Pediatric Rheumatology (2025) 23:93
https://doi.org/10.1186/s12969-025-01138-8

Pediatric Rheumatology

MEETING ABSTRACTS

Open Access

Proceedings of the 32nd European Paediatric Rheumatology Congress

Helsinki, Finland. 17-20 September 2025
Published online: 16 September 2025

O01

Reconstitution of the B cell compartment following anti-CD19 CAR-T cell therapy in refractory patients with Juvenile Dermatomyositis (JDM)

E. Marasco[1], R. Nicolai[1], A. Ariolli[1], M. Becilli[2], C. Bracaglia[1], P. Merli[3], M. I. Petrone[1], F. Del Bufalo[3], M. Algeri[3], M. G. Cefalo[3], F. Locatelli[3], F. De Benedetti[1]
[1]Rheumatology Unit, [2]Department of Hematology/Oncology, Cell and Gene Therapy, [3]Department of Hematology/Oncology, Cell and Gene Therapy, Ospedale Pediatrico Bambino Gesù, Rome, Italy
Correspondence: E. Marasco
Pediatric Rheumatology, **23(2):** O01

Introduction: CD19 CAR T-cell therapy is an innovative strategy to induce profound B cell depletion in patients with refractory idiopathic inflammatory myopathies (IIM). However, its effects on B cell phenotypes in pediatric patients remain largely unknown.
Objectives: To characterize the reconstitution profile of B cell subsets in three patients with juvenile dermatomyositis (JDM) treated with anti-CD19 CAR T-cell therapy.
Methods: Three patients with refractory JDM received a single infusion of autologous, second-generation anti-CD19 CAR T cells (1×10^6 CAR T cells/kg; lentiviral vector), manufactured on the CliniMACS Prodigy system. Lymphodepletion was achieved using cyclophosphamide (1000 mg/m^2 over 2 days) and fludarabine (90 mg/m^2 over 3 days). B cell immunophenotyping was performed according to standard operating procedures (SOPs) before and after CAR T-cell infusion. A comparator group of five JDM patients treated with rituximab (RTX) was included.
Results: B cell reconstitution occurred at a median of 8 weeks (IQR: 8.0-12.0) post-CAR T therapy, with an immature transitional B cell phenotype. B cell subsets distribution was assessed at a median of 27.3 weeks (IQR: 22.5–40.2) after treatment, when all B cell subsets were present for each patient, and compared to pre-treatment profiles. In the RTX group, B cell phenotyping was performed at a median of 47 weeks (IQR: 33.4–50.7) post-treatment. The proportion of CD19$^+$ B cells among lymphocytes was similar before and after CAR T-cell treatment (pre: 32% [IQR: 23–40], post: 21% [IQR: 20–24]). B cell subset analysis showed comparable levels of transitional, naïve and plasmablast populations pre- and post-treatment. However, there was a notable reduction in total memory B cells (MBCs) post-treatment (pre: 6.4% [IQR: 6.3–9.1], post: 3.9% [IQR: 3.1–4.0]), particularly in the switched MBC subset. Interestingly, JDM patients treated with RTX showed higher frequencies of switched MBCs during B cell reconstitution compared to those treated with CAR T cells: CAR T treated-patients 16.0 % [IQR: 8.5-18.0], RTX group 52.0% [IQR: 28.0, 60.0].
Conclusion: These data show that following CAR T cell treatment, the memory B cell compartment presents a lower frequency of switched MBCs when compared to pre-treatment levels and to patients treated with RTX, suggesting a specific effect of CAR T cell treatment in regulating the memory B cell compartment in JDM patients.
Disclosure
None declared

O02

Anti-CD19 Car-T cell therapy in refractory juvenile dermatomyositis (JDM): a single-center case series

R. Nicolai[1], M. Becilli[2], E. Marasco[1], P. Merli[2], C. Bracaglia[1], F. Del Bufalo[2], M. I. Petrone[1], M. G. Cefalo[2], M. Algeri[2], F. De Benedetti[1], F. Locatelli[2,3]
[1]Division of Rheumatology, [2]Department of Hematology/Oncology, Cell and Gene Therapy, IRCCS Ospedale Pediatrico Bambino Gesù, [3]Catholic University of the Sacred Heart, Rome, Italy
Correspondence: R. Nicolai
Pediatric Rheumatology, **23(2):** O02

Introduction: CD19 CAR T-cell therapy represents an innovative approach emerging as a promising treatment option in patients with refractory idiopathic inflammatory myopathies (IIM), but the experience in children so far is limited.
Objectives: To report on the safety and efficacy of anti-CD19 CAR T-cell therapy in 3 JDM patients.
Methods: All 3 patients received a single infusion of fresh, autologous second-generation anti-CD19 CAR T product (lentiviral vector) manufactured on the Prodigy device ($1x10^6$ CAR T cells/kg), after lymphodepletion with cyclophosphamide (1000 mg/m^2 over 2 days) and fludarabine (90 mg/m^2 over 3 days).
Results: Maximum follow-up after CAR T-cell therapy was 20 months. Patients 1 and 2 had a history of severe chronically active disease with extensive calcinosis and ulcerations. Patient 3 presented interstitial lung disease (ILD) and persistently active muscle and skin disease with ulcerations. Short-term effects of CAR T-cell therapy on Patient 1 have been previously reported (Nicolai A&R 2024). All patients were refractory to multiple immunosuppressive treatment lines and presented significant side effects from chronic glucocorticoid treatment. After infusion, CAR T cells rapidly expanded, reaching peak concentrations after a median of 7 days (range 7-9). At peak, the median number of circulating CAR T cells was 32.69 per microliter (range 31.04-535.02). CD19+ B cells were undetectable in peripheral blood after a mean of

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

6.33 days (median 7, range 5-7). B-cell reconstitution started after a mean of 65.33 days (median 56, range 56-84). All patients achieved a major clinical response after 3 months of CAR T cell-treatment, despite discontinuation of glucocorticoids and immunosuppressive medications. Patient 1 reached and maintained clinically inactive disease starting from month 9 after infusion and showed complete resolution of calcinosis. Two out of 3 patients presented a grade 1 cytokine release syndrome (G1), not requiring treatment; Patient 2 presented a mild (G1) immune effector cell–associated neurotoxicity syndrome (ICANS), characterized by confusion and transient EEG abnormalities, resolving spontaneously after 72 hours. Transient anemia (range G2-G3) and neutropenia (range G3-G4) were recorded in all patients, but cytopenia was limited to the first weeks after infusion. No severe infections where observed. Patient 2 presented a mild upper respiratory tract infection 4 months after infusion and Patient 3 contracted type A influenza 2 months after treatment, without worsening of underlying ILD.

Conclusion: These data add evidence supporting the short- and long-term safety and efficacy of CD19 CAR T-cell therapy in patients with refractory JDM.

Disclosure

R. Nicolai: None declared, M. Becilli: None declared, E. Marasco: None declared, P. Merli Speaker Bureau with: Miltenyi, Medac, Amgen, C. Bracaglia: None declared, F. Del Bufalo: None declared, M. Petrone: None declared, M. Cefalo: None declared, M. Algeri: None declared, F. De Benedetti Consultant with: Abbvie, Apollo, Elixiron, Kliniksa, Novartis, Roche, Pfizer, Sanofi, SOBI, F. Locatelli Speaker Bureau with: Amgen, bluebird bio, Gilead, Jazz Pharmaceuticals, Medac, Miltenyi, Neovii, Novartis, Sanofi, SOBI

Reference

1. Nicolai R, Merli P, Moran Alvarez P, Bracaglia C, Del Bufalo F, Marasco E, Caiello I, Prencipe G, Algeri M, Cefalo MG, Becilli M, Quintarelli C, Sinibaldi M, Hanssens L, De Benedetti F, Locatelli F. Autologous CD19-Targeting CAR T Cells in a Patient With Refractory Juvenile Dermatomyositis. Arthritis Rheumatol. 2024 Oct;76(10):1560-1565.

O04

Unexplored Type I Interferon Signalling Heterogeneity In Childhood-Onset SLE Reveals Novel Considerations For personalised Therapy

H. Cross, J. Peng, T. McDonnell, B. Goulden, E. Jury, C. Ciurtin, G. A. Robinson
Ageing, Rheumatology and Regenerative Medicine, University College London, London, United Kingdom
Correspondence: G. A. Robinson
Pediatric Rheumatology, **23(2):** O04

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a severe autoimmune disease that causes significant morbidity in children and adolescents, with more aggressive clinical manifestations compared to adult-onset SLE. This is largely attributed to heightened type I interferon (IFN-I) signalling. In this study, we investigate the heterogeneity of IFN-I signalling in cSLE patients using a novel multi-omic approach, aiming to better understand disease mechanisms and identify therapeutic strategies.

Objectives: To explore the heterogeneity of IFN-I signalling in cSLE, assess its immunological impact, clinical relevance, and identify potential biomarkers for stratified therapy.

Methods: We performed RNA sequencing on peripheral blood mononuclear cells (PBMCs) from 74 female cSLE patients (mean age 19 years, disease duration 6.5 years) and 20 age/sex-matched healthy controls (HCs). Serum pan-IFNα levels were quantified using single-molecule array (SIMOA), and IFN-I activity was assessed using firefly luciferase reporter cells. We analysed IFN-I-sensitive BST2 expression by spectral flow cytometry, and serum proteins were quantified by Olink proteomics with selected proteins validated by ELISA. Clinical data informed disease endotyping.

Results: Gene expression analysis revealed 51 upregulated differentially expressed genes in cSLE. Sparse partial least squares discriminant analysis (sPLS-DA) revealed robust separation between cSLE and HC groups, with the strongest upregulation in IFN-I pathways ($p<0.0001$). Patients clustered into two groups: IFN-High (65%) and IFN-Low (35%), independent of disease activity, as validated by SLE IFN-stimulated gene (ISG) scores (AUC=1.00, $p<0.0001$). IFN-High patients had reduced lymphocyte counts ($p=0.0048$). Serum IFNα levels ($p=0.0014$) and reporter cell responses ($p<0.0001$) were significantly elevated in the IFN-High group and showed a greater reduction following anifrolumab treatment ($p=0.013$) compared to IFN-Low patients, supporting stratified therapy. These patterns were absent in HCs and systemic juvenile idiopathic arthritis (sJIA) disease controls, highlighting cSLE specificity. Proteomics identified LAMP3 as the most predictive biomarker for the IFN-High group (AUC=0.95, $p<0.0001$), validated by ELISA, with longitudinal stability regardless of disease activity across 82 data points. Cellular analysis showed increased BST2 expression in plasmacytoid dendritic cells, CD4+, and CD8+ T-cells, with functional consequences on activation, exhaustion, and abundance, indicating heightened IFN-I sensitivity in these subsets. Clustering multi-level IFN-I data revealed six patient endotypes with unique IFN-I activity and clinical phenotypes, including serum IFNα levels, ISG patterns, cell subset sensitivity to IFN-I, and profiles of disease activity, organ damage, anti-double-stranded DNA antibodies and lymphocyte counts. Thus, the impact of IFN-I signalling exists on a heterogeneous spectrum in cSLE.

Conclusion: This study provides novel and detailed insights into the heterogeneity of IFN-I signalling in cSLE with clinically relevant subgroups identified. These findings support stratified use of IFN-I-targeted therapies in cSLE, with LAMP3 as a promising biomarker for monitoring IFN-I activity and guiding personalised treatment for patients.

Disclosure

None declared

O05

Molecular mechanisms in chronic nonbacterial osteomyelitis (CNO) and their therapeutic potential

A. Charras[1], S. R. Hofmann[2], F. Schulze[2], S. Russ[2], J. Hawkes[1], C. M. Hedrich[1,3]
[1]Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [2]Department of Paediatrics, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany, [3]Department of Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom
Correspondence: A. Charras
Pediatric Rheumatology, **23(2):** O05

Introduction: Chronic non-bacterial osteomyelitis (CNO) is an autoinflammatory bone disease mainly affecting children and adolescents. It can cause pain, hyperostosis and fractures, affecting patients' quality of life and psychomotor development. We recently identified rare P2RX7 variants in a large proportion of CNO patients (32.4% versus 4.4% of controls) and demonstrated their functional impact. CNO-associated P2RX7 variants are associated with impaired K^+ efflux, promoting NLRP3 inflammasome activation and pro-inflammatory cytokine release. Notably, P2RX7 variants also associated with prolonged survival (reduced pyroptosis) of monocyte-derived macrophages.

Objectives: To understand how P2XR7 variants contribute to prolonged cell survival, this project investigated effects of CNO-associated P2RX7 variants on Ca^{2+} mobilisation, reactive oxygen species (ROS) production, mitochondrial integrity, and cytokine expression in THP-1 derived macrophages.

Methods: Genetically modified THP-1 monocytes were differentiated into macrophage-like cells, and used to investigate effects of CNO-associated P2RX7 variants (c.349C>T, rare gain-of-function; c.920G>A rare loss-of-function; c.489C>T common gain-of-function). Activation of the NLRP3 inflammasome (ASC speck assay), K^+ (ELISA) and Ca^{2+} flux (flow cytometry), expression of pro- and anti-inflammatory cytokines (MSD and Luminex assays), ROS production (2',7'-dichlorofluorescein diacetate/DCFDA and Lucigenin assays) and mitochondrial function (MitoTracker) were studied. Effects of small molecule P2X7 (A-804598) and NLRP3 (MCC950) inhibitors were interrogated.

Results: Compared to cells expressing wild-type P2X7, THP-1-derived macrophages expressing CNO-associated c.349C>T and c.489C>T variants associated with increased K^+ and sustained Ca^{2+} flux, enhanced inflammasome activation, increased IL-1β and IL-18 secretion, and reduced LDH release (approximating prolonged cell survival). Prolonged survival associated with reduced ROS content for all CNO-associated variants, reduced mitochondrial stress for the c.920G>A loss-of-function variant (superoxide production), and increased numbers of functional mitochondria for the c.349C>T and c.920G>A variants. Co-culture with the P2X7 inhibitor A-804598, across cell lines, resulted in reduced cellular K^+ and increased $Ca2^+$content, reduced inflammasome assembly, ASC speck and cytokine release, and reduced mitochondrial damage. These P2X7 inhibitor mediated effects were greater when compared to co-culture with the NRLP3 inhibitor MCC950.
Conclusion: Imbalanced K^+ and Ca^{2+} mobilization in THP-1-derived macrophages expressing CNO-associated P2RX7 variants associates with reduced mitochondrial stress and prolonged survival. Understanding the contribution of CNO-associated variation in P2RX7 will promote the development of target-directed treatments.
Disclosure
None declared

Reference

1. Charras A, Hofmann SR, Cox A, Schulze F, Russ S, Northey S, Liu X, Fang Y, Haldenby S, Hartmann H, Bassuk AG, Carvalho A, Sposito F, Grinstein L, Rösen-Wolff A, Meyer-Bahlburg A, Beresford MW, Lainka E, Foell D, Wittkowski H, Girschick HJ, Morbach H, Uebe S, Hüffmeier U, Ferguson PJ, Hedrich CM. P2RX7 gene variants associate with altered inflammasome assembly and reduced pyroptosis in chronic nonbacterial osteomyelitis (CNO). J Autoimmun. 2024 Apr;144:103183. doi: https://doi.org/10.1016/j.jaut.2024.103183. Epub 2024 Feb 23. PMID: 38401466.

O06

BCAP is an interferon stimulated gene that enhances type i interferon activity in response to lipopolysaccharide

A. Tesser[1], M. Di Rosa[2], G. M. Piperno[3], A. Pin[1], G. Sospiro[3], E. Valencic[1], V. Boz[1], M. Girardelli[1], E. De Martino[1], F. Benvenuti[3], A. Taddio[1,2], A. Tommasini[1,2], S. Pastore[1]
[1]Institute for Maternal and Child Health IRCCS Burlo Garofolo, [2]University of Trieste, [3]International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy
Correspondence: A. Tesser
Pediatric Rheumatology, **23(2):** O06

Introduction: B-cell adapter for PI3K (BCAP) is a protein that connects membrane receptors signaling to the PI3K-AKT-mTOR pathway. In fibroblasts and dendritic cells, priming the cGAS nucleic acid-sensing pathway increases BCAP expression and enhances Type I Interferon (IFN) production upon LPS stimulation (1). These findings corroborate the idea that BCAP may bias cytokine production towards IFN during inflammation, indicating its potential involvement in IFN-driven diseases like Systemic Lupus Erythematosus (SLE).
Objectives: To investigate the role of BCAP in regulating the inflammatory response in SLE and its relationship with IFN-mediated inflammation.
Methods: BCAP gene expression and IFN signature were analyzed in 36 subjects with SLE and 20 healthy donors. Two cellular models (murine HoxB8-derived macrophages and human fibroblasts) were used to assess BCAP's role in cGAS priming, LPS stimulation, and IFN signaling.
Results: We found a correlation between BCAP expression and Interferon Stimulated Genes (ISGs) in subjects affected by SLE (R = 0.56, p-value = 0.00043). Tofacitinib and anifrolumab blocked BCAP overexpression triggered by cGAS signaling in human fibroblasts, confirming BCAP as an ISG. Additional studies in BCAP Knock-Out HoxB8 murine cells revealed that, in the absence of BCAP, these cells reduced IFN production when stimulated with LPS after pre-exposure to cGAMP.
Conclusion: BCAP could be considered an ISG that acts like a positive regulator of TLR4-mediated IFN production, and its increased expression in SLE may contribute to a positive feedback loop, enhancing IFN production during bacterial infections. These results pave the way for the possibility of studying pharmacological interventions with PI3K-AKT-mTOR pathway inhibitors to modulate the inflammatory response in diseases characterized by IFN hyper-responsiveness.
Disclosure
None declared

Reference

1. Tesser A, Piperno GM, Pin A, Piscianz E, Boz V, Benvenuti F, Tommasini A. Priming of the cGAS-STING-TBK1 Pathway Enhances LPS-Induced Release of Type I Interferons. Cells. 2021;10(4).

O07

Systemic juvenile idiopathic arthritis-associated lung disease: frequency and risk factors

A. Eravsar[1], A. A. Kilinc[2], M. Yildiz[1], E. Aslan[1], N. Akay[1], U. Gul[1], E. Aslan[1], E. K. Konte[1], A. Gunalp[1], S. Sahin[1], O. Kasapcopur[1], K. Barut[1]
[1]Pediatric Rheumatology, [2]Pediatric Pulmonology, Istanbul University-Cerrahpasa, Istanbul, Türkiye
Correspondence: K. Barut
Pediatric Rheumatology, **23(2):** O07

Introduction: In recent years, an increase in lung disease has been reported in patients with sJIA, with a frequency 7%–12%. This condition shares similarities with other rheumatologic diseases, presenting with parenchymal damage and hypoxemia, restricting the diffusion capacity of the lungs, and showing a wide range of radiological spectra, from mild subpleural reticulations to extensive ground-glass opacities. The clinical presentation can vary from being asymptomatic to severe respiratory failure with interstitial pattern.
A consensus developed by the Boston Children's Hospital recommends CT evaluation for patients with sJIA showing HLADRB115 positivity, disease onset before age 2, macrophage activation syndrome (MAS) attacks and atypical rashes for sJIA. Tissue typing for HLADRB115 is also recommended for all patients diagnosed with sJIA.
Objectives: This study aims to determine the frequency of lung involvement in sJIA and to identify patients at risk for developing lung disease, as well as to develop effective screening strategies.
Methods: Exclusion Criteria:
1. Presence of other diseases causing lung involvement (infectious, rheumatologic).
2. Currently active MAS attacks.

A total of 87 patients were included in the study.
Patients with any of the following risk factors were considered at risk and underwent thoracic CT imaging: diagnosis before age 2, Down syndrome, MAS attacks, subclinical MAS, adverse reactions to biologics, persistent cough, clubbing of fingers, and suspicious lung X-ray findings. The relationship between sJIA-LD, disease activity, HLADRB1*15 positivity and biologic agent usage was also analyzed.
Results: Out of the 87 patients with sJIA, 56 were considered at risk and underwent CT imaging. LD was found in 15 patients (17%). Among these, 8 patients (53%) were completely asymptomatic.
Statistically significant relationships were found between lung disease and early disease onset, asymptomatic inflammation indicative of disease activity, number of MAS attacks, number of subclinical MAS attacks, adverse reactions to biologics, use of canakinumab, and HLADRB1*15 positivity.
Multivariate regression analysis identified the frequency of MAS attacks (p=0.009, OR 95% CI = 6.67 (1.82-19.08)) and subclinical MAS attacks (p=0.005, OR 95% CI = 2.28 (1.5-5.78)) as independent risk factors for lung disease. Although a strong association was found between HLADRB1*15 and sJIA-related lung disease, a direct cause-and-effect relationship could not be demonstrated.
Conclusion: The increase in sJIA-related lung disease (sJIA-LD) has emerged debates about its etiology. Some researchers have pointed to biologic agents as potential trigger, suggesting that changes in immunity caused by these medications may lead to sJIA-LD. However, other researchers argue that the primary factor in the development of lung disease is the inability to control disease activity, asserting that

biologics remain the first-line treatment. Our study supports this by demonstrating a strong relationship between HLADRB1*15 positivity and sJIA-LD, alongside the finding that disease activity itself is an independent risk factor. Our results endorse the PRES consensus recommendation for HLADRB1 tissue typing for all sJIA patients.

Disclosure

None declared

O08

Bronchoalveolar fluid cytokine profile in patients with the lung disease associated with systemic juvenile idiopathic arthritis

I. Romankevych[1], D. Do[1], A. Sproles[1], L. Auld[1], T. Sabit[1], R. Chhaing[1], J. Baker[1], J. Brewington[2], C. Towe[2], A. Grom[1], G. Schulert[1]
[1]Rheumatology, [2]Pulmonary Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, United States
Correspondence: I. Romankevych
Pediatric Rheumatology, **23(2):**O08

Introduction: The lung disease associated with systemic JIA (SJIA-LD) remains poorly understood. Measurement of cytokine levels in bronchoalveolar lavage fluid (BALF) may offer insights into disease pathogenesis, activity, and progression. However, there is currently limited data on the bronchoalveolar inflammatory environment in children with SJIA-LD.

Objectives: The objective of our study was to measure levels of pro-inflammatory cytokines and other biomarkers in BALF collected from patients with SJIA-LD.

Methods: Children with SJIA-LD were included in the study at the time of diagnostic bronchoscopy as part of routine clinical care. As controls we included patients undergoing routine bronchoscopy for tracheostomy surveillance or other known inflammatory diseases, including SJIA without LD, autoimmune alveolar proteinosis, IBD with lung disease, and lymphoma. Children from the control group were divided into inflammatory (IC, n=9) and non-inflammatory (NIC, n=7) controls based on underlying disease. Interleukin 6, 8 and 18, S100A8/9, S100A12, CD25, CCL25, CCL11, CCL17, MMP7 and CXCL9 were measured by ELISA or Multiplex.

Results: BALF samples were obtained from 14 patients with SJIA-LD (mean age 7.4±1.98 years and disease duration 4.4±0.9 years) and 16 patients without SJIA-LD (mean age 8.6±0.24 years). Seven (50%) SJIA-LD patients required O2 support intermittently or continuously. Serial samples were obtained for two patients before and after whole lung lavage and BMT, respectively.

BAFL level of IL18 was elevated in the main group (1012.2±289.6 pg/mL, p<0.05) vs IC (154±59 pg/mL) and NIC (37.1±15.1 pg/mL). CCL11 (20.48±2.22 pg/mL in children with SJIA-LD vs 8.71±4.1 pg/mL in controls, p<0.05) and MMP7 (17952.8±2869.2 pg/mL in SJIA-LD vs 10675.6±8485.4 pg/mL in NIC, p<0.001) were significantly elevated in children with SJIA-LD as well, while CXCL9 was significantly higher in general control 227.4±101.1 pg/mL (p<0.05) vs 122.8±36.35 pg/mL in main group, and the NIC group had higher IL6 (27.6±20.1 pg/mL vs 10.6±3.2 pg/mL in main group, p<0.05) and IL8 (1056.7±769.2 pg/mL vs 319±96.1 pg/mL in main group). Levels of CD25, CXCL9, CCL11 and CCL17 were undetectable in most patients from both groups, but detection of CD25 ($\chi 2=2.16$, $p= 0.0027$) occurred more often in SJIA-LD Linear regression didn't show the relationship between BALF IL-18 level and disease duration ($p=0.15$); oxygen requirement ($p=0.11$); dose of Anakinra ($p=0.4$) or plasma levels of ferritin ($p=0.9$), CXCL-9 ($p=0.6$) and IL-18 ($p=0.9$). There was a direct relation with daily prednisone dose ($p=0.03$) and number of immunosuppressive medications ($p=0.0015$).

Of the 3 SJIA-LD patients who underwent BMT, we observed a higher BALF/plasma IL-18 ratio compared to other patients, although this was not significant (176±99 vs 34±16.5 ($p=0.1$)).

Analysis of cytokines before and after BMT showed a decrease of IL18 (pre 1182 pg/mL vs post 532.99 pg/mL) and S100A8/9 (pre 10500 pg/mL vs post 3028.5 pg/mL), and no notable changes of MMP7 (pre 17589.36 pg/mL vs post 19808.8 pg/mL) in BALF 6 months after. Similar changes were observed after therapeutic whole lung lavage: level of IL18 fell from 1205 to 477.5 pg/mL.

Conclusion: Patients with SJIA-LD showed a distinct BALF cytokine profile, with elevated IL-18, MMP7, and CCL11 but lower levels of other cytokines. These profiles also vary with flares and management, including WLL and BMT. Further prospective work is needed to determine the relationship with disease course and treatments.

Disclosure

None declared

O09

Long-term treatment efficacy of intra-articular triamcinolone hexacetonide injections in juvenile idiopathic arthritis patients starting tumor necrosis factor inhibitor therapy: 48-week results from a randomized, phase 4 trial - the myjia trial

P. Bøyesen[1], A.-B. Aga[1], V. Lilleby[1], M. Pesonen[2], M. Rygg[3,4], E. Nordal[5,6], B. Barstad[7], K. Tylleskär[8], H. Sanner[1,9], N. K. Sande[1], S. O. Hetlevik[1], I. C. Olsen[2,10], S. Lillegraven[11], E. A. Haavardsholm[9,11], A. V. Ramanan[12], Ø. Molberg[1,9], B. Flatø[1]
[1]Rheumatology, [2]Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, [3]Department of Pediatrics, Trondheim University HospitalDepartment of Pediatrics, [4]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, [5]Department of Pediatrics, University Hospital of North Norway (UNN), [6]Department of Clinical Medicine, The Arctic University of Norway, Tromsø, [7]Department of Pediatrics, Stavanger University Hospital, Stavanger, [8]Department of Pediatrics, Haukeland University Hospital, Bergen, [9]Faculty of Medicine, University of Oslo, [10]Department of Research Support for Clinical Trials, Oslo University Hospital, [11]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet hospital, Oslo, Norway, [12]Bristol Royal Hospital for Children and Translational Health Sciences, University of Bristol, Bristol, United Kingdom
Correspondence: P. Bøyesen
Pediatric Rheumatology, **23(2):**O09

Introduction: Modern therapies have improved outcomes in patients with juvenile idiopathic arthritis (JIA), but up to 60% of patients treated with tumor necrosis factor inhibitors (TNFi) have persisting disease activity. Intra-articular (IA) triamcinolone hexacetonide injections are often used as adjunctive therapy to TNFi treatment even though no controlled studies have examined their potential added benefit.

Objectives: To assess the efficacy and safety of IA triamcinolone hexacetonide injections compared to no injections in children with JIA starting TNFi therapy.

Methods: The MyJIA trial is a randomized, controlled, multicenter, parallel group, blinded-assessor, open-label, phase 4 clinical trial. Main inclusion criteria were non-systemic JIA, age 1 to 18 years, clinical indication for TNFi therapy, and at least one joint with arthritis suited for IA steroid injection. Participants were assigned by a computer randomization procedure (1:1) to IA triamcinolone hexacetonide injections of active joints or no joint injections. Core outcome variables for JIA were collected at baseline, weeks 6, 12, 24, 36 and 48. Participants randomized to intra-articular/IA steroid injections had joints with arthritis injected at baseline and if clinically indicated at follow-up visits with triamcinolone hexacetonide (large joints 0.5-1 mg/kg (max 40 mg), medium joints 0.3-0.5 (max 20 mg), small joints, 0.1-0.3 (max 15 mg), maximum total dose per visit 3.5mg/kg or <140mg). Primary endpoint was the proportion of patients with sustained inactive disease, as defined by the JIA-ACR/Wallace 2011 criteria, at both weeks 24 and 36.

Results: In total 187 children (119 (64%) girls and 68 (36%) boys) with non-systemic JIA, median (IQR) age 11(6.5) years, were randomized. 92 (49%) patients were allocated to the intervention group and received at least one intra-articular steroid injection, and 95 (50%) to the no-injection group. In the IA steroid injection group, mean number (SD) of joints injected at baseline were 2.7 (2.1), and the total triamcinolone hexacetonide dose 1.2 (1.0) mg/kg. The primary endpoint, the proportion of patients with sustained inactive disease at weeks 24 to 36, was 35% in the intra-articular steroid injection group compared to 33% in the control group (risk difference (RD) 0.02, 95% CI −0.12–0.15, p 0.80). The mean time to JIA-ACR inactive disease during the 48-week follow-up period was 184 days in the steroid injection group and 188 days in the no-injection group (mean difference −4.5 days, 95% CI −37.4, 28.5). JIA-ACR response rates increased in both groups during follow-up. JIA-ACR30 response rate at week 48 was 96% in the injection group and 88% in the no-injection group (RD 0.03, 95% CI −0.01, 0.08, $p=0.15$).

JIA-ACR 50/70/90 response rates at week 48 were 96%/88%/74% in the injection group and 87%/75%/70% in the control group. Betweeen group differences were similar at week 48 for JIA-ACR50, 70 and 90 with RD (95% CI) of 0.03 (−0.01–0.07), 0.08 (−0.01–0.18) and 0.02 (−0.11–0.15), respectively. JIA-ACR core set variables showed no between-group differences at any time point (data not shown). Median (IQR) JADAS71 were 1.5 (2.2) and 2.3 (3.2) in the IA injection group and no-injection group at week 48, respectively (p=0.2). AEs/SAEs occurred in 67%/7% in the injection group and in 75%/8% in the control group. Subcutaneous atrophy occurred in 8 of 288 steroid injected joints (3%).
Conclusion: Intra-articular triamcinolone hexacetonide injections did not increase the proportion of children with JIA reaching sustained inactive disease at weeks 24 and 36 after starting TNFi therapy. Our findings suggest that concomitant therapy with intra-articular steroid injections might be redundant in children with JIA starting TNFi therapy.
Trial registration identifying number: Clinical trials NCT 04614311, EUCT number:2023-510118-21-00
Disclosure
None declared

O10

How to choose second-line biologics in juvenile idiopathic arthritis: insights into treatment effectiveness from a real-life experience

A. Marino[1], M. R. Pellico[2], E. A. Conti[2], M. Rossano[3], S. Lanni[3], S. Germinario[2], A. Amati[2], M. Pandolfi[2], C. Iannone[2], S. Costi[1], F. Baldo[1], F. Minoia[3], G. Filocamo[3], R. Caporali[1], C. Chighizola[1]
[1]Pediatric Rheumatology, ASST G.Pini-CTO, [2]University of Milan, [3]Pediatric Immuno-Rheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
Correspondence: A. Marino
Pediatric Rheumatology, **23(2):**O10

Introduction: Currently, there are few and weak evidence supporting the choice of the second-line biological disease-modifying anti-rheumatic drug (bDMARD) for non-systemic juvenile idiopathic arthritis (JIA).
Objectives: To describe prescription patterns of second-line bDMARDs in non-systemic JIA and to assess the effectiveness of TNFα inhibitors (TNFi) and non-TNFi as second-line bDMARDs.
Methods: This retrospective cohort study included non-systemic JIA patients treated with at least two bDMARDs and followed at two Rheumatology Pediatric tertiary centers. The presence of clinically inactive disease (CID) at both 6 and 12 months during the second course of bDMARD treatment was used as the dependent variable in a logistic regression analysis. Since repeated measurements were obtained from the same subjects at both time points, multivariate analyses were performed using logistic Generalized Estimating Equations (GEE) models with robust standard errors, specifying an exchangeable correlation structure. Propensity scores stratified into quintiles were included as an indicator variable in the regression models.
Results: A total of 127 patients were included. The main reason for switching to a second bDMARD was ineffectiveness, reported in 109 out of 127 patients (86%), with active uveitis accounting for 25 out of those 109 switches (23%). Adalimumab was the most frequently prescribed second-line TNFi (59%). In 25% of cases, a non-TNFi was chosen, with tocilizumab being the most common (66%). The choice of second-line bDMARD was influenced by the calendar year of prescription. Non-TNFi treatments had a median initiation year of 2021 [interquartile range (IQR) 2017–2023], compared to 2019 (IQR 2013–2022) for TNFi treatments (p = 0.03).
Time on the first TNFi did not significantly impact the likelihood of achieving CID during the second TNFi course [odd ratio (OR) 0.98, 95% confidence interval (CI) 0.79–1.21, p = 0.83]. Interestingly, the median duration of the second bDMARD (censored at discontinuation or last follow-up) was significantly longer in the TNFi group compared to the non-TNFi group [2.2 years (IQR 0.7–5.3) vs. 0.8 years (IQR 0.5–3.6); p = 0.02]. In the multivariate GEE model adjusted for propensity score quintiles, switching to a second TNFi rather than a non-TNFi was significantly associated with achieving CID (OR 5.42, 95% CI 1.91–15.40, p < 0.01). Additionally, in the same model, male sex (OR 3.37, 95% CI 1.08–10.49, p = 0.04) and switching due to an adverse event (OR 4.61, 95% CI 1.16–18.31, p = 0.03) were significantly associated with CID. Patients who switched due to active uveitis also showed a higher likelihood of achieving CID compared to those switching for active arthritis (OR 18.38, 95% CI 4.33–78.07, p < 0.01).
Conclusion: Our findings suggest that TNFi remains a viable and effective option as second-line bDMARDs in non-systemic JIA, regardless of the duration of prior TNFi exposure.
Disclosure
None declared

O11

Data-driven trajectories of physical function in children with Juvenile idiopathic arthritis: results from the capri registry

C. Cunningham[1], R. A. Berard[2], M. Berkowitz[3], B. M. Feldman[4], N. Johnson[5], L. S. Lim[6], T. Loughin[3], M. McPherson[6], P. Miettunen[5], J.-P. Proulx-Gauthier[7], D. Rumsey[8], H. Schmeling[5], L. B. Tucker[1], K. Houghton[1], J. Guzman[1], on behalf of CAPRI Registry Investigators
[1]Pediatrics, UBC, Vancouver, [2]Pediatrics, Western University, London, [3]Statistics, Simon Fraser University, Burnaby, [4]Pediatrics, Sick Kids and U of Toronto, Toronto, [5]Pediatrics, U of Calgary, Calgary, [6]Pediatrics, U of Manitoba, Winnipeg, [7]Pediatrics, CHU de Quebec Universite Laval, Quebec, [8]Pediatrics, U of Alberta, Edmonton, Canada
Correspondence: J. Guzman
Pediatric Rheumatology, **23(2):**O11

Introduction: In historical cohorts many children with Juvenile Idiopathic Arthritis (JIA) had lifelong disability. In contrast, most children in modern JIA cohorts are expected to recover function after treatment with synthetic and biologic DMARDs.
Objectives: To identify data-driven longitudinal trajectories of physical function in children with JIA treated with modern treatments, and the baseline characteristics that may predict these trajectories.
Methods: We included newly-diagnosed JIA patients recruited in the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry between 2017 and 2024, whose parents provided Kids Disability Screen (KDS) scores for 4 or more visits. The KDS considers the help needed from parents and difficulties for run and play atributted to JIA, and has been validated against the Childhood Health Assessment Questionnaire (CHAQ)[1]. Relative to the CHAQ, a KDS=0 means no impairment, >0 to 1.5 mild, >1.5 to 4.0 mild to moderate, and >4 to 10 moderate to severe impairment. Data-driven trajectories were identified with latent class trajectory analysis (LCTA), and classification trees were used to identify predictors of trajectories with persisting functional impairments.
Results: A total of 727 patients were included and the best-fitting LCTA model identified 5 distinct data-driven trajectories. Trajectory A had little measurable impairment throughout 7 years of follow-up (41% of patients); Trajectory B had mild-to-moderate impairment resolving over 1 year (23%); and Trajectory C had moderate impairment resolving over 2 years (6%). Two trajectories had persisting mild functional impairments: Trajectory D had initial mild-to-moderate impairment that improved but did not resolve (18% of patients), and Trajectory E had persisting mild impairment throughout (12%). There were no trajectories with persisting moderate or severe impairments. Age at diagnosis, JIA category, time since disease onset, disease activity scores, pain and fatigue scores, presence of enthesitis, and hip, ankle and foot involvement at baseline differed across the 5 trajectories (p<0.05). The best predictor of trajectories with persisting mild impairments was the baseline KDS. At baseline, 63% of the cohort had a KDS of 1.5 or higher and this cut-off captured 80% of patients in trajectories with persisting functional impairment.
Conclusion: Most children in the CAPRI JIA Registry had mild to moderate functional impairments upon diagnosis that resolved with treatment within 2 years. However, about 30% reported persisting mild functional impairments beyond 2 years, and 80% of those had a baseline KDS of 1.5 or more.
Trial registration identifying number: ClinicalTrials.gob: NCT03245801
The CAPRI JIA Registry has been funded by grants from The Arthritis Society and the Canadian Institutes of Health Research, Canada.
Disclosure
None declared

Reference
1. Houghton et al, Rheumatology (Oxford) 2022; 61 (12): 4835-4844

O12

Impact of body weight on treatment response to TNF-inhibitors in children With Juvenile idiopathic arthritis

G. Mastrangelo[1], G. Damianakis[2], A. H. H. Cheng[1,2], D. Marshall[3,4,5], S. J. J. Vastert[6,7], J. F. Swart[6,7], S. M. Benseler [8], R. S. Yeung[1,2,9]
[1]Division of Rheumatology, Department of Paediatrics, [2]Cell and Systems Biology Program, The Hospital for Sick Children, Toronto, [3]Alberta Children's Hospital Research Institute, [4]Department of Community Health Sciences, Cumming School of Medicine, [5]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Canada, [6]Department of Pediatric Rheumatology and Immunology, University Medical Center Utrecht, [7]Faculty of Medicine, Utrecht University, Utrecht, Netherlands, [8]Rheumatology, Children's Health Ireland,, University College Dublin, Trinity College Dublin, Royal College of Surgeons of Ireland, Dublin City University, Dublin, Ireland, [9]Department of Immunology and Institute of Medical Science, University of Toronto, Toronto, Canada
Correspondence: G. Mastrangelo
Pediatric Rheumatology, **23(2):**O12

Introduction: Tumor necrosis factor inhibitors (TNFi) are effective in the treatment of juvenile idiopathic arthritis (JIA). Recommended treatment dosing of TNFi in children was extrapolated from adults. The relationships between the child's weight, the recommended and prescribed TNFi dose, and the treatment response are not well understood; available data are controversial.
Objectives: We aimed to investigate the impact of body weight and TNFi dosing on treatment response in children with JIA.
Methods: A prospective multi-center cohort study of consecutive children with JIA starting TNFi between October 2018 and March 2025 was performed. Demographics, physician assigned JIA subtypes according to the International League of Associations for Rheumatology (ILAR), joint counts, laboratory markers, clinical Juvenile Arthritis Disease Activity Score (cJADAS), well-being measures and concomitant treatments were captured. Weight-associated parameters included total body weight, body max index (BMI), and body surface area (BSA). TNFi dose and interval were documented. Dosing was normalized and expressed as proportion of prescribed TNFi dosing over optimal TNFi dosing, the latter based on actual patient weights, approved product labelling and/or clinical dosing practices. The primary outcome measure was JIA American College of Rheumatology Pediatric 70 (ACR Pedi70) treatment response at 6 months. Analytic approaches included parametric and nonparametric tests for comparisons between groups as appropriate; Spearman's correlation testing; and subgroup analyses performed for BMI groupings, TNFi types, and prior biologic exposure.
Results: A total of 315 children were included, median age was 13.0 years (IQR 8.3-15.9), 66% were female and 64% were Caucasian, 36% had polyarticular JIA. The majority (78%) were healthy-weight, 3% were underweight, overweight or obese accounted for 10% and 9%, respectively. Adalimumab (69%) and etanercept (22%) were the most commonly used TNFi. A total of 159 patients (50%) were TNFi responders, and 156 (50%) non-responders. At baseline the responder and non-responder groups had similar ethnicity, JIA ILAR subtypes, disease duration, laboratory findings, disease activity, time to TNFi initiation and type of TNFi received. Importantly, at baseline weight, BMI and BSA were significantly higher in non-responders (p= 0.01, 0.02, 0.01, respectively). In contrast, treatment responders received significantly higher proportion of TNFi dosing at 6 months (p= 0.01). Correlation analysis showed significant negative correlation between baseline total body weight, BMI, and BSA with the proportion of TNFi dosing received (ρ= −0.7,−0.6,−0.7, respectively), and a small but significant negative correlation between percentage change of ACR Pedi core set variables between baseline and 6-month follow-up and proportion of TNFi dosing. These findings were consistent regardless of overweight/obese status, TNFi type, or prior biologic exposure.
Conclusion: Non-response to TNFi in JIA patients is closely associated with higher body weight. This important observation warrants further investigation into appropriately weight-adjusted TNFi dosing in children with JIA.

Disclosure
None declared

O13

Multiomic investigation of juvenile idiopathic arthritis synovium reveals immune cell heterogeneity

A. R. Thielbar[1], T. V.-Y. Ting[2], L. Auld[2], K. Rogers[2], M. Quinlan-Waters[2], S. T. Angeles-Han[1,3], E. A. Ogbu[2], D. J. Lovell[2], J. L. Huggins[2], G. Schulert[2], P. Vega-Fernandez[2], Y. Baglaenko[1,3]
[1]Human Genetics, [2]Rheumatology, Cincinnati Children's Hospital, [3]Pediatrics, University of Cincinnati, Cincinnati, United States
Correspondence: Y. Baglaenko
Pediatric Rheumatology, **23(2):**O13

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease of childhood, affecting 1:1,000 children worldwide. The hallmark of JIA is immune-mediated chronic inflammation in the synovium – clinically reflected by the presence of arthritis or a combination of joint pain, swelling, or limitation of joint movement. If inadequately treated, JIA can lead to profound lifelong joint deformity and disability. Thus, early diagnosis and treatment initiation is essential in the management of patients with JIA. Histological examination of synovium, although limited in scope, has identified immune cell infiltration of lymphocytes, plasma cells, macrophages as well as proliferation of fibroblast- and macrophage-like synoviocytes. To date, no comprehensive studies of JIA synovium have been performed as current best-practices do not routinely collect tissue biopsies for diagnosis or analysis. Recent single cell methodologies that assay open chromatin and transcriptome have made great strides in bridging this gap in adult rheumatic conditions by directly examining the synovium.
Objectives: The objective of this study is to leverage novel multiomic single cell strategies to characterize cell heterogeneity in the synovium of children with JIA.
Methods: Ultrasound guided synovial biopsies were performed in two children to isolate synovium. Tissue was enzymatically digested, sorted for viability, nuclei isolated, and single cell libraries generated with the 10X multiome (RNA + ATAC) pipeline. A PBMC sample from a JIA patient was also included to define tissue enrichment. Data was aligned with cellranger and processed with custom analysis pipelines.
Results: We obtain high quality data from three samples for single cell RNA and ATAC sequencing with a median of 1350 genes and 6233 ATAC peaks from 5771 cells. Integration of gene expression and open chromatin data, harmonization by donor, and clustering identifies 11 broad populations including T, B and fibroblasts cells. Comparison between tissue and blood sample identifies an enrichment of activated/memory CD4 and CD8 T cells and a decrease in monocytes populations specific to the synovium. Pathogenic HLA-DR+ fibroblasts are exclusively identified in synovium. Fine-grained analysis of T cells with our recently developed T cell annotation program (TCAT) identifies evidence of proliferation in Tfh/Tph and T regulatory cells.
Conclusion: To our knowledge, this is the first multiomic single cell study of JIA synovium that simultaneously captures gene expression and open chromatin. We implement a high-quality processing pipeline and identify cell heterogeneity specific to the synovium. In particular, we find evidence of immune cell activation and proliferation in Tfh/Tph and T regulatory cells from synovium.
Disclosure
None declared

O14

Genome-wide association study and xqtl analysis in syndrome of undifferentiated recurrent fever (SURF): A multi-omics approach for identifying novel candidate biomarkers and molecular pathophysiological mechanisms

G. Cavalca[1,2], P. Uva[1], S. Gattulli[1], A. Petretto[3], S. Palmeri[4,5], C. Speziani[6], F. Penco[4], F. Rizzi[7], S. Decherchi[8], Y. Rodina[8], K. Vierlinger[9], G. A. Vignolle[9], J. I. Arostegui[10], S. Ozen[11], M. Gattorno[4], I. Ceccherini[6]on behalf of PerSAIDs consortium, G. Fiorito[1]

[1]Clinical Bioinformatics Unit, IRCCS Istituto Giannina Gaslini, Genoa, [2]University of Bologna, Bologna, [3]Core Facilities Proteomics Laboratory, [4]Rheumatology and Autoinflammatory Diseases Unit, IRCCS Istituto Giannina Gaslini, [5]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, [6]UOSD Aggregation Area for Research Laboratories, IRCCS Istituto Giannina Gaslini, Genoa, [7]Istituto di Management Sanitario, IMS, Milan, [8]Data Science and Computation Facility, Fondazione Istituto Italiano di Tecnologia, Genoa, Italy, [9]Center for Health & Bioresources, Competence Unit Molecular Diagnostics, AIT Austrian Institute of Technology GmbH, Wien, Austria, [10]Department of Immunology, Hospital Clínic-IDIBAPS, Barcelona, Spain, [11]Department of Pediatrics, Hacettepe University, Ankara, Türkiye
Correspondence: Y. Baglaenko
Pediatric Rheumatology, **23(2):**O14

Introduction: The Syndrome of Undifferentiated Recurrent Fever (SURF) is characterized by recurrent fever episodes and systemic inflammation whose etiology is currently unknown, being probably multifactorial.
Objectives: This study aimed to identify genetic variants underlying SURF and characterize their functional impact through comprehensive multi-omics analysis.
Methods: We collected Whole-Genome Sequencing (WGS) data from 79 SURF patients and 321 healthy controls. Genome-wide association study (GWAS) and sequence kernel association test optimal (SKAT-O) were performed to identify common and rare genetic variants associated with the disease. Candidate variants were further investigated through quantitative trait loci (xQTL) analysis using machine learning (ML) methods to evaluate their impact on multiple omics profiles: immunomics, lipidomics, metabolomics, transcriptomics, proteomics, and epigenomics. Pathway enrichment analysis was performed on candidate biomarkers to identify biological processes involved in the disease pathogenesis.
Results: We identified several candidate SNPs and rare variants-enriched genomic regions associated with the disease, mostly localized in non-coding areas. Subsequent xQTL analyses revealed novel expression quantitative trait loci (eQTLs), methylation QTLs (meQTLs), protein QTLs (pQTLs), and metabolite QTLs (mQTLs), suggesting a functional impact across multiple omics layers. A systematic comparison across different ML algorithms demonstrated that integrating multiple omics layers yields a more comprehensive and reliable set of putative QTL associations. We prioritized our findings based on evidence from publicly available datasets and manually-curated lists of autoinflammatory diseases-related genes, generating a focused set of high-confidence candidate variants/genes for future functional validation.
Conclusion: To the best of our knowledge, this is the first genome-wide study on SURF. We identified several significant genetic associations that need to be validated on an independent dataset. Functional characterization suggests that many identified variants may influence clinical phenotype through regulatory QTL mechanisms. Our multi-omics approach reveals candidate biomarkers potentially underlying SURF pathogenesis, while demonstrating how ML effectively links genomic findings with their functional impacts across multiple molecular layers, enhancing our understanding of this complex condition.
Disclosure
None declared

Reference
1. This work was supported within the framework of ERA PerMed (PerSAIDs Consortium), which is funded from the European Union's Horizon 2020 research and innovation program under grant agreement No. 779282.

O15

Validation of human phenotype ontology (HPO) terms and development of an AI-based diagnostic tool for saids: the odino project

C. Matucci Cerinic[1], M. Vergani[2], G. Cavalca[2], R. Caorsi[1], M. E. Van Gijn[3], L. Pape[3], G. Boursier[4], E. Mosci[5], G. Fiorito[2], P. Uva[2], M. Gattorno[1]
[1]Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, [2]Clinical Bioinformatics, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [3]Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, [4]Institute for Regenerative Medicine and Biotherapy, University of Montpellier,, Montpellier, France, [5]Gaslini Trial Center, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: C. Matucci Cerinic
Pediatric Rheumatology, **23(2):**O15

Introduction: An accurate classification of systemic autoinflammatory diseases (SAIDs) is crucial for an early diagnosis and therapy optimization. The Human Phenotype Ontology (HPO) project provides a standardized terminology for describing phenotypic features of genetic diseases. HPO help clinicians prioritize diagnosis by ranking diseases based on similarity scores between HPO terms and patient's symptoms. In 2022 the AutoInflammatory diseases section was revised, but the accuracy of the new terms has not yet been validated in real patients.
Objectives: i) to evaluate the diagnostic accuracy of HPO terms in a cohort of real patients, ii) to evaluate the accuracy of *Phenomizer* compared to different machine-learning algorithms based on a provided real-life patients' dataset. iii) to develop a novel diagnostic tool for SAIDs.
Methods: From the Eurofever Registry, 2,866 patients diagnosed with Familial Mediterranean Fever (FMF), Cryopyrin-Associated Periodic Syndrome (CAPS), Mevalonate Kinase Deficiency (MKD), Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis (PFAPA), or Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) were included. Eurofever clinical variables were codified with HPO terms, and missing terms were retained. The patients' dataset was split into training (n=2,005) and test sets (n=861). Four machine learning classifiers were evaluated: Elastic Net regression (EN), k-Nearest Neighbors (kNN), Random Forest (RF), and eXtreme Gradient Boosting (XGBoost), comparing their performance to *Phenomizer*.
Results: 224 Eurofever variables were codified into HPO terms. Of these, 195 had full HPO correspondence, 12 partial, and 17 no correspondence. XGBoost emerged as the best-performing algorithm in assigning the correct diagnosis to the analyzed patients, achieving an average accuracy of 0.80, and significantly outperforming *Phenomizer*, even when *Phenomizer* was trained on Eurofever HPO terms' frequencies. The addition of the terms "fever duration" and "ethnicity" (present in Eurofever but absent in HPO) improved the algorithm accuracy, highlighting the need for new HPO codes. Finally, based on the best-performing algorithm, a user-friendly web app where clinicians can input HPO terms to receive the probability of each SAID diagnosis (among those used in the training model) was developed.
Conclusion: Our results suggest that the HPO database should be updated including Eurofever patients' term frequencies. The developed web app correctly identifies the two most probable SAIDs in over 85% of cases, offering a valuable tool for early diagnosis. Further updates will refine the model as additional data from underrepresented diseases become available.
Disclosure
None declared

O16

Dominant negative ADA2 mutations cause ADA2 deficiency in heterozygous carriers

M. Wouters[1], L. Ehlers[1], W. Van Eynde[2], M. E. Kars[3], S. Delafontaine[1], V. Kienapfel[1], M. Dzhus[1], R. Schrijvers[1], P. De Haes[4], S. Struyf[1], G. Bucciol[1], Y. Itan[3], A. Bolze[5], A. Voet[2], A. Hombrouck[1], L. Moens[1], B. Ogunjimi[6], I. Meyts[1]
[1]Microbiology, Immunology and Transplantation, [2]Chemistry, KU Leuven, Leuven, Belgium, [3]Icahn School of Medicine at Mount Sinai, New York City, United States, [4]General Internal Medicine, UZ Leuven, Leuven, Belgium, [5]Helix, San Mateo, United States, [6]Pediatrics, Antwerp University Hospital, Antwerp, Belgium
Correspondence: M. Wouters
Pediatric Rheumatology, **23(2):**O16

Introduction: Human ADA2 deficiency (DADA2) is an inborn error of immunity with a broad clinical phenotype encompassing

vasculopathy including livedo racemosa and lacunar strokes as well as hemato-immunological manifestations. Combination of decreased serum ADA2 activity and the identification of biallelic deleterious alleles in the *ADA2* gene are used for diagnosis. DADA2 carriers harbor a single pathogenic variant in *ADA2* and are mostly considered healthy and asymptomatic. However, some DADA2 carriers present a phenotype compatible with DADA2 (1–4).
Objectives: We sought to investigate whether being heterozygote for specific variants in *ADA2* could explain the patients DADA2 phenotype.
Methods: A HEK293T cell overexpression system was used to evaluate impact of ADA2 variants on WT ADA2 protein expression/secretion and enzymatic activity. Finngen, UK biobank and the Bio*Me* Biobank were used to assess population genetics and evaluate correlation with DADA2 phenotypes. ADA2 enzyme activity was measured in a colorimetric assay adapted by Giusti et al (1974)
Results: In addition to diseased DADA2 carriers in literature (1–4), we report a cohort of 10 heterozygous carriers of pathogenic *ADA2* variants presenting with DADA2 clinical features. To study the potential effect of heterozygous pathogenic variants in ADA2 on WT ADA2 protein expression, secretion and enzymatic activity, we performed transient transfection of each *ADA2* variant together with WT *ADA2* to mimic carrier status. In vitro study of the *ADA2* variants identified in this patient cohort revealed that R169Q, H424N and Y453C affect secretion of WT ADA2 protein. Moreover, we demonstrate a dominant negative effect on the enzymatic activity of WT ADA2 by variants G47A, G47R, G47V, R169Q, E328K, H424N and Y453C both intracellularly and extracellularly. Data from PheWAS show that the heterozygous state for pLOF variants in *ADA2* is associated with phenotypes that align with DADA2. When studying the most frequent allele, R169Q, the enriched phenotypes are even more striking, despite the overall low number of cases.
Conclusion: Here, we describe how specific heterozygous variants cause ADA2 deficiency through distinct dominant negative effects on either ADA2 enzyme activity, dimerization and/or secretion. At the molecular level, heterozygosity for these variants mimics what is observed in DADA2. We conclude that humans with heterozygous dominant negative missense variants in *ADA2* are at risk of DADA2.
Disclosure
None declared

References
1. Rama, M. et al. European Journal of Human Genetics 26, 960–971 (2018)
2. Moi, L. et al. Journal of Clinical Immunology 42, 959–961 (2022)
3. Nihira, H. et al. Journal of Allergy and Clinical Immunology 148, 550–562 (2021)
4. Izumo, H. et al. Cureus (2023)

O17

Lipopolymer/sirna precision nanotherapy targeting NLRP3 in autoinflammatory diseases

M. Nasrullah[1], A. P. Rajendran[2], B. Bulut[2], M. Romano[3], L. Piskin[4], S. Suresh[5], M. Osman[6], H. Ostergaard[7], E. Demirkaya[4], H. Uludağ[2]
[1]Faculty of Pharmacy and Pharmaceutical Sciences, [2]Department of Chemical and Materials Engineering, University of Alberta, Edmonton, [3]Division of Paediatric Rheumatology, Department of Paediatrics, [4]Department of Paediatric Rheumatology, Schulich School of Medicine and Dentistry, Western University, London, [5]Department of Pediatrics, [6]Department of Medicine, [7]Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Canada
Correspondence: E. Demirkaya
Pediatric Rheumatology, **23(2):**O17

Introduction: Autoinflammatory disorders like Cryopyrinopathies (CAPS), TNF receptor-associated periodic syndrome (TRAPS) and familial Mediterranean fever (FMF) involve dysregulated innate immune responses. The NLRP3 inflammasome, part of the nucleotide-binding oligomerization-like receptor (NLR) family, activates caspase-1, leading to the maturation of the pro-inflammatory cytokine interleukin-1β (IL-1β). While IL-1 blockers (e.g., anakinra, canakinumab) can help many patients, challenges such as therapeutic resistance and partial responses persist 1. Moreover, certain autoinflammatory conditions like CAPS, TRAPS and FMF do not respond well to anti-IL 1, as their underlying mechanisms are not effectively suppressed by these drugs. Precision medicine using short interfering RNA (siRNA)-based therapeutics offers a promising alternative for gene-specific silencing of pathogenic targets. However, clinical use of siRNA-based therapy is challenged by poor stability in circulation and inefficient cellular uptake.
Objectives: This study aims to develop a lipid-substituted polyethyleneimine-based lipopolymer (PEI-C) system for safe and efficient siRNA delivery to immune cells, specifically targeting *NLRP3* to suppress inflammatory responses in autoinflammatory disorders.
Methods: We designed three siRNAs targeting murine *Nlrp3* and complexed them with PEI-C to formulate lipopolymer nanoparticles (LPNPs). These LPNPs were used to transfect RAW264.7 murine macrophages stimulated with lipopolysaccharide (LPS). 24 hours post-transfection, *Nlrp3* gene expression and IL-1β secretion were quantified using RT-qPCR and ELISA, respectively. The most effective siRNA sequence (siNlrp3-3) was further tested *in vivo* using an LPS-induced inflammation mouse model. IL-1β levels were measured in the spleen, liver, lung, kidney, heart, and bone marrow 24 hours post-treatment. In addition, *ex vivo* studies were conducted using LPS-stimulated PBMCs from healthy human donors transfected with LPNPs containing a human-specific siNLRP3.
Results: In vitro, siNlrp3 LPNPs effectively silenced *Nlrp3* expression in LPS-stimulated RAW264.7 cells, resulting in a marked reduction in IL-1β secretion compared to scrambled control (CsiRNA) LPNPs. Among the three tested sequences (siNlrp3-1, siNlrp3-2, and siNlrp3-3), siNlrp3-3 outperformed the other 2 sequences. Based on this outcome, siNlrp3-3 LPNPs were evaluated in an LPS-induced inflammatory mouse model (n=5), where IL-1β levels were measured 24 hours post-treatment in different tissues, including spleen, liver, lung, kidney, heart, and bone marrow. Reductions of IL-1β levels were observed in the liver and bone marrow, with significant decreases in the spleen (p=0.0086) and lung (p=0.0030). To assess translational relevance, siNLRP3 LPNPs were tested *ex vivo* in LPS-stimulated human PBMCs (n=15), leading to a significant reduction in IL-1β secretion compared to CsiRNA LPNPs (p=0.0107).
Conclusion: Our study demonstrates that PEI-C–based LPNPs offer a robust, non-viral delivery system for siRNA-mediated silencing of *NLRP3*, leading to effective suppression of IL-1β in murine and human immune models, highlighting the therapeutic potential of siRNA nanomedicine in autoinflammatory diseases, especially where conventional therapies fall short.
Disclosure
M. Nasrullah: None declared, A. P. Rajendran: None declared, B. Bulut: None declared, M. Romano: None declared, L. Piskin: None declared, S. Suresh: None declared, M. Osman: None declared, H. Ostergaard: None declared, E. Demirkaya: None declared, H. Uludağ Shareholder with: The lipopolymer, PEI-C, is being commercialized with a different brand name via a U. of Alberta spin-off company, RJH Biosciences Inc. (Edmonton, AB). H.U. has ownership of patents on the indicated lipopolymers and own shares in RJH Biosciences Inc.

Reference
1. Fanlo, P., Gracia-Tello, B. del C., Aizpuru, E.F., Álvarez-Troncoso, J., Gonzalez, A., Prieto-González, S., Freire, M., Argibay, A.B., Pallarés, L., Todolí, J.A., et al. (2023). Efficacy and Safety of Anakinra Plus Standard of Care for Patients With Severe COVID-19: A Randomized Phase 2/3 Clinical Trial. JAMA Netw Open *6*, e237243–e237243. https://doi.org/10.1001/JAMANETWORKOPEN.2023.7243.

O18

Changes in pharmacodynamic markers (PD) in response to emapalumab in children and adults with macrophage activation syndrome (MAS) in still's disease: results from a pooled analysis of two prospective trials

S. J. Vastert[1], J. Antón[2], P. Quartier[3], B. Fautrel[4,5,6], P. Brogan[7,8], E. M. Behrens[9], M. Elder[10], F. Minoia[11], P. Dolezalova[12], R. Biesen[13], M. Shimizu[14], U. Ullmann[15], A. Mahmood[16], A. Danquah[15], E. Burillo[15], M. Petrimpol[15], S. Mallett[16], B. D. Jamieson[17], A. Grom[18], F. De Benedetti[19]

[1]Pediatric Rheumatology & Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, Netherlands, [2]Hospital Sant Joan de Déu, Department of Pediatric Rheumatology, University of Barcelona, Barcelona, Spain, [3]Université Paris-Cité, IMAGINE Institute, RAISE
Reference centre, Pediatric Immuno-Hematology and Rheumatology Unit, Necker Hospital, Assistance Publique-Hôpitaux de Paris, [4]Department of Rheumatology, Pitié-Salpêtriere Hospital, Assistance Publique-Hôpitaux de Paris, Sorbonne University, [5]CRI-IMIDIATE Clinical Research Network and ERN Rita, CEREMAIA
Reference Center, [6]Pierre Louis Institute of Epidemiology and Public Health, INSERM UMR-S 1136, Paris, France, [7]Great Ormond Street Hospital for Children NHS Foundation Trust, [8]University College London Great Ormond Street Institute of Child Health, London, United Kingdom, [9]Division of Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, [10]College of Medicine, University of Florida, Gainesville, United States, [11]Pediatric Immuno-Rheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [12]Paediatric Rheumatology and Autoinflammatory Diseases Unit, General University Hospital, Prague, Czech Republic, [13]Department of Rheumatology and Clinical Immunology, Charité Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität, Berlin, Germany, [14]Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, [15]Sobi, Basel, Switzerland, [16]Sobi, Stockholm, Sweden, [17]Sobi Inc., Morrisville, [18]Cincinnati Children's Hospital, Division of Rheumatology, Cincinnati, United States, [19]Division of Rheumatology, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy
Correspondence: S. J. Vastert
Pediatric Rheumatology, **23(2):** O18

Introduction: MAS is a life-threatening complication of Still's disease, characterized by interferon-gamma (IFNg)-driven macrophage activation and systemic hyperinflammation. Emapalumab binds free and receptor-bound IFNg, providing rapid and targeted neutralization of IFNg. Emapalumab achieved rapid control of MAS in a pooled patient population from two single-arm interventional studies (NI-0501-06[1] and NI-0501-14 [EMERALD]).
Objectives: To evaluate changes in key PD markers by response status 8 weeks after treatment initiation and time to response.
Methods: Patients with MAS in Still's disease who had an inadequate response to high-dose glucocorticoids (GCs), or investigator-assessed rapid worsening of clinical condition, were treated with emapalumab for 4 weeks. Patients were administered a 6 mg/kg loading dose of emapalumab, followed by 3 mg/kg every 3 days from days 4–16, then 3 mg/kg twice weekly until Day 28 (or longer). The primary efficacy endpoint was complete response (CR) at Week 8, defined as resolution of clinical signs according to investigator assessment (MAS clinical activity visual analog score [VAS] ≤1/10 cm) and normalization of 7 MAS-related laboratory parameters. Overall response (OR) was defined as a CR or partial response (PR; VAS <4 cm and normalization of ≥3 abnormal baseline laboratory parameters included in the composite primary endpoint). Key biomarkers included chemokine C-X-C motif ligand 9 (CXCL9), ferritin and soluble CD25 (sCD25).
Results: 39 patients were enrolled (31 [79.5%] females; median age, 12 years [range, 9 m–64 y]). 85% of patients received concomitant treatments for their underlying condition, including anti-IL-1 (66.6%) and cyclosporine (43.6%). At Week 8, 21/39 (53.8%) patients achieved a CR (95% CI, 37.2–69.9%) and 29/38 patients (76.3%) achieved an OR. The median time to first OR was 16 days. 32/39 (82.1%) patients achieved an OR up to Week 8 and 6 more patients after Week 8. Patients with CR (n=20) or PR (n=9) at Week 8 had higher geometric mean levels of CXCL9 (CR, 3206 ng/mL; PR, 2371 ng/mL), ferritin (CR, 8186 µg/mL; PR, 8452 µg/mL) and sCD25 (CR, 5654 ng/mL; PR, 7436 ng/mL) at baseline versus Week 8 non-responders (n=5; CXCL9, 291 ng/mL; ferritin, 2633 µg/mL; sCD25, 1531 ng/mL). All patients had rapid and sustained CXCL9 and ferritin declines over time: at Week 8, CXCL9 and ferritin median percentage reductions from baseline were −99% and −92% in patients with CR or PR, respectively. NR had similar declines in CXCL9 (n=2; −86%) and ferritin (n=5; −89%) at Week 8, though sCD25 remained relatively unchanged vs baseline (n=2; +21%).
Conclusion: Emapalumab treatment enabled rapid responses and reduction of key PD markers in patients with MAS in Still's disease who had an inadequate response to high-dose GCs. The treatment effect was sustained with a trend of increased response levels at Week 8.
Trial registration identifying number: Trial registration numbers: NCT03311854 and NCT05001737
Disclosure
S. Vastert Grant/Research Support with: Sobi, Consultant with: Sobi, Novartis, Speaker Bureau with: Sobi, Novartis, J. Antón Grant/Research Support with: Sobi, Speaker Bureau with: Sobi, P. Quartier: None declared, B. Fautrel Grant/Research Support with: AbbVie, Eli Lilly & Co, MSD, Pfizer, Consultant with: AbbVie, Alternative, Biogen, BMS, Celgene, Celltrion, Chugai, Eli Lilly & Co, Fresenius Kabi, Galapagos, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche, Room, Sandoz, Sanogi-Genzyme, UCB, P. Brogan Speaker Bureau with: Sobi, E. Behrens Grant/Research Support with: Sobi, Consultant with: Sobi, Ab2Bio, M. Elder: None declared, F. Minoia Consultant with: Sobi, Novartis, Speaker Bureau with: Sobi, Novartis, P. Dolezalova Speaker Bureau with: Sobi, Novartis, Pfizer, Medac, R. Biesen: None declared, M. Shimizu Grant/Research Support with: Medical and Biological Laboratories Co., Ltd, U. Ullmann Consultant with: Sobi, A. Mahmood Consultant with: Sobi, A. Danquah Employee with: Sobi, E. Burillo Employee with: Sobi, M. Petrimpol Employee with: Sobi, S. Mallett Consultant with: Sobi, B. Jamieson Employee with: Sobi Inc., A. Grom Grant/Research Support with: National Institutes of Health, Novartis, SJIA FOundation, Sobi, Consultant with: Kiniksa, Novartis, Sobi, F. De Benedetti Grant/Research Support with: Abbvie, Apollo, Elixiron, Kiniska, Novartis, Sanofi, Sobi, Consultant with: Abbvie, Apollo, Elixiron, Kiniska, Novartis, Sanofi, Sobi

Reference
1. De Benedetti F, et al. *Ann Rheum Dis* 2023;82:857–865.

O19

Spatial transcriptomic profiling reveals interferon activation and CD8$^+$ t cell dominance in systemic juvenile idiopathic arthritis-macrophage activation syndrome liver inflammation

E. Eloseily[1], T. Sabit[2], L. Berklite[2], G. Schulert[2], A. Grom[2]
[1]Dallas, UT Southwestern Medical Center, Texas, [2]Cincinnati, Cincinnati Children's Hospital Medical Center, Ohio, United States
Correspondence: E. Eloseily
Pediatric Rheumatology, **23(2):**O19

Introduction: Systemic juvenile idiopathic arthritis (SJIA) with macrophage activation syndrome (MAS) involves severe systemic inflammation and hepatocellular injury. Our prior histopathology studies showed increased CD8$^+$ T cell and CD163$^+$ macrophages in SJIA-MAS compared to SJIA without MAS (1). However, distinguishing SJIA-MAS liver involvement from autoimmune hepatitis (AIH), familial hemophagocytic lymphohistiocytosis (FHLH), and steatohepatitis (SH) remains challenging.
Objectives: We aimed to define spatial immune signatures across SJIA-MAS, AIH, FHLH, SH, and healthy controls (HC) using spatial transcriptomics with the ultimate goal to develop diagnostic biomarkers for clinical practice.
Methods: Formalin-fixed, paraffin-embedded liver tissues from SJIA-MAS (n=6), SJIA without MAS (n=1), AIH (n=7), FHLH (n=6), SH (n=5), and HC (n=6) were analyzed using the NanoString GeoMx DSP® platform. Immunofluorescent staining for CD18, CD68, CDE, and nuclear DNA was used to select regions of interest (ROIs) enriched for (1) hepatocytes; (2) macrophages, and (3) lymphocytes. Spatially resolved gene expression was Q3 normalized. In the initial analysis, levels of expression of the IFN-induced signature genes (ISG) (2) as well as markers specific for CD4+ T cells, cytotoxic T cells (CD8, GZMb, PRF) and macrophages (CD163) were compared between the clinical groups in macrophage- and T cell-enriched compartments.
Results: SJIA-MAS samples showed strong interferon-stimulated gene (ISG) activation (STAT1, EPSTI1, CXCL9) in both macrophage and T lymphocyte enriched ROIs and higher expression of cytotoxic markers (GZMB), particularly in T cell–enriched areas, compared to mild ISG activation in SJIA without MAS (figure 1). AIH samples exhibited

heterogeneous immune profiles with variable but modest CD4⁺ T cell expression with less prominent ISG (figure 2). FHLH shared partial interferon signatures but had lower overall ISG expression. LY6E was selectively elevated in FHLH macrophages (table 1).
Conclusion: SJIA-MAS is defined by activation and expansion of CD8⁺ T cells in addition to strong type I/II interferon responses, distinct from SJIA without MAS, AIH, and FHLH. Particularly high expression of CXCL9 distinguished SJIA-MAS. This suggests that serum CXCL9 may help distinguish MAS-related liver injury from other SJIA-associated pathologies. Global gene expression analysis in the same samples is ongoing.
Disclosure
None declared

Reference
1. Eloseily E, Berklite L, Picarsic J, Schulert G, Sheridan R, Grom A, editors. Histopathological Features of Liver Tissue Biopsies in SJIA Patients with and Without Clinical Macrophage Activation Syndrome. ARTHRITIS & RHEUMATOLOGY; 2024: WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.
2. Kim H, de Jesus AA, Brooks SR, Liu Y, Huang Y, VanTries R, et al. Development of a validated interferon score using NanoString technology. Journal of Interferon & Cytokine Research. 2018;38(4):171-85.

O20

Analysis of clinical parameters and transcriptional biomarkers for the prediction of Il-1 inhibitor treatment non-response in the carra first-line options for systemic juvenile idiopathic arthritis treatment (FROST) study

M. Matt[1], M. C. Marques[2], L. Auld[1], G. Tomlinson[3], Y. Kimura[4], M. Ombrello[2], G. Schulert[1], on behalf of the CARRA FROST Investigators
[1]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, [2]Translational Genetics and Genomics Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, United States, [3]University of Toronto, Toronto, Canada, [4]Division of Pediatric Rheumatology, Hackensack Meridian Medical Center, Hackensack, United States
Correspondence: M. Matt
Pediatric Rheumatology, **23(2):**O20

Introduction: Many patients with systemic juvenile idiopathic arthritis (sJIA) will experience incomplete response to first-line interleukin-1 (IL-1) inhibitors, however, the biologic mechanisms underlying treatment non-response are not well understood.
Objectives: We sought to characterize the clinical phenotype, inflammatory cytokines, and gene expression profile of responders and non-responders to IL-1 inhibitors in a real-world cohort of new-onset sJIA patients in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.
Methods: We identified all patients in the FROST study who were started on IL-1 inhibitors. Responders were classified as those patients who fulfilled either the Wallace criteria of clinically inactive disease (CID), or criteria of low disease activity (LDA; cJADAS < 2.5 without fever or corticosteroid use) after 6 months. Children who did not fulfill these requirements were characterized as non-responders. In all patients with available serum or plasma, IL-18 and CXCL9 levels were measured using an Ella assay, and other cytokine and inflammatory protein levels were obtained using a custom Luminex panel. Candidate gene targets for a custom Nanostring panel were selected based on data from prior studies.
Results: Among the 61 patients who received IL-1 inhibitors, we identified 34 responders and 27 non-responders. A higher baseline physician global score was observed in non-responders (mean 7.2 vs 5.5; p = 0.006). Responders trended towards a higher neutrophil count at baseline, but this was not significant (mean 11,560 cells/μL vs 9,160; p= 0.09). There were no significant differences in the baseline joint count, arthritis joint count at one month, or in days to initiation of therapy between responders and non-responders. There were 30 total patients who received IL-1 inhibitors with existing baseline biosamples; of these, 17 were responders and 13 were non-responders. At baseline, median IL-18 levels were higher in non-responders (46,823 pg/mL; range 4,612-157,713) vs responders (23,435; range 1,485- 150,479), but this difference was not significant (p=0.65). Luminex data revealed decreased baseline CCL25 (p=0.019) and MCP-1 (p=0.05) levels in non-responders when compared to responders. Finally, we performed blood transcriptional profiling using Nanostring. A 29 gene score previously associated with response to canakinumab showed no significant difference between responders and non-responders. However, baseline gene expression levels of genes associated with canakinumab non-response - *STAB1*, *CD163*, and *VCAN* – were significantly higher in non-responders compared to responders. A composite geomean score of these three genes >545 yielded 78% sensitivity and 93% specificity for IL-1 inhibitor non-response.
Conclusion: In the FROST cohort, non-responders to IL-1 inhibitors by CID or LDA had higher baseline physician global scores and significantly decreased CCL25 and MCP-1 levels compared to responders. We also validated a previously described IL-1 non-response gene expression signature of *STAB1*, *CD163*, and *VCAN*. These findings support the hypothesis that subgroups of sJIA patients with different immunologic phenotypes exist, and that immune phenotyping could assist in predicting IL-1 inhibitor non-response.
Disclosure
M. Matt: None declared, M. Marques: None declared, L. Auld: None declared, G. Tomlinson: None declared, Y. Kimura: None declared, M. Ombrello: None declared, G. Schulert Grant/Research Support with: IpiNovyx, Consultant with: Novartis and Sobi

O21

Ev-mirna and T cell profiles identify oligoarticular Jia at risk for severe outcomes

F. Raggi[1], C. Rossi[1], B. Salvatori[2], S. Pelassa[1], F. Briasco[1], F. Antonini[3], S. M. Orsi[4], M. Burrone[4], G. Del Zotto[3], A. Ravelli[5], D. Cangelosi[2], M. Gattorno[1], A. Consolaro[1], M. C. Bosco[1]
[1]Unit of Rheumatology and Autoinflammatory Diseases, Department of Pediatric Sciences, [2]Clinical Bionformatics Unit, Scientific Direction, [3]Core facilities Laboratory, Integrated Department of Services and Laboratories, IRCCS G.Gaslini Institute, [4]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, [5]Scientific Direction, IRCCS G.Gaslini Institute, Genova, Italy
Correspondence: F. Raggi
Pediatric Rheumatology, **23(2):**O21

Introduction: Oligoarthritis is the most frequent form of Juvenile Idiopathic Arthritis (JIA), characterized by a variable course. Although many patients maintain a benign phenotype, up to 40% may develop polyarticular extension (pcJIA), requiring more aggressive treatment. Another complication is iridocyclitis, which may cause vision loss. Early identification of patients at risk for disease progression remains a major clinical challenge.
Objectives: This study aims to identify extracellular vesicle–derived miRNAs (EV-miRs) and immune cell phenotype present at disease onset that predict long-term outcomes in oligoarticular JIA, through integrated omics, immunophenotyping, and machine learning (ML).
Methods: Ninety-four treatment-naïve oligoarthritis patients were enrolled at onset and followed for 24 months. EV-miR profiling was performed in plasma (PL) and synovial fluid (SF). Clinical and laboratory features (e.g., age, sex, ANA, ESR, CRP, joint count, and EV-miRNAs at onset; therapy at onset and within 2 years) were included as predictor variables, whereas relapse, pcJIA, iridocyclitis, and remission were outcome measures for supervised ML models. Dataset was split into training and test sets to assess predictive capabilities of predictors. Four predictive models were developed using Random Forest classifiers, with feature selection performed via Recursive Feature Elimination and model optimization through 5-fold cross-validation. Matthews Correlation Coefficient (MCC) was used as metric for assessing model performance. Diagnostic segregation between groups of patients based on outcome was visualized by Receiver Operating Curves (ROC) and assessed by Area Under the Curve (AUC). Flow cytometry on peripheral blood and SF mononuclear cells from 28 patients was used to assess immune signatures associated with pcJIA progression.
Results: ML models were trained on EV-miR signatures from both PL and SF; however, only PL-derived profiles demonstrated robust predictive performance across clinical outcomes. In the test set, the highest prediction performance, with a MCC of 0.688, was achieved for relapse

within 2 years using a model including hsa-miR-150, ESR, and therapy at 2 years. For pcJIA, the most accurate model included miR-20b, miR-331, ESR, joint count at onset, and therapy at 2 years (MCC = 0.508). Iridocyclitis was best predicted by a model comprising let-7e, miR-30b, and ESR (MCC = 0.508). Flow cytometry revealed that patients progressing to pcJIA exhibited significant alterations in T cell phenotypes, including increased frequencies of HLA-DR+ cells within both CD4+ and CD8+ subsets (AUC = 0.9), an expansion of CD4+ and CD8+ effector memory T cells (AUC = 0.9), and a marked reduction in naïve CD4+ (AUC = 0.8) and CD8+ (AUC = 0.9) T cell populations.
Conclusion: Systemic EV-miRs and immune cell phenotypes at disease onset represent valuable prognostic biomarkers in oligoarticular JIA. The integration of omic and immunophenotypic data through ML approaches allows for early identification of patients at increased risk of severe outcomes, supporting the implementation of personalized therapeutic strategies.
Disclosure
None declared

O22

Cumulative social disadvantage mediates the impact of neighborhood deprivation on Jia disease activity in a U.S. population

W. D. Soulsby[1], J. Boscardin[1], D. Horton[2], A. Knight[3], K. Toupin-April[4], E. von Scheven[1]
[1]University of California, San Francisco, San Francisco, CA, [2]Robert Wood Johnson Medical School at Rutgers University, New Brunswick, NJ, United States, [3]The Hospital for Sick Children, University of Toronto, Toronto, Ontario, [4]University of Ottawa, Ottawa, Ontario, Canada
Correspondence: W. D. Soulsby
Pediatric Rheumatology, **23(2):** O22

Introduction: Social determinants of health (SDOH) interact across individual, family, and community levels and are known contributors to health disparities. We previously demonstrated that cumulative social disadvantage, a score of individual and family-level SDOH, was associated with persistent disease activity among U.S. children with JIA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.
Objectives: To assess the role of community-level SDOH and its interaction with cumulative social disadvantage in relation to persistent disease activity in a cohort of U.S. youth with JIA.
Methods: This cohort study included children with JIA enrolled in the CARRA Registry (July 2015-January 2022). A cumulative social disadvantage score (range 0–3) was calculated using three binary indicators: family income <$50,000/year, guardian education <high school, and public or no insurance. Community-level SDOH was assessed using the U.S. Area Deprivation Index (ADI), a validated geocoded measure of neighborhood disadvantage. Demographic and clinical characteristics were summarized by ADI quartile. Mixed-effects logistic regression models evaluated the association between ADI and active disease by cJADAS-10 thresholds (>1.1 for oligoarticular JIA; >2.5 for others), adjusting for cumulative social disadvantage and covariates. Multiple imputation (50 cycles) addressed missing data: ADI (17%), income (25%), and education (16%). Causal mediation analysis assessed whether cumulative social disadvantage and its components mediated the ADI–disease activity relationship.
Results: Among 9,612 U.S. children with JIA, cumulative social disadvantage was more common in disadvantaged neighborhoods (ADI quartile 4: 64.9% with score >0 vs. quartile 1: 18.8%). Neighborhood disadvantage was independently associated with persistent disease activity (ADI Q4: OR 1.43, 95% CI: 1.15–1.76), but this was attenuated after adjusting for cumulative social disadvantage and covariates (quartile 4: aOR 1.06, 95% CI: 0.85–1.32). Causal mediation analysis identified cumulative social disadvantage as a significant mediator, accounting for 68% of the ADI-disease activity relationship. Low income (80%) and public/no insurance (75%) were significant mediators; guardian education was not (27%).
Conclusion: Neighborhood disadvantage (ADI) was associated with persistent JIA disease activity, but this relationship was largely mediated by individual and family-level SDOH. These findings highlight the need to address modifiable social risk factors, especially financial insecurity and insurance access, when developing strategies to reduce JIA health disparities. Interventions such as social work support or patient navigation may help mitigate these inequities. This conceptual framework should be studied in European settings, where socioeconomic disparities exist but healthcare systems differ from the U.S. and may require alternative intervention.
Disclosure
None declared

O23

"Confused by what it all means" – using a creative method to explore rheumatological conditions with children

K. Kupiec[1,2], P. Livermore[2,3] on behalf of IMPACT Study Steering Group
[1]Great Ormond Street Hospital NHS Foundation Trust, [2]Infection, Immunity, and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, [3]NIHR GOSH BRC, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom
Correspondence: K. Kupiec
Pediatric Rheumatology, **23(2):** O23

Introduction: Living with a rheumatological condition is associated with a range of daily challenges. Children frequently experience higher levels of pain, fatigue, and physical disabilities despite access to treatments that aim to control disease activity [1,2].
Objectives: The IMPACT study is a UK wide study to design, develop and test a technology intervention to support parents of children with rheumatological conditions. As part of the first phase of this study we invited children to share with us their experiences and perspectives in focus groups. In order to support families better it is important to explore children's understanding of their conditions and how it affects them.
Methods: The children's groups were all conducted virtually on Teams. They were asked to consider how they would support a friend who has received a recent diagnosis. They were also encouraged to explore emotions and feelings associated with getting a diagnosis, but also the impact this may have on their 'friend's' everyday life. Using 'Teams Whiteboard' children were invited to share their thoughts and ideas as they were exploring different pre-written scenarios for their fictional character. The aim of using a storyboard was to ensure each child didn't feel they needed to share their own personal experiences, which they may have found upsetting.
Results: We conducted 3 focus groups with the help of one of our child representatives from the Steering Group who co-led the sessions. In total 10 children (aged 8-13 (M = 10.51, SD = 1.60); 58.33% were female), with a range of different rheumatological conditions (JIA (N=5), JDM (N=2) and other conditions such as Behcet's, fever syndromes, CRMO, and Scleroderma (N=5)) participated in the sessions. They discussed challenges and implications in relation to having a health condition, especially around taking medicines, and sometimes not understanding side effects. Most prominently, children were very encouraging and provided hints and tips on how to support their 'friend' when it comes to blood tests, taking medicines, and doing regular exercises. They explored advantages of telling their friends, and how informing school is important to get extra help where needed. The children voiced how they really enjoyed the opportunity to meet others during the focus groups, and some even swapped contact details to stay in touch.
Conclusion: It is crucial to understand children's views to know how to better support them. Providing them with creative ways to explore their ideas and share their emotions is important to allow children to discuss their thoughts freely in a safe space. Using Teams Whiteboard as an interactive way for children to express themselves worked really well, with resultant high levels of engagement and energy in all three groups. Having a young Steering group member co-leading the sessions as both an expert as well as a peer, has provided a unique view and enriched the experience.
Disclosure
None declared

References

1. Shaw KL, Southwood TR, Duffy CM, McDonagh JE. Health-related quality of life in adolescents with juvenile idiopathic arthritis. Arthritis Care & Research:

Official Journal of the American College of Rheumatology. 2006 Apr 15;55(2):199-207. https://doi.org/10.1002/art.21852
2. Jones JT, Cunningham N, Kashikar Zuck S, Brunner HI. Pain, fatigue, and psychological impact on health-related quality of life in childhood onset lupus. Arthritis care & research. 2016 Jan;68(1):73-80. https://doi.org/10.1002/acr.22650

O24

Elevated trajectories of biomarkers galectin-9 and CXCL10 are associated with high risk of flare in Juvenile dermatomyositis – a multicohort study

S. R. Veldkamp[1], J. Drylewicz[1], J. G. Yeo[2,3], T. R. Moreau[4], D. Bletry[4], K. L. Teh[3], J. Wienke[1], S. J. Vastert[5], J. F. Swart[5], E. Van Nieuwenhove[5], W. Armbrust[6], J. M. van den Berg[7], P. C. Hissink Muller[8], E. Hoppenreijs[9], S. Kamphuis[10], E. Schatorjé[9], I. Melki[11], M. P. Rodero[4], T. Arkachaisri[3], B. Bader-Meunier[11], B. M. Feldman[12,13], A. van Royen-Kerkhof[5], F. van Wijk[1], M. H. Jansen[5]
[1]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, **[2]**Translational Immunology Institute, SingHealth Duke-NUS Academic Medical Centre, **[3]**KK Women's and Children's Hospital, Singapore, Singapore, **[4]**Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques UMR8601, CNRS, Paris, France, **[5]**Department of Paediatric Rheumatology and Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, **[6]**Department of Paediatric Rheumatology and Immunology, University Medical Center Groningen, Groningen, **[7]**Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam University Medical Centres, location AMC, Emma Children's Hospital, Amsterdam, **[8]**Department of Paediatric Rheumatology, Leiden University Medical Centre, Willem Alexander Children's Hospital, Leiden, **[9]**Department of Paediatric Rheumatology, Radboud University Medical Centre, Amalia Children's Hospital, Nijmegen, **[10]**Department of Paediatric Rheumatology, Erasmus University Medical Centre, Sophia Children's Hospital, Rotterdam, Netherlands, **[11]**Paediatric Haematology-Immunology and Rheumatology Department, Necker-Enfants Malades Hospital, AP-HP, Paris, France, **[12]**Division of Rheumatology, **[13]**Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada
Correspondence: S. R. Veldkamp
Pediatric Rheumatology, **23(2):** O24

Introduction: Juvenile dermatomyositis (JDM) has a heterogeneous and unpredictable disease course, with half of patients experiencing recurrent or persistent disease. Although there is a clear need for objective biomarkers to guide personalized treatment strategies, few novel candidates are successfully translated into clinical practice. Galectin-9 and CXCL10 have previously been validated as robust indicators of disease activity in JDM and may serve as reliable prognostic biomarkers.
Objectives: To validate Galectin-9 and CXCL10 as biomarkers for an impending flare.
Methods: We measured Galectin-9 and CXCL10 in >1,100 longitudinal serum or plasma samples from 158 JDM patients from four countries. Mean biomarker levels in the 2 years prior to flare were compared with levels in patients without flares. We applied joint latent class mixed models (jointLCMM) to jointly analyze biomarker trajectories and time to flare. For the jointLCMM, the total cohort was split in a training and validation cohort. Models with 1 to 5 classes were fitted and the optimal model was selected based on the lowest Bayesian Information Criterion (BIC). Mean posterior probabilities were used to assess classification quality (1 indicating perfect classification). The trained models for Galectin-9 and CXCL10 were applied to predict class membership in the validation cohort. A flare was defined as the moment of treatment intensification due to worsening of disease.
Results: Galectin-9 and CXCL10 both started rising around 1 year prior to flare, while levels remained low in those without a flare. In contrast, conventional biomarker CK showed a slight increase only in the final 4 months, similar to the Physician's Global Assessment (PGA) score. For both Galectin-9 and CXCL10, two latent classes were identified; one class containing one-fifth of patients was characterized by elevated biomarker levels and a high flare risk, with flare rates of 91.3% (Galectin-9) and 77.8% (CXCL10). Median time-to-flare was 7.1 months from the first measurement. When comparing flares among the two classes, skin-only flares were relatively more common in the Galectin-9 class with low biomarker levels (50% vs 14% of flares, p = 0.03). In the validation cohort, 41 and 47% of patients were predicted to be in the class with high Galectin-9 and high CXCL10, respectively, with a mean posterior probability of 0.90 and a flare rate of 100%. The sole flare predicted to be in the low Galectin-9 class was limited to the skin.
Conclusion: In this comprehensive international cohort, patients with increased longitudinal measurements of Galectin-9 and CXCL10 had a high risk of flaring within a year. Skin-only flares were less likely to be preceded by increased levels of Galectin-9. Validation on an independent cohort confirmed the reproducibility of these findings. Our data indicate that Galectin-9 and CXCL10 could guide medication tapering decisions and timely treatment intensifications, reducing chronic inflammation and improving outcomes in children with JDM.
Disclosure
None declared

O25

Spatial transcriptomic analysis reveals mitochondrial dysfunction in treatment-naïve juvenile dermatomyositis muscle

A. E. Syntakas[1,2,3], M. Kartawinata[1,2,3], H. D. Nguyen[1,2], C. Papadopoulou[2,4], M. Al-Obaidi[2,4], C. Pilkington[2,4], Y. Glackin[2,4], C. B. Mahony[5], A. P. Croft[5], S. Eaton[2,6], M. Cortina-Borja[7], N. M. L. Evans[1,2,3], A. White[8], M. Mshanga[8], M. Mshanga[8], O. Ogunbiyi[8], A. Merve[8], L. R. Wedderburn[1,2,3], M. L. G. Wilkinson[1,2,3] on behalf of UK JDM Cohort and Biomarker Study (JDCBS)
[1]Infection, Immunity and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, **[2]**NIHR Biomedical Research Centre at Great Ormond Street Hospital, **[3]**Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCL Hospital and Great Ormond Street Hospital, **[4]**Department of Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, **[5]**Department of Inflammation and Ageing, University of Birmingham, **[6]**Developmental Biology and Cancer Research & Teaching Department, **[7]**Population Policy and Practice Research & Teaching, UCL Great Ormond Street Institute of Child Health, **[8]**Department of Histopathology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
Correspondence: A. E. Syntakas
Pediatric Rheumatology, **23(2):** O25

Introduction: Juvenile dermatomyositis (JDM) is a pediatric autoimmune disease characterized by chronic inflammation of muscle and skin tissues. While interferon (IFN)-driven inflammation is well-documented, the role of mitochondrial dysfunction in muscle pathology remains unclear. This study investigates spatial transcriptomic alterations in JDM muscle, focusing on mitochondrial pathways and their relationship to IFN signalling.
Objectives: To characterize the spatial transcriptomic landscape of muscle biopsies from treatment-naïve JDM patients, comparing mitochondrial and IFN-related gene expression with healthy controls.
Methods: Muscle biopsies from three JDM patients recruited from the JDCBS and three age-matched controls were analyzed using the Nanostring GeoMx Digital Spatial Profiler. Regions of interest (ROIs) included muscle fibres, immune-infiltrated muscle, and CD68+ macrophage-enriched regions. Differential gene expression, pathway enrichment, and pathway clustering analyses were performed. Findings were validated in a bulk RNA-sequencing dataset (JDM n=4; controls n=5; PMID: 34997119) and a cohort of 19 JDM cases from the JDCBS using immunohistochemistry (IHC) for myxovirus-resistant-protein A (MxA, an IFN-driven protein marker) and histochemistry (HC) with COX-SDH staining (indicating mitochondrial deficiency).
Results: Spatial transcriptomics identified 448 differentially expressed genes (|LogFC|>1.5, FDR <0.05) between JDM and control muscle regions, with pathway analysis revealing concurrent IFN pathway activation and mitochondrial dysfunction. To quantify these patterns across ROI types, two gene expression scores were calculated: a 15-gene IFN score was elevated across all JDM regions (Kruskal-Wallis p=0.0034), while a 41-gene mitochondrial score showed significant suppression of genes associated with mitochondrial function (ANOVA p<0.0001), most marked in CD68+ macrophages. These mitochondrial abnormalities were confirmed in bulk RNA-sequencing from 5 additional JDM cases, demonstrating consistent suppression of oxidative

phosphorylation pathways, linked to both nuclear-encoded and mitochondrial-encoded gene transcription. Critically, IFN and mitochondrial signatures were clinically distinct: mitochondrial dysfunction was evident even in patients with minimal weakness or lower IFN activity. This was further validated in 19 JDM cases, where IHC demonstrated no association between MxA and COX-SDH scores (*U*-statistic permutation test, p=0.657), reinforcing that mitochondrial defects could occur independently of IFN-associated inflammation. Importantly, higher MxA expression was associated with more severe muscle symptoms, while mitochondrial deficiency showed no such association.

Conclusion: These data suggest that mitochondrial dysfunction is a consistent and IFN-independent feature of JDM muscle, involving genes encoded by both nuclear and mitochondrial genomes, and is detectable regardless of disease severity. These findings, validated across spatial transcriptomics, bulk RNA-sequencing, and IHC, highlight the potential for mitochondrial-targeted therapies alongside immunosuppressive treatment.

Disclosure

A. Syntakas: None declared, M. Kartawinata: None declared, H. Nguyen: None declared, C. Papadopoulou: None declared, M. Al-Obaidi: None declared, C. Pilkington: None declared, Y. Glackin: None declared, C. Mahony: None declared, A. Croft: None declared, S. Eaton: None declared, M. Cortina-Borja: None declared, N. Evans: None declared, A. White: None declared, M. Mshanga: None declared, M. Mshanga: None declared, O. Ogunbiyi: None declared, A. Merve: None declared, L. Wedderburn Grant/Research Support with: Pfizer, Consultant with: Pfizer and Cabaletta, M. Wilkinson: None declared

O26

The ISSAID/Pres recommendations for the diagnosis, treatment and monitoring of pediatric behcet's disease and monogenic mimickers

M. Romano[1], N. Zitoun[2], D. Poddighe[3], E. Sag[4], S. Demir[5], D. Rigante[6], D. Piskin[2], S. Al-Mayouf[7], P. Brogan[8], Y. Butbul[9], K. Devia[10], D. Diotte[1], A. Elhamamy[11], F. Garcia-Bournissen[2], M. Gattorno[12], A. Gul[13], M. C. B. Poli[14], A. Insalaco[15], O. Kasapcopur[16], D. Kastner[17], J. Kuemmerle-Deschner[18], R. Laxer[19], S. Ozen[4], J. Park[1], G. Simonini[20], S. Venkateswaran[1], V. Ziaee[21], I. Tugal-Tutkun[22], I. Aksentijevich[17], I. Kone-Paut[23], E. Demirkaya[1]

[1]Pediatrics, [2]Western University, London, Canada, [3]VinUniversity, Hanoi, Viet Nam, [4]Hacettepe University School of Medicine, Ankara, [5]Osmangazi University School of Medicine, Eskisehir, Türkiye, [6]Università Cattolica Sacro Cuore, Roma, Italy, [7]King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, [8]UCL Great Ormond St Institute of Child Health, University College London, London, United Kingdom, [9]Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, Israel, [10] Hôpitaux de Paris, Hôpitaux Universitaires Paris Saclay, Site Bicêtre, Paris, France, [11]University of Windsor, Windsor, Canada, [12] IRCCS Istituto G. Gaslini, Gaslini, Genoa, Italy, [13]Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Türkiye, [14]Universidad del Desarrollo, Santiago, Chile, [15]IRCCS Ospedale Pediatrico Bambino Gesù, Roma, Italy, [16]Cerrahpasa Medical School, Istanbul University-Istanbul, Istanbul, Türkiye, [17]National Human Genome Research Institute, NIH, Marylan, United States, [18]Universitatsklinikum Tubingen, Tubingen, Germany, [19]Hospital for SickKids, University of Toronto, Toronto, Canada, [20]Meyer Children's Hospital IRCCS, University of Florence, Florence, Italy, [21]Department of Pediatrics, Tehran University of Medical Science, Tehran, Iran, Islamic Republic Of, [22]Department of Opthalmology, Istanbul University, Istanbul Medical Faculty, Istanbul, Türkiye, [23]Department of Paediatric Rheumatology and CEREMAIA, Bicêtre University Hospital, APHP, university of Paris Saclay Paris, Paris, France

Correspondence: M. Romano

Pediatric Rheumatology, **23(2):** O26

Introduction: Behçet's disease (BD) is a polygenic condition with a complex immunopathogenetic background and challenging diagnostic and therapeutic concepts. Despite the presence of classification criteria, the diagnosis of pediatric BD is still difficult due to multisystemic character of the disease, absence of definitive diagnostic biomarkers, and the incomplete manifestations in childhood cases. Due to the difficulties in diagnosing pediatric BD as well as the absence of randomized clinical trials, there is a lack of standardized treatment protocols for managing this condition.

Objectives: To establish evidence-based recommendations on diagnosis, treatment, and monitoring to standardize the management of patients with paediatric BD and identified monogenic mimics (TNFAIP3, RELA, Trisomy 8, NFKB1, ELF4).

Methods: A multinational, multidisciplinary task force consisting of physician experts including rheumatologists, neurologists, ophthalmologist, pharmacologist, geneticist, patient/caregivers, and allied health care professionals was established. Evidence synthesis including systematic literature review (EMBASE, Medline, PubMed, CINAHL, Cochrane, Clinical Trials.gov) and Delphi questionnaire via RedCap were conducted. Consensus meeting was convened in May 2025 in London, Ontario,Canada. Face to face consensus methodology (Round Robin Discussion) was utilized to formulate and vote on statements to guide optimal patient care.

Results: For pediatric BD, of 13043

References identified, 100 articles were selected for inclusion. For genetic mimickers, of 357

References identified, 96 studies were selected for inclusion. Delphi questionnaire consisted of 79 questions and was sent to 41 experts from 13 countries across Europe, United States, Canada, South America, and Asia.

The task force devised 33 statements including 4 overarching principles. Major themes endorse the importance of acknowledging that pediatric Behcet disease can be a challenging diagnosis, as symptoms emerge gradually over time. It's crucial to consider genetic or genomic conditions in the differential diagnosis, especially for patients with early-onset or family history of Behcet-like disease. In these cases, evaluation should include genetic testing using NGS-based autoinflammatory gene panels or WES or WGS as well as screening (immunephenotyping) for immune dysregulation, and disease-associated comorbidities. Monoclonal Anti TNFs should be used as a first-line biologic treatment for patients with severe major organ such as ocular, neuro, vascular and GI involvement. Close monitoring for disease progression and complications is essential as well as the access to specialized, multidisciplinary care at referral centers.

Conclusion: These recommendations represent state-of-the-art knowledge based on published data and expert opinion to guide diagnostic evaluation, treatment, and monitoring of patients with pediatric BD, and to standardize and improve care, quality of life and disease outcomes.

Disclosure

None declared

O27

Treating juvenile dermatomyositis to target: pres/carra-endorsed recommendations from an international task force

S. Rosina[1], J. M. MacMahon[2,3,4], T. Baird[2], A. I. Rebollo-Giménez[5], C. Hinze[6], L. J. McCann[7,8], A. M. Reed[9], L. G. Rider[10], F. Bovis [11], A. Consolaro[1,12], B. M. Feldman[2,13], A. Ravelli[12,14] on behalf of on behalf of the JDM T2T International Task Force

[1]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [2]Division of Rheumatology, The Hospital for Sick Children, [3]Department of Paediatrics, University of Toronto, [4]Child Health Evaluative Sciences, Sickklds Research Institute, Toronto, Canada, [5]Health Research Institute Gregorio Marañón (IiSGM, Hospital General Universitario Gregorio Marañón, Madrid, Spain, [6]Department of Pediatric Rheumatology and Immunology, University Hospital Münster, Münster, Germany, [7]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, [8]University of Liverpool, Liverpool, United Kingdom, [9]Department of Pediatrics, Duke University, Durham, [10]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, United States, [11]Department of Health Sciences (DISSAL), [12]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, Genoa, Italy, [13]Departments of Pediatrics, Medicine, Faculty of Medicine, and Institute of Health Policy Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada, [14]Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genoa, Italy

Correspondence: S. Rosina

Pediatric Rheumatology, **23(2):** O27

Introduction: Despite the recent prognostic improvement, a sizeable proportion of patients with juvenile dermatomyositis (JDM) respond suboptimally to available therapies and experience chronic disease activity. The treat-to-target (T2T) strategy, which mandates the explicit definition of a therapeutic target and the adaptation of treatment interventions depending on whether the target is reached or not reached over time, has been recently proposed for juvenile idiopathic arthritis and childhood-onset systemic lupus erythematosus.
Objectives: To develop the recommendations for treating JDM to target.
Methods: A Steering Committee formulated a set of provisional recommendations based on evidence derived from a systematic literature review (SLR) and a retrospective chart review of patients followed in two tertiary care pediatric rheumatology centers. The provisional recommendations were shared with an international Task Force (TF) through an online consensus survey. The TF included 28 paediatric rheumatologists, two specialists in neuromuscular diseases, one dermatologist, one physical therapist, one research nurse, two patients with JDM and one parent of a patient with JDM. Based on the comments provided by the respondents, some recommendations were amended or reworded. The recommendations were, then, discussed, amended and voted by the TF members at a consensus conference convened in Genoa, Italy, on 7-8 October 2024.
Results: The TF reached consensus on 7 overarching principles and 12 recommendations. It was agreed that both patients/parents and treaters should share in setting treatment targets and therapeutic strategies, with inactive disease (ID) as the preferred target and minimal disease activity as an alternative target. ID is aimed to be achieved within 12 months after treatment start. Interim targets include minimal and moderate clinical improvement within 6 weeks and 3 months, respectively, and normalization of muscle strength within 6 months. High-dose glucocorticoids remain fundamental in the initial management, but progressive tapering and discontinuation within 12 months through optimisation of concomitant immunomodulatory therapy was advised. All items were agreed by more than 80% of TF members. A research agenda was formulated.
Conclusion: The TF developed recommendations for treating JDM to target, being aware that the evidence is not strong and needs to be expanded by future research. Implementation of the recommendations in clinical practice will help to reach optimal outcomes for JDM.
Disclosure
None declared

PT001

Frequency of tissue-specific activated CD8+ t cells is correlated to disease severity in juvenile idiopathic arthritis

A. R. Thielbar[1], T. V.-Y. Ting[2], L. Auld[2], K. Rogers[2], M. Quinlan-Waters[2], S. T. Angeles-Han[1,3], E. A. Ogbu[2], D. J. Lovell[2], J. L. Huggins[2], G. Schulert[2], Y. Baglaenko[1,3], P. Vega-Fernandez[2]
[1]Human Genetics, [2]Rheumatology, Cincinnati Children's Hospital, [3]Pediatrics, University of Cincinnati, Cincinnati, United States
Correspondence: Y. Baglaenko
Pediatric Rheumatology, **23(2):** PT001

Introduction: Juvenile Idiopathic Arthritis (JIA) is characterized by joint pain and inflammation. Persistent oligoarticular JIA(oligoJIA) is defined by the involvement of up to 4 joints throughout disease course. OligoJIA can progress to an extended form of arthritis (extended-oligoJIA), involving 5 or more joints after the first 6 months of disease. Polyarticular JIA is defined as affecting 5 or more joints in the first 6 months of disease. Over 30% of children with extended-oligoJIA experience uncontrolled disease requiring the use of several immunosuppressive medications even after 8-year follow-up. Moreover, even with current treatment options, 50-60% of children with extended-oligoJIA continue to experience pain, functional disability, disease activity, and impaired quality of life extending into adulthood. There is limited understanding of the cellular composition of inflammatory tissues in JIA, particularly in the affected synovium, which is a major barrier for the identification of disease biomarkers, diagnosis, and therapeutic targeting.
Objectives: The purpose of this study was to identify cell subsets associated with disease progression and severity in the synovium of children with JIA.
Methods: Fourteen synovial tissue biopsies of children with oligoJIA or polyarticular JIA, were collected by ultrasound guided biopsy. Cryopreserved synovial tissue was thawed and enzymatically digested in Liberase and DNAse I, prior to staining with a comprehensive antibody panel encompassing all major immune and non-immune cell types. Matching PBMC samples were also stained for flow analysis from 5 of the individuals. Synovial fluid biomarkers were measured by Luminex.
Results: Flow cytometry analysis revealed significant differences in the cellular composition of B cells, fibroblasts, and T-cell subtypes between PBMC and synovium samples from patients with JIA. Interestingly, we note a significant difference in tissue-specific HLA-DR+ CD8+ activated T cells in polyarticular JIA when compared to oligoJIA. Extending this analysis, we discovered significant correlations of activated and regulatory CD8+ T cell states with Juvenile Arthritis Disease Activity Scores (JADAS). Synovial fluid biomarkers such as IL-18, CD25, IL-6, and IL-23 were similarly correlated to disease activity and the frequency of tissue-specific activated T cells (PD-1+ CD-8+), T peripheral helper cells (HLA-DR+ CD4+), and HLA-DR+ fibroblasts.
Conclusion: With comprehensive flow cytometry analysis, we characterized the heterogenous cellular composition of JIA in both PBMC and disaggregated synovium. We observed increased frequencies of activated T cells specifically within the synovium correlated to disease severity and synovial fluid biomarkers.
Disclosure
None declared

PT002

Are clinical disease activity measures used in juvenile idiopathic arthritis (JIA) interchangeable with the adult disease activity measures? Results from the population-based nordic Jia cohort

L. G. Hansen[1], E. Olsen[1], M. Rypdal[2], K. Aalto[3,4], E. D. Arnstad[5,6], L. Berntson[7], M. Ekelund[7,8], A. Fasth[9], M. Glerup[10], T. Herlin[10], C. Myrup[11], S. Peltoniemi[4,12], N. T. Songstad[1], A. Szentpetery[7,13], F. Oliveira Ramos[14,15], M. Rygg[5,16], E. Nordal[1,2], V. G. Rypdal[1,2], on behalf of the Nordic Study Group of Pediatric Rheumatology (NoSPeR)
[1]University Hospital of North Norway, [2]UiT the Artic University of Norway, Tromsø, Norway, [3]New Children's Hospital, Helsinki University Hospital, [4]University of Helsinki, Helsinki, Finland, [5]Norwegian University of Science and Technology, Trondheim, [6]Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway, [7]Uppsala University, Uppsala, [8]Ryhov County Hospital, Jönköping, [9]Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [10]Aarhus University Hospital, Aarhus, [11]Copenhagen University Hospital, Copenhagen, Denmark, [12]Helsinki University Hospital, Helsinki, Finland, [13]Uppsala University Hospital, Uppsala, Sweden, [14]Santa Maria University Hospital, [15]Lisbon University, Lisbon, Portugal, [16]St. Olavs University Hospital, Trondheim, Norway
Correspondence: L. G. Hansen
Pediatric Rheumatology, **23(2):** PT002

Introduction: The choice of disease activity measures in juvenile idiopathic arthritis (JIA) is crucial, particularly during the transition from pediatric to adult rheumatology care. Since pediatric and adult rheumatology use different composite scores, it is essential to evaluate how they compare. However, data on the interchangeability of these measures remains limited.
Objectives: This study aims to evaluate whether the Juvenile Arthritis Disease Activity Score (JADAS) is interchangeable with the Disease Activity Score in 28 joints (DAS28), the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) in adults with JIA, and to identify factors contributing to discrepancies in disease activity states across these measures.
Methods: Patients who underwent a clinical examination nearly two decades after JIA onset, meeting the International League of Associations for Rheumatology (ILAR) criteria, were included. Spearman's rank correlation was used to assess relationships between outcome measures. Pediatric measures included cJADAS10, JADAS10 and JADAS27 while adult measures included DAS28, SDAI, and CDAI. Each measure has distinct cut-off values to define disease activity levels: inactive disease (ID)/remission, low/minimal (LDA), moderate (MDA), and high/severe (HDA). Reasons for discrepancies in disease activity classification were analyzed statistically, focusing on the patients classified to

have remission with respect to adult scores yet HDA with respect to JADAS.
Results: A total of 329 patients (71% female) were examined at a median of 17.6 years after JIA onset, with a median age of 24 years (IQR 20–27). Disease activity measures showed strong correlations (ρ > 0.70), with the lowest between DAS28 and the JADAS versions, while SDAI, CDAI, and JADAS versions had higher correlations (0.92–0.98). Among patients in remission per DAS28, 32–37% were classified as having HDA by JADAS versions. For these, physician global assesment of disease activity (PhGA) and patient global assessment (PaGA) were significantly higher in the HDA subgroup defined using cJADAS10, JADAS10, or JADAS27 compared to patients with ID, LDA, and MDA (p < 0.0001). No patients in remission per SDAI or CDAI were classified as HDA by the JADAS versions. All patients with HDA according to DAS28, SDAI, and CDAI were correctly identified as HDA by the JADAS.
Conclusion: Pediatric and adult disease activity measures correlate strongly. However, DAS28 shows discrepancies in identifying HDA compared to JADAS. This discrepancy is related to the PhGA and PaGA. SDAI and CDAI correlate more strongly with the JADAS offering better interchangeability for JIA patients transitioning to adult care.
Trial registration identifying number: NA
Disclosure
None declared

PT003

From paediatric to adult care: validating the jadas for juvenile idiopathic arthritis in adulthood

F. Oliveira-Ramos[1], L. Kearsley Fleet[2], D. Vinha[3], A. I. Rebollo Giménez[4], J. Humphreys[2], V. Rypdal[5], J. J. B. Baute[6], A. Zacarias[7], J. A. Lopez[7], M. J. Santos[8], E. F. Mateus[9], C. Gomes[9], A. Consolaro[10], S. J. W. Shoop-Worrall[2]
[1]University Hospital ULS Santa Maria, Lisbon School of Medicine, University of Lisbon, Lisbon, Portugal, [2]Children and Young Person's Rheumatology Research Programme, University of Manchester, Manchester, United Kingdom, [3]NOVA School of Science and Technology, Lisbon, Portugal, [4]Hospital General Universitario Gregorio Marañón, Health Research Institute Gregorio Marañón (IiSGM), Madrid, Spain, [5]University Hospital of North Norway, Arctic University of Norway, Tromsø, Norway, [6]Hospital Universitario de Canarias, Tenerife, [7]Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain, [8]Hospital Garcia de Orta, Almada, Lisbon School of Medicine, University of Lisbon, [9]ANDAI - National Association of Patients with Juvenile Arthritis, Lisbon, Portugal, [10]Istituto Giannina Gaslini, Università di Genova, Genoa, Italy
Correspondence: S. J. W. Shoop-Worrall
Pediatric Rheumatology, **23(2):** PT003

Introduction: Many children with Juvenile Idiopathic Arthritis (JIA) continue to experience active disease into adulthood, yet no validated disease activity measure exists for adult use. While the Juvenile Arthritis Disease Activity Score (JADAS) is established for children, its relevance and validation for adults remain unexplored.
Objectives: Validate the JADAS for JIA patients aged >18 years, focusing on criterion, convergent, construct, and discriminant validity.
Methods: Adults with JIA were selected if recruited to the EPOCA cross-sectional cohort or two prospective cohorts: Rheumatic Diseases Portuguese Registry (Reuma.pt), and Spanish national registry for adults with JIA (JUVENSER). Those selected were >18 years old, met ILAR criteria for JIA, and had available data for both pediatric and adult disease activity scores (JADAS, DAS28, SDAI, CDAI). Demographic details, disease characteristics, and clinical assessments were extracted from patient's most recent visits (range January 2001 to February 2024).
Construct validity of JADAS and its components (joint counts, physician, and patient global assessment) were evaluated through Spearman's rank correlation and Cohen's weighted kappa with adult measures of disease activity (DAS28/SDAI/CDAI). Convergent validity of the JADAS with Health Assessment Questionnaire (HAQ) scores was tested using Spearman's rank correlation. Criterion and discriminant validity were assessed through the sensitivity and specificity of the JADAS at detecting clinically inactive disease between versus adult constructs, respectively. Differences in optimal JADAS cut-offs relating to i) the achievement/non-achievement of DAS28 EULAR response criteria and ii) clinically important differences in HAQ scores between two clinical visits were assessed via ROC curve analysis.
Results: A total of 1315 adult JIA patients, from Reuma.pt (N=545), JUVENSER (N=392), and EPOCA (N=378) across 39 nationalities were included. Median age at disease onset was 9 years for Reuma.pt (IQR 4-13) and JUVENSER (IQR 4-13) patients, and 11 years (IQR 7-14) for EPOCA patients. Reuma.pt patients were older (25 versus 19-21 years), with longer disease duration (18 versus 8-13 years). EPOCA patients had a median JADAS27 of 3.5 versus 2 (Reuma.pt) and 0 (JUVENSER).
High construct validity of the JADAS10 was demonstrated, particularly against the SDAI (correlation coefficient: 0.95; kappa: 0.72 (0.70-0.74) and CDAI (correlation coefficient: 0.96; kappa: 0.72 (0.70-0.74). Correlation between JADAS10 and DAS28 was lower (correlation coefficient: 0.69; kappa: 0.51 (95% CI 0.48-0.54). Similar correlations were seen for JADAS27 and JADAS71.
High convergent validity of the JADAS10 and HAQ was observed (correlation coefficient: 0.64), with clinical significant differences in JADAS 10 scores between those with low/mild disability (JADAS10 cut-off: < 2.95), moderate disability (JADAS10 cut-off: 2.95-4.85) and high disability (JADAS10 cut-off: >4.85).
High criterion validity of the JADAS10 was demonstrated, with sensitivities of detecting clinically inactive disease according to the CDAI at 88%, SDAI at 86%, and lower with the DAS28 at 64%. High discriminant ability was also demonstrated with specificities of excluding clinically inactive disease according to the CDAI at 97%, SDAI at 97% and DAS28 at 96%.
The JADAS10 had moderate to high classification ability at detecting DAS28 EULAR response between two-time points, with a change of 1.9 for moderate response and 4.3 for good response. The results were similar for all JADAS versions. AUC values were 0.73 for detecting moderate DAS28 EULAR response, and 0.74 for good response.
Conclusion: The JADAS is a valid tool for measuring disease activity in adults with JIA. Its strong performance in criterion, convergent, construct, and discriminant validity against existing adult tools supports its potential for broader use in clinical practice, helping to bridge the gap in transition care from pediatric to adult rheumatology. Of note, the DAS28, common practice for use in adults with JIA, does not include relevant joint counts for JIA, and had poorer validity against the JADAS. Further studies are needed to explore the feasibility of implementing the JADAS in adult practice.
Disclosure
None declared

PT004

Identifying distinct subgroups in early juvenile psoriatic arthritis using machine learning: results from a multinational collaboration of inception cohorts

S. J. W. Shoop-Worrall[1], on behalf of CAPS Investigators, K. L. Hyrich[1,2] on behalf of CAPS Investigators, J. Guzman[3], on behalf of ReACCh-Out Investigators, K. Minden[4,5], J. Klotsche[6], R. Queiro [7], M. Yates [8,9], G.-M. Alenius[10], N. Geifman[11], L. Coates[12] on behalf of CAPS Investigators, ReACCh-Out Investigators
[1]Children and Young Person's Rheumatology Research Programme, Centre for Musculoskeletal Research, University of Manchester, [2]NIHR Manchester BRC, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom, [3]UCB, Vancouver, Canada, [4]Programme area Epidemiology and Health Services Research, Deutsches Rheuma-Forschungszentrum, [5]Department of Paediatric Respiratory Medicine, Immunology and Critical Care Medicine, [6]Programme area Epidemiology and Health Services Research, Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt - Universität zu Berlin, Berlin, Germany, [7]Rheumatology Division & Oviedo University School of Medicine, Hospital Universitario Central de Asturias, Oviedo, Spain, [8]Norwich Medical School, University of East Anglia, [9]Department of Rheumatology, Norfolk and Norwich University Hospital, Norwich, United Kingdom, [10]Deprtment of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, [11]School of Health Sciences, Faculty of Health and Medical Sciences, University of Surrey, Surrey, [12]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom
Correspondence: S. J. W. Shoop-Worrall[1]
Pediatric Rheumatology, **23(2):** PT004

Introduction: The heterogenous presentation and variable clinical response of juvenile psoriatic arthritis (JPsA) to DMARDs suggests the presence of clinically-meaningful subgroups with different pathophysiologies. Previously identified subgroups are driven by suspected significant age ranges, rather than large-scale data. To improve stratified treatment of this rare disease, such subgroups must be uncovered and interrogated.
Objectives: To identify novel, phenotypically consistent subgroups of children and young people (CYP) with JPsA in early disease.
Methods: CYP were selected if enrolled to one of four multicentre inception/population cohorts of JIA: CAPS (UK), ReACCh-Out (Canada), ICON (Germany) or NPRD (Germany) between January 2001 and December 2023 with a physician's diagnosis of JPsA, enthesitis-related JIA (ERA) or undifferentiated JIA.
Clinical features used for ILAR JPsA classification were clustered: an active joint count and the presence or absence of psoriasis, dactylitis and nail abnormalities. We tested two methods of including CYP (those with a JPsA diagnosis vs. those with JPsA, ERA or undifferentiated JIA who fulfilled ILAR JPsA criteria) and two timeframes for accumulation of clinical features (within one vs. two years of disease onset). Latent class analysis was used to identify one to ten clusters, with optimal models selected based on statistical fit (AIC, BIC), entropy and likelihood ratio testing. Differences in outcomes between clusters were tested via Chi-squared, Mann-Whitney U-tests and Kruskall-Wallis tests.
Results: Among 719 CYP with a diagnosis of JPsA within two years of symptom onset, 190 fulfilled ILAR JPsA criteria. An additional 91 CYP with ERA and 87 with undifferentiated JIA also fulfilled ILAR JPsA criteria.
Within one year of symptom onset, optimal models identified two clusters of JPsA. In those with a JPsA diagnosis (n=674), there was a large oligoarticular (95%, median active joint count 1, IQR 0, 4) and smaller polyarticular cluster (5%, median 14, IQR 21, 21). The polyarticular cluster had more CYP with dactylitis (17% vs 35%, p<0.001), though similar proportions had psoriasis and nail abnormalities. In those fulfilling ILAR criteria for JPsA (n=320), oligoarticular (93%, median active joint count 3, IQR 1, 5) and polyarticular clusters (7%, median 22, IQR 18, 29) were also evident. The polyarticular cluster had a higher proportion of CYP with dactylitis (66% vs 73%, p<0.001) and nail abnormalities (17% vs 36%, p=0.021).
When extending to two years, a third cluster was evident. In those diagnosed with JPsA (n=719), two oligoarticular clusters (Oligo 1: 51%, median active joint count 1, IQR 0, 2; Oligo 2: 38%, median 2, IQR 1, 4) and a polyarticular cluster (11%, median 14, IQR 12, 18) were evident. Psoriasis was highly evident in one of the oligoarticular clusters (Oligo 1: 12%, Oligo 2: 71%, Poly: 46%, p<0.001) and dactylitis highest in the polyarticular cluster (44% vs. 0% vs. 53%, p<0.001). In those fulfilling ILAR JPsA criteria (n=320), oligoarticular (88%, median active joint count 2, IQR 2, 5), intermediate (7%, median 6, IQR 2, 12) and polyarticular (5%, median 26, IQR 22, 37) clusters were evident. The oligoarticular group had more psoriasis (Oligo: 100%, intermediate: 0%, poly: 79%, p<0.001), the intermediate group more nail abnormalities (15%, 64%, 42%, p<0.001), and the polyarticular group more dactylitis (63%, 71%, 84%, p=0.136), respectively.
Conclusion: Unique clusters of JPsA were identified with different combinations of disease manifestations, including a polyarticular cluster with higher rates of dactylitis and an oligoarticular cluster with the most psoriasis. These subgroups require further validation and characterisation. Links identified between joint activity and psoriatic manifestations may have ramifications for early stratified medicine in CYP with JPsA.
Disclosure
None declared

PT005

Guselkumab for treatment of juvenile psoriatic arthritis: data extrapolation from studies in adjacent adult and pediatric populations

H. Crauwels[1], S. Ringold[2], S. Howard[3], B. Van Hartingsveldt[4], V. Smith[2], M. Jett[2], T. Baguet[1], E. Adamson[5], S. D. Chakravarty[5,6], J. H. Leu[2]

[1]Johnson & Johnson, Beerse, Belgium, [2]Johnson & Johnson, Spring House, United States, [3]Johnson & Johnson, High Wycombe, United Kingdom, [4]Johnson & Johnson, Leiden, Netherlands, [5]Johnson & Johnson, Horsham, [6]Drexel University College of Medicine, Philadelphia, United States
Correspondence: S. Howard
Pediatric Rheumatology, **23(2):** PT005

Introduction: Psoriatic arthritis (PsA) and juvenile PsA (jPsA) are chronic inflammatory diseases with similar traits that differ by age of onset.[1] PsA and psoriasis (PsO) share comparable pathology and clinical features in children and adults. While interleukin (IL)−23 is a key cytokine in PsA and PsO pathophysiology, no approved pediatric treatment selectively targets IL-23 signaling. Guselkumab (GUS), a fully human IL-23p19-subunit inhibitor, was shown safe and effective in adult PsO and PsA in the phase 3 VOYAGE (V)1/2 and DISCOVER (D)1/2 trials, respectively, with consistent clinical benefits and safety in pediatric PsO in the phase 3 PROTOSTAR study.
Objectives: As jPsA is rare and shares similarities with adult PsO and PsA, extrapolation based on similarity of GUS systemic exposure and clinical response across Phase 3 populations of children with PsO, adults with PsO, and adults with PsA was used to establish GUS efficacy and safety in jPsA. This FDA-endorsed[2] extrapolation method was previously applied to support the use of ustekinumab in jPsA.[3]
Methods: One-year pharmacokinetic (PK), clinical response, and safety data from V1 (N=494), V2 (N=727), D1 (N=127), D2 (N=248), and PROTOSTAR (N=92; 3 with jPsA) pts receiving GUS were included. V1/2 adults with PsO and D1/2 adults with PsA received GUS 100 mg at Week (W)0, W4, then every 8W (Q8W). PROTOSTAR pediatric pts (≥6 to <18 years) <70kg received GUS 1.3 mg/kg and ≥70kg received GUS 100 mg at W0, 4, then Q8W. Serum GUS levels were measured and compared between pediatric PsO pts, adults with PsO, and adults with PsA at common time points. Investigator Global Assessment clear (0) or minimal (1) (IGA0/1) and Psoriasis Area and Severity Index (PASI)75/90/100 response rates were assessed. GUS safety outcomes were summarized across studies.
Results: Serum GUS concentrations over 1 year were similar between pediatric and adult PsO pts, adult PsO and PsA pts, and pediatric PsO and adult PsA pts (max median range: 3.1-4.2 µg/mL). IGA0/1 response rates for GUS through W16 were comparable in pediatric (max: 71%) and adult PsO (85%) pts. In children with PsO and adults with PsA, similar W16 IGA0/1 (67% and 77%, respectively) and PASI100 (33% and 22%) response rates were also observed for GUS. GUS safety outcomes were similar across children and adults.
Conclusion: Comparable PK, efficacy, and safety results from GUS studies in children with PsO (3 with jPsA) and adult PsO and PsA pts corroborate extrapolation of efficacy and safety data from adults to children with jPsA. These findings support the use of GUS in children with jPsA.
Trial registration identifying number: NCT0220723, NCT02207244, NCT03162796, NCT03158285, NCT03451851
Disclosure
H. Crauwels Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, S. Ringold Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, S. Howard Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, B. Van Hartingsveldt Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, V. Smith Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, M. Jett Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, T. Baguet Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, E. Adamson Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, S. Chakravarty Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson, J. Leu Shareholder with: Johnson & Johnson, Employee with: Johnson & Johnson

References

1. Martini. Nat Rev Dis Primers. 2022.
2. US FDA. E11A Pediatric extrapolation. 2024.
3. Leu. Paediatr Drugs. 2022.

PT006

Adalimumab serum levels and associations with disease activity in juvenile idiopathic arthritis

I. Herder[1,2], S. O. Hetlevik[1], J. E. Gehin[3], M. Pesonen[4], V. Lilleby[1], M. Rygg[5,6], E. Nordal[7,8], B. Barstad[9], K. B. Tylleskär[10], N. Bolstad[3], S. Syversen[2,11], S. Lillegraven[11], E. A. Haavardsholm[2,11], B. Flatø[1,2], Ø. Molberg[1,2], P. Bøyesen[1], A.-B. Aga[1]

[1]Department of Rheumatology, Oslo University Hospital, [2]Faculty of Medicine, University of Oslo, [3]Department of Medical Biochemistry, [4]Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, [5]Department of Pediatrics, St. Olavs Hospital, Trondheim University Hospital, [6]Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences (IKOM), Norwegian University of Science and Technology (NTNU), Trondheim, [7]Department of Pediatrics, University Hospital of North Norway (UNN), [8]Department of Clinical Medicine, The Arctic University of Norway (UiT), Tromsø, [9]Department of Pediatrics, Stavanger University Hospital, Stavanger, [10]Child and Youth Clinic, Haukeland University Hospital, Bergen, [11]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway

Correspondence: I. Herder

Pediatric Rheumatology, **23(2):** PT006

Introduction: Measurement of tumor necrosis factor inhibitor (TNFi) serum levels might be a valuable tool in management of juvenile idiopathic arthritis (JIA), but in children there is still a knowledge gap with regards to whether TNFi serum levels are associated with disease activity.

Objectives: To describe adalimumab serum levels in children and adolescents with JIA following initiation of treatment with adalimumab, and to describe adalimumab serum levels in patients with or without active joints.

Methods: Consecutive patients who fulfilled the International League of Associations for Rheumatology (ILAR) classification criteria for non-systemic JIA, age >1 to 18 years with active disease and clinical indication for TNFi therapy, were recruited from five Norwegian university hospitals (ClinicalTrials.gov NCT 04614311) when initiating adalimumab treatment. Core outcome variables for JIA including active joints (joints with swelling or limitation of movement and tenderness) and non-trough serum samples were collected at week 12 and 48. Serum adalimumab levels were measured using automated fluoresence assays.

Results: From December 2020 to March 2024, 176 children were included: 111 (63%) girls, mean (SD) age 10.5 (4.4) years and mean (SD) disease duration 1.6 (3.1) years. At baseline, the number of active joints was median (IQR) 3 (1-6), patient/parent global VAS (mm) mean (SD) 44.4 (22.8), physician global VAS (mm) mean (SD) 43.4 (20.6), ESR (mm/hr) median (IQR) 12 (7-25). Methotrexate was used as co-medication in 155 (88%). Four patients (2%) had previously used a TNFi.

At week 12, 171 of the 176 patients had measurements of both s-adalimumab and number of active joints, and median (IQR) s-adalimumab was 14.3 mg/L (9.5-17.8). 57/171 (33%) patients had ≥1active joint, 114/171 (67%) had no active joints. In patients with ≥1 active joint median s-adalimumab was 12.1 mg/L (IQR 7.6-16.0) and in patients with no active joints s-adalimumab was 15.1 mg/L (IQR 10.1-19.5) (p=0.01).

At week 48, 153 of the 176 patients who started adalimumab at baseline had measurements of both s-adalimumab and number of active joints, and median (IQR) s-adalimumab was 14.9 mg/L (10.1-20). 20/153 (13%) patients had ≥1 active joint, 133/153 (87%) had no active joints. In patients with ≥1 active joint median s-adalimumab was 12.9 mg/L (IQR 7.7-17.4) and in patients with no active joints s-adalimumab was 15.5 mg/L (IQR 10.7-20.6) (p=0.14).

Conclusion: Our results suggest an association between adalimumab serum levels and disease activity 12 weeks after treatment initiation, indicating a possible role of monitoring TNFi drug level in the early treatment course. The association was no longer evident at 48 weeks follow-up, possibly related to the high proportion of patients without active joints at that stage. Further analyses are needed to possibly identify a therapeutic level for adalimumab in JIA.

Trial registration identifying number: ClinicalTrials.gov NCT 04614311

Disclosure
None declared

PT007

Sarilumab in polyarticular-course juvenile idiopathic arthritis: long-term safety and efficacy from a phase 2B extension study

F. De Benedetti[1], I. C. Penadés[2], I. Nikishina[3], I. Foeldvari[4], A. J. Spindler[5], A. Kozlova[6], N. Rubio-Pérez[7], P. Quartier[8,9], Z. Žuber[10], R. Barria[11], D. Clemente[12], G. V. Cornejo[13], K. Marzan[14], N. Liu[15], J. Msihid[16], L. Araujo[17], V. Batarilo[15], S. DiMartino[18], B. Akinlade[18], L. Baret-Cormel[19]

[1]Division of Rheumatology, Ospedale Pediatrico Bambino Gesù IRCCS, Rome, Italy, [2]Hospital Universitario y Politécnico la Fe, Valencia, Spain, [3]V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, [4]Hamburg Center for Pediatric and Adolescent Rheumatology, Am Schoen Klinik Eilbek, Hamburg, Germany, [5]Centro Médico Privado de Reumatologia, Tucumán, Argentina, [6]Centre of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation, [7]Departamento de Pediatría, Hospital Universitario "Dr. J.E. González", Universidad Autónoma de Nuevo León, Monterrey, Mexico, [8]Pediatric Immunology-Hematology and Rheumatology unit, Necker-Enfants Malades hospital, Assistance Publique-Hopitaux de Paris, Paris, France, [9]Université Paris-cité, Paris, France, [10]Andrzej Frycz Modrzewski Krakow University, Krakow, Poland, [11]Bioreuma, Concepción, Chile, [12]Hospital Infantil Universitario Niño Jesús, Madrid, Spain, [13]CREA de Guadalajara, Jalisco, Mexico, [14]Division of Rheumatology, Children's Hospital Los Angeles, Keck School of Medicine of USC, University of Southern California, Los Angeles, United States, [15]Sanofi, Morristown, New Jersey, United States, [16]Sanofi, Gentilly, France, [17]Sanofi, Cambridge, Massachusetts, United States, [18]Regeneron, Tarrytown, New York, United States, [19]Sanofi, Paris, France

Correspondence: F. De Benedetti

Pediatric Rheumatology, **23(2):** PT007

Introduction: A 156-week (W), open-label, 2 part study (12W core and 144W extended)[1] evaluated the efficacy and safety of sarilumab [3/4mg/kg every 2 weeks] in two weight groups (Group A/B: body weight ≥30kg/≥10kg–<30kg) of patients with polyarticular-course juvenile idiopathic arthritis (pcJIA).

Objectives: To report the long-term efficacy and safety of sarilumab in patients with pcJIA, up to 3 years.

Methods: This 156W study assessed the efficacy and safety of sarilumab in patients with pcJIA aged 2-17 years, who received the selected dose identified after core phase of part 1.[1] Efficacy was evaluated by improvements in specified disease activity levels at W48, 96 and 156. Safety was assessed by reported adverse events (AEs) for up to 3 years.

Results: Ninety-three patients received ≥1 dose of the selected dose (primary safety population) during the 156W study phase. The primary efficacy population (73 patients who received the selected dose from baseline [BL]) had mostly RF-negative pJIA (48/73 [65.8%]), a high cJADAS-10 (mean±SD: 20.1±4.1) and CHAQ-DI (mean±SD: 1.24±0.66). At BL, 14/73 (19.2%) had ≥1 prior bDMARD, 62/73 (84.9%) were receiving csDMARD, and 10/73 (13.7%) systemic glucocorticoid (GC). Improvements in specified disease activity levels as assessed by cJADAS-10≤2.5 (W48/96/156: 70.3%/72.9%/81.8%), clinically inactive disease (CID) per Wallace criteria[1] (W48/96/156: 70.3%/78.9%/84.4%), CID per Wallace criteria with no GC use (W48/96/156: 60.9%/70.2%/78.1%), and clinical remission [inactive disease per Wallace criteria ≥6 consecutive months] (W48/96/156: 51.6%/64.6%/77.4%) were observed in patients with available measurement at each visit. Functional ability of patients, as assessed by the CHAQ-DI score, improved with a mean change of −0.96, −1.01, and −1.13 from BL to W48, W96, and W156 respectively. Treatment-emergent AEs (TEAEs) were reported in 89/93 (95.7%) patients with any exposure to the selected dose. Among these, 6/93 (6.5%) patients had ≥1 serious TEAE (core-treatment phase: 1 patient; W12 to W52: 3 patients; after W52: 2 patients). All serious TEAEs were unrelated to the study drug. In patients with grade 3/4 neutropenia (35/41, 85.4%), the incidence of infections was comparable to those without grade 3/4 neutropenia (50/60, 83.3%) following exposure to any sarilumab dose (N=101).

Conclusion: Clinical remission as assessed by the Wallace Criteria was observed in over three-fourths of the patients with pcJIA at W156. Long-term safety was consistent with the known safety profile of sarilumab with no new safety concerns. There was no association of neutropenia with increased risk of infection.
Trial registration identifying number: NCT02776735
Disclosure
F. De Benedetti Grant/Research Support with: AbbVie, Novartis, Novimmune, Pfizer, Roche, Sanofi, SOBI, and UCB, Consultant with: Novartis, Roche, and SOBI, I. Penadés Grant/Research Support with: AbbVie, Bristol-Myers Squibb, Clementia, MSD, Novartis, Pfizer, Roche, and Sanofi, Speaker Bureau with: AbbVie, Novartis, Roche, and SOBI, Advisory Boards with: AbbVie and Novartis, I. Nikishina Speaker Bureau with: AbbVie, Ipsen, Janssen, Novartis, Pfizer, and R-Pharm, I. Foeldvari Speaker Bureau with: Boehringer, Lilly, Mitsubishi, Advisor with: Boehringer, Lilly, Mitsubishi, A. Spindler Speaker Bureau with: Eli Lilly, A. Kozlova: None declared, N. Rubio-Pérez Speaker Bureau with: AbbVie and Roche, P. Quartier Consultant with: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi (also member of a data safety monitoring board), and SOBI, Speaker Bureau with: AbbVie, Bristol-Myers Squibb, Chugai-Roche, Novartis, Pfizer, and SOBI, Z. Żuber: None declared, R. Barria Consultant with: Tecnofarma, Speaker Bureau with: Pfizer and Roche, D. Clemente Speaker Bureau with: Novartis and Roche, G. Cornejo Grant/Research Support with: Bristol-Myers Squibb, Parexel, and Sanofi, K. Marzan Grant/Research Support with: Novartis, Pfizer, and Sanofi, N. Liu Shareholder with: Sanofi, Employee with: Sanofi, J. Msihid Shareholder with: Sanofi, Employee with: Sanofi, L. Araujo Shareholder with: Sanofi, Employee with: Sanofi, V. Batarilo Shareholder with: IQVIA (supporting current analysis for Sanofi), Employee with: IQVIA (supporting current analysis for Sanofi), S. DiMartino Shareholder with: Regeneron, Employee with: Regeneron, B. Akinlade Shareholder with: Regeneron, Employee with: Regeneron, L. Baret-Cormel Shareholder with: Sanofi, Employee with: Sanofi

Reference
1 De Benedetti F, et al. *PReS*. 2023. Poster (PT012).

PT008

Patient, parent and physician global assessment discordance related to pain coping strategies in juvenile arthritis

A. Halttu[1,2], M. Backström[1,3], M. Tarkiainen[4,5], E. Lehtinen[3], S. Sard[2], P. Keskitalo[2], K. Markula-Patjas[6,7], K. Rebane[4,5], K. Aalto[4,5], T. Remes-Pakarinen[8], J. Kärki[9,10], M. Hietanen[11], H. Pohjankoski[12], K. Korkatti[13], E. Kosonen[9,14], E. Löyttyniemi[15], L. Kröger[8], P. Vähäsalo[1,16]
[1]Research Unit of Clinical Medicine, Oulu University, [2]Department of Pediatrics, Oulu University Hospital, Oulu, [3]Department of Pediatrics, The Wellbeing Services County of Ostrobothnia, Vaasa, [4]New Children's Hospital, Helsinki University Hospital, [5]Pediatric Research Center, University of Helsinki, Helsinki, [6]Faculty of Medicine and Health Technology, Center for Child, Adolescent and Maternal Health Research, Tampere University, [7]Department of Pediatrics, Wellbeing Services of Pirkanmaa, Tampere University Hospital, Tampere, [8]Department of Children and Adolescents, Kuopio University Hospital, Kuopio, [9]Department of Children and Adolescents, Kanta Häme Central Hospital, Hämeenlinna, [10]The Finnish Rheumatology Quality Register, The Finnish Institute for Welfare and Health, Helsinki, [11]Department of Paediatrics, [12]Department of Pediatrics, Päijät-Häme Central Hospital, Lahti, [13]Department of Pediatrics, Central Ostrobothnia Central Hospital, Kokkola, [14]Department of Children and Adolescents, Wellbeing Services of Pirkanmaa, Tampere University Hospital, Tampere, [15]Department of Biostatistics, University of Turku, Turku, [16]Department of Pediatrics, Medical Research Center, Oulu University Hospital, Oulu, Finland
Correspondence: M. Backström
Pediatric Rheumatology, **23(2):** PT008

Introduction: It has previously been shown that there can be a discordance between patient and physician global assessment in patients with juvenile idiopathic arthritis (JIA). Only a few studies on the factors influencing the discordance have been done in children [1-3].
Objectives: We aim to investigate the factors underlying the discordance in physicians', patients', and caregivers' perceptions of disease state in patients with newly diagnosed or suspected JIA.
Methods: We invited all children in eight centres in Finland from November 2021 to March 2024 presenting with newly confirmed or suspected diagnoses of JIA and the accompanying parents to participate. Children over 8.0 years and all the parents filled in the patient's and parent's proxy pain and global assessment at 0 and 3 months and the pain coping scale for both children and their parents [4] at 3 months after diagnosis. The discordance between patient or parent global assessment and physician global assessment was determined by subtracting the physician global assessment from the patient or parent global assessment. The factors explaining discordance between the global assessments were evaluated by a multivariable linear model.
Results: In total, 186 families participated in the study. Children and caregivers used effective pain coping strategies more often than catastrophizing. Discordance between the patient or parent and physician global assessment of less than +/−10 mm was seen in 51% of the children and 52% of the parents. When a discordance of more than +/−10 mm was seen, it was mainly positive, i.e. the patients' and parents' perception of the disease state was higher than the physician's. A global assessment discordance of +/- 30 mm or greater was seen in 17% of the children and 11% of the parents. In the patients, the lower the active joint count (AJC) (p=0.006) and the higher the pain assessment (p<0.001), the greater the discordance between patient and physician global assessment. In parents, the lower the AJC (p<0.001) and the higher the parent proxy pain assessment (p<0.001) and catastrophizing score (p=0.005), the greater the discordance between parent and physician global assessment.
Conclusion: The discordance between the parent and physician global assessment is greater among parents who use catastrophizing as a pain coping strategy. The lower the AJC and the higher the pain assessment score, the greater the discordance between the patient or parent and physician global assessment. Children and caregivers used effective pain coping strategies more often than catastrophizing.
Disclosure
None declared

References
1. Sztajnbok F, Coronel-Martinez D L, Diaz-Maldonado A et.al. Discordance between physician's and parent's global assessments in juvenile idiopathic arthritis. Rheumatology 2007;46:141–5.
2. Consolaro A, Vitale R, Pistorio A et al. Physicians' and parents' ratings of inactive disease are frequently discordant in juvenile idiopathic arthritis. J Rheumatol 2007;34:1773-6.
3. Trachtman R, Issa R, Pan S et al. The value of the patient global health assessment in polyarticular juvenile idiopathic arthritis: a nested cohort study. *J Patient Rep Outcomes* 2021;5:50.
4. Backström M, Vuorimaa H, Tarkiainen M, et al. Pain-coping scale for children and their parents: a cross-sectional study in children with musculoskeletal pain. Pediatr Rheumatol Online J. 2023;21(1):9.

PT009

Comparative performance of disease activity indices in juvenile idiopathic arthritis during transition of care

A. Pilato[1], G. Tarantino[2], M. I. Petrone[2], A. Aquilani[2], E. Marasco[2], R. Nicolai[2], L. Navarini[1], R. Giacomelli[1], F. De Benedetti[2], S. Magni Manzoni[2]
[1]Rheumatology and Clinical Immunology, University of Rome Campus Biomedico, [2]Rheumatology Unit, "Bambino Gesù" Children Hospital IRCSS, Rome, Italy
Correspondence: A. Pilato
Pediatric Rheumatology, **23(2):** PT009

Introduction: Monitoring disease activity is a crucial aspect of the treat-to-target strategy in rheumatic diseases. However, no standardized protocols exist for monitoring disease activity in patients with Juvenile Idiopathic Arthritis (JIA) during the transition of care.
Objectives: The aim of this study is to compare different disease activity indices across JIA categories (excluding systemic JIA), and to assess

their relative performance and clinical consistency in a real-life transition setting.
Methods: Young adult JIA patients eligible for transition of care underwent a prospective clinical evaluation by both paediatric and adult rheumatologists. Disease activity was assessed using validated clinical indices. All patients were evaluated with cJADAS, JADAS10, JADAS27, and JADAS71. Additional indices were applied according to JIA subtype: SDAI, CDAI, and DAS28 were used in persistent oligoarticular (oJIA-p), extended oligoarticular (oJIA-e), and RF-positive and RF-negative polyarticular JIA (polyJIA RF^-/RF^+); DAPSA was used for the psoriatic JIA (jPsA) category; and jSpADA, ASDAS-CRP, and BASDAI were used for enthesitis-related arthritis (ERA). Ultrasound data were collected as additional marker of articular inflammation when arthritis was clinically suspected or for disease monitoring, to detect active synovitis according to OMERACT ultrasound paediatric definitions. Spearman's correlation was used to assess associations between disease activity indices. ROC analyses were conducted to compare the relative performance of different clinical indices in relation to ultrasound-detected synovitis. Statistical analyses were performed using R software (version 4.5.0).
Results: A total of 124 JIA patients were included (median age 19 years, IQR 17–23). Disease activity was highest in jPsA compared to lower values in oJIA-e/polyJIA RF^-, and oJIA-p. Strong correlations were observed in oJIA-p, oJIA-e, and polyJIA RF^- among JADAS scores, CDAI, and SDAI ($\rho > 0.87$; $p < .001$), with slightly lower values for DAS28. Similar findings were confirmed in prospective analyses, with strong correlations between changes in JADAS, SDAI, and CDAI over time in both oJIA-e/polyJIA RF^- patients (ΔJADAS71 vs ΔSDAI: $\rho = 0.944$; $p < .001$) and oJIA-p ($\rho = 0.993$; $p < .001$). In jPsA, a moderate-to-strong correlation was observed between JADAS scores and DAPSA ($\rho \approx 0.87$, $p < .001$). In ERA, jSpADA correlated moderately with ASDAS-PCR ($\rho = 0.51$; $p = 0.161$), but not with BASDAI. Ultrasound was performed in 84.7% of patients, with a total of 1612 assessed joints. In oJIA-e and polyJIA RF^-, JADAS71-PCR and SDAI showed the highest AUCs (0.844–0.845) for ultrasound-detected synovitis; in prospective analyses, changes in these scores showed good discriminative ability for predicting new onset ultrasound-detected synovitis over time (AUC = 0.789 and 0.812, respectively). In oJIA-p, all indices performed well (AUCs ≥ 0.926). In jPsA, DAPSA showed the highest AUC (0.818) at baseline.
Conclusion: In this real-life transition cohort, both paediatric and adult-derived indices performed comparably across most JIA subtypes. In prospective evaluation, changes in JADAS71 and SDAI showed the strongest association with new-onset ultrasound-detected synovitis, particularly in oJIA-e and polyJIA RF^-. In jPsA, DAPSA demonstrated the highest baseline performance. In ERA, divergent correlations among available indices were observed. These findings highlight the need for a targeted approach to disease activity monitoring, tailored to the specific JIA subtype during the transition of care.
Disclosure
None declared

PT010

Development of a scoring system to assist clinicians in the early referral of patients with suspected juvenile idiopathic arthritis: the easy Jia score

A. Marino[1], C. A. Scirè[2], P. Baldassarre[3], C. Ferrigno[3], S. Costi[1], F. Baldo[1], M. V. Gattinara[1], D. Rozza[4], C. B. Chighizola[1], R. F. Caporali[5]
[1]Pediatric Rheumatology, ASST G.Pini-CTO, Milan, [2]Rheumatology Unit, IRCCS San Gerardo dei Tintori Foundation, Monza, [3]Buzzi Children's Hospital, [4]Epidemiology, Italian Society for Rheumatology (SIR), [5]ASST G.Pini-CTO, Milan, Italy
Correspondence: A. Marino
Pediatric Rheumatology, **23(2):** PT010

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic pediatric rheumatic disease. The diagnosis of JIA relies on specialist expertise and the exclusion of other conditions. However, children with JIA often face significant referral delays following the initial contact with primary care providers. Timely referral to pediatric rheumatology is crucial for early diagnosis, highlighting the need for fast-track pathways to specialized care.
Objectives: This study aims to develop and validate a scoring system to assist clinicians in efficiently identifying and referring patients suspected of having non-systemic JIA.
Methods: We conducted a cohort study with a mixed design (retrospective and prospective) involving consecutive patients presenting with joint complaints who were referred for the first time to the Pediatric Rheumatology Unit at ASST G. Pini-CTO Hospital, Milan, Italy, between April 1, 2022, and July 31, 2024. Patients with fever at the time of referral or with a pre-existing conditions that may affect musculoskeletal functions and examination were excluded.
The model was developed using multivariate logistic regression with bootstrap resampling and the Lasso (Least Absolute Shrinkage and Selection Operator) method for variable selection.
Results: A total of 342 patients were included, of whom 61 (18%) were diagnosed with JIA. The most common JIA subtype was oligoarticular (38 patients, 62%), followed by polyarticular (15 patients, 25%), and enthesitis-related arthritis (8 patients, 13%). Using the bootstrap method and LASSO regression, we generated a list of variables ranked by their frequency. The process involves repeatedly running LASSO on bootstrapped samples and calculating how often each variable is selected. From the covariates with a frequency exceeding 250 (indicating choice in more than 50% of cases), we selected the following based on clinical judgment: joint type (large), daily symptoms, joint swelling, activity as a precipitating factor, a positive squeeze test of the metatarsophalangeal/metacarpophalangeal (MTP/MCP) joints, normal bending of the interphalangeal (IF) joints of the hands, morning limping and/or stiffness, and the presence of sacroiliac pain. To improve usability in routine clinical practice, a simplified model was developed by rounding the regression coefficients to the nearest integer. Negative coefficients were transformed into positive values by inverting the expected outcomes. This resulted in a streamlined scoring system consisting of eight items, with a total possible score ranging from 0 to 10. The ROC curve, based on the model's regression score, showed an AUC of 0.92 with an overall accuracy of 0.84 (95% CI: 0.80–0.88) with a cutoff of 4 points yielding a sensitivity of 87% and a specificity of 83%. The model was internally validated using a bootstrap approach to create a validation dataset, onto which the developed model was applied. The resulting AUC was 0.92, with a 95% confidence interval (CI) ranging from 0.89 to 0.95.
Conclusion: We presented and validated a simple, time-efficient scoring system designed to assist clinicians in the early referral of patients suspected of having non-systemic JIA. This tool could also be utilized to identify patients who require further workup, including imaging studies, autoantibody testing, and screening for anterior uveitis.
Disclosure
None declared

PT011

Prognostic value of interleukin-18 in still's disease: associations with disease activity, course, and mas development

M. Trevisan[1], M. Pardeo[1], C. Bracaglia[1], A. De Matteis[1], I. Caiello[2], V. Matteo[2], E. Loricchio[2], F. De Benedetti[1,2], G. Prencipe[2]
[1]Division of Rheumatology, [2]Laboratory of Immuno-Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy
Correspondence: M. Trevisan
Pediatric Rheumatology, **23(2):** PT011

Introduction: Still's disease (SD) is a systemic inflammatory disorder characterized by nonspecific clinical and laboratory features, which pose diagnostic challenges at onset (e.g. Kawasaki disease, leukemia). Although IL-1 inhibitors (IL-1i) are standard treatment, reliable biomarkers to predict disease activity, clinical course, and complications such as macrophage activation syndrome (MAS) are lacking. Interleukin-18 (IL-18) has been proposed as a potential biomarker, but its predictive value remains unclear.
Objectives: To assess the association between IL-18 levels at disease onset and subsequent disease activity and course. A secondary aim was to evaluate whether IL-18 levels could predict the risk of MAS.
Methods: We retrospectively analyzed 64 pediatric patients with newly diagnosed SD, all treated with IL-1i for at least 12 months. Demographic, clinical and laboratory data, including IL-18 levels, were collected at onset (T0), before treatment initiation and at 3 (T3),

6 (T6) and 12 (T12) months of therapy. Disease activity was defined according to EULAR/PReS 2024 criteria; disease course was classified as monocyclic, polycyclic, or chronic-persistent. Statistical adjustments were made for potential confounders, including MAS and concomitant treatments.
Results: The median IL-18 level at onset was 59.215 pg/ml (IQR 14.261–630.037). MAS was present in 23 (35%) patients at disease onset. Sixty-one patients were treated with anakinra and 3 with canakinumab. IL-18 levels significantly decreased during treatment (median pg/ml: T0 59.215; T3 1.984; T6 1.100; T12 788). However, patients with active disease (AD) had consistently higher IL-18 levels than those in clinical inactive disease (CID) at all time points. Patients with AD at 12 months had significantly higher IL-18 levels at baseline compared to those who achieved CID. IL-18 levels >45.000 pg/ml at onset predicted AD at 12 months with an area under the curve (AUC) of 78% (Se 91%, Sp 53%, *p*=0,001). Regarding disease course, 54% patients had a monocyclic, 26% a polycyclic, and 20% a chronic-persistent course. After treatment initiation, IL-18 levels significantly decreased in mono-/poly-cyclic course patients, but remained stable over-time in those with a chronic-persistent course. IL-18 levels >45.000 pg/ml at disease onset predicted a chronic-persistent course (AUC 72%, *p*=0,01, Se 91% Sp 56%). Furthermore, IL-18 levels >15,000 pg/ml at three months (T3) more accurately predicted a persistent course, yielding an AUC of 91% (p<0.0001; se 90%, sp89%). Additionally, elevated IL-18 levels at baseline were strongly associated with MAS development (AUC 81%, *p*=0.004, Se 100%, Sp 77%).
Conclusion: Baseline IL-18 levels are predictive of disease activity, clinical course, and MAS risk in Still's disease. IL-18 may serve as a valuable biomarker, offering a valuable tool for tailoring treatment strategies and improving patient outcomes.
Disclosure
None declared

References
1. Fautrel B et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis*. 2024
2. Yasin S et al. IL-18 as a biomarker linking systemic juvenile idiopathic arthritis and macrophage activation syndrome. *Rheumatol*. 2020.
3. Mizuta M et al. Clinical significance of interleukin-18 for the diagnosis and prediction of disease course in systemic juvenile idiopathic arthritis. *Rheumatol*. 2021.

PT012

Monitoring IL-18 in pediatric still's disease: diagnostic and prognostic value

M. Thilloy[1], A. BELOT[1], A.-P. FORAY[2], P. Quartier-dit-Maire[3], F. Benjamin[3]
[1]Pediatric Rheumatology, [2]Immunology, HCL, LYON, [3]Pediatric Rheumatology and Immunology, APHP, Paris, France
Correspondence: M. Thilloy
Pediatric Rheumatology, **23(2):** PT012

Introduction: Systemic juvenile idiopathic arthritis (sJIA), also known as Still's disease in children, is a rare autoinflammatory disorder of unknown etiology. Interleukin-18 (IL-18) has emerged as a key cytokine implicated in the pathogenesis of Still's disease in both children and adults. Its role in diagnosis and disease monitoring remains an active area of investigation.
Objectives: This study aimed to assess the diagnostic value of IL-18 levels in pediatric Still's disease by comparing them with those observed in other pediatric rheumatic conditions. Moreover, the study evaluated the potential of IL-18 as a biomarker for monitoring disease activity and therapeutic response over time.
Methods: Data were collected from pediatric rheumatology departments at multiple French hospitals including Lyon's Hôpital Femme Mère Enfant, Necker-Enfants Malades, Kremlin-Bicêtre, Valence Hospital, Villefranche Hospital, and Lille Hospital. Patients included in the study had IL-18 measurements performed either at Henri Mondor Hospital (Paris) or the Immunology Laboratory at Lyon Sud, both of which used the same testing protocols. Over 170 patients including 100 patients with Still disease and more than 500 IL-18 measurements were analyzed. Among them, 30 patients had IL-18 levels measured at the time of diagnosis prior to treatment initiation, and longitudinal data were available for 60 patients.
Results: IL-18 levels were significantly higher in patients diagnosed with Still's disease compared to those with other rheumatic conditions. Elevated IL-18 concentrations were particularly associated with active disease states. Patients experiencing macrophage activation syndrome (MAS) exhibited especially high IL-18 levels, which remained elevated even in the absence of acute flares. Longitudinal follow-up revealed that IL-18 levels correlated with disease activity over time, suggesting its potential utility in predicting disease progression and treatment response.
Conclusion: In line with previous findings, this study reinforces the diagnostic relevance of IL-18 in identifying pediatric Still's disease. In addition, persistently high IL-18 levels appear to be associated with severe disease phenotypes, including chronic MAS and pulmonary involvement. These findings support the integration of IL-18 monitoring into routine clinical practice to aid in diagnosis, risk stratification, and longitudinal disease management in pediatric patients with Still's disease.
Disclosure
None declared

References
1. Quartier-dit-Maire P, Belot A, Protocole National de Dlagnostic et de Soins. Arthrites Juvéniles Idiopathiques. 2023.
2. Sur LM, Sur G, Investigations of cellular immunity in juvenile idiopathic arthritis. Cent Eur J Immunol. 2019
3. Fautrel B, Mitrovic S, De Matteis A, Bindoli S, Antón J, Belot A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. Annals of the Rheumatic Diseases. déc 2024;83(12):1614
4. Mitrovic S, Fautrel B. New Markers for Adult-Onset Still's Disease. Joint Bone Spine. mai 2018;85(3):285

PT013

Peripheral T helper cells dominate the synovial CD4⁺ T cell compartment in still`s disease and are shaped by IL-1B and IL-18

J. Dirks[1], J. Fischer[1], L. Harrer[1], C. Bracaglia[2], G. Prencipe[2], M. Pardeo[2], A. T. Holl-Wieden[1], H. Girschick[3], C. Kessel[4], H. Morbach[1]
[1]Pediatric Rheumatology and Immunology, University Hospital Würzburg, Würzburg, Germany, [2]Division of Rheumatology, Ospedale Pediatrico Bambino Gesù, Rome, Italy, [3]Children's Hospital, Vivantes Klinikum im Friedrichshain, Würzburg, [4]Pediatric Rheumatology and Immunology, University Hospital Muenster, Muenster, Germany
Correspondence: H. Morbach
Pediatric Rheumatology, **23(2):** PT013

Introduction: Still`s Disease (SD) begins as a predominantly autoinflammatory disorder but often transitions into chronic arthritis, implicating a role for dysregulated adaptive immunity (1, 2). The molecular mechanisms linking innate immune activation to adaptive T cell responses within inflamed joints remain poorly defined. While IL-1β is known to promote Th17 differentiation and peripheral blood (PB) T cells from SD patients exhibit Th17 skewing (3), recent data show that PB naïve CD4⁺ T cells also favor differentiation into IL-21–producing peripheral T helper (Tph)–like cells (5). Tph cells, key contributors to local inflammation and B cell help in autoimmunity, are enriched in ANA-positive oligo-/polyarticular (o/p)-JIA joints (5). However, the phenotype, function, and clonal structure of synovial CD4⁺ T cells in SD remain largely unexplored.
Objectives: To characterize the transcriptional landscape, clonal architecture, and inflammatory cues shaping CD4⁺ T cell responses in SD joints, and to compare these with those in o/p-JIA.
Methods: Synovial fluid (SF) CD4⁺ T cells from SD and o/p-JIA patients were analyzed via flow cytometry, single-cell RNA and TCR sequencing. T cell–mediated B cell help and cytokine secretion were assessed in vitro. Bulk RNA-seq and multiplex ELISA were used to evaluate the impact of IL-1β and IL-18 on T cell differentiation.
Results: SD joints contained a dominant population of clonally expanded CD4⁺ T cells with a Tph phenotype, characterized by high IL-21

and CXCL13 expression and potent B cell helper activity. Single-cell transcriptomics revealed a diverse CD4⁺ T cell compartment, with a striking convergence of Tph and regulatory T cell gene programs, particularly in SD. A subset of these cells showed transcriptional hallmarks consistent with differentiation from Tph precursors. In vitro, IL-1β and IL-18 compensated for limited CD28 co-stimulation signals to induce proliferation and synergistically with IFN-α promoted upregulation of effector Tph gene signatures. These *in vitro* derived IL-1β- or IL-18-induced gene signatures were enriched in Tph cells within the SD SF scRNA-seq dataset.
Conclusion: We demonstrate that synovial CD4⁺ T cells in SD are dominated by clonally expanded Tph cells with robust B cell helper function. IL-1β and IL-18, targetable key mediators of innate immunity, actively promote Tph differentiation, aligning with findings from a complementary functional study (6). These results reveal a mechanistic link between innate-driven inflammation and adaptive immune dysregulation in SD, highlighting Tph cells as potential mediators of chronic arthritis.
Disclosure
J. Dirks: None declared, J. Fischer: None declared, L. Harrer: None declared, C. Bracaglia Consultant with: SOBI and Novartis, Speaker Bureau with: GSK, G. Prencipe: None declared, M. Pardeo Consultant with: SOBI and Novartis, A. Holl-Wieden: None declared, H. Girschick: None declared, C. Kessel: None declared, H. Morbach Speaker Bureau with: Novartis

References
1. Kessel C, Hedrich CM, Foell D. Arthritis Rheumatol. 2020 Feb;72(2):210
2. Nigrovic PA. Arthritis Rheumatol. 2014 Jun;66(6):1405
3. Henderson LA, JCI Insight. 2020 Mar;26(5):e132508
4. Kuehn J,..., Kessel C. Arthritis Rheumatol. 2023 May;75(5):826
5. Fischer J,..., Morbach H. Arthritis Rheumatol. 2022 Jan;74(1):150
6. Schleifenbaum S,..., Kessel C. independent PReS 2025 abstract (PReS25-ABS-1160)

PT014

Real-life treatment strategies for refractory still's disease: results from a worldwide survey, the metaphor project

G. Rogani[1,2], F. Baldo[3], C. Bracaglia[4], D. Foell[5], M. Gattorno[6], M. Jelusic[7], J. Anton[8], P. Brogan[9], S. W. Canna[10], R. Q. Cron[11], F. De Benedetti[4], A. Grom[12], M. Heshin Bekenstein[13], A. Horne[14], R. Khubchandani[15], M. Mizuta[16], S. Ozen[17], P. Quartier Dit Maire[18], A. Ravelli[6], M. Shimizu[19], G. Schulert[12], C. Scott[20], R. Sihna[21], N. Ruperto[22], J. Swart[2], B. Fautrel[23], S. Vastert[1,2], F. Minoia[24] on behalf of PReS MAS/sJIA Working Party
[1]Center for Translational Immunology, [2]Department of Pediatric Rheumatology, University Medical Center Utrecht, Utrecht, Netherlands, [3]Pediatric Rheumatology, ASST G. Pini-CTO, Milan, [4]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [5]University Hospital Muenster, Muenster, Germany, [6]IRCCS Giannina Gaslini, Genoa, Italy, [7]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia, [8]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat, Barcelona, Spain, [9]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [10]Children's Hospital of Philadelphia, Philadelphia, [11]University of Alabama at Birmingham, Birmingham, [12]Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [13]Dana Dwek Children's Hospital, Tel Aviv Medical Center, Tel Aviv University, Tel Aviv,, Israel, [14]Karolinska Institute, Sollentuna, Sweden, [15]SRCC Childrens Hospital, Mumbai, India, [16]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan, [17]Department of Pediatrics, Hacettepe University, Ankara, Türkiye, [18]Université Paris-Cite, IMAGINE Institute, Necker Children's Hospital, Paris, France, [19]Tokyo Medical and Dental University, Bunkyo-ku, Tokyo, Japan, [20]Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Canada, [21]Systemic JIA Foundation, Cincinnati, United States, [22]Fondazione IRCCS San Gerardo dei Tintori, Università degli Studi Milano-Bicocca, Monza, Italy, [23]Department of Rheumatology, AP-HP, Pitié-Salpêtrière Hospital, Sorbonne University, Paris, France, [24]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
Correspondence: G. Rogani
Pediatric Rheumatology, **23(2):** PT014

Introduction: The outcome of Still's disease (SD) has significantly improved in the past 15 years due to new therapeutic options[1], treatment strategies based on early biologic initiation (window of opportunity)[2,3] and a treat-to-target approach[4]. Nonetheless, a substantial proportion of patients still experiences a refractory course, severely impacting their quality of life. Recent reports have also highlighted an increasing occurrence of severe SD-associated lung disease (SD-LD)[5]. Treatment strategies in these cases are not standardized and are affected by medication availability and clinician experience.
Objectives: To describe current treatment practices and major unmet needs, fostering a uniform approach to refractory SD.
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize therapy in SD and Macrophage Activation Syndrome (MAS), a global survey on refractory SD treatment was developed, with the following proposed subtypes: 1) persistent arthritis, 2) recurrent/refractory MAS and 3) SD-LD. Topics were selected by 22 expert pediatric rheumatologists, including 1 patient representative and 1 adult rheumatologist. The survey covered demographic data, clinical practice insights and a patient-focused section on unmet needs. International physicians part of the PReS/PRINTO network together with adult rheumatologists involved in SD care were invited to complete the web-survey between 3/12/24 and 14/2/25.
Results: A total of 206 physicians completed the survey, predominantly pediatric rheumatologists (91%), from 56 countries. Methotrexate was the most common 1st-line choice for SD-refractory arthritis, followed by anti-TNF agents and intra-articular steroids. JAK inhibitors (JAK-i) were considered mainly as 2nd- or 3rd-line option. If systemic symptoms co-occurred, 62% of respondents would modify their strategy, favoring methylprednisolone (MPN) pulses, JAK-i and ciclosporin. In SD patients with recurrent/refractory MAS, ciclosporin, anakinra, and MPN pulses were the most frequently selected medications. Treatment decisions were mainly guided by clinical severity, inflammatory markers, history of ICU admission and concomitant complications. Biomarkers played a minor role, partly due to limited access, reported by 22% of clinicians. For SD-LD, 41% would continue ongoing biologics, 30% withdraw and 29% decide case by case. Factors influencing withdrawal included persistent disease activity, history of adverse reactions and impending MAS. HLA genotyping was rarely considered relevant. The most used 1st-line agents for SD-LD included JAK-i, mycophenolate mofetil, and ciclosporin and only 8% would add Pneumocystis Jiroveci prophylaxis. Most respondents (82%) would consider Hematopoietic Stem-Cell Transplantation (HSCT) in difficult-to-treat SD patients, particularly for refractory MAS or SD-LD.
Conclusion: Management for refractory SD is widely heterogeneous and varies by phenotype. JAK-i are the most commonly used agents alongside standard therapies and HSCT is increasingly considered a potential option, especially for refractory MAS and SD-LD. A consensus effort is essential to refine the definition and identify optimal treatment strategies for refractory cases.
Disclosure
G. Rogani: None declared, F. Baldo: None declared, C. Bracaglia: None declared, D. Foell: None declared, M. Gattorno Grant/Research Support with: Novartis, Consultant with: Novartis, SOBI, Speaker Bureau with: Fresenius Kabi SwissBioSim GmbH, Novartis, SOBI, M. Jelusic: None declared, J. Anton: None declared, P. Brogan Speaker Bureau with: SOBI, S. W. Canna Grant/Research Support with: Simcha Therapeutics, Consultant with: AB2Bio; Bristol-Myers Squibb(BMS); Novartis, Speaker Bureau with: SOBI, R. Q. Cron Grant/Research Support with: Sobi, Consultant with: AbbVie/Abbott; American Board of Pediatrics; AS2 Biotherapeutics; CareerPhysician; Neurogene; Pfizer; Sobi; VIDA Ventures, F. De Benedetti Grant/Research Support with: AbbVie; Apollo; Elixiron; Kiniksa; Novartis; Sanofi; Sobi, Consultant with: AbbVie; Apollo; Elixiron; Kiniksa; Novartis; Sanofi; Sobi, A. Grom Grant/Research Support with: Novartis; Sobi, Consultant with: Novartis; Sobi, M. Heshin Bekenstein: None declared, A. Horne: None declared, R. Khubchandani: None declared, M. Mizuta: None declared, S. Ozen Speaker Bureau with: Novartis, Pfizer, Sobi, P. Quartier Dit Maire Grant/Research Support with: Amgen; Bristol-Myers Squibb(BMS); Lilly; Novartis; Pfizer; Sanofi; Sobi, Consultant with: AbbVie/Abbott; Amgen; Bristol-Myers Squibb(BMS); Lilly; Novartis; Pfizer; Sanofi; Sobi, Speaker Bureau with: Chugai-Roche; Novartis; Pfizer, A. Ravelli Grant/Research Support with: AbbVie; Alexion; Bristol-Myers Squibb(BMS); Galapagos; Johnson

& Johnson, Novartis; Pfizer; Roche; SOBI, Consultant with: AbbVie; Alexion; Bristol-Myers Squibb(BMS); Galapagos; Johnson & Johnson, Novartis; Pfizer; Roche; SOBI, Speaker Bureau with: AbbVie; Alexion; Bristol-Myers Squibb(BMS); Galapagos; Johnson & Johnson, Novartis; Pfizer; Roche; SOBI, M. Shimizu: None declared, G. Schulert Grant/Research Support with: IpiNovoyx, Consultant with: Novartis; SOBI, C. Scott: None declared, R. Sihna: None declared, N. Ruperto Consultant with: Abbvie; AClaris; AlfaSigma; Amgen; AstraZeneca; Aurinia; Boehringer-Ingelheim; Bristol Myers and Squibb; Eli Lilly; Galapagos; Genentech; Guidepoint; Idorsia; Janssen; Novartis; Pfizer; Roche; Sanofi; Takeda, Speaker Bureau with: Abbvie; AClaris; AlfaSigma; Amgen; AstraZeneca; Aurinia; Boehringer-Ingelheim; Bristol Myers and Squibb; Eli Lilly; Galapagos; Genentech; Guidepoint; Idorsia; Janssen; Novartis; Pfizer; Roche; Sanofi; Takeda, J. Swart: None declared, B. Fautrel Grant/Research Support with: AbbVie; Eli Lilly&Co.; MSD; Pfizer, Consultant with: AbbVie; Amgen; Biogen; BMS; Celltrion; Chugai; Eli Lilly&Co.; Fresenius Kabi; Galapagos; Janssen; Medac; MSD; Nordic Pharma; Novartis; OW KIN; Pfizer; Roche; Sandoz; Sanofi-Genzyme; SOBI; UCB; Viatris, S. Vastert Grant/Research Support with: SOBI, Consultant with: Novartis; SOBI, Speaker Bureau with: Novartis; SOBI, F. Minoia: None declared

Reference

1. PMID 37923864; 2. PMID 24623686; 3. PMID 30848528; 4. PMID 39317417; PMID 31562126

PT015

Transcriptional diversity of human normal-density and low-density granulocytes in systemic juvenile idiopathic arthritis

N. Inoue[1,2], A. Kuenzi Davis[1], A. Paranjpe[1], R. De[1], T. Do[1], E. Baker[1], G. S. Schulert[1,3]
[1]Cincinnati Children's Hospital, Cincinnati, United States, [2]Pediatrics, Kanazawa University, Kanazawa City, Japan, [3]University of Cincinnati College of Medicine, Cincinnati, United States
Correspondence: G. S. Schulert
Pediatric Rheumatology, **23(2):** PT015

Introduction: Systemic juvenile idiopathic arthritis is a severe systemic inflammatory disorder with features of autoinflammation. Disease onset is marked by profound neutrophilia, which is a marker for clinical response to IL-1 blockade. However, transcriptional activation of neutrophils persists even in clinically inactive disease.
Objectives: The objectives of this study were to define the transcriptional diversity of neutrophil subpopulations, including normal (NDG) and low-density granulocytes (LDG), in SJIA.
Methods: This protocol was approved by the CCHMC IRB and all patients/guardians provided informed consent. Neutrophils were analyzed for flow cytometry from whole blood. Alternatively, paired NDG and LDG populations were isolated using a two-step method. Total neutrophils were isolated by negative selection using the MACSxpress® Whole Blood human Neutrophil Isolation Kit (Miltenyi Biotec). This population was then separated using density-gradient centrifugation to obtain purified NDG and LDG. Flow cytometric analysis was performed using the Aurora platform. Cell capture for scRNA-sequencing was performed using HIVES (Honeycomb). Libraries were sequenced using Novaseq. Initial alignment and quality control were performed using the beenet analyze pipeline. Cells with fewer than 200 genes or 400 transcripts were excluded. Downstream processing, integration, and label transfer were conducted using Seurat.
Results: Flow cytometry analysis of SJIA neutrophils showed variable levels of more immature CD10- neutrophils, but with increased abundance in association with flares. Immature neutrophils, and in particular CD10-CD16- neutrophils, were highly enriched in the LDG population compared to the NDG population. To examine the transcriptional diversity of these populations, we captured paired LDG and NDG populations from 3 patients with SJIA, compared to total neutrophils from 2 healthy control children. We sequenced 34,442 NDG, 25,979 LDG, and 10,200 control neutrophils. Integrated analysis revealed 24 transcriptionally distinct clusters, which contained cells from each sample; there were no patient-specific or LDG-specific clusters. Both NDG and LDG showed increased abundance of more transcriptionally active clusters (3, 17) with high *NEAT1* expression, as well as interferon-stimulated gene (ISG) high expressing cluster 1. Patient LDG samples showed an increased abundance of more immature neutrophil clusters 21 and 24, including *PADI4* expression associated with NETosis. Performing pathway analysis on LDG to NDG transcriptomes, we found significant enrichment in pathways in innate immune response (z-score 16.7, adjusted p=3.75e-7) and antibacterial humoral response (z-score 59.8, adjusted p=2.49e-4), with differentially expressed genes including CD177, DEF4A, PADI4, and S100A12.
Conclusion: Neutrophils in SJIA are highly diverse, including CD10- immature neutrophils that are enriched in LDGs. Transcriptionally, SJIA LDGs do not represent a defined population but rather a diverse compartment with shared transcriptional changes reflecting innate immune activation.
Disclosure
None declared

PT016

Flipping the switch –classical complement activation closely linked to IFN-signalling in stills disease

F. Huijsmans[1,2], A. Bodelón de Frutos[2], L. Sijbers[2], S. M. Benseler[3,4,5], J. F. Swart[1], R. S. Yeung[6,7,8,9], B. J. Vastert[1,2], J. van Loosdregt[1,2]
[1]Pediatric Rheumatology and Immunology, UMC Utrecht, Wilhelmina Children's Hospital, [2]Center for Translational Immunology, UMC Utrecht, Utrecht, Netherlands, [3]Alberta Children's Hospital Research Institute, [4]Division of Rheumatology, Department of Pediatrics, Alberta Children's Hospital, Cumming School of Medicine, University of Calgary, Calgary, Canada, [5]Rheumatology, Paediatrics, Children's Health Ireland, Dublin, Ireland, [6]Division of Rheumatology, Department of Pediatrics, [7]The Institute of Medical Science, The Hospital for Sick Children, [8]Immunology, University of Toronto, [9]Cell Biology Program, The Hospital for Sick Children, Toronto, Canada
Correspondence: F. Huijsmans
Pediatric Rheumatology, **23(2):** PT016

Introduction: Stills disease (SD) is an autoinflammatory syndrome characterized by severe innate immune dysregulation. The complement system, an essential component of innate immunity, can drive inflammatory cascades through the classical, lectin or alternative pathway. Although complement activation has been implicated in various inflammatory disorders, its involvement in SD remains largely undefined. Elucidating the role of complement in SD may provide valuable insights into disease mechanisms and uncover novel therapeutic targets.
Objectives: To determine whether the complement pathway is activated in SD patients.
Methods: RNA was extracted from whole blood of SD (active n=27, inactive n=26) and active non-systemic juvenile idiopathic arthritis (JIA) patients (n=538). Gene expression of classical complement components C1QB, C1QC and IFN-regulated genes (IFN-score) was quantified by NanoString. Additionally, RNA sequencing was conducted on sorted monocytes from SD patients (active n=7, inactive n=7). Inflammatory mediators (IL-18, CXCL9, CXCL10) and complement activation products (C1q, C3a, C5a) were quantified using Luminex and ELISA. Classical complement activity was evaluated in sera of SD (active n=32, inactive n=66) and non-systemic JIA patients (active n=12, inactive n=12). To explore potential mechanisms underlying complement activation, in vitro experiments were conducted to assess which inflammatory stimuli could induce C1q production in monocytes.
Results: RNA expression of classical complement protein C1q is upregulated in both whole blood and isolated CD14+ monocytes from active SD patients compared to those with inactive disease (NanoString: *C1QB* 43 vs. 11, p<0.01; *C1QC* 24 vs. 6, p<0.01; Monocytes: *C1QB* $\log_2$FC 3.6, p<0.01; *C1QC* $\log_2$FC 3.9, p<0.01) and to active non-systemic JIA patients (*C1QB* 43 vs 15, p<0.01; *C1QC* 24 vs 8, p<0.01). Moreover, whole blood C1QB and C1QC expression levels positively correlate with the IFN-score (r=0.34, p=0.01), plasma levels of IL18 (r=0.5, p<0.01) and IFN related chemokines CXCL9 (r=0.4, p<0.01) and CXCL10 (r=0.6, p<0.01) in SD. Protein analysis revealed elevated levels of C1q, C3a, and C5a, as well as enhanced classical complement activity in active SD compared to inactive SD (94% vs 74%, p<0.01) and active non-systemic JIA patients (94% vs 81%, p=0.02). Furthermore, in vitro stimulation of healthy control monocytes with IFNγ robustly and

specifically induces C1q mRNA expression. Flow cytometry analysis confirmed that IFNγ stimulation promotes the emergence of a distinct monocyte subset characterized by high C1q expression.
Conclusion: Our findings indicate activation of the classical complement pathway in SD, closely linked with IFN-signalling. Obtaining a better understanding of the role of the complement system, particularly the role of C1q-high monocytes, may open novel avenues for personalized therapeutic approaches in SD.
Disclosure
F. Huijsmans: None declared, A. Bodelón de Frutos: None declared, L. Sijbers: None declared, S. Benseler: None declared, J. Swart: None declared, R. Yeung: None declared, B. Vastert Grant/Research Support with: SOBI, Consultant with: Novartis and SOBI, J. van Loosdregt: None declared

PT017

Therapeutic strategies in newly diagnosed still's disease: real-life clinicians' choices from the metaphor project worldwide survey

F. Baldo[1], G. Rogani[2], C. Bracaglia[3], D. Foell[4], M. Gattorno[5], M. Jelusic[6], J. Anton[7], P. Brogan[8], S. Canna[9], R. Cron[10], F. De Benedetti[3], A. Grom[11], M. Heshin Bekenstein[12], A. Horne[13], R. Khubchandani[14], M. Mizuta[15], S. Ozen[16], P. Quartier[17], A. Ravelli[5], M. Shimizu[18], G. Schulert[11], R. Sinha[19], C. Scott[20], N. Ruperto[21], J. Swart[2], B. Fautrel[22], S. Vastert[2], F. Minoia[23]
[1]PAediatric Rheumatology Unit, ASST-G.Pini-Cto, Milano, Italy, [2]Univeristy Medical Center, Utrecht, Netherlands, [3]IRCCS Ospedale Pediatrico Bambin Gesù, Rome, Italy, [4]University Hospital Muenster, Muenster, Germany, [5] IRCCS Giannina Gaslini, Genova, Italy, [6]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia, [7]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [8]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [9]Children's Hospital of Philadelphia, Philadelphia, [10]University of Alabama at Birmingham, Birmingham, [11]Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [12]Dana Dwek Children's Hospital, Tel Aviv Medical Center, Tel Aviv, Israel, [13]Karolinska Institute, Sollentuna, Sweden, [14]SRCC Childrens Hospital, Mumbai, India, [15]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kanazawa, Japan, [16]Department of Pediatrics, Hacettepe University, Ankara, Türkiye, [17]Université Paris-Cite, IMAGINE Institute, Necker Children's Hospital, Paris, France, [18]Tokyo Medical and Dental University, Tokyo, Japan, [19]Systemic JIA Foundation, Cincinnati, United States, [20] Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Canada, [21]Fondazione IRCCS San Gerardo dei Tintori, Università degli Studi Milano-Bicocca, Monza, Italy, [22]Department of Rheumatology, AP-HP, Pitié-Salpêtrière Hospital, Sorbonne University, Paris, France, [23]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy
Correspondence: F. Baldo
Pediatric Rheumatology, **23(2):** PT017

Introduction: Despite continuous advances in care and the recent publication of updated international recommendations, relevant discrepancies in the management of Still's disease (SD) may still exist, mainly due to the heterogeneity of its clinical expression and the differences in access to medications worldwide.
Objectives: To assess current intial treatment strategies in SD worldwide, and to identify factors influencing clinical decision-making, particularly related to different settings and clinical scenarios.
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize treatment in SD and macrophage activation syndrome, a global survey on SD treatment was developed based. Topics were selected by 22 experts, including 1 patient representative and 1 adult rheumatologist. The survey included demographic data, clinical practice insights, a patient-led section on unmet needs. International physicians part of the PReS/PRINTO network and adult rheumatologists involved in SD care were invited to complete the anonymous online survey (Dec 3, 2024–Feb 14, 2025).
Results: A total of 206 clinicians, mainly pediatric rheumatologists (91%), from 56 countries completed the survey. In newly diagnosed SD patients without MAS, 34% of respondents would initiate anti-IL1/IL6 biologic without glucocorticoids (GCs); the rest would use GCs alone (24%) or in combination with biologics (42%). Factors favoring GCs use included severe pericarditis (64%), severe arthritis (55%), and refractory disease risk factors (16%), as hyperferritinemia, lung involvement, early onset and Trisomy 21. Anakinra was the most frequently used biologic in 1 st line (59%), followed by Tocilizumab (25%). Only 1.5% reported unavailability of any anti-IL1/IL-6 therapy. Factors driving anakinra's choice were safety (72%), cost (41%), and predominant systemic phenotype (73%), while Tocilizumab was chosen for compliance (56%) and arthritis-dominant profile (80%). Difficult access to medication influenced decisions for Rilonacept (67%), Canakinumab (27%), Anakinra (17%); Tocilizumab was rarely unavailable (1.5%). In systemic-predominant SD, clinicians used NSAIDs (50%), GCs (46%), GCs pulses (42%), and Anakinra (45%) as first-line options. Second-line strategies included Tocilizumab (39%), GCs (31%), Anakinra (29%), GCs pulses (22%), and MTX (21%), while Tocilizumab (37%), JAK inhibitors (29%), and cyclosporin (24%) were the most selected options as third-line therapies. In SD patients with a prominent articular involvement at onset, half of the respondents would not change their therapeutic approach. Physician who modified thor strategy would use as a first line therapy GCs (47%), oral steroids (44%), Tocilizumab (39%), MTX (34%), and intra-articular steroids (31%) respectively. Second-line choices were mostly Tocilizumab and MTX (~40%).
Conclusion: Still's disease still represents a therapeutic challenge, mainly due to its heterogeneity in clinical expression. Our data reveals significant differences in treatment approaches, driven by clinical phenotype and drug availability. Future research is essential to optimize clustering of patients to foster tailored target treatments, while ensuring equitable access to effective therapies worldwide.
Disclosure
None declared

PT018

Diverging paths within juvenile spondyloarthropathies: axial involvement in enthesitis-related arthritis and juvenile psoriatic arthritis in a large national cohort study

F. G. Demirkan[1], V. Guliyeva[1], S. D. Arık[1], S. Türkmen[2], I. Bağrul[3], Ç. Kaşıkçı[4], N. Z. Özaslan[5], E. Küçük[6], Z. Kızıldağ[7], H. Kısaoğlu[8], B. Kasap Demir[4], D. Gezgin Yıldırım[9], S. Özdel[3], K. Öztürk[6], H. E. Sönmez[5], S. A. Bakkaloğlu Ezgü[9], M. Kalyoncu[8], E. Ünsal[7], B. Sözeri[2], N. Aktay Ayaz[1]
[1]İstanbul University, [2]Ümraniye Research and Training Hospital, İstanbul, [3]Etlik City Hospital, Ankara, [4]İzmir City Hospital, İzmir, [5]Kocaeli University, Kocaeli, [6]Göztepe Prof. Dr. Süleyman Yalçın City Hospital, İstanbul, [7]Dokuz Eylül University, İzmir, [8]Karadeniz Technical University, Trabzon, [9]Gazi University, Ankara, Türkiye
Correspondence: F. G. Demirkan
Pediatric Rheumatology, **23(2):** PT018

Introduction: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are considered within the broader context of juvenile spondyloarthropathies (JSpA). However, emerging evidence highlights distinct differences in pathophysiology, clinical presentation, and treatment response, particularly in relation to axial disease manifestations.
Objectives: This study aimed to evaluate and compare axial involvement in patients with ERA and JPsA, identifying shared features, overlapping characteristics, and key differences in disease expression and treatment response.
Methods: We utilized data from PERA research group, a large, real-world national cohort. Eligible patients were those with axial involvement of either JPsA or ERA who had at least 6 months of follow-up and imaging to assess axial disease. Data collected included age, sex, disease duration, joint and skin findings, laboratory parameters, HLA-B27 status, and disease activity scores.
Results: Overall, 314 ERA (65%, male) and 58 JPsA (72%, female) patients were included. The median age at disease onset was 11.4 years (IQR:8.7–13.2) in the JPsA group and 12.1 years (IQR:9.5–14.3) in the ERA group. In terms of clinical features, peripheral arthritis was universal in both groups at onset, but dactylitis was more commonly observed in JPsA (48.7% vs. 10.6%, $p < 0.001$), while enthesitis was significantly more prevalent in ERA (85.1% vs. 28.2%, $p < 0.001$). Uveitis occurred in 10.3% of ERA and none of JPsA patients, predominantly anterior and non-granulomatous. HLA-B27 positivity was significantly

more frequent in ERA (72.4%) compared to JPsA (28.6%, p < 0.01). Axial involvement as defined by imaging (MRI evidence of sacroiliitis and/or spinal inflammation) was present in 61.7% of ERA patients and 35.9% of JPsA patients (p = 0.03). The pattern of axial disease also differed: symmetric sacroiliitis was more frequent in JPsA, whereas ERA patients more commonly exhibited unilateral or asymmetric sacroiliac inflammation. Disease activity score (JSpADA) was higher in ERA patients with axial disease compared to their JPsA counterparts, although treatment response at 12 months was comparable between groups following anti-TNF therapy initiation. ERA patients demonstrated more frequent bone marrow edema of the sacroiliac joints and spine, while JPsA patients occasionally showed coexisting joint arthritis and diffuse enthesopathy. Ultrasound confirmed active enthesitis in 18.6% of ERA patients and 4% of JPsA patients with axial disease.
Conclusion: The higher prevalence of HLA-B27 and enthesitis in ERA supports its closer resemblance to adult-onset axial spondyloarthritis. In contrast, the occurrence of axial disease in JPsA patients-often HLA-B27 negative and more frequently female- suggests that axial involvement in JPsA may represent a distinct clinical entity, potentially reflecting a psoriatic spondyloarthritis phenotype.
Disclosure
None declared

References
1. Srinivasalu H, Sikora KA, Colbert RA. Recent Updates in Juvenile Spondyloarthritis. Rheum Dis Clin North Am. 2021 Nov;47(4):565-583.
2. Demir S, Ergen FB, Taydaş O, Sağ E, Bilginer Y, Aydıngöz Ü, Özen S. Spinal involvement in juvenile idiopathic arthritis: what do we miss without imaging? Rheumatol Int. 2022 Mar;42(3):519-527.

PT019

Molecular signatures and early therapeutic effects in the pro-kind SJIA biomarker inception cohort

C. Hinze[1], G. Varga[1], M. Saers[1], S. Schleifenbaum[1], G. Horneff[2], K. Tenbrock[3], J. Kümmerle-Deschner[4], M. Hufnagel[5], K. Mönkemöller[6], H. Morbach[7], D. Foell[1] on behalf of the German PRO-KIND Rheuma Study Group
[1]Klinik für Pädiatrische Rheumatologie und Immunologie, Universitätsklinikum Münster, Münster, [2]Klinik für Kinder- und Jugendmedizin, Asklepios Kinderklinik, Sankt Augustin, [3]Klinik für Kinder- und Jugendmedizin, Uniklinik RWTH Aachen, Aachen, [4]Zentrum für Kinder- und Jugendrheumatologie, Universitätsklinikum Tübingen, Tübingen, [5]Klinik für Allgemeine Kinder- und Jugendmedizin, Universitätsklinikum Freiburg, Freiburg, [6]Klinik für Kinder- und Jugendmedizin, Kliniken Köln, Köln, [7]Kinderklinik und Poliklinik, Uniklinikum Würzburg, Würzburg, Germany
Correspondence: C. Hinze
Pediatric Rheumatology, **23(2):** PT019

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is a severe inflammatory disease of childhood, characterized by marked innate immune activation. The PRO-Kind initiative promotes harmonized treat-to-target strategies in pediatric rheumatology, including a prospective cohort of newly diagnosed SJIA patients. An embedded biomarker module investigated molecular signatures and treatment effects, aiming to better understand early disease mechanisms and response predictors.
Objectives: To explore longitudinal gene expression patterns and their modulation by different first-line therapies in SJIA, and to identify molecular correlates of inflammation and treatment response in the early disease course.
Methods: In the multi-center prospective PRO-Kind SJIA inception cohort, RNA was extracted from peripheral blood and analyzed using a 67-gene NanoString panel targeting immune-related pathways. Sampling covered five timepoints or time frames: baseline, >0–2 weeks, >2–12 weeks, >12–36 weeks, and >36 weeks. Clinical and laboratory data were recorded in parallel. Differential gene expression was analyzed across treatment groups (glucocorticoids vs. IL-1 blockade) with FDR correction. Hierarchical clustering and T-score transformations were used to define expression modules. Additional analyses included correlation of gene expression with routine inflammatory markers, immune phenotyping, and serum protein biomarkers (ongoing).
Results: A total of 121 biosamples from 30 patients were included. Four consistent gene expression clusters emerged: neutrophil/innate immunity, type I interferon, erythropoiesis, and T-cell/EOMES-regulated modules. Compared to healthy controls, baseline SJIA samples showed profound dysregulation in all clusters, as well as markedly elevated serum protein biomarkers, e.g. S100A8/A9 67769 ng/ml (4429-157568), IL-18 19062 pg/ml (4025-37438), CXCL9 737 pg/ml (463-1794) (median [interquartile range]). Notably, treatment type was associated with distinct expression profiles during the follow-up: IL-1 blockade more strongly suppressed neutrophil/innate-related signatures than glucocorticoids (adjusted p<0.05). Routine inflammation markers correlated with specific gene modules, and ongoing analyses are exploring links to therapeutic outcomes. Immune phenotyping revealed dynamic changes in neutrophil S100 protein content, inversely reflecting S100 protein gene expression and serum S100 protein levels.
Conclusion: The PRO-Kind SJIA biomarker module reveals characteristic transcriptional signatures in active disease and demonstrates that early therapy induces distinct molecular effects. IL-1 blockade appears to modulate key inflammatory pathways more effectively than glucocorticoids. These insights support the concept of a therapeutic "window of opportunity" and offer a foundation for identifying biomarkers predictive of treatment response. Further analyses, including ongoing serum protein and cellular profiling, aim to refine personalized approaches in early SJIA management.
Disclosure
None declared

PT020

The systemic Jia synovial fluid environment supports development and prevalence of specific inflammatory T helper cell phenotypes

S. Schleifenbaum[1], A. Swoboda[1], J. Dirks[2], C. Bracaglia[3], T. Hinze[4], I. Caiello[3], G. Prencipe[3], M. Pardeo[3], S. Fuehner[1], C. Park[1], C. Hinze[1], H. Wittkowski[1], D. Windschall[4], D. Foell[1], H. Morbach[2], C. Kessel[1]
[1]Pediatric Rheumatology & Immunology, University Hospital Muenster, Muenster, [2]Pediatric Inflammation Medicine, Department of Pediatrics, University Hospital Würzburg, Würzburg, Germany, [3]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [4]Clinic for Pediatric and Adolescent Rheumatology, Sendenhorst, Germany
Correspondence: C. Kessel
Pediatric Rheumatology, **23(2):** PT020

Introduction: Still's Disease (SD) encompasses a unique childhood arthritis entity in that it features characteristics of both autoinflammation and autoimmunity(1, 2). Importantly, in a recent study we reported a skewing of SD naïve peripheral Th cell differentiation toward a functional T peripheral/follicular helper (Tph/Tfh) cell phenotype(3). Previously, both Tph and Tfh subsets have been reported as essential for supporting B cellular antibody production in secondary lymphoid organs (Tfh cells) or within inflamed tissues (Tph cell) and have been linked to the pathology of autoimmune conditions in rheumatoid arthritis or systemic lupus erythematosus but also juvenile idiopathic arthritis (JIA; 4). In this context, our previous analysis in SD(3) was limited to investigations on peripheral immune cells and serum biosamples and thus lacked data reflecting immune perturbations at sites of inflammation, such as the synovium.
Objectives: In the present study, we investigated whether and how the inflammatory environment in SD *versus* JIA synovial fluid (SF) may differentially impact T helper (Th) cell polarization and activation.
Methods: Synovial fluid samples from SD (n=7) and JIA (n=7) patients were tested in various cell culture setups, with or without recombinant cytokines or cytokine-blocking drugs, to assess their effects on healthy donor Th cell activation. We analyzed cellular surface marker, transcription factor, and effector molecule expression using flow cytometry, Luminex, ELISA, and digital PCR.
Results: Both SD and JIA SF represents a highly pro-inflammatory environment. Compared to JIA, SD SF was hallmarked by significant overexpression of IL-1β, IL-18, GM-CSF, S100A9 and MPO. Soluble FasL and IL-17A were elevated by trend in JIA SF. SD SF selectively induced significant elevation of CD4 T cellular ICOS expression and $CXCR3^{pos}CCR6^{pos}$ Th cell expansion, while JIA SF increased $CXCR3^{neg}CCR6^{pos}$ Th cell numbers. $CCR6^{pos}$ Th cell expansion was sensitive to IL-1 blocking

treatment in *in vitro* experiments. Furthermore, SD SF selectively supported the prevalence of recombinant cytokine induced (Th1-like) T follicular/peripheral Th (Tf/ph) phenotypes. These phenotypic data were supported by cytokine and transcription factor expression profiles assessed at protein and gene expression level. Tf/ph prevalence upon exposure to SD SF was associated with several inflammatory mediator levels in SF, but IL-1β, IL-18 and GM-CSF, in particular. Spiking JIA SF with a cocktail of these cytokines recapitulated some T cellular phenotypic features as observed in T cell cultures with SD SF.
Conclusion: Compared to JIA, SD SF drives distinct Th cell polarization, including differential and sustained Tf/ph cell activation. These findings complement our earlier observations in SD peripheral blood(3) and align with deep phenotyping data of JIA and SD synovial T cells performed in a paralleling back-to-back study(5).
Disclosure
None declared

References
1. Kessel C, Hedrich CM, Foell D. Arthritis Rheumatol. 2020. PMID:31524322
2. Schulert GS, Kessel C. Rheum Dis Clin North Am. 2023. PMID:37821202
3. Fischer J,..., Morbach H. Arthritis Rheumatol. 2022. PMID:34196496
4. Kuehn J,..., Kessel C. Arthritis Rheumatol. 2023. PMID:36409585
5. Dirks J,..., Morbach H. independent PReS 2025 abstract (PReS25-ABS-1458)

PT021

Fever resolution and treatment outcomes in pfapa and surf: evaluating the role of tonsillectomy in a pediatric autoinflammatory cohort

Y. Vyzhga[1,2], I. Y. Goh[1,3], E. Garibeh[1], B. M. Feldman[1,2,3,4], R. M. Laxer[1,2,3], D. Dissanayake[1,2]
[1]Division of Rheumatology, The Hospital for Sick Children, [2]Department of Paediatrics, University of Toronto, [3]Child Health Evaluative Sciences, SickKids Research Institute, [4]Dalla Lana School of Public Health, University of Toronto, Toronto, Canada
Correspondence: Y. Vyzhga
Pediatric Rheumatology, **23(2):** PT021

Introduction: While periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome is traditionally considered a benign and self-limited syndrome, treatment strategies such as corticosteroids and tonsillectomy are often used to accelerate fever resolution. In contrast, patients with syndrome of undifferentiated recurrent fever (SURF) remain understudied, and treatment approaches are largely extrapolated from PFAPA management.
Objectives: To evaluate fever resolution rates and the impact of tonsillectomy in PFAPA and SURF, and to explore how clinical phenotype influences treatment outcomes using principal component analysis (PCA).
Methods: Fever resolution was defined as ≥12 months without febrile episodes since the recent follow up with reported absence of febrile episodes. Time-to-resolution was assessed using Kaplan-Meier and Cox regression models. Separate subgroup analysis examined the effect of tonsillectomy by diagnosis. PCA was used to identify clinical phenotypes associated with resolution trends.
Results: We retrospectively analyzed 235 children with recurrent fever (PFAPA: n = 155; SURF: n = 80) followed at the Autoinflammatory Clinic of The Hospital for Sick Children from 2016 to 2024. Patients were classified using using established Eurofever/PRINTO classification criteria for PFAPA and proposed empirical indications for SURF. Among the 235 patients analyzed, fever resolution was achieved in 147 cases (62.6%), with higher resolution rates observed in the PFAPA group (68.4%) compared to the SURF group (51.2%). The median time to fever resolution was significantly longer in the SURF group compared to PFAPA (2,068 vs. 1,738 days; log-rank p = 0.037). Multivariable Cox regression analysis revealed that tonsillectomy was not an independent predictor of fever resolution (HR = 1.046; p = 0.803). However, diagnosis of SURF remained significantly associated with prolonged fever persistence (HR = 0.683; 95% CI: 0.476–0.980; p = 0.038), indicating a substantially lower likelihood of resolution over time in this group. PCA of clinical features across the cohort identified three distinct phenotypic clusters: a classic PFAPA cluster characterized by pharyngitis and cervical lymphadenopathy; a gastrointestinal-dominant cluster marked by abdominal pain, nausea, and fatigue; and an intermediate overlapping group. The GI-dominant cluster was predominantly composed of patients with SURF and exhibited the slowest trajectory toward fever resolution, with minimal response to tonsillectomy. These findings suggest that clinical phenotype may be a stronger determinant of treatment response than diagnostic label alone.
Conclusion: Tonsillectomy did not significantly accelerate fever resolution in either PFAPA or SURF cohorts and was associated with a paradoxical trend toward longer disease persistence in SURF. These findings suggest that treatment effects differ by phenotype, and tonsillectomy may have limited benefit outside of classic PFAPA presentations. Tailored treatment approaches, informed by clinical phenotype and symptom clustering, are needed for optimized management of pediatric autoinflammatory syndromes.
Disclosure
None declared

PT022

Evaluation of monocyte subtypes in patients with mevalonate kinase deficiency

S. Ozdemir Cicek[1,2,3], B. S. Demir[3,4], Z. B. Azizoglu[3,4], F. Kardaş[5], H. Gunes[6], R. M. Kisla Ekinci[7], B. Sozeri[8], A. Pac Kisaarslan[1,3], M. H. Poyrazoğlu[1,2,3], A. Eken[2,3,4,9], E. W. Hsieh[9], H. Canatan[2,3,4]
[1]Department of Pediatric Rheumatology, Erciyes University Faculty of Medicine, [2]Department of Molecular Biology and Genetics, Gevher Nesibe Genome and Stem Cell Institute, [3]Genome and Stem Cell Center (GENKÖK), Erciyes University, [4]Department of Medical Biology, [5]Department of Pediatric Metabolism, Erciyes University Faculty of Medicine, Kayseri, [6]Department of Pediatric Metabolism, University of Health Sciences Behcet Uz Children Training and Research Hospital, İzmir, [7]Department of Pediatric Rheumatology, Cukurova University Faculty of Medicine, Adana, [8]Department of Pediatric Rheumatology, University of Health Sciences Umraniye Training and Research Hospital, İstanbul, Türkiye, [9]Department of Immunology and Microbiology, University of Colorado Anschutz Medical Campus Faculty of Medicine, Denver, United States
Correspondence: S. Ozdemir Cicek
Pediatric Rheumatology, **23(2):** PT022

Introduction: Mevalonate kinase deficiency (MKD) is a monogenic autoinflammatory disease caused by loss of function mutations in *MVK* gene which results in reduced isoprenoids synthesis due to impaired mevalonate kinase enzyme. The mevalonate pathway controls the innate immune response via protein geranylgeranylation. Impairement of geranylgeranylation results in overproduction of pro-inflammatory cytokines, increased pyrin inflammasome. Past research shows that monocytes display inflammasome dysregulation and aberrant innate immune responses.
Objectives: The aim of our study was to evaluate the changes in monocyte subtypes in patients with MDK in flare and remission period and to compare them with healthy controls and patients using statins due to hereditary hyperlipidemia.
Methods: Nineteen MKD patients were included our study, and peripheral blood mononuclear cells (PBMCs) were obtained during remission (n=12) and flare (n=7) phases and patients with hypercholesterolemia using statins (n=7) and healthy controls (10). The flow cytometer was used to evaluate classical CD14++CD16- monocytes and intermediate CD14++CD16+ monocytes and non-classical CD14+CD16+ monocytes. Plasma cytokine levels as well as post-LPS stimulation cytokine production was examined via Legend Plex™ Inflammation Panel 1. Lastly, gene expression of pattern recognition receptors *MAVS, AIM2, MDA5, DDX58, STING, cGAS, IL-33R, IL-17R, TLR2, TLR3, TLR7* and *TLR9* were evaluated with real-time qPCR.
Results: A decrease in the frequency of CD14++CD16- classical monocytes was observed in MKD patients during flare and remission. Intermediate and non-classiacl monocytes did not show significant difference. Serum IL-18 and IL-6 levels were increased in MKD patients with disease flare compared to healthy controls. After LPS stimulation, IL-1β, IL-6, IL-8, IFN-α2, IFN-γ and MCP-1 cytokine levels were found to be significantly lower in PBMCs of MKD patients in flare compared to healthy controls. *DDX58 (RIG-I)* gene expression was significantly

decreased in MKD patients in the flare and remission period compared to healthy controls.
Conclusion: The subsets and inflammatory response of classical monocytes appear to be altered in MKD patients. Those defects could explain both autoinflammatory phenotype and perhaps immunodeficiency to select pathogens.
Disclosure
None declared

References
1. Akula MK, Shi M, Jiang Z, Foster CE, Miao D, Li AS, Zhang X, Gavin RM, Forde SD, Germain G, Carpenter S, Rosadini CV, Gritsman K, Chae JJ, Hampton R, Silverman N, Gravallese EM, Kagan JC, Fitzgerald KA, Kastner DL, Golenbock DT, Bergo MO, Wang D. Control of the innate immune response by the mevalonate pathway. *Nat Immunol.* 2016, 17(8):922-9.
2. Bekkering S, Arts RJW, Novakovic B, Kourtzelis I, van der Heijden CDCC, Li Y, Popa CD, Ter Horst R, van Tuijl J, Netea-Maier RT, van de Veerdonk FL, Chavakis T, Joosten LAB, van der Meer JWM, Stunnenberg H, Riksen NP, Netea MG. Metabolic Induction of Trained Immunity through the Mevalonate Pathway. *Cell.* 2018, 172(1-2):135-146.e9.

PT023

Phoenixin-14 as a potential limiting neuropeptide for inflammatory attacks in familial mediterranean fever and pfapa syndrome: a comparative study

S. Ayduran[1], S. N. Tığrak[1], G. Oğuz[1], G. Kılbaş[1], I. Kaleli[2], S. Türkuçar[1]
[1]Division of Pediatric Rheumatology,, [2]Division of Microbiology, Pamukkale University Faculty of Medicine, Denizli, Türkiye

Correspondence: S. Ayduran
Pediatric Rheumatology, **23(2):** PT023

Introduction: Familial Mediterranean Fever (FMF) and Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA) syndrome are the most common autoinflammatory diseases in childhood with similar clinical features. Both are characterized by recurrent, self-limited hyperinflammatory attacks due to exaggerated IL-1β secretion.
Phoenixin-14 (PNX-14) is a recently identified neuropeptide shown to exert anti-inflammatory effects in preclinical studies by downregulating IL-1β. However, its role in pediatric autoinflammatory conditions has not yet been explored.
Objectives: This study aimed to evaluate serum PNX-14 levels during febrile and attack-free periods in children with FMF and PFAPA, and to compare them with healthy controls to assess its potential anti-inflammatory effects.
Methods: A total of 140 children were included: 46 with FMF, 48 with PFAPA, and 46 age- and sex-matched healthy controls. Demographic, clinical, and genetic data were reviewed retrospectively, laboratory parameters such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum amyloid A protein (SAA), fibrinogen with serum PNX-14 levels were measured both during attack and attack-free periods
Results: PNX-14 levels were significantly elevated during febrile attacks in both FMF (130.1 ± 42.5 pg/mL) and PFAPA (131.0 ± 51.0 pg/mL) groups compared to their respective attack-free periods (71.5 ± 32.2 and 85.8 ± 33.5; $p < 0.001$ for both) and healthy controls (52.0 ± 34.7; $p < 0.001$). However, no significant differences were observed between the patient groups in either the attack or attack-free phases.
PNX-14 levels showed no significant correlation with demographic features, clinical findings, MEFV mutations, or PRAS scores (all $p > 0.05$). Similarly, no associations were found with common inflammatory markers, including ESR ($p = 0.27$), SAA ($p = 0.19$), and fibrinogen ($p = 0.31$).
Interestingly, a significant positive correlation was identified between PNX-14 and CRP levels during attacks in both patient groups (rho = 0.222, $p = 0.0357$). Moreover, PNX-14 levels demonstrated a stronger correlation with the time elapsed since the onset of fever episodes (rho = 0.360, $p = 0.0004$). Notably, both CRP and PNX-14 levels exhibited a parallel trend, rising during the early phase and declining in the later phase of attacks.
Conclusion: This study is the first to demonstrate that PNX-14 levels significantly increase during febrile attacks in both FMF and PFAPA, independent of clinical or genetic factors. The parallel rise and fall of PNX-14 and CRP suggest a possible compensatory, anti-inflammatory role for PNX-14 in acute inflammation. These findings highlight PNX-14 as a potential endogenous modulator of IL-1β-mediated responses. Overall, the results provide novel insights into neuroimmune regulation in autoinflammatory diseases and point toward PNX-14's promise as a future therapeutic target.
Disclosure
None declared

References
1. Ozen S, Batu ED, Demir S. Familial Mediterranean Fever: Recent developments in pathogenesis and new recommendations for management. *Front Immunol.* 2019;10:1130
2. Van Gijn ME, Soler-Palacin P, Franco-Jarava C, et al. Pathogenesis and diagnosis of PFAPA syndrome. *Nat Rev Rheumatol.* 2022;18(7):423–435
3. Schalla MA, Stengel A. Phoenixin-a pleiotropic gut-brain peptide. *Endocrine.* 2018;59(1):22–32

PT024

Evaluating consensus treatment plans for chronic nonbacterial osteomyelitis using real-world data

N. Z. Özaslan[1], E. Tunce[2], S. Tuncez[3], B. Menentoğlu[4], B. Sözeri[2], S. Özdel[3], N. Aktay Ayaz[4], S. Türkuçar[5], S. Yüksel[6], M. Kalyoncu[7], S. Atamyıldız Uçar[2], S. Ayduran[5], S. Türkmen[2], F. Gündoğmuş[7], M. Özen Balcı[8], K. Öztürk[8], N. Karacayır[9], S. Bakkaloğlu[9], G. Vatansever[10], S. S. Kılıç[10], M. Çakan[11], H. Adıgüzel Dündar[12], K. Ulu[13], F. Demir[14], B. Bozkaya[15], H. Ilgaz[16], B. Kasap Demir[16], F. Çakmak[17], Ö. Altuğ Gücenmez[12], F. G. Demirkan[18], N. Şahin[1], H. E. Sönmez[1]
[1]Division of Pediatric Rheumatology, Kocaeli University, Faculty of Medicine, Kocaeli, [2]Division of Pediatric Rheumatology, Ümraniye Training and Research Hospital, İstanbul, [3]Division of Pediatric Rheumatology, Etlik City Hospital, Ankara, [4]Division of Pediatric Rheumatology, Istanbul University Faculty of Medicine, İstanbul, [5]Division of Pediatric Rheumatology, Pamukkale University Faculty of Medicine, Denizli, [6]Division of Pediatric Rheumatology, Çanakkale Onsekiz Mart University, Çanakkale, [7]Division of Pediatric Rheumatology, Karadeniz Technical University, Faculty of Medicine, Trabzon, [8]Division of Pediatric Rheumatology, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, İstanbul, [9]Division of Pediatric Rheumatology, Gazi University, Faculty of Medicine, Ankara, [10]Division of Pediatric Rheumatology, Uludağ University, Faculty of Medicine, Bursa, [11]Department of Pediatric Rheumatology, Zeynep Kamil Training and Research Hospital, İstanbul, [12]Department of Pediatric Rheumatology, Dr. Behçet Uz Children's Training and Research Hospital, İzmir, [13]Department of Pediatric Rheumatology, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, [14]Division of Pediatric Rheumatology, Acıbadem Ataşehir Hospital, İstanbul, [15]Department of Pediatric Rheumatology, Samsun Training and Research Hospital, Samsun, [16]Department of Pediatric Rheumatology, İzmir Katip Çelebi University, İzmir, [17]Department of Pediatric Rheumatology, Başakşehir Çam and Sakura City Hospital, [18]Department of Pediatric Rheumatology, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
Correspondence: N. Z. Özaslan
Pediatric Rheumatology, **23(2):** PT024

Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare autoinflammatory bone disease of childhood. Due to the lack of standardized assessment tools in the diagnosis and treatment process, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed three consensus treatment plans (CTPs) for CNO. The Clinical Disease Activity Score (CDAS) for CNO was created to assess disease activity in the absence of imaging findings.
Objectives: To evaluate the applicability and effectiveness of the CNO CTPs in real-world settings using the CNO CDAS, and to assess the diagnostic and therapeutic processes as well as the outcomes at final visit to determine the practical success of current treatment approaches.
Methods: This retrospective study included 171 patients diagnosed with CNO across 18 centers. Disease activity was assessed at diagnosis, treatment modification, and final visit using the CNO CDAS, which is based on the number of clinically active lesions, patient pain

assessment, and global disease activity. Responses to the CTPs—comprising DMARDs, biologics (anti-TNF agents), and pamidronate—were analyzed.
Results: Of 171 patients, 68 (39.8%) were female and 103 (60.2%) male. Median age at symptom onset was 10 years (IQR: 4), at diagnosis 11 (IQR: 4.8), and at final visit 14 (IQR: 4); median follow-up was 30 months (IQR: 5). Bone pain (95.3%), functional limitation (67.8%), and fatigue (35.1%) were the most common presenting symptoms. Regional MRI was performed in 139 patients (81.3%) and whole-body MRI in 71 (42.1%), revealing a median of 6 lesions (IQR: 9). Frequently involved sites included the lower extremities (66%), pelvis (33.9%), and spine (15.7%). NSAIDs were used in 156 patients (91.2%), methotrexate in 146 (85.4%), anti-TNF agents in 93 (54.4%), and corticosteroids in 90 (52.6%). Remission was achieved in 69 patients (40.3%) with anti-TNF therapy, 52 (30.4%) with methotrexate, 9 (5.3%) with sulfasalazine, and 5 (2.9%) with pamidronate. Among 89 patients requiring treatment modifications, 83 switched from DMARDs to anti-TNF agents. At final follow-up, 106 patients (62%) achieved medicated remission, 50 (29.2%) were in drug-free remission, and 15 (8.8%) had persistent active disease. Median CDAS scores declined from 15 (IQR: 5) at diagnosis to 15 (IQR: 5) after treatment modification and 0 (IQR: 5) at final visit ($p < 0.05$), indicating a significant improvement over time.
Conclusion: This study demonstrates the real-life applicability of the CNO CTPs. Anti-TNF therapy was associated with the highest remission rate (40.3%). Significant reductions in CDAS scores were observed following treatment modifications, supporting the clinical utility of these strategies in CNO management.
Disclosure
None declared

References

1. Zhao Y, Wu EY, Oliver MS, Cooper AM, Basiaga ML, Vora SS, et al. Consensus Treatment Plans for Chronic Nonbacterial Osteomyelitis Refractory to Nonsteroidal Antiinflammatory Drugs and/or With Active Spinal Lesions. Arthritis Care Res (Hoboken). 2018 Aug 1;70(8):1228–37
2. Wu EY, Oliver M, Scheck J, Lapidus S, Akca UK, Yasin S, et al. Feasibility of Conducting Comparative Effectiveness Research and Validation of a Clinical Disease Activity Score for Chronic Nonbacterial Osteomyelitis [Internet]. 2022. Available from: http://medrxiv.org/lookup/doi/10.1101/2022.10.03.22280351

PT025

Comparative performance of the eurofever/printo classification criteria and tel hashomer criteria for fmf diagnosis: a systematic review

A. N. Ahmad[1], S. Haroon[1], O. F. Razouk[1], A. O. Al Nidawi[2], A. R. Al Midani[3]
[1]College of Medicine, University of Sharjah, Sharjah, United Arab Emirates, [2]Faculty of Medicine in Hradec Králové, Charles University, Hradec Králové, Czech Republic, [3]Tawam Hospital, Al Ain, United Arab Emirates
Correspondence: S. Haroon
Pediatric Rheumatology, **23(2):** PT025

Introduction: Until recently, Familial Mediterranean Fever (FMF) diagnosis has primarily relied on the Tel-Hashomer criteria, historically recognized for high diagnostic accuracy [1]. In 2019, the Eurofever/Pediatric Rheumatology International Trials Organization (PRINTO) introduced new classification criteria for hereditary recurrent fevers, including FMF [2]. However, it remains unclear whether these updated criteria provide superior diagnostic accuracy compared to the traditional Tel-Hashomer criteria.
Objectives: In this systematic review, we aimed to directly compare the diagnostic accuracy of the Tel-Hashomer criteria and the Eurofever/PRINTO criteria for FMF.
Methods: We systematically searched PubMed, Embase, CINAHL, and Web of Science databases from inception to March 29, 2025, for relevant observational studies assessing diagnostic accuracy. The primary outcomes evaluated were sensitivity and specificity of the Tel-Hashomer criteria and the Eurofever/PRINTO criteria (clinical-only or clinical + genetic versions). True positives (TP), true negatives (TN), false positives (FP), and false negatives (FN) were calculated based on the reported sensitivity, specificity, and sample sizes.
Results: Out of 130 studies screened, four met inclusion criteria, comprising a total of 1,291 FMF patients and 373 controls. The Tel-Hashomer criteria demonstrated a sensitivity ranging from 82.6% to 96.0% and specificity from 73.1% to 92.6%, with the highest sensitivity observed in genetically confirmed cases [3]. The Eurofever clinical-only criteria had slightly lower sensitivity (70.0%–93.1%) but good specificity (80.5%–96.0%). When genetic testing was added (Eurofever clinical + genetic), sensitivity increased to 94.0%–96.0%, similar to Tel-Hashomer, while specificity remained high (82.9%–90.0%). Notably, false-negative rates were lower with Eurofever+genetic (FN = 7-9) versus Tel-Hashomer (FN = 17-224).
Conclusion: The Eurofever/PRINTO criteria demonstrate comparable diagnostic performance to Tel-Hashomer, particularly when incorporating genetic testing, offering a modern alternative for FMF diagnosis while maintaining high accuracy.
Disclosure
None declared

References

1. Livneh A, Langevitz P, Zemer D, Zaks N, Kees S, Lidar T, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis Rheum. 1997;40(10):1879–85.
2. Gattorno M, Hofer M, Federici S, Vanoni F, Bovis F, Aksentijevich I, et al. Classification criteria for autoinflammatory recurrent fevers. Ann Rheum Dis. 2019;78(8):1025–32.
3. Tanatar A, Sönmez HE, Karadağ ŞG, Çakmak F, Çakan M, Demir F, et al. Performance of Tel-Hashomer, Livneh, pediatric and new Eurofever/PRINTO classification criteria for familial Mediterranean fever in a referral center. Rheumatol Int. 2020;40(1):83-91. doi:https://doi.org/10.1007/s00296-019-04463-w.

PT026

Idiopathic recurrent pericarditis in children and adults: clinical and diagnostic differences

M. Angela[1], E. Bizzi[2], M. Sandini[1], R. Mascolo[2], V. Collini[3], M. Imazio[3], L. Bernardo [1], A. Brucato [4]
[1]Department of Childhood and Developmental Medicine, [2]Internal Medicine Department, ASST Fatebenefratelli-Sacco, Milan, [3]Cardiothoracic Department, University Hospital "Santa Maria della Misericordia, Udine, [4]Department of biomedical and clinical sciences, ASST Fatebenefratelli-Sacco, Milan, Italy
Correspondence: M. Angela
Pediatric Rheumatology, **23(2):** PT026

Introduction: Current guidelines for diagnosis and treatment of recurrent pericarditis are based on adult populations. Few scientific data regarding recurrent pericarditis in pediatric patient are reported in literature.
Objectives: Due to limited pediatric data, this study aims to highlight clinical, laboratory, and therapeutic differences between idiopathic recurrent pericarditis in children and adults to optimize pediatric disease management.
Methods: This retrospective multicentric cohort study analyzed data from patients with recurrent pericarditis (idiopathic or post-cardiac injury). Clinical, laboratory, and outcome data were compared between pediatric (<18 years) and adult (>18 years) patients. A total of 61 children and 289 adults were included.
Results: Follow-up was significantly longer in children (8 vs. 4 years, $p < 0.001$). Males were predominantly affected in pediatric patient's cohort (30.3% female vs 69.7% male), while gender distribution was similar in adults (51.6% female vs. 48.4% male). Children were hospitalized more frequently than adult (81.8% vs. 58.5%, $p < 0.05$). From the clinical point of view, chest pain was the most common symptom in both group (100% vs. 57.1%), whereas dyspnea was exclusive to adults (31.5%, $p < 0.05$). Pericardial effusion was less common in children (63.6% vs. 80.6%, $p < 0.05$) and no pediatric patients developed constrictive pericarditis requiring pericardiectomy. Pediatric patient's cohort had a higher incidence of ST-segment elevation on ECG (64.7%

vs. 32.4%, p < 0.01) and a higher relative lymphocyte count (p < 0.05) with a lower neutrophil-to-lymphocyte ratio (3.65 vs. 4.71, p < 0.05). Recurrence of pericarditis was more frequent in adults (9.59 vs. 4.4 episodes/10 years, p < 0.001), but children had significantly longer relapse-free periods (68.31 vs. 31.72 months, p < 0.001).There were no significant differences observed in the treatment between the two groups. A total of 48 children (78.8%) and 237 adults (82.0%) were treated with NSAIDs. Colchicine was prescribed to 22 children (36.4%) and 136 adults (47.1%), while 15 children (24.2%) and 73 adults (25.3%) received Anakinra. The only notable difference was in the dosage of prednisone, with children receiving significantly higher doses compared to adults (37.25 mg vs. 25 mg, p = 0.023).
Conclusion: Recurrent pericarditis in children follows a different course than in adults, with fewer recurrences, prolonged symptom-free periods, and typical ECG abnormalities. The higher corticosteroid use in children raises some concerns because of its potential side effects, including growth impairment and osteoporosis. IL-1 inhibitors should be considered to minimize corticosteroid administration. These findings emphasize the importance of developing a pediatric age-specific guideline.
Disclosure
None declared

PT027

Functional study of mrtf-a gene variants: a novel gene associated with a monogenic disorder mimicking behçet's disease?

M. Di Rosa[1], G. Posern[2], E. De Martino[3], M. Girardelli[3], R. Rodrigues De Moura [4], A. Pin[3], E. Valencic[1,3], V. Boz[3], G. Zucca[3], A. Tesser[3], S. Pastore[3], A. Tommasini[1,3], A. K. Singh[2], A. Taddio[1,3]
[1]University of Trieste, Trieste, Italy, [2]Medical Faculty, Martin Luther University Halle-Wittenberg, Institute for Physiological Chemistry, Halle (Saale), Germany, [3]Department of Pediatrics, [4]Department of Advanced Diagnostics, Institute for Maternal and Child Health-IRCCS Burlo Garofolo, Trieste, Italy
Correspondence: M. Girardelli
Pediatric Rheumatology, **23(2):** PT027

Introduction: The pathophysiology of Behçet's disease (BD), a complex condition affecting multiple systems, remains unclear. However, monogenic disorders resembling BD may uncover biological pathways potentially relevant to understanding the complex etiology of multifactorial BD cases.
Objectives: We found two variants of uncertain significance (VUS) via whole exome sequencing in two families with BD-like complaints and evaluated their possible pathogenic impact through *in silico* and *in vitro* investigations.
Methods: Molecular dynamic analysis (MD) was performed by Gromacs software. Gene expression and protein quantification were performed through qPCR and cytofluorometry, respectively. Relative activity of MRTF-A was evaluated in NIH3T3 cells stimulated by increasing concentrations of Fetal Bovine Serum (FBS) after starvation by dual luciferase reporter assay system.
Results: The first variant (c.1864G>A p.D622N NM_020831) was observed to segregate in a family exhibiting BD-like complaints, which included recurrent fever, aphtous stomatitis, gastrointestinal involvement, arthritis and erythema nodosum, across three generations. The second one (c.1720G>A p.D574N) was found in a girl with recurrent bouts of fever accompanied by acute hepatitis and oral ulcers. Both variants were relatively rare in population databases and classified as VUS due to conflicting predictors tools. MD simulations showed that overall structural stability was similar between wild-type (wt) and mutant proteins, while mutants displayed altered local flexibility and adopted a less compact conformation. Gene and protein expression showed no differences between subjects with mutated MRTF-A and the control group. Luciferase assays demonstrated that MRTF-A mutants exhibited higher transcriptional activity compared to wt under both steady-state conditions (10%FBS) and upon serum resupply after starvation (0.5%FBS).
Conclusion: Our findings show that nucleotide changes in the *MRTF-A* gene, initially classified as VUS, actually lead to increased activity of the MRTF-A protein, enhancing gene expression. Given its crucial role as a transcriptional co-activator of Serum Response Factor and its established link to actin cytoskeleton dynamics, the observed hyperactivation likely disrupts these cellular processes. The clinical presentation in individuals carrying these variants, mimicking aspects of Behçet's disease, points toward a novel potential monogenic mimicker of BD. This is because reduced G-actin levels, a consequence of such defects, promote the translocation of MRTF-A into the nucleus, thereby increasing its activity. Consequently, gain-of-function variants of *MRTF-A* may exhibit effects analogous to those observed in actin depolymerization disorders, such as WDR1 deficiency, a recognized monogenic mimic of Behçet's disease, thereby reinforcing the hypothesis that cytoskeletal imbalance may play a role in the pathogenesis of Behçet's disease spectrum disorders.
Disclosure
None declared

PT028

OGFRL1 gene mutations may link cherubism to chronic recurrent multifocal osteomyelitis (CRMO)

L. Rossi-Semerano[1], C. Borocco[2], H. J. G. VAN DE WERKEN [3], P. KATSIKIS[4], G. BOURSIER[5], O. OZISIK[6], V. SOUMELIS[6,7,8], I. Koné-Paut[1] on behalf of ImmunAID consortium
[1]Department of Paediatric rheumatology and CEREMAIA, Hôpital Bicêtre, Université Paris Saclay, Le Kremlin Bicetre, [2]Paediatrics, Aix en Provence hospital, Aix en provence, France, [3]Department of Immunology, [4]Departmet of Immunology, Erasmus University Medical Center, Rotterdam, Netherlands, [5]Department of Molecular Genetics and Cytogenomics, Rare and Auto Inflammatory Diseases Unit, CHU Montpellier, Univ Montpellier, CEREMAIA, Montpellier, [6]INSERM, U976 HIPI, Université Paris Cité, [7]Department of Immunology-Histocompatibility,, Saint-Louis Hospital, AP-HP Nord, Université Paris Cité, [8]Owkin France, Paris, France
Correspondence: L. Rossi-Semerano
Pediatric Rheumatology, **23(2):** PT028

Introduction: Cherubism (OMIM 118400) is characterized by destructive bilateral jawbone expansion due to inflammatory fibrous lesions. Recently, autosomal recessive loss-of-function variants in the *OGFRL1* (opioid growth factor receptor-like 1) gene were identified in two families from Syria and India with cherubism. These families carried homozygous frameshift mutations, presumed highly pathogenic. Despite attempts to model the disease in *OGFRL1* knockout mice, the human phenotype could not be replicated.
Objectives: To investigate the relationship between OGFRL1 gene mutations and the co-occurrence of cherubism and chronic recurrent multifocal osteomyelitis (CRMO) in a newly identified family, and to explore the molecular mechanisms underlying this phenotype by analyzing genomic variants and proteomic profiles.
Methods: We identified a new family with a phenotype linking cherubism and CRMO. Whole genome sequencing (WGS) was performed on both parents and two affected brothers. Proteomics analysis using SomaScan 7 K from blood plasma compared the blood proteome of one patient to CRMO patients and controls from the IMMUNAID cohort. Only proteins significant in both comparisons were analysed further.
Results: The younger brother developed recurrent fevers, developmental delay, sterile pyogenic arthritis, and severe abscesses post-vaccination at the age of 1, along with jawbone osteitis and diffuse CRMO lesions. Imaging revealed mandibular osteosclerosis with heterogeneous osteolytic lesions and multifocal metaphyseal involvement on whole-body MRI. A major inflammatory syndrome was noted (leukocytes 16,000, CRP 180 mg/L, ESR 110 mm). The older brother displayed a milder phenotype with post-vaccination abscesses and osteoarticular pain starting at age 10. MRI identified a single epiphyseal-metaphyseal lesion in the right clavicle, suggesting CRMO. Inflammatory markers were moderately elevated (CRP 7 mg/L, ESR 40 mm). Cherubism-related features were absent. WGS revealed a rare missense variant in *OGFRL1* exon 7, p.(Arg241His), predicted deleterious *in silico* in both brothers. Proteomics analysis of the younger brother highlighted a higher abundance of proteins involved in osteoclast differentiation (NOTCH2, EFNA2, FOSL2, PIAS3), cartilage development

(FOSL2, RUNX3, DLX2), and immune function (TXN, ITGB2/ITGAL, HERC1, ULBP1). Conversely, anti-inflammatory proteins BCHE, SIGLEC5, and SIGLEC14 were less abundant.
Conclusion: This report extends the spectrum of *OGFRL1*-related disorders to include a phenotype combining cherubism and CRMO. Unlike previously reported cases, our patients exhibit CRMO, pyogenic arthritis, and skin pathergy. We investigated the KEGG pathways involving significant proteins and known cherubism-related genes. Our results suggest that the *OGFRL1* mutation in our patients may affect the MAPK signaling pathway, shedding light on the potential molecular mechanisms underlying this condition. Consent to published had been obtained.
Disclosure
None declared

Reference
1. Kittaka M, Mizuno N, Morino H, Yoshimoto T, Zhu T, Liu S et al. Loss-of-function *OGFRL1* variants identified in autosomal recessive cherubism families. JBMR Plus. 2024 Apr 9;8(6):ziae050.

PT029

Transcriptome analysis of unmedicated heterozygous familial mediterranean fever patients reveals a type I interferon signature driving increasing pyrin expression

E. Sag[1,2], G. Imren[3], L. Vande Walle[4], E. A. Arslanoglu Aydin[5], Y. Bayindir[1], V. Cam[1], D. Unal[1], H. Ercan Emreol[1], A. Pac Kısaarslan[6], S. Ozdel[5], O. Basaran[1], B. Karaosmanoglu[3], M. Alikasifoglu[3], Y. Bilginer[1], M. Lamkanfi[4], E. Z. Taskiran[3], S. Ozen[1,2]
[1]Department of Pediatric Rheumatology, [2]Translational Medicine Laboratories, Pediatric Rheumatology Unit, [3]Department of Medical Genetics, Hacettepe University, Ankara, Türkiye, [4]Laboratory of Medical Immunology, Department of Internal Medicine and Paediatrics,, Ghent University, Ghent, Belgium, [5]Department of Pediatric Rheumatology, Etlik City Hospital, Ankara, [6]Department of Pediatric Rheumatology, Erciyes University, Kayseri, Türkiye
Correspondence: E. Sag
Pediatric Rheumatology, **23(2):** PT029

Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disorder, characterized by recurrent episodes of systemic inflammation. Although this largely is an autosomal recessive condition, a subset of heterozygous carriers of *MEFV* mutations exhibit a clinical phenotype consistent with FMF. The mechanisms underlying this phenomenon remain poorly understood.
Objectives: We aimed to identify differential molecular signatures and potential diagnostic pathways by comparing the transcriptomic profiles of patients with a single pathogenic mutation that display the classical FMF phenotype with those of healthy heterozygous carriers. We also assessed our results with FMF patients with two mutations and validated key results at the protein level.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from 10 FMF patients (5 homozygous/compound heterozygous, 5 heterozygous exon 10 mutations) and 5 healthy heterozygous carriers (exon 10 mutations) recruited from tertiary centers. Patients met 2019 Eurofever/PRINTO criteria and were sampled during asymptomatic, treatment-naïve phases (prior to colchicine initiation) to avoid confounding effects.
For transcriptome profiling, total RNA from pooled groups (heterozygous FMF, homozygous FMF, healthy carriers) was extracted (Norgen Kit), followed by globin mRNA depletion (Qiaseq Fast Select) and library preparation (Qiaseq Stranded mRNA Kit). Libraries were sequenced on an Illumina NextSeq 500/550 (2×74 bp paired-end reads). Reads were aligned to hg19 (CLC Genomic Workbench), with differential expression analyzed via a negative binomial Generalized Linear Model (TMM-normalized; adjusted *p*<0.01, $|\log_2 FC|>1$). REACTOME pathways were assessed using ExpressAnalyst.
Protein studies utilized healthy donor-derived monocytes/PBMCs. Monocytes (isolated with Miltenyi Kit) and PBMCs were stimulated with IFN-α (1000 U/mL), and lysates were immunoblotted for IRF-3, ISG15, Pyrin, STAT1, AIM2, caspase-5, and β-actin. CXCL10 in supernatants was quantified via Luminex (Bio-Rad).
Results: We included 10 familial Mediterranean fever (FMF) patients (6 males/4 females; median age 9–11 years) and 5 healthy heterozygous carriers (1 male/4 females). All patients were treatment-naïve, with normal acute-phase reactants. Transcriptomic profiling of PBMCs identified 147 differentially expressed genes (DEGs; FDR ≤0.001, |Fold Change (fc)|≥2) between heterozygous FMF patients and healthy carriers (96 upregulated and 51 downregulated genes), including upregulated interferon-stimulated genes (*STAT1*, *STAT2*, *IRF7*, *ISG15*, *IFIT2*, *IFIT3*, *USP18*). Gene Ontology revealed enriched type I interferon responses, cytokine signaling, and inflammatory pathways (p-adj <0.01), with JAK-STAT signaling implicated. REACTOME analysis confirmed pronounced type I interferon activation (p-adj <0.01), particularly in IFN-α/β clusters. STRING network analysis highlighted interactions among innate immune genes (*STAT1*, *IRF7*, *ISG15*, *OAS1*).
Inflammasome-associated genes (*CASP5*, *GBP1*, *NLRC4*) and *MEFV* (encoding Pyrin) were upregulated in heterozygous FMF (p-adj <0.05). Compared to homozygous patients, heterozygotes exhibited heightened cytokine signaling and persistent interferon-related gene expression. Kinetic analysis of IFN-α-stimulated monocytes/PBMCs from healthy donors demonstrated time-dependent increases in CXCL10 secretion and elevated expression of Pyrin, STAT1, ISG15, AIM2, and caspase-5, while IRF3 remained unchanged. These findings support a model wherein chronic type I interferon signaling acts as a "second hit" in heterozygous *MEFV* carriers, driving mutant Pyrin overexpression and inflammasome activation, thereby precipitating the FMF phenotype.
Conclusion: These findings suggest that type I IFN signaling acts as a critical 'second hit,' amplifying Pyrin expression in heterozygous individuals and enabling disease manifestation despite a single *MEFV* mutation. This study offers an explanation for the much-debated issue of the carriers expressing disease phenotypes in diseases such as FMF, and presents novel insights for precision diagnosis and therapeutic intervention.
Disclosure
None declared

PT031

Total volume of heterotopic ossifications underlies functional impairment in fibrodysplasia ossificans progressiva

V. Matkava[1], I. Nikishina[1], S. Arsenyeva[1], E. Gasymov[2], M. Shalygina[3]
[1]Paediatric, [2]Radiology, [3]Junior Researchers Departments, V.A. Nasonova Scientific Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** PT031

Introduction: Fibrodysplasia ossificans progressiva (FOP) is an extremely rare genetic disorder which caused by mutation in the ACVR1 gene characterized by progressive heterotopic ossification (HO) and severe mobility restrictions. Low-dose whole body computed tomography (WBCT) is the most preferable option of observation the HO development. It seems that HO volume may be correlated with age and a cumulative analogue joint involvement scale (CAJIS).
Objectives: To evaluate HO volume and analyze correlations with age of pts and functional status according to CAJIS.
Methods: In single-center prospective study 32 pts with FOP were underwent WBCT without contrast in a 128-slice CT scanner. HO volume was determined by segmentation of each axial slice using semi-automatic algorithms in AW Server 3.2 with manual contouring for optimization. HO volume was calculated separately for each body region and then summarized. The CAJIS was used for functional status assessment.
Results: From July 2022 to March 2025 the WBCT was performed in 32 pts (15 female/17 male) with a verified FOP. 31/97% pts have «typical» c.617G>A (p.Arg206His) and 1 pt have ultra-rare (p.Gly356Asp) heterozygous missense substitution in the ACVR1 gene. All pts have congenital malformed great toes as a classic phenotypical FOP features. In 18 pts WBCT was done twice (9 female/9 male), in 4 pts 3 times (2 female/2 male), in 1 male pt – 4 times. HO volume was calculated in 23 pts (repeated in 13). WBCT was repeated after 1-year period. At the moment of first performed WBCT the median age of pts was 10 [interquartile range (IQR) 7;16] years, the median CAJIS was 7 [IQR 5;11], the

median HO volume (n=23) was 89.7 [IQR 9.2;297.1]. We detected significant correlation between HO volume and CAJIS (r=0.554, *p*=0.006) and between age and CAJIS (r=0.554, *p*=00009). At the moment of second examination with WBCT the median age of pts was 11 [IQR 8;15] years, the median CAJIS was 7,5 [IQR 4;11], the median HO volume (n=13) was 89,7 [IQR 49,3;352,3]. We detected significant correlation between HO volume and CAJIS (r=0.741, *p*=0.003) and between age and CAJIS (r=0.656, *p*=0.003). Pts were compared into 4 age groups (at the moment of performing WBCT): 0-5 y.o. (n=5); 5-10 y.o. (n=12); 11-15 y.o. (n=6); >16 y.o.(n=9). Significant association with CAJIS was detected in two age groups: 5-10 y.o. and >16 y.o. (*p*=0.04). Tendency to significant association with HO volume was detected in other two age groups: 0-5 y.o. and 11-16 y.o. (*p*=0.08).
Conclusion: Our preliminary data confirmed that HO volume significantly increased according the age and correlate with CAJIS score. It is extremely needed to find medications that can prevent the development of HO with the possibility of their use in early childhood.
Disclosure
None declared

PT032

Chronic fatigue and inflammatory fatigue – roughly the same? Comparing fatigue in juvenile rheumatic diseases, chronic pain, post-infectious conditions, and chronic fatigue syndrome

S. Hajek[1], U. Thoma[1], M. Krumrey-Langkammerer[1], A. Schramm[2], L. Harms[2], J. von der Beek[2], N. Draheim[2], S. Dollinger[1], A. Sprengel[1], J.-P. Haas[3], L. Höfel[2]
[1]German Center for Pediatric and Adolescent Rheumatology, [2]Center for Pain Therapy for Young People, [3]German Center for Pediatric and Adolescent Rheumatology, Center for Pain Therapy for Young People, Children's Hospital Garmisch-Partenkirchen, Garmisch-Partenkirchen, Germany
Correspondence: S. Hajek
Pediatric Rheumatology, **23(2):** PT032

Introduction: Fatigue is a common and severe symptom in many pediatric chronic conditions. In juvenile rheumatic diseases, it is frequently reported and linked to disease activity, pain, sleep issues, and psychosocial factors. Likewise, children with chronic pain often experience fatigue, which impairs physical, emotional, and school functioning. In post-infectious conditions and in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fatigue is a defining and persistent symptom, often involving post-exertional malaise.
Objectives: Comparing similarities and differences of fatigue in different pediatric chronic conditions.
Methods: Patients were recruited from a single specialized pediatric inpatient center. Fatigue was assessed as part of the routine admission process using the PROMIS® Fatigue – Short Form 10a (10 items, rated 1–5). Total scores and item responses from 08/2024 until 03/2025 were analyzed by diagnostic group.
Groups:
Rheumatic diseases, incl. autoimmune and autoinflammatory conditions (n = 188, 72.3% ♀, mean age (M) = 13.6, SD = 3.7).
Chronic pain, incl. complex regional pain syndrome (n = 123, 82.9% ♀, M = 13.9, SD = 2.4).
Post-infectious conditions, incl. SARS-CoV-2, EBV, and others (n = 22, 68.2% ♀, M = 15, SD = 3.6).
ME/CFS (n = 13, 84.6% ♀, M = 15.4, SD = 2.2).
Results: Fatigue severity varied between groups. Rheumatic disease patients reported the lowest sum scores (*M* = 22.23, *SD* = 10.26; mean item score (MIS) = 2.22), followed by patients with chronic pain (*M* = 29.09, *SD* = 10.44; MIS = 2.91). Higher scores were found in post-infectious conditions (*M* = 39.75, *SD* = 7.51; MIS = 3.98), while patients with ME/CFS showed the highest (*M* = 42.54, *SD* = 7.21; MIS= 4.25).
When asked about the most appropriate wording for their fatigue (exhausted or tired), descriptions varied between groups. Among those with rheumatic diseases, 56.80% described themselves as exhausted, 36.80% as tired, and 6.40% chose both. In the chronic pain group, a similar pattern emerged, with a stronger tendency toward exhausted (65.45%), followed by tired (28.18%) and both (6.36%). Patients with post-infectious conditions showed a p
Reference for exhausted (90.48%), with 4.76% each choosing tired or both. All patients with ME/CFS (100%) identified exhausted as the most accurate description of their experience.
Conclusion: Fatigue severity differed across diagnostic groups, with the lowest levels reported in rheumatic diseases, higher levels in chronic pain, and the highest in post-infectious conditions and ME/CFS. A key limitation of the study is the unequal group sizes, which may influence the generalizability of findings. We are currently analyzing the correlations between disease activity in rheumatic diseases, as well as different patterns of chronic pain.
Fatigue is a relevant and variable symptom across pediatric chronic conditions. The findings emphasize the need for diagnosis-specific assessment and targeted management strategies in clinical care.
Disclosure
None declared

PT033

Evaluating bone health in familial mediterranean fever: impact of inflammation and treatment

S. N. Tiğrak[1], S. A. Aydıncık[2], N. Sabir Akkoyunlu [3], S. Tiğrak[4], A. Gültekin[5], S. Ayduran[1], G. Kılbaş[1], G. Oğuz[1], S. Türkuçar[1]
[1]Pediatric Rheumatology, [2]Pediatric Endocrinology, [3]Radiology, Pamukkale University, [4]Pediatric Radyology, Denizli State Hospital, [5]Nuclear Medicine, Pamukkale University, Denizli, Türkiye
Correspondence: S. N. Tiğrak
Pediatric Rheumatology, **23(2):** PT033

Introduction: Familial Mediterranean Fever(FMF) is an inherited autoinflammatory disorder characterized by recurrent episodes of hyperinflammation and persistent subclinical inflammation during attack-free periods. This chronic inflammatory burden has been implicated in various long-term complications, including impaired bone health. Current literature suggests that sustained inflammation may contribute to reduced bone mineral density(BMD) and an increased risk of vertebral fractures. However, the relationship between disease activity, treatment modalities, and bone health remains unclear.
Objectives: This study aimed to evaluate bone health parameters in pediatric FMF patients and explore their associations with inflammatory markers, disease severity (PRAS score), and MEFV mutations. Additionally, the potential protective effect of treatment on BMD and vertebral fracture risk was investigated.
Methods: A total of 87 FMF patients were included. Demographic and clinical data were retrospectively reviewed, while laboratory tests (CRP, ESR, SAA), bone mineral density (BMD) measurements (based on bone age, calendar age, and height age), and lateral vertebral radiographs were prospectively obtained during attack-free periods. PRAS scores were categorized as mild(≤5), moderate(6–7), or severe(≥8). To assess the impact of treatment on bone health, patients receiving colchicine or anti-IL-1 treatment (firstly anakinra, followed by canakinumab) were analyzed in separate subgroups.
Results: The mean age was 161.7±37.1 months, with a disease duration of 78.0±44.2 months. The gender distribution was 50.5% male and 49.5% female.
BMD z-scores for chronological age, height age, and bone age were recorded as −0.16±1.25, −0.10±1.34, and −0.31±1.29, respectively. The prevalence of vertebral fractures was 3.5% (n=4).
No significant associations were found between disease severity parameters, including inflammatory markers(CRP, ESR, SAA), MEFV gene mutations, and PRAS score, and bone health outcomes(BMD and vertebral fractures)(p > 0.05 for all).
Analysis of treatment subgroups revealed no significant effect of colchicine on BMD or vertebral fracture risk (p>0.05 for all). On the other hand, patients treated with anti-IL-1 treatment showed significantly higher BMD values adjusted for both bone age and calendar age(*p*=0.037 for both). However, no significant difference was observed in vertebral fracture risk(*p*=0.634) or height age–adjusted BMD(p>0.05) in this group.
Conclusion: Our findings did not reveal a significant association between disease severity and bone mineral density or vertebral fracture risk in FMF patients, suggesting that bone health may not directly reflect clinical or inflammatory burden. Notably, despite higher

disease activity, patients receiving IL-1 blocking treatments exhibited higher BMD values, raising the possibility of a protective role of IL-1β inhibition in bone metabolism.

Disclosure

None declared

References

1. Salah S, El-Masry SA, Sheba HF, El-Banna RA, Saad W. Bone Mineral Density in Egyptian Children with Familial Mediterranean Fever. Iran J Med Sci. 2016 Jan;41(1):2-8. PMID: 26722138; PMCID: PMC4691266.
2. Aydin, E.A., Baglan, E., Kocamaz, N.G. *et al.* The effect of canakinumab treatment on growth parameters in children with familial Mediterranean fever. *Clin Rheumatol* 43, 387–392 (2024). https://doi.org/10.1007/s10067-023-06752-z

PT034

The SOS project: to switch or to swap after adalimumab failure for the management of childhood non-infectious uveitis in an international cohort

I. Maccora[1], M. Chang[2], S. Angeles-Han[3], A. Taddio[4], L. Fotis[5], C. de Libero[6], M. Mangin[2], A. Duell[3], M. Gabrielli[7], K. Chiotopoulou[5], L. Sutton[2], V. Miraldi-Utz[8], G. Simonini[1]
[1]Rheumatology Unit, ERN ReCoNNET Center, Meyer Children's Hospital IRCCS, Florence, Italy, [2]Division of Immunology, Boston Children's Hospital, Boston, [3]Rheumatology Division, Cincinnati Children's Hospital, Cincinnati, United States, [4]Burlo Garofalo IRCCS, Rheumatology Division, Trieste, Italy, [5]Division of Pediatric Rheumatology, ATTIKON General Hospital, National and Kapodistrian University of Athens, Athene, Greece, [6]ophthalomology division, Meyer Children's Hospital IRCCS, Florence, [7]university of trieste, Trieste, Italy, [8]Ophthalmology Unit, Cincinnati Children's Hospital, Cincinnati, United States

Correspondence: I. Maccora
Pediatric Rheumatology, **23(2):** PT034

Introduction: Childhood chronic non-infectious uveitis (cNIU) is a sight-threatening condition that can lead to blindness if not appropriately treated. cNIU is typically associated with Juvenile Idiopathic Arthritis or can occur in isolation when idiopathic. Adalimumab is the only approved treatment for cNIU and TNF inhibitors (TNFi) are the recommended first line-biologic treatment of cNIU. However, 25% of patients do not achieve disease remission. In these cases, there is no consensus whether switching to another TNFi or swapping drug class is more effective.
Objectives: We aim to evaluate the efficacy of the switch OR swap therapeutic approach to treating cNIU refractory to primary TNFi and the efficacy of the different drugs in these patients.
Methods: In a multicentre international retrospective study involving pediatric rheumatology centres in Florence, Boston, Cincinnati, Athens and Trieste, we enrolled children with a diagnosis of cNIU unresponsive to adalimumab and required the use of another biologic. Remission on treatment was determined according to the grading of ocular inflammation using the Standardization of Uveitis Nomenclature (SUN) criteria. Statistical analysis was performed using Spss 29 for windows. A p-value <0.05 was considered significant.
Results: We collected the data of 79 children with cNIU, of whom 57 had JIA-associated uveitis (JIA-U) and 17 had idiopathic uveitis (IU). Seventy-nine were treated with adalimumab as first-line TNFi. Forty-one children did not respond to treatment and were "switched" to a second TNFi (38 infliximab, 3 golimumab), and 38 "swapped" to a non-TNFi biologic (20 tocilizumab, 2 baricitinib, 2 tofacitinib, 11 abatacept, 1 canakinumab). We identified a significant difference in treatment approach, European swapped more frequently than American (χ^2 0.078 p 0.78). We did not find significant differences in remission between switching TNFi and swapping drug class (χ^2 0.078 p 0.78) or amongst the different drugs (χ^2 32.87p <0.001). On sub-analysis of the different sub-types of uveitis (JIA-U and Idiopathic), we did not find significant differences in remission of patients for either switching TNFi or swapping to non-TNFi ($\chi^2$0.021 p0.88 and χ^2 0.016 p 0.90 respectively) or for the different drugs regardless of switch/swap ($\chi^2$5.03 p0.754 and $\chi^2$2.57 p 0.463 respectively). There were no significant differences based on anatomical location- anterior NIU (switch vs swap $\chi^2$0.219 p0.64 and based on the drugs $\chi^2$4.97 p0.760) and non-anterior NIU ($\chi^2$0.117 p0.733 and $\chi^2$2.97 p0.395). Furthermore no significant differences were assessedconsidering the responder to the primary TNFi ($\chi^2$0.012 p0.912 and $\chi^2$3.35 p0.851) and non-responder ($\chi^2$0.024 p0.877 and $\chi^2$5.4 p0.24).
Conclusion: Management of childhood cNIU is challenging and evidence is scarce on treatment after failure of first-line TNFi. This is one of the largest multicentre international cohorts that showed that TNFi and non-TNFi biologics are reasonable next treatment and there is no p
Reference for a specific class of biologics and all are reasonable therapeutic approach for the management of cNIU. The use of the European and US cohort allowed us to make a comparison between the two treatments approach. Further data are needed to make specific comparison among drugs.
Trial registration identifying number: Not applicable
Disclosure
None declared

PT035

Rantes and CXCL10 as potential tear-based biomarkers associated with ocular damage in pediatric chronic anterior uveitis

I. Maccora[1], M. Pavlenko[2], M. Altaye[3], H. I. Brunner[2,4], A. Duell[2], M. Quinlan-Waters[2], A. Sproles[2,4], S. Thornton[2,4], G. Schulert[2,4], V. Miraldi Utz[5,6], S. T. Angeles-Han[2,4]
[1]Rheumatology Unit, ERN ReCoNNET, Meyer Children's Hospital IRCCS, Florence, Italy, [2]Rheumatology Division, [3]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, [4]Department of Pediatric, University of Cincinnati College of Medicine, [5]Abrahamson Pediatric Eye Institute, Cincinnati Children's Hospital Medical Center, [6]Department of Ophthalmology, University of Cincinnati College of Medicine, Cincinnati, United States
Correspondence: I. Maccora
Pediatric Rheumatology, **23(2):** PT035

Introduction: Pediatric chronic anterior uveitis (CAU) leads to sight-threatening complications in approximately 50% of affected children. Among complications, cataract and glaucoma are among the most common ocular complications of CAU.
Objectives: We aim to identify tear-based biomarkers associated with ocular damage in pediatric CAU.
Methods: This cross-sectional study included children ≥5 years old diagnosed with CAU (juvenile idiopathic arthritis-associated (JIA-U) or idiopathic (iCAU)) from our local registry. Tear samples were collected from both eyes by Schirmer strips. Ocular complications included cataract, glaucoma, synechiae, band keratopathy, macular edema, epiretinal membrane, and optic disc oedema. Levels of S100A8, A9, and A12 were measured by ELISA, and IL-18, IL-8, CXCL10 (IP-10), MCP-1, RANTES, and sICAM-1 by Luminex assays. Biomarker levels were compared by the number of ocular complications (0, 1, >1). An exploratory Spearman correlation (ρ) analysis was performed and a Heatmap was developed to identify potential significant associations. A p-value<0.05 was considered significant.
Results: Forty-one children (29 JIA-U; 12 iCAU) with CAU contributed 121 tear samples (86 JIA-U; 35 iCAU), of whom 77 samples are from eyes with complications (51 by JIA-U and 26 by iCAU, $\chi^2$2.41 p0.088). We assessed significant differences regarding the number of complications between JIA-U vs iCAU (mean 1.88 vs 2.15 p<0.001).
We observed an increased level of RANTES in children with complications compared to those without complications (0.752 vs 0.389, p=0.028), and when considering the number of [0, 1, or >1] (0.389 vs 0.675 vs 0.824 respectively, p=0.022) complications. Conversely, CXCL10 was decreased in children with complications (2.82 vs 2.99 p=0.010), and when stratified by the number of complications (2.991 vs 2.881 vs 2.785 respectively p=0.004).
There were several significant correlations between the level of candidate biomarkers and ocular parameters: RANTES levels were positively correlated with the presence of complications (ρ=271, p=0.005) and glaucoma (ρ=306, p=0.015), while CXCL10 was negatively correlated with the presence of complications(ρ=0.27; p=0.005, the number of complications (ρ=0.31, p=0.006), and the presence of macular oedema/and papillitis (ρ=245, p=0.031). Moreover we found a positive

correlation between S100A9 and the presence of cataract (ρ=384, p=0.003) and a negative correlation with uveitis activity (ρ=292, p=0.007).
Conclusion: We identified RANTES, CXCL10 and S100A9 as potential tear-based biomarkers associated with ocular damage in pediatric patients with CAU. RANTES appears to be higher with ocular complications, whereas CXCL10 is decreased. The role of RANTES has been demonstrated in experimental autoimmune uveitis models and patients with uveitis. It has also been shown to differentiate patients with glaucoma. Further, we identified CXCL10 and S100A9 correlations with specific complications. Next steps are to determine biomarkers that are associated with specific ocular complications and differentiate activity from damage (chronicity).
Disclosure
None declared

PT036

Confirming the validity of the new eular/ACR classification criteria for pediatric chronic nonbacterial osteomyelitis

G. Mastrangelo[1,2], E. Itzkovitz[1,2], K. Sawicka[3,4,5], Y. I. Goh[1,3], A. Bitnun[2,6], S. Hopyan[7,8,9,10], P. Nathan[2,4,11], R. M. Laxer[1,2], B. M. Feldman[1,2,3,4]
[1]Division of Rheumatology, Department of Pediatrics, The Hospital for Sick Children, [2]Department of Paediatrics, Temerty Faculty of Medicine, University of Toronto, [3]Child Health Evaluative Sciences Program, SickKids Research Institute, The Hospital for Sick Children, [4]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, [5]Division of Neurology, Department of Medicine, University of Toronto, [6]Division of Infectious Disease, Department of Pediatrics, [7]Division of Orthopedics, Department of Surgery, [8]Developmental, Stem Cell & Cancer Biology, SickKids Research Institute, The Hospital for Sick Children, [9]Department of Molecular Genetics, [10]Department of Surgery, Temerty Faculty of Medicine, University of Toronto, [11]Division of Hematology-Oncology, Department of Pediatrics, The Hospital for Sick Children, Toronto, Canada
Correspondence: G. Mastrangelo
Pediatric Rheumatology, **23(2):** PT036

Introduction: Chronic nonbacterial osteomyelitis (CNO) is a noninfectious autoinflammatory bone disease which remains a diagnosis of exclusion, as existing diagnostic criteria are not widely accepted. Recently, the European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) developed new classification criteria for CNO, demonstrating 82% sensitivity and 98% specificity in an initial study.
Objectives: We aimed to investigate sensitivity and specificity of the new EULAR/ACR classification criteria for pediatric CNO, in a distinct real-world clinical setting and compare it to the sensitivity and specificity of the existing Jansson and Bristol diagnostic criteria.
Methods: This was a single-center cross-sectional study including children ≤18 years, diagnosed with CNO, acute infectious osteomyelitis (AOM) and bone malignancy from June 1, 2018 to May 31, 2024. Patients with other mimicking conditions, immunodeficiency, sickle cell disease, or those previously included in the original development cohort were excluded. Patients were divided into two groups: a CNO group and a non-CNO group (AOM and bone malignancy), from the latter a representative, random, sample was selected (www.random.org). Demographic, clinical, laboratory, imaging and pathology data were collected at disease onset. EULAR/ACR criteria were retrospectively applied to the entire cohort, independently from the initial diagnosis. Patients with an aggregate score ≥ 55 points were classified as having CNO. A sensitivity analysis was also conducted where patients with criteria with missing data were excluded. Classification results using the new criteria were compared with the final clinical diagnosis based on physician assessment (criterion standard). The same analysis was applied to Jansson and Bristol criteria. From contingency tables, sensitivity and specificity were calculated.
Results: Of the 164 children included, 82 had CNO, 41 were randomly selected from 274 cases of AOM, and 41 from 849 cases of bone malignancy. The median age was 10 years (IQR 3–16), with 62% girls and 37% boys, 66% had a bone biopsy. Overall, 40% scored ≥ 55 and 60% did not, with 3 false positive and 19 false negative. The EULAR/ACR criteria demonstrated 77% sensitivity and 96% specificity, with a positive predictive value (PPV) of 95% and negative predictive value (NPV) of 80%. In our sensitivity analysis excluding patients with incomplete data, results remained consistent (sensitivity 79%, specificity 96%, PPV 95%, NPV 81%). In comparison, the Jansson criteria showed 78% sensitivity, 67% specificity, PPV of 70%, and NPV of 75%. The Bristol criteria yielded 89% sensitivity, 70% specificity, PPV of 86%, and NPV of 74%.
Conclusion: Based on its favorable sensitivity and specificity, especially in comparison to existing criteria, the new EULAR/ACR criteria appeared to be more effective in distinguishing CNO from AOM and bone malignancy at disease onset. These results were consistent with findings from the original validation cohort.
Disclosure
None declared

PT037

Clinical and cellular phenotype in an MTORC1-driven mouse model of still's disease–associated macrophage activation syndrome

F. Bauer[1,2], J. Kuehn[1], R. Darbousset[1], H.-M. Lorenz[2], P. Y. Lee[1], P. A. Nigrovic[1]
[1]Division of Immunology, Boston Children's Hospital, Boston, MA, United States, [2]Department of Rheumatology, Heidelberg University Hospital, Heidelberg, Germany
Correspondence: F. Bauer
Pediatric Rheumatology, **23(2):** PT037

Introduction: Macrophage activation syndrome (MAS) is a life-threatening hyperinflammatory syndrome occurring in 10-30% of pediatric patients with Still's disease and is characterized by a high activation of mechanistic target of rapamycin complex 1 (mTORC1). Accordingly, overactivation of mTORC1 can induce experimental MAS in mice.
Objectives: To characterize the cellular phenotype of murine MAS by inducible deletion of tuberous sclerosis complex 2 (Tsc2), a negative regulator of mTORC1. With this leading to mTORC1 overactivation in hematopoietic cells, we aimed to assess the value of this model for studying human MAS.
Methods: Tsc2 deletion was induced in male and female Mx1-Cre$^+$ Tsc2 fl/fl mice (C57BL/6, 4-11 weeks of age) by intraperitoneal injection of 250 µg poly(I:C) on days 0, 2, and 4. Tissues were collected and analyzed on day 25 by flow cytometry, complete blood count, histology and Olink-based cytokine profiling. In vivo MRI scans of the brain were conducted in seven males on days 0, 4 and 24 as an exploratory study after findings in brain histology.
Results: Mx1-Cre$^+$ Tsc2 fl/fl mice of all age groups and both sexes developed hemophagocytosis in bone marrow and hepatosplenomegaly with disruption of normal lymphoid follicle formation in the spleen – phenotypes not apparent in poly(I:C)-treated Mx1-Cre$^-$ littermate controls. While anemia was detected in the blood, leukocytopenia was observed only in the bone marrow. Weight loss and joint swelling were not observed. By flow cytometry, F4/80$^+$ macrophages were highly increased in bone marrow and Ly6G$^+$ neutrophils were increased in the spleen. Pro-inflammatory Ly6C^{hi} CX3CR1$^-$ monocytes were increased, whereas Ly6C^{lo} CX3CR1$^+$ monocytes were diminished in both marrow and spleen. Natural killer (NK) cell proportions were lower in both compartments. Cytokine analysis in serum from 24 mice revealed an upregulation of macrophage-associated inflammatory markers such as CCL4, CCL5 and CXCL1, while the anti-inflammatory cytokine CCL22 was decreased. Histology of brain tissue revealed a greater abundance of F4/80$^+$ macrophages, particularly in the choroid plexus. However, hydrocephalus or other evidence of CNS-MAS was not observed by MRI.
Conclusion: mTORC1 overactivation induced by Tsc2 deletion replicates key cellular features of human MAS including hemophagocytosis in bone marrow and myeloid cell expansion. These findings support this model's relevance for investigating mTORC1-driven hyperinflammation in Still's disease and MAS.
Disclosure
F. Bauer Grant/Research Support with: German Academic Scholarship Foundation and German Society of Internal Medicine (merit-based scholarships), J. Kuehn: None declared, R. Darbousset: None declared, H.-M. Lorenz: None declared, P. Lee Consultant with: Pfizer (reviewing of a slide deck), P. Nigrovic: None declared

Reference
1. Huang, Z., et al., mTORC1 links pathology in experimental models of Still's disease and macrophageactivation syndrome. Nat Commun, 2022. **13**(1): p. 6915.

PT038

Comparing childhood-onset and adult-onset sjogren's disease: results of a national multicentre study

E. Kilic Konte[1], S. Sahin[1], E. Firat Sentürk[2], A. Yekeduz Bulbul[3], M. O. Erkan[4], B. Kucukali[5], C. Arslanoglu[3], Y. Ugur Es[6], N. Kara Canlioglu[7], G. Kilbas[8], G. Oguz[8], M. S. Kul[2], C. Sahin[2], G. Sumer[9], O. Akın[10], H. Ilgaz Tuzen[11], H. Kisaoglu[12], B. Bozkaya[13], M. Ozen Balci[14], E. C. Eroglu[15], M. H. Kacmaz[16], R. Isguder[17], S. Sener[17], F. G. Demirkan[18], F. Cakmak[19], F. Haslak[14], S. Türkucar[8], R. M. Kisla Ekinci[20], O. Koker[21], E. Celikel[6], D. Gezgin Yildirim[5], H. E. Sonmez[22], S. Demir[10], E. Sag[4], O. Basaran[4], M. Kalyoncu[15], B. Kasap Demir[11], A. Balat[16], S. S. Kilic Gultekin[9], A. Pac Kisaarslan[3], N. Aktay Ayaz[19], B. Sozeri[7], S. Yuksel[23], S. Ugurlu[2], O. Kasapcopur[1]
[1]Pediatric Rheumatology, [2]Internal Medicine, Rheumatology, Istanbul University- Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, [3]Pediatric Rheumatology, Erciyes University Faculty of Medicine, Kayseri, [4]Pediatric Rheumatology, Hacettepe University, Faculty of Medicine, [5]Pediatric Rheumatology, Gazi University Faculty of Medicine, [6]Pediatric Rheumatology, Ankara Bilkent City Hospital, Ankara, [7]Pediatric Rheumatology, Health Sciences University, Istanbul Umraniye Training and Research Hospital, Istanbul, [8]Pediatric Rheumatology, Pamukkale University Faculty of Medicine, Denizli, [9]Pediatric Rheumatology, Uludağ University Faculty of Medicine, Bursa, [10]Pediatric Rheumatology, Osmangazi University Faculty of Medicine, Eskişehir, [11]Pediatric Rheumatology, İzmir City Hospital, İzmir, [12]Pediatric Rheumatology, Kayseri Training and Research Hospital, Kayseri, [13]Pediatric Rheumatology, Samsun Training and Research Hospital, Samsun, [14]Pediatric Rheumatology, Medeniyet University Faculty of Medicine, Istanbul, [15]Pediatric Rheumatology, Karadeniz Technical University Faculty of Medicine, Trabzon, [16]Pediatric Rheumatology, Gaziantep University Faculty of Medicine, Gaziantep, [17]Pediatric Rheumatology, Adana Training and Research Hospital, Adana, [18]Pediatric Rheumatology, Istanbul Kanuni Sultan Süleyman Training and Research Hospital, [19]Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, [20]Pediatric Rheumatology, Çukurova University Faculty of Medicine, Adana, [21]Pediatric Rheumatology, Marmara University Faculty of Medicine, Istanbul, [22]Pediatric Rheumatology, Kocaeli University Faculty of Medicine, Kocaeli, [23]Pediatric Rheumatology, Çanakkale Onsekiz Mart Üniversitesi, Çanakkale, Türkiye
Correspondence: E. Kilic Konte
Pediatric Rheumatology, **23(2):** PT038

Introduction: Sjögren's disease (SjD) is an autoimmune disorder affecting exocrine glands. No studies to date have directly compared the childhood-onset SjD (coSjD) with adult-onset SjD (aoSjD), representing a critical knowledge gap in Sjögren's disease research.
Objectives: In our study, we aimed to highlight the differences between coSjD and aoSjD by comparing the clinical features, immunological profiles, activity/damage patterns, and long-term disease outcomes of SjD.
Methods: Data were evaluated for 115 patients diagnosed with coSjD across 22 pediatric rheumatology centers and for 82 patients followed at a single center with aoSjD. The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and the Sjögren's Syndrome Damage Index (SSDI) were used to assess activity and damage.
Results: In this nationwide study, 84.3% of childhood-onset patients and 94% of adult-onset patients were female. The mean age at diagnosis was 12.6 years for coSjD and 49.7 years for aoSjD. The fulfillment of the EULAR/ACR criteria at diagnosis was statistically significantly lower among those with coSjD(73.0% vs. 98.7%). Dry eye (60.0% vs. 82.9%) and dry mouth (55.6% vs. 84.1%) were the most common clinical symptoms in both groups; however, they were significantly more prevalent in the adult group. Constitutional symptoms (49.5% vs. 24.3%), lymphadenopathy (46.4% vs. 17.0%), recurrent parotitis (43.4% vs. 8.5%), and Raynaud's phenomenon (15.6% vs. 2.4%) were significantly more common in coSjD, whereas hematologic involvement (15.6% vs. 39%), pulmonary involvement (5.2% vs. 12.1%), and anti-SSA positivity (63.4% vs. 84.1%) were found to be more frequent in aoSjD. Salivary gland biopsy positivity was the most common diagnostic parameter, with a rate exceeding 90% in both groups. Schirmer test positivity (53.1% vs. 76.1%) was statistically significantly more prevalent in aoSjD. The median ESSDAI score at diagnosis was 8 (5-12) in the childhood-onset group and 3 (2-8.5) in the adult-onset group, with the score being statistically significantly higher in coSjD. The ESSDAI score at the last visit showed similar results, with a median score of 2 (0-5) for both groups. A damage score greater than 0 (36.5% vs. 59.8%) was found to be significantly higher in the adult-onset group at the last visit SSDI.
Conclusion: Childhood-onset Sjögren's disease might exhibit a different clinical course compared to adults. Our study emphasizes the necessity for updated criteria in this age group.
Disclosure
None declared

References
1. Randell RL, Stern SM, Van Mater H, Schanberg LE, Lieberman SM, Basiaga ML. Pediatric rheumatologists' perspectives on diagnosis, treatment, and outcomes of Sjögren disease in children and adolescents. Pediatr Rheumatol Online J 2022; 20(1): 79. 2022/09/06. doi: https://doi.org/10.1186/s12969-022-00740-4.
2. Wright TB. Updates in childhood Sjogren's syndrome. Curr Opin Pediatr 2022; 34(2): 217-22. 2021/12/09. doi: https://doi.org/10.1097/mop.0000000000001093.
3. Ramos-Casals M, Acar-Denizli N, Vissink A, et al. Childhood-onset of primary Sjögren's syndrome: phenotypic characterization at diagnosis of 158 children. Rheumatology (Oxford) 2021; 60(10): 4558-67. 2021/01/26. doi: https://doi.org/10.1093/rheumatology/keab032.

PT039

Identification of an optimal cut-off of laser flare photometry for diagnosis and monitoring of pediatric uveitis

A. Meneghel[1], F. Tirelli[1], M. Mazzarolo[2], N. Rocco[2], F. Vittadello[3], F. Zulian[1], M. E. Zannin[2]
[1]Department of Woman's and Child's Health, University Hospital of Padova, Pediatric Rheumatology Unit, [2]Department of Woman's and Child's Health, University Hospital of Padova, Ophthalmology Unit, [3]Research and Statistical Analysis, Explora, Padova, Italy
Correspondence: A. Meneghel
Pediatric Rheumatology, **23(2):** PT039

Introduction: Systemic inflammatory diseases, such as Juvenile Idiopathic Arthritis (JIA), vasculitis and connective tissue diseases, often present with ocular manifestations, especially uveitis. Early diagnosis is crucial to prevent ocular complications, sometimes leading to vision loss. Traditional evaluation of intraocular inflammation relies on slit-lamp biomicroscopy, a subjective and operator-dependent method. More recently, Laser Flare Photometry (LFP) has emerged as a non-invasive, objective, and quantitative tecnique to assess anterior chamber inflammation. To date,
Reference values and diagnostic thresholds in pediatric populations have not been clearly defined, yet.
Objectives: To assess and establish normative values and diagnostic cut-off for chronic pediatric uveitis for LFP
Methods: This retrospective, single-center study included pediatric patients with uveitis associated with systemic inflammatory disease, isolated uveitis, or systemic inflammatory conditions with no ocular involvement. All LFPs have been performed as part of standard ocular evaluation over a 1 year-period. Demographic and clinical data, including age, sex, systemic disease, uveitis subtype, presence of ocular complications were collected in standardized format. Mean LFP values and standard deviations (SD) were measured and recorded for each evaluated eye. Healthy eyes were used to define
Reference values. ROC curve analysis was conducted to determine the diagnostic threshold for inflammation.
Results: A total of 286 pediatric patients (74.8% female; median age 13 years) were included: 253 with systemic autoimmune disease (219 JIA), 34 with other systemic conditions, 33 isolated ocular disease. Of

these, 151 (52.8%) presented at least one previous uveitis flare at baseline, while 135 (47.2%) underwent LFP as part of routineocular screening. Uveitis was diagnosed in 151 patients; ocular complications were observed in 65. The overall mean LFP value in the cohort was 4.4 ph/ms. LFP values were significantly higher in eyes with uveitis than in those without (21.7 ph/ms ± 55.1 vs 4.4 ph/ms ± 2.7, p < 0.001) with the highest level observed in JIA-associated uveitis (25.1 ph/ms ± 62.4, p < 0.001) and in particular eyes with uveitic structural ocular complications (38.3 ph/ms ± 2.7, p < 0.001). ROC analysis identified 5.5 ph/m as the optimal cut-off for diagnosing intraocular inflammation with 67.3% sensitivity and 83.2% specificity.
Conclusion: LFP is a reliable tool for quantifying anterior chamber inflammation in pediatric patients. Its reliability and diagnostic precision make it a valuable tool, complementary to traditional ophtalmological assessment, particularly in the early stages of ocular inflammatory disease. Notably, this is the first study that clearly defines the optimal cut-off value for both diagnosis and monitoring of pediatric uveitis.
Disclosure
None declared

PT040

Clinical indicators of methotrexate response in juvenile idiopathic arthritis (JIA) and Jia with uveitis (JIA-U)

A. Jagger[1], M. Becker[2], S. Thompson[1], M. Altaye[1], J. Bohnsack[3], H. Brunner[1], M. Chang[4], A. Cooper[5], S. Davidson[6], A. Duell[1], B. Gangwani[4], C. Langefeld[7], M. Lerman[6], M. Lo[4], S. Pastore[8], M. Pavlenko[1], S. Prahalad[9], M. Quinlan-Waters[1], L. Ramsey[5], G. Schulert[1], G. Simonini[10], E. Stahl[5], G. Stocco[8], M. Sudman[1], A. Taddio[8], V. Miraldi Utz[1], R. Yeung[11], S. Angeles-Han[1] on behalf of This work could not have been accomplished without the aid of the following organizations: The NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) & the Arthritis Foundation (AF). We would also like to thank all participan
[1]Cincinnati Children's Hospital Medical Center, Cincinnati, **[2]**Duke University, Durham, **[3]**University of Utah, Salt Lake City, **[4]**Boston Children's Hospital, Boston, **[5]**Children's Mercy, Kansas City, **[6]**Children's Hospital of Phillidelphia, Philadelphia, **[7]**Wake Forest University, Raleigh, United States, **[8]**Institute of Child and Maternal Health, Trieste, Italy, **[9]**Emory, Atlanta, United States, **[10]**Meyer Children's Hospital IRCCS, Firenze, Italy, **[11]**The Hospital for Sick Children, Toronto, Canada
Correspondence: H. Brunner
Pediatric Rheumatology, **23(2):** PT04

Introduction: Patients with JIA are at high risk for development of chronic anterior uveitis (CAU), impacting 10-20% of this population. Although methotrexate (MTX) is the first-line systemic treatment for JIA-U patients, only 50% respond to therapy. Poor MTX response and delayed escalation of therapy can lead to sight-threatening complications. Non-white race, male sex, ANA positivity, and young age at JIA diagnosis have been associated with a lack of response.
Objectives: We aim to identify clinical risk factors associated with non-response to MTX in JIA-U patients.
Methods: This is a multicenter, prospective study – PEDIA-U and PROMOTE. Patients diagnosed with JIA or JIA-U who were prescribed MTX and who had 12 months follow-up were included. Patients were grouped as MTX non-responders (MTX-NR) vs responders (MTX-R). MTX-NR for CAU was defined as active or worse CAU by Standardization of Uveitis Nomenclature (SUN) criteria, presence of new or worsening complications, and/or need for > 2 drops/day of topical or oral steroids after 3 months. MTX-NR for arthritis was defined as no change in active joint count after 3 months. Clinical phenotypes were compared between MTX-NR and MTX-R using Chi-square and two sample tests. Odds ratios were calculated by multiple logistic regression.
Results: A total of 635 patients with JIA were identified, 187 (29.4%) of whom had JIA-U (Table 1). The overall cohort was predominately white (73.7%) and female (74.9%), with 298 (46.9%) being identified as MTX-NR. Average MTX oral and subcutaneous dose was similar at 16.5 mg/m^2 (SD 6.6) and 17.4 mg/m^2 (SD 5.7), respectively. White race was associated with MTX-NR on bivariate (X^2=20.0, p=0.0012) and multivariate (OR 2.429, CI 1.512-3.904) analysis, with no other significant clinical variables identified. Of the 187 JIA-U patients, 91 (48.6%) were identified as being MTX-NR (Table 2). Of the 91 JIA-U MTX-NR, a majority were non-responders due to arthritis activity (61.5%), followed by both CAU and arthritis activity (26%) and isolated CAU activity (12%). In contrast to the overall cohort, MTX intolerance (MTX-IT) was associated with MTX-NR (X^2=9.3, p=0.00023) in the JIA-U group. The most common reason for MTX-IT being GI symptoms (76.2%), followed by laboratory abnormalities (11.9%). The most initiated biological DMARD in MTX-NR patients was adalimumab (37.9%). No significant differences in predictors of response were found between JIA and JIA-U groups across clinical and demographic variables.
Conclusion: Patients of white race and those who experience MTX-IT were significantly more likely to be MTX-NR in the combined and JIA-U cohorts, respectively. Risk factors of MTX-NR from previously reported smaller cohorts were not significant in our population. Our study does not support evidence of using clinical criteria alone to identify at-risk populations for MTX-NR. Future investigation could include ocular findings on novel imaging modalities, biomarkers, and genetics as risk factors of MTX-NR, with the potential for developing individualized JIA-U therapy plans while minimizing ophthalmic morbidity.
Disclosure
None declared

PT041

Analysis of environmental exposures in pediatric chronic non-infectious uveitis: a case-control study

M. Kasap Cuceoglu[1], Y. Kapucu[2], S. Kadayifcilar[2], Y. Bilginer[1], S. Ozen[1], S. Yalcın[3]
[1]Division of Rheumatology, Department of Pediatrics, **[2]**Department of Opthalmology, **[3]** Division of Social Pediatrics, Department of Pediatrics,, Hacettepe University, Ankara, Türkiye
Correspondence: M. Kasap Cuceoglu
Pediatric Rheumatology, **23(2):** PT041

Introduction: Chronic uveitis in pediatric rheumatology practice have due to diagnostic difficulties, latent course and treatment-resistant conditions. The most common non-infectious cause of chronic uveitis in children is juvenile idiopathic arthritis (JIA), but idiopathic uveitis is also seen quite frequently. The importance of environmental factors in the development of rheumatological diseases is increasing day by day.
Objectives: The aim of this study was to investigate the effects of air pollution and some other environmental factors on the development of non-infectious uveitis.
Methods: The study was planned as a case-control study. The data of 102 patients (<18 years of age) who were followed up in tertiary center between January 2015 and January 2023 were reviewed using electronic medical records. Patients were divided into 3 groups as JIA, idiopathic uveitis and uveitis associated with JIA (JIA-U), 34 patients from each group. Then, pairwise comparison was made between these three groups. Demographic and clinical characteristics of the patients, recurrence frequency, treatments, various familial and environmental factors (smoking exposure during pregnancy, breast milk use), and Mediterranean diet compliance were assessed with KIDMED questionnaires[1] during outpatient clinic visits. Air quality indexes and air pollutants data were recorded for the place of residence one year before the last uveitis attack, and for the place of residence of those without remission of the attack and those with a diagnosis of JIA.
Results: 102 patients (66 female, 64.7%) were included in the study. In total (101 eyes for sixty-eight patients) were 38 (55.9%) were bilateral and 25 eyes (36.8 %) were unilateral.The median disease durations for JIA, JIA-U, and idiopathic uveitis were 9.9, 7, and 3 years, respectively.
There were no significant differences between the groups in demographic factors such as parental consanguinity, parental age and number of siblings, except for maternal smoking during pregnancy (p<0.001). However, caesarean section rates were significantly higher in the idiopathic uveitis groups compared with JIA and JIA-U (p=0.007). The Mediterranean diet quality scores were evaluated between patient groups, the median KIDMED score differed significantly between JIA-U and idiopathic uveitis (p=0.007).
Environmental factors including air pollutants (PM10, PM2.5, SO2) and weather parameters (precipitation, daily maximum temperature, daily diurnal temperature difference, average relative humidity) were found to influence disease severity and frequency. In particular, air pollutants (PM10, PM2.5, SO2) above defined thresholds were associated

with an increased risk of disease, while SO2 showed a potentially protective effect. Statistical analysis of total precipitation, daily maximum temperature, and daily diurnal temperature difference across the three groups revealed significant differences, with the most pronounced variations observed in the uveitis group, evident throughout the year and in the last 3 months.
Conclusion: Our study found that environmental factors, especially PM10 air pollution and climate parameters, were significantly different between JIA and JIA-U. In contrast, familial effects, smoking exposure during pregnancy and caesarean section delivery were more influential in differentiating idiopathic uveitis from JIA-U. In particular, maternal exposure to cigarette smoke during pregnancy emerged as a significant cause of uveitis. These findings highlight the importance of environmental factors in the management of JIA, JIA-U and idiopathic uveitis.
Disclosure
None declared

Reference
1. Sahingoz SA, Sanlier N. Compliance with Mediterranean Diet Quality Index (KIDMED) and nutrition knowledge levels in adolescents. A case study from Turkey. Appetite. 2011;57(1):272-7.

PT043

Monocytes upregulate M1 and M2 markers upon migration to the synovial fluid in oligo- and polyarticular jia

C. Kleimeyer[1,2], S.-J. Bremer[1,2], L. Finger[1,2], J. Pagel[1,2,3,4]
[1]Department of pediatrics, [2]University childrens' research, Universitätsklinikum Hamburg Eppendorf, [3]Partner Site Hamburg-Lübeck-Borstel-Riems,, German Center for Infection Research (DZIF), [4]Partner Site Hamburg, German Center for Child and Adolescent Health (DZKJ), Hamburg, Germany

Correspondence: L. Finger
Pediatric Rheumatology, **23(2):** PT043

Introduction: Juvenile idiopathic arthritis is the most common rheumatic disease in children. Upon inflammation circulating monocytes infiltrate the synovia and the synovial fluid. In vivo, recruited monocytes are capable of perpetuating inflammation e.g. by secretion of chemoattractants leading to immune cell infiltration into the joint. On the other hand monocytes can aid in resolving an inflammation by expression and secretion of CD163, Arginase-1 or cytokines such as IL-1 RA [1, 2]. Previous studies have highlighted the role of monocytes in rheumatoid arthritis but their role in JIA is much less understood.
Objectives: We aim to characterize synovial fluid monocyte polarization patterns and cytokine profiles to deliver a better understanding of JIA pathogenesis.
Methods: We collected peripheral blood mononuclear cells (PBMC), plasma, synovial fluid cells (SFC) and synovial fluid (SF) from 27 patients with JIA (persistent and extended oligoarthritis, RF + and RF - polyarthritis). Samples were frozen at −80 °C until the time of analysis. We performed flow cytometry based immunephenotyping of PBMC (n=29) and SFC (n=24) and Legendplex™ multiplex cytokine analysis in plasma and SF.
Results: Monocytes from PBMC and SFC of JIA patients showed a significantly different surface marker profile. Classical and intermediate monocytes from the SF showed an upregulation of CD64, CD68 indicating a mature and macrophage like differentiation. M1 polarization markers CD86 and HLA-DR were increased on classical and intermediate monocytes in the SF compared to PBMCs. Non-classical monocytes did not aquire an M1 polarization upon migration to the joint cavity. Interestingly, non-classical, intermediate and classical monocytes displayed an upregulation of CD163 and CD206, indicative of an M2 phenotype. In line with this mixed phenotype, legendplex cytokine profiling revealed an upregulation of CXCL10, IL-6 and IL-1 RA in the SF compared to plasma, as described before. Additionally, we saw a strong upregulation of Arginase activity in SF.
Conclusion: Synovial fluid monocytes display a mixed activation profile with both, M1 and M2 polarization markers upregulated upon migration into the SF. This is reflected by the cytokine profile of SF showing upregulated pro-inflammatory factors (IL-6, CXCL10) as well as an upregulation of immunoregulatory factors (Arginase, IL-1 RA). Since Arginase-1 expression has been reported on monocytes in SF of JIA patients, we hypothesize that monocytes might employ an Arginase dependant pathway for immunemetabolic regulation in the inflamed joint. Nonetheless, despite upregulation of M2-like markers and immunoregulatory agents JIA patients show chronic synovial inflammation, substantiating the notion of immune dysregulation is a key component in JIA disease pathogenesis.
Disclosure
None declared

References
1. Schmidt, T., Berthold, E., Arve-Butler, S. *et al.* Children with oligoarticular juvenile idiopathic arthritis have skewed synovial monocyte polarization pattern with functional impairment—a distinct inflammatory pattern for oligoarticular juvenile arthritis. *Arthritis Res Ther* **22**, 186 (2020).
2. Giacalone, V.D., Cammarata-Mouchtouris, A., Moncada-Giraldo, D. *et al.* Immunometabolic Analysis of Synovial Fluid from Juvenile Idiopathic Arthritis Patients. *Immunohorizons* 1 November 2022; 6 (11): 768–778.

PT044

Novel hemizygous TLR8 gain-of-function variants: a genetic cause of polyarteritis nodosa and polychondritis in male children

J. Sormani[1,2], A. Chenel[1,3], N. Poursac[4], P. Pillet[5], S. Tiriau[6], M. Broly[7], G. Boursier[7], C. David[8], E. Chopin[9], A. Nombel[1,10], T. Walzer[1], M. Tusseau[1,11], A.-L. Mathieu[1], A. Belot[1,12]
[1]LYACTS team, Centre International de Recherche en Infectiologie, [2]Internal medicine department, Hospices Civils de Lyon, [3]Biology department, Ecole Normale Superieure Lyon - UCBL, Lyon, [4]Rheumatology department, [5]Paediatric department, Bordeaux University Hospital Pellegrin, Bordeaux, [6]Paediatric department, Nantes University Hospital, Nantes, [7]Molecular Genetic department, Montpellier University Hospital, Montpellier, [8]Laboratory of Neurogenetics and Neuroinflammation, Imagine Institute, Paris, [9]Cellular Biotechnology department and Biobank, Hospices Civils de Lyon, Lyon, [10]Immunology laboratory, Hospices Civils de Lyon, Oullins-Pierre-Bénite, [11]Genetic department, [12]Paediatric rheumatology department, Hospices Civils de Lyon, Lyon, France
Correspondence: J. Sormani
Pediatric Rheumatology, **23(2):** PT044

Introduction: Germline TLR8 gain-of-function is a recently described inborn error of immunity (1–3).
Objectives: We aimed to assess the pathogenicity of an undescribed NM_138636.5: c.1027G>C (p.D343H) variant of *TLR8* in two kindreds and describe its clinical presentation.
Methods: We performed *in silico* analyses of the c.1027G>C variant, reported the genetic and clinical familial segregation and explored the impact of the variant on the NF-κB pathway using a luciferase reporter assay.
Results: Familial segregation revealed an X-linked transmission of the disease, and genetic assessment found a c.1027G>C variant of *TLR8*. This variant was predicted pathogenic by CADD score and AlphaMissense. This mutation was not disclosed in healthy genetic database, but another variant at the same position was recorded in a healthy female, carrying c.1028A>T, p.D343V variant. As both variants were located on the same residue, we explored the impact on the protein function using a NF-κB reporter luciferase assay. After TLR stimulation, both variants presented an increased NF-κB activity compared to wild type TLR8 and were activated at lower concentration. Interestingly, p.D343H variant exhibits a marked loss of ligand specificity and unexpectedly responds to R837, a specific agonist of TLR7. Location of the mutation was shown to be in the site of interaction with degraded RNA, which likely explains TLR8 overactivation (4).
From a clinical perspective, female carriers were mainly asymptomatic, as previously described (2,3). Several symptoms presented by the patients were evocative of ADA2 deficiency and were reported as polyarteritis nodosa diagnoses with thrombotic vasculitis, *livedo* or *erythema nodosum*, and infectious manifestations that could be fatal. Moreover, vasculitis, uveitis, neutrophilic dermatitis and polychondritis were as many manifestations compatible with *UBA1* somatic

mutation and could be evocative of another somatic disease, the VEXAS syndrome. These manifestations, associated with the effect of TLR8 variants on hematopoietic stem cells, provide promising clues to understand how NF-κB overactivation in myeloid cells contributes to these phenotypes (1,3).
Conclusion: We characterized two novel gain-of-function variants of TLR8 and highlighted the proximity of the clinical manifestations with two genetic diseases: ADA2 deficiency and VEXAS syndrome. Due to the clinical overlap, common explorations of these diseases will enable us to better understand their pathophysiology.
Disclosure
None declared

References
1. Aluri J et al. Immunodeficiency and bone marrow failure with mosaic and germline TLR8 gain of function. Blood. 2021 May 6;137(18):2450–62.
2. Fejtkova M et al. TLR8/TLR7 dysregulation due to a novel TLR8 mutation causes severe autoimmune hemolytic anemia and autoinflammation in identical twins. Am J Hematol. 2022 Mar 1;97(3):338–51.
3. Liang J et al. Erythroid-intrinsic activation of TLR8 impairs erythropoiesis in inherited anemia. Nat Commun. 2024 Jul 6;15(1):5678.
4. Tanji H et al. Toll-like receptor 8 senses degradation products of single-stranded RNA. Nat Struct Mol Biol. 2015 Feb;22(2):109–15.

PT045

Sex-specific mechanisms associated with female childhood-onset sle revealed by transcriptomic analysis of transgender adolescents undergoing gender-affirming sex hormone therapy

H. Cross[1], H. Peckham[1,2], G. Butler[2,3], E. Rosser[1], E. Jury[1], G. Robinson[1], C. Ciurtin[1,3]
[1]Ageing, Rheumatology and Regenerative Medicine, University College London, [2]Great Ormond Street Institute of Child Health, Infection, Immunity and Inflammation Research and Teaching Department, [3]University College London Hospital, London, United Kingdom
Correspondence: H. Cross
Pediatric Rheumatology, **23(2):** PT045

Introduction: Sex determinants may play a role in the immunological sexual dimorphism of childhood-onset systemic lupus erythematosus (cSLE).
Objectives: This study aimed to investigate the impact of sex determinants on immune transcriptomic changes and their association with cSLE.
Methods: We performed PBMC RNAseq analysis on post-pubertal cis-female adolescents with cSLE (n=74) and healthy controls (HCs, n=20), as well as transgender adolescents (trans-male, XX TM; trans-female, XY TF, n=32 samples) undergoing gender-affirming hormone therapy (GAHT) across 3 timepoints; pre-treatment, on gonadotrophin-releasing hormone agonist (GnRHa, puberty blocker) and on GAHT, TM on testosterone (T) and TF on oestradiol (E). Rstudio was used to identify the significantly differentially expressed genes (DEGs, DEseq2). Pathway enrichment analysis (PEA), clustering and normalised gene count analysis were conducted with compatible software.
Results: We identified 40 DEGs (fold change>1.5, P<0.05) in the cis-female cSLE cohort vs. HCs (defining a post-pubertal cSLE signature) that overlapped with the transgender cohort (on GAHT). Specifically, in the XY TF group (on E vs. GnRHa), there were 24 upregulated/1 downregulated DEGs, including *TLR2* (upregulated, p= 0.0077), and *IL1R2* (upregulated, p= 0.048 which overlapped with the cSLE signature. Similarly, in the XX TM group (on T vs. GnRHa), there were 6 upregulated/4 downregulated overlapping DEGs, including *IL15* (upregulated, p= 0.019). PEA revealed DEGs linked to the inflammatory response processes, cell migration/activation and lipid regulation.
Additionally, we discovered 63 X-linked DEGs (P <0.05) in the GAHT vs. GnRHa groups across both XX and XY backgrounds, however, these did not overlap with the cSLE signature, suggesting a lesser impact of sex hormones on X-linked transcripts related to cSLE susceptibility. However, the X-linked non-coding RNA X-inactive specific transcript (*XIST*) and the *XIST* antisense non-coding RNA *TSIX*, were both significantly increased in cSLE vs. HCs (p=0.018 and 0.0007). *XIST* correlated negatively with cSLE interferon scores (p=0.0010, r=−0.38) and X-linked *TLR7* expression (p=0.0004, r=−0.40), but *TSIX* did not, supporting a role for X chromosome inactivation in controlling the pathogenic mechanisms associated with cSLE in females.
Conclusion: This analysis demonstrated unique inflammatory transcriptomic changes (DEGs) induced by GAHT in transgender adolescents, which overlapped with cis-female cSLE adolescents, as well as sex hormone-independent associations between *XIST* expression and inflammatory cSLE pathogenic mechanisms. To our knowledge, this is the first exploration of the impact of sex hormones disaggregated from their corresponding sex chromosomal background in driving transcriptomic changes potentially relevant for understanding female cSLE pathogenesis.
Disclosure
None declared

PT046

Shared tcr VB21.3+ t cell immunological signature between MIS-C and MIS-A

L. Khoryati[1], S. Bech Sørensen [2], C. Parizot[3,4], R. Lautraite[3,4], G. Gorochov[3,4], T. Hyrup Mogensen [2,5], A. Belot [1,6] on behalf of MIS-A & COVID-19 taskforce
[1]Centre International de Recherche en Infectiologie (INSERM U1111), Lyon, France, [2]Department of Biomedicine, Aarhus University, Aarhus, Denmark, [3]Centre d'Immunologie et des Maladies Infectieuses (CIMI-Paris), [4]Département d'Immunologie, Hôpital La Pitié-Salpêtrière, Paris, France, [5]Department of Infectious Diseases, Aarhus University Hospital, Aarhus, Denmark, [6]Pediatric Rheumatology department, Hospices Civils de Lyon, Lyon, France
Correspondence: L. Khoryati
Pediatric Rheumatology, **23(2):** PT046

Introduction: Multisystem inflammatory syndrome in children (MIS-C) emerged shortly after the onset of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, characterized by life-threatening myocarditis and systemic symptoms. In adults, myocarditis was mainly associated to acute COVID-19 and mRNA-based coronavirus vaccines. Although extremely rare, a similar presentation to MIS-C with features of multisystem involvement and myocarditis was reported in adults and termed as Multisystem Inflammatory Syndrome in Adults (MIS-A). The pathophysiology of MIS is not fully understood. Several studies reported an aberrant immune activation in MIS-C involving autoantibodies, inborn errors of immunity, and a unique T cell signature defined by a polyclonal expansion of Vβ21.3+ T cells. In contrast, due to the rarity of MIS-A cases, T cell repertoire anomalies in MIS-A remain underexplored.
Objectives: We investigated the T cell response in a total of 16 cases of MIS-A to determine whether MIS-A shares the T cell receptor (TCR) Vβ repertoire skewing observed in MIS-C.
Methods: We explored the T cell response in cryopreserved peripheral blood mononuclear cells and fresh blood from Danish (n=5 patients) and French (n=11 patients) MIS-A cohorts, respectively. TCR Vβ repertoire and T cell phenotype were analyzed by spectral flow cytometry.
Results: Five Danish MIS-A patients were hospitalized between December 2020 and February 2022 upon SARS-CoV-2 infection. The patients presented with persistent fever, signs of hyperinflammation, gastrointestinal symptoms, and myocardial dysfunction. Laboratory results from the first days of hospital admission showed elevated levels of C-reactive protein in all five individuals. High levels of D-dimer, brain-type natriuretic peptide, and troponin were seen in several patients. Our data from the analysis of the TCR Vβ repertoire showed an expansion of Vβ21.3+ T cells in at least one of the three T cell subsets, CD3+, CD4+, or CD8+ T cells in 3 MIS-A patients. We also observed in all MIS-A patients an upregulation of the expression of activation and exhaustion markers (CD38, HLA-DR, TIM-3, and PD-1) on Vβ21.3+ cells compared to Vβ21.3- T cells. Additionally, we found a higher abundance of effector memory T cells (CD45RA- CCR7-) within the Vβ21.3+ T cells compared to the Vβ21.3- T cells.
To confirm these findings, we analysed data from the largest MIS-A published cohort to date (11 patients). TCR Vβ repertoire screening was performed in MIS-A patients and control cohorts including patients with COVID-19 associated myocarditis, post BNT162b2 mRNA vaccine-related myocarditis, and flu associated myocarditis. We found

an expansion of Vβ21.3+ T cells in 6/11 MIS-A patients versus 3/15 control patients.
Conclusion: Our results highlight a skewing of the TCR Vβ repertoire towards a Vβ21.3 response in MIS-A similar to what was previously reported in MIS-C, in CD3, CD4, and CD8 T cells. Thus, the immunological signature of expanded and activated Vβ21.3+ T cells is also common between MIS-C and MIS-A and provide further evidence that these two medical conditions are highly similar and may be manifestations of the same immune dysregulation in children and adults.
Disclosure
None declared

PT047

Classification, clinical phenotypes and long-term outcomes of childhood sjogren disease into adulthood

C. Ciurtin[1], R. Gotch[1], H. Peckham[1], R. Wilson[1], M. Al Obaidi[2], E. C. Jury[3]
[1]Centre for Adolescent Rheumatology, University College London, [2]Department of Paediatric Rheumatology, Great Ormond Street Hospital, [3]Department of Ageing, Rheumatology and Regenerative Medicine, University College London, London, United Kingdom
Correspondence: C. Ciurtin
Pediatric Rheumatology, **23(2):** PT047

Introduction: Childhood Sjögren Disease (cSjD) is a rare clinical phenotype lacking robust classification or research into its long-term outcomes and impact on young people (YP).
Objectives: To characterise the natural history of cSjD into adulthood mapped onto the available classification or diagnostic criteria.
Methods: A single centre long-term longitudinal cohort of cSjD has been characterized over time, including assessment of disease activity, symptom severity and damage using validated scores (ESSDAI, ESSPRI and SSDDI), and stratification according to the Newcastle Sjögren's Stratification Tool (1) and the Florida Scoring System (FSS)-derived classification for cSjD (2). Paediatric diagnostic criteria, Bartunkova et al.,1999 (3) and a diagnostic algorithm proposal, Tomiita et al., 2021 (4), as well as the 2016 ACR/EULAR adult classification criteria (5) were tested at disease onset vs. last assessment.
Results: We identified 30 YP with cSjD (F:M=14:1, 60% White, 23.3% Black African, 16.6% Asian), aged 25.8+/−5.2 years, with symptoms onset at age 12.7+/- 3.3 years, follow-up 1-25 years (mean 10.5+/−5.4 years), and diagnosis delay of median one year (IQR, 1-3; range 3 weeks-5 years). The most common manifestations at onset were: fatigue (73.3%), arthralgia (70%), dryness (56.6%), glandular swelling (33.6%), and skin rashes (30%). All patients diagnosed >3 years from disease onset (n=9) reported dryness compared to those diagnosed within 3 years (100% vs. 38%, p<0.001). All YP with cSjD but one were ANA positive, while 83.3%, 40% and 43.3% were anti-Ro, anti-La and rheumatoid factor positive, respectively. All had US features compatible with sialadenitis at diagnosis and 40% had salivary/lachrymal gland diagnostic biopsies. Three patients were diagnosed with lymphoma (10%), all within 3 years from diagnosis. All patients were treated with hydroxychloroquine, 19 with various cDMARDs, seven with rituximab, one with belimumab and three with cyclophosphamide throughout the disease course. At the last assessment, the median ESSDAI was 2 (IQR 2-8), median ESSPRI was 5.33 (IQR 3-7); and 56.6% (n=17) cSjD patients had damage associated with decreased saliva/tear secretion, and three patients (10%) experienced tooth loss. At the time of diagnosis compared to most recent assessment, 12(40%) vs. 20(66.6%) fulfilled the ACR/EULAR criteria, 9(29%) vs. 14(46.6%) fulfilled the Bartunkova criteria and 12(40%) vs. 19(61.2%) had at least a 'probable' diagnosis of cSjD based on Tomiita algorithm. At the last assessment, 36.6% had high vs. 30% low symptom burden, while 26.6% had dominant pain and 6.66% dominant dryness with fatigue symptoms. At presentation, 56.6% patients could not be mapped onto any of the FSS-derived clusters as they presented with either high or low symptom burden and positive diagnostic test results, potentially reflecting their longer diagnosis delay compared to the cSjD cohort used for the FSS classification.
Conclusion: This is the largest cSjD cohort with long-term follow-up ever described, which revealed differences between the paediatric and adult clinical phenotypes, and poor performance of the FSS for cSjD classification at presentation. Almost 2/3 patients could not be initially classified/diagnosed by any of the available criteria, and 1/3 still could not be classified even after 10 years of follow-up, highlighting the critical unmet need for better research in this rare condition characterised by early irreversible damage accumulation and increased risk of lymphoma.
Disclosure
None declared

PT048

The synovial fluid of jia patients is enriched in cytotoxic immune cells and granzyme A and B

S.-J. Bremer[1,2], C. Kleimeyer[1,2], L. Finger[1,2], J. Pagel[1,2,3,4]
[1]Department of pediatrics, [2]University childrens' research, Universitätsklinikum Hamburg Eppendorf, [3] Partner Site Hamburg-Lübeck-Borstel-Riems, German Center for Infection Research (DZIF), [4]Partner Site Hamburg, German Center for Child and Adolescent Health (DZKJ), Hamburg, Germany
Correspondence: C. Kleimeyer
Pediatric Rheumatology, **23(2):** PT048

Introduction: Juvenile idiopathic arthritis is the most common rheumatic disease in childhood and adolescence. Previous studies have shown an immunological imbalance leading to chronic inflammation of affected joints. Granzymes are secreted by cytotoxic immune cells, in particular CX3CR1 expressing CD8+ T cells, and are capable of extracellular matrix degradation and remodeling[1, 2]. Whether granzymes are involved in JIA pathogenesis is not yet understood.
Objectives: We aim to deliver a better understanding of the implication of cytotoxic immune cells and granzymes in the pathogenesis of JIA.
Methods: We collected peripheral blood mononuclear cells (PBMC), plasma, synovial fluid cells (SFC) and synovial fluid (SF) from 27 patients with JIA. Samples were frozen at −80 °C until the time of analysis. We performed flow cytometry based immunephenotyping of PBMC (n=45) and SFC (n=31) and Legendplex™ multiplex cytokine analysis in plasma and SF.
Results: The immune composition in the blood of patients differed significantly from the immune composition in the synovial fluid. In particular, we observed a marked increase in the level of cytotoxic immune cells such as NK bright cells and CD8+ T cells in the SF compared to PBMCs. In addition, we show that CX3CR1 is expressed on synovial fluid CD8+ T cells. Granzyme A, granzyme B and granulysin, all of which are secreted by cytotoxic immune cells are significantly enriched in the synovial fluid compared to plasma samples of JIA patients.
Conclusion: Our study delivers a comprehensive overview of the immune signature (cellular composition and major cytokines) of JIA patients during active disease. The observed high levels of granzyme A, granzyme B and granulysin in the synovial fluid of JIA patients indicate an increased presence of cytotoxic immune cells. These findings are in line with an increased infiltration of NK bright and CD8+ T cells in the synovial fluid compared to PBMCs of JIA patients. Delineating the contribution of cytotoxic immune cells to inflammatory dysregulation in the affected joints of JIA patients could help to identify novel treatment targets.
Disclosure
None declared

References

1. Obasanmi G, Uppal M, Cui JZ, Xi J, Ju MJ, Song J, To E, Li S, Khan W, Cheng D, Zhu J, Irani L, Samad I, Zhu J, Yoo HS, Aubert A, Stoddard J, Neuringer M, Granville DJ, Matsubara JA. Granzyme B degrades extracellular matrix and promotes inflammation and choroidal neovascularization. Angiogenesis. 2024 Aug;27(3):351-373.
2. Böttcher, J., Beyer, M., Meissner, F. et al. Functional classification of memory CD8+ T cells by CX3CR1 expression. Nat Commun 6, 8306 (2015).

PT049

Transposable element expression and cytokine profiling in Mis-C patients: insights from telomere-to-telomere genome alignment

B. Jenko Bizjan[1,2], L. Leko[1], A. Markez[1], M. Rob[1], T. Tesovnik[1,2], B. Vrhovsek[1], J. Kovac[1,2], N. Emersic[3], M. Z. Avramovic[2,3], T. Avcin[2,3]

[1]Clinical Institute of Special Laboratory Diagnostics, 1University Children's Hospital, University Medical Centre Ljubljana, [2]Faculty of Medicine, University of Ljubljana, [3]Department of Allergology, Rheumatology and Clinical Immunology, 1University Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia
Correspondence: B. Jenko Bizjan
Pediatric Rheumatology, **23(2):** PT049

Introduction: Multisystem Inflammatory Syndrome in Children (MIS-C) is characterized by severe hyperinflammation following SARS-CoV-2 infection; however, underlying genomic and immune mechanisms remain incompletely understood.
Objectives: This study aimed to investigate differential expression of transposable elements (TEs) and cytokine profiles during MIS-C flare compared to remission phases, using comprehensive genomic alignments.
Methods: Bulk RNA sequencing was performed on blood samples from pediatric MIS-C patients (n=18) during flare and remission. Differential TE expression analysis was conducted using both hg38 and the comprehensive Telomere-to-Telomere (T2T)
Reference genome, facilitating identification of previously inaccessible repetitive genomic regions. Cytokine levels were measured using multiplex assays, and statistical significance was assessed using the Wilcoxon test with FDR adjustment.
Results: We identified significant upregulation (log2 fold change ≥1) of endogenous retroviruses (ERV1, ERVL, ERVK families), LTR retrotransposons, and LINE elements during MIS-C flares compared to remission. Notably, LTR161-ERV1 and LTR108e_Mam-ERVL were among the highest expressed elements (log2FC=2). T2T alignment exclusively uncovered additional TE transcripts, including unknown and poorly characterized elements (e.g., UCON61, UCON63), further emphasizing genomic regions traditionally underrepresented in
Reference genomes. Elevated TE expression coincided with significantly increased cytokine levels, including IL-6 (median flare: 484.81 vs remission: 2.40 pg/mL, adjusted p=0.019), IFN-γ (median flare: 2184.48 vs remission: 70.71 pg/mL), VEGF (median flare: 179.74 vs remission: 134.78 pg/mL, adjusted p=0.024), and CCL2 (median flare: 531.99 vs remission: 219.58 pg/mL, adjusted p=0.024). These cytokines are known to promote inflammatory responses and immune cell recruitment, potentially contributing to the transcriptional activation of TEs observed during MIS-C flares.
Conclusion: Comprehensive genomic analysis using the T2T
Reference genome revealed significant differential expression of transposable elements uniquely associated with MIS-C flares, strongly correlating with elevated cytokines such as IL-6, IFN-γ, VEGF, and CCL2. These findings highlight a potential interplay between cytokine-driven inflammation and epigenetic activation of TEs, suggesting novel mechanistic insights into MIS-C pathology and offering new avenues for diagnostic biomarker development and targeted therapies.
Disclosure
None declared

Reference
1. Grants This study was supported by grants from the Slovenian Research Agency (J3-50115, J3-50122), Interreg Concerto, and SLING.

PT050

PRG4 as a regulator of joint homeostasis

A. Hackland[1], G. Neag[1], C. Bolton[1,2,3], C. B. Mahony[1], C. G. Smith[1], S. Kemble[1], L.-J. Marsh[1], R. Gentek[4], A. Filer[1,5], D. Elewaut[6], M. Kurowska-Stolarska[7], M. C. Coles[3], L. R. Wedderburn[2,8], E. Al-Abadi[9], A. P. Croft[1,5]
[1]Department of Inflammation and Ageing, University of Birmingham, Birmingham, [2]Infection, Immunity and Inflammation Research and Teaching Department, University College London, London, [3]Kennedy Institute of Rheumatology, University of Oxford, Oxford, [4]Centre for Inflammation Research and Centre for Reproductive Health, University of Edinburgh, Edinburgh, [5]NIHR Biomedical Research Centre, University of Birmingham, Birmingham, United Kingdom, [6]Ghent University, Ghent, Belgium, [7]University of Glasgow, Glasgow, [8]NIHR Biomedical Research Centre, Great Ormond Street Hospital, London, [9]Birmingham Women's and Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom
Correspondence: A. Hackland
Pediatric Rheumatology, **23(2):** PT050

Introduction: The lining layer of the synovial membrane is increasingly recognised as a key tissue niche determining joint health, producing synovial fluid components, including proteoglycan-4 (PRG4), to nourish and lubricate the joint(1-3). The rare monogeneic condition Camptodactyly-Arthropathy-Coxa Vara-Pericarditis (CACP) syndrome, caused by mutations in the *PRG4* gene, manifests with progressive arthropathy of the large joints arising in early childhood, demonstrating a critical for PRG4 in mediating normal joint homeostasis(4).
Objectives: We aim to investigate the role of PRG4 in maintaining joint homeostasis, particularly through its regulation of synovial lining layer macrophages, to better understand regulators of the lining layer niche and the pathophysiology of this rare condition.
Methods: Using synovial tissue biopsy samples from 6 individuals with CACP syndrome, as well as a Prg4 knockout mouse model that phenocopies the disease, we have undertaken histological, 2D/3D immunofluorescence (IF) imaging, flow cytometric, spatial and single cell transcriptomic analysis of synovial tissue to investigate the mechanisms underpinning synovial tissue pathology in the absence of PRG4.
Results: Single cell and spatial transcriptomic analyses of CACP syndrome synovium demonstrated an increased proportion of myofibroblasts and extracellular matrix deposition, which we validated at the protein level in human and mouse tissue using IF staining and flow cytometry, in accordance with the clinical manifestation of this condition. Interestingly, we observed multi-nucleated macrophages in the hyperplastic synovial lining layer in CACP syndrome, an uncommon feature of joint pathology. These lining layer macrophages displayed polarisation towards an *SPP1+* program, which is associated with fibrosis in the fibrotic liver and lung, and *in vitro* stimulation determined SPP1 expression to be directly regulated by PRG4. 3D imaging analysis of synovial lining macrophages in Prg4-knockout mice demonstrated altered morphology, suggesting impaired capacity to undergo immunoregulatory efferocytosis of synovial fluid debris.
Conclusion: We demonstrate that PRG4 suppresses the emergence of a pro-fibrotic *SPP1+* macrophage program in the synovial lining, which, in the absence of PRG4, promotes differentiation of myofibroblasts that drive synovial fibrosis, leading to restricted movement in the joints of individuals affected by CACP syndrome. Our further work aims to characterise defects in efferocytic capacity of lining macrophages in the absence of PRG4 and elucidate the role of efferocytosis in the healthy and inflamed synovium.
Disclosure
None declared

References
1. Kemble S, Croft AP. Critical Role of Synovial Tissue–Resident Macrophage and Fibroblast Subsets in the Persistence of Joint Inflammation. Frontiers in Immunology. 2021 Sep 3;12.
2. Kurowska-Stolarska M, Alivernini S. Synovial tissue macrophages in joint homeostasis, rheumatoid arthritis and disease remission. Nature Reviews Rheumatology. 2022 Jun 7;18(7):384–97.
3. Jay GD, Waller KA. The biology of Lubricin: Near frictionless joint motion. Matrix Biology. 2014 Oct;39:17–24.
4. Maniscalco V, Pizzetti C, Marrani E, Perrone A, Maccora I, Pagnini I, et al. Pseudo-rheumatic manifestations of limping: Camptodactyly–arthropathy–coxa vara–pericarditis syndrome: Single case report and review of the literature. Frontiers in Pediatrics. 2022 Dec 5;10.

PT051

Can fitness testing increase physical activity in adolescents with juvenile idiopathic arthritis?

U. Nilsson[1], M. Skattør[1], H. Sanner[1,2], K. Risum[1,3]
[1]Oslo University Hospital, [2]University of Oslo, [3]Oslo Metropolitan University, Oslo, Norway
Correspondence: U. Nilsson
Pediatric Rheumatology, **23(2):** PT051

Introduction: Juvenile idiopathic arthritis (JIA) impairs physical function and limits engagement in physical activity (PA). Our physiotherapy practice emphasizes education to encourage adherence to PA recommendations. Encouraging PA is important for managing JIA and enhancing overall health.

Objectives: To investigate whether the introduction of submaximal treadmill fitness testing could increase PA levels, estimated peak oxygen uptake (VO_{2peak}), walking distance, physical function, and health-related quality of life (HRQoL) in adolescents with JIA. Also, to examine associations between PA levels, VO_{2peak} and walking distance.
Methods: A longitudinal clinical study with a pre-test (visit 1) and post-test (visit 2) design was conducted. The planned test interval was 3-6 months. Adolescents aged 10-18 years with non-systemic JIA were recruited at Oslo University Hospital between June 2019 and September 2021. The intervention included a submaximal treadmill test during routine physiotherapy assessments. The test involved walking at a self-selected pace on a treadmill with a 0% incline for 4 minutes, followed by a 5% incline for the next 4 minutes. Estimated VO_{2peak} was calculated based on walking speed, age, sex, and heart rate increase. PA was measured using the International Physical Activity Questionnaire (IPAQ). Physical function and HRQoL were assessed using the Juvenile Arthritis Multidimensional Assessment Report.
Results: Thirty-four participants were initially enrolled in the study; however, only 24 completed the follow-up assessments within 3-11 months after visit 1. The COVID-19 pandemic adversely affected recruitment efforts and led to the cancellation of several planned follow-up tests. Between visits, there was no significant change in PA levels measured by IPAQ. However, significant improvements were observed in estimated VO_{2peak} (2.4 $mL \cdot kg^{-1} \cdot min^{-1}$, p=0.012) and walking distance (31 meters, p=0.038). Moderate, positive correlations were found between vigorous PA and estimated VO_{2peak} at both visits (Visit 1: rho=0.36, p=0.035; Visit 2: rho=0.51, p=0.01), and between vigorous PA and walking distance at Visit 2 (rho=0.42, p=0.04). Additionally, there were significant correlations between moderate-to-vigorous PA and estimated VO_{2peak} (rho=0.43, p=0.04), and between total PA and estimated VO_{2peak} (rho=0.41, p=0.049) at Visit 2. Even if changes in PA levels, physical function and HRQoL were non-significant, there were positive trends, indicating that our study was underpowered.
Conclusion: Submaximal treadmill fitness testing may enhance estimated VO_{2peak} and walking distance in adolescents with JIA. While no significant changes in PA levels or HRQoL were observed, the positive trends and correlations indicate that fitness testing could be a valuable tool in clinical practice to motivate increased PA.
Disclosure
None declared

PT052

Towards standardized data collection in pediatric antiphospholipid syndrome: a consensus-based core dataset

M. Zajc Avramovič[1], S. Demir[2], E. Sloan[3], J. Pandja Bhatt[4], D. Erkan[5], S. Ozen[6], T. Avcin[1]
[1]Pediatric Allergology, Rheumatology and Clinical Immunology, University Medical Center Ljubljana, Ljubliana, Slovenia, [2]Pediatric Rheumatology, Eskisehir Osmangazi University, Eskisehir, Türkiye, [3]Pediatric Rheumatology, The University of Texas Southwestern Medical Center (UT Southwestern), Texas, [4]Pediatric Rheumatology, AdventHealth for Children, Orlando, [5]Rheumatology, Hospital for Special Surgery, New York, United States, [6]Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye
Correspondence: M. Zajc Avramovič
Pediatric Rheumatology, **23(2):** PT052

Introduction: Pediatric antiphospholipid syndrome (APS) is a rare, thrombo-inflammatory autoimmune disease characterized by thrombosis and nonthrombotic manifestations in patients with persistent positive antiphospholipid antibodies, with clinical features that differ from adult APS. Current APS classification criteria are derived from adult data, and pediatric APS data collection is fragmented and inconsistent between institutions and regions.
Objectives: This project aims to develop an international consensus that defines critical data fields to facilitate international registry-based pediatric APS research.
Methods: Data fields were compared from existing International Ped-APS Registry and CARRA Registry, which identifies patients with APS within the lupus cohort. The 2023 ACR/EULAR APS classification criteria were reviewed and systematic literature review of pediatric APS between 2003-2024 was conducted to identify potential data elements for future registries (Figure 1). Delphi surveys were completed by physicians with APS experience, which included pediatric rheumatologists, med/peds rheumatologists, adult rheumatologists, and pediatric hematologists representing 12 countries and two caregiver representatives. Items were scored from 1 (not important) to 9 (very critical). Consensus "in" was reached for core items scored > 7 by > 70% of experts, as well as all items included in the adult 2023 APS Classification Criteria. Consensus "out" was reached for items with average score < 5. The remaining items were labeled "equivocal" for voting at a hybrid consensus meeting. During the meeting, items with ≥80% agreement were included in the final dataset (either Core or Expanded), and items failing to meet consensus were either excluded or revised and re-evaluated when appropriate. Items scoring ≥6 were eligible for either Core or Expanded datasets. Items scoring ≥ 5 but < 6 were only voted upon for the Expanded dataset.
Results: A total of 32 experts completed the first-round Delphi survey, and 26 participated in the second round. Two caregiver representatives completed a modified version of the survey. Of 316 total candidate items, 72 reached consensus "in," 87 were rated "out," and 157 were classified as "equivocal." These equivocal items were reviewed and voted upon by 19 experts during a hybrid consensus meeting. Based on >80% agreement thresholds, additional items were included. Ultimately, a final dataset comprising **60 core** and **22 expanded data elements** was established. These were categorized under **18 thematic domains**, including demographics, thrombotic and non-thrombotic features, laboratory parameters, comorbidities, therapies, and outcomes. The resulting dataset reflects both expert consensus and parent perspectives and is intended to support consistent international data collection in future pediatric APS research initiatives.
Conclusion: Through systematic evaluation of existing registries, literature review, and Delphi process, we have identified several critical variables to inform future pediatric APS registries. By leveraging international expertise and integrating it with patient patient perspectives, we are laying a solid foundation for the development of a harmonized dataset to advance pediatric APS research efforts globally.
Disclosure
None declared

PT053

Long-term outcomes and prediction of juvenile idiopathic arthritis-related dentofacial deformity: a 17-year follow-up study in the nordic jia cohort

K. Lindberg Larsen[1,2], P. Stoustrup[3], V. Rypdal[4,5], E. Nordal [4,5], P. Frid[6,7,8], E. Dalen Arnstad[9,10], M. Rygg[9,11], M. Ekelund[12,13], L. Berntson[13], A. Fasth[14], H. Nilsson[15], S. Peltoniemi[16], K. Aalto[17], A. Suomalainen[18], C. Myrup[19], S. Kreiborg[20,21], T. Herlin[1,2], T. Klit Pedersen[3,22], M. Glerup[1,2] on behalf of The Nordic Study Group of Pediatric Rheumatology (NoSPeR)
[1]Department of Pediatrics, Aarhus University Hospital, [2]Institute of Clinical Medicine, [3]Sections of Orthodontics, Department of Dentistry and Oral Health, Aarhus University, Aarhus, Denmark, [4]Department of Pediatrics, University Hospital of North Norway, [5]Department of Clinical Medicine, UIT The Arctic University of Norway, [6]Department of Otorhinolaryngology, Division of Oral and Maxillofacial Surgery, University Hospital of North Norway, [7]Public Dental Service Competence Centre of North Norway, [8]Department of Clinical Dentistry, UIT The Arctic University of Norway, Tromsø, [9]Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, [10]Department of Pediatrics, Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, [11]Department of Pediatrics, St. Olavs Hospital, Trondheim, Norway, [12]Department of Pediatrics, Ryhov County Hospital, Jönköping, [13]Department of Women´s and Children´s Health, Uppsala University, Uppsala, [14]Department of Pediatrics, Sahlgrenska Academy, University of Gothenburg, Gothenburg, [15]Section 3, Department of Orofacial Pain and Jaw Function, Faculty of Odontology, Malmö University, Malmö, Sweden, [16]HUS Inflammation Center, Rheumatology, [17]Paediatric Research Center, New Children's Hospital, [18]HUS Medical Imaging Center, Department of Radiology, Helsinki University Hospital, University of Helsinki, Helsinki, Finland, [19]Department of Pediatrics, Rigshospitalet, Copenhagen University Hospital, [20]Department of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, [21]Department of Oral and Maxillofacial Surgery, Copenhagen University Hospital Rigshospitalet, Copenhagen, [22]Department of Oral and Maxillofacial Surgery, Aarhus University Hospital, Aarhus, Denmark
Correspondence: K. Lindberg Larsen
Pediatric Rheumatology, **23(2):** PT053

Introduction: Temporomandibular joint (TMJ) involvement in juvenile idiopathic arthritis (JIA) can lead to dentofacial deformities. Early and timely diagnosis remains both urgent and challenging, and predictive markers have not been identified.
Objectives: We aimed to identify predictors of dentofacial deformity in JIA that could inform early intervention and improve long-term outcomes.
Methods: Participants were included from the population-based, Nordic JIA cohort with baseline visits (1997–2000) and 17 years of follow-up. All met the ILAR criteria for JIA. Of the original cohort, 420 were eligible for clinical orofacial and radiographic evaluation. Full-face cone-beam computed tomography (CBCT) scans were used to assess dentofacial morphology. The validated dentofacial deformity index was applied to CBCT scan data to classify dentofacial deformities into four grades: Normal, minor deformity, severe deformity, and very severe deformity. Ordinal regression and cluster analysis (recursive partitioning) were conducted using baseline variables such as gender, age at onset, JIA categories, CRP, height-for-age standard deviation score (height SDS), and weight-for-age standard deviation score (weight SDS) to explore associations with deformity grade.
Results: Of the 420 eligible participants, 245 (58%) underwent full-face CBCT and were included in the present study. The deformity grades were distributed as follows: Normal = 74 (30.2%), minor deformity = 104 (42.9%), severe = 50 (20.4%), and very severe = 16 (6.5%). Cluster analysis showed limited predictive value and failed to classify deformity severity accurately. However, baseline CRP (threshold value = 29 mg/ml), height SDS (threshold value 0.56 SD), and weight SDS (threshold value −0.38 SD) were the most relevant predictors in the cluster analysis. In the ordinal regression, a high height SDS (OR = 0.74, 95% CI [0.59, 0.92], p = 0.009) and high weight SDS (OR = 0.74, 95% CI [0.60, 0.92], p = 0.006) were protective of developing severe deformity. Baseline CRP as a continuous variable (OR = 1.00, 95% CI [0.99; 1.01], p = 0.788) was not significantly associated with deformity grade in the ordinal regression. Dentofacial deformities were found in all JIA categories.
Conclusion: In the Nordic JIA cohort, 27% of patients exhibited severe or very severe dentofacial deformity 17 years after disease onset. Our findings suggest a potential association between baseline height and weight SDS, and the severity of dentofacial deformity, which has not been previously described. Given the limited predictive utility of the cluster analysis applied, our findings emphasize the importance of regular orofacial assessments for all JIA patients, regardless of their JIA categories, to enable early detection and intervention.
Disclosure
None declared

PT054

Gaps in transitional care for young adults with chronic arthritis: insights from german health insurance data

F. Milatz[1,2], M. Niewerth[1], U. Marschall[3], I. Liedmann[1], N. Grösch[1], C. Sengler[1], G. Erbis[4], I. Foeldvari[5], S. Hansmann[4], A. Maier[6], C. Reiser[4,7], E. Seipelt[8], S. Tatsis[9], A. Wörner[10], K. Mönkemöller[11], J. Klotsche[1], S. Schalm[12], K. Minden[1,2]
[1]German Rheumatology Research Center, [2]Charité - Universitätsmedizin Berlin, Berlin, [3]BARMER Health Insurance, Wuppertal, [4]Universitätsklinikum Tübingen, Tübingen, [5]Hamburger Zentrum Kinder- und Jugendrheumatologie, Hamburg, [6]St. Josef Stift Sendenhorst, Sendenhorst, Germany, [7]LKH Bregenz, Bregenz, Austria, [8]Immanuel Krankenhaus Berlin, Berlin, [9]Kath. Marienkrankenhaus Hamburg, Hamburg, Germany, [10]Universitäts-Kinderspital beider Basel, Basel, Switzerland, [11]Kliniken der Stadt Köln, Köln, [12]Rheumatologie im Zentrum, München, Germany
Correspondence: F. Milatz
Pediatric Rheumatology, **23(2):** PT054

Introduction: The transition from pediatric to adult rheumatology care presents a vulnerable phase for young people with chronic inflammatory arthritis. Disruptions during this process may compromise therapeutic continuity, health status, and long-term participation. Despite growing awareness of transition challenges, real-world data on care continuity and psychosocial outcomes remain limited.
Objectives: To examine healthcare utilization, treatment continuity, and psychosocial well-being among young adults with juvenile-onset arthritis following pediatric rheumatology care.
Methods: A cross-sectional survey was conducted in 2022 among individuals aged 20–25 years insured by BARMER, one of the largest statutory health insurance funds in Germany. Eligible participants had ICD-10 diagnoses of juvenile idiopathic arthritis, rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis. Self-reported data included healthcare access, treatment status, health status, pain (numeric rating scale 0–10), and mental well-being (WHO-5). These data were linked to retrospective claims data covering the years 2018 to 2021 to assess healthcare utilization and antirheumatic medication use.
Results: Among 2,144 eligible individuals, 723 responded, including 325 aged 20–25 years. Of 269 respondents with a history of pediatric rheumatology care, 50% reported no longer receiving specialist follow-up. Reported barriers included limited access (16%), time constraints (12%), treatment fatigue or refusal (8%), and uncertainty or fear (5%). Compared to those in specialist care, patients without specialist follow-up were less frequently employed (37% vs. 44%), had higher sick leave rates (40% vs. 32%) and more sick days annually (28.4 vs. 18.7). DMARD therapy remained stable in the specialist care group (63%) but declined in the group without specialist follow-up (30% to 18%). Among those with polyarthritis, only 19% of those without specialist care received DMARDs. In contrast, 72% of their counterparts with specialist care did. Mental well-being was lower among patients without specialist care, with 34% scoring ≤28 on the WHO-5, compared to 19% among those receiving specialist care.
Conclusion: These findings highlight the importance of structured, multidisciplinary transition models to support continuity of specialist rheumatology care beyond adolescence. Structured transition models and early adult care engagement may reduce treatment discontinuities, improve psychosocial health, and safeguard participation in education and employment for young adults with chronic arthritis.
The InfoTrans project is funded by the Innovation Fund of the Federal Joint Committee (G-BA), grant number 01VSF20012.
Disclosure
None declared

PT055

Comparable efficacy of FK-tocilizumab and Reference tocilizumab in Covid-19 vaccinated and unvaccinated rheumatoid arthritis patients

F. de Benedetti[1], K. Klama[2], A. Illes[3], P. Baker[3], M. Romanova Michailidi[3], A. Zubrzycka-Sienkiewicz[4]
[1]Ospedale Pediatrico Bambino Gesù, Rome, Italy, [2]Solumed Clinical Research Center, Poznan, Poland, [3]Fresenius Kabi Swiss BioSim GmbH, Eysins, Switzerland, [4]Reumatika - Centrum Reumatologii, Warsaw, Poland
Correspondence: F. de Benedetti
Pediatric Rheumatology, **23(2):** PT055

Introduction: Biosimilars offer comparable efficacy and safety to their originators, thereby improving patient access to affordable treatments. This is particularly important in pediatric patients, where early treatment accessibility and continuity are crucial. FK-Tocilizumab (FK-toci) is the first tocilizumab biosimilar approved by both FDA and EMA for the treatment of autoimmune diseases including moderate-to-severe Rheumatoid Arthritis (RA) and Juvenile Idiopathic Arthritis. Therapeutic equivalence of FK-toci to
Reference tocilizumab was shown in subjects with moderate to severe RA in APTURA-1, a randomized, double blind efficacy study. Since its launch in 2024, FK-toci has accumulated ~50,000 patient-treatment-years of exposure with no new safety information affecting its benefit-risk balance.
Objectives: As vaccination is a key consideration in immunomodulatory therapies, especially in pediatric populations, this analysis assessed the efficacy of FK-toci in the subgroup of COVID-19 vaccinated and unvaccinated RA patients included in the APTURA-1 study.
Methods: Subjects (M/F) over 18 years with moderate to severe RA were randomized to subcutaneous (SC) injections of 162 mg FK-toci or Reference tocilizumab (originator) for 24 weeks (W). Randomization was stratified by previous exposure to biological treatment for RA (yes/

no). A cohort of patients were switched from the originator to FK-toci at W24. The primary objective was to demonstrate therapeutic equivalence, with 90% and 95% CIs for the difference in DAS28-ESR LS mean change from baseline at W24 falling within predefined equivalence intervals ([−0.6, 0.5] and [−0.6, 0.6], respectively). ACR20 response at W24 was an important secondary endpoint. Both endpoints were also analyzed by COVID-19 vaccination status.
Results: 604 patients were randomized, 302 patients on FK-toci and 302 on originator; 68 (38 and 30, respectively) were COVID-19 vaccinated. Gender, race, ethnicity, age and disease characteristics were all well balanced at baseline. In total, 58/68 (85.3%) of vaccinated patients reached ACR20 at W24, versus 442/536 (82.5% for subjects not vaccinated against COVID-19, with similar ACR20 response rates in the two treatment groups. Similar reduction of DAS28-ESR at W24 was observed in both subgroups and in the two treatment groups. Overall COVID-19 vaccination had no effect on occurrence of adverse events over the 24 weeks: 63% vs 56.7% vaccinated subjects had at least one AE in FK-toci and
Reference group respectively – and 66% vs 64% in non-vaccinated subjects.
Conclusion: Subgroup analyses by COVID-19 vaccination status support the therapeutic equivalence between FK-tocilizumab and originator, with no clinically meaningful differences in efficacy observed relative to vaccination status. These findings support the consistency of FK-tocilizumab's performance across patient subgroups and are relevant to its use in pediatric populations.
Trial registration identifying number: Trial registration : NCT04512001
Disclosure
None declared

PT056

The pediatric rheumatology workforce in europe – results from a eular paed rheumafacts survey

D. Foell[1], J. Anton[2] on behalf of EULAR PAED committee
[1]Pediatric Rheumatology, University of Muenster, Muenster, Germany, [2]Pediatric Rheumatology, Hospital Sant Joan de Déu, Barcelona, Spain
Correspondence: D. Foell
Pediatric Rheumatology, **23(2):** PT056

Introduction: EULAR has launched the RheumaFacts initiative to collect data about rheumatic and musculoskeletal diseases (RMDs) and their impact on individuals, society and the health economy across all Europe. RheumaFacts aims at creating a definitive standardized source of information for data-driven advocacy, research, and policy-making to highlight the disease burden, healthcare gaps, and inequalities around RMDs across European and EULAR member countries. This data repository will be based on up-to-date general health and RMD-related information, gathered primarily by the world statistic organizations, and scientific societies at the national levels.
Objectives: The EULAR Paediatric Committee contributed to the RheumaFacts initiative via a survey among pediatric rheumatologists.
Methods: We aimed at identifying experts who represent the field of pediatric rheumatology in respective countries in Europe,
either as officially appointed representative or as recognized leading experts. Via a survey we asked for the number of pediatric rheumatologists who care for children in the different countries. We also gathered information on the training and the recognition of pediatric rheumatology as a subspecialty. Finally, we asked for the actual time and effort spent in the care for children with RMDs (full time, part time approximately 25-75%, or less).
Results: We received data from 31 countries. In 12 countries, the colleagues in the field reported to have an own legal entity that serves as their representation (i.e., a national society of pediatric rheumatology). In 14 countries, the physicians are represented by the "adult" society of rheumatology, while in 5 countries representation is via the society of pediatrics. An official national recognition for pediatric rheumatology as subspecialty exists in 15 of the 31 countries, whereas 17 reported to have a training curriculum. The number of people working in the field in the 31 countries sums up to 1320 physicians, with almost half of them (n=586) being certified pediatric rheumatologist. The full time equivalent of these experts actually spent in the care for children with RMDs sums up to 362 FTE.
Conclusion: The data collected in RheumaFacts will be available to researchers and stakeholders who can advance public health at a European level.
Finding the exact number of pediatric rheumatologists in Europe is challenging. Our survey suggests that there are approximately 600 certified pediatric rheumatologists across Europe, but their training varies substantially. It is a major task for EULAR and PReS to provide guidance and standards.
The European Syllabus for Training in Paediatric Rheumatology Syllabus, approved by the European Academy of Paediatrics - Union Européenne des Médecins Spécialistes (EAP-UEMS) should be the basis for optimized training programs in Europe.
Disclosure
None declared

PT057

Perceptions and attitudes toward biologic therapy among families of pediatric rheumatology patients: a cross-sectional survey study

B. Başer Taşkın[1], A. Doğru[1], M. T. Karadoğan[2], F. Çakmak[2], F. G. Demirkan[3], Ö. Akgün[1], N. Aktay Ayaz[1]
[1]Pediatric Rheumatology, Istanbul Faculty of Medicine, Istanbul University, [2]Pediatric Rheumatology, Basaksehir Cam and Sakura City Hospital, [3]Pediatric Rheumatology, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Türkiye
Correspondence: M. T. Karadoğan
Pediatric Rheumatology, **23(2):** PT057

Introduction: Childhood rheumatic diseases are chronic conditions that require long-term follow-up and may cause both physical and psychosocial challenges. In cases unresponsive to conventional treatments, biologic agents have become effective alternatives. However, treatment success depends not only on pharmacological efficacy but also on the child's and parents' adherence, knowledge, and attitudes toward therapy.
Objectives: This study aimed to assess parents' knowledge, attitudes, emotional responses, challenges, and satisfaction related to their child's biologic treatment using a structured questionnaire.
Methods: The study involved primary caregivers of 61 children on biologic therapy. After informed consent, participants completed a 64-item structured questionnaire covering six main categories with closed-ended, open-ended, and multiple-choice questions.
Results: Among participants, 70.5% were mothers and 65.6% of the children were girls. The most common diagnosis was juvenile idiopathic arthritis (57.4%). The most frequently used biologics were etanercept (34.4%), adalimumab (24.6%), and canakinumab (16.4%), mostly administered subcutaneously (88.5%) and weekly (32.8%). While 42.6% of parents reported sufficient knowledge, 88.5% cited the physician as their main information source, and 90.2% trusted the physician's decision. The most frequently requested topic for clarification was side effects (50.8%). Reported benefits included improved physical functioning (70.5%), school/social participation (55.8%), and family life (55.8%). Nevertheless, 24.6% experienced emotional distress and 50.8% reported feelings of loneliness and indecision. Adherence issues were noted in 14.8%, and 24.6% reported difficulties accessing treatment. Common challenges included injection-related issues (24.6%) and the child's reluctance (21.3%). While 26.2% had attended an informational event, 80.3% were willing to join future sessions.
Conclusion: The findings underscore the need to address both medical and psychosocial aspects of parents' experiences during biologic treatment, supporting a more family-centered approach with structured information and caregiver support.
Disclosure
None declared

References

1. Calvo Penadés I, Moreno Ruzafa E, Calzada-Hernández J, Mosquera Angarita J, López Montesinos B, Bou R, López Corbeto M, Sánchez-Manubens J, González Fernández MI, Carriquí Arenas S, Bittermann V, Estepa Guillén C, Rodríguez Díez L, Iglesias E, Marti Masanet M, LaCruz Pérez L, Peral C, De Lossada A, Valderrama M, Llevat N, Montoro M, Antón J. Real-world psychosocial impact among patients with juvenile idiopathic arthritis and families in Spain. Pediatr Rheumatol Online J. 2024 Nov 26;22(1):102. doi:

https://doi.org/10.1186/s12969-024-01035-6. PMID: 39593042; PMCID: PMC11600913.
2. Lipstein EA, Lovell DJ, Denson LA, Kim SC, Spencer C, Ittenbach RF, Britto MT. High Levels of Decisional Conflict and Decision Regret When Making Decisions About Biologics. J Pediatr Gastroenterol Nutr. 2016 Dec;63(6):e176-e181. doi: https://doi.org/10.1097/MPG.0000000000001425. PMID: 27749390; PMCID: PMC5123667.

PT058

A composite fitness profile in juvenile idiopathic arthritis and familial mediterranean fever compared to healthy peers: fast and fit

A. Albayrak[1,2], N. Arman[3], A. Yekdaneh[1,4], A. Namli Seker[1,5], I. Donmez[6], Y. Acıkgoz[6], K. Ucar[3], F. Cakmak[7], N. Aktay Ayaz[8]
[1]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [2]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [3]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [4]Physiotherapy English Program, Fenerbahçe University, Vocational School of Health Services, Istanbul, [5]Program of Podology, Aydin Adnan Menderes University, Nazilli Vocational School of Health Services, Aydın, [6]Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [7]Department of Pediatric Rheumatology, Basaksehir Cam ve Sakura Hospital, [8]Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Department of Pediatrics, Istanbul, Türkiye
Correspondence: A. Albayrak
Pediatric Rheumatology, **23(2):** PT058

Introduction: Physical fitness (PF) is a key determinant of health outcomes, and its assessment in children and adolescents provides an effective means of estimating overall health status and functional ability (1).
Objectives: The aim of this study was to evaluate the PF profile of patients diagnosed with Juvenile Idiopathic Arthritis (JIA) and Familial Mediterranean Fever (FMF) and to compare the results with healthy peers.
Methods: A total of 343 children and adolescents aged 8–18 years participated in the study (JIA: 117, FMF: 61, Healthy: 166). PF was assessed using FitnessGram tests: Curl-Up Test (CT), Push-Up Test (PT), Trunk Lift Test (TLT), Back-Saver Sit and Reach Test (BSSRT), and the Progressive Aerobic Cardiovascular Endurance Run (PACER), along with estimated VO_2max. Functional capacity was evaluated using the 6-Minute Walk Test (6MWT), 30-Second Sit-to-Stand Test (30SST), and 10-Stair Climb Test (10SCT). Group comparisons were performed using ANOVA, post-hoc Tukey, and ROC analysis. A Composite Fitness Score (CFS) was calculated by averaging the z-scores of ten fitness and functional capacity tests. Each raw score was standardized and averaged to generate a single composite indicator of physical fitness.
Results: The mean ages of participants with JIA, FMF, and healthy controls were 13.19±1.34, 13.52±1.45, and 13.32±1.34 years, respectively. Patients with JIA and FMF had significantly lower PF and functional capacity compared to their healthy peers ($p<0.05$). The 30SST demonstrated the highest discriminative accuracy (AUC = 0.85), PT (AUC = 0.75) and CT (AUC = 0.72) also showed good discriminative value, whereas the 6MWT and BSSRT were less predictive (AUC = 0.67 each). The healthy group had a significantly higher CFS (+0.22) compared to JIA (−0.20) and FMF (−0.23) ($p<0.001$) however, no significant difference was observed between the JIA and FMF ($p>0.05$). According to the Random Forest regression analysis based on participants' CFS scores, PT, BSSRT, and PACER were identified as the most important predictors of PF.
Conclusion: The findings of this study demonstrate that PF and functional capacity outcomes are significantly lower in patients with JIA and FMF, particularly among those with JIA. The primary determinants of PF were identified as upper extremity muscular endurance and strength, flexibility, and aerobic performance. One of the key outcomes of the study is the identification of the 30SST as an excellent potential for rapid fitness screening in adolescents. Furthermore, the incorporation of the PT, BSSRT and PACER into the evaluation process has been shown to be valuable in identifying risk factors and planning of targeted exercise interventions.
This study was supported by Scientific and Technological Research Council of Turkey (TUBITAK) under the Grant Number 121E690.
Disclosure
None declared

Reference
1. Day et al. 2023. NYC FITNESSGRAM:population-level physical fitness surveillance for New York City youth. American Journal of Epidemiology

PT059

Digital home monitoring in patients with juvenile idiopathic arthritis to increase intervals of hospital visits

A. J. Sellies[1,2], J. W. van Straalen[1,2], G. C. de Joode-Smink[1,2], M. J. Doeleman[1,2], M. H. Jansen[1,2], E. van Nieuwenhove[1,2], A. van Royen-Kerkhof[1,2], B. J. Vastert[1,2], N. M. Wulffraat[1,2], S. de Roock[1,2], J. F. Swart[1,2]
[1]Department of Paediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, University Medical Centre Utrecht, [2]Faculty of Medicine, Utrecht University, Utrecht, Netherlands
Correspondence: A. J. Sellies
Pediatric Rheumatology, **23(2):** PT059

Introduction: Children with juvenile idiopathic arthritis (JIA) commonly visit their paediatric rheumatologist at regular standardized intervals, which is costly in time and money for patients, parents/guardians, hospital and other stakeholders.
Objectives: This non-inferior, single-centre study aims to test if JIA patients with inactive disease can safely increase a visit interval by home monitoring disease activity using the EuroQol five-dimensional youth questionnaire with five levels (EQ-5D-Y-5L) and Juvenile Arthritis Multidimensional Assessment Report (JAMAR).
Methods: JIA patients with inactive arthritis from the Wilhelmina Children's Hospital in Utrecht, the Netherlands, skipped one three-monthly control visit and instead completed online EQ-5D-Y-5L and JAMAR questionnaires at home. Patients were included in 2022. Home monitoring questionnaires were evaluated by a research nurse to determine if a short-term control visit at the hospital was necessary. To test non-inferiority, rates of study-wide flares and flares after an actual prolonged visit interval were compared with a historical cohort flare rate and with matched JIA patients using relative risks (RR) with 95% confidence intervals (95% CI) and a non-inferiority margin of 15%. Secondary outcomes were the number of reminders sent for home monitoring, the number of patients that failed to complete questionnaires, rescheduled visits, and patient satisfaction with home monitoring.
Results: A total of 84 patients participated in the study. Seven participants had rescheduled visits before, and eleven after evaluation of the questionnaires. 63 participants completed the six-month visit without returning to the hospital earlier, of whom seven experienced a flare. The study-wide flare rate was 18.5%, compared to a historical flare rate of 18.4% (including non-inferiority margin) and the flare rate after an actual prolonged visit interval within the total study population was 8.6%. In comparison to matched controls, RRs were measured as 0.52 (95% CI: 0.25–1.06) for study-wide flares and 0.86 (95% CI: 0.29–2.54) for flares of patients with a prolonged visit interval. The RR for study-wide flares falls within the boundaries for non-inferiority, whereas the study was underpowered for the RR for flares after a prolonged visit interval. Two participants failed to complete home monitoring despite two reminders. 92% of participants who completed the patient satisfaction questionnaire indicated they would be willing to skip a hospital visit using home monitoring more often.
Conclusion: The findings indicate no clear evidence that replacing one hospital control visit with home monitoring poses a significant risk for JIA patients with inactive disease. There was a high questionnaire response, although reminders and rescheduled visits were necessary. Patient satisfaction with home monitoring was high.
Trial registration identifying number: The THUIS study is registered at ClinicalTrials.gov: NCT05603286
Disclosure
None declared

PT060

Tofacitinib and baricitinib in the treatment of juvenile idiopathic arthritis(JIA)- effectiveness and safety data from the biker-registry

A. Zimmer[1], A. Klein[1], N. Brueck[2,2], J. Kuemmerle-Deschner[3], F. Dressler[4], J.-P. Haas[5], C. Hillekamp[1], A. Hospach[6], J. Klotsche[7], K. Minden[8], R. Trauzeddel[9], W. Daniel[10], G. Horneff[1]
[1]Pediatric Rheumatology, Asklepios Hospital for Children, Sankt Augustin, [2]Pediatric Rheumatology, Uniklinik Dresden, Carl Gustav Carus, Dresden, [3]Pediatric Rheumatology, Uniklinik Tübingen, Tübingen, [4]Pediatric Rheumatology, Medizinische Hochschule Hannover, Hannover, [5]Pediatric Rheumatology, Deutsches Zentrum für Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Garmisch-Partenkirchen, [6]Pediatric Rheumatology, Olgahospital, Stuttgart, [7]Pediatric Rheumatology, Deutsches Rheuma Forschungszentrum, [8]Pediatric Rheumatology, Kinderklinik der Charité, Campus Virchow, [9]Pediatric Rheumatology, Helios Klinikum Berlin-Buch, Berlin, [10]Pediatric Rheumatology, Sankt Josef Stift, Sendenhorst, Germany

Correspondence: A. Zimmer
Pediatric Rheumatology, **23(2):** PT060

Introduction: Tofacitinib and baricitinib are oral Januskinase inhibitors (JAKi) recently approved for polyarticular juvenile idiopathic arthritis (JIA), juvenile psoriatic arthritis, and (for baricitinib) enthesitis related arthritis. Due to limited long-term data, the German BiKeR-registry monitors their safety and effectiveness in clinical practice.
Objectives:
To assess long-term safety, tolerability, and effectiveness of tofacitinib and baricitinib in JIA-patients.
Methods: JIA-patients aged 2–18 treated with tofacitinib or baricitinib were included. Baseline data and disease activity at 3, 6, 12, and 24 months were evaluated. Safety was assessed via adverse events (AE), focusing on serious infections, zoster/opportunistic infections, thrombosis, and therapy discontinuation.
Results: In total, 100 patients were exposed to tofacitinib (107.5 patient years (PY)) and 28 to baricitinib (42.9 PY). In the tofacitinib-cohort the mean JADAS 10 dropped from 10.8 to 5.6/4.3/3.9/1.8 after 3/6/12/24 months of therapy; the mean CHAQ DI from 0.6 to 0.4/0.3/0.2/0.3; the mean physician global assessment of disease activity score from 36.9 to 12.9/10.9/9.8/4.3 and the mean active joint count from 4.1 to 2.3/0.6/1.0/0.2;
PED ACR90 score was met by 17.4/35.3/40.6/44.4 % and ACR defined inactive disease by 27.1/34.7/51.4/55.6 % of patients. Safety data showed 113 total AE (incl. 1 SAE) resulting in an AE rate of 105.1/100PY (95%CI 87.4-126.4). 35 % of patients discontinued therapy, in mostly due to lack of efficacy (24%).
In the baricitinib-cohort, after 3/6/12/24 months of therapy the mean JADAS 10 dropped from 14.7 to 8.0/4.8/6.0/1.7; the mean CHAQ DI from 0.7 to 0.4/0.3/0.2/0.4; the mean physician global assessment of disease activity score from 41.1 to 17.3/13.1/7.9/0.6 and the mean active joint count from 7.1 to 2.7/1.5/1.6/0;
PED ACR90 score was met by 8.3/21.4/27.3/42.9 % and ACR inactive disease by 18.2/42.9/36.4/100 % of documented patients. Safety data showed 36 total AE (1 SAE) resulting in an AE rate of 84.0/100PY (95%CI 60.6-116.4). 25 % of patients discontinued therapy, mostly due to lack of efficacy (7.1%).
There were no reported cases of serious or opportunistic infections, herpes zoster reactivation or thrombosis in both cohorts.
Conclusion: - Tofacitinib and baricitinib showed good therapeutic response despite often prior inadequate response/intolerance to conventional synthetic or biological DMARDs.
- No new safety signals were identified.
- No cases of serious or opportunistic infections, herpes zoster reactivation or thrombosis were reported in both cohorts.
- Numbers are still limited, enrolment in this ongoing registry is therefore highly appreciated
Disclosure
A. Zimmer Grant/Research Support with: Travel grants: Novartis, Lilly, Speaker Bureau with: Speakers bureau: Lilly, Glaxo-Smith-Kline, A. Klein Speaker Bureau with: Speakers fee: Novartis, Lilly, N. Brueck Consultant with: Advisory Board Fresenius, Kabi, Speaker Bureau with: honorary fee Chougai Pharma, J. Kuemmerle-Deschner: None declared, F. Dressler Consultant with: advisory Boards: Novartis and Mylan, Speaker Bureau with: speakers bureau: Abbvie, Novartis, Pfizer,, J.-P. Haas: None declared, C. Hillekamp: None declared, A. Hospach Consultant with: Consulting fees: Novartis, SOBI, Speaker Bureau with: Speakers bureau: Novartis and SOBI, J. Klotsche: None declared, K. Minden Speaker Bureau with: honoraria from Amgen, Biogen, gsk, Novartis and medac, R. Trauzeddel: None declared, W. Daniel Grant/Research Support with: Novartis, Roche, Pfizer, Abbvie, Speaker Bureau with: received honorary fees from Novartis, Pfizer, Abbvie, MEDAC, Roche, and Sobi, G. Horneff Grant/Research Support with: Grants Novartis, MSD, Roche, Grant/research support from: Pfizer, Roche,MSD, AbbVie, Chugai, Novartis, Consultant with: Advisory Speaker: Pfizer, Novartis, Sobi; Consultant MSD, Lilly, Speaker Bureau with: Speakers bureau: Pfizer, Roche, MSD, Sobi, GSK, Sanofi, AbbVie, Chugai, Bayer, Novartis,

Reference

1. Wallace CA, Giannini EH, Huang B, Itert L, Ruperto N. American College of Rheumatology provisional criteria for defining clinical inactive disease in select categories of juvenile idiopathic arthritis. Arthritis Care Res (Hoboken). 2011;63(7):929-936.

PT061

Jak-inhibitors safety and efficacy in a group of patients with autoinflammatory diseases (AIDS): single center experience

Z. Nesterenko, V. Burlakov, N. Kuzmenko, A. Mukhina, Y. Rodina, A. Shcherbina
Immunology, Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation
Correspondence: Z. Nesterenko
Pediatric Rheumatology, **23(2):** PT061

Introduction: AIDs are a group of diseases caused by genetic or multifactorial defects of the innate immune response mechanisms and characterized by systemic inflammation and a plethora of manifestations, that represent a significant therapeutic challenge
Objectives: To analyze response to treatment with JAK-inhibitors (JAKinibs) in a group of patients with AIDs
Methods: We retrospectively analyzed data of 48 patients (24-females) treated with JAKinibs at our Center in 2014-2025.
The forms of AIDs included: type I Interferonopathies - 14, genetically undefined AIDs –13, adenosine deaminase 2 deficiency (DADA2) – 5, PSTPIP1-associated syndrome (PAID) - 4, SAMD9 deficiency - 2, SOCS1 haploinsufficiency – 2, SAMD9L deficiency - 1, A20 haploinsufficiency (HA20) - 1, proteasome-associated autoinflammatory syndrome (PRAAS) – 1, IL-18–mediated PAP and recurrent MAS –1, NLRP1- associated autoinflammation with arthritis and dyskeratosis (NAIAD) – 1, RELA haploinsufficiency –1, NEMO-NDAS – 1, C1q deficiency – 1.
JAKinibs were used as monotherapy in 19 cases, and in combination with other immunosuppressive therapy (steroids, anti-IL1, anti-TNFα and others) - in 29. Before initiation of JAKinibs therapy, 27 patients received therapy with other immunosuppressive drugs which was not effective
Results: Median age of onset of any disease symptoms was 0.1 years (range 0; 16). Median age at diagnosis was 3 years (range 0; 17), with the mean diagnostic delay of 3.7 years.
24 patients had autoinflammatory, 22 – autoinflammatory and hematological and 2 - hematological manifestations.
Tofacitinib was used in 32/48 cases, and ruxolitinib - in 16/48. Average initial dose was 0.9±0.2 mg/kg. Median duration of therapy – 3.0 years (0.3; 10.0). Median age of initiation of therapy – 5.0 years (0.5; 17.0).
JAKinibs therapy led to a complete remission in 23/48 cases, partial remission in 20/48, and had no effect in 5/48.
Side effects that were attributed to JAKinibs were noted in 8/48 patients and included infections in 5, lymphopenia in 2, hepatotoxicity in 1, none of them were severe and led to discontinuation of treatment.
Conclusion: Based on our experience JAKinibs are effective and safe in a variety of AIDs
Disclosure
None declared

PT062

Predictive factors for therapeutic response and cluster analysis in syndrome of undifferentiated recurrent fever (SURF)

S. Palmeri[1,2], M. Ponzano[3], G. Recchi[2], C. Conti[1,2], S. La Bella[2], D. Sutera[2], M. Bustaffa[2], C. Matucci-Cerinic[1,2], R. Bertelli[4], F. Penco[2], I. Prigione[2], R. Papa[2], I. Ceccherini[5], S. Volpi[1,2], R. Caorsi[1,2], M. Gattorno[2]
[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, [2]Rheumatology and Autoinflammatory Diseases Unit, IRCCS Istituto Giannina Gaslini, [3]Department of Health Sciences (DISSAL), University of Genoa, [4]Laboratory of Human Genetics, [5]Laboratory of Genetics and Genomics of Rare Diseases, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: S. Palmeri
Pediatric Rheumatology, **23(2):** PT062

Introduction: Syndrome of Undifferentiated Recurrent Fever (SURF) defines a group of patients with recurrent fevers lacking a clear monogenic cause. Despite clinical similarities to Familial Mediterranean Fever (FMF) and frequent colchicine responsiveness, no causative mutations are found, even with next-generation sequencing. (1) Recent studies suggest SURF may represent a distinct autoinflammatory entity, with unique inflammatory features and altered pyrin inflammasome activation. (2, 3, 4) However, its clinical spectrum, therapeutic response predictors, and optimal management remain poorly defined.
Objectives: To study a homogeneous cohort of SURF patients longitudinally, differentiate their phenotype from other recurrent fevers, evaluate their response to colchicine, identify factors linked to colchicine resistance, and assess the efficacy of interleukin-1 (IL-1) inhibitors.
Methods: A longitudinal study was conducted on 101 SURF patients, excluding those with Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical adenitis (PFAPA), Familial Mediterranean Fever (FMF), and other known monogenic systemic autoinflammatory diseases (SAIDs). Demographic, clinical, and therapeutic data were analyzed to identify predictors of colchicine response and define subgroups using cluster analysis.
Results: The predominantly European cohort had a median diagnostic delay of 2.6 years. Less than 20% had a family history of recurrent fever. Common symptoms included arthralgia, abdominal pain, and myalgia, while PFAPA-like features (lymphadenopathy, tonsillitis, oral aphthae) were observed in one-third of cases, sporadically. Colchicine was effective in nearly half of the patients, but resistance was linked to PFAPA-like symptoms and prolonged fever. Tonsillectomy was ineffective. Multivariate analysis identified aphthous stomatitis as a predictor of colchicine inefficacy. IL-1 blockade showed benefits in refractory cases, with anakinra having a better response than canakinumab. Cluster analysis revealed three distinct subgroups with varying symptoms and colchicine responses.
Conclusion: These findings offer new insights into SURF, highlighting predictors of colchicine resistance and supporting IL-1 blockade efficacy. Cluster analysis suggests heterogeneity within SURF, emphasizing the need for refined diagnostic criteria and personalized treatment strategies.
Disclosure
S. Palmeri: None declared, M. Ponzano: None declared, G. Recchi: None declared, C. Conti: None declared, S. La Bella: None declared, D. Sutera: None declared, M. Bustaffa: None declared, C. Matucci-Cerinic: None declared, R. Bertelli: None declared, F. Penco: None declared, I. Prigione: None declared, R. Papa: None declared, I. Ceccherini: None declared, S. Volpi Consultant with: Boehringer, Speaker Bureau with: Speaker fee from SOBI, R. Caorsi Consultant with: SOBI, M. Gattorno Consultant with: Novartis, Sobi, Fresenius Kabi, Kiniksa, Speaker Bureau with: Novartis, Sobi, Fresenius Kabi, Kiniksa

References

1. Papa R, Penco F, Volpi S, Sutera D, Caorsi R, Gattorno M. Syndrome of Undifferentiated Recurrent Fever (SURF): An Emerging Group of Autoinflammatory Recurrent Fevers. J Clin Med. 2021 May 3;10(9):1963. 2. Luu I, Nation J, Page N, Carvalho D, Magit A, Jiang W, et al. Undifferentiated recurrent fevers in pediatrics are clinically distinct from PFAPA syndrome but retain an IL-1 signature. Clin Immunol. 2021 May;226:108697.
3. Macaraeg M, Baker E, Handorf E, Matt M, Baker EK, Brunner H, et al. Clinical, Immunologic, and Genetic Characteristics in Patients With Syndrome of Undifferentiated Recurrent Fevers. Arthritis Rheumatol. 4. Palmeri S, Penco F, Bertoni A, Bustaffa M, Matucci-Cerinic C, Papa R, et al. Pyrin Inflammasome Activation Defines Colchicine-Responsive SURF Patients from FMF and Other Recurrent Fevers. J Clin Immunol. 2024 Jan 17;44(2):49.

PT063

Risk assessment for pediatric rheumatic diseases in children with a history of kawasaki disease: a long-term retrospective comparative big data cohort study

R. Kasem Ali Sliman, M. Hamad Saied
Pediatrics, Carmel medical center, Haifa, Israel
Correspondence: R. Kasem Ali Sliman
Pediatric Rheumatology, **23(2):** PT063

Introduction: Kawasaki disease (KD) is an acute systemic vasculitis predominantly affecting children under 5 years old. Although primarily known for its cardiac complications, the long-term immune-related outcomes remain poorly understood. Recent evidence suggests a potential link between KD and subsequent development of autoimmune conditions, possibly due to immune dysregulation and Th1/Th2 cytokine imbalance.
Objectives: To assess the long-term risk of pediatric rheumatic diseases in children with a history of KD compared to the general pediatric population.
Methods: This comprehensive 20-year retrospective cohort cohort study analyzed Clalit Health Services data in Israel between 2002-2022. KD patients (N=2126) were compared with matched controls (N=10630) with follow-up assessments conducted at multiple intervals (2, 5, 10, 15, and 20 years). Primary outcomes included juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and Henoch-Schönlein purpura (HSP) development.
Results: Children with KD demonstrated a significantly higher risk of developing pediatric rheumatic diseases compared to controls. JIA incidence was markedly elevated at 2 years (117.83 vs. 9.41 per 100,000 person-years; HR 12.51, 95% CI: 2.43-64.50, p=0.003), with this significance persisting throughout the 20-year follow-up (HR 4.38, 95% CI: 1.59-12.09, p=0.004). SLE showed consistently significantly higher incidence from early follow-up (HR 15.01, 95% CI: 1.56-144.30, p=0.019) at 2 years, through 15 years (HR 5.01, 95% CI: 1.01-24.80, p=0.049), though not at 20-years. HSP risk was elevated at 2 years (HR 5.01, 95% CI: 1.45-17.30, p=0.011), with an approximately two-fold increased risk thereafter, without statistical significance.
Conclusion: Our findings reveal a crucial message for clinicians caring for children with KD: the battle doesn't end when the fever subsides. These children face significantly higher risks of developing pediatric rheumatic diseases, with JIA risk up to 12.5 times higher at 2 years post-diagnosis and consistently elevated through 20 years of follow-up. SLE risk was significantly higher up to 15 times at early follow-up and 5 at 15 years. Additionally, we observed a significant initial five-fold increased risk of HSP at 2 years, with a persistent approximately two-fold elevated risk thereafter. Our findings support a paradigm shift in post-KD care that extends beyond traditional cardiac monitoring to include systematic screening for pediatric rheumatic diseases in susceptible children, particularly during the first decade following diagnosis.
Disclosure
None declared

PT064

Relationship among a pediatric-specific ultrasound scoring system for the evaluation of arthritis and biologic markers of inflammation

P. Vega-Fernandez[1], K. Rogers[1], M. Quinlan-Waters[1], J. Huggins[1], D. Lovell[1], S. Angeles-Han[1], H. Brunner[1], S. Thornton[1], A. Cassedy[2], T. V. Ting[1]
[1]Rheumatology, [2]Biostatistics, Cincinnati Children's Hospital Medical Center, Cincinnati, United States
Correspondence: P. Vega-Fernandez
Pediatric Rheumatology, **23(2):** PT064

Introduction: Musculoskeletal ultrasound (MSUS) is a point-of care instrument that is increasingly being utilized for the evaluation of joint inflammation in children with juvenile idiopathic arthritis (JIA). To provide objective assessments of arthritis, reliable and validated MSUS scoring systems are needed

Objectives: Evaluate the construct validity of a pediatric-specific MSUS scoring system in relation to biologic markers of inflammation assessed in serum and synovial fluid (SF).
Methods: Children with JIA presenting to Cincinnati Children's Hospital Rheumatology clinics and able to tolerate a MSUS were eligible for this study. During a study visit, clinical information including the clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS-10), serum, SF -following a clinically indicated arthrocentesis-, and MSUS images were collected. MSUS examination of 10 joints (bilateral wrist, knee, ankle, 2nd and 3rd MCPs) was performed by MSUS-expert pediatric rheumatologist. B-mode and Power Doppler (PD) mode MSUS images were scored by pediatric MSUS experts using a reliable joint-specific semiquantitative MSUS scoring system (MSUS-10, graded 0-normal to 3-severe). Synovitis on MSUS was defined as MSUS findings of grades >=2. *MSUS-10 count* resulted from the sum of the positive MSUS joints for synovitis (*MSUS-10 count* range 0-10). SF was collected from a subset of participants that received a clinically indicated knee joint injection after MSUS of the knee (MSUS-knee) was completed. MSUS-knee score (range 0-6) assess severity of knee joint recess distention at 3 different anatomic locations. To evaluate the association of MSUS findings with biomarkers of inflammation, the following biomarkers in serum and SF were measured: TNFR1, IL-6, IL-10, MCP-1, ANG-1, ANG-2, MMP-2, MMP-8, CCL18, CCL20, IFNg, IL-17a, IL-2Ra, IL-23, IL-18, resistin, CXCL9, VEGF, TIMP-1 by Luminex, and S100A12, S100A8/A9 by ELISA. Descriptive statistics were done. Spearman correlation (r_s) was used to assess the relationship between MSUS, clinical variables, and biomarkers.
Results: Clinical, MSUS-10, and serum samples were collected in 50 children with polyarticular-course JIA (pJIA) [mean age 14.2 (SD 3.3)]. Their median cJADAS score was 2.5 (IQR 0.5-8.5). MSUS-10 count was 0 in 25% of the children while 17% of them had a MSUS-10 count >=4. No significant correlations were noted between the MSUS-10 count and serum biomarkers. Nevertheless, Ang-1 and IL-17a were found to be significantly elevated in children with no active synovitis on the MSUS-10 examination (MSUS-10 count of 0) when compared to children with MSUS-10 count >=4 (p-value 0.022 and 0.016, respectively).
A total of 28 children [mean age 11.8 (SD 5.60)] with JIA (oligoarticular JIA 54%, pJIA 32%) contributed 32 SF samples. MSUS-knee score median was 5 (IQR 4-6). MSUS-knee score was <=4 in 37% of the knees while 31% had a score of 6 (severe findings of MSUS synovitis). Moderate to strong associations between the MSUS-knee score and Ang-2 [0.40 (0.06-0.66), p 0.021], VEGF [0.39 (0.04-0.65), p 0.028], IL-2Ra [0.66 (0.2-0.88), p 0.008] were found. Additionally, Ang-2, VEGF, and IL-2Ra levels were significantly higher in children with MSUS-knee score of 6 when compared to those with a MSUS-knee score <=4 (p-value <0.05). Ang-2, VEGF, and IL-2Ra levels were significantly higher in children with oligoarticular course-JIA when compared with children with pJIA (p-value <0.05).
Conclusion: In JIA, VEGF and Ang-2 have been related to angiogenic activity in synovium, while IL-2Ra has been associated with T and B cell activation. The significantly moderate to strong association between MSUS knee findings of synovitis and local biomarkers of inflammation (i.e., VEGF, Ang 2 and IL-2Ra), found in this preliminary analysis suggest that MSUS can provide an objective assessment of the local inflammatory response. Remarkably, no association between serum biomarkers and MSUS findings of arthritis was found. MSUS has the potential to enhance current clinical standard of care to improve assessment of JIA disease burden.
Trial registration identifying number: n/a
Disclosure
None declared

Reference

1. Vega-Fernandez P, Ting TV, Oberle EJ, et al. Musculoskeletal ultrasound in childhood arthritis limited examination: a comprehensive, reliable, time-efficient assessment of synovitis. Arthritis Care Res (Hoboken) 2023;75(2):401–9

PT065

Association of preliminary musculoskeletal ultrasound activity scores with clinical outcomes of disease activity in juvenile arthritis

P. Vega-Fernandez[1], K. Rogers[1], J. Huggins[1], D. Lovell[1], H. Brunner[1], M. Altaye[2], A. Cassedy[2], T. V. Ting[1]
[1]Rheumatology, [2]Biostatistics, Cincinnati Children's Hospital Medical Center, Cincinnati, United States
Correspondence: P. Vega-Fernandez
Pediatric Rheumatology, **23(2):** PT065

Introduction: Musculoskeletal ultrasound (MSUS) can be used to evaluate the presence and severity of joint inflammation in juvenile idiopathic arthritis (JIA). Two measures have been proposed for the assessment of MSUS-based JIA disease activity using a 10 joint examination protocol: *MSUS10-count* and *MSUS10-score*. The association of the MSUS10-count and MSUS10-score with clinical and patient-reported outcomes (PRO) measures is not known
Objectives: Evaluate the construct validity of the MSUS10-count and MSUS10-score in relation to clinical and PRO measures of disease activity in JIA
Methods: Children with a history of polyarticular JIA (pJIA) presenting to Cincinnati Children's Hospital Rheumatology clinics were enrolled. During a study visit, clinical and PRO data (including the clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS-10) score, the Pediatric Quality of Life Inventory generic core (PedsQL-gen) and rheumatology module (PedsQL-rhe)) and a MSUS of 10 joints (MSUS10, bilateral wrists, knees, ankles, 2nd and 3rd MCPs) were collected. B-mode MSUS images were scored by pediatric MSUS experts, who were blinded to clinical information using joint-specific semiquantitative MSUS scoring systems (range 0-normal to 3-severe). Synovitis on MSUS was defined as B-mode findings of grades ≥ 2 for a given joint. The *MSUS10-score* was calculated from the sum of graded inflammation per joint as per MSUS. To correct for biasing joints with more MSUS views (2 views for MCP, 3 for wrist and knee, and 4 for ankle), the contribution from each joint was weighted equally (range: 0-120). *MSUS10-count* reflects the total number of joints with MSUS-confirmed inflammation (range 0-10). Descriptive statistics were done. Spearman correlation (r_s) was used to assess the relationship between MSUS, clinical, and PRO measures variables.
Results: Sixty children with pJIA were enrolled [mean age 13.6±3.6; median cJADAS 3.5 (IQR: 1-9.5)]. The median *MSUS10-count* was 1 (IQR: 0-3) and the *MSUS10-score* was 6 (IQR: 0-16). PRO suggest moderately reduced quality of life (mean±SD; PedsQL-gen 76.1±18.8; PedsQL-rhe 77.8±15.2). There were moderately strong correlations of *MSUS10-count* with cJADAS (r_s:0.38, p=0.003), PedsQL-gen (r_s:−0.31, p=0.05) and PedsQL-rhe (r_s:−0.38, p=0.016). Similar results were observed for the *MSUS10-score:* cJADAS(r_s:−0.42, p=0.001), PedsQL-gen (r_s:−0.35, p=0.027) and PedsQL-rhe (r_s:−0.41, p=0.008). The correlations between *MSUS10-count* and *MSUS10-score* was 0.90 (p<0.001).
Conclusion: There was moderate association between *MSUS10-count* and the *MSUS10-score* using the MSUS-10 joint examination in pJIA with clinical measures of JIA activity and PRO. This supports the construct validity of both MSUS10 measures (count, score). Further research is needed to delineate the preferred MSUS-based activity measure for JIA.
Trial registration identifying number: N/A
Disclosure
None declared

PT066

Cutaneous manifestations of autoinflammatory bone diseases: a retrospective multicenter study

N. Öner[1], M. Kasap Cüceoğlu[2], E. Kılıç Könte[3], E. Kayhan[4], M. Çakan[5], S. Demir[6], Ö. Baba[7], G. Kılbaş[8], N. Karaçayır[9], M. M. Kaplan[1], E. D. Batu[2], M. Yıldız[3], A. Yekedüz Bülbül[4], Z. Ekici Tekin[1], F. Haşlak[3], A. Paç Kısaarslan[4], Y. Bilginer[2], S. A. Bakkaloğlu[9], S. Yüksel[10], M. Kalyoncu[7], Ö. Kasapçopur[3], S. Özen[2], B. Çelikel Acar[1]
[1]Pediatric Rheumatology, Ankara Bilkent City Hospital, [2]Pediatric Rheumatology, Hacettepe University, Ankara, [3]Pediatric Rheumatology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, [4]Pediatric Rheumatology, Erciyes University Medical Faculty, Kayseri, [5]Pediatric Rheumatology, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, İstanbul, [6]Pediatric Rheumatology, Eskisehir Osmangazi University, Eskişehir, [7]Pediatric Rheumatology, Karadeniz Technical University, Trabzon, [8]Pediatric Rheumatology, Pamukkale University, Denizli, [9]Pediatric Rheumatology, Gazi University, Ankara, [10]Pediatric Rheumatology, Çanakkale Onsekiz Mart University, Çanakkale, Türkiye
Correspondence: N. Öner
Pediatric Rheumatology, **23(2):** PT066

Introduction: Autoinflammatory bone diseases are a group of disorders characterized by sterile osteomyelitis, caused by impaired regulation of the innate immune system [1]. Cutaneous manifestations may include palmoplantar pustulosis, generalized pustulosis, pyoderma gangrenosum, and acne. In addition to cutaneous manifestations, CNO may be coexistent with psoriasis and palmar plantar pustulosis [2]. Cutaneous manifestations are considered to be secondary to increased inflammation. The treatment for cutaneous manifestations is not clear. The management of the disease and local therapies are effective in the treatment of cutaneous manifestations [3].
Objectives: The aim of this study was to describe the cutaneous manifestations of patients with autoinflammatory bone diseases and to evaluate the relationship between cutaneous manifestations, bone involvement, and systemic inflammation in Turkish children.
Methods: This retrospective multicenter study was conducted in 9 pediatric rheumatology centers between the years 2013 and 2023 in patients with a diagnosis of autoinflammatory bone disease with cutaneous manifestations. Demographic data, laboratory findings, cutaneous manifestations, bone involvement, and treatments were recorded.
Results: Two hundred and sixty-nine autoinflammatory bone disease patients were evaluated. Fifty-one patients with cutaneous manifestations [46 CNO and 5 Majeed syndrome] were included in this study. Cutaneous manifestations preceded bone symptoms in 21 (41.2%) patients. The mean diagnostic delay was 16.1 ± 11.7 months in those with cutaneous manifestations and 25.3 ± 9.9 months in those with bone involvement (p=0.02). The most common skin lesions were acne (n=26), pustules (n=23), and papules (n=10). In a comparison of patients with and without acne, patients with acne had more frequent male sex and higher ESR, CRP levels (p=0.01, p=0.03, and p=0.04, respectively). In a comparison of patients with and without pustules, patients with pustules had younger age at symptom onset and age at diagnosis and higher ESR and CRP levels (p=0.04, p=0.04, p=0.04, p=0.02, p=0.03, respectively). In patients with CNO, the mean time to remission was 2.1 ± 0.7 years for cutaneous manifestation and 2.9 ± 1.4 years for bone involvement (p=0.04).
Conclusion: Skin lesions may appear before bone lesions in autoinflammatory bone diseases, serving as an important early warning sign for diagnosis, lesions such as acne and pustules are more common in these conditions and may contribute to the severity of inflammation in autoinflammatory bone diseases.
Disclosure
None declared

References
1. Masters SL, Simon A, Aksentijevich I, Kastner DL. Horror autoinflammaticus: the molecular pathophysiology of autoinflammatory disease (*). Annu Rev Immunol 2009;27:621–68.
2. Giovannelli E, Iacono A, Sprocati M. Osteomielite cronica non-batterica: descrizione di tre casi pediatrici [Chronic nonbacterial osteomyelitis: description of three pediatric cases.]. Recenti progressi in medicina 2021;112(7), 532–7.
3. Koker O, AktayAyaz N. Autoimmune and autoinflammatory diseases with mucocutaneous manifestations: A pediatric rheumatology perspective. International journal of dermatology 2023;62(6),723–36.

PT067

Genome-wide dna methylation analysis in familial mediterranean fever

K. Cetin Gedik[1], D. Casares Marfil[1], B. Baser Taskin[2], E. Kilic Konte[3], S. Sahin[3], M. Bowes[1], F. Guzel[4], M. Romano[5], O. Kasapcopur[3], N. Aktay Ayaz[2], E. Demirkaya[5], A. H. Sawalha[1]
[1]Department of Pediatrics, Division of Pediatric Rheumatology, University of Pittsburgh, Pittsburgh, PA, United States, [2]Department of Pediatrics, Division of Pediatric Rheumatology, Istanbul University Medical School, [3]Department of Pediatrics, Division of Pediatric Rheumatology, Istanbul University Cerrahpasa Medical School, [4]Department of Research and Development, Ant Biotechnology, Istanbul, Türkiye, [5]Department of Pediatrics, Division of Pediatric Rheumatology, Schulich School of Medicine Dentistry, University of Western Ontario, London, Ontario, Canada
Correspondence: K. Cetin Gedik
Pediatric Rheumatology, **23(2):** PT067

Introduction: Familial Mediterranean fever (FMF) is an autoinflammatory disease most commonly associated with biallelic mutations in the *MEFV* gene. Patients carrying the same pathogenic variant in *MEFV* can exhibit a broad spectrum of clinical phenotypes. Identifying factors contributing to this clinical variability is essential for understanding disease mechanisms. DNA methylation has been proposed as a potential modifier of *MEFV* mutations and clinical presentation. However, prior studies exploring this hypothesis included heterogeneous cohorts, lacked genome-wide methylation analyses, and yielded inconsistent findings.
Objectives: We aimed to investigate the role of DNA methylation in FMF using a genome-wide DNA methylation approach.
Methods: We conducted a cross-sectional, genome-wide DNA methylation analysis using whole blood samples from 32 pediatric FMF patients and 16 age- and ethnicity-matched healthy controls (2:1 ratio), all recruited from Istanbul University Medical School. To minimize confounding, we included only patients homozygous for the M694V mutation and from the same geographical region. DNA methylation profiling was performed using the Illumina Infinium MethylationEPIC v2.0 BeadChip array, covering over 930,000 CpG sites. Data analysis was conducted in R (v4.4.0), adjusting for age, sex, and cell composition.
Results: We identified 22 differentially methylated CpG sites in FMF patients compared with healthy controls. Of these, 18 were hypomethylated—including a CpG site within the *MEFV* gene—and four were hypermethylated. Notably, several differentially methylated CpGs were located in genes encoding zinc finger proteins, a family of transcriptional regulators. Of the 22 CpGs, 13 were found on chromosome 16, where *MEFV* is located. Three hypomethylated CpGs were within 1.1 kb of the *MEFV* transcription start site, two of which overlapped with enhancer regions, suggesting a potential regulatory role. Cell-type–specific analysis revealed significant differential methylation in NK cells, $CD8^+$ T cells, and $CD4^+$ T cells in FMF patients compared with controls.
Conclusion: Our findings suggest that DNA methylation changes may contribute to the pathogenesis of FMF. The enrichment of differentially methylated sites near *MEFV* on chromosome 16 and in immune cell subsets supports a role for epigenetic regulation in disease expression. These results highlight DNA methylation as a potential modifier of FMF and a promising target for future biomarker development and personalized therapeutic strategies.
Disclosure
None declared

PT068

The impact of genotype on nutritional status in pediatric fmf patients: linking anthropometrics to mutations and dietary interventions in colchicine-resistant cases

H. M. Kaçmaz, O. Nurlu, A. Girgeç, A. Balat
Pediatric Rheumatology, Gaziantep University, Gaziantep, Türkiye
Correspondence: H. M. Kaçmaz
Pediatric Rheumatology, **23(2):** PT068

Introduction: Familial Mediterranean Fever (FMF) is an autoinflammatory disorder caused by mutations in the *MEFV* gene, characterized by recurrent fever, abdominal pain, and serositis attacks. Chronic inflammation may lead to metabolic disturbances, increasing the risk of growth retardation and malnutrition.
Objectives: This study aims to evaluate the impact of *MEFV* genotypes on malnutrition in pediatric FMF patients by comparing nutritional status and anthropometric measurements across different genotypes. Furthermore, we aim to investigate the relationship between genotype and malnutrition to identify high-risk populations. To date, only a limited number of studies have examined the relationship between genotype and malnutrition in this specific population.
Methods: This study was designed as a cross-sectional, single-center investigation. Patients aged ≤18 years with a diagnosis of familial Mediterranean fever (FMF), who had been followed for at least two years, were included. Demographic data (age, sex, age at diagnosis, disease duration) were recorded from medical files and socioeconomic status was assessed based on family income. Malnutrition was evaluated

using weight and height percentiles, nutritional status, mid-upper arm circumference, height-for-age, and body mass index (BMI) z-scores. The Pediatric Yorkhill Malnutrition Score (PYMS) and Tool for Risk On Nutritional status and Growth in Kids (STRONGkids) scores were compared. Laboratory parameters, including C-reactive protein (CRP) and serum amyloid A (SAA) levels during attack-free periods, were analyzed. Comorbidities, chronic diseases, and known food allergies were documented. Statistical analyses were performed using IBM SPSS version 27.0, with a significance threshold of $p < 0.05$.

Results: A total of 224 patients were enrolled in the study. Female patients accounted for 56.7% (n = 129) of the study cohort.The mean age was 11.9 (7.6–15.0) years; age at diagnosis was 7.0 (4.0–10.0) years; disease duration was 3.0 (2.0–6.0) years; and colchicine treatment duration was 24.0 (12.0–48.0) months. It was determined that 17% (n=38) of the patients had at least one comorbid condition, while 67.4% (n=151) had a families with intermediate socioeconomic status. Among the patients, 46% (n=104) carried at least one M694V mutation in the MEFV gene, and 12.5% (n=28) were diagnosed with colchine resistant FMF. Patients with at least one M694V mutation in exon 10 exhibited significantly higher rates of mild and moderate malnutrition (59.7% and 18.8%, respectively) compared to those without the mutation (16.0% and 5.3%, p<0.001). Additionally, patients with homozygous M694V mutations in exon 10 demonstrated significantly lower mid-upper arm circumference z-scores and height-for-age z-scores (median [IQR]: 2 [2–2] and −1.86 [−2.96–−0.72], respectively) compared to non-carriers (3 [3–3] and −0.72 [−1.24–−0.12], p=0.002 and p=0.004, respectively).The PYMS and STRONGkids total scores were significantly higher in patients with colchine resistant FMF (1.03 ± 0.74 and 0.96 ± 0.42, respectively) than in those without (0.37 ± 0.62 and 0.35 ± 0.49, p<0.001 for both). Furthermore, a statistically significant positive correlation was observed between SAA levels and both PYMS and STRONGkids scores (r=0.204, p=0.002 and r=0.229, p=0.001, respectively).

Conclusion: Children with homozygous M694V mutations exhibit anthropometric measurements significantly associated with malnutrition, suggesting that this genotype may adversely affect growth parameters. These findings underscore the importance of close monitoring and targeted nutritional interventions in this patient population.

Disclosure

None declared

Reference

1. Kişla Ekinci RM, Balci S, Akay E, Doğruel D, Altintaş DU, Yilmaz M. Disease Severity and Genotype Affect Physical Growth in Children With Familial Mediterranean Fever. Arch Rheumatol. 2019;34(3):288-293.

PT069

A comparison between the omeract and carra synovitis ultrasound scoring systems in juvenile idiopathic arthritis: results of a multicentre reliability study

D. Lazarevic[1], S. Sawhney[2], L. Rossi[3], A. Pistorio[4], N. Maronese[5], J. Vojinovic[6], C. Malattia[5]

[1]1Clinic of Pediatrics, University Clinical Center Nis, Nis, Serbia, [2]Pediatric and Adolescent Rheumatology, Sir Ganga Ram Hospital, New Delhi, India, [3]Pediatric Rheumatology, Bicêtre Hospital, Assistance Publique-Hôpitaux de Paris, Le Kremlin Bicêtre, France, [4]Direzione Scientifica, [5]Pediatric Rheumatology, Istituto Giannina Gaslini, Genoa, Italy, [6]Pediatric Rheumatology, University of Nis, Nis, Serbia

Correspondence: D. Lazarevic

Pediatric Rheumatology, **23(2):** PT069

Introduction: Musculoskeletal ultrasound (MSUS) is becoming increasingly prevalent in the assessment of JIA. Semi-quantitative scores have been proposed to quantify synovitis. The OMERACT paediatric US group and the CARRA MSUS Workgroup have proposed different definitions for the individual grades of synovitis, but there is currently no consensus on which scoring system should be used.

Objectives: To compare the reliability of the OMERACT and CARRA synovitis scores.

Methods: Four experienced sonographers analysed 2480 static US images of the following joints: elbow, wrist/hand, knee, tibio-talar (TT), subtalar (ST), talonavicolar (TN) and metatarsophalangeal (MTP). US images were obtained from 40 JIA patients at different ages and disease stages. For each joint recess, synovitis was graded in both B mode and Doppler mode according to the OMERACT and CARRA scoring systems. The inter-reader reliability was analysed using the Cohen kappa coefficient. According to Landis and Koch, kappa values between 0.21- 0.40 were considered fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-1 almost perfect.

Results: The inter-reader reliability for synovitis in B mode was found to be fair for the OMERACT (k 0.37) and moderate for the CARRA (k 0.57) elbow score; moderate for the OMERACT (k 0.43) and substantial for the CARRA (k 0.66) wrist score; moderate for both the OMERACT (k 0.50) and CARRA (k 0.44) dorsal MCP scores; moderate for the OMERACT (k 0.49) and substantial for the CARRA (k 0.72) volar MCP score; moderate for both the OMERACT (k 0.46) and CARRA (k 0.47) PIP scores; substantial for both the OMERACT (k 0.64) and CARRA (k 0.76) knee scores; moderate for the OMERACT (k 0.41) and almost perfect for the CARRA (k 0.81) TT score; fair for the OMERACT (k 0.35) and substantial for the CARRA (k 0.61) ST score; fair for the OMERACT (k 0.33) and moderate for the CARRA (k 0.49) TN score; moderate for both the OMERACT (k 0.41) and CARRA (k 0.46) MTP scores. The inter-reader reliability for synovitis in Doppler mode was found to be substantial for the OMERACT (k 0.61) and fair for the CARRA (k 0.37) elbow score; substantial for both the OMERACT (k 0.78) and CARRA (k 0.63) wrist scores; moderate for the OMERACT (k 0.45) and fair for the CARRA (k 0.38) dorsal MCP scores; moderate for both the OMERACT (k 0.42) and CARRA (k 0.52) knee scores; substantial for both the OMERACT (k 0.65) and CARRA (k 0.69) TT scores; substantial for the OMERACT (k 0.73) and moderate for the CARRA (k 0.55) ST score; moderate for both the OMERACT (k 0.65) and CARRA (k 0.55) TN scores.

Conclusion: The CARRA synovitis score demonstrated greater reliability when using grayscale, while the OMERACT score exhibited higher reliability on pD. These results indicate the need for a collaborative effort to develop a unified synovitis score for utilisation in clinical practice and multicentre studies.

Funding

This study is supported by the Foundation for Research in Rheumatology

Disclosure

None declared

References

1. Rossi-Semerano L et al. Application of the OMERACT synovitis ultrasound scoring system in juvenile idiopathic arthritis: a multicenter reliability exercise. Rheumatology 2021;60:3579-3587.
2.Vega-Fernandez P et al. Musculoskeletal Ultrasound in Childhood Arthritis Limited Examination: A Comprehensive, Reliable, Time-Efficient Assessment of Synovitis. Arthritis Care Res 2023;75:401-409.

PT070

Retrospective analysis of clinical manifestations, genetic findings and treatment strategies in patients with behçet-like symptoms: almost two decades of experience from a tertiary rheumatology centre

A. M. Vrinceanu[1], S. Pastore[2], E. De Martino[2], M. Girardelli[2], A. Tesser[2], V. Boz[2], A. Tommasini[1,2], A. Taddio[1,2]

[1]University of Trieste, [2]Institute for Maternal and Child Health - IRCCS Burlo Garofolo, Trieste, Italy

Correspondence: A. M. Vrinceanu

Pediatric Rheumatology, **23(2):** PT070

Introduction: Behçet's disease (BD) is a chronic, complex inflammatory disorder with unclear multifactorial pathogenesis.[1] Recently, monogenic disorders mimicking BD have emerged, whose identification may improve understanding of pathogenesis and allow tailored therapies.[2,3]

Objectives: To describe the demographic, clinical, genetic features, and treatment approaches in a pediatric cohort with BD-like symptoms.

Methods: A retrospective study of patients with BD-related symptoms (e.g., mucosal ulceration, erythema nodosum) and systemic inflammation, referred to a tertiary center (Jan 2007 - Apr 2025), who underwent genetic testing for monogenic BD-mimics. Data included demographics, clinical details, genetic results (Sanger, panel, WES), laboratory findings (monocyte SIGLEC-1, Interferonic Signature), and treatments. The cohort was grouped by genetics: A (pathogenic variant), B (VUS), C (benign variant or negative). Descriptive statistics were used.
Results: 47 patients (71% female, median age at onset: 4.5 years) underwent genetic analysis. 14 (29.8%) had a pathogenic variant (TNFAIP3, DNASE1L3, PTPN22); 19 (40.5%) had one or more VUS (MRTF-A, IFIH1, SOCS1, RIPK1, MEFV, NLRP3, NCF4, ELF4); 14 (25.5% negative, 4.2% likely benign) formed the rest. Interferon inflammation markers (SIGLEC-1/Interferonic score) were raised in 20% A, 14% B, 17% C. Most common manifestations: oral ulcers (100% A and C, 89% B), genital ulcers (14% A, 0% B, 64% C), arthralgia (14% A, 37% B, 50% C). Ocular involvement in 7% A and C, 5.2% B. Vascular complications only in C (14.2%). Recurrent fever in 14% A, 47% B, 42.8% C; recurrent abdominal pain in 21.4% A, 29.4% B, 35.7% C. Neurological involvement in 7.1% A, 10.5% B, 14.2% C. HLA-B51 positive in 14.2% tested in A, 5.3% B, 28.5% C. Pathergy test negative. Colchicine was the most used treatment. Group A: 85.7% colchicine, 57% conventional immunosuppressant, 42.8% thalidomide, 42.8% biological, 28.6% corticosteroids, 14.2% apremilast. Group B: 87.5% colchicine, 62.5% corticosteroids. Group C: 70% corticosteroids, 50% colchicine, 40% biological, 30% conventional immunosuppressant, 20% apremilast, 10% thalidomide.
Conclusion: Patients with BD-like symptoms and systemic inflammation show a spectrum based on genetic results. Group A (pathogenic variant) often presents only oral ulcers and systemic inflammation. Group C (negative/benign) is more similar to classical BD (more HLA-B51, genital, vascular, ocular, neurological lesions). Group B (VUS) showed intermediate traits. While colchicine was the most used treatment in all groups, classical symptoms correlated with more corticosteroids/thalidomide use, and defined variants with targeted biological therapies.
Disclosure
None declared

References

1. Saadoun D, Bodaghi B, Cacoub P. Behçet's Syndrome. N Engl J Med. 2024 Feb 15;390(7):640-651.
2. Perazzio SF, Allenspach EJ, Eklund KK, et al. Behçet disease (BD) and BD-like clinical phenotypes: NF-κB pathway in mucosal ulcerating diseases. *Scand J Immunol*. 2020; 92:e12973.
3. Burleigh A, Omoyinmi E, Papadopoulou C, Al-Abadi E, Hong Y, Price-Kuehne F, Moraitis E, Titheradge H, Montesi F, Xu D, Eleftheriou D, Brogan P. Genetic testing of Behçet's disease using next-generation sequencing to identify monogenic mimics and HLA-B*51. Rheumatology (Oxford). 2024 Dec 1;63(12):3457-3470.

PT071

Recombinant Dnase1l3 analogue for targeted therapy of monogenic SLE caused by dnase1l3 deficiency

T. Avcin[1], M. Bizjak[1], T. Vesel Tajnsek[1], B. Jenko Bizjan[1], B. Cugalj Kern[1], C. Lood[2], R. Lambalot[3], A. Prasanna[3], G. Gouya[3], A. Hakkim[3], T. A. Fuchs[3], A. Reiff[3]
[1]University Children's Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia, [2]Division of Rheumatology, University of Washington, Seattle, WA, [3]Neutrolis, Inc., Cambridge, MA, United States
Correspondence: T. Avcin
Pediatric Rheumatology, **23(2):** PT071

Introduction: DNASE1L3 deficiency is a rare genetic disorder that typically presents with features of systemic autoimmunity, particularly early onset systemic lupus erythematosus (SLE) and hypocomplementemic urticarial vasculitis syndrome (HUVS). The disease is based on loss-of- function mutations in the endonuclease DNASE1-like 3 (*DNASE1L3*), which is secreted by immune cells and typically degrades chromatin into small fragments and effectively dismantles neutrophil extracellular traps (NETs). The persistence of undigested chromatin and cell-free DNA can result in the formation of autoantibodies such as anti-dsDNA antibodies and is implicated in the development of various autoimmune diseases including SLE. Additionally, the presence of anti-DNASE1L3 autoantibodies detected in patients with idiopathic SLE correlates with disease severity, suggesting that DNASE1L3 plays a critical role in NET associated autoimmune disease.
Objectives: To demonstrate clinical evidence that degrading NETs with a DNASE1L3 analogue can resolve autoimmune symptoms in monogenic SLE caused by DNASE1L3 deficiency.
Methods: Proof-of-concept was established in a 16.5–year-old white male with a homozygous loss-of-function mutation of c.643del consistent with DNASE1L3 deficiency, and severe longstanding treatment refractory monogenic SLE characterized by recurrent disseminated urticarial rashes, autoimmune hepatitis, arthritis, episcleritis, fevers, vomiting, abdominal pain, poor weight gain, malaise, fatigue and marked systemic inflammation since the age of 1.5 years. The patient was refractory to several immunosuppressive drugs including high dose steroids, cyclosporine, azathioprine, cyclophosphamide, MMF, intravenous immunoglobulins, rituximab and tofacitinib. He was treated with 5 weekly intravenous infusions of a recombinant DNASE1L3 analogue (NTR-441, Neutrolis, Inc., Cambridge, MA, USA) as add-on therapy to his background immunosuppression with steroids, antimalarials and tofacitinib.
Results: Within 6 hours after the first infusion of NTR-441, all clinical symptoms completely resolved and did not reoccur during the 14-week post-treatment observation period, except for the rash, which rebounded but subsequently significantly decreased. The patient tolerated the treatment well without severe adverse events except an infusion-related reaction with a concomitant rise in anti-drug antibodies during his fifth infusion. He was subsequently successfully desensitized and continued treatment with a reduced dose and infusion schedule. Analysis of serial blood samples showed a peak of NET-degradation products, i.e., MPO-DNA complexes and small DNA fragments 8 hours after dosing, demonstrating effective degradation of NETs in affected tissues by NTR-441.
Conclusion: We provide the first clinical evidence that the degradation of NETs by a recombinant analogue of endogenous DNASE1L3 can lead to a rapid and sustained resolution of autoimmune symptoms in a patient with monogenic SLE caused by DNASE1L3 deficiency whose condition was refractory to all prior treatments. The temporal association between NET degradation and clinical improvement provides a proof-of-concept that NETs play a central pathogenic role in autoimmune disease.
Disclosure
T. Avcin Consultant with: Octapharma, Speaker Bureau with: Novartis, Octapharma, Pfizer, Takeda, M. Bizjak: None declared, T. Vesel Tajnsek: None declared, B. Jenko Bizjan: None declared, B. Cugalj Kern: None declared, C. Lood Shareholder with: Redd Pharma, Grant/Research Support with: Archon, Boehringer-Ingelheim, Gilead Sciences, Neutrolis, Pfizer, Redd Pharma, Consultant with: Citryll, Redd Pharma, R. Lambalot Shareholder with: Neutrolis, Employee with: Neutrolis, A. Prasanna Shareholder with: Neutrolis, Employee with: Neutrolis, G. Gouya Shareholder with: Neutrolis, Consultant with: Neutrolis, A. Hakkim Shareholder with: Neutrolis, Employee with: Neutrolis, T. Fuchs Shareholder with: Neutrolis, Employee with: Neutrolis, A. Reiff Shareholder with: Neutrolis, Employee with: Neutrolis

PT072

Novel autoantibodies predictive of atherosclerosis progression and statin response in juvenile-onset systemic lupus erythematosus

J. Peng[1,2], P. Dönnes[3], T. McDonnell[1], S. P. Ardoin[4], L. E. Schanberg[5], L. Lewandowski[6] on behalf of APPLE trial investigators and CARRA Registry Investigators, E. C. Jury[1], G. Robinson[1,2], C. Ciurtin[1,2,7]
[1]Department of Ageing, Rheumatology and Regenerative Medicine, Division of Medicine, [2]Centre for Adolescent Rheumatology, Division of Medicine, University College London, London, United Kingdom, [3]Scicross AB, Skövde, Sweden, [4]Department of Pediatrics, Nationwide Children's Hospital, Ohio State University, Ohio, [5]Duke Clinical Research Institute, Duke University School of Medicine, Durham, [6]Lupus Genomics and Global Health Disparities Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, United States, [7]NIHR University College London Hospitals Biomedical Research Centre, University College London Hospital, London, United Kingdom
Correspondence: J. Peng
Pediatric Rheumatology, **23(2):** PT072

Introduction: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (JSLE). There is an urgent need to identify biomarkers that can predict atherosclerosis progression and therapeutic responses, enabling personalised CVD-risk management in JSLE.
Objectives: This study aimed to investigate whether novel autoantibody signatures can predict atherosclerosis progression and atorvastatin response in young people with JSLE.
Methods: We conducted a biomarker discovery study using baseline serum samples from a sub-cohort of the APPLE (Atherosclerosis Prevention in Pediatric Lupus Erythematosus) trial, a large, multi-centre, randomised, double-blind, placebo-controlled trial of atorvastatin versus placebo (1:1) to prevent atherosclerosis progression in JSLE [1]. The trial was conducted across 21 sites in North America. Ninety-four JSLE patients (mean [SD] age 15.3 [2.4] years; 78% female), with matched baseline serum samples and complete longitudinal carotid intima-media thickness (CIMT) measurements over 36 months, were included (45 randomized to the placebo and 49 to the atorvastatin arm). Unsupervised cluster analysis based on CIMT progression over 36 months was used to identify groups with high and low atherosclerosis progression within each treatment arm. Differential autoantibody expression at baseline between these groups was assessed using Empirical Bayes moderated t-tests, and predictive performance was evaluated using logistic regression and receiver operating characteristic (ROC) analysis. Pathway enrichment analysis was performed using Metascape [2].
Results: A total of 579 autoantibodies were identified as true signals in the 94 baseline serum samples analysed. In the placebo arm, six autoantibodies (STK24, RAD23B, HDAC4, STAT4, SEPTIN9 and NFIA) were significantly associated with high versus low CIMT progression over 36 months, achieving a combined area under the curve (AUC) of 87% for distinguishing progression patterns. In the atorvastatin arm, a distinct autoantibody profile was identified that predicted response to statin treatment. Eight autoantibodies (ABI1, ATP5B, CSNK2A2, NRIP3, PRKAR1A, PDK4, BATF and NUDT2) were significantly associated with CIMT progression despite atorvastatin therapy, achieving an exceptional combined AUC of 96%. Enriched pathway analysis of the autoantibody profile in atorvastatin arm revealed lipid-independent mechanisms, potentially contributing to atherosclerosis progression in atorvastatin-treated patients. Based on the predictive models generated from these distinct autoantibody profiles, we can propose a two-step stratification strategy: first, identify JSLE patients at high risk using the placebo atherosclerosis progression signature, and second, stratify them for statin vs. other CVD-risk management strategies based on the statin response signature.
Conclusion: In this biomarker discovery cohort study, novel autoantibody signatures were identified as the first JSLE-specific biomarkers for atherosclerosis progression and prediction of statin response, suggesting possible autoimmune mechanisms underlying the increased CVD-risk associated with JSLE. These findings support the potential application of autoantibody profiling for precision medicine approaches for CVD-risk research and management in JSLE for ultimate patient benefit.
Disclosure
None declared

References

1. Schanberg LE, Sandborg C, Barnhart HX, Ardoin SP, Yow E, Evans GW, et al. Use of atorvastatin in systemic lupus erythematosus in children and adolescents. Arthritis Rheum. 2012;64(1):285-96.
2. Zhou Y, Zhou B, Pache L, Chang M, Khodabakhshi AH, Tanaseichuk O, et al. Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. Nature Communications. 2019;10(1):1523.

PT073

Epigenetic profiling of childhood-onset lupus reveals distinct epigenetic clusters and suggests epigenetic drivers of disease activity

G. Kavrul Kayaalp[1,2], D. Casares-Marfil[2], V. Guliyeva[1], O. Akgün[1], S. Türkmen[3], E. Kılıç Könte[4], S. Sener[5], S. Sahin[4], O. Kasapcopur[4], B. Sözeri[3], S. Sözer Tokdemir[6], S. Ozen[5], N. Aktay Ayaz[1], A. Sawalha[7]
[1]Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Türkiye, [2]Department of Pediatrics, Division of Rheumatology, University of Pittsburgh, Pittsburgh, United States, [3]Department of Pediatric Rheumatology, University of Health Sciences, Umraniye Research and Training Hospital, [4]Department of Pediatric Rheumatology, Istanbul University-Cerrahpaşa, Istanbul, [5]Department of Pediatric Rheumatology, Hacettepe University, Faculty of Medicine, Ankara, [6]Department of Genetics, Istanbul University, Aziz Sancar Institute of Experimental Medicine, Istanbul, Türkiye, [7]Departments of Pediatrics, Medicine, and Immunology, Lupus Center of Excellence, University of Pittsburgh, Pittsburgh, United States
Correspondence: G. Kavrul Kayaalp
Pediatric Rheumatology, **23(2):** PT073

Introduction: Childhood-onset lupus is generally associated with a more severe disease course than adult-onset lupus. DNA methylation alterations are known to play a key role in lupus pathogenesis. While we previously showed that childhood-onset lupus is linked to a higher genetic risk burden compared to adult-onset disease, the epigenetic landscape of childhood-onset lupus remains largely unexplored.
Objectives: This study aimed to characterize DNA methylation changes in childhood-onset lupus, and explore their potential association with clinical features and disease activity.
Methods: A total of 64 patients with childhood-onset lupus and 47 healthy controls were included in this study, along with an independent validation cohort of 38 additional patients. DNA was isolated from PBMCs in the study cohort and from whole blood in the validation cohort to assess DNA methylation using the Infinium MethylationEPIC v2.0 array (Illumina). Quality controls and statistical analyses were performed using *minfi* and *limma* R packages. Methylation differences among groups were tested through linear regression, adjusting for age, sex, medication use, and cell subset compositions. Differences in clinical manifestations were assessed using Fisher's exact tests. Gene ontology enrichment analyses were performed with Metascape and GREAT.
Results: Case-control differential DNA methylation analysis revealed significant hypomethylation in interferon-regulated genes in lupus, such as *DTX3L*, *PARP9*, *IFI44L*, and *MX1*. The enrichment analysis confirmed the presence of type I interferon signature-related biological processes, consistent with adult-onset lupus. Hypomethylation in genes related to B cell activation and cellular senescence was correlated with more active disease, as measured by SLEDAI scores. K-means clustering analysis of patients based on DNA methylation patterns identified 3 distinct lupus clusters. Cluster 1 was characterized by the enrichment of hypomethylated genes involved in cell adhesion and response to growth factor pathways; Cluster 2 exhibited hypomethylation in genes related to regulation of cell differentiation and cell fate determination; and Cluster 3 was enriched in response to oxidative stress and Rap1 signaling pathway in hypomethylated genes. Sex-based analysis revealed hypomethylation in males at sites enriched in immune response pathways, with over 80% of differentially methylated positions in male individuals with childhood-onset lupus validated in the replication cohort.
Conclusion: Childhood-onset lupus is marked by significant hypomethylation in interferon-regulated genes, with DNA methylation changes correlating with disease activity and revealing distinct epigenetic molecular subgroups. Sex-specific patterns further suggest epigenetic contributions to sex-based disease heterogeneity in lupus.
Disclosure
None declared

PT074

Common toll-like receptor 7 variants define disease risk and phenotypes in juvenile-onset systemic lupus erythematosus

F. Sposito[1], Y. Renaudineau[2,3], A. Charras[1], J. Hawkes[1], J. Roachdown[1], V. Natoli[1,4], M. Fusaro[2,3], E. M. Smith[1,5], M. W. Beresford[1,5], C. M. Hedrich[1,5]
[1]Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [2]Immunology Department Laboratory, Referral Medical Biology Laboratory, Institut Fédératif de Biologie, Toulouse University Hospital Center, [3]INFINITy, Toulouse Institute for Infectious and Inflammatory Diseases, INSERM U1291, CNRS U5051, University Toulouse III, Toulouse, France,

[4]Dipartimento di Neuroscienze, riabilitazione, oftalmologia, genetica e scienze materno-infantili, DINOGMI, Università degli Studi di Genova, Genoa, Italy, [5]Department of Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom
Correspondence: F. Sposito
Pediatric Rheumatology, **23(2):** PT074

Introduction: While the pathophysiology of juvenile-onset systemic lupus erythematosus (jSLE) is incompletely understood, genetic variation significantly contributes to increased type 1 interferon (IFN) expression.
Objectives: This study investigated genetic variability of *TLR7* and associations with disease outcomes in 319 jSLE patients enrolled in the UK JSLE Cohort Study.
Methods: Sequence capture enrichment (NimbleGen/Roche), followed by next-generation sequencing (MiSeq2500/Illumina) was performed. Allele frequencies were extracted from Allele Frequency Aggregator, 1000 genomes, and the Genome Aggregation Database. Haplotype analyses and linkage disequilibrium parameters were investigated using SNPstats, and associations with organ domain involvement (pBILAG-2004) were analysed. Functional impacts of *TLR7* variants were studied in HEK293T cells following transfection with reporter plasmids including the *TLR7* promoter and plasmids carrying the *TLR7* cDNA sequence. Transcription factor recruitment was evaluated through chromatin immunoprecipitation (ChIP). Messenger RNA (mRNA) stability was investigated through the transcriptional inhibitor 5,6-Dichloro-1-β-D-ribofuranosylbenzimidazole (DRB).
Results: Three jSLE-associated variants with a minor allele frequency ≥5% and an *in silico* predicted impact on gene function were retrieved: rs2302267/n.–20T>G (promoter); rs179008/c.32A>T/p.Gln11Leu (loss-of-function); and rs3853839/c.*881C>G (3′ untranslated region/UTR). Among girls carrying rs3853839 GC/GG, JSLE risk was increased in African/Caribbean girls (OR: 1.8; 95% CI: 1.2-2.9) and reduced in those of European ancestry (OR: 0.5; 95% CI: 0.4-0.7). The SLE-associated rs2302267 minor G allele associated with reduced leukopenia. The non-random rs79008/rs3853839 T-C/TT-CC haplotype associated with increased overall disease activity, and activity in the constitutional and musculoskeletal domains. Two SNPs lacked functional data in the literature: rs2302267/n.–20T>G and rs3853839/c.*881C>G. To study rs2302267, cells were transfected with reporter plasmids and promoter luciferase activity was reduced for the minor G allele when compared to the major T allele. Recruitment of the negative transcriptional regulator transcription factor 7-like 1 (TCF7L1) was higher for the G allele, suggesting reduced *TLR7* expression and a protective effect against leukopenia. Cells transfected with *TLR7* expression plasmids carrying the rs3853839 minor G allele showed increased *TLR7* and IFN expression. As 3′UTRs are involved in fine-tuning gene expression through microRNAs, mRNA stability was investigated and found to be elevated in transcripts carrying the rs3853839 G variant.
Conclusion: Common *TLR7* variants may influence jSLE risk and organ involvement in an ancestry-specific manner, supporting the rationale for genetic risk stratification and future consideration of TLR7-targeted treatments.
Disclosure
None declared

PT075

Cross-cohort international validation of treat-to-target endpoints in childhood lupus: data from the UK JSLE cohort and carra registry

F. Alves[1], L. B. Lewandowski[2], E. Smitherman[3], C. Sarker[1], A. Belot[4], M. W. Beresford[1,5], A. L. Jorgensen[6], J. Cooper[7], R. Sadun[8], E. M. Smith[1,9,10] on behalf of On behalf of the UK JSLE Study Group and CARRA Registry Investigators
[1]Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, [3]Department of Pediatrics, University of Alabama at Birmingham, Alabama, United States, [4]Service de Pediatrie, Centre Hospitalier Universitaire de Lyon, Lyon, France, [5]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, [6]Department of Health Data Science, Institute of Population Health, University of Liverpool, Liverpool, United Kingdom, [7]Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, [8]Departments of Medicine and Pediatrics, Divisions of Rheumatology, Duke University School of Medicine, Durham, North Carolina, United States, [9]School of Infection & Immunity, University of Glasgow, [10]Paediatric Rheumatology, Royal Hospital for Children, Glasgow, United Kingdom
Correspondence: F. Alves
Pediatric Rheumatology, **23(2):** PT075

Introduction: Consensus treat-to-target (T2T) endpoints for childhood-onset lupus, including the Childhood Lupus Low Disease Activity State (cLLDAS) (1), cSLE clinical remission on (cCR) and off-corticosteroids (cCR-0) (2), have been endorsed by the PReS. Validation in large international cohorts is needed to support their use in clinical care and research.
Objectives: To compare cSLE-specific T2T target attainment (cLLDAS, cCR, cCR-0) across UK and North American cohorts, identify predictors of sustained cLLDAS attainment, and assess the association between target attainment and future high disease activity.
Methods: Analysis included patients from the UK JSLE Cohort Study and CARRA Registry, diagnosed before age 18 and meeting ACR-1997 or SLICC-2012 classification criteria. Target attainment, time to target, and proportion of follow-up time in target were assessed; Wilcoxon signed-rank tests compared variables between cohorts. Further analysis was undertaken for the most easily attainable target, cLLDAS. Multivariable logistic regression identified independent predictors of spending above-median cumulative time in cLLDAS, reported as odds ratios (ORs). Risk of subsequent high disease activity (SLEDAI-2K ≥10) after cLLDAS attainment was assessed using Prentice-Williams-Peterson (PWP) models, adjusted for the cohort.
Results: Among 1,566 patients (11,965 visits [median disease duration 3.3 years]; UK JSLE: n=492, 5,923 visits [median 4.4 years]; CARRA: n=1,074, 6,042 visits [median 3.0 years]), 59% achieved cLLDAS (UK JSLE: 67% vs CARRA: 56%; p<0.001), 52% cCR (UK JSLE: 58% vs CARRA: 49%; p=0.003), and 43% cCR 0 (UK JSLE: 43% vs CARRA: 44%; p=0.756). Median time to cLLDAS was significantly shorter (13.1 vs 17.0 months; p<0.001) and cumulative time in cLLDAS was significantly greater (32% vs 23%; p<0.001) in CARRA compared to UK JSLE patients respectively. Multivariable logistic regression identified low complement C4 (OR 0.73 [CI 0.56, 0.96]; p=0.024), older diagnosis age (OR 0.87 [CI 0.84, 0.91]; p<0.001), and higher baseline SLEDAI 2 K (OR 0.97 [CI 0.96, 0.99]; p=0.007) as independent predictors of reduced cumulative time in cLLDAS. In multivariable PWP models, longer disease duration (HR 0.26; p<0.001) and ever attaining any target (HR 0.35; p<0.001), were independently associated with a reduced risk of subsequent high disease activity. Black (HR 1.94; p<0.001) and Hispanic (HR 1.61; p=0.002) ethnicities were independently associated with a higher risk of high disease activity.
Conclusion: This is the first study to evaluate cSLE-specific T2T endpoints across international registries, identifying predictors of sustained target attainment and confirming the protective effect of target attainment against subsequent high disease activity, supporting the integration of T2T strategies into clinical care and research.
Disclosure
None declared

Reference

1. Smith E, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clinical Immunology. 2023;250:109296.

PT077

Preceding mental health diagnosis does predict eventual neuropsychiatric disease in childhood-onset systemic lupus erythematosus

E. Ogbu[1,2], C. Treutel[2,3], A. Merritt[1], M. Wagner[1,2], H. Brunner[1,2]
[1]Cincinnati Children's Hospital Medical Center, [2]College of Medicine, University of Cincinnati, [3]College of Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, United States
Correspondence: E. Ogbu
Pediatric Rheumatology, **23(2):** PT077

Introduction: Childhood-onset Systemic Lupus Erythematosus (cSLE) affects approximately 1 in 10,000 children in the United States, with the estimated prevalence of childhood neuropsychiatric SLE (NPSLE) at 43 - 95%. Risk factors of NPSLE are poorly understood though NPSLE could severely impact cognitive development and long-term neurologic outcomes. Thus, identification of accurate predictors of increased NPSLE risk are greatly needed.
Objectives: The objective of our study was to understand whether premorbid mental health history predicted neuropsychiatric disease in cSLE. We hypothesized that mental health diagnoses and prescriptions occurring before cSLE diagnosis are predictive of future NPSLE.
Methods: Retrospective case-control study using a federated patient database (TriNetX Research network). We included patients aged ≤18 years at first SLE diagnosis between January 2014 and April 2025. We defined NPSLE using the 19 American College of Rheumatology classified neuropsychiatric syndromes with corresponding ICD-10 codes (1). Premorbid mental health diagnosis was defined as a neuropsychiatric diagnosis any time up to one day before initial SLE diagnosis using specific ICD-10 codes [(i.e. mood disorders (F30 - 39), depression (F32), anxiety disorders (F40–48; F41, F41.1, F41.9), adjustment disorders (F43.2) and attention deficit hyperactivity disorder (F90)]; and prescriptions using Veterans Affairs National Drug File (VA NDF) codes (CN300, CN301, CN302, CN309, CN400, CN600, CN601, CN609). The risk of NPSLE occurrence in relation to premorbid mental health diagnosis or prescription was analyzed over 2 time periods:(a)18-months and (b) total observation period, prior to SLE diagnosis. Propensity score matching was based on patient sex and race, and regression analyses conducted for the risk of NPSLE compared between cases and controls.
Results: The total TriNetX population queried included approximately 140 million patients from 102 healthcare organizations. A total of 8504 cSLE patients (5,880 cSLE patients with NPSLE and 2,624 without NPSLE) were identified. After propensity matching by sex, ethnicity, and race, 2,313 patients were included in each cohort. Premorbid diagnosis of mood disorders, depression and anxiety disorders within 18 months prior to cSLE diagnosis were associated with > 2-fold risk of subsequent NPSLE (RR: 3.4, 3.6, 3.0; all p <0.05. Similarly, the risk of developing NPSLE was increased with a diagnosis of mood disorders, depression, anxiety and attention-deficit hyperactivity disorder at any time point prior to cSLE diagnosis (RR: 2.9, 3.0, 3.0,2.1; all p <0.05). History of use of anticonvulsant, antidepressants and sedatives within 18 months or at any time prior to cSLE diagnosis was also associated with increased risk of subsequent NPSLE.
Conclusion: Preceding mental health diagnoses predict future neuropsychiatric disease in cSLE. Further research is needed to understand earlier clinical, laboratory and neuroimaging indicators of NPSLE development to delineate surveillance measures and interventions.
Disclosure
E. Ogbu Grant/Research Support with: Supported by the Lupus Research Alliance Empowering Lupus Research Career Development Award, Consultant with: Cartesian Therapeutics, C. Treutel: None declared, A. Merritt: None declared, M. Wagner: None declared, H. Brunner Grant/Research Support with: Supported by National Institutes of Arthritis and Musculoskeletal Skin Diseases under Award Number P30AR076316, Consultant with: Abbie, Astra Zeneca-Medimmune, Merck, Novartis, R-Pharm, Sanofi, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lily, EMD Serono, Genzyme, GlaxoSmithKline, F.Hoffmann-La Roche, Johnson &Johnson, Speaker Bureau with: GlaxoSmithKlein, Novartis, Roche (speaker bureau includes symposia and expert witness for all)

Reference

1. Gao S, Yu Z, Ma X, Sun J, Ren A, Gao S, et al. Childhood-onset systemic lupus erythematosus in China, 2016-21: a nationwide study. Lancet Child Adolesc Health. 2024;8(10):762-72.

PT078

Clinically feasible detection of cognitive dysfunction in association with abnormal cortical morphology: a prospective study in adolescents with childhood-onset lupus

D. Valdés Cabrera[1], T. El Tal[2], O. Mwizerwa[3], A. Jeyanathan[3], L. Ng[3], S. Mossad[1], B. Ertl-Wagner[4], A. E. Yeh[5], H. Branson[4], A. Davis[6], L. Hiraki[3], D. Levy[3], B. Zapparoli[7], A. Danguecan[7], A. M. Knight[3]

[1]Neurosciences and Mental Health, The Hospital for Sick Children, Toronto, [2]Dermatology/Rheumatology, Children's Hospital of Eastern Ontario, Ottawa, [3]Rheumatology, [4]Diagnostic Imaging, [5]Neurology, The Hospital for Sick Children, [6]Emergency Medicine, Children's Hospital of Eastern Ontario, [7]Psychology, The Hospital for Sick Children, Toronto, Canada

Correspondence: A. M. Knight
Pediatric Rheumatology, **23(2):** PT078

Introduction: Clinical identification of diffuse neuropsychiatric syndromes like cognitive dysfunction (CD) in youth with childhood-onset SLE (cSLE) remains challenging due to limited resources and diagnostic tools. Computerized neurocognitive batteries such as the Pediatric Automated Neuropsychological Assessment Metrics (Ped-ANAM) show promise for time- and resource-feasible assessment of CD when neuropsychiatric SLE (NPSLE) is suspected. Ped-ANAM and quantitative neuroimaging present a potential clinically viable framework to improve CD detection and attribution in cSLE; however, they have not been assessed together in cSLE.
Objectives: To evaluate differences in Ped-ANAM and advanced metrics of cortical brain morphology between adolescents with cSLE and healthy controls (HC) and to examine the relationship between cognitive and brain metrics in each group.
Methods: Global performance ($CPS_{Multiscore}$) and domain-specific cognitive efficiency throughput (TP_{std}) scores were calculated from Ped-ANAM in 68 adolescents with cSLE (10 females, 2 patients with NPSLE diagnosis; 15 patients with NPSLE concern) and 62 age/sex-matched HC, aged 11-17 years. T1w MRI was cross-sectionally acquired at 3T, and cortical brain metrics (volume and thickness) were calculated using Freesurfer. Group differences in cognitive and brain metrics were calculated with analyses of covariance. Associations between cognitive and brain metrics were evaluated with regression analyses, adjusted for covariates. Family-wise error corrections for multiple tests were performed.
Results: Compared to HC, adolescents with cSLE showed worse global and domain-specific (speed/efficiency, $t=4.23$; reasoning, $t=2.99$; $p<0.0042$) cognitive scores and similar age/sex/education distributions. They also showed both lower volume and thinner cortex in several clusters, mostly in frontal, as well as in parietal and occipital regions (all cluster areas>108 mm^2; all stats $log_{10}p>2.32$). Higher speed/efficiency and reasoning associated with greater thickness on occipital (isthmus cingulate, lingual) and frontal (precentral/caudal middle frontal) clusters on the left hemisphere in HC (all cluster areas>56 mm^2; all stats $log_{10}\ p>2.54$) while the inverse association (lower thickness) was observed in cSLE (all cluster areas>74 mm^2; all stats $log_{10}\ p<-2.08$).
Conclusion: Patients with cSLE exhibited worse global performance, speed/efficiency and reasoning, regional atrophy, and cortical thinning compared to HC. By combining the strengths of ped-ANAM and MRI-based cortical morphology, we present a clinical framework for enhancing CD screening/monitoring in cSLE and potential cognitive training therapies. Next, this approach should be validated by comparing it to gold standards for CD screening and clinical neuropsychiatric diagnosis. The distinct relationships between cognitive speed, reasoning, and regional brain morphology in the cSLE and HC groups suggest a link to SLE pathology, treatment and/or comorbidities that requires further longitudinal investigation.
Disclosure
None declared

PT079

International validation and simplification of clldas: findings from the UK JSLE cohort and carra registry

C. Sarker[1], F. Alves[1], A. Belot[2], M. W. Beresford[1,3], J. Cooper[4], A. L. Jorgensen[5], L. B. Lewandowski[6], R. Sadun[7], E. Smitherman[8], E. M. Smith[1,9,10] on behalf of for the UK JSLE Cohort Study and CARRA Registry Investigators
[1]Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [2]Centre Hospitalier Universitaire de Lyon, Service de Pediatrie, Lyon, France, [3]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, United Kingdom, [4]Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States, [5]Department of Health Data Science, Institute of Population Health, University of Liverpool, Liverpool, United Kingdom,

[6]National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin diseases, Bethesda, [7]Departments of Medicine and Pediatrics, Divisions of Rheumatology, Duke University School of Medicine, Durham, North Carolina, [8]Department of Pediatrics, University of Alabama at Birmingham, Alabama, United States, [9]School of Infection & Immunity, University of Glasgow, [10]Paediatric Rheumatology, Royal Hospital for Children, Glasgow, United Kingdom
Correspondence: C. Sarker
Pediatric Rheumatology, **23(2):** PT079

Introduction: Consensus-derived Childhood Lupus (cSLE) treat-to-target (T2T) endpoints have been endorsed by PReS including Childhood Lupus Low Disease Activity State (cLLDAS) (1). Validation with large international cohorts is needed to support their clinical implementation.
Objectives: Use a data-driven approach to evaluate whether the cLLDAS definition can be simplified, without compromising its ability to protect against subsequent high disease activity.
Methods: Data from UK JSLE Cohort Study and CARRA Registry patients, <18 years at diagnosis, with ≥4 ACR/SLICC criteria for SLE were included. Data were available from 1566 cSLE patients (11965 visits; UK JSLE: n=492, 5923 visits; CARRA: n=1074, 6042 visits). Criteria from the consensus-derived cLLDAS were either removed or transformed (18 variations in total). Prentice-Williams-Peterson (PWP) gap-time models assessed the impact of variations of cLLDAS, on episodes of high disease activity (SLEDAI-2K ≥10) over time. Hazard ratios (HRs) from the original and modified definitions were compared using Student's t-test. When variations of multiple target criteria showed comparable HRs to the original definition, they were evaluated in combination. Target attainability was also compared between original and modified cLLDAS definitions using Wilcoxon tests.
Results: Original cLLDAS attainment reduced the hazard of high disease activity by 72% (HR 0.28 [CI 0.21, 0.36]; p<0.001). Removing the PGA (HR 0.33 [CI 0.27, 0.41]), SLEDAI-2K (HR 0.30 [CI 0.23, 0.38]), or stable immunosuppression (HR 0.31 [CI 0.24, 0.39]) criteria statistically significantly diminished the protective effect of cLLDAS attainment. In contrast, (a) removing 'no new SLEDAI features,' (b) removing 'no major active organ involvement,' or (c) replacing the SLEDAI-2K criterion with the simpler clinical-SLEDAI ≤4 definition, did not significantly alter the hazard of subsequent high disease activity. A model evaluating a simplified cLLDAS definition combining modifications (a–c) yielded a statistically comparable hazard reduction (HR 0.32 vs. HR 0.28 for original cLLDAS). Additionally, the simplified version showed faster time to target attainment (12.9 vs. 16.3 months) and a greater proportion of follow-up time spent in target (54.5% vs. 46.6%) compared to the original cLLDAS definition.
Conclusion: These data suggest that refining the cLLDAS definition by applying the aforementioned changes, could serve to simplify targets for use in clinical and research settings, allowing real-time cLLDAS assessment during visits and removing the need to review past data or await serological results. Of note, the current analyses do not compare the consensus and modified cLLDAS definitions for the crucial prevention of cSLE-related damage.
Disclosure
None declared

Reference
1. Smith E, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clinical Immunology. 2023;250:109296.

PT080

Interdisciplinary clinical practice guidelines for patient-centered management of juvenile-onset systemic lupus erythematosus

K. Mönkemöller[1], L. T. Weber[2], M. Häusler[3], T. Kallinich[4], S. Benseler[5], H. I. Brunner[6], J. Brunner[7], C. Deuter[8], G. Hahn [9], C. Hedrich[10], C. Hinze[11], A. Hospach[12], H. K. Hoyer-Kuhn[13], A. Janda[14], D. Kamitz[15], M. A. Lee-Kirsch[16], U. Neudorf[17], J. Reichert[16], M. Aringer[18], S. Schanze[19], N. Schwerk[20], F. Speth[21], N. Wagner[22], M. Schneider[23], B. Tönshoff[24], D. Haffner[25], K. Tenbrock[22,26], on behalf of Gesellschaft fuer Kinder- und Jugendrheumatologie (Germany, Austria, Switzerland), C. Schuetz[27]

[1]Pediatric Rheumatology, Kinderkrankenhaus Amsterdamer Strasse, [2]Pediatric Nephrology, University of Cologne, Köln, [3]Division of Pediatric Neurology, RWTH Aachen, Aachen, [4]Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité-Universitätsmedizin Berlin, Berlin, Germany, [5]Rheumatology, Childrens Health Ireland, and University College Dublin, Dublin, Ireland, [6]Dept of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [7]Dept of Pediatrics, Medical University Innsbruck, Innsbruck, Austria, [8]Centre for Ophthalmology, University Hospital Tuebingen, Tuebingen, Germany, [9]Department of Pediatric Radiology, University Children`s Hospital Basel UKBB, Basel, Switzerland, [10]Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, United Kingdom, [11]Department of Pediatric Rheumatology and Immunology, Münster University Hospital, Münster, [12]Center for Pediatric Rheumatology, Klinikum Stuttgart, Stuttgart, [13]Dept of Pediatrics, University of Cologne, Köln, [14]Dept of Pediatrics, Ulm University Medical Center, Ulm, [15]Kinderrheumatologie, Praxis Kamitz, Aachen, [16]Dept of Pediatrics, Medizinische Fakultät an der TU Dresden, Dresden, [17]Division of Pediatric Cardiology and Rheumatology, University Hospital Essen, Essen, [18]Rheumatology, University Medical Centre and Faculty of Medicine, Dresden, [19]Lupus Erythematodes Selbsthilfegemeinschaft e.V., Wuppertal, [20]Clinic for Pediatric Pneumology, Allergology and Neonatology, Hannover Medical School, Hannover, [21]Dept of Pediatrics, University Medical Center Hamburg-Eppendorf, Hamburg, [22]Dept of Pediatrics, RWTH Aachen, Aachen, [23]Department of Rheumatology & Hiller Research Unit Rheumatology,, Heinrich-Heine Universität, Düsseldorf, [24]Dept of Pediatrics, University Children's Hospital, Heidelberg, Heidelberg, [25]Department of Pediatric Kidney, Liver and Metabolic Diseases, Hannover Medical School, Hannover, Germany, [26]Pediatric Rheumatology, Inselspital Universität Bern, Bern, Switzerland, [27]Pediatric Immunology, Medizinische Fakultät an der TU Dresden, Dresden, Germany
Correspondence: C. Schuetz
Pediatric Rheumatology, **23(2):** PT080

Introduction: Children and teenagers living with juvenile SLE (jSLE) on average have a higher disease activity and a worse prognosis than adults [1]. The majority of jSLE patients continue to require immunomodulatory drugs, and glucocorticoids (GC) into adulthood [2]. jSLE patients have a significantly increased pre-mature risk of developing atherosclerosis and GC-related toxicity [3]. These updated consensus guidelines build on the 2017 SHARE recommendations. They include detailed recommendations for juvenile lupus nephritis that are closely aligned with the recently published KDIGO recommendations for glomerular diseases [4]. As published evidence for the treatment of jSLE remains scarce by 2025, our recommendations take into account the EULAR recommendations for adults [5], to facilitate a process of presenting evidence-based recommendations to the community wherever applicable.
Objectives: To develop updated interdisciplinary clinical practice guidelines for the management of juvenile-onset systemic lupus erythematosus (jSLE) in a patient-centered, treat-to-target (T2T) approach.
Methods: Recommendations were developed based on T2T principles around shared decision-making by a multidisciplinary team of experts including pediatric and adult rheumatologists, pediatric nephrologists, neurologists, cardiologists, pneumologists, radiologists, immunologists, and infectious disease specialists, geneticists, and ophthalmologists from Germany, Switzerland, Austria, United Kingdom and Ireland, a psychologist and a patient representative. The process followed the standard operating procedures of the German AWMF (Association of the Scientific Medical Societies in Germany). The team conducted an extensive literature review (2012-2024) of 40 clinically selected PICO questions. Overarching principles (OAP), overarching treatment strategies (OATS), and recommendations were formulated and explored in 2 online pre-consensus meeting Delphi surveys with the experts. The results were discussed in 3 virtual consensus meetings using a modified nominal group technique to discuss, modify and vote on the OAP, OATS, and recommendations. All final document was approved by all 15 medical societies involved in the process, 2 external reviewers and the AWMF.

Results: We reached consensus on 45 recommendations on the general assessment, diagnosis, monitoring, non-pharmacologic and pharmacologic management of jSLE. We highlight organ specific manifestations such as CNS disease, jSLE related APS, and juvenile lupus nephritis, and consider disease severity for treatment recommendations.
Conclusion: We have developed updated interdisciplinary clinical practice guidelines to facilitate a patient-centered T2T approach to the management of patients with jSLE in daily practice. We also incorporated shared decision making as a hallmark of a state-of-the-art T2T approach to jSLE care.
Disclosure
None declared

References

1. Ambrose N, Morgan TA, Galloway J, *et al.* Differences in disease phenotype and severity in SLE across age groups. *Lupus*. 2016;25:1542–50. doi: https://doi.org/10.1177/0961203316644333
2. Groot N, Shaikhani D, Teng YKO, *et al.* Long-Term Clinical Outcomes in a Cohort of Adults With Childhood-Onset Systemic Lupus Erythematosus. *Arthritis Rheumatol Hoboken NJ*. 2019;71:290–301. doi: https://doi.org/10.1002/art.40697
3. Heshin-Bekenstein M, Trupin L, Yelin E, *et al.* Longitudinal disease- and steroid-related damage among adults with childhood-onset systemic lupus erythematosus. *Semin Arthritis Rheum*. 2019;49:267–72. doi: https://doi.org/10.1016/j.semarthrit.2019.05.010
4. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021;100:S1–276. doi: https://doi.org/10.1016/j.kint.2021.05.021
5. Fanouriakis A, Kostopoulou M, Andersen J, *et al.* EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis*. 2024;83:15–29. doi: https://doi.org/10.1136/ard-2023-224762

PT081

Monocyte siglec-1 as an ifn-inducible biomarker in juvenile dermatomyositis: correlation with disease activity and treatment response

S. VR, V. Pandiarajan, A. Dod, S. Sharma, A. Rawat
Allergy Immunology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India
Correspondence: V. Pandiarajan
Pediatric Rheumatology, **23(2):** PT081

Introduction: Juvenile dermatomyositis (JDMS) is the most common inflammatory myositis in children, characterized by proximal muscle weakness and distinctive skin features. Its pathogenesis involves a vasculopathy with an exaggerated type 1 interferon (IFN) response, driving immune cell activation and muscle inflammation (1). Siglec-1, an IFN-inducible marker, is elevated in JDMS and other autoimmune diseases, correlating with disease activity. Studies by Lerkvaleekul et al. (2) and Graf et al. (3) highlight Siglec-1 as a promising biomarker for JDMS, aiding in disease assessment and treatment response evaluation.
Objectives: To estimate Siglec-1 (CD169) expression in monocytes of children with JDMS and healthy controls, and to prospectively assess Siglec-1 levels after immunosuppressive treatment, and correlate Siglec-1 expression with disease activity in JDMS patients.
Methods: Siglec-1 was assessed by flow cytometry on circulating monocytes of 14 newly diagnosed JDMS patients and 6 relapsed cases. 16 of them were also assessed at 2 months and 13 of them at 6 months. 26 patients in remission and 8 patients with persistent skin disease activity on treatment were also assessed cross sectionally. Siglec-1 was assessed on CD14+ monocytes using [CD14 Alexa flour 700, CD169 FITC]. Gating was performed using (FlowJo), with isotype controls for background subtraction. Siglec-1% is the percentage of Siglec-1+ monocytes and ΔMFI is the change in mean fluorescence intensity.
Results: Monocyte Siglec-1 expression, measured by flow cytometry was significantly elevated at disease onset in children with juvenile dermatomyositis JDMS (n=14) compared to controls (n=20): Siglec-1% AUC=0.986 (95% CI: 0.957–1, p<0.001); Siglec-1 ΔMFI AUC=1.0 (95% CI: 1–1, p<0.001). Expression levels substantially reduced with treatment in newly diagnosed patients-Siglec-1%: Friedman $\chi^2(2)=13.55$, $p=0.001$; Siglec-1 ΔMFI: Friedman $\chi^2(2)=18.00$, $p<0.001$-and in relapsed cases-Siglec-1 ΔMFI: Friedman $\chi^2(2)=6.50$, $p=0.039$. Monocyte Siglec-1 expression also remained significantly higher in patients in remission (n=27) compared to controls (Siglec-1 ΔMFI: AUC=0.681, 95% CI: 0.528–0.835, $p=0.035$). Isolated skin disease activity had an independent effect on monocyte Siglec-1 levels (Siglec-1%: $U=61.0$, $p<0.05$; Siglec-1 ΔMFI: $U=77.0$, $p<0.05$), whereas calcinosis did not (Siglec-1%: $U=32.5$, $p=0.372$; Siglec-1 ΔMFI: $U=37.0$, $p=0.576$). Clinical markers of muscle disease activity such as CMAS, MMT8, and MDAS, showed moderate correlations with Siglec-1 expression (r=0.4–0.52, $p<0.05$), while skin disease activity exhibited only weak correlations (r=0.2–0.3, $p<0.05$).
Conclusion: Siglec-1 on monocytes is a newly identified IFN-inducible biomarker in JDMS that correlates with clinical disease activity and reduces with treatment.
Disclosure
None declared

References

1. Papadopoulou C, Chew C, Wilkinson MGL, McCann L, Wedderburn LR. Juvenile idiopathic inflammatory myositis: an update on pathophysiology and clinical care. Nat Rev Rheumatol. 2023 Jun;19(6):343–62.
2. Lerkvaleekul B, Veldkamp SR, van der Wal MM, Schatorjé EJH, Kamphuis SSM, van den Berg JM, et al. Siglec-1 expression on monocytes is associated with the interferon signature in juvenile dermatomyositis and can predict treatment response. Rheumatol Oxf Engl. 2022 May 5;61(5):2144–55.
3. Graf M, von Stuckrad SL, Uruha A, Klotsche J, Zorn-Pauly L, Unterwalder N, et al. SIGLEC1 enables straightforward assessment of type I interferon activity in idiopathic inflammatory myopathies. RMD Open. 2022 Feb;8(1):e001934.

PT082

A clear pattern of clinical presentation in juvenile systemic scleroderma is associated with interstitial lung disease

I. Foeldvari[1], J. Klotsche[2], K. Torok[3], O. Kasapcopur[3], A. Adrovic[3], F. Sztajnbok[3], M. T. Terreri[3], A. P. Sakamoto[3], J. Anton[3], R. Khubchandani[3], S. Johnson[3], G. Özomay Baykal[3], B. Feldman[3], D. Schonenberg-Meinema[3], S. Sawhney[3], V. Smith[3], E. Al-Abadi[3], S. Appenzeller[3], S. Hajek[3], M. Katsicas [3], M. Kostik[3], S. Li[3], H. Malcova[3], A. Patwardhan[3], W.-A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], T. Avcin [3], P. Costa Reis[3], S. O. Hetlevik[3], M. Janarthanan [3], E. Marrani[3], C. Pain[3], M. J. Santos[3], V. Stanevicha[3], S. Abu Al-Saoud[3], E. Alexeeva[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], D. Eleftheriou[3], L. Harel[3], T. Kallinich[3], D. Lazarevic[3], K. Minden[2], D. Nemcova [3], S. Nielsen[3], F. Nuruzzaman[3], M. Sparchez[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, [2]German Rheumatism Research Center, Berlin, [3]jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** PT082

Introduction: Juvenile systemic sclerosis(jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. In adult systemic sclerosis is interstitial lung disease (ILD) one of the main leading causes of mortality. High resolution computer tomography (HRCT) is the gold standard to assess ILD. To find risk factors or predictive factors for ILD in jSSc has a significant clinical importance.
Objectives: To compare clinical characteristics of patients with jSSc, who had a positive or negative finding for ILD on HRCT.
Methods: We extracted data from patients till March 2025, who had an HRCT evaluation at the time of inclusion into the juvenile scleroderma inception cohort(jSScIC)(1). We compared the clinical presentation of patients with positive (HRCT+) and negative (HRCT-) findings for ILD.
Results: 216 patients had an HRCT result at time of the inclusion in the cohort. 76 of them were HRCT+. In both groups around 70% of the patients had diffuse subset. Median age at the time of the first non-Raynaud´s presentation was 10.8 and 11.3 in the HRCT+ versus

HRCT- group. Median disease duration was around 2 years. Significantly more patients had decreased FVC<80% (44% versus 25%, *p*=0.011) and DLCO<80% (62% versus 36%, *p*=0.004) in the HRCT + then HRCT- group. Median MRSS was lower in the HRCT+ then HRCT- group (8.5 versus 12.5, *p*=0.031). Lower number of patients had sclerodactyly in the HRCT+ then HRCT- group (68% versus 81%, *p*=0.039). Nailfold capillary changes occurred more often in the HRCT+ then in HRCT- group (88% versus 73%, *p*=0.042). In the HRCT+ group pulmonary hypertension occurred more frequently (14% versus 2%, *p*=0.001). Oesophageal involvement was more frequent in the HRCT+ group (58% versus 34%, *p*=0.001). We could not find any significant difference regarding antibody profile, cardiac, renal and musculoskeletal
Conclusion: We found a remarkable clinical pattern associated with HRCT+, with increased capillary changes, more frequent oesophageal involvement and pulmonary hypertension and lower MRSS. This pattern may help to predict ILD. We must remark that we had no central reading of the HRCT imaging. We need more patients and more long term observation period to prove our findings.
Disclosure
None declared

Reference
1. Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Terreri MT, Sakamoto AP, et al. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.

PT083
Juvenile and adult-onset dermatomyositis: a comparative study in a cohort from a tertiary center
E. Aslan[1], A. Karakoç[2], P. Öztürk[3], A. Günalp[1], N. Akay[1], Ü. Gül[1], E. Kılıç Könte[1], E. Aslan[1], M. Yıldız[1], S. Şahin[1], A. Adrovic[1], K. Barut[1], S. Uğurlu[2], Ö. Kasapçopur[1]
[1]Pediatrics, Pediatric Rheumatology Department, [2]Internal Medicine, Rheumatology Department, [3]Internal Medicine Department, Istanbul University- Cerrahpasa, Istanbul, Türkiye
Correspondence: E. Aslan
Pediatric Rheumatology, **23(2):** PT083

Introduction: Dermatomyositis (DM) is a rare inflammatory myopathy with distinct clinical features in juvenile (JDM) and adult (ADM) forms. Both present with symmetrical proximal muscle weakness and characteristic skin lesions; notable differences exist in organ involvement, disease course, and malignancy risk (1). Identifying these differences is crucial for the development of age-specific diagnostic, therapeutic, and follow-up strategies.
Objectives: To define the differences and similarities between JDM and ADM in terms of clinical presentations, diagnostic procedures, autoantibody profiles, treatment options, and disease outcomes.
Methods: We retrospectively reviewed medical records of DM patients diagnosed per 2017 EULAR/ACR criteria (2) at the pediatric and adult rheumatology clinics of Istanbul University-Cerrahpasa from January to April 2025. Patients were classified as JDM if diagnosed under 16 years and ADM if 16 years or older.
Data were analyzed using SPSS (v.27). Non-normally distributed variables were assessed with the Mann-Whitney U test, while categorical data were compared using the Chi-square or Fisher's exact tests. Statistical significance was set at p<0.05.
Results: A total of 164 patients were included: 84 with JDM (63.1% female) and 80 with ADM (67.7% female). Age at diagnosis showed a bimodal distribution, peaking at 6.9 and 44.2 years.
Joint involvement was more prevalent in JDM (*p*=0.019), whereas cardiac involvement was more common in ADM (*p*=0.038). Calcinosis occurred in 33.3% of JDM cases but only in one ADM case (p<0.001). Among the myositis-specific and myositis-associated antibodies, Anti-NXP2 and Anti-TIF1g were more prevalent in JDM, whereas Anti-Mi2, Anti-Jo1 and Anti-SSa were more common in ADM.
Acute phase reactants were higher in ADM at both diagnosis and last visit (p<0.005 for all). While MRI was more frequently utilized to demonstrate myositis in JDM cases, biopsy, EMG and PET/CT were more commonly employed in ADM (p<0.001 for all)
Glucocorticoids were initiated in nearly all patients (>98%) in both groups. At follow-up, most ADM patients remained on treatment, while only 11.6% of JDM patients were still receiving steroids (p<0.001). Malignancy was observed in 26.2% of ADM cases, whereas no such association was found in JDM (p<0.001). The hospitalization and mortality rates were higher in the ADM group (p<0.001 for both).
Conclusion: JDM and ADM have distinct clinical features: ADM is characterized by more severe organ involvement, particularly cardiac and respiratory, higher acute phase reactants, prolonged steroid rates, and poorer outcomes, including higher rates of malignancies, hospitalization, and mortality. In contrast, JDM is associated with more frequent calcinosis and joint involvement, along with a relatively better prognosis.
These differences emphasize that JDM should not be approached merely as the pediatric form of ADM, but as a distinct clinical entity requiring tailored management strategies.
Disclosure
None declared

References
1. Robinson AB, Reed AM. Clinical features, pathogenesis and treatment of juvenile and adult dermatomyositis. Vol. 7, Nature Reviews Rheumatology. 2011. p. 664–75.
2. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, et al. 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis and Rheumatology. 2017 Dec 1;69(12):2271–82.

PT084
Evaluation of microcirculation in patients with childhood-onset systemic lupus erythematosus
S. Sener[1], B. Ergin[2], D. Schonenberg-Meinema[3], C. Ince[2], S. Kamphuis[4]
[1]Pediatric Rheumatology, Adana City Training and Research Hospital, Adana, Türkiye, [2]Intensive Care Medicine, Laboratory of Translation Intensive Care, Erasmus University Medical Center, Rotterdam, [3]Pediatric Immunology, Rheumatology and Infectious Diseases, Emma Children's Hospital, Amsterdam University Medical Center, Amsterdam, [4]Pediatric Rheumatology, Sophia Children's Hospital, Erasmus University Medical Center, Rotterdam, Netherlands
Correspondence: S. Sener
Pediatric Rheumatology, **23(2):** PT084

Introduction: Microcirculatory involvement is an underrecognized yet critical aspect of childhood-onset systemic lupus erythematosus (cSLE), potentially contributing to irreversible organ damage. Two techniques can be used to evaluate microcirculation in cSLE. These are nailfold (video) capillaroscopy (NFC) reflecting peripheral microvascular anatomy and Incident Dark Field (IDF) imaging reflecting central microvascular anatomy. While NFC studies in cSLE are scarce, to our knowledge this is the first study to explore central microvascular anatomy in cSLE.
Objectives: We aimed to evaluate peripheral and central microvascular alterations in patients with cSLE using NFC and IDF imaging and to assess the concordance between these two imaging modalities.
Methods: In this prospective cross-sectional single-center observational pilot study, 29 cSLE patients fulfilling the SLICC classification criteria were evaluated at the Erasmus University Medical Center, Rotterdam, Netherlands. NFC was performed in all patients, while 10 patients underwent IDF imaging. Capillary morphology, density, apical diameter, and presence of hemorrhages were assessed in NFC. IDF imaging analysis included total vessel density (TVD), functional capillary density (FCD), proportion of perfused vessels (PPV), red blood cell velocity (RBCv), capillary hematocrit (cHct), and total red blood cell perfusion (tRBCp). Microangiopathy pattern was defined as abnormal capillary pattern (with abnormal capillary morphology and/or capillary hemorrhages and without criteria for a scleroderma pattern). All results are reported as mean ± SD.
Results: NFC revealed a mean capillary density of 7.5 ± 1.5/mm and a mean apical diameter of 18.4 ± 4.9 µm. Five patients exhibited dilated capillaries (range 20–50 µm), seven showed abnormal morphology, and four had hemorrhages. No scleroderma pattern was observed; seven patients displayed a microangiopathy pattern. IDF imaging in 10

patients showed TVD of 19.39 ± 3.94 mm/mm², FCD of 18.83 ± 3.91 mm/mm², and PPV of 0.97 ± 0.02. Mean RBCv was 321.2 ± 42.7 µm/s, with cHct 0.07 ± 0.01 and tRBCp 43.51 ± 11.98. All these results were within the normal range. Interestingly, two patients with microangiopathy on NFC did not exhibit pathological findings in IDF imaging.
Conclusion: This study provides the first combined data of NFC and IDF imaging in cSLE. These findings support the need for further studies exploring multimodal vascular monitoring in pediatric autoimmune diseases to better understand central and peripheral microvascular involvement.
Funding
This study was supported by The Scientific and Technological Research Council of Türkiye (TÜBİTAK) under the 2219 International Postdoctoral Research Fellowship Programme.
Disclosure
None declared

PT085

Damage accrual and transition from pediatric to adult care in patients with childhood-onset systemic lupus erythematosus

N. Kifer[1], I. Padjen[2], M. Bakula[2], M. Scepovic Ljucovic[2], M. Sestan[1], M. Frkovic[1], M. Baresic[2], M. Mayer[2], B. Anic[2], M. Jelusic[1]
[1]University of Zagreb School of Medicine, Department of Pediatrics, UHC Zagreb, [2]University of Zagreb School of Medicine, Department of Internal Medicine, UHC Zagreb, Zagreb, Croatia
Correspondence: N. Kifer
Pediatric Rheumatology, **23(2):** PT085

Introduction: Childhood-onset SLE (cSLE) is associated with significant morbidity and early organ damage, and transitioning these patients to adult care presents notable challenges.
Objectives: We aimed to analyze damage accrual in a retrospective cohort of cSLE patients who transitioned from tertiary pediatric to tertiary adult rheumatology care within our institution.
Methods: We retrospectively analyzed cSLE patients diagnosed before age 18, followed at our Pediatric Rheumatology Department and transitioned to Adult Rheumatology between 2005 and 2020. All patients met the 1997 ACR or 2019 ACR/EULAR classification criteria. We analyzed demographics, cumulative fulfillment of 1997 ACR criteria, disease activity (SLEDAI-2k), damage accrual (SDI), and immunosuppressive treatment. Kaplan-Meier analysis assessed damage-free survival (DFS). Chi-square or Fisher's exact test were used for categorical variables, and T-test or Mann-Whitney U-test for continuous variables.
Results: A cohort of 33 patients was analyzed (7 males, 21%), with 3 having a family history of SLE. The mean age at diagnosis was 13.8 years (SD 2.7), with a mean follow-up of 14.4 years (SD 5.0). Median transition was 4 months (IQR 2-10). Transition occurred over several joint visits with both pediatric and adult rheumatologists. A psychologist was regularly included in the transition. Cumulatively, the most frequent clinical classification criteria were malar rash (24/33), arthritis (21/33) and photosensitivity (15/33). Lupus nephritis was biopsy-proven in 11 patients (class III: 3; IV: 6; V: 2). Frequent laboratory criteria included anti-dsDNA antibodies (28/33) and cytopenia (26/33), mostly leukopenia (23/33). Hemolytic anemia was seen in 9 patients, mostly autoimmune, and one microangiopathic due TTP. Secondary APS was diagnosed in one patient. Damage (SDI ≥1) occurred in 15/33 patients, with SDI ≥2 in 6: Most frequent damage types included cataract (4/15); deforming arthritis (3/15); osteoporosis with fracture, muscle atrophy, nephrotic-range proteinuria (2/15 each). In 10/15 patients, damage was observed at pediatric age (<18 years). Damage-free survival (DFS) was 71% at 5 years and 59% at 10 years, much lower in those with lupus nephritis. Renal disorder and photosensitivity were more frequent in the damage group (p=0.026 and p=0.016). No differences were observed in disease activity (at diagnosis or one year after) or most treatments, except cyclophosphamide, which was more common in the damage group (10/15 vs. 1/18, p=0.026).
Conclusion: Our analysis highlights the long-term burden of disease in cSLE, with lupus nephritis emerging as a key contributor to damage accrual in these patients. Despite regular physician visits and a well coordinated transition team, damage accrual increased, emphasizing the need for more effective strategies to support patients during the transition to adult care.
Disclosure
None declared

PT086

Beyond echocardiography: cardiovascular MRI findings in juvenile systemic sclerosis

F. Tirelli[1], E. Reffo[2], A. Leo[1], B. Castaldi[2], A. Meneghel[1], F. Zulian[1]
[1]Pediatric Rheumatology, [2]Pediatric Cardiology, Department of Woman and Child Health, University Hospital of Padova, Padova, Italy
Correspondence: F. Tirelli
Pediatric Rheumatology, **23(2):** PT086

Introduction: Cardiac involvement is reported in up to 25% of Juvenile Systemic Sclerosis (JSSc) cases and is a leading cause of mortality. Conventional methods like electrocardiography (EKG) and transthoracic echocardiography often fail to detect the subclinical nature of early cardiac abnormalities. Cardiovascular magnetic resonance imaging (CMR) is a highly sensitive modality able to detect structural, functional, and inflammatory myocardial abnormalities. Its use in JSSc cardiac assessment, however, remains limited.
Objectives: To investigate whether subclinical cardiac involvement could be detected using CMR in a cohort of JSSc patients.
Methods: We included patients newly diagnosed with JSSc, per PRES/EULAR/ACR criteria[1] and/or EULAR PRES adult SSc criteria[2], at our Centre from 2007 onward. Demographic and clinical data were retrospectively collected from medical records. Cardiologic assessment included conventional echocardiography, strain rate echocardiography (STE), and CMR with contrast and optional T1/T2 mapping.
Results: 32 patients, 18 (56.3%) females, mean age at onset 10.7 years (range 4.2–15.9), were enrolled. Seventeen had diffuse JSSc, 7 limited, 5 *sine scleroderma*, and 3 overlap syndromes. Four patients (12.5%) had symptomatic cardiac involvement: three had left ventricular dysfunction and arrhythmias requiring ICD placement; one had pulmonary hypertension with right ventricular dysfunction; all had unfavorable outcomes (3 transplants, 1 death). Standard echocardiography and EKG were performed in all but resulted altered only in the symptomatic patients. STE revealed GLS abnormalities in 7/26 (26.9%) of patients undergoing this assessment: 3 symptomatic with Left Ventricular Ejection Fraction (LVEF) reduction and 4 asymptomatic. CMR was performed in 21 patients, including two symptomatic, and was abnormal in 7 (33%). CMR-measured LVEF was reduced in two with known dysfunction. Fibrosis (LGE+) was found in 4: two symptomatic, two asymptomatic with normal LVEF and GLS. T1/T2 mapping was abnormal in 3 of 9 in whom was performed, all asymptomatic with no prior cardiac findings. Abnormal left atrial strain was available for 10 patients and found altered in 1 asymptomatic patient with known reduction of GLS.
Conclusion: CMR identified myocardial abnormalities both in patients with overt cardiac symptoms and in asymptomatic individuals, most of these without detectable changes with other cardiac tests. These findings strongly highlight the added value of CMR in detecting early, subclinical myocardial involvement in JSSc, supporting its integration into the diagnostic and monitoring work-up.
Trial registration identifying number:
Disclosure
None declared

References
1. Zulian F, et al. Arthritis Rheum 2007;57(2):203-12
2. van den Hoogen F, *Arthritis Rheum.* 2013;65(11):2737–47.

PT087

The role of nailfold capillaroscopy in the assessment of juvenile rheumatic diseases

F. Tirelli[1], M. Binda[2], B. Moccaldi[2], V. Sanetti[1], A. Benini[2], A. Cuberli[2], A. Meneghel[1], E. Zanatta[2], F. Zulian[1]
[1]Pediatric Rheumatology, Department of Woman and Child Health, University Hospital of Padova, [2]Rheumatology Unit, Department of Medicine-DIMED, University Hospital of Padova, Padova, Italy
Correspondence: F. Tirelli
Pediatric Rheumatology, **23(2):** PT087

Introduction: Nailfold videocapillaroscopy (NVC) represents a reliable, non-invasive tool for the diagnosis of several adult rheumatic diseases, and the assessment of peripheral microvascular abnormalities may serve as a potential biomarker of disease severity in these patients[1]. However, data on NVC findings and their clinical significance in pediatric patients are limited.
Objectives: To evaluate nailfold videocapillaroscopy (NVC) findings in children with primary
Raynaud's phenomenon (PRP) and connective tissue diseases (CTDs). In juvenile CTDs, we aimed to assess potential associations between NVC features and clinical or organ involvement.
Methods: NVC was performed in patients followed at the Paediatric Rheumatology Unit of our hospital for PRP or a definite diagnosis of CTD. For each child, 32 images were acquired, and microvascular alterations were analysed and classified as either non-specific or scleroderma patterns (early, active, and late) by two independent observers. A semi-quantitative rating scale from 0 to 3 was adopted to score six capillary abnormalities[2] (enlarged capillaries, giant capillaries, microhaemorrhages, loss of capillaries, microvascular disarray, and capillary ramifications) and calculate an average score. The capillary density score was identified as "avascular score".
Results: A total of 800 NVC images from 50 subjects (30 females; mean age 16.4±4.0 years) were evaluated. Scleroderma pattern was significantly more frequent in juvenile systemic sclerosis (jSSc) compared to both juvenile dermatomyositis and PRP (p=0.003 and p<0.001, respectively). In terms of capillaroscopic alterations, differences were observed only in PRP vs. jSSc for reduction of capillary density (p<0.001) and presence of giants (p=0.01). Scleroderma pattern was associated with skin sclerosis (21/25 vs. 0/9; p<0.001), digital ulcers (8/25 vs. 0/9; p=0.07) and gastrointestinal involvement (17/25 vs. 1/9; p=0.006). Avascular score was higher in children with interstitial lung disease (ILD) than in those without (p<0.05). Patients with severe reduction of capillary density (≤4/mm) were more likely to have ILD (5/10 vs. 4/13; p=0.02). Multivariate logistic regression analysis showed that the association between severe reduction of capillary density and ILD was independently of the presence of scleroderma pattern (OR 3.2; 95%CI 0.9-11.6) and skin fibrosis (OR 2.7; 95%CI 0.8-9.3).
Conclusion: As in the adult population, NVC may help differentiate primary from secondary RP, supporting the early diagnosis of CTDs. In these patients, NVC may have a role in risk stratification for organ involvement, particularly ILD.
Disclosure
None declared

References

1. Smith V, Decuman S, Sulli A, Bonroy C, et al. Do worsening scleroderma capillaroscopic patterns predict future severe organ incolvement? A pilot study. Ann Rheum Dis 2012; 71:1636–9.
2. Sulli A, Secchi ME, Pizzorni C, Cutolo M. Scoring the nailfold microvascular changes during the capillaroscopic analysis in systemic sclerosis patients. Ann Rheum Dis 2008; 67:885–7.

PT089

Associations of myositis-specific autoantibodies with specific clinical features in juvenile dermatomyositis in a large real-world multi-site registry

B. Y. Yi[1], M. Sherman[2], K. Ardalan[3], S. Kim[4], S. Tarvin[5], H. Kim[6], B. M. Feldman[7] on behalf of CARRA JDM Therapeutics Workgroup for the CARRA Registry Investigators
[1]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, [2]Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases, National Institute of Health, Bethesda, [3]Department of Pediatrics, Duke University School of Medicine, Durham, [4]Department of Pediatrics, University of California, San Francisco, San Francisco, [5]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, [6]Juvenile Myositis Pathogenesis and Therapeutics Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute of Health, Bethesda, United States, [7]Department of Medicine, University of Toronto, Toronto, Canada
Correspondence: B. Y. Yi
Pediatric Rheumatology, **23(2):** PT089

Introduction: Myositis-specific autoantibodies (MSAs) are associated with distinct clinical features in juvenile dermatomyositis (JDM) and are increasingly being used to tailor treatment. However, there is a paucity of data on sensitivity and positive likelihood ratios (LR) of MSAs for specific clinical manifestations in a real-world multi-site JDM cohort.
Objectives: To determine the sensitivity and LR of MSAs with specific baseline and chronic clinical features of JDM in a large multi-site registry.
Methods: Patients with JDM enrolled between January 2019 and June 2024 in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) North America-based Registry with MSA testing were included. Sensitivity and LR of MSAs for clinical features were calculated for those with more than 2 observations per MSA group. MSA groups with more than 5 patients were analyzed.
Results: There were 395 patients diagnosed with JDM per enrolling providers. 303 were tested for at least 1 MSA, and 141 were positive for 1 MSA. 16 who were positive for more than 1 MSA were excluded. MSA testing was most commonly performed at Oklahoma Medical Research Foundation (n=49, 35%) and Associated Regional and University Pathologists, Inc., (n=35, 25%), both in the USA. The most common MSA was anti-TIF1 (n=46, 33%) then anti-NXP2 (n=41, 29%), anti-Mi2 (n=24, 17%), and anti-MDA5 (n=24, 17%). Overall, the MSAs were poorly sensitive (5-70%) for specific clinical features. Significant associations for anti-TIF1 included LR for baseline V-sign (2.23, 95% CI 1.19-4.18) and baseline malar/facial erythema (2.10, 95% CI 1.06-4.14). For anti-MDA5, LR for interstitial lung disease (7.78, 95% CI 4.23-14.30), baseline arthritis (6.21, 95% CI 2.56-15.06), and baseline skin ulcer (3.88, 95% CI 1.75-8.60) were significant. Of note, LR for lipodystrophy in anti-TIF1 (1.19, 95% CI 0.43-3.30) and for calcinosis in anti-NXP2 (0.95, 95% CI 0.33-2.74) were not significant.
Conclusion: MSAs had low sensitivity for specific disease features. Anti-TIF1 and anti-MDA5 had significant LR for a few known associated disease manifestations. Strengths of this study include large sample size and multi-site data source. Limitations include missing data in setting of retrospective study design and variable MSA assays with potential for antibody status misclassification. More studies are needed to better understand the sensitivity and predictive value of MSAs for clinical manifestations in JDM.

Acknowledgements
NIH Intramural Research Program (IRP). This work could not have been accomplished without the aid of the following organizations: The NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the Arthritis Foundation (AF), and the Cure JM Foundation (Cure JM). We would also like to thank all participants and hospital sites that recruited patients for the CARRA Registry.

Disclaimer
This study utilized data collected in the CARRA Registry. The views expressed are the authors' and do not necessarily represent the view of CARRA.
Disclosure
B. Yi: None declared, M. Sherman: None declared, K. Ardalan Grant/Research Support with: Rheumatology Research Foundation, Childhood Arthritis & Rheumatology Research Alliance/Arthritis Foundation, Chan Zuckerberg Initiative, Cure JM Foundation, Patient-Centered Outcomes Research Institute, National Institutes of Health/Technical Resources International., Consultant with: Cabaletta Bio (scientific advisory board, paid consulting), Childhood Arthritis & Rheumatology Research Alliance (Vice Chair JDM Committee paid consultant position), Paid Instructor with: Rheumatology Research Foundation Pediatric Visiting Professorship travel reimbursement and honorarium 2024-2025, American College of Rheumatology travel reimbursement for invited speaker 2024, SingHealth - honorarium (paid to my institution, not directly to me) for grant pre-review program, S. Kim: None declared, S. Tarvin: None declared, H. Kim Grant/Research Support with: Intramural Research Program of the National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin diseases (NIAMS) (AR041215)., Consultant with: Juvenile myositis expert panel member for Cabaletta Bio (unpaid), part of NIAMS CRADA with provision of drug (deucravacitinib) with Bristol Myers Squibb, previous part of NIAMS CRADA with study support and drug (baricitinib) with Eli Lilly and Company., B. Feldman: None declared

PT090

Deep immunophenotyping in patients with juvenile localized scleroderma reveals two distinct immunological endophenotypes

A. Ariolli, A. Aquilani, I. Caiello, F. De Benedetti, R. Nicolai, E. Marasco
Rheumatology Unit, Ospedale Pediatrico Bambino Gesù, Rome, Italy
Correspondence: A. Ariolli
Pediatric Rheumatology, **23(2):** PT090

Introduction: Juvenile localized scleroderma (JLS) is a rare autoimmune disorder causing skin inflammation and fibrosis in children under the age of 16 years. Disease hallmarks include dermal sclerosis and inflammatory infiltration, linking inflammation and fibroblast activation with excess extracellular matrix production (1). Current clinical tools may struggle to distinguish active from inactive lesions, highlighting the need for reliable biomarkers to assess activity and predict response to therapy.
Objectives: The aim of this project is to perform immunophenotyping of JLS patients and healthy controls to assess dysregulated immunological pathways in JLS, and to identify biomarkers able to predict clinical features.
Methods: We included in this study pediatric patients diagnosed with linear and mixed JLS. PBMC and plasma samples at diagnosis and before the initiation of treatment were analyzed. Levels of 50 cytokines were measured in the plasma by protein array. Lymphocyte and monocyte subsets were analysed with a 26-colour flow cytometry panel and acquired on a FACSymphony.
Results: We identified samples at baseline from 11 patients with JLS and 10 controls. Cytokine array identified 15 cytokines that were significantly elevated in JLS patients compared to controls. Using Principal Component Analysis (PCA), we observed a distinct distribution between patients and controls, with approximately 50% of patients clustering away from controls, and the remaining 50% aligning closely with them. Patients clustering near controls exhibited the lowest cytokine levels and were designated as non-inflammatory JLS (no_inf JLS), whereas those clustering away had the highest cytokine levels and were classified as inflammatory JLS (inf_JLS). Flow cytometry analysis identified 81 subpopulations of interest; PCA analysis highlighted significant differences in the distribution of lympho-monocytic subsets between patients and controls. We observed a reduction in monocyte populations, including classical ($CD14^+CD16^-$) and atypical monocytes ($CD14^+CD16^+$), and an expansion of dendritic cells compared to controls. Within lymphocyte subsets, significant differences were observed in the frequency of $CD4^+$ T cells, particularly of activated $CD4^+$ T cells ($CD38^+$ $HLA\text{-}DR^+$). Patients stratified into inf_JLS and no_inf JLS groups based on cytokine levels showed minimal differences in cellular subpopulations upon PCA. However, two subpopulations demonstrated significant variability: activated $CD4^+$ T cells ($CD38^+$ $HLA\text{-}DR^+$) and terminally differentiated effector memory $CD4^+$ T cells (TEMRA) expressing PD1, were significantly expanded in patients with inf_JLS.
Conclusion: This study identified two distinct groups of patients with JLS: a non-inflammatory group, characterized by normal levels of circulating proinflammatory cytokines, and an inflammatory group, marked by elevated levels of circulating cytokines and increased levels of activated $CD4^+$ T cells. Our findings highlight the central role of activated T cells in JLS pathogenesis, particularly in patients within the inflammatory group. Furthermore, these results pave the way for novel therapeutic approaches for JLS, including the potential use of treatments targeting T cells.
Disclosure
None declared

Reference
1. Walker D, J Am Acad Dermatol. 2017

PT091

Anakinra for infants under six months with kawasaki disease and coronary artery lesions: a multicenter experience

G. Inguscio[1], S. Romano[1], M. Fabi[2], L. Gargiullo[3], A. Marchesi[3], M. C. Maggio[4], V. mastolia[1], G. B. Calabri[5], G. Simonini[1,6], T. Giani[1]
[1]Rheumatology, Meyer Children's Hospital IRCCS, Florence, [2]emergency, 2Pediatric Emergency Unit, IRCCS Azienda Ospedaliero Universitaria Di Bologna, Bologna, [3]General Pediatric and Infectious Disease Unit, Bambino Gesù Children's Hospital, IRCSS, Rome, [4]Department of Health Promotion, Maternal and Infantile Care, Department of Internal Medicine and Medical Specialties, "G. D'Alessandro", University of Palermo, Palermo, Italy., Palermo, [5]Cardiology, Meyer Children's Hospital IRCCS, [6]Rheumatology, University of Florence, Florence, Italy
Correspondence: T. Giani
Pediatric Rheumatology, **23(2):** PT091

Introduction: Infants with Kawasaki Disease (KD) have a higher risk of incomplete presentations, IVIG resistance, and coronary artery lesions (CALs). IL-1 plays a key role in the pathogenesis, highlighting its potential as a therapeutic target.
Objectives: To report a multicenter Italian experience and review the literature on anakinra use in KD infants with CALs.
Methods: We retrospectively reviewed charts of patients aged ≤6 months treated with anakinra at four Italian centers between January 2015 and May 2025.
Results: Eight infants were included. The median age at diagnosis was 2.75 months. Six had incomplete KD. All were resistant to first-line treatment and all developed CALs, which were detected at a median of 9.5 days from fever onset. Anakinra was initiated at a median of 18 days from fever onset and 1.5 days after CALs detection. One patient received only subcutaneous anakinra. Seven infants underwent intravenous administration (median dose 8.5 mg/kg/day), four of whom received an initial bolus (median dose 2.75 mg/kg), and six were subsequently switched to subcutaneous dosing. Median total treatment duration was 22.5 days. CALs completely resolved in five patients and improved in two. One treatment-related adverse event was reported.
Conclusion: Anakinra appears to be a promising and well-tolerated option for infants with KD and CALs, especially in IVIG-resistant or high-risk cases. While adverse events were unusual, further studies are needed to confirm its safety and efficacy.
Trial registration identifying number:
Disclosure
None declared

References
1. Jone PN, Tremoulet A, Choueiter N, et al. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association. *Circulation*. Published online 2024. doi:https://doi.org/10.1161/CIR.0000000000001295
2. Kone-Paut I, Cimaz R, Herberg J, et al. The use of interleukin 1 receptor antagonist (Anakinra) in Kawasaki disease: A retrospective cases series. *Autoimmun Rev*. 2018;17(8). doi:https://doi.org/10.1016/j.autrev.2018.01.024
3. Atici AE, Noval Rivas M, Arditi M. The Central Role of Interleukin-1 Signalling in the Pathogenesis of Kawasaki Disease Vasculitis: Path to Translation. *Can J Cardiol*. 2024;0(0). doi:https://doi.org/10.1016/J.CJCA.2024.07.023/ASSET/48C0A149-121F-4E08-BD82-D3CFD4A0B187/MAIN.ASSETS/GR2.JPG

PT092

Investigation of the expression of MIR-185-5P in adenosine deaminase 2 deficiency

M. Kasap Cuceoglu[1], T. H. Akbaba[2], S. Caglayan[3], B. Sen[2], E. Nalbant[2], M. E. Ozkan[2], Y. Z. Akkaya Ulum[2], S. Sahin[4], M. Kısla Ekinci[5], Y. Bayindir[1], B. Guven Taskin[6], E. D. Batu [1], H. O. Basaran[1], S. Unal Cangul[7], O. Kasapcopur[4], B. Sözeri[8], S. Ozen[1], B. Peynircioğlu[2], Y. Bilginer[1]
[1]Pediatric Rheumatology, [2]Department of Medical Biology, Faculty of Medicine, Hacettepe University, Ankara, [3]Department of Rheumatology, Umraniye Training and Research Hospital, [4]Pediatric Rheumatology, Istanbul University Cerrahpasa Faculty of Medicine, İstanbul, [5]Pediatric Rheumatology, Çukurova University,, Adana, [6]Pediatric Rheumatology, Izmir City Hospital, İzmir, [7]Department of Hematology, Hacettepe University, Ankara, [8]Pediatric Rheumatology, Umraniye Training and Research Hospital, İstanbul, Türkiye
Correspondence: M. Kasap Cuceoglu
Pediatric Rheumatology, **23(2):** PT092

Introduction: Adenosine Deaminase 2 (ADA2) deficiency (DADA2) is an autoinflammatory disease associated with loss-of-function mutations in the ADA2 gene, presenting with vasculitic and hematological features(1).The clinical manifestations of DADA2 are heterogeneous, and the differences observed among patients with the same mutation are thought to be related to changes in the expression of microRNAs(miRNAs), which are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level(2).
Objectives: In this study, the possible role of miRNAs in the formation of phenotypic findings in individuals with the same or different homozygous mutations in DADA2 patients who are heterozygous but show clinical phenotype was investigated.
Methods: Individuals with homozygous or heterozygous ADA2 mutations (G47R, V217D, R381S, G5R, H335R, K314R), asymptomatic carriers, and healthy controls followed at five pediatric rheumatology centers between 2021–2024 were included. Bioinformatic analyses identified candidate miRNAs, and miR-185-5p, targeting the highest number of genes, was selected. RT-qPCR was performed using RNU6 as a
Reference gene to measure miR-185-5p expression in all groups. Expression levels were compared across groups to evaluate significance.
Results: The study included 24 participants: nine homozygous patients, four heterozygous symptomatic patients, five asymptomatic heterozygous carriers, one asymptomatic homozygous individual, and five healthy controls. Among those with the G47R mutation (n=9), four were homozygous, two heterozygous with symptoms, and three heterozygous without symptoms. Of the heterozygous symptomatic individuals, three exhibited a vasculitic phenotype with stroke; two had the G47R/- mutation, one had H335R/-. miR-185-5p expression was significantly elevated in homozygous and heterozygous patients with clinical findings compared to carriers and healthy controls (p=0.018). Furthermore, patients with severe disease showed higher miR-185-5p expression than those with mild/moderate or no symptoms (p=0.062). Stroke patients had markedly increased expression compared to non-stroke individuals (p<0.001).
Conclusion: Our findings show that miR-185-5p expression is significantly increased in DADA2 patients with vasculitic phenotypes, especially in those with severe disease and stroke. This expression pattern, which changes during clinical deterioration, suggests that miR-185-5p may serve as a potential biomarker and contribute to the suppression of protective pathways against vasculitis and stroke. Thus, our study lays the groundwork for future functional research on candidate genes involved in DADA2-related mechanisms.
Acknowledgments
This project was supported by Hacettepe University BAP Coordination Unit (Project No: 323S389) and the TÜBİTAK under the 1002-B support program. 'We would like to express our sincere gratitude to the Scientific and Technological Research Council of Turkey (TÜBİTAK) for their invaluable support.'
Disclosure
None declared

References
1. Ombrello MJ. 2021. 'Genetic and Pediatric Rheumatic Diseases.' Eighth Edi. Textbook of Pediatric Rheumatology. Elsevier Inc.; pp. 12-23.e3.
2. Vulture TH. 2020. 'Epigenetics for Clinicians from the Perspective of Pediatric Rheumatic Diseases.' Current Rheumatology Reports. July; 22(8):46.

PT093

Performance of kobayashi and kawanet scores in predicting ivig resistence: data from the Kiwi study

M. V. Mastrolia[1,2], V. Pandiarajan[3], M. Cattalini[4], A. Taddio[5], S. Vergnano[6], J. Anton[7], W. Sontichai[8], B. Sozeri[9], S. Ozen[10], S. Rosina[11], J. Sánchez-Manubens[12], R. Haviv[13], P. Pal[14], A. Rodrigues Fonseca[15], A. Gagro[16], N. Bagri[17], L. Verdoni[18], D. Montin[19], M. C. Maggio[20], M. Garrone[21], E. Patrone[21], E. Barbi[22], G. Ciacci[22,23], A. Barucci[23], N. Ruperto[24], G. Simonini[1,2] on behalf of for the Pediatric Rheumatology European Society (PReS)
[1]Rheumatology Unit, ERN ReCONNET center, Meyer Children's Hospital IRCCS, [2]NEUROFARBA Department, University of Florence, Firenze, Italy, [3]Pediatric Allergy Immunology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, [4]Pediatric Clinic, University of Brescia and Spedali Civili di Brescia, Brescia, [5]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", University of Trieste, Trietse, Italy, [6]Department of Paediatric Infectious Diseases and Immunology, Bristol Royal Hospital for Children, Bristol, United Kingdom, [7]Department of Pediatric Rheumatology, Universitat de Barcelona, Hospital Sant Joan de Déu, Barcelona, Spain, [8]Faculty of Medicine, Chiang Mai University, Division of Rheumatology, Department of Pediatrics, Chiang Mai, Thailand, [9]Umraniye Training and Research Hospital, Department of Pediatric Rheumatology, Health Sciences University,, Instanbul, [10]Department of Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye, [11]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslin, Genoa, Italy, [12]Parc Taulì Hospital Universitari,Institut d'Investigaciò I Innovaciò Parc Taul' (I3PT-CERCA), Unitat de Reumatologia Pediatrica - Servei de Pediatria, Barcelona, Spain, [13]and School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv University, Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, Tel Aviv, Israel, [14]Institute of Child Health, Department of Pediatric Rheumatology, Kolkata, India, [15]Universidade Federal do Rio de Janeiro, Instituto de Puericultura e Pediatria Martagao Gesteira (IPPMG),, Rio de Janeiro, Brazil, [16]Children's Hospital Zagreb, Department of Pediatrics, Department of pulmology,allergology, clinical immunology and rheumatology, Zagreb, Croatia, [17]All India Institute of Medical Sciences, Division of Pediatric Rheumatology - Department of Pediatrics, New Delhi, India, [18]Paediatric Department, Hospital Papa Giovanni XXIII, Bergamo, [19]Regina Margherita Children Hospital, Immunology and Rheumatology Unit, Turin, [20]Rheumatology Unit, Children Hospital "G. Di Cristina", Palermo, [21]IRCCS Giannina Gaslini Institute, UOC Servizio di Sperimentazioni Cliniche Pediatriche/PReSTaR, Genoa, [22]Meyer Children's Hospital IRCCS, Neuroscience and Human Genetics Department, Firenze, [23]Consiglio Nazionale delle Ricerche, CNR-IFAC, Istituto di Fisica Applicata 'Nello Carrara', Sesto Fiorentino (FI), [24]Reumatologia Pediatrica, Monza, Italy; Università degli Studi di Milano-Bicocca, Pediatria, Fondazione IRCCS San Gerardo dei Tintori di Monza, Milan, Italy
Correspondence: M. V. Mastrolia
Pediatric Rheumatology, **23(2):** PT093

Introduction: Between 10% and 20% of patients with Kawasaki disease (KD) exhibit resistance to intravenous immunoglobulin (IVIg) therapy. The Kobayashi scoring system demonstrated a good sensitivity (77–86%) and specificity (67–86%) for predicting IVIg resistance in Japanese KD cohorts. However, its predictive accuracy has not been confirmed in European, American, or other Asian populations. The Kawanet group proposed a new scoring model that showed promising sensitivity (77%) and acceptable specificity (60%) in non-Asian KD populations
Objectives: To evaluate the performance of the Kobayashi and Kawanet scores in a multicenter cohort of European, Asian and Indian KD children. To identify demographic, clinical, and biological factors associated with IVIg resistance.
Methods: Retrospective-prospective, observational, international multicenter study, supported by the 2020 PRINTO/PReS grant. KD patients, diagnosed according to the AHA criteria were enrolled from April 2022 to January 2024. Retrospective data were also collected for patients diagnosed from January 1st, 2015.
Results: 723 KD patients were included across 19 paediatric rheumatology units. 62.0% (448) were male, with a median age of 2.40 years (IQR 1.19–4.30). The cohort comprised 57.9% (418) Caucasian, 20.5% (148) Indian, 14.2% (102) Asian, 5.3% (38) African, and 2.4% (17) Hispanic patients. Complete KD was diagnosed in 396 patients (54.8%), incomplete KD in 296 (41.0%), and atypical features were noted in 18 (2.5%). KD shock syndrome was observed in 12 patients (1.7%). Coronary ectasia was observed in 87 cases (12%), and coronary aneurysms in 181 (25.1%). IVIg resistance rate was 19.8% (143). No significant differences in ethnicity or age were observed between IVIg responders and non-responders. However, extremity desquamation (p=0.017), musculoskeletal signs (p=0.006), cardiac involvement (p < 0.001), longer fever duration (p<0.001) and long-term sequelae (p<0.001) were significantly more common in the IVIg-resistant group. Higher ESR (p = 0.002), neutrophil count (p=0.021), ALT (p=0.001), and AST (p<0.001) values were more commonly observed in IVIg-resistant patients. The Kobayashi score demonstrated a balanced accuracy of 55.3% with sensitivity and specificity of 71.3% and 39.2%, respectively. The Kawanet score showed a balanced accuracy of 53.3% with a sensitivity and specificity of 16.1% and 90.4%, respectively. When analysed across the

three main ethnic subgroups—Caucasian, Indian, and Asian—the performance of both scores remained consistent with that observed in the overall cohort.
Conclusion: In our multicenter, multiethnic cohort, the Kobayashi score retained a sensitivity comparable to that reported in the original Japanese population but demonstrated a lower specificity. In contrast, the Kawanet score proved to be poorly sensitive but highly specific in predicting IVIg resistance. Both scores maintained similar performance across different ethnic subgroups.
Trial registration identifying number: Trial registration identifying number: NCT06305611
Disclosure
None declared

References
1. Kobayashi T, et al. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. Circulation 2006.
2. Piram M, et al. Defining the risk of first intravenous immunoglobulin unresponsiveness in non-Asian patients with Kawasaki disease. Sci Rep. 2020

PT094

Predicting flare after low disease activity: an Asian childhood-onset systemic lupus erythematosus cohort experience

K. L. Teh[1,2], J. C. Huang[1,2], L. Das[1], Y. X. Book[1], S. F. Hoh[3], X. Gao[3], T. Arkachaisri[1,2]
[1]Department of Paediatric Subspecialties, Rheumatology and Immunology, KK Women's and Children's Hospital, [2]Duke-NUS Medical School, [3]Division of Nursing, KK Women's and Children's Hospital, Singapore, Singapore
Correspondence: K. L. Teh
Pediatric Rheumatology, **23(2):** PT094

Introduction: Sustaining childhood lupus low disease activity state (cLLDAS) is an important treatment goal in childhood-onset systemic lupus erythematosus (cSLE) therapy, but recurrent flares remain a clinically significant challenge.
Objectives: To evaluate the frequency and predictors of recurrent flares following episodes of cLLDAS in an Asian cSLE cohort.
Methods: Prospective longitudinal data from a cSLE cohort at KK Women's and Children's Hospital, Singapore, were included. Patients were recruited from inception in 2009 to 2025 with at least 6 months of follow-up. Demographic data, disease manifestations, treatment and disease activity outcomes were collected. Patients who achieved at least one cLLDAS episode (clinical SLEDAI-2K ≤ 4 without major organ activity, prednisolone ≤0.15mg/day or ≤7.5mg/day, whichever lower, no new lupus activity, Physician Global Assessment ≤1/3, and stable immunosuppressants) were included. Multiple cLLDAS and flare episodes were recorded per patient. Kaplan-Meier survival analysis, Cox and Poisson regressions were used where appropriate.
Results: Among 148 patients (83% female, median age at diagnosis 13.1 years [IQR 10.9–14.6], median follow-up duration 6.1 years [IQR 3.2 - 8.6]), 135 (91%) achieved at least one cLLDAS episode. Of these, 67 (49.6%) experienced 91 flare episodes, with 20 (29.9%) having more than one flare. Median duration of initial cLLDAS before first flare was 17.2 months (IQR 7.2-30.0), while median duration of subsequent cLLDAS remained similar before flares (14.4 months, IQR 10.3–18.5, p=0.958).
Kaplan-Meier analysis demonstrated significantly shorter flare-free intervals among patients with neuropsychiatric involvement (log-rank p=0.003), discoid rash (p = 0.040) and photosensitivity (p=0.005). Cox regression identified neuropsychiatric involvement (hazard ratio [HR] 2.51, 95% confidence interval [CI] 1.35–4.69, p=0.004) and photosensitivity (HR 2.13, 95% CI 1.21–3.73, p=0.008) as independent predictors of time to flare. The duration in first cLLDAS did not correlate with duration of first flare (p=0.683) nor flare severity (p=0.942).
Poisson regression showed shorter duration in first cLLDAS (Incidence Rate Ratio [IRR] 1.05 per decreasing month, 95% CI 1.03-1.06, p<0.001) and older age at diagnosis (IRR 1.53 per increasing year, 95% CI 1.29-1.80, p<0.001) were associated with higher flare rate when accounting for follow-up duration.
Conclusion: Despite achieving cLLDAS, half of our cSLE patients experienced flares. Neuropsychiatric involvement and photosensitivity predicted shorter time to flare. One-third of patients will experience recurrent flares, with lower flare rates in younger patients. Time in first cLLDAS also functions as a protective buffer, hence maintaining disease control is critical. These findings highlight the need for tailored maintenance strategies following cLLDAS in cSLE.
Disclosure
None declared

PT095

Anti TNFA and recombinant ADA2 have beneficial effect in vitro on bone marrow mononuclear cells growth

F. Schena[1], M. Lupia[2], R. Caorsi[1], F. Barzaghi[3,4], M. Giarratana[2], A. Corcione[1], F. Penco[1], P. Terranova[5], A. Mortellaro[4], A. Aiuti[3,4], A. Cafaro[6], G. Cangemi[6], S. Signa[1], A. Grossi[7], E. Traggiai[8], I. Ceccherini[7], M. Miano[2], M. Gattorno[1], C. Dufour[2]
[1]UOC Reumatologia e Malattie Autoinfiammatorie, [2]Haematology Unit, IRCCS ISTITUTO GIANNINA GASLINI, GENOVA, [3]Pediatric Immunohematology and Bone Marrow Transplantation Unit, [4]San Raffaele Telethon Institute for Gene Therapy, IRCCS San Raffaele Scientific Institute, MILAN, [5]U.O.C. Servizio Immunoematologia e Trasfusionale, Laboratorio Citofluorimetria, [6]Biochemistry, Pharmacology and Newborn Screening Unit, Central Laboratory of Analysis, [7]Research Laboratories Aggregation Area, IRCCS ISTITUTO GIANNINA GASLINI, GENOVA, Italy, [8]Novartis Institutes for BioMedical Research, Basel, Switzerland
Correspondence: F. Schena
Pediatric Rheumatology, **23(2):** PT095

Introduction: Deficiency of adenosine deaminase 2 (DADA2) is a monogenic form of systemic vasculopathy that often presents during early childhood. Linked to biallelic mutations in ADA2, DADA2 was initially described as a syndrome of recurrent fever, livedo racemosa, early-onset strokes, and peripheral vasculopathy. However, the wide spectrum of clinical findings and heterogeneity of disease, including variable haematological manifestations, has been recognized.
Anemia is present in more than 50% of cases and several patients with DADA2 present with pure red cell aplasia and transfusion dependence, mimicking Diamond-Blackfan anaemia. Hematopoietic stem cell transplant may be needed to treat refractory cytopenia. Bone marrow biopsy typically demonstrates hypoplasia of the affected lineage(s), suggesting a defect in cell production.
Objectives: How a plasma protein produced mainly by macrophages affects multi-lineage hematopoiesis is unclear. ADA2 knockdown in the Zebrafish model caused neutropenia, supporting an intrinsic role of ADA2 in normal haematopoiesis. In vitro, human ADA2 can promote T cell-dependent monocyte maturation.
The objectives of the present work are: (i) to quantify and characterize hematopoietic progenitor cells on bone marrow samples of DADA2 patients, (ii) to test the apoptosis of CD34+cells, (iii) to explore if in the bone marrow there is an inflammatory milieu by testing the presence of proinflammatory cytokines in BM plasma and (iv) to assess the effect of anti-TNFα, human recombinant ADA2 or Eltrombopag on the growth of BM patients' progenitors.
Methods: Fresh or frozen BM samples from DADA2 patients and healthy donors (HD) were analyzed by in-vitro colony forming unit assay (CFU) in presence of anti-TNFα, human recombinant ADA2 or Eltrombopag.
BFU-E (Burst-Forming Unit-Erythroid) and CFU-GM (Colony-Forming Unit-Granulocyte Macrophage) were analyzed by flow cytometry. Apoptosis and pro-inflammatory cytokines were measured by flow cytometry.
Results: DADA2 patients show a defect of proliferation and maturation of progenitors regardless of the clinical phenotype. There is a trend towards and increased CD34+ cells and B cell progenitors' apoptosis. TNFα, Fas Ligand and IL18 marrow plasma levels were significantly higher and IFNγ was increased almost significantly in DADA2 patients compared to healthy controls. Eltrombopag seem to have a positive effect on erythroid marrow progenitor cell growth. The addition of anti-TNFa to cultures significantly stimulates the growth of myeloid bone marrow progenitors in patients with severe bone marrow

damage whereas recombinant ADA2 also had a positive effect on erythroid progenitors.
Conclusion: Our preliminary data suggest that the bone marrow of DADA2 patients is characterized by an inflammatory microenvironment and reduced growth of marrow progenitor cells. In vitro treatment with anti-TNFα and human recombinant ADA2 restores the growth of bone marrow progenitor cells.
Disclosure
None declared

PT096

Evaluation of enzyme activity and genotypes in patients suspected of adenosine deaminase 2 (ADA2) deficiency in pediatric rheumatology clinics across türkiye: a functional analysis study

E. Tunce[1], M. Kasap Cüceoğlu[2], A. Tanatar[3], N. G. Kocamaz[4], H. K. Zora[5], G. Kılbaş[6], E. Gümüşsoy Ay[7], C. Arslanoğlu[8], T. Aydın[9], H. Kazanasmaz[10], Z. Ekici Tekin[11], B. Bozkaya Yücel[12], E. Atalay[13], S. Atamyıldız Uçar[1], N. Kara Çanlıoğlu[1], S. Türkmen[1], T. Coşkuner[1], M. Kalyoncu[10], M. K. Gürgöze[7], S. Demir[14], S. Yüksel[6], E. Ünsal[9], K. Öztürk[15], Y. Bilginer[2], S. S. Kilic[5], A. Paç Kısaarslan[8], S. Özdel[4], Ö. Kasapçopur[16], N. Aktay Ayaz[3], S. Özen[2], P. Eker[17], B. Sözeri[1]
[1]Pediatric Rheumatology, University of Health Science, Ümraniye Training and Research Hospital, İstanbul, **[2]**Pediatric Rheumatology, Hacettepe University, Faculty of Medicine, Ankara, **[3]**Pediatric Rheumatology, İstanbul University, İstanbul, **[4]**Pediatric Rheumatology, Ankara Etlik City Hospital, Ankara, **[5]**Pediatric Rheumatology, Uludağ University, Bursa, **[6]**Pediatric Rheumatology, Pamukkale University, Denizli, **[7]**Pediatric Rheumatology, Fırat University, Elazığ, **[8]**Pediatric Rheumatology, Erciyes University, Kayseri, **[9]**Pediatric Rheumatology, Dokuz Eylül University, İzmir, **[10]**Pediatric Rheumatology, Karadeniz Technical University, Trabzon, **[11]**Pediatric Rheumatology, Bilkent City Hospital, Ankara, **[12]**Pediatric Rheumatology, University of Health Sciences, Samsun Training and Research Hospital, Samsun, **[13]**Pediatric Rheumatology, Şanlıurfa Training and Research Hospital, Şanlıurfa, **[14]**Pediatric Rheumatology, Eskisehir Osmangazi University, Eskişehir, **[15]**Pediatric Rheumatology, Istanbul Medeniyet University, **[16]**Pediatric Rheumatology, İstanbul University-Cerrahpaşa, **[17]**Medical Biochemistry, Maltepe University, İstanbul, Türkiye
Correspondence: E. Tunce
Pediatric Rheumatology, **23(2):** PT096

Introduction: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive monogenic vasculitis syndrome.It typically presents in early childhood with clinical features such as vasculitis, stroke, hematological abnormalities, and immune dysregulation.Diagnosis of DADA2 is based on the presence of pathogenic variants in the *ADA2* gene and low serum ADA2 enzyme activity.However, due to the high cost and time-consuming nature of genetic testing, enzymatic activity measurement is increasingly important, particularly for screening and differential diagnosis in symptomatic patients.
Objectives: To evaluate the association between serum ADA2 enzyme levels and genetic variants in patients suspected of DADA2 across pediatric rheumatology clinics in Türkiye, and to assess the diagnostic sensitivity and specificity of ADA2 enzyme activity measurement
Methods: This multicenter, cross-sectional observational study was conducted across 16 pediatric rheumatology centers and included a total of 97 pediatric patients, comprising 83 symptomatic, 14 asymptomatic cases.ADA2 enzyme activity was measured using a kinetic enzymatic assay developed with BioSystems GLDH reagent.To ensure the specificity of ADA2 measurement, ADA1 activity was selectively inhibited using EHNA (erythro-9-(2-hydroxy-3-nonyl) adenine).Patients were classified into three groups based on ADA2 gene status determined by Sanger sequencing: biallelic, monoallelic, or no variants.
Results: Among 83 symptomatic patients, ADA2 enzyme levels varied significantly based on genetic findings. Patients with biallelic ADA2 variants (n=26) had a median enzyme level of 6.6 U/L (range: 2.8–16.4; IQR: 4.5–8.8), while monoallelic variants (n=10) had a higher median 9 U/L (range: 5.8–27.4; IQR: 6.5–12.3). Patients without any detected pathogenic variants detected (n=47) showed the highest median ADA2 levels at a median 13.1 U/L (range: 3–30.2; IQR: 8.9–17.7). The difference among these three groups was statistically significant ($p < 0.001$). Comparison between symptomatic (n=10) and asymptomatic (n=10): monoallelic carriers revealed no significant difference in enzyme levels (median 9 U/L vs. 11.2 U/L, $p=0.65$). In evaluating the diagnostic performance of ADA2 enzyme activity, a threshold of <8 U/L predicted the presence of biallelic mutation with a sensitivity of 79% and a specificity of 69.2%.
Conclusion: This study demonstrated that ADA2 enzyme levels are significantly lower in patients with biallelic pathogenic variants, and that a cut-off value of <8 U/L has meaningful diagnostic utility for identifying such mutations. The EHNA-inhibition-based kinetic enzymatic assay is a rapid and reliable tool for the screening of DADA2. When supported by genetic testing, this approach may facilitate early identification of affected individuals, particularly among symptomatic pediatric patients.
Disclosure
None declared

References

1. Escherich C, Bötticher B, Harmsen S, et al. The Growing Spectrum of DADA2 Manifestations-Diagnostic and Therapeutic Challenges Revisited. *Front Pediatr*. 2022;10:885893. Published 2022 Jun 14.
2. Lee PY, Kellner ES, Huang Y, et al. Genotype and functional correlates of disease phenotype in deficiency of adenosine deaminase 2 (DADA2). *J Allergy Clin Immunol*. 2020;145(6):1664-1672.e10.
3. Gibson KM, Morishita KA, Dancey P, et al. Identification of Novel Adenosine Deaminase 2 Gene Variants and Varied Clinical Phenotype in Pediatric Vasculitis. *Arthritis Rheumatol*. 2019;71(10):1747-1755.

PT097

Persistent serological activity predicts risk of flare after T2T goal attainment in childhood-onset systemic lupus erythematosus

M. O. Kerr[1], V. Natoli[2,3,4], C. Sarker[3,5], M. Beresford[3,6], A. Jorgensen[5], E. Smith[6,7] on behalf of on behalf of the UK JSLE Study Group
[1]School of Medicine, University of Liverpool, Liverpool, United Kingdom, **[2]**UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, **[3]**Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, **[4]**Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili, Università degli Studi di Genova, Genoa, Italy, **[5]**Department of Health Data Science, University of Liverpool, **[6]**Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital,, Liverpool, **[7]**University of Glasgow, School of Infection & Immunity, Glasgow, United Kingdom
Correspondence: M. O. Kerr
Pediatric Rheumatology, **23(2):** PT097

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) is a multisystem autoimmune disease. Disease flares contribute significantly to organ damage, morbidity, and mortality. The utility of ongoing biomarker monitoring, including anti-dsDNA antibodies, complement levels (C3, C4), and erythrocyte sedimentation rate (ESR) in predicting flares after achieving treat-to-target (T2T) goals remains unclear.
Objectives: To evaluate the association between biomarker levels and flare occurrence in patients with cSLE who had attained T2T goals.
Methods: Patients from the UK JSLE Cohort Study (<18 years at diagnosis, ≥4 ACR/SLICC criteria) were included. Flares were defined using the BILAG-2004 flare index. Longitudinal biomarker data (anti-dsDNA, C3, C4, ESR) were analysed using Prentice–Williams–Peterson (PWP) gap-time models for recurrent flares, adjusted for T2T attainment: Childhood Lupus Low Disease Activity State (cLLDAS), clinical remission on-treatment (cCR), and off-treatment (cCR-0), and for covariates found to be significant ($p < 0.01$) with each T2T state. As cLLDAS includes dsDNA, C3, and C4 in its definition, only ESR was evaluated for additional prognostic value within that model. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported, representing the change in flare risk per 1-unit change in the corresponding biomarker.
Results: 401 patients from the UK JSLE Cohort Study were included, contributing 4,602 visits. In univariable PWP analyses of patients who had attained either cCR and cCR-0, each unit change in both anti-dsDNA (cCR model HR 1.0004, 95% CI 1.0001–1.0007, $p=0.0035$, cCR-0 model HR 1.0004, 95% CI 1.0001–1.0007, $p=0.0048$) and ESR levels (cCR model HR 1.0046, 95% CI 1.0028–1.0063, $p<0.0001$, cCR-0 model HR

1.0050, 95% CI 1.0032–1.0070, p<0.0001) was associated with significantly increased risk of subsequent flare. In contrast, C3 and C4 levels were not statistically significantly associated with flare risk (p>0.05). In the multivariable model, both anti-dsDNA and ESR remained independently associated with risk of subsequent flare in the cCR (anti-dsDNA: HR 1.0005, 95% CI 1.0001–1.0008, *p*=0.0078; ESR: HR 1.0041, 95% CI 1.0020–1.0063, *p*=0.0002) and cCR-0 (anti-dsDNA: HR 1.0004, 95% CI 1.0000–1.0008, *p*=0.0188; ESR: HR 1.0045, 95% CI 1.0023–1.0067, p<0.0001) models. In the univariable model of patients in cLLDAS, ESR was also significantly associated with subsequent risk of flare (HR 1.0047, 95% CI 1.0029–1.0065, p<0.0001).
Conclusion: Despite attainment of T2T goals, elevated anti-dsDNA and ESR levels independently predicted flare risk in cSLE. These findings support continued biomarker monitoring even in clinically stable patients to guide long-term disease management. Further studies with larger international cohorts are needed to confirm these associations.
Disclosure
None declared

PT098

Predicting the recurrence risk of immunoglobulin a vasculitis due to clinical and laboratory features in children

D. Gezgin Yildirim[1], E. N. Sunar Yayla[2], C. G. Yildiz[1], N. Karacayir[1], B. Kucukali[1], N. Belder[1], M. Kutlar Tanıdır[1], P. Esmeray Senol[3], K. Ahmadova[1], B. Acun Sayili[1], O. Ozenli Yagci[1], S. A. Bakkaloglu[1]
[1]Pediatric Rheumatology, Gazi University, [2]Pediatric Rheumatology, Etlik City Hospital, Ankara, [3]Pediatric Rheumatology, Mersin City Hospital, Mersin, Türkiye
Correspondence: D. Gezgin Yildirim
Pediatric Rheumatology, **23(2):** PT098

Introduction: Immunoglobulin A vasculitis (IgAV) is the most common vasculitis in childhood, characterized by affecting the small vessels of the skin, gastrointestinal tract, and kidneys. Although IgAV is a benign and self-limited disorder, relapses may occur during follow-up.
Objectives: The aim of this study is to evaluate the frequency and predictors of IgAV relapses according to clinical and laboratory features in children.
Methods: We retrospectively reviewed the medical records of 546 pediatric IgAV patients between 2005 and 2025. IgAV-related recurrence was accepted as a recurrence of skin lesions and/or any systemic organ involvement after an asymptomatic period of at least 6 months. Patients were divided into two subgroups: Group 1, which consisted of IgAV patients who had at least one recurrence related to IgAV, and Group 2, which consisted of IgAV patients who had no recurrence.
Results: There were 546 IgAV patients with a male dominance. A total of 40 (7.3%) patients had a relapse related to IgAV after an asymptomatic period of at least 6 months (Group 1). Patients' characteristics and laboratory features were presented in Table 1. Male predominance, diarrhoea, bloody stool, bloody vomiting, gastrointestinal involvement, testicular involvement, WBC, creatinine, and pediatric vasculitis assessment scale (PVAS) at first visit were significantly higher, while mean age at diagnosis of IgAV was significantly lower in Group 1 than Group 2 (*p*=0.033, *p*=0.015, *p*=0.013, *p*=0.045, *p*=0.047, *p*=0.003, *p*=0.012, *p*=0.012, *p*=0.000, and *p*=0.015, respectively). The most recurrent clinical finding was purpuric skin eruption (65%) (Table 2). Recurrence free survival of Group 1 was illustrated in Fig1. Logistic regression analysis for the prediction of recurrence of IgAV was shown in Table 3. Male sex, diarrhoea, testicular involvement, Hb value, and PVAS were found as independent risk factors for the prediction of IgAV recurrence in the long-term follow-up (*p*=0.033, *p*=0.015, *p*=0.003, *p*=0.025, and *p*=0.005, respectively).
Conclusion: In this study, we have shown that male sex, diarrhoea, testicular involvement, higher Hb value, and higher PVAS at first visit were found as independent risk factors for the prediction of IgAV recurrence in the long-term follow-up. Close follow-up is important especially in the presence of male gender, testicular involvement in boys, presence of diarrhoea and high PVAS at first visit, considering that the disease may recur in the long term.
Disclosure
None declared

PT099

Coronary evolution and inflammatory response in ivig-resistant kawasaki disease treated with anakinra: a longitudinal study from a French tertiary center

C. Matucci Cerinic[1], M. Gattorno[1], I. Kone-Paut[2], P. Dusser-Benesty[2]
[1]IRCCS Istituto Giannina Gaslini, Rheumatology and autoinflammatory diseases, Genoa, Italy, [2]Department of Paediatric Rheumatology and CEREMAIA, Bicêtre University Hospital, APHP, university of Paris Saclay, Paris, France
Correspondence: C. Matucci Cerinic
Pediatric Rheumatology, **23(2):** PT099

Introduction: Treatment of intravenous immunoglobulin (IVIG)-resistant Kawasaki disease (KD) remains non-standardized. IL-1 blockade with anakinra (ANK) has shown promising results in case series and a phase II open-label trial.
Objectives: To describe the longitudinal clinical and coronary evolution of IVIG-resistant KD patients treated with anakinra, from treatment initiation to long-term follow-up.
Methods: We retrospectively analyzed IVIG-resistant KD patients treated with ANK at a French tertiary referral center and enrolled in the JIR cohort. Clinical, laboratory, treatment, and echocardiographic data were collected at predefined timepoints: baseline (T0), day 7, day 14, day 30, day 365, and last follow-up. Coronary artery aneurysms (CAA) were defined according to American Heart Association (AHA) criteria. Z-score normalization was defined as <2.
Results: Thirty patients were included (56.7% male, mean age 2.17 ± 2.31 years). Mean follow-up duration was 16.95 ± 17.26 months. All received aspirin and IVIG (63.3% one dose, 30% two doses, 6.7% three doses). Before ANK, 40% received corticosteroids and 6.6% infliximab. At ANK initiation, all had persistent inflammation, and 11 (36.6%) had CAA (2 at diagnosis). Two had myocarditis. Three additional patients developed new CAA under ANK, all affecting the proximal right coronary artery (RCA). CRP normalized in 77% of patients at day 14, and in 82.6% (19/23) during follow-up (median time 33 days, IQR 33.5). The median duration of ANK therapy was 14 days (range 1–324); 26.6% received corticosteroids after ANK. Seven patients were switched to another biologic.
Among patients with CAA, the proximal RCA showed the highest initial Z-score (median 3.48 [IQR 2.6–7.6]). Despite a frequent transient increase in coronary Z-scores around day 7 to 14 after ANK initiation, the median time to normalization across all coronary segments was 5 days (IQR 0–181; n=13). At last follow-up, only 3 patients had persistent CAA.
Conclusion: In this French tertiary cohort, anakinra was associated with favorable 1-year outcomes regarding systemic inflammation and coronary artery evolution in IVIG-resistant KD. Prospective studies are needed to confirm these findings.
Disclosure
None declared

PT100

Elevated serum brain injury markers correlate with disease features and interferons in children with systemic lupus erythematosus

G. Ramanathan[1], O. Mwizerwa[1], J. Ledochowski[1], T. El Tal[2], L. Ng[1], A. Jeyanathan[1], A. Davis[1], L. Hiraki[1], D. Levy[1], J. Wither[3], Z. Touma[3], A. Yeh[1], A. Knight[1]
[1]Hospital for Sick Children, Toronto, [2]Children's Hospital of Eastern Ontario, Ottawa, [3]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto, Canada
Correspondence: A. Knight
Pediatric Rheumatology, **23(2):** PT100

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) involves interferon (IFN)-mediated inflammation emerging during the critical period of adolescent brain development. Neuropsychiatric lupus (NPSLE) manifests as syndromes like cognitive dysfunction, seizures, and psychiatric Clinicians face challenges diagnosing/treating brain inflammation in cSLE, due to suboptimal diagnostic tools. Neuronal/glial structural proteins may be useful biomarkers of brain injury in cSLE.

Objectives: We compared serum levels of brain injury markers and IFNs between children with cSLE and controls and investigated the relationship of markers to cSLE disease features and serum-IFN levels.
Methods: We utilized prospectively-collected cross-sectional data from cSLE participants (ages 12-17) recruited from the Lupus Clinic at a Canadian tertiary children's hospital from January 2020–December 2023 and age-, sex-matched healthy controls. Serum brain injury markers (serum neurofilament light (sNFL), glial fibrillary acidic protein (GFAP), Tau) were quantified using Simoa Human Neurology 4–Plex B assay; IFN-α and IFN-γ were also quantified by their respective Simoa assays (Quanterix, Billerca, MA, USA). Disease features included disease activity (SLEDAI-2K), damage (SLICC damage index, SDI >0), glucocorticoid (GC) dose at study visit, and cumulative GC exposure (prednisone-equivalent). Wilcoxon rank sum test compared markers and IFNs; Spearman correlation tested associations.
Results: 56 cSLE participants (mean age=15.1±1.8 years, 86% female) and 43 controls (mean age=15.1±1.7 years, 81% female) were included. For cSLE, median disease duration was 22.6 months (IQR 12.5-43.9), median SLEDAI-2K was 2.5 (IQR, 2-5.5), 13% had disease damage, 41% were using glucocorticoids at study visit, and median cumulative GC exposure was 1.9 grams (IQR 0.6-6.9). One patient had a NPSLE diagnosis. GFAP (114.0 vs 74.3 pg/mL) and Tau (3.57 vs 2.58 pg/mL) levels were significantly higher in cSLE compared to controls ($p<0.05$), as were serum IFN-α (0.278 vs 0.018 pg/mL) and IFN-γ (0.100 vs 0.068 pg/mL). All brain injury markers had significant positive correlations with SLEDAI-2K and GC dose; sNFL and Tau associated with disease damage. Higher levels of sNFL and GFAP correlated with IFN-α, while GFAP also associated with IFN-γ. No correlations were found between Tau and IFNs.
Conclusion: Serum brain injury markers and IFNs were elevated in cSLE, with brain injury markers correlating with disease features, IFN-α, and IFN-γ. This suggests a link between IFN-mediated inflammation and neuronal/glial injury, and potential utility of sNFL, GFAP and Tau as diagnostic and monitoring biomarkers in cSLE. Future studies will explore relationships between brain injury markers and IFNs in larger cSLE cohorts over time.
Disclosure
None declared

P003

Comparative evaluation of chatgpt and llama for reliability, quality and accuracy in familial mediterranean fever

A. Uzun Bektaş, S. E. Ünsal, B. Bora
Pediatric Rheumatology, Dokuz Eylul University, İzmir, Türkiye
Correspondence: A. Uzun Bektaş
Pediatric Rheumatology, **23(2):** P003

Introduction: In the era of advanced technology, large language models (LLMs) such as OpenAI's ChatGPT and Meta's LLaMA offer rapid access to medical information for both patients and healthcare professionals. Unlike traditional search engines, LLMs empower clinicians to retrieve clinical data rapidly, facilitating decision-making processes. Despite their broad potential and widespread accessibility, studies have highlighted their accuracy and reliability concerns. The utilization of LLMs in rheumatology, particularly in the context of Familial Mediterranean Fever (FMF) remains underexplored.
Objectives: This study aims to evaluate and compare the accuracy, quality, and reliability of responses generated by ChatGPT-4o and LLaMA-3.1 405B models to medical questions related to FMF.
Methods: A total of 31 questions related to FMF were prepared from a clinician's perspective, based on the SHARE and EULAR guidelines. Each question was asked to ChatGPT-4o and LLaMa-3.1 405B only once in separate chat sessions. The randomized responses were independently and blindly evaluated by two pediatric rheumatologists, each with over 20 years of experience, in terms of reliability, quality, and accuracy. Reliability was assessed using the Modified DISCERN score, and quality using the Global Quality Scale (1). The accuracy of the responses was evaluated according to the evidence-based guideline on the genetic diagnosis of FMF published by SHARE and the guideline on FMF management published by EULAR (2,3). The Shapiro-Wilk test, the Intraclass Correlation Coefficient, and the Wilcoxon Signed Rank test were used to analyze the score distribution, inter-rater agreement, and the models' comparative performance, respectively. Readability was assessed using the Flesch Reading Ease, Flesch-Kincaid Grade Level, Gunning Fog Index, Coleman-Liau Index, and SMOG Index (4).
Results: Both models demonstrated moderate reliability according to the modified DISCERN score and high response quality on the Global Quality Score. Although both models aligned with guidelines in terms of accuracy on average, LLaMA exhibited notable inconsistencies. Despite achieving a high average score, some of its responses either directly contradicted guideline-based protocols or contained partially aligned guidelines but erroneous information. In contrast to LLaMA, ChatGPT's responses adhered to guidelines without contradictions; however, certain responses demonstrated informational gaps. Statistical analyses showed that ChatGPT's responses were superior to LLaMA's, with significantly higher scores in accuracy, quality, and reliability. Readability assessments showed that understanding the answers from both LLMs required at least a college-level education.
Conclusion: It is crucial for the clinicians to consider that LLMs may provide incomplete or misleading information.
Disclosure
None declared

References

1. Charnock D, Shepperd S, Needham G, Gann R. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. J Epidemiol Community Health (1978) [Internet]. 1999 [cited 2025 Feb 4];53(2):105. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC1756830
2. Ozen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, Giancane G, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis [Internet]. 2016 Apr 1 [cited 2025 Feb 2];75(4):644–51. Available from: https://ard.bmj.com/content/75/4/644
3. Giancane G, Haar NMT, Wulffraat N, Vastert SJ, Barron K, Hentgen V, et al. Evidence-based recommendations for genetic diagnosis of familial Mediterranean fever. Ann Rheum Dis [Internet]. 2015 Apr 1 [cited 2025 Feb 2];74(4):635–41. Available from: https://ard.bmj.com/content/74/4/635
4. Derivation of New Readability Formulas (Automated Readability Index, Fog Count and Flesch Reading Ease Formula) for Navy Enlisted Personnel [Internet]. [cited 2025 Feb 4]. Available from: https://apps.dtic.mil/sti/citations/ADA006655

P004

Is it possible to predict the need for tonsillectomy in children with PFAPA?

B. Öksel[1], Z. Özaslan[1], A. Şen[2], S. Atamyıldız Uçar[3], M. Çakan[4], S. N. Tığrak[5], B. Menentoğlu[6], F. Kaya[7], D. Alkan[2], G. O. Yener[8], H. Adıgüzel Dündar[9], Ö. Altuğ Gücenmez[9], F. Demir[10], H. Ilgaz Tüzen[11], N. Belder[12], A. Tanatar[13], G. Vatansever[14], H. Kazanasmaz[15], K. Ulu[16], A. U. Bektaş[17], F. G. Demirkan[18], B. Bozkaya Yücel[19], T. Kasap[20], B. K. Demir[11], D. G. Yıldırım[12], S. S. Kilic[21], M. Kalyoncu[15], S. Yüksel[22], B. Bora[17], K. Öztürk[7], N. A. Ayaz[6], S. Türkuçar[5], S. Balcı[23], N. Şahin[1], S. Özdel[2], B. Sözeri[3], H. E. Sönmez[1]
[1]Department of Pediatric Rheumatology, Kocaeli University, Kocaeli, [2]Department of Pediatric Rheumatology, Ankara Etlik City Hospital, Ankara, [3]Department of Pediatric Rheumatology, Health Sciences University, Umraniye Training and Research Hospital, [4]Department of Pediatric Rheumatology, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, İstanbul, [5]Department of Pediatric Rheumatology, Pamukkale University, Denizli, [6]Department of Pediatric Rheumatology, İstanbul University, [7]Department of Pediatric Rheumatology, İstanbul Medeniyet University, İstanbul, [8]Department of Pediatric Rheumatology, Eskişehir City Hospital, Eskişehir, [9]Department of Pediatric Rheumatology, Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir, [10]Department of Pediatric Rheumatology, Acıbadem Ataşehir Hospital, İstanbul, [11]Department of Pediatric Rheumatology and Nephrology, İzmir Katip Çelebi University, İzmir, [12]Department of Pediatric Rheumatology, Gazi University, Ankara, [13]Department of Pediatric Rheumatology, Gaziantep City Hospital, Gaziantep, [14]Department of Pediatric Rheumatology, Bursa Uludag University Faculty of Medicine, Bursa, [15]Department of Pediatric Rheumatology, Karadeniz Technical University, Trabzon, [16]Department of Pediatric Rheumatology, Sancaktepe Prof. Dr Ilhan Varank Training and Research Hospital, İstanbul, [17]Department of Pediatric Rheumatology, Dokuz Eylul University, İzmir,

[18]Department of Pediatric Rheumatology, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, [19]Department of Pediatric Rheumatology, Samsun Training and Research Hospital, Samsun, [20]Department of Pediatrics, Çanakkale Onsekiz Mart University, Çanakkale, [21]Department of Immunology and Rheumatology, Bursa Uludag University Faculty of Medicine, Bursa, [22]Department of Pediatric Rheumatology, Çanakkale Onsekiz Mart University, Çanakkale, [23]Department of Biostatistics and Medical Informatics, Faculty of Medicine, Kocaeli University, Kocaeli, Türkiye
Correspondence: B. Öksel
Pediatric Rheumatology, **23(2):** P004

Introduction: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis syndrome (PFAPA) is the most common periodic fever disorder in children. Tonsillectomy is considered an important option due to its positive effects on the resolution of attacks.
Objectives: This study aims to identify clinical and laboratory predictors for recommending tonsillectomy in PFAPA patients.
Methods: This retrospective, multicenter, cross-sectional study included 20 pediatric rheumatology centers in Turkey. Patients diagnosed with PFAPA according to the Eurofever/PRINTO classification criteria between January 2019 and January 2024 were included. Demographic, clinical, and laboratory data were recorded. Surgical outcomes and satisfaction were evaluated in operated patients.
Results: This study included 1205 PFAPA patients. Tonsillectomy was recommended for 332 patients, and 167 underwent the procedure. After tonsillectomy, 69.5% of patients experienced complete resolution of symptoms, while 26% had partial recovery. Overall, 89.2% of patients were satisfied with the procedure. The absence of exudative tonsillitis during attacks, along with the presence of pharyngitis or abdominal pain, were significant factors influencing a decision to recommend tonsillectomy. Multivariate analysis showed exudative tonsillitis was a negative predictor (p=0.012), while pharyngitis ($p < 0.001$) and abdominal pain ($p < 0.001$) were positive predictors. Longer attack duration was also associated with tonsillectomy (p=0.043).
Conclusion: Identifying which PFAPA patients would benefit from tonsillectomy may contribute to more effective disease management. In particular, patients with prolonged attack duration, absence of exudative tonsillitis, and the presence of pharyngitis or abdominal pain may be appropriate candidates for surgical intervention. Given its significant impact on quality of life, tonsillectomy is associated with high patient satisfaction.
Disclosure
None declared

References
1. Gattorno M, Hofer M, Federici S et al. Eurofever Registry and the Paediatric RheumatologyInternational Trials Organisation (PRINTO). Classification criteria for autoinflammatory recurrent fevers. Ann Rheum Dis. 2019 Aug;78(8):1025–32.
2. Byars SG, Stearns SC, Boomsma JJ. Association of Long-Term Risk of respiratory, allergic, and infectious diseases with removal of adenoids and tonsils in childhood. JAMA Otolaryngol Head Neck Surg. 2018;144(7):594-603.
3. Efficacy of partial tonsillectomy in periodic fever, aphthous stomatitis, pharyngitis and adenitis syndrome: a STROBE retrospective observational study.

P005
Early use of baricitinib in aicardi-goutières syndrome type 4: a case report
B. Alattas[1], S. Hussain[2], K. Mahmood [1]
[1]Pediatric Rheumatology, Sheikh Shakhboot Medical city, [2]Pediatric Neurology, Sheikh Khalifa Medical city, Abudhabi, United Arab Emirates
Correspondence: B. Alattas
Pediatric Rheumatology, **23(2):** P005

Introduction: Aicardi-Goutieres Syndrome (AGS) is rare genetic disorder characterized by dyysregulation of the innate immune system, particularly type 1 interferon pathway persistant activation. Patients with AGS usually presents with developmental delay or regression, seizure activity, spasticity, cutaneous leisons and other system involvement in early infancy. Janus kinase (JAK) inhibitors such as Baricitinib, are being explored to reduce the chronic autoinflammatory response. While preliminary data suggest potential benefit, yet only limited data are available.
Objectives: To report the clinical course and early developmental outcomes of an infant with genetically confirmed AGS Type 4 who initiated Baricitinib therapy at six month of age.
Methods: We describe the case of a full term female infant, who was diagnosed antenatlly with IUGR, posnatally, she was noted to have microcephaly, dystonia, visual problems and delayed milestones. Neuroimaging revealed basal ganglia and periventricular calcifications. Metabolic work up was normal and infectious causes were ruled out. Genteic testing was sent and revealed pathogenic variant in the ADAR gene, confirming the diagnosis of AGS Type 4. Baricitnib initiated at age of 6 months, represting the youngest reported patient to receive the therapy so far. No adverse reaction was reported with medication administration. Follwoing treatment initiation, the patient demonestrated modest developmental gains and she has no seizure activity reported until now.
Results: This case supports the potential role of early intervention with Baricitinib in infants with AGS. Although developmental improvements were limited, timely modulation of interferon signaling pathway may help preserving neurological function and improve neurological outcomes.
Conclusion: Our case highlight the importance of timely genetic diagnosis, and treatment initiation to optimize neurodevelopmental outcomes. Consent to published had been obtained.
Disclosure
None declared

P006
Kawasaki disease in an infant with chikungunya infection
C. Lafay, M. Ruin, A. Burtz, on behalf of Select...
Pediatrics, Saint Pierre University Hospital, Saint Pierre, France
Correspondence: C. Lafay
Pediatric Rheumatology, **23(2):** P006

Introduction: Kawasaki disease (KD) is an acute systemic vasculitis that primarily affects children. To this day, its cause is still unknown. Multiple studies have reported virus in children presenting with KD, in particular Epstein-Barr virus, measles virus, herpesvirus, varicella-zoster virus, influenza virus, coxsackie virus, bocavirus, sars-cov-2 virus. So far, most described viruses were transmitted by air, by droplets or by contact.
Considerably less information is available on arbovirus in children with KD. However, some observational studies have reported an overlap between KD outbreaks and seasonal peaks of arboviral infections, suggesting the possible role of these pathogens as triggers of KD.
In the beginning of the year 2025, there was a massive outbreak of Chikungunya infection on the Reunion Island with many children affected. Paediatric presentations for Chikungunya infection usually include high fever, skin, joint and neurological manifestations.
Although Kawasaki disease is known to be triggered by certain virus, no cases of kawasaki-like disease have been yet described in these patients.
Objectives: Here we reported the case of a 9 years-old boy diagnosed with a Chikungunya infection who presented with Kawasaki-like disease 2 weeks after the beginning of the infection.
Methods: A 9-years-old caucasian male was first diagnosed with Chikungunya infection by his general practitioner. He had fever, arthralgia and cutaneous rash. The symptoms improved and the fever stopped for 7 days before starting up again. After 1 week of high fever (40°), he developed gastrointestinal symptoms with diarrhea, vomit and weight loss. The general practitioner prescribed an abdominal ultrasound which was normal and bacterial urinalysis which was negative. Given the deterioration of the general condition, he was put on antibiotics for a week.
Two weeks after the beginning of the fever, he developped inflammation of both cervical and inguinal lymph nodes which a pustular raash that led him to the emergency room Saint Pierre University Hospital in La Reunion. At arrival he had a major blood inflammation with a CRP of 284mg/l with anemia 11g/L and hepatic cytolysis (<2N). During his hospitalisation, in addition to his fever, the other major criteria

of kawasaki disease were rapidly observed: supracentimetric cervical and inguinal lymphnode, cheilitis with strawberry tongue, conjunctival hyperemia and erythematous rash all over his body.
Blood tests revealed : anemia 11g/dl, negative EBV PCR, negative viral multiplex PCR, negative Chikungunya/Leptospirosis/Dengue PCR.
The Chikungunya serology came back positive with a profile suggesting a recent infection: IgM positive at 20 and IgG positive at 2.9. Dengue serology was negative. COVID serology was positive for IgG not IgM.
Bacteriological and mycological swab from the pustules was positive for Candida albicans. A Chest X-ray showed no infectious focus or effusion. Urinalysis showed aseptic leukocyturia. A cardiac ultrasound was then performed, showing dilation of both coronary arteries with Z-score>2.The patient was administered intravenous immunoglobulin (IVIG) 2g/kg, corticosteroids 2mg/kg/j IV and aspirin. The fever and all of the other symptoms resolved after 1 dose of IVIG. The CRP went down quickly and was negative 6 days after the begining of IVIG.
Results: Here the precise mechanism by which chikungunya infection may contribute to the onset of KD remains to be clarified. Chikungunya could just be a confounding bystander to another case of multisystem inflammatory syndrome linked to sars-cov-2 since the serology was positive. However, previous studies have shown that the KD seasonality in certain countries may support an arbovirus infection trigger, mainly with dengue infection, but more rarely with chikungunya infection.
Conclusion: In endemic regions for chikungunya infection, physicians should be aware regarding the possibility of the arboviruses as triggers for kawasaki-like disease. Any prolonged fever in a patient with chikungunya infection should be investigated. Consent to published had been obtained.
Disclosure
None declared

P002

Impact of familial mediterranean fever on health-related quality of life: a systematic review

A. N. Ahmad[1], K. Mustafa[1], O. F. Razouk[1], M. Al Khalidi[1], A. A. Albast[1], A. Al Khalidi[1], A. R. Al Midani[2]
[1]College of Medicine, University of Sharjah, Sharjah, [2]Tawam Hospital, Al Ain, United Arab Emirates
Correspondence: O. F. Razouk
Pediatric Rheumatology, **23(2):** P002

Introduction: Familial Mediterranean Fever (FMF) is a chronic autoinflammatory disease that leads to repeated fever and inflammation episodes that typically start during childhood [1]. The symptoms can affect many areas of functioning in daily life, including how children feel and what they can do.
Objectives: We aimed to synthesize evidence on the relationship between childhood FMF and children's health-related quality of life (HRQoL), as well as the discrepancy of children's HRQoL between parent- and child-reported HRQoL.
Methods: Following PRISMA guidelines, we systematically searched four databases, PubMed, Embase, CINAHL, and Web of Science, from inception until March 26th, 2025. Observational studies reporting HRQoL using the Pediatric Quality of Life Inventory 4.0 Generic Core Scale (PedsQL 4.0 GCS) were included. Quality of included articles was assessed using the Newcastle-Ottawa Scale. Primary outcomes were child-reported and parent-proxy scores. Information on study characteristics and clinical history of pediatric FMF patients was also recorded.
Results: We screened a total of 557 articles; eight of them were included, involving 576 children with FMF, aged 8 to 18 years. The mean of total scores among FMF patients ranged from 65.0 to 81.3, which are lower than those reported for healthy controls (84.43–88.37). Physical functioning scores ranged from 65.0 to 83.0, emotional from 70.0 to 86.3, social from 73.0 to 96.4, and school functioning from 73.0 to 84.6, indicating varying degrees of impairment. Parent proxy reports aligned with child reports, especially in physical and psychosocial domains. Based on the Newcastle-Ottawa Scale, case-control studies had a median quality score of 7 (IQR: 7–8) out of 9, while cross-sectional studies scored a median of 6 (IQR: 4.5–6.5) out of 8.
Conclusion: Findings highlight that FMF in children has a clear negative impact on quality of life across most domains. Both the child and proxy scores were consistently lower compared to those of healthy peers. The results of this review point to the importance of care that addresses the emotional and social challenges these children face.
Disclosure
None declared

Reference

1. The International FMF Consortium. Ancient missense mutations in a new member of the RoRet gene family are likely to cause familial Mediterranean fever. *Cell*. 1997;90(4):797–807. doi:https://doi.org/10.1016/S0092-8674(00)80539-5.

P007

PFAPA outcomes: experience from a tertiary centre in bristol, United Kingdom

C. Govardhan[1], A. Batchu Prithvi[1], K. Darma[2], M. R Roderick[2], A. V Ramanan[1]
[1]Paediatric Rheumatology, [2]Paediatric Immunology, Bristol Royal Hospital for Children, Bristol, United Kingdom
Correspondence: C. Govardhan
Pediatric Rheumatology, **23(2):** P007

Introduction: Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenitis Syndrome (PFAPA) is an autoinflammatory condition of childhood, that presents with regular attacks of some or all of the named features.(1) Whilst the disease has a good prognosis with potential spontaneous resolution prior to teenage life, the impact of frequent attacks on social and educational development can be significant.
Objectives: To describe our experience and outcomes with different treatment options in our cohort of children with PFAPA at Department of Paediatric Rheumatology and Immunology, Bristol Royal Hospital for Children.
Methods: Outpatient lists and electronic patient records were used to identify referred children with a diagnosis of PFAPA.
Results: A total of 61 children were identified with a diagnosis of PFAPA. 38 (62%) underwent a tonsillectomy. Whist awaiting tonsillectomy, 44 (72%) received colchicine of whom 36 reported improvement in symptoms. 5 children during this period were offered a trial of steroids at the start of the flare (all 5 reported partial improvement in symptoms). 26 had resolution of symptoms; 25 had significant improvement in symptoms while 2 had no improvement. Of note, the two children that did not respond to tonsillectomy also did not respond to colchicine.
Conclusion: Though this is a small retrospective observational study, we demonstrate 84% of children with PFAPA reported improvement or cure following tonsillectomy $\pm$ colchicine.
Trial registration identifying number: Nil
Disclosure
None declared

Reference

1. Wang A, Manthiram K, Dedeoglu F, Licameli GR. Periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome: A review. World J Otorhinolaryngol - Head Neck Surg. 2021 Jul;7(3):166–73.

P008

Safety and efficacy of IV neridronate in patients with chronic nonbacterial osteomyelitis (CNO)

D. Iacono, S. Della Paolera, G. Martini
Pediatric Unit, University Hospital,S Maria della Misericordia, Udine, Italy, Udine, Italy
Correspondence: G. Martini
Pediatric Rheumatology, **23(2):** P008

Introduction: Chronic Nonbacterial Osteomyelitis (CNO) is an aseptic inflammatory skeletal disease, that primarily affects the pediatric population and rarely adults[(1,2)]. The presentation of CNO is tipically non-specific, with local bone pain, and sometimes with other clinical features including low grade fever, swelling, warmth, focal tenderness, and unspecific radiological findings. For this reason, the diagnostic process is one of exclusion[(2)]. First-line therapeutic agents are non-steroidal anti-inflammatory drugs (NSAIDs) while use of corticosteroids, disease-modifying antirheumatic agents and anti-TNF agents have

also been reported. In refractory cases, there is increasing evidence on the use of bisphosphonates[3].
Objectives: Aim of this report is to describe the safety and efficacy of of Neridronate in pediatric CNO.
Methods: One 13-years old girl had CNO with localization in the temporo-mandibular joint, clavicle and pelvic bones, one 9-years old girl was involved on the jaw and one 10-years old boy was affected at the diaphysis of both femurs and the metacarpal bone of the left first finger. All patients underwent Neridronate infusions at three months interval and were evaluated before starting and after completing treatment by whole body Magnetic Resonance Imaging (WB-MRI), blood exams evaluating acute phase reactants, calcium-phosphorous metabolism, particularly C-terminal telopeptide of type I collagen (CTX) and Procollagen Type I N-terminal Propeptide (P1NP) levels.
Results: All patients received four, three and four infusions of Neridronate, respectively. During treatment clinical symptoms progressively resolved, with all children experiencing the disappearance of pain. CTX and P1NP levels declined steadily throughout therapy. Follow-up WB-MRI revealed no new bone lesions and showed significant improvement in pre-existing ones. The treatment was well tolerated as the patients experienced only mild flu-like syndrome after the first infusion.
Conclusion: According to our knowledge, this is the first study reporting efficacy and safety of Neridronate in pediatric patients with CNO. Bisphosphonates are commonly used in a variety of diseases, especially in adults, and in children with osteogenesis imperfecta, osteoporosis etc. Our results suggest that Neridronate may be a promising and well-tolerated option for the management of pediatric CNO, particularly in cases unresponsive to NSAIDs. Further research is encouraged to confirm these observations and to develop standardized treatment protocols. Consent to published had been obtained.
Disclosure
None declared

References

1. Chronic non-bacterial osteomyelitis (CNO) in childhood and adolescence – a disease with many faces. Marc Steinborn, Veronika Huf 2024 Mar;196(3):243-252. doi: https://doi.org/10.1055/a-2143-7564. Epub 2023 Sep 12.
2. A clinico-radiological review of chronic non-bacterial osteomyelitis in paediatrics, adolescents, and adults: demystifying a forgotten differential. Clin Radiol 2024 Mar;79(3):170-178. doi: https://doi.org/10.1016/j.crad.2023.12.004. Epub 2023 Dec 20.
3. Challenges in the imaging and diagnosis of chronic non-bacterial osteomyelitis (CNO). DOI: https://doi.org/10.1016/j.crad.2025.106905.

P009

Neurological involvement in children with familial mediterranean fever

S. La Bella[1,2], A. Corsello[3], D. Bayraktar[4,5], A. Di Ludovico[6], G. Scorrano[7,8], M. Rinaldi[9], Y. Bayindir[10], S. Ozen[10], G. P. Milani[3,11], M. Gattorno[1], R. Caorsi[1,12]
[1]UOC Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, Genova, **[2]**UO Pediatric Rheumatology, "G. D'Annunzio" University of Chieti-Pescara, Chieti, **[3]**Department of Clinical Sciences and Community Health, Università Degli Studi Di Milano, Milano, Italy, **[4]**Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Izmir Katip Celebi University, Izmir, Türkiye, **[5]**Arthritis Research Canada, British Columbia, Vancouver, Canada, **[6]**Department of Pediatrics, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, **[7]**Department of Pediatric Neurology,
Reference Centre for Rare Epilepsies, Necker Enfants Malades University Hospital, AP-HP, Université Paris Cité, Paris, France, **[8]**UO Pediatric Neurology, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, **[9]**Pediatric Department, John Radcliffe Hospital - Oxford University Hospitals, Thames Valley Deanery, Oxford, United Kingdom, **[10]**Division of Pediatric Rheumatology, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Türkiye, **[11]**Department of Pediatrics, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, **[12]**Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), Università degli Studi di Genova, Genova, Italy
Correspondence: D. Bayraktar
Pediatric Rheumatology, **23(2):** P009

Introduction: Although typical findings of familial Mediterranean fever (FMF), such as brief fever episodes and abdominal and/or chest pain, have been largely described and incorporated into the current EuroFever/PRINTO classification criteria (1), little is known about the neurological manifestations of the disease in childhood.
Objectives: The aim of this study was to systematically define the neurological involvement in children with FMF.
Methods: A systematic search of the literature was conducted in PubMed/Medline, Cochrane, and Web of Science databases according to the PRISMA guideline. The search involved the articles published in English up to March 1st, 2025, with no filter set for publication date. Papers detailing FMF patients less than 18 years of age with clinical neurological involvement or assessing neurological outcomes were selected. All study designs were considered, including case series and case reports. When there was a clear distinction between patients aged less than 18 years and adults only pediatric patients were included in the dataset. Given the multiple classification criteria available for FMF, all patients diagnosed based on the authors' decision were included. Non-peer reviewed content such as congress abstracts, papers published in languages different than English, and papers not distinguishing between pediatric and adult patients were excluded. The following data were extracted from the articles: first author name, demographic data, study design, FMF classification criteria, characteristics of neurological involvement, *MEFV* genotype, diagnostic work-up, treatment, and outcome.
Results: Sixty-four studies, comprising 4753 children with FMF, were included. Approximately 33.9% of them had some degree of neurological involvement and were categorized into six groups: headache, seizures, demyelinating disorders, cochlear/vestibular involvement, optic nerve/retinal abnormalities, and other manifestations. Headache emerged as the most common neurological symptom in children with FMF, affecting 766 (female to male ratio: 1.28) out of 3143 children (24.4%) and was often associated with FMF flares, with frequencies ranging from 4.8% to 58.8%. Reports describe various headache phenotypes, spanning from migraine with and without aura (107 children diagnosed with migraine, 73 with probable migraine) to tension-type headaches (TTH) and secondary headache syndromes such as pseudotumor cerebri and cerebral vasculitis. Seizures were reported in 127 (female to male ratio: 0.78) out of 1890 patients from 12 studies. Reports and cohort studies describe a spectrum of seizure types that mostly occur during FMF flares and are rarely accompanied by electroencephalographic abnormalities. Indeed, febrile seizures emerged as relevant manifestations, as expected in children with FMF since they have more and high fever during childhood, with frequencies ranging from 1% to 15.2%. Demyelinating disorders, such as multiple sclerosis, were rarely reported, mostly in female adolescents with the homozygous M694V *MEFV* genotype. A few studies have shown that cochlear and retinal involvement due to chronic and recurrent inflammation may contribute to sensorineural hearing loss and retinal abnormalities. However, the causality of neurological involvement in children with FMF has not been shown and a report bias cannot be ruled out.
Conclusion: Febrile conclusions and headaches may be expected to be more common in children with FMF whose disease is poorly controlled. Case reports and series describe a heterogeneous range of neurological manifestations, including demyelinating disorders, cochlear/vestibular and retinal abnormalities. However, the causal relation has not been established, and a reporting bias cannot be overruled. Hence children with FMF should be assessed for such comorbidities to provide more substantial answers.
Trial registration identifying number: NA
Disclosure
None declared

Reference

1. Gattorno M et al, Classification criteria for hereditary recurrent fevers. Ann Rheum Dis 2019

P010

Pediatric autoinflammatory diseases with pulmonary manifestations: a retrospective cohort study

D. Unal[1], Y. Bayindir[1], E. Aliyev[1], V. Cam[1], H. Ercan Emreol[1], M. O. Erkan[1], O. Necipoglu Banak[1], H. Kisaogku[2], S. Caglayan[3], R. M. Kisla Ekinci[4], N. Emiralioglu Ordukaya[5], E. Sag[1], O. Basaran[1], M. Kalyoncu[2], Y. Bilginer[1], E. E. Yalcin[5], S. Ozen[1]

[1]Pediatric Rheumatology, Hacettepe University, Ankara, [2]Pediatric Rheumatology, Karadeniz Technical University, Trabzon, [3]Pediatric Rheumatology, University of Health Sciences, Antalya Research and Training Hospital, Antalya, [4]Pediatric Rheumatology, Çukurova University Faculty of Medicine, Adana, [5]Pediatric Pulmonology, Hacettepe University, Ankara, Türkiye
Correspondence: D. Unal
Pediatric Rheumatology, **23(2):** P010

Introduction: Autoinflammatory diseases (AID) represent a spectrum of disorders involving innate immune dysregulation. Among these, interferonopathies such as STING-associated vasculopathy with onset in infancy (SAVI) and COPA syndrome frequently manifest with interstitial lung disease (ILD). Pulmonary disease contributes significantly to morbidity and mortality in these conditions.
Objectives: To evaluate the clinical and radiological characteristics of pulmonary involvement in autoinflammatory diseases, and to identify factors contributing to morbidity in these conditions.
Methods: This retrospective study included 7 patients with pulmonary involvement due to AID followed in a single center between 2007 and 2024. Patients were categorized into SAVI, COPA, and an unclassified group presenting with diffuse alveolar hemorrhage (DAH) and arthritis. Clinical, radiological, histopathological findings, treatments, and outcomes were analyzed. Pulmonary function tests (PFTs), diffusing capacity of the lungs for carbon monoxide (DLCO), thoracic CT scans, and histopathological evaluations were systematically reviewed.
Results: The cohort consisted of four genetically confirmed SAVI cases, one COPA case, and two unclassified cases with DAH and arthritis. Pulmonary findings ranged from asymptomatic ILD to progressive respiratory failure requiring lung transplantation. Notable complications associated with therapy included infectious events such as BK virus reactivation and nocardial brain abscess. We identified a distinct "unclassified" group within our cohort, consisting of two patients presenting with diffuse alveolar hemorrhage (DAH), polyarthritis, and systemic inflammation. Despite thorough genetic analyses, no definitive disease-causing mutations were detected in these patients.
Conclusion: This study underscores the heterogeneity of pulmonary involvement in pediatric AID and emphasizes the need for early and comprehensive lung assessment. In addition to genetically confirmed COPA and SAVI cases, our cohort also included two patients presenting with DAH, arthritis, autoantibody positivity, and persistent systemic inflammation. Despite clinical similarities to COPA and SAVI, the absence of pathogenic mutations suggests the possibility of a distinct, previously unclassified monogenic interferonopathy-like phenotype. These findings highlight the need to consider such undefined presentations within the broader spectrum of early-onset pulmonary-autoimmune syndromes.
Disclosure
None declared

References

1. Crow YJ. Type I interferonopathies: a novel set of inborn errors of immunity. Ann N Y Acad Sci. 2011;1238:91-8.
2. Liu Y, Jesus AA, Marrero B, Yang D, Ramsey SE, Sanchez GAM, et al. Activated STING in a vascular and pulmonary syndrome. N Engl J Med. 2014;371(6):507-18.
3. Rodero MP, Crow YJ. Type I interferon-mediated monogenic autoinflammation: The type I interferonopathies, a conceptual overview. J Exp Med. 2016;213(12):2527-38.

P011

Challenges in measuring serum calprotectin in autoinflammation: a comparative study of commercial assays

H. Wittkowski[1], C. Park[1], M. Saers[1], S. Schleifenbaum[1], S. Fuehner[1], M. Fobker[2], A. Karolin[3], C. Schneiter[3], M. Horn[3], B. Schlueter[2], D. Foell[1]
[1]Paediatric Rheumatology and Immunology, [2]Central Laboratory, University Hospital Muenster, Münster, Germany, [3]Central Laboratory, University Hospital Insel Bern, Bern, Switzerland
Correspondence: D. Foell
Pediatric Rheumatology, **23(2):** P011

Introduction: Serum calprotectin (S100A8/A9 complex) is increasingly utilized in the clinical evaluation of autoinflammatory diseases (AID), particularly in pediatric populations. However, systematic comparisons of commercially available assays for serum calprotectin quantification remain limited, hindering the establishment of standardized diagnostic thresholds.
Objectives: To assess the performance, comparability, and clinical applicability of multiple commercially available calprotectin assays, aiming to support standardized biomarker-guided diagnostics in inflammatory and autoinflammatory diseases.
Methods: Serum samples from 40 individuals—systemic juvenile idiopathic arthritis (sJIA, n=10), adult-onset Still's disease (AOSD, n=10), familial Mediterranean fever (FMF, n=10), PAPA syndrome (n=2), infections (n=5), leukemia (n=3), and healthy pediatric controls (n=10)—were analyzed. Calprotectin levels were measured using four ELISAs (Bühlmann, R&D, BioLegend, BMA), two PETIAs (sCAL turbo, gCAL), and one CLIA (Werfen), strictly following manufacturers' protocols. A secondary dilution (10-fold) was applied for ELISA-based assays. Additional spiking experiments with purified S100A8, S100A9, and S100A8/A9 were conducted to evaluate recovery.
Results: All assays, except gCAL (r = 0.35), showed strong correlation with the Bühlmann ELISA
Reference (r = 0.99). However, median values in healthy controls varied substantially (0.29–3.22 µg/mL), with inter-assay differences exceeding one log scale. Most assays failed to accurately quantify extremely high calprotectin levels (>50 µg/mL), likely due to Hook effects. Maximum measurable concentrations were limited in R&D (95 µg/mL), BioLegend (82 µg/mL), gCAL (118 µg/mL), and Werfen (227 µg/mL), whereas only the BMA ELISA reliably measured up to 1000 µg/mL. sCAL turbo demonstrated partial capacity to estimate high values, albeit with underestimation. Spike recovery ranged from 79–268%, with sCAL turbo showing the most consistent recovery (116%).
Conclusion: Commercial assays reliably measure serum calprotectin in the normal to moderately elevated range (<50 µg/mL), but results are not interchangeable across platforms. Significant variability in upper detection limits and susceptibility to Hook effects can lead to underestimation in patients exhibiting severe inflammation. Clinicians should interpret results in the context of assay-specific
Reference ranges. For suspected extreme elevations, additional dilution steps are recommended to prevent false-low values and ensure accurate clinical decision-making.
Disclosure
None declared

P012

Predicting FMF50 response in pediatric FMF: evaluating disease activity scores and colchicine resistance risk

E. N. Dizman, F. Haslak
Pediatric Rheumatology, Istanbul Medeniyet University, Istanbul, Türkiye
Correspondence: E. N. Dizman
Pediatric Rheumatology, **23(2):** P012

Introduction: Familial Mediterranean Fever (FMF), the most common monogenic autoinflammatory disease characterised by recurrent episodes of fever, polyserositis, and arthritis, is assessed using various tools: the Auto-Inflammatory Diseases Activity Index (AIDAI), Pras, Mor scores, and the International Severity Score for FMF (ISSF) are utilised to measure disease activity; the FMF50 score measures treatment response; and the TURPAID score is used to predict the risk of colchicine resistance at diagnosis.
Objectives: The aim of this study was to determine whether these scores and acute-phase reactants can predict the FMF50 response earlier.
Methods: Children diagnosed with FMF according to the Eurofever/PRINTO criteria and treated with colchicine for ≥6 months were included. Patients with poor adherence or those without exon 10 mutations were excluded. Disease activity was assessed using AIDAI, Pras, Mor, and ISSF, while FMF50 criteria evaluated treatment response. TURPAID score was used to assess risk of colchicine resistance at diagnosis. Concordance between scores was analysed using Cohen's kappa and Fleiss' Kappa. The patients were classified as FMF50 responders or non-responders. Predictors of non-response were identified via

logistic regression. The association between TURPAID score categories (≥2 vs. <2) and FMF50 response was analyzed with chi-square test.
Results: Among 117 patients (44.4% female), 73 (62.4%) and 84 (71.8%) achieved FMF50 response at 3 and 6 months, respectively. The ISSF, AIDAI, and Pras scores were significantly higher in non-responders (p<0.001). Elevated CRP (OR 1.035, 95% CI 1.002–1.070, p=0.038), ISSF (OR 1.703, 95% CI 1.135–2.557, p=0.010), and AIDAI (OR 1.253, 95% CI 1.053–1.491, p=0.011) at three months were significantly associated with FMF50 non-response at sixth month. Multivariate analysis identified high ISSF (OR 1.745, 95%CI 1.129–2.698, p=0.012) and AIDAI (OR 1.265, 95%CI 1.056–1.514, p=0.011) as independent predictors. Although the TURPAID score was not significantly associated with the FMF50 response, patients with higher TURPAID scores tended to have lower FMF50 achievement rates. APRs were significantly correlated with ISSF, Pras, and AIDAI. Kappa coefficients revealed poor agreement among the activity scores (Kappa values = 0.157 to –0.048).
Conclusion: The ISSF and AIDAI scores may predict the FMF50 response as early as the third month. While the TURPAID score was not a statistically significant predictor, its potential role in early risk stratification warrants further exploration in clinical settings.
Disclosure
None declared

References

1. Batu ED, Şener S, Arslanoğlu Aydın E, Aliyev E, Bağrul İ, Türkmen Ş, et al. A score for predicting colchicine resistance at the time of diagnosis in familial Mediterranean fever: Data from the TURPAID registry. Rheumatology. 2024;63(3):791–797.
2. Eroglu Kara F, Beşbaş N, Topaloglu R, and Ozen S. Treatment of colchicine-resistant Familial Mediterranean fever in children and adolescents, Rheumatol Int, 2015;35(10):1733-37.
3. Ozen S, Demirkaya E, Duzova A, Erdogan O, Erken E, Gul A, Kasapcopur O et al. FMF50: a score for assessing outcome in familial Mediterranean fever. Ann Rheum Dis, 2014;73:897–901.

P013

Clinical spectrum and genetic analysis of recurrent fevers in childhood

E. De Martino[1], A. Pin[1], A. Gentile [2], M. Girardelli[1], A. Tesser[1], M. Klanjscek[2], L. De Nardi [3,4], G. M. Severini[1], S. Pastore[1], A. Tommasini[1,2], A. Taddio[1,2]
[1]Institute for Maternal and Child Health IRCCS Burlo Garofolo, [2]University of Trieste, Trieste, [3]Bambino Gesù Children's Hospital, [4] Tor Vergata University, Rome, Italy
Correspondence: E. De Martino
Pediatric Rheumatology, **23(2):** P013

Introduction: Recurrent fever syndromes are a group of autoinflammatory disorders, including hereditary recurrent fevers (HRFs), like Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD), TNF Receptor-Associated Periodic Fever Syndrome (TRAPS), and cryopyrinopathies, as well as multifactorial conditions like PFAPA (Periodic Fever, Pharyngitis, Aphthous Stomatitis, and Adenitis) syndrome. Subjects with recurrent fevers that don't meet the diagnostic criteria for hereditary periodic fever syndromes or PFAPA have also been described and referred to as "Syndrome of Undifferentiated Recurrent Fevers" (SURF).
Objectives: The aim of this study is to describe the clinical characteristics of patients with recurrent fevers referred to a third-level hospital, to evaluate the utility of Eurofever/PRINTO classification criteria in a real-life setting, and to compare the existing classification with subgroups formed by machine-learning techniques (unsupervised clustering).
Methods: This retrospective study is based on the clinical records of patients consecutively referred to the Pediatric Department of the IRCCS Burlo Garofolo of Trieste for recurrent fevers over the past 10 years. The Sanger method, Next Generation Sequencing (NGS) and Whole Exome Sequencing (WES) were applied for genetic analysis. The hclust function in RStudio was used to perform the unsupervised clustering analysis.
Results: Our analysis demonstrated distinct clinical features among PFAPA, SURF, and HRF. Simultaneously, unsupervised clustering analysis revealed novel subgroups that can expand the PFAPA spectrum beyond the existing definition provided by the Eurofever/PRINTO criteria. Furthermore, numerous patients categorized as SURF were allocated to these newly established subgroups.
Conclusion: The findings of this study indicate that the clinical spectrum of PFAPA-like syndrome is broader than previously documented in the literature, including symptoms typically linked to HRFs, infections, and atypical clinical presentations. Based on this concept, certain SURF patients may be reclassified, highlighting the healing of recurrent fever episodes after tonsillectomy in the subjects or in one of his/her family members.
Disclosure
None declared

P014

Characterizing biologic therapy requirements in FMF patients with sacroiliitis

E. Tunce, S. Atamyıldız Uçar, N. Kara Çanlıoğlu, B. Sözeri
Pediatric Rheumatology, University of Health Science, Ümraniye Training and Research Hospital, İstanbul, Türkiye
Correspondence: E. Tunce
Pediatric Rheumatology, **23(2):** P014

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease, particularly prevalent in populations of Mediterranean origin. Although FMF primarily manifests with recurrent febrile episodes and serositis, musculoskeletal involvement, including sacroiliitis, can occasionally complicate the clinical course. Sacroiliitis in FMF patients may be underrecognized due to overlapping symptoms and variable imaging findings. The treatment of FMF-associated sacroiliitis often requires more than colchicine; in some cases, biologic agents such as anti-IL-1 or anti-TNF therapies are used depending on the dominant clinical features, including inflammatory attack patterns and axial joint involvement. However, there is limited data on the factors influencing the choice and effectiveness of these biologics in FMF patients with sacroiliitis.
Objectives: To evaluate the requirement and response to biological treatments in patients with FMF-associated sacroiliitis, and to analyze correlations with genotypic (MEFV mutations, HLA-B27) and phenotypic features (acute-phase response, attack findings).
Methods: We retrospectively and cross-sectionally evaluated FMF patients followed in our pediatric rheumatology clinic between 2016 and 2025 who had biallelic pathogenic MEFV mutations in exon 10 and a diagnosis of sacroiliitis confirmed by MRI. Patients were grouped according to their biological therapy status. Demographic, clinical, genetic, and laboratory characteristics were compared between groups.
Results: Among 24 patients with FMF-associated sacroiliitis, 13 (54%) required biological disease-modifying antirheumatic drugs (bDMARDs). The biological treatment group had a higher male predominance and earlier age of FMF and sacroiliitis diagnoses. M694V homozygosity (77% vs. 64%) and HLA-B27 positivity (39% vs. 27%) were more frequent among biologically treated patients. Median erythrocyte sedimentation rate and serum amyloid A (SAA) levels were also higher. Anti-IL-1 agents (Anakinra or Canakinumab) were preferred in patients with frequent attacks and elevated acute phase reactants, while anti-TNF agents (Adalimumab) were used in patients without these features. Three patients required switching between anti-TNF and anti-IL-1 agents due to evolving attack profiles or sacroiliitis progression. Notably, one patient who initially received Canakinumab due to frequent FMF attacks required anti-TNF therapy for sacroiliitis progression, then returned to Canakinumab upon re-emergence of attack symptoms.
Conclusion: Biological treatment is more frequently needed in FMF patients with sacroiliitis who are male, have M694V homozygosity, are HLA-B27 positive, and demonstrate elevated acute-phase reactants. Phenotypic profiling can guide initial biologic selection: anti-IL-1 agents may be preferable in attack-dominant patients with systemic inflammation, while anti-TNF agents may be effective in those with isolated axial disease.
Disclosure
None declared

References
1. Kaçmaz H, Aldemir E, Tanatar A, et al. Sacroiliitis in children and adolescents with familial Mediterranean fever. *Adv Rheumatol*. 2021;61(1):29. Published 2021 Jun 5. doi:https://doi.org/10.1186/s42358-021-00188-2
2. Özçelik E, Çelikel E, Tekin ZE, et al. Sacroiliitis in familial Mediterranean fever: A rare joint involvement of the disease. *J Paediatr Child Health*. 2024;60(10):511-515. doi:https://doi.org/10.1111/jpc.16623

P015

Phenotypic discordance despite genotypic identity: insights from fmf siblings with biallelic exon 10 variants

E. Tunce[1], M. S. Öz[2], S. Atamyıldız Uçar[1], B. Sözeri[1]
[1]Pediatric Rheumatology, [2]Pediatrics, University of Health Sciences, Ümraniye Training and Research Hospital, İstanbul, Türkiye
Correspondence: E. Tunce
Pediatric Rheumatology, **23(2):** P015

Introduction: FMF is an autosomal recessive autoinflammatory disorder caused by biallelic mutations in the MEFV gene. Despite identical genotypes, considerable phenotypic variability is frequently observed, especially among siblings who share both genetic and environmental backgrounds. Reported differences include age at symptom onset, attack frequency, disease severity, and response to colchicine. Even monozygotic twins may follow divergent clinical courses. While homozygous M694V mutations are associated with severe, early-onset FMF and increased risk of amyloidosis, some affected siblings remain asymptomatic or show milder manifestations. These discrepancies suggest the involvement of non-genetic modifiers such as epigenetic regulation, environmental factors, and sex-based immune differences.
Objectives: To assess the degree of clinical similarity among pediatric sibling pairs diagnosed with FMF who share identical biallelic mutations in exon 10 of the MEFV gene, and to investigate the potential influence of non-genetic factors on phenotypic variation.
Methods: This cross-sectional analysis involved 194 children with FMF from 97 families, all carrying the same pathogenic biallelic mutations in exon 10 of the MEFV gene. Four monozygotic twins from two families were excluded, leaving 190 non-twin siblings for evaluation. Data on demographics, clinical presentation, genetic profile, disease severity (using Pras and ISSF scores), and colchicine responsiveness were collected and analyzed.
Results: In 88 out of 95 families, the older sibling was the first to be diagnosed. Older siblings experienced significantly longer diagnostic delays and had higher disease severity scores at the time of diagnosis. Arthritis was observed more frequently in older siblings (30% vs. 13%, p = 0.006), while other FMF-related symptoms showed no notable differences. Complete concordance in clinical manifestations was found in 41% of sibling pairs, and colchicine response was consistent in 79%. Differences in disease severity scores and attack frequency were also recorded. Among monozygotic twins, both concordant and discordant phenotypes were present.
Conclusion: The study reveals considerable clinical diversity among pediatric FMF sibling pairs despite having identical exon 10 MEFV mutations. Significant differences in disease severity and arthritis prevalence suggest that genetic identity alone does not fully account for clinical expression. Recognizing this variability is important for improving early diagnosis and tailoring patient management strategies.
Disclosure
None declared

References
1. Özçakar, Z. B., Erdogan, B. D., Elhan, A. H., & Yalçinkaya, F. (2012). Familial Mediterranean fever in siblings. *The Journal of rheumatology*, *39*(11), 2170–2174.
2. Arslanoglu Aydin, E., Baglan, E., Bagrul, İ., Emine Nur, S. Y., Kocamaz, N. G., & Semanur, O. (2025). Characteristics of Siblings with Familial Mediterranean Fever: A Single-Center Experience. *Turkish archives of pediatrics*, *60*(1), 57–62.
3. Mauvais-Jarvis, F., Bairey Merz, N., Barnes, P. J., Brinton, R. D., Carrero, J. J., DeMeo, D. L., De Vries, G. J., Epperson, C. N., Govindan, R., Klein, S. L., Lonardo, A., Maki, P. M., McCullough, L. D., Regitz-Zagrosek, V., Regensteiner, J. G., Rubin, J. B., Sandberg, K., & Suzuki, A. (2020). Sex and gender: modifiers of health, disease, and medicine. *Lancet (London, England)*, *396*(10250), 565–582.

P016

Diagnostic delay in systemic autoinflammatory disease: preliminary results from the eurofever registry

D. Piskin[1], M. Romano[1], N. Zitoun[1], R. Caorsi[2], Y.-H. Choi[1], M. Gattorno[2], E. Demirkaya[1]
[1]Western University, London, Canada, [2]IRCCS Istituto G. Gaslini, Genoa, Italy
Correspondence: E. Demirkaya
Pediatric Rheumatology, **23(2):** P016

Introduction: Systemic Autoinflammatory Diseases (SAIDs) are an umbrella term that consists of monogenic and polygenic or multifactorial origin disorders. These are rare diseases with the estimated prevalence lowest as 1-3/1,000,000. Most of the SAIDs have an early disease onset, so that many patients present in childhood or adolescence. These complex patients often see many medical practitioners over time, resulting in fragmented care, emergency room visits and hospitalizations leading to diagnostic delays. Even though the early diagnosis is essential to prevent mortality and life-long complications, the rarity of the SAIDs and the variety of clinical spectrum limit the understanding of potential diagnosis for health-care professionals.
Objectives: We aimed to identify and evaluate possible factors related with diagnostic delay in selected SAIDs from the Eurofever database.
Methods: The most common monogenic SAIDs, including Familial Mediterranean Fever (FMF), cryopyrin-associated periodic syndromes (CAPS), Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) and Mevalonate Kinase Deficiency (MKD), were selected for this study. Data on diagnostic delay is retrieved from the Eurofever database and defined as the time between symptom onset and diagnosis. Ages at disease onset and years of diagnostic delay were reported as median and interquartile range. Mann Whitney U and Kruskal Wallis tests were used to compare groups where appropriate.
Results: In total, 2249 patients (1519, FMF; 271, TRAPS; 254, CAPS; 205, MKD) from 32 countries were included in the study. 51.9% (n=1168) were male and 64.4% were Caucasian-European (n=1448). The median age at disease onset was 3.1[IQR 1-7.8] overall and, 3.6 [IQR 1.6-8] for FMF, 4.4 [IQR 1-13.4] for TRAPS, 1.2 [IQR 0-6.1] for CAPS and 0 [IQR 0-2.6] for MKD. The median age at diagnosis was 8 [IQR 4.1-16.5] overall and, 7 [IQR 4-13.2] for FMF, 16.1 [IQR 6.2-38.4] for TRAPS, 12.3 [IQR 4.3-30.5] for CAPS and 7.4 [IQR 3.7-15.2] for MKD. The median diagnostic delay in years was 2.9 [IQR 1-8.3] overall and, 2.3 [IQR 0-5.7] for FMF, 5.8 [IQR 1.4-21] for TRAPS, 5.8 [IQR 2-20] for CAPS and 5 [IQR 1.6-14.2] for MKD. Frequency of having at least one concomitant disease was 17.7% (n=399) and 14.9% (n=334) had at least one complication. Diagnostic delay was shorter in patients with FMF compared to others (p<0.001). There was no statistically significant difference in diagnostic delay between males and females (2.9 [IQR 1-8.2] and 3 [IQR 1-8.7] years, respectively, p=0.82). However, diagnostic delay was significantly higher in patients with at least one concomitant disease (4.2 [IQR 1.4-10.2] vs 2.7 [IQR 1-7.9] years, p<0.001) and patients with at least one complication (8.2 [IQR 2.4-24.2] vs 2.6 [IQR 1-6.5] years, p<0.001).
Conclusion: FMF patients have a shorter diagnostic delay compared to other SAIDs, which could be explained by the familiarity of the disease. Patients with concomitant disease and complications have longer diagnostic delay compared to others. One possible explanation could be that having concomitant diseases may confound physician's decision process. The next step of the project is to create a subset of patients fulfilling the Eurofever classification criteria and further identify and evaluate possible individual-, disease-, and country-level factors associated with diagnostic delay.
Disclosure
None declared

P017

Imaging findings in pediatric familial mediterranean fever patients with exertional leg pain

F. Aydın[1], S. Kaynak Şahap[2], Ö. S. Fitöz[2], Z. B. Özçakar[1]
[1]Pediatric Rheumatology, [2]Pediatric Radiology, Ankara University Faculty of Medicine, Ankara, Türkiye
Correspondence: F. Aydın
Pediatric Rheumatology, **23(2):** P017

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease, characterised by recurrent episodes of fever, serositis and arthritis/arthralgia. Exertional leg pain, which has been shown to be associated with a more severe disease phenotype, is a common musculoskeletal symptom of FMF, reported by 30–50% of patients. The association between leg pain and musculoskeletal findings in paediatric patients using radiological examinations has not been previously investigated.
Objectives: This study aimed to evaluate the changes in the joints and entheses of the lower leg in paediatric FMF patients with exertional leg pain, using magnetic resonance imaging (MRI) and ultrasonography (USG).
Methods: The study included patients with FMF who attended to our clinic between June 2023 and May 2024 with a complaint of exertional leg pain, and who carried at least one exon 10 mutation in the MEFV gene. All patients underwent grey-scale and colour Doppler ultrasonography of the lower extremities, including a total of ten enthesis areas, the knee and ankle joints bilaterally. All patients underwent unilateral (right) ankle MRI scanning. Imaging protocols were performed when patients developed leg pain after standing or walking for a while.
Results: Thirty patients were included in the study, 15 (50%) of whom were male. The mean age was 159.40 ± 7.70 months. USG revealed bursitis of the knee and/or ankle in 24 patients (80%) and increased tendon thickness around the knee in 16 patients (53.3%). USG also showed oedema in the heel in 11 patients (36.7%), increased Doppler flow in the tendons in five patients (16.7%) and fluid in the knee joint in one patient (3%). MRI scans of the right foot showed retrocalcaneal bursitis in 10 of 30 patients (36.6%). MRI also showed tenosynovitis in three patients (10%), calcaneal oedema in seven patients (23.3%) and an enthesophyte in one patient (3%).
Conclusion: Bursitis of the knee and/or ankle joints was found in majority of paediatric FMF patients presenting with exertional leg pain. Furthermore, an increase in tendon thickness around the knee was observed in over half of the patients. Leg pain in FMF patients may be caused by inflammation of the tendons and bursae after exercise.
Disclosure
None declared

References

1. Eshed I, Kushnir T, Livneh A, et al. Exertional leg pain as a manifestation of occult spondyloarthropathy in familial Mediterranean fever: an MRI evaluation. Scand J Rheumatol. 2012;41(6):482–486.
2. Livneh A, Langevitz P, Zemer D, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis (10):1879–1885.
3. Langevitz P, Livneh A, Zemer D, et al. Seronegative spondyloar thropathy in familial Mediterranean fever. Semin Arthritis Rheum. 1997;27(2):67–72.
4. Kushnir T, Eshed I, Heled Y, Livneh A, Langevitz P, Ben Zvi I, Konen E, Lidar M. Exertional muscle pain in familial Mediterranean fever patients evaluated by MRI and 31P magnetic resonance spectroscopy. Clin Radiol. 2013 Apr;68(4):371-5.

P018

Identifying high-risk fmf patients: a prospective validation of the predict-crfmf score

N. Aktay Ayaz[1], Ö. Akgün[1], F. G. Demirkan[1], S. D. Arık[1], B. Menentoğlu[1], B. Başer[1], A. Dudaklı[1], E. Tunce[2], A. Doğru[1], G. Kavrul Kayaalp[1], M. Çakan[3], B. Sözeri[2], H. E. Sönmez[4]
[1]İstanbul University, [2]Ümraniye Research and Training Hospital, [3]Zeynep Kamil Children's Hospital, İstanbul, [4]Kocaeli University, Kocaeli, Türkiye
Correspondence: F. G. Demirkan
Pediatric Rheumatology, **23(2):** P018

Introduction: Recognizing the value of predictive models in guiding treatment strategies, we developed the *PREDICT-crFMF score*—a novel tool designed to predict colchicine resistance in children with FMF. This model was externally validated in a large, independent cohort, demonstrating robust performance with a sensitivity of 82% and specificity of 79%.
Objectives: To prospectively validate the *PREDICT-crFMF* score and assess its performance in predicting colchicine resistance based on patients' baseline characteristics.
Methods: Data from patients presenting for the first time after the introduction of the *PREDICT-crFMF* scoring system were analyzed. Preliminary findings from two tertiary pediatric rheumatology centers were reviewed. Eligible patients were diagnosed after 2022, were under 18 years of age at diagnosis, and had a minimum follow-up of 6 months. The score's performance was evaluated using a predefined cut-off value of 9, derived from logistic regression modeling.
Results: Between January 2023 and December 2024, 83 patients were admitted to the paediatric rheumatology outpatient clinics and newly diagnosed with FMF. Among these, 73 patients (88%) showed a favorable response to colchicine treatment, while 10 patients (12%) met the criteria for colchicine-resistant FMF (cr-FMF), having experienced more than three clinically and laboratory-confirmed inflammatory attacks within a six-month period despite regular colchicine use. Approximately half (43.4%) of the entire cohort and 60% of the cr-FMF patients were female.The cr-FMF group and the responsive group were similar in terms of age at diagnosis ($p = 0.75$). The follow-up period was significantly longer in the resistant FMF group ($p = 0.03$).At least one pathogenic exon 10 mutation was found in 90.4% (n=74) of the patients. All patients with colchicine resistance had exon 10 homozygous or compound heterozygous mutations on exon 10. In colchicine-responsive patients, 50.7% had exon 10 homozygous or compound heterozygous mutations on exon 10 and 49.3% had other exon mutationson *MEFV* gene.
The *PREDICT-crFMF* score, applied prospectively to this cohort, demonstrated a sensitivity of 80% and a specificity of 91% at the cut-off value of 9. Notably, 8 out of 10 colchicine-resistant patients had scores ≥9, while only 7 of the 73 colchicine-responsive patients were incorrectly classified as high-risk, indicating a high level of predictive accuracy.
Conclusion: The PREDICT-crFMF score proved to be a reliable and practical tool for identifying pediatric FMF patients at risk for colchicine resistance. Its strong predictive performance supports its use in routine clinical practice to enable early, individualized treatment approaches. Prospective validation in larger cohorts is warranted.
Disclosure
None declared

References

1. Aktay Ayaz N, Demirkan FG, Coşkuner T, Demir F, Tanatar A, Çakan M, Karadağ ŞG, Yener GO, Öztürk K, Bağlan E, Çakmak F, Çağlayan Ş, Özdel S, Ulu K, Sözeri B, Sönmez HE. PREDICT-crFMF score: A novel model for predicting colchicine resistance in children with familial Mediterranean fever. Mod Rheumatol. 2023 Dec 22;34(1):220-225.
2. Mosad Mosa D, Shokry D, Ahmed DB, Sobh A. Early predictors of colchicine resistance in familial Mediterranean fever. Mod Rheumatol. 2023 Jul 4;33(4):830-835.

P019

Tackling the diagnosis of HA20 in children: challenges of a highly variable clinical and genetic spectrum

F. Anselmi[1,2], M. L. Fremond[3], C. Fieschi[4], A. Laurent[5], A. Schvartz [6], A. desdoits[7], M. C. Besse[8], E. Jesiorski [9], G. Boursier[10], H. Remaux[11], P. Dusser[1,2], I. Kone- Paut[1,2]
[1]Paediatric rheumatology department and CEREMAIA, Bicêtre university hospital, [2]Faculty of Medecine, University of Paris-Saclay, [3]Paediatric Haematology-Immunology and Rheumatology Unit,, Necker Hospital, [4]Department of Clinical Immunopathology, University of Paris - Saint-Louis Hospital, Paris, [5]Pediatric Nephrology, Rheumatology, Dermatology Unit, Hôpital Femme Mère Enfant, Hospices Civils de Lyon, lyon, [6]Imagine Institute,INSERM, Laboratory of Inflammatory Responses and Transcriptomic Networks in Diseases, Paris, [7]epartment of Pediatric Surgery and Rheumatology, Caen University hospital, caen, [8]Department of Internal Medicine and Clinical Immunology, CHU de Tours, tours, [9]aediatric Infectious and Immunology Unit, CHU Montpellier, [10]Laboratory of Genetics for Rare and Autoinflammatory Diseases, Montpellier university hospital,, Montpellier, [11]Department of Pediatric Rheumatology, CHU de Lille, Lille, France
Correspondence: F. Anselmi
Pediatric Rheumatology, **23(2):** P019

Introduction: Heterozygous pathogenic mutations in the ***TNFAIP3*** gene lead to haploinsufficiency of the A20(HA20)protein,which is

associated with a complex inflammatory disorder at the intersection of autoinflammation and autoimmunity.To date there is little data available regarding paediatric presentation.
Objectives: This observational study aims to enhance the understanding of HA20 in paediatric patients by describing the phenotype,the disease course and the treatment strategies.
Methods: We conducted a retrospective analysis of HA20 patients in France, utilizing both the SOFREMIP(Francophone Society of Paediatric Rheumatology and Inflammatory Medicine)mailing list and data from the referent.Inclusion criteria were disease onset <18 years, the presence of a *TNFAIP3* mutation,and the reasonable exclusion of other similar conditions.Data on demographics, clinical and laboratory features,disease progression and treatment efficacy were analysed and compared to previous reports in literature.
Results: We included 20 patients(45%female,90% Caucasian)from 13 non-consanguineous families, carrying distinct *TNFAIP3* mutations. The median age at disease onset was 4 years(1 month–17 years). Age at onset was significantly lower in boys compared to girls(2.5 vs. 6 years,$p = 0.004$).Clinical presentations varied widely among patients and among siblings carrying the same mutation.At disease onset,65% of patients presented with oral ulcers and 20% with genital ulcers.Over the disease course,these proportions increased to 80% and 60%,respectively.Other frequent features included fever(70.6%)and gastrointestinal manifestations, such as abdominal pain(63.2%),diarrhoea(45%),and colitis(20%).Arthralgia was significantly more frequent in children with disease onset <5 years of age($p = 0.015$).Acute-phase reactants were moderately elevated during flares(medianCRP 93 mg/L vs. 7 mg/L out of flares).None of the patients suffered from a definitive rheumatic autoimmune disease, although 40%of patients had positive ANA titers,and 14.3% tested positive for rheumatoid factor.Colchicine monotherapy was effective in 20% of patients.Among biological DMARDs,infliximab was the most effective,with a 100% response rate (4/4 patients).
Conclusion: This study highlights the wide phenotypic variability of HA20 syndrome, even among siblings carrying the same mutation. Our study revealed that oral and genital ulcers may be absent, both at disease onset and throughout its course.Additionally, we highlight key distinctions between HA20 and pediatric Behçet's disease,notably the median age of onset(4 years vs 11years),the predominance of GI involvement,which may be severe, and the peculiar aspect of mucosal ulcerations which are deeper and distinct from common cankers sores. Despite providing new insights, the limited sample size precludes definitive conclusions regarding phenotype-genotype correlations. Further studies involving larger cohorts are essential to clarify the phenotype-genotype correlation as well as to achieve a deeper understanding of the factors influencing clinical expression and disease progression of paediatric HA20.
Disclosure
None declared

P020

Use of secukinumab in a pediatric patient with sapho syndrome: clinical efficacy in a rare autoinflammatory condition

G. De Toro
Department of Translational Medical Sciences, Section of Pediatrics, University of Naples Federico II, Naples, Italy, University of Naples Federico II, Naples, Italy, naples, Italy

Pediatric Rheumatology, **23(2):** P020

Introduction: SAPHO syndrome in children is a rare autoinflammatory disorder presenting with a combination of dermatological and musculoskeletal manifestations, often including severe acne and osteitis. The pathogenesis involves dysregulation of innate immunity and elevation of pro-inflammatory cytokines including IL-17, with no standardized treatment available.
Objectives: To report the clinical response and safety of secukinumab, an IL-17A inhibitor, in a pediatric patient with SAPHO syndrome, focusing on cutaneous and muscoloskeletan symptom control.
Methods: A 14-year-old male presented with acne fulminans-like papulo-pustular lesions on the face, trunk, back and bilateral sternoclavicular swelling. Previous treatment with systemic antibiotics (vancomycin and ceftazidime) and corticosteroids failed to achieve symptom control. Lesions worsened following corticosteroid withdrawal, with increased inflammation and elevated IL-6 levels. Based on Kahn's criteria, SAPHO syndrome was diagnosed. Given the role of IL-17 in its pathogenesis, secukinumab was started at 4 mg/kg subcutaneously. The patient received four weekly doses followed by monthly injections for six months in a hospital setting. Monitoring at each visit included Global Acne Grading System (GAGS), Dermatology Life Quality Index (DLQI), ESR, CRP, IL-6, and photographic documentation. Genetic analysis excluded primary immunodeficiencies but revealed a heterozygous PRF1 variant of uncertain significance.
Results: Secukinumab was well tolerated with no reported adverse events. Skin lesions gradually improved, with reduced inflammation and fewer pustules, especially in facial and upper trunk regions. GAGS decreased from 38 to 33. DLQI improved from 17 to 11, indicating a notable improvement in quality of life. The sternoclavicular swelling showed partial regression. ESR and CRP remained negative throughout therapy, and IL-6 levels normalized. Photographic comparisons supported the observed clinical improvement. The patient maintained emotional stability and better social interaction over the course of treatment. Clinical response was sustained, and lesion distribution became more localized and less inflammatory.
Conclusion: This case highlights the promising role of IL-17A inhibition in pediatric SAPHO syndrome, with marked improvement in both dermatologic and skeletal symptoms. Secukinumab demonstrated clinical effectiveness and a favorable safety profile. Given the lack of established pediatric treatment guidelines, biologic agents such as secukinumab offer a potential therapeutic option. Future multicenter studies are essential to validate these findings and support evidence-based management in pediatric patients with refractory SAPHO syndrome. Consent to published had been obtained.
Disclosure
None declared

References

1. Kahn, M.F. and Khan, M.A. (1994) 'The SAPHO syndrome', *Baillière's Clinical Rheumatology*, 8(2), pp. 333–362
2. Liu, S., Tang, M., Cao, Y., Li, C. and Dai, Y. (2020) 'The role of interleukin-17 in the pathogenesis of SAPHO syndrome', *Therapeutic Advances in Musculoskeletal Disease*, 12, pp. 1–10
3. Wendling, D., Prati, C., Aubin, F., Cazzola, M. and Toussirot, E. (2017) 'IL-23/Th17 targeted therapies in SAPHO syndrome. A case series', *Joint Bone Spine*, 84(6), pp. 733–735
4. Daoussis, D., Konstantopoulou, G., Kraniotis, P., Kalogeropoulou, C. and Andonopoulos, A.P. (2019) 'Biologics in SAPHO syndrome: a systematic review', *Seminars in Arthritis and Rheumatism*, 48(4), pp. 618–625

P021

Insights into corticosteroid use for PFAPA: a study by the jir-clips survey

G. Özomay Baykal[1], C. Vinit[2,3], N. Toplak[4], O. Boyarchuk[5], H. E. Sönmez[6], K. Pateras[7], F. Hofer[8], M. Gattorno[9], M. Hofer[8,10], E. D. Batu[11]
[1]Pediatric Rheumatology, Mardin Training, Mardin, Türkiye, [2]General Pediatrics, Jean Verdier Hospital, Bondy, [3]Pediatric Rheumatology, Robert Debre Hospital, Paris, France, [4]Allergology, Rheumatology and Clinical Immunology, UCH, UMC, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [5]Children's Diseases and Pediatric Surgery, I. Horbachevsky Ternopil National Medical University,, Ternopil, Ukraine, [6]Pediatric Rheumatology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye, [7]Biostatistics, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands, [8]Fondation RES, Lausanne, Switzerland, [9]Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [10]Paediatrics, Hôpital Riviera-Chablais, Rennaz, Switzerland, [11]Pediatric Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Türkiye
Correspondence: G. Özomay Baykal
Pediatric Rheumatology, **23(2):** P021

Introduction: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is a recurrent fever disorder affecting young children. This study evaluates corticosteroid (CS) use in

PFAPA, emphasizing the need for standardized treatment strategies to improve outcomes across diverse populations.
Objectives: This study aims to formulate Clinical Practice Strategies (CliPS) regarding CS use in patients with PFAPA that reflect real-life experience of physician in the field.
Methods: This study is part of the Juvenile Inflammatory Rheumatisms (JIR)-CliPS project, an international cross-sectional online survey led by the JIR-network (www.jircohorte.org) and conducted on 5 JIR medical conditions by a consortium of pediatric and adult rheumatologists and immunologists from Europe and beyond. Questionnaires on diagnosis, treatment and follow-up were sent to physicians taking care of PFAPA patients. Data were exported on September 18, 2024, yielding 313 responses from 41 countries. After excluding incomplete or irrelevant entries, 164 responses specifically addressing CS use in PFAPA were analyzed. The current analysis focused on 15 questions on CS use in patients with PFAPA. Analyses were conducted to explore associations between responses and factors such as professional experience, Gross Domestic Product (GDP), and Health Assessment Questionnaire (HAQ) indices.
Results: A total of 164 participants (117 women and 46 men) from 41 countries completed the survey. Seven countries—Türkiye, France, Brazil, Ukraine, Germany, Switzerland, and the UK—accounted for 58% (n=95) of responses. Among participants, 57% (n=94) had over 10 years of experience, 62.2% (n=102) worked in university hospitals, and 63.3% (n=103) were pediatric rheumatologists. A majority (92%, n=151) recognized CS response at the onset of flares as a key diagnostic tool for PFAPA, with no significant differences by professional experience.
Regarding CS prescription practices during flares, 60% (n=99) administered CS once or twice per flare. Child-friendly formulations, such as oral solutions, were available to 73% (n=119) of participants. Nearly half (49%, n=80) reported using CS no more than 5–10 times annually. Most participants (81%, n=133) observed clinical improvement within 3–4 hours of administration, or at most within 12 hours. Six CS formulations were identified and standardized for analysis, with no significant p
Reference differences linked to professional experience. 32% (n=53) routinely prescribed CS at flares, while 68% (n=111) did so non-routinely. Complex Medical Reasons (such as combinations involving attack frequency and severity) tend to appear more frequently in high GDP categories. (p<0.05).
Criteria for nonresponse to CS included the need for more than two doses (50.6%, n=83), lack of fever improvement within 24 hours (38.4%, n=63) or 12 hours (36.6%, n=60), recurrence of fever after CS administration (35.4%, n=58), and the requirement for more than one dose of CS (12.8%, n=21). Regarding indications for alternative treatments, 57% (n=93) cited severe attacks, 36% (n=59) flare intervals shorter than two weeks, 27% (n=44) highlighted flare intervals shorter than three weeks or attacks persisting beyond three weeks, and 4% (n=6) noted attacks lasting over one year.
Conclusion: CS at flare onset is a treatment prescribed in most PFAPA patients from the 41 countries studied. However, we observed wide variations in the indication of CS treatment, the modalities of prescription and the criteria for treatment efficacy and failure. Our results emphasize the importance of individualized approaches, particularly in severe or frequent flares. Standardized clinical practice strategies (CliPS) are needed to optimize care and ensure consistent management across diverse healthcare settings.
Disclosure
None declared

P022

Adherence to colchicine therapy among pediatric familial mediterranean fever patients: role of demographic and clinical determinants

G. Özomay Baykal[1,2], E. Oğultekin Vazgeçer[3], B. Sözeri[2]
[1]Pediatric Rheumatology, Mardin Training and Research Hospital, Mardin, [2]Pediatric Rheumatology, [3]Pediatrics, Ümraniye Training and Research Hospital, İstanbul, Türkiye
Correspondence: G. Özomay Baykal
Pediatric Rheumatology, **23(2):** P022

Introduction: Familial Mediterranean Fever (FMF) is a monogenic autoinflammatory disorder marked by recurrent febrile episodes and serosal inflammation, predominantly affecting individuals of Mediterranean descent. Colchicine remains the standard of care for preventing disease flares and amyloidosis; however, challenges related to lifelong adherence and the absence of clear discontinuation criteria necessitate further investigation.
Objectives: To evaluate the demographic and clinical characteristics of Familial Mediterranean Fever (FMF) patients carrying a heterozygous MEFV mutation, focusing on those who discontinued colchicine therapy, and the factors associated with successful treatment discontinuation.
Methods: A retrospective analysis was conducted on FMF-diagnosed patients presenting to the Pediatric Rheumatology Clinic of Ümraniye Training and Research Hospital between October and December 2024. Data included patient and parental age, parental education, maternal employment, number of siblings, annual FMF-related hospital visits, and mode of colchicine administration (self vs. parent-administered). Adherence was assessed via a standardized medication adherence scale. Genetic mutations and clinical features of attacks were also analyzed.
Results: A total of 91 patients (46 female, 45 male; mean age 7.43 ± 3.44 years) were included. No significant correlation was found between mode of administration and maternal education or annual attack frequency (p>0.05). No association was observed between genotype or attack features and adherence. However, a significant association was noted between longer disease duration and self-administration of colchicine (p<0.05).
Conclusion: In pediatric FMF patients, disease follow-up duration appears to influence colchicine adherence. Prolonged monitoring promotes self-management, suggesting a need for strategies fostering patient independence in in treatment.
Disclosure
None declared

P023

Attitudes toward genetic testing in PFAPA syndrome: unveiling clinical trends from the JIR-clips survey

H. E. Sönmez[1], C. Vinit[2,3], N. Toplak[4], O. Boyarchuk[5], M. Gattorno[6], G. Ozomay Baykal[7], K. Pateras[8], E. D. Batu[9], F. Hofer[10], C. JURCUT[11], M. Rodrigues[12], O. Gillaux[13], K. Laskari[14], M. Santos Faria[15], R. Craveiro da Costa[16], M. Hofer[17]
[1]Department of Pediatric Rheumatology, Kocaeli University, Kocaeli, Türkiye, [2]Department of General Pediatrics, Jean Verdier Hospital, Bondy, Bondy, [3]Department of Pediatric Rheumatology, Robert Debre Hospital, Paris, France, [4]Department of Allergology, Rheumatology and Clinical Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [5]Department of Children's Diseases and Pediatric Surgery,. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine, [6]Department of Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [7]Department of Pediatric Rheumatology, Umraniye Training and Research Hospital, Istanbul, Türkiye, [8]Department of Biostatistics, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands, [9]Department of Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye, [10]Fondation RES, Lausanne, Switzerland, [11]Internal Medicine and Rheumatology Specialist, Central Military Hospital, Bucharest, Romania, [12]Pediatric and Young Adult Rheumatology Unit, Centro Hospitalar Universitário São João, Porto, Portugal, [13]ediatric Immunology and Rheumatology, Centre Hospitalier Universitaire de Charleroi, Charleroi, Belgium, [14]First Department of Propaedeutic and Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece, [15]Department of Rheumatology, Hospital Central do Funchal, Funchal, [16]Unidade Local de Saúde de Coimbra, Coimbra, Portugal, [17]Department of Pediatric Immunology, Allergology, and Rheumatology, Lausanne University Hospital, Lausanne, Switzerland
Correspondence: H. E. Sönmez
Pediatric Rheumatology, **23(2):** P023

Introduction: PFAPA syndrome (Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical Adenitis) is a frequent autoinflammatory

recurrent fever syndrome. While its exact cause remains unclear, genetic testing is increasingly used to rule out monogenic autoinflammatory diseases. Clinicians' views on genetic analysis in PFAPA vary, with some questioning its necessity and cost-effectiveness, as the diagnosis is primarily clinical. Currently, there is no standardized algorithm for incorporating genetic testing into PFAPA management. A better understanding of current used clinical strategies could enable the development of useful recommendations, minimizing unnecessary testing.
Objectives: This study aims to formulate Clinical Practice Strategies (CliPS) regarding genetic testing in patients suspected of PFAPA that reflect real-life experience of physician in the field.
Methods: This study is part of the Juvenile Inflammatory Rheumatisms (JIR)-CliPS project, an international cross-sectional online survey led by the JIR-network (www.jircohorte.org) and conducted on 5 JIR medical conditions by a consortium of pediatric and adult rheumatologists and immunologists from Europe and beyond. Questionnaires on diagnosis, treatment and follow-up were sent to physicians taking care of PFAPA patients. The current analysis focused on 12 questions on genetic testing in patients suspected of PFAPA. We analyzed the responses according to the participant's professional profile and geographical origin. Based on the results, we propose a decision algorithm for genetic testing in patients suspected of PFAPA.
Results: As of May 2024, a total of 130 participants (95 female, 35 male) from 43 countries provided responses on genetic testing questions. Half of the participants came from the five most represented countries (Turkey, France, Brazil, Germany, and Switzerland), 53% from medium-GDP, 28% were from high-GDP and 18% from low-GDP countries. The majority cared for pediatric patients (n=111), 80 worked at university hospitals, 92 were pediatric rheumatologists, 73 had more than ten years of experience.
Two thirds of the participants reported occasionally performing genetic tests, 15% never, 8% always, and 12% often. Sixty-one percent favored autoinflammatory gene panels, and 20% preferred single-gene tests (Table 1). The choice of the test did not significantly differ according to the country's GDP. Physicians with < 10 years of experience preferred single-gene tests compared to those with > 10 years (21 vs. 7, p<0.001). Atypical presentation was the most reported reason for performing a genetic test. A variant of unknown significance (VUS) was considered as a causative variant in 73% of the responders, mainly based on expert opinion and compatible clinical findings. Based on the results we have drawn a flowchart representing the different strategies used by the participants.
Conclusion: Examining physicians' genetic testing practices can provide valuable information for improving the management of patients with PFAPA syndrome.
Trial registration identifying number: Funding
This article/publication is based upon work from COST Action CA21168 – Improving outcome of Juvenile Inflammatory Rheumatism via universally applicable clinical practice strategies (JIR-CliPS), supported by COST (European Cooperation in Science and Technology) - www.cost.eu.
Disclosure
H. Sönmez Grant/Research Support with: This article/publication is based upon work from COST Action CA21168 – Improving outcome of Juvenile Inflammatory Rheumatism via universally applicable clinical practice strategies (JIR-CliPS), supported by COST (European Cooperation in Science and Technology) - www.cost.eu., C. Vinit: None declared, N. Toplak: None declared, O. Boyarchuk: None declared, M. Gattorno: None declared, G. Ozomay Baykal: None declared, K. Pateras: None declared, E. Batu: None declared, F. Hofer: None declared, C. JURCUT: None declared, M. Rodrigues: None declared, O. Gillaux: None declared, K. Laskari: None declared, M. Santos Faria: None declared, R. Craveiro da Costa: None declared, M. Hofer: None declared

P024

Genotypic correlations of serum amyloid a levels before colchicine initiation in children with familial mediterranean fever

N. S. Ciftci[1], B. Celik[1], H. Kisaoglu[2]
[1]Pediatrics, [2]Pediatric Rheumatology, University of Health Sciences Kayseri Medical Faculty, Kayseri, Türkiye
Correspondence: H. Kisaoglu
Pediatric Rheumatology, **23(2):** P024

Introduction: Serum amyloid A (sAA) is frequently used for the detection of subclinical inflammation in patients with familial Mediterranean fever (FMF) [1]. However, frequency of elevated sAA levels in attack-free period before initiation of colchicine treatment and genotypic correlations of sAA levels has not been previously studied.
Objectives: We aimed to investigate sAA levels in the attack-free period of children with FMF before initiation of colchicine and genotypic correlations of sAA.
Methods: Medical charts of children diagnosed with FMF according to EUROFEVER criteria [2], between June 2023 and January 2025, were reviewed. Patients presented with FMF attacks, patients without sAA measurement before initiation of colchicine and patients with inflammatory comorbidities were excluded. sAA levels higher than 10 mg/L were accepted as elevated sAA [3]. Genotypes of patients were classified as confirmatory and non-confirmatory as described in the EUROFEVER criteria.
Results: Among 109 children diagnosed with FMF, 60 patients were excluded (18 with FMF attack, 38 without sAA measurement, 4 with inflammatory comorbidity). Of the remaining 49 patients, confirmatory genotype was observed in 38 (77.6%) patients with homozygous M694V in 9 (18.4%). In 24 (49%) patients, sAA level was elevated and median sAA level was 8.4 mg/L (Q1-Q3: 2.9–39.0). Elevated sAA despite normal CRP levels were observed in 6 (12.2%) patients. sAA levels did not display significant correlation with age, attack frequency and attack duration (p >0.05). Frequency of patients with elevated sAA levels was not differed between confirmatory and non-confirmatory genotypes (47.4% vs. 57.5%, p: 0.74). However, frequency of elevated sAA was significantly higher in homozygous M694 genotype than non-homozygous M694V genotypes (89.9% vs. 40.0%, p: 0.01). Additionally, patients with homozygous M694V displayed significantly higher sAA levels than other confirmatory genotypes [median(Q1-Q3): 44.7 (18.0–200.6) vs. 4.4 (3,4–16,3), p: 0.015]. However, there was no significant difference between patients with non-confirmatory genotype and confirmatory genotype excluding homozygous M694V in terms of sAA levels.
Conclusion: Elevated sAA levels could be observed in half of the children during the attack-free period before the initiation of colchicine. More frequent observation of elevated sAA along with higher levels in children with homozygous M694V supports the severe phenotype of homozygous M694V in FMF patients. However, attack-free sAA levels could not discriminate against confirmatory genotype from non-confirmatory variations.
Disclosure
None declared

References

1. Berkun Y, Padeh S, Reichman B, Zaks N, Rabinovich E, Lidar M, Shainberg B, Livneh A. A single testing of serum amyloid a levels as a tool for diagnosis and treatment dilemmas in familial Mediterranean fever. Semin Arthritis Rheum 2007; 37:182-8.
2. Gattorno M, Hofer M, Federici S, Vanoni F, Bovis F, Aksentijevich I, et al. Classification criteria for autoinflammatory recurrent fevers. Ann Rheum Dis. 2019; 78: 1025-32.
3. Liu Q, Li Y, Yang F, Xu T, Yao L, Sun J, Liang W. Distribution of serum amyloid A and establishment of
Reference intervals in healthy adults. J Clin Lab Anal 2020; 34: e23120.

P025

Pediatric familial mediterranean fever: a retrospective cohort study from a spanish tertiary hospital

M. I. Gonzalez Fernandez[1], B. Lopez Montesinos[1], M. Marti Masanet[1], L. Lacruz Perez[1], I. Burgos Berjillos[2], S. de Vicente Revenga[3], I. Calvo Penades[1]
[1]Pediatric Rheumatology Unit, Health Research Institute Hospital La Fe (IIS La Fe), Hospital Universitario y Politecnico La Fe, [2]Hospital Universitario y Politecnico La Fe, Valencia, [3]Medical Lead Immunology, Novartis, Madrid, Spain
Correspondence: I. Calvo Penades
Pediatric Rheumatology, **23(2):** P025

Introduction: Familial Mediterranean fever (FMF) is an autoinflammatory disease belonging to inflammasomopathies and caused by

variants in the MEFV gene, with autosomal recessive inheritance. It is characterized by self-limited episodes of fever and polyserositis with increased acute phase reactants. Its main complication is amyloidosis. Colchicine is the therapy of choice. However, approximately 10-20% of patients with FMF are resistant to colchicine and approximately 2-10% are intolerant to colchicine, mainly due to gastrointestinal adverse effects.
There are few series describing the clinical and genetic characteristics of FMF, as well as its management and progression in Spain.
Objectives: To describe the demographic, clinical, genetic and treatment characteristics of a cohort of patients diagnosed with FMF during childhood at a Spanish tertiary center.
Methods: A retrospective, non-interventional, single-center study was conducted at a Spanish tertiary care hospital. Patients with a clinical diagnosis of FMF during childhood, between January 2005 and December 2021, and with a minimum follow-up of 3 months after diagnosis, were included. Demographic, clinical, genetic and treatment data were collected.
Results: 44 patients included. Mean age at inclusion (standard deviation [SD]) 17.6 (6.3) years; 59.1% men; 97.7% Caucasian (70.5% Spanish, 11.4% Armenian, 9.1% Romanian, 4.5% Syrian). Mean (SD) age at symptom onset 5.2 (4.3) years. Median time (P25;P75) between symptom onset and diagnosis 1.8 (1.0;3.5) years. 100% of patients had at least one pathogenic and/or variant of uncertain significance in MEFV. At diagnosis, the most frequent symptoms, in addition to recurrent fever, were abdominal pain (47.7%) and arthralgia (47.7%), and others (61.4%) such as diarrhea, oral thrush, headache and vomiting, the most frequent remaining during follow-up. At diagnosis, 38.6% of patients had comorbidities (11.8% vasculitis, 11.8% juvenile idiopathic arthritis). At some point during the study, all patients received colchicine, and 27.3% received anti-IL-1 inhibitors. At the end of follow-up, 55.6% of patients with anti-IL-1 inhibitors were receiving standard doses, while 33.3% had optimized treatment. Three patients (6.8%) were intolerant to colchicine.
Conclusion: This study describes a predominantly Spanish cohort of patients with FMF diagnosed in childhood at a tertiary center. Demographic, phenotypic, genotypic and treatment characteristics were collected. We found the need for additional therapies to colchicine, such as IL-1 blockade, in 25% of patients.
Disclosure
None declared

P026

Interleukin-18 as a potential biomarker of disease activity in major monogenic autoinflammatory diseases

A. Sukhanina, S. Salugina, E. Fedorov, M. Diatroptova, S. Glukhova, I. Nikishina
V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P026

Introduction:
In recent years, interleukin-18 (IL-18) has attracted attention as a promising biomarker of inflammatory activity, a tool for patient stratification, and a potential therapeutic target in various immune-mediated inflammatory diseases.
Objectives: To assess serum IL-18 levels in patients with major monogenic autoinflammatory diseases (mAID).
Methods: The study included 78 patients with mAID (47 males, 36 females) followed at the V.A. Nasonova Research Institute of Rheumatology, diagnosed with: familial Mediterranean fever (FMF, n=37), cryopyrin-associated periodic syndromes (CAPS, n=29), and TRAPS (n=12). Patient age ranged from 1.8 to 59 years (median 14 [7; 18] years). The median disease duration was 7 [4.5; 13.5] years. Serum IL-18 and ferritin levels were measured using ILISA. The
Reference values for IL-18 and ferritin were >223 pg/mL and 20–150 µg/L, respectively.
Results: Patients were stratified by disease activity (active, n=40; remission, n=38) and by disease subtype (FMF, CAPS, TRAPS).
Elevated IL-18 levels were found in 60 (77%) patients (me 357.8 [215.3; 1032.9] pg/mL), including 27 (68%) in remission (me 309.4 [207.9; 443.8]) and 28 (76%) with active disease (me 418.5 [249.6; 1385.6]). IL-18 levels were higher in patients with active disease, though the difference was not statistically significant. Elevated IL-18 levels were more frequent in FMF (81%) compared to CAPS (69%) and TRAPS (42%) (p=0.03). Median IL-18 levels were significantly higher in FMF (553.1 [308.9; 1516.4]) than in CAPS (347.5 [216.3; 396.1]) and TRAPS (178.6 [156; 278.4]) (p<0.05), and higher in CAPS than in TRAPS (p=0.028). In active disease, IL-18 levels were higher in FMF than in CAPS (p=0.003). No significant differences were observed between groups during remission. Comparing ferritin and IL-18 levels in active vs. remission subgroups, IL-18 elevation was observed in 76% of patients with low ferritin (<20 ng/mL) during active disease and 65% in remission. However, the differences were not statistically significant.
Among CAPS patients, higher IL-18 levels were found in those with low ferritin (median 380.6 [303.5; 640.2] pg/mL) compared to those with normal ferritin levels (median 216.8 [153.1; 333.2] pg/mL). This association was not observed in FMF or TRAPS.
Conclusion: Elevated IL-18 levels were observed in patients with major mAIDs during both active disease and clinical-laboratory remission. No significant differences in IL-18 levels were found between subgroups stratified by disease activity. The observed association between elevated IL-18 and low ferritin in CAPS patients is of interest and warrants further research to clarify its pathogenic and clinical relevance.
Disclosure
None declared

P027

Clinical and genetic features of confirmed FMF and symptomatic heterozygotes: a cohort study of 185 patients

I. Mahé, F. Anselmi , L. Rossi , C. Galeotti, I. Kone-paut, P. Dusser
Rhumatologie pédiatrique, Hôpital Bicetre, APHP, Kremlin Bicetre, France
Correspondence: I. Mahé
Pediatric Rheumatology, **23(2):** P027

Introduction: Familial Mediterranean fever (FMF) is a monogenic autoinflammatory disease caused by mutations in the *MEFV* gene. While the clinical phenotype is well characterized in homozygous or compound heterozygous patients (confirmed FMF, cFMF), some heterozygous individuals also present with FMF-like symptoms requiring treatment (symptomatic heterozygotes, HetFMF). The distinction between these two populations and their clinical trajectories remains poorly understood.
Objectives: To compare the clinical and genetic characteristics of patients with cFMF and HetFMF to identify potential subgroups and better understand their disease course.
Methods: Retrospective study including pediatric and adult patients followed between 2004 and 2025 in a French tertiary center. Clinical and biological characteristics were analyzed during attacks and in the intercritical period. Cluster analysis was performed to identify subgroups, and swimmer plots will illustrate the evolution of patients during follow-up.
Results: We included 185 patients (87 females, 98 males), with comparable group sizes (cFMF: 92, HetFMF: 93), and a median follow-up of 5.5 years. Age at onset was <5 years in 56% of cFMF and 47% of HetFMF. Male predominance was higher in HetFMF (58% vs 48%).
Fever duration was similar (2–3 days). Compared to cFMF, HetFMF patients had lower frequencies of abdominal pain (75% vs 90%, p=0.04), chest pain (33% vs 62.5%, p=0.001), myalgia (36.6% vs 65.6%, p<0.01), and erysipelas-like erythema (8.6% vs 26.6%, p=0.007). Orchitis and purpura were reported only in cFMF. During attacks, aphthous ulcers (14% vs 11%) and pharyngitis (20% in both) were reported with similar frequency. Cervical lymphadenopathy was also observed in both groups.
Between flares, HetFMF more often had aphthous ulcers (19.4% vs 9.4%, p=0.01) and reported fewer triggers: no trigger 62% vs 47% (p<0.05). Stress (22% vs 35%), exertion (9% vs 20%), sleep deprivation (4% vs 13%) were more frequent in cFMF. *M694V* was the most common mutation in both groups. C-reactive protein levels during attacks were elevated in both groups, with no significant difference (median CRP: 50 vs 89 mg/L). Colchicine duration was shorter in HetFMF (median 48 vs 96 months, p<0.001). High-dose colchicine was less frequent (54.5% vs 89.1%, p<0.001), and interruptions over one year were more common (10.4% vs 1.6%).

Clustering analysis identified five groups. Cluster 1 (C1): homozygous genotype, very symptomatic attacks requiring colchicine and anti-IL1 therapy. C2: highly symptomatic, heterogeneous genotype, only partial response to colchicine. C3: predominantly HetFMF, variable attack frequency, moderately symptomatic, well response to high-dose colchicine. C4: HetFMF, few or no symptoms, no specific treatment. C5: moderately symptomatic form, predominantly HetFMF, requiring colchicine, often high doses.
Conclusion: Although fever duration and inflammation were similar, HetFMF patients had fewer classical FMF symptoms and required less intensive colchicine treatment. More frequent aphthous ulcers between attacks may reflect mild phenotypic variation within the FMF spectrum. These findings suggest that HetFMF represents a milder clinical presentation. Ongoing cluster analysis may help refine this classification.
Disclosure
None declared

P028

Beyond behçet: unveiling trisomy 8–associated autoinflammatory disease (TRIAD) in a paediatric patient

J. B. Lima[1], B. P. Correia[2,3], S. Azevedo[4], I. Esteves[5], M. Rodrigues[6], A. Martins[7], R. Campanilho-Marques[2,3], F. O. Ramos[2,3]
[1]Paediatrics Department, Unidade Local de Saúde de Santo António (ULSSA), Porto, [2]Paediatric Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde de Santa Maria (ULSSM), [3]Faculdade de Medicina, Universidade de Lisboa, [4]Paediatric Gastroenterology Unit, Paediatrics Department, [5]Pediatric Infectious Diseases, Pediatric Department, [6]Department of Medical Genetics, [7]Paediatri Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde de Santa Maria (ULSSM), Lisboa, Portugal
Correspondence: J. B. Lima
Pediatric Rheumatology, **23(2):** P028

Introduction: Behçet's disease (BD) is an autoinflammatory (AI) disorder of unknown cause, marked by recurrent oral and genital ulcers, uveitis, and skin lesions. Trisomy 8, a chromosomal anomaly often linked to myelodysplastic syndromes, is also associated with Behçet-like and other AI features. TRIAD (Trisomy 8–associated AI disease) has been recently proposed to describe this overlap, though reported cases remain limited.
Objectives: To describe a case of TRIAD.
Methods: Case-report
Results: We report the case of a now 12-year-old girl with an early onset of a persistent AI syndrome. Family history included recurrent oral aphthosis (mother) and BD (2nd-degree maternal cousin). Symptoms began at 18 months with recurrent high-grade fevers (40ºC), painful oral ulcers,myalgias and arthralgias. She was initially diagnosed with Periodic Fever, Aphthous stomatitis, Pharyngitis and Adenitis and treated with corticosteroids during flares, with only partial response. At age 4, she developed periumbilical abdominal pain and marked perianal aphthosis. Endoscopic studies were unremarkable. At age 10, she presented panniculitis. During flares—marked by oral aphthous ulcers and severe abdominal pain—she required frequent hospital admissions and total enteral nutrition, with limited improvement. Diagnostic workup revealed leukocytosis, elevated C-reactive protein and persistently high serum amyloid A levels (peak 710 mg/L). HLA-B51 was negative. Urinary mevalonic acid, urinalysis and proteinuria were normal. Faecal calprotectin was intermittently elevated (max 9531µg/g). New endoscopy showed nonspecific mucosal erosions and ulcerations in the cecum, with histopathology revealing mild nonspecific inflammation. Enteral MRIwas normal. Genetic testing identified a mosaic trisomy 8, confirmed by FISH in peripheral blood but not in buccal cells, alongside a pathogenic variant in TNFRSF13B inherited from her asymptomatic father. Therapeutic management was challenging. Initial treatment with azathioprine and colchicine was ineffective. Adalimumab provided partial relief, while tofacitinib showed no benefit. Infliximab was recently started. She currently has episodic abdominal pain and perianal aphthosis, with some improvement, alongside stable inflammatory markers. Haematological evaluation shows no evidence of myelodysplastic changes.
Conclusion: This case illustrates the diagnostic and therapeutic challenges of early-onset BD-like syndromes and the importance of investigating genetic or chromosomal causes in atypical or refractory cases. Mosaic trisomy 8 has recently been linked to AI diseases, often with gastrointestinal involvement and poor therapeutic response. It is also a known cytogenetic abnormality in myelodysplastic syndromes, raising concerns about long-term risk. These overlapping features highlight the need for multidisciplinary care and follow-up. Consent to published had been obtained.
Disclosure
None declared

P029

Validation of the health-related quality of life scale (FMF-QOL) in pediatric patients with familial mediterranean fever

K. Ulu[1,2], M. K. Erener[3], T. Duruöz[4], B. Sözeri[1]
[1]Pediatric Rheumatology, Ümraniye Training and Research Hospital, [2]Pediatric Rheumatology, Sancaktepe Training and Research Hospital, [3]Internal Medicine, İstanbul-Cerrahpaşa University Faculty of Medicine, [4]PMR Dept & Rheumatology Division, Marmara University Faculty of Medicine, İstanbul, Türkiye
Correspondence: K. Ulu
Pediatric Rheumatology, **23(2):** P029

Introduction: Familial Mediterranean Fever (FMF) is a chronic autoinflammatory disease that can significantly impair quality of life. The FMF-QoL scale is a disease-specific instrument originally developed for adults to assess physical, emotional, and social functioning.
Objectives: This study aimed to evaluate the validity and reliability of the FMF-QoL scale in a pediatric FMF population.
Methods: A total of 187 pediatric FMF patients and 50 healthy controls were evaluated. The FMF-QoL scale was administered to all participants. Internal consistency was assessed using Cronbach's alpha. Construct validity was analyzed through Principal Component Analysis (PCA), utilizing KMO and Bartlett's tests. Components with eigenvalues greater than 1 were retained.
Results: The FMF-QoL was applied to 187 patients with FMF and 50 control subjects. The median age (IQR) was 13 (10.3-15.8) years for the FMF group and 11 (9-13) years for the control group. The female/male ratio was 90/97 (48.1% female) in the patient group and 25/25 (50% female) in the control group. Forty-three (22.9%) patients with FMF were resistant to colchicine. The total median FMF quality of life score was 16 (9-32) for colchicine-resistant FMF patients, 20.5 (10.2-31) for patients receiving only colchicine treatment, and 9.5 (6-14) for the control group. The quality-of-life score was statistically significantly lower in the control group compared to the patient group (p=0.00). The Kaiser-Meyer-Olkin (KMO) measure was 0.668, indicating sampling adequacy. Bartlett's test of sphericity was significant ($p < 0.001$), confirming the data's suitability for factor analysis. Most items loaded strongly (>0.50) on the first component, which appeared to represent a general quality of life dimension. The FMF-QoL scale showed good internal consistency with a Cronbach's alpha of 0.75.
Conclusion: The FMF-QoL scale demonstrates strong psychometric properties when applied to pediatric FMF patients. High internal consistency and clear factor structure support its use in clinical and research settings for assessing quality of life in children with FMF. FMF substantially impairs quality of life in pediatric patients regardless of age, gender, or colchicine responsiveness. Broader psychosocial factors, including illness perception, may also contribute to reduced QoL scores. However, further refinement or development of a pediatric-specific version may improve conceptual alignment with age-related functional and emotional experiences.
Disclosure
None declared

Reference

1. Unal-Ulutatar C, Duruoz MT. Development and validation of a quality of life scale in Familial Mediterranean Fever (FMFQoL). Mod Rheumatol. 2021 May;31(3):710-717. doi: https://doi.org/10.1080/14397595.2020.1775946. Epub 2020 Jun 26. PMID: 32475195.

P030

Mofetil mycophenolate and ruxolitinib: a combination not to be recommended in 3 patients with savi syndrome

L. De Nardi[1,2], C. Celani[1], V. Messia[1], S. Federici[1], F. De Benedetti[1], A. Insalaco[1]
[1]Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, [2]University of Roma "Tor Vergata", Rome, Italy
Correspondence: L. De Nardi
Pediatric Rheumatology, **23(2):** P030

Introduction: Mutations affecting the TMEM173 gene cause STING-associated vasculopathy with onset in infancy (SAVI). Janus kinase (JAK) inhibitor ruxolitinib has been reported to control disease progression in such patients through targeting type I IFN signaling.$_1$ Recurrent viral infections are known side effects of JAK inhibitors.$_2$
Objectives: To describe a small cohort of patients with SAVI syndrome treated with the combination of mofetil mycofenolate (MMF) and ruxolitinib with good disease control, but increased risk of severe infections.
Methods: We used DNA sequencing to identify mutations in TMEM173.
Results: Pt 1 (12 years old boy) presented at the age of 9 with polyarthritis previously treated with TNF-a inhibitor. He suffered from recurrent episodes of pulmonary infections since the first years of life, and chest CT scan performed at the admission showed focal thickening of the interlobular septa with multiple not calcific peri-lymphatic nodules. Heterozygous variant c.463G>A (V155M) in STING1 was found. He started MMF and ruxolitinib with marked improvement of both arthritis and lung disease. After 1 year of such therapy he developed severe pneumonia and lymphadenitis with colliquation, whose biopsy resulted positive for atypical mycobacterium. Pt 2 (10 years old girl) presented since the first months of life with erythematous vesicular rash on nose and cheeks, later spreading to hand and feet with pustular evolution, resulting in neutrophilic dermatosis at skin biopsy. Chest CT revealed ground glass opacities with thickening of the interlobular septa. She presented de novo heterozygous mutation in TMEM173 c.461A>G (N154S). Ruxolitinib was started at 2 years of life. MMF was added at 3 years for a better disease control. At 8 years, she developed bilateral submandibular lymphadenitis with colliquation, whose biopsy showed atypical mycobacterial infection. Pt 3 (5 years old girl) started at 14 months with acute respiratory failure, clubbing and ground glass evidence at chest CT scan. She also presented a de novo heterozygous variant c.463G>A (V155M) in STING1. Therapy with mycophenolate and ruxolitinib was started. She developed several viral infections needing ruxolitinib periodical suspension and monthly administration of substitutive IVIg. During the last year of combined therapy with MMF and ruxolitinib she developed 3 episodes of severe pneumonia requiring IV antibiotics. MMF was suspended.
Conclusion: We do not recommend the combined use of mofetil mycofenolate and ruxolitinib in SAVI patients, since two patients developed atypical mycobacteriosis needing long-term antitubercolar therapy, and the third developed 3 pneumonias in the same year. Mycophenolate was suspended in all patients with beneficial on infective risk.
Disclosure
None declared

References

1. Cetin Gedik K, Lamot L, Romano M, et al. Ann Rheum Dis 2022;81:601–613.
2. Volpi S, Insalaco A, Caorsi R, et al. Journal of Clinical Immunology (2019) 39:476–485.

P031

Familial chilblain lupus with a novel pathogenic variant in the trex1 gene in a girl from the czech republic, complicated by social background

M. Schüller[1], H. Grombiříková[2], J. Fráňová[1], E. Nedorost[1], M. Macků[1], T. Freiberger[2]
[1]Department of Pediatrics, Masaryk University and University Hospital Brno, [2]Molecular Genetics Laboratory, Center of Cardiovascular Surgery and Transplantation, Brno, Czech Republic
Correspondence: M. Schüller
Pediatric Rheumatology, **23(2):** P031

Introduction: Familial chilblain lupus (FCL) is an autosomal dominantly inherited type I interferonopathy, mostly caused by a pathogenic variant in the *TREX1* gene. Its typical symptoms are painful erythematous changes on the acral parts of the body, aggravated by cold, and starting in early childhood. Diagnosis is based on clinical and histological findings and genetic testing. Recently, Janus kinase inhibitors (JAKi) have been mainly used in treatment[1].
Objectives: To demonstrate the challenge of finding a proper diagnosis and therapy of a rare autoinflammatory disease in association with social aspects
Methods: A case report
Results: In 2014, a 10-year-old girl was referred to our pediatric rheumatology center due to skin changes aggravated by cold, similar to those her mother had experienced since childhood. Erythematous macules, papules, and scarce ulcerations on the patient's fingers, toes, knees, auricles, and nose were observed from age 2. Skin biopsy revealed lymphocytic perivascular infiltrates. Criteria for systemic connective tissue disease or vasculitis, immunodeficiency, and cryoglobulinemia were not met. In 2014–15, we treated the girl with prednisone and azathioprine. Due to the insufficient efficacy, adverse effects, and the mother's frustration, compliance was poor, genetic testing was not performed, and from 2015–19, the girl dropped out of our follow-up. Paradoxically, care resumed thanks to the children's shelter, where she chose to live at age 15. At that time, we noted substantial progression of acral changes including reduction of distal parts of fingers and toes, with stenoses and occlusions of the distal finger arterioles and capillaries on the upper limb angiography. Newly, predominantly sensory peripheral polyneuropathy was found. Whole-exome sequencing of her genomic DNA identified a new pathogenic heterozygous variant c.388G>A; p.Asp130His in the *TREX1* gene, which was also confirmed in her mother. After the FCL diagnosis, baricitinib was added to the therapy, leading to an improvement in skin symptoms and a significant drop in the concomitant prednisone dose. At age 19, the patient was referred to an adult rheumatologist in good condition. In contrast, her mother unfortunately kept refusing all medical care and died before age 40.
Conclusion: In a girl with an inherited mutilating vasculopathy and peripheral neuropathy, identifying a novel pathogenic variant in the *TREX1* gene eventually resulted in a diagnosis of type I interferonopathy, and targeted JAKi therapy was initiated with a positive effect. This case shows that successful and timely diagnosis and treatment depend on both medical expertise and strong family cooperation that may be affected by psychosocial challenges. Consent to published had been obtained.
Disclosure
None declared

Reference

1. Boucher E, Morand EF. Familial chilblain lupus: what can we learn from type I interferonopathies? *Curr Rheumatol Rep*. 2017;19(10):61.

P032

Personalized medicine for systemic autoinflammatory diseases: the european multicenter "persaids" project

C. Speziani[1], M. Gattorno[2], P. Uva[3], F. Rizzi[4], G. Cavalca[3], G. Fiorito[3], S. Gattulli[3], S. Palmeri[5], F. Penco[2], S. Fuehner[6], Y. Rodina[7], S. Decherchi[8], G. Vignolle[9], A. Petretto[10], E. D. Batu[11], F. Akal[12], J. I. Arostegui[13], D. Foell[6], K. Vierlinger[9], I. Ceccherini[1], S. Ozen[11]
[1]UOSD Aggregation Area for Research Laboratories, [2]UOC Pediatric Rheumatology, [3]Clinical Bioinformatics, IRCCS Gaslini Institute, Genoa, [4]Istituto di Management Sanitario, IMS, Milan, [5]Rheumatology and Autoinflammatory Diseases Unit, IRCCS Gaslini Institute, Genoa, Italy, [6]Dept Rheumatology and Immunology, University of Muenster, Muenster, Germany, [7]Data Science and Computation Facility, [8]Computational and Chemical Biology (CCB) lab, Fondazione Istituto Italiano di Tecnologia, Genoa, Italy, [9]Center for Health and Bioresources/Molecular Diagnostics, Austrian Institute of Technology, Wien, Austria, [10]Core Facilities-Proteomics Laboratory, IRCCS Gaslini Institute, Genoa, Italy, [11]Pediatric Rheumatology Unit, [12]Dept Computer Engineering, Hacettepe University Faculty of Medicine, Ankara, Türkiye, [13]Department of Immunology, Hospital Clinic-IDIBAPS, Barcelona, Spain
Correspondence: M. Gattorno
Pediatric Rheumatology, **23(2):** P032

Introduction: Systemic autoinflammatory diseases (SAIDs) are a rapidly growing group of rare monogenic and polygenic/multifactorial conditions that display dysregulation of mechanisms controlling the innate immune response. While monogenic SAIDs clearly benefit from personalized medicine approaches, "undefined" SAIDs (uSAIDs) are characterized by a lack of knowledge of the underlying molecular defect and the absence of specific treatments.
Objectives: To improve the classification, diagnosis and prognosis of uSAIDs and to support the discovery of personalized therapies through the use of multi-omics signatures. Moreover, we also aimed to develop tools for SAID diagnosis and management in clinical practice.
Methods: We have used some of the largest registries and bio-sample repositories on SAID in Europe to: i) analyse already available data and producing new data from SAIDs and uSAIDs, by integrating structured clinical data and multi-omics approaches; ii) generate standardised protocols and bioinformatics pipelines for data management and analysis; iii) simplify reuse of data in compliance with FAIR principles and GDPR. To decode the disease complexity, we applied appropriate tools to all datasets, including Artificial Intelligence technologies, supervised and unsupervised learning algorithms and statistical genetics approaches.
Results: Clinical and omics data have been collected and harmonized through a uniform semantic schema implemented in the MOLGENIS database. Biological samples (DNA, RNA and serum) from 173 patients enrolled from three clinical centers were used to generate 1657 datasets using 9 different technologies (i.e. genomics, transcriptomics, proteomics, metabolomics, lipidomics, epigenomics, immunomics, OLINK inflammation panel and miRNA profile). Preliminary results using hierarchical clustering followed by differential expression analysis and supervised Machine Learning approaches on individual omics showed relevant stratification between different SAIDs and uSAIDs and highlighted the presence of differentially expressed disease-associated markers that can provide insights into which biological processes/pathways differ between disease groups. A relevant degree of concordance was observed for some disease groups between different omics.
Conclusion: In the present study, we addressed an omics-based clustering of undefined SAIDs. In the future, the definition of multi-omics analysis will further increase and integrated datasets will reveal novel associations between biological markers and disease phenotypes relevant for clinical decision-making.
Disclosure
None declared

Reference

1. This work was supported within the framework of ERA PerMed (PerSAIDs Consortium), which is funded from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 779282.

P033

Neridronate vs pamidronate in chronic nonbacterial osteomyelitis (CNO): a comparative effectiveness and safety study

M. L. Cagnato[1], A. Meneghel[1], F. Tirelli[1], F. Biscaro[2], G. Fichera[3], C. Giraudo[4], F. Zulian[1]
[1]Department of Women's and Child's Health, Pediatric Rheumatology Unit, Padua, [2]Cà Foncello Hospital ULSS 2, Pediatric Unit, Treviso, [3]University Hospital of Padova, Pediatric Radiology Unit, [4]DCTV, University of Padova, Unit of Advanced Clinical and Translational Imaging, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, Padua, Italy
Correspondence: M. L. Cagnato
Pediatric Rheumatology, **23(2):** P033

Introduction: Chronic Nonbacterial Osteomyelitis (CNO) is a rare autoinflammatory bone disorder. Whole-body MRI (WB-MRI) is the gold standard for diagnosis and monitoring, although bone biopsy is necessary in doubtful cases. Currently, there is no consensus on treatment which may include anti-inflammatory drugs, corticosteroids, bisphosphonates and anti-TNF agents. Pamidronate has the strongest evidence of efficacy but alternative therapies are being explored.
Objectives: To compare the efficacy and safety of Neridronate (NER) with Pamidronate (PAM) in the treatment of pediatric CNO.
Methods: A retrospective study was conducted in patients under 18 years diagnosed with CNO (according to Bristol criteria) and treated with PAM or NER at the Pediatric Rheumatology Unit in Padua. Clinical, laboratory, imaging and therapeutic data were collected at baseline (T0) and after 6 and 12 months (T6, T12). Radiological involvement was measured (T0, T12) using a Whole Body Imaging Score (WBI score), based on WB-MRI or bone scintigraphy. Disease activity was assessed using two scoring systems by three independent evaluators: the standard Physician Global Assessment (PGA; T0, T6, T12), based on clinical findings, and a redefined PGA (r-PGA; T0, T12), which incorporated clinical and radiological scores. Clinical outcomes were defined at T12 as remission off therapy (CR), remission on medication (CRM) or active disease (AD).
Results: Twenty-nine patients (59% female) were included: 9 NER, 20 PAM. Mean age at diagnosis: 10.9 years. At T0, 97% had bone pain, 93% had multifocal disease. At T0, PGA scores were significantly higher in the NER group [6.6 ± 1.4 vs 5.2 ± 1.3, p = 0.02], along with higher ESR and fever prevalence. At T6 and T12, PGA scores decrease significantly in both groups, with more marked reduction in the PAM cohort in the first 6 months. No major adverse events were reported. A slight WBI score reduction was noticed in both groups at T12. At baseline mean rPGA score were lower than PGA in the NER group and higher in the PAM group. At T12 mean rPGA scores were higher than PGA in both groups. Final clinical outcomes: NER- 44% CR, 33% CRM, 22% AD; PAM-35% CR, 25% CRM, 40% AD.
Conclusion: This is the first study comparing the use of NER and PAM for the treatment of pediatric CNO. Clinical and radiological responses were comparable, although NER showed slightly better final outcome. Clinical improvement appeared to precede radiological response at T12, underscoring the need for standardized timing in radiological follow-up. Overall, NER appears to be a valid and safe therapeutic alternative to PAM.
Disclosure
None declared

P034

Clinical presentation, radiological patterns, and therapeutic approaches in cno patients: real-world data from the eurofever registry

M. V. Mastrolia[1,2], A. Insalaco[3], O. Kasapcopur[4], A. Gagro[5], E. Legger[6], J. Anton[7], A. N. Olivieri[8], M. Alessio[9], F. Licciardi[10], M. Cattalini[11], A. Taddio[12], J. Kuemmerle-Deschner[13], E. Hoppenreijs[14], J. Brunner[15], J. Sánchez-Manubens[16], B. Ogunjimi[17], E. B. Nordal[18], T. Avcin[19], A. Miniaci[20], G. Conti[21], M. Gattorno[22], G. Simonini[1,2] on behalf of on behalf of EUROFEVER registry
[1]Rheumatology Unit, ERN ReCONNET center, Meyer Children's Hospital IRCCS, [2]NEUROFARBA Department, University of Florence, Firenze, [3]Division of Rheumatology, ERN RITA center, IRCCS Ospedale Pediatrico Bambino Gesù, Roma, Italy, [4]Cerrahpasa Medical School, Istanbul University-Cerrahpasa, Department of Pediatric Rheumatology, Instanbul, Türkiye, [5]Children's Hospital Zagreb, Department of Pediatrics, Department of pulmology,allergology, clinical immunology and rheumatology, Zagreb, Croatia, [6]Department of Pediatric Rheumatology, Beatrix Kinderkliniek, University Medical Center, Groningen, Netherlands, [7]Department of Pediatric Rheumatology, Universitat de Barcelona, Hospital Sant Joan de Déu, Barcelona, Spain, [8]Dipartimento della Donna del Bambino e di Chirurgia Generale e Specialistica, Università degli Studi della Campania L.Vanvitelli, [9]Department of Translational Medical Sciences, Federico II University of Naples, Napoli, [10]Regina Margherita Children Hospital, Immunology and Rheumatology Unit, Turin, [11]Pediatric Clinic, University of Brescia and Spedali Civili di Brescia, Brescia, [12]Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", University of Trieste, Trietse, Italy, [13]Division of Pediatric Rheumatology and Autoinflammation Reference Center, University Hospital Tuebingen, Department of Pediatrics, Tuebingen, Germany, [14]Paediatric Rheumatology, CUKZ 435, Radboud UMC, Nijmegen, Netherlands, [15]Faculty of Medicine and Dentistry, Danube Private University, Department of Pediatrics, Innsbruck Medical University,, Innsbruck, Austria, [16]Parc Taulì Hospital Universitari,Institut d'Investigaciò I Innovaciò Parc Taul' (I3PT-CERCA), Unitat de Reumatologia Pediatrica - Servei de Pediatria, Barcelona, Spain, [17]Department of Paediatrics, Antwerp University Hospital, Centre for Health Economics Research and Modeling of Infectious Diseases (CHERMID), Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium,

[18]University Hospital of Northern Norway, and Department of Clinical Medicine, UiT The Arctic University of Norway,, Department of Child and Adolescent Health, Tromso, Norway, [19]Department of Allergology, Rheumatology and Clinical Immunology, University Children's Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia, [20]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Pediatric Unit, Bologna, [21]materno Infantile – UO Nefrologia E Reumatologia Pediatrica, Azienda Ospedaliera Universitaria Gaetano Martino Messina, Messina, [22]Department of Pediatrics and Rheumatology, IRCCS Istituto G. Gaslini, Center of Autoinflammatory Diseases and Immunodeficiencies, Genoa, Italy
Correspondence: M. V. Mastrolia
Pediatric Rheumatology, **23(2):** P034

Introduction: CNO treatment is currently based on personal experience, case reports and retrospective analysis. CARRA consensus treatment plans (CTPs) suggest that in cases refractory to NSAIDs, bisphosphonates, conventional or biologic DMARDs may be equally considered as second-line options.
Objectives: To evaluate potential differences in achievement of radiologial improvement and complete clinical remission among CNO patients treated with different therapeutic regimens.
Methods: Clinical, imaging, and treatment data were collected from a cohort of CNO patients belonging to the Eurofever registry, with available clinical and radiological follow-up of at least 6 months post-diagnosis.
Results: 215 CNO patients followed at 21 international pediatric rheumatology centers were included. 92 (42.8%) were male with a median age at diagnosis of 10.6 years (IQR 8.6–13.0). At onset, the most common clinical manifestations associated with musculoskeletal complaints were constitutional (45.6%), mucocutaneous (16.3%), and gastrointestinal (9.8%) symptoms. Whole-body MRI revealed a median of 4 bone lesions (IQR 2–8.75); 21 patients (9.8%) had unifocal disease. The most frequently affected sites were the metaphyseal extremities (52.6%), the epiphyseal (36.7%) and pelvic (35.8%) regions. Spinal involvement was observed in 33.5% of patients.158 patients (73.5%) received NSAIDs as first-line therapy, while the remaining 57 (26.5%) were initially treated with bisphosphonates, cDMARDs, or bDMARDs. The median follow-up was 2.9 years (IQR 1.7–5.3). At the last available follow-up, 56 patients (35.4%) were off treatment, 83 (38.6%) had achieved a complete clinical remission and 47 (21%) showed radiological improvement with >50% reduction in bone lesions. Persistent disease activity was significantly associated with the presence of constitutional symptoms ($p<0.001$). Among CNO patients initially treated with NSAIDs, 117 (54.4%) required a second-line therapy including bisphosphonates (41.1%), cDMARDs (44.9%) and bDMARDs (29.1%). These treatments were administered as monotherapy in 59 patients (27.4%), in combination in 42 (19.5%) patients, and introduced sequentially in 16 patients (7.4%). At the last follow-up, patients who had received an alternative first-line treatment reported a significantly higher rate of both radiological improvement ($p=0.035$) and complete clinical remission compared to those initially treated with NSAIDs ($p=0.016$). No statistically significant differences in remission rates were observed among the different second-line treatment regimens or between sequential and combined treatment approaches.
Conclusion: The characteristics of our CNO patient cohort are consistent with previously published data. While no significant differences were observed among the three second-line drug classes proposed by the CARRA CTPs in inducing clinical remission, their early use as first-line therapy—alternative to NSAIDs—was significantly associated with a higher likelihood of achieving complete clinical remission and radiological improvement.
Disclosure
None declared

Reference
1. Zhao Y et al. Arthritis Care Res 2018;70(8):1228-1237

P035

Autoinflammatory and periosteal involvement: a new autoinflammatory disease or a de novo TGFBR1 mutation?

M. Rossano[1], L. Capra[2], F. A. Vianello[1], F. Di Stasio[1], S. Torreggiani[3], L. A. Baselli[1], F. Minoia[1], G. Filocamo[1]

[1]Pediatric immunorheumatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, [2]Pediatric immunorheumatology, University of Milan, Milan, Italy, [3]Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health, Bethesda, United States
Correspondence: M. Rossano
Pediatric Rheumatology, **23(2):** P035

Introduction: Loeys-Dietz syndrome (LDS) is a connective tissue disorder caused by mutations in genes affecting TGF-β signaling. It typically presents with cardiovascular, craniofacial, skeletal, and neurocognitive abnormalities. Although inflammatory bowel disease-like symptoms have been reported, systemic inflammation and bone involvement have not been described.
Objectives: To describe the diagnostic challenges and therapeutic strategies in a patient presenting with an unclassified autoinflammatory disease.
Methods: Patient data were retrospectively collected from medical records.
Results: A 12-month-old girl presented with left arm pain, functional impairment, and swelling of the ipsilateral lower limb. Radiographs revealed atraumatic fractures, periosteal thickening, and bone irregularities, raising suspicion of a connective tissue disorder. Trio whole-exome sequencing identified a de novo heterozygous c.696G>C (p.Lys232Asn) mutation in TGFBR1, absent in gnomAD v4 and All of Us, predicted to be deleterious (CADD 25.5, REVEL 0.834), and previously associated with LDS. The patient exhibited grey sclerae, velvety skin, and ligamentous hyperlaxity. However, her inflammatory phenotype, particularly with periostosis, had not been reported in LDS.
Her condition progressively worsened with increased pain, functional limitation, fever, and elevated inflammatory markers. WB MRI showed extensive bone marrow edema and periosteal thickening.
Bone biopsy excluded malignancy and revealed chronic osteomyelitis with osteoclastic bone resorption. Cytokine profiling showed elevated IL-18, IL-6, IL-1Ra, and TNFR1, with a negative interferon signature.
Antibiotic therapy was ineffective. High-dose methylprednisolone initially improved symptoms but relapses occurred during tapering. Biologic therapies were introduced: anakinra and etanercept showed no benefit.
Bisphosphonate therapy was ineffective.
Weekly adalimumab with methotrexate led to transient clinical improvement and allowed steroid tapering. However, disease activity recurred, and canakinumab was added without achieving sustained control.
Following steroid tapering, new lesions appeared, with worsening periostitis and involvement of new skeletal sites. Infliximab was introduced with partial improvement, though she presented another flare during tapering with new skin involvement. Due to the patient's steroid dependence and impaired quality of life, ustekinumab (anti–IL-23) was added to the therapy at the time of reporting.
Conclusion: The pathogenic link between the de novo TGFBR1 mutation and the severe autoinflammatory phenotype with periosteal involvement remains unclear. While TGF-β plays a crucial role in bone matrix regulation, such inflammatory manifestations have not been previously associated with TGFBR1 mutations. This case underscores the complexity of managing refractory inflammation and the need to better understand underlying molecular pathways to halt disease progression and enable steroid discontinuation. Consent to published had been obtained.
Disclosure
None declared

P036

Musculoskeletal manifestations in h syndrome: results from a national cohort of SLC29A3-mutated patients

M. Jouret[1], on behalf of
Reference Center for Histiocytosis (MARIH), D. Benasla[1], B. Neven[2], P. Pillet[3], B. Bader-Meunier[4], A. Felix[5], E. Lazaro[6], S. Dealmeida[7], F. Chasset[8], H. Reumaux[9], M. Gerfaud-Valentin[10], J. Wourms[11], B. Faucher[12], F. Cohen[13], J. Haroche[13], S. Barete[14], S. Georgin-Lavialle[15], C. Kevorkian[16], G. Le Guenno[17], L. Rossi[18], J.-F. Emile[19], P.-Y. Jeandel[20], G. Boursier [21], S. Boussouar[22], J. Donadieu[23], A. Belot[1]

[1]Pediatric Rheumatology, Dermatology, and Nephrology Department, Hôpital Femme Mère Enfants, Hospices Civils de Lyon, Lyon, [2]Pediatric Immuno-Hematology and Rheumatology Department, Necker-Enfants Malades Hospital, AP-HP, Paris, [3]General Pediatrics, Pediatric Rheumatology, and Internal Medicine Department, Hôpital des Enfants CHU Bordeaux,
Reference Center for Pediatric Autoimmune and Systemic Diseases (RAISE), Bordeaux, [4]Pediatric Immuno-Hematology and Rheumatology Department, Necker-Enfants Malades Hospital, Necker-Enfants Malades Hospital,
Reference Center for Pediatric Autoimmune and Systemic Diseases (RAISE); Université Paris Cité, Paris, [5]General Pediatrics Department, RAISE Competence Center Antilles-Guyane, EpiCliV Research Unit, Université des Antilles, CHU de la Martinique, Fort-de-France, [6]Internal Medicine Department,
Reference Center for Rare Systemic Autoimmune Diseases of the East and Southwest, USN Building, Hôpital du Haut-Lévêque, Pessac, [7]Internal Medicine Department, CHU de Toulouse, Toulouse, [8]Dermatology and Allergology Department, AP-HP, Hôpital Tenon, Paris, [9]General Pediatrics, Emergency, Infectious Diseases, and Pediatric Rheumatology Clinic, Hôpital Jeanne de Flandre, CHU de Lille, Lille, [10]Internal Medicine, Hôpital Saint-Joseph Saint-Luc, Lyon, [11] Clinical Genetics, Neonatology Children's Unit, CHRU Nancy, [12]Internal Medecine Departement, La Timone Hospital, Assistance Publique Hôpitaux de Marseille, Marseille, [13]Internal Medicine, [14] AP-HP, La Pitié-Salpétrière, [15]Internal Medicine Department, AP-HP, Hôpital Tenon, Paris, [16]Department of Pediatrics, CHU Grenoble-Alpes, Grenoble, [17]Internal Medicine Department, CHU Estaing, Clermont-Ferrand, [18]Department of Pediatrics, Pediatric Rheumatology, National Referral Centre of Auto-inflammatory Diseases, CEREMAI, APHP, CHU Bicêtre, Paris, [19]Department of Pathology, Versailles SQY University, EA4340-BECCOH, Assistance Publique–Hôpitaux de Paris (AP-HP), Ambroise-Paré Hospital, Boulogne, [20]Internal Medecine Departement, Hôpital Archet 1, Université Côte d'Azur, Nice, [21]Laboratory of Genetics of Rare and Auto-Inflammatory Diseases, Hôpital A. De Villeneuve – CHU de Montpellier, University of Montpellier, Montpellier, [22]Department of Cardiovascular Imaging, AP-HP, La Pitié-Salpétrière, [23]Pediatric Hematology, AP-HP, Trousseau Hospital, Paris, France
Correspondence: M. Jouret
Pediatric Rheumatology, **23(2):** P036

Introduction: H syndrome is a rare genetic disorder caused by biallelic *SLC29A3* mutations, characterized by histiocytic infiltration, bone abnormalities, and autoinflammatory features.
Objectives: This retrospective study aimed to characterize musculoskeletal involvement in patients with confirmed *SLC29A3* mutations.
Methods: Medical records from a national French cohort were reviewed.
Results: Musculoskeletal involvement was present in 26 of 35 patients (74%).
- **Joint involvement** occurred in 19 patients (54%), with 14 (40%) presenting fixed flexion contractures (camptodactyly) of fingers or toes. These early-onset contractures mimic arthrogryposis and represent a hallmark of H syndrome.
- **Tenosynovitis** was observed in 4 patients (14%), including one misdiagnosed with juvenile idiopathic arthritis.
- **Joint hyperlaxity** was reported in 4 cases, suggesting features of connective tissue disorders.
- **Bone abnormalities** (34%) included skull osteosclerosis (n=6), vertebral anomalies, enlarged thumbs/metatarsals, and lytic lesions in small bones and the patella.
- **Muscle inflammation** was identified by MRI in 8 patients (23%), revealing signs of myositis or fasciitis.
Radiological and histological evaluations revealed histiocytic infiltration in musculoskeletal tissues, particularly at the myotendinous junction of the flexor hallucis longus and in the fascia of the inner thighs. These findings were confirmed by immunohistochemical and anatomopathological analyses, which demonstrated $CD68^+/CD163^+$ histiocyte-rich infiltrates.
Therapeutic Response
IL-6 inhibitors were used in five patients with musculoskeletal symptoms (Tocilizumab in 4; Sarilumab in 1). Two achieved complete clinical responses, two had partial improvements in tenosynovitis and two had pain relief. One patient showed complete resolution of fibrotic tendon lesions on MRI after six months.Additionally, eleven patients received Tocilizumab for non-articular indications. Despite treatment, two developed progressive camptodactyly, supporting the hypothesis that *SLC29A3* deficiency impairs bone homeostasis. This mirrors findings in *Slc29a3−/−* mice, which exhibit defective bone and cartilage development (1).
Conclusion: Musculoskeletal manifestations are frequent in H syndrome and may mimic juvenile arthritis. They result from histiocytic infiltration, inflammation, and impaired osteogenesis. Further research is needed to elucidate the underlying mechanisms and guide targeted therapies.
Disclosure
None declared

Reference
1. Nair S, Strohecker AM, Persaud AK, Bissa B, Muruganandan S, McElroy C, et al. Adult stem cell deficits drive Slc29a3 disorders in mice. Nat Commun. 2019 Jul 3;10(1):2943.

P037

The role of demographics in the nature of familial mediterranean fever: a comparative international study

B. Han Egeli[1,2], K. Marzan[1,2], T. Stein[3], M. Heshin-Bekenstein[4,5]
[1]Pediatric Rheumatology,, Children's Hospital Los Angeles, [2]University of Southern California, Los Angeles, United States, [3]Pediatrics, [4]Pediatric Rheumatology, Dana Children's Hospital of Tel Aviv Medical Center, [5]School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel
Correspondence: M. Heshin-Bekenstein
Pediatric Rheumatology, **23(2):** P037

Introduction: Existing research on Familial Mediterranean fever (FMF) suggest that patients in North America are more treatment responsive and get less complicated compared to patients in Middle Eastern countries, due to unclear reasons.
Objectives: To compare the clinical and genetic characteristics of an Israeli and US cohort, and evaluate for differences in disease presentation, severity, and treatment response.
Methods: Medical records of children diagnosed with FMF from 2 tertiary rheumatology centers, Tel Aviv, Israel, and Los Angeles, US, were analyzed retrospectively. Data were recorded from at least three time points: time of diagnosis prior to treatment, one year after diagnosis and at the last charted visit, including clinical, laboratory, and genetic information.
Results: The Israeli and US cohorts consisted of 36 and 63 patients, respectively. The Israeli cohort mostly originated from Morocco (44%) and Iraq (33%), whereas more than 75% of the US cohort originated from Armenia. The clinical characteristics in Israel vs. the US were similar. Fever was the most common (80% vs. 90%, p=0.16), followed by abdominal pain (83% vs. 79%, p=0.63), and joint pain (56% vs. 59%, p=0.76). Age of symptom onset was significantly younger in the Israeli cohort (6.2 months vs. 35 months, p<0.001), despite similar percentages of patients homozygous to MEFV mutations (11% vs. 17%, p=0.7) and with positive family history (53% vs. 49%, p=0.9). Time from symptom onset to diagnosis (2.3 ±6.9 vs. 27±53 months, p<0.001) and to colchicine initiation (2.3 ±2.3 vs. 28.9±28.2 months, p<0.001) were significantly shorter in Israel. The mean follow-up duration was 33.4 months (SD± 30.3) in Israel and 53.7 months (SD± 34.3) in the US. Attack frequency declined over time in both cohorts from diagnosis to the last charted follow-up, from an average of 12.3/year to 3.3/year and 16.2/year to ~1/year for Israel and the US, respectively. At the last recorded visit, none of the patients in either cohort demonstrated kidney injury. However, seven (11.1%) US patients and one (3.3%) Israeli patient presented with new, mild proteinuria (p= 0.14). Of the patients with proteinuria in the US cohort, 3 had homozygous M694V mutation, 3 had compound heterozygous MEFV mutations, and 1 had heterozygous M694V mutation. Six started colchicine an average of 21.5 months after symptom onset, similar to the rest of the cohort without renal involvement. The Israeli child with proteinuria had a homozygous M694V mutation and was never treated with colchicine.

Conclusion: The US and Israel cohorts showed similar clinical presentations despite the differences in their ethnic distribution. Attack frequency at the time of presentation was similar in both cohorts, but the Israeli children had an earlier age of symptom onset. In Israel, the time to diagnosis and treatment initiation was significantly shorter, possibly due to the increased awareness due to a higher prevalence of FMF and/or better access to pediatric rheumatology. Despite delays in diagnosis and treatment in the US cohort, the US children seemed to have favorable outcomes. Studies with a longer follow-up are needed to determine renal outcomes.

Disclosure
None declared

Reference

1. Gattorno M et al. Ann Rheum Dis. 2019 Aug;78(8):1025-1032.

P038

Evaluation of pulmonary involvement in colchicine resistant FMF patients

E. Hepkaya[1], N. Z. Özaslan[2], T. Özer[3], B. Öksel[2], Y. Anık[3], N. Şahin[2], H. E. Sönmez[2]
[1]Department of Pediatric Pulmonology, Kocaeli City Hospital, [2]Department of Pediatric Rheumatology, [3]Department of Radiology, Kocaeli University, Kocaeli, Türkiye
Correspondence: N. Z. Özaslan
Pediatric Rheumatology, **23(2):** P038

Introduction: Familial Mediterranean Fever (FMF) is characterized by self-limited episodes of fever and polyserositis, accompanied by a significant acute phase response. Approximately 40% of pediatric FMF patients experience pleuritic episodes, which lead to symptoms such as chest pain, breathlessness, and cough. Colchicine remains the cornerstone of FMF management, effectively reducing the frequency and severity of attacks while preventing organ complications. However, 5–10% of patients are colchicine-resistant. A recent study in adults reported pulmonary findings in 68.7% of cases, with apical fibrosis being the most common feature. Although pediatric data on radiological pulmonary findings are lacking, it is essential to monitor children for pulmonary involvement.
Objectives: To determine the prevalence and characterize the pulmonary involvement in pediatric patients with colchicine-resistant FMF.
Methods: This cross-sectional study included 31 colchicine-resistant FMF patients and 31 age- and sex-matched healthy volunteers who had undergone chest computerized tomography (CT) for trauma. Pulmonary function was assessed using spirometry, and chest CT scans performed during disease progression were evaluated. Demographic data, including age, gender, age at diagnosis, genotype, and medication history, were recorded, along with information on atopic status, respiratory symptoms, tobacco exposure, and attack characteristics.
Results: A total of 31 colchicine-resistant FMF patients were evaluated, including 20 girls (64.5%) and 11 boys (35.5%).The median ages at symptom onset and diagnosis were 55 months (6–115) and 66 months (18–144), respectively. The most common MEFV mutation was M694V/M694V (74.2%), followed by M694V/M680I (16.1%). The median attack frequency was 5 per year (4–12), lasting a median of 3 days (1–5). Abdominal pain (96.8%), fever (90.3%), and arthralgia (87.1%) were the most common symptoms. Chest pain occurred in 71% of patients, but none had amyloidosis. The median age at pulmonary evaluation was 11 years (5–20), with a median colchicine treatment duration of 36 months (12–192). Respiratory complaints included shortness of breath in 5 patients (16.1%), a history of atopy in 3 (9.7%), asthma in 2 (6.5%), and pneumonia in 3 (9.7%). Pulmonary function tests showed normal results in 18 patients (58.1%), an obstructive pattern in 2 (6.5%), and a restrictive pattern in 5 (16.1%), while 6 (19.4%) were unable to cooperate. Chest CT findings were normal in 8 patients (25.8%) but abnormal in 23 (74.2%), compared to 11 in the control group (p=0.002). Nodules, all solid in nature, were more common in patients, predominantly peri-lymphatic and located near the pleura, fissures, and bronchovascular tree (Table 1).
Conclusion: In this study, increased peri-lymphatic nodules were observed in FMF patients, and it is hypothesized that this may be related to previous pleuritic attacks.

Disclosure
None declared

References

1. Sen N, Acer Kasman S, Baysal T, Dizman R, Yilmaz-Oner S, Tezcan ME. Apical fibrosis was the most common incidental pulmonary finding in a familial Mediterranean fever cohort. Clin Rheumatol. 2023;42(5):1363-1370.
2. Ozturk K, Coskuner T, Baglan E, et al. Real-Life Data From the Largest Pediatric Familial Mediterranean Fever Cohort. Front Pediatr. 2021;9:805919.
3. Tsur AM, Watad A, Gendelman O, Nissan D, Cohen AD, Amital H. Familial Mediterranean fever and asthma. Rheumatology (Oxford). 2021;60(12):5642-5646.

P039

Clinical differences between colchicine-resistant familial mediterranean fever patients responding to colchicine preparation switching and those requiring biological therapy

N. Kara Çanlıoğlu, E. Tunce, S. Atamyıldız Uçar, B. Sözeri
Pediatric Rheumatology, Ümraniye Training and Research Hospital, Istanbul, Türkiye
Correspondence: E. Tunce
Pediatric Rheumatology, **23(2):** P039

Introduction: In patients with colchicine-resistant Familial Mediterranean Fever (FMF), switching to a different colchicine preparation has been shown to reduce attack frequency before initiating biological therapy (1).
Objectives: In this study, we aimed to compare patients who benefited from switching to an imported colchicine preparation after failing to respond to the domestic formulation in Türkiye, with those who required biological treatment.
Methods: A retrospective review was conducted of patients who had undergone colchicine preparation switching. A total of 108 colchicine-resistant FMF patients were included in the analysis. Patients who had changed colchicine formulations solely due to side effects such as diarrhea were excluded.
Results: Among 108 colchicine-resistant FMF patients with biallelic pathogenic exon 10 mutations, 72 (66%) showed clinical improvement after switching colchicine formulations and did not require biological therapy, while 36 (33%) did not benefit and needed anti-IL-1 treatment.
In the group responding to colchicine switching alone, MEFV analysis showed compound heterozygosity in 17 patients, homozygous M680I in 1, V726A in 1, and homozygous M694V in 53. In the biologic-treated group, 9 had compound heterozygosity, 2 had homozygous V726A, 1 had homozygous M680I, and 24 had homozygous M694V.
The mean age at FMF attack onset, diagnosis, and colchicine switch was 3.9, 5.6, and 12.3 years respectively in responders, and 4.8, 5.7, and 10.9 years in biologic-treated patients. Mean age at biologic therapy initiation was 11.4 years. There were no statistically significant differences between groups regarding age at onset, diagnosis, or colchicine switch. Among responders, 63 had fever, 65 abdominal pain, 18 chest pain, 34 arthritis, 30 erysipelas-like erythema (ELE), and 46 a positive family history. In the biologic group, 35 had fever, 33 abdominal pain, 11 chest pain, 7 arthritis, 6 ELE, and 20 a family history.
There were no significant differences in the frequency of fever, abdominal pain, or chest pain. However, arthritis, ELE, and positive family history were significantly more common in the group responding to colchicine switching.
These findings suggest that the need for biological therapy is more closely related to attack frequency than specific clinical manifestations. Evaluating patient response to different colchicine formulations may help avoid unnecessary escalation to biologics in a substantial proportion of colchicine-resistant FMF cases.
Conclusion: Among our cohort of 108 patients who underwent colchicine preparation switching, only 36 ultimately required biological therapy. These results underscore that, in colchicine-resistant patients, switching colchicine formulations should be considered as a therapeutic step prior to initiating anti-IL-1 treatment.
Disclosure
None declared

Reference
1. Baglan E, Ozdel S, Bulbul M. Do all colchicine preparations have the same effectiveness in patients with familial Mediterranean fever? *Mod Rheumatol*. 2021 Mar;31(2):481-484.

P040

Evaluation of CD9 blood levels in pediatric patients with familial mediterranean fever (FMF)

N. Gorpuz[1], U. Sarıkaya[2], H. Dursun[3], F. Sonmez[4]
[1]Faculty of Medicine, [2]Department of Clinical Biochemistry, Bezmialem Vakıf University, [3]Department of Pediatric Nephrology, University of Health Sciences, [4]Depatment of Pediatric Nephrology, Bezmialem Vakıf University, Istanbul, Türkiye
Correspondence: N. Gorpuz
Pediatric Rheumatology, **23(2):** P040

Introduction: Familial Mediterranean Fever (FMF) is a clinically diagnosed autoinflammatory disease in which CD9, a tetraspanin protein involved in immune regulation, may play a role in its underlying inflammatory mechanisms.
Objectives: The objective of this study is to investigate CD9 levels in FMF patients and examine their asssociation with clinical features, genetic findings and inflammatory characteristics.
Methods: Clinical, genetic, and laboratory data (serum amyloid A (SAA), white blood cell count (WBC), fibrinogen, C- reactive protein (CRP), estimated sedimentation rate (ESR), 24-hour urine) were collected from pediatric FMF patients (subdivided into attack and remission groups) and compared with a healthy control group. CD9 blood levels were measured by ELISA and re-tested after 15 days in the attack group. Data were analyzed using Mann–Whitney U, Chi-square, and correlation tests via SPSS.
Results: The study included 40 FMF patients (23 girls, 17 boys; mean age 11.3 ± 3.8 years) (6 during attack, 34 in remission) and 28 healthy controls (20 girls, 8 boys; mean age 9.1 ± 4.8 years). The most common clinical manifestations were abdominal pain (78%) and arthritis (50%). The most common genetic mutations were M694V (27,5%) and E148Q (17,5%). CD9 levels were significantly lower in the FMF patients compared to the control group ($p<0.01$). No significant difference was observed between the remission group and the attack group ($p > 0.05$). CD9 levels did not correlate significantly with inflammatory markers (CRP, ESR, SAA), nor were they associated with gender, genetic variations or symptoms ($p > 0.05$).
Conclusion: Despite the limitations in sample size and the restricted attack group due to the study's prospective design, the findings indicate that CD9 may have a significant role in the pathophysiology of FMF. Further large-scale, multicentered studies are required to comprehensively elucidate its role.
Disclosure
None declared

P041

Subclinical inflammation in pediatric familial mediterranean fever: predictors and follow-up results

O. Bahçeci, F. Aydin, O. Tas, B. Oksuz Aydin, D. Sarisoy, Z. B. Ozcakar
Pediatric Rheumatology, Ankara University Faculty of Medicine, ANKARA, Türkiye
Correspondence: O. Bahçeci
Pediatric Rheumatology, **23(2):** P041

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease of childhood. Subclinical inflammation, characterised by persistently elevated acute phase reactants in the absence of clinical episodes, is an increasingly recognised risk factor for long-term complications. Undetected inflammation can lead to severe outcomes such as amyloidosis, organ damage such as renal failure, and growth retardation. Despite the significant clinical relevance of the issue, there is a paucity of research on the predictors and outcomes of subclinical inflammation in paediatric FMF patients.
Objectives: The aim of this study was to determine the frequency and clinical predictors of subclinical inflammation in pediatric FMF patients and to evaluate the response to treatment adjustments for subclinical inflammation.
Methods: The medical records of FMF patients followed up at our clinic between December 2011 and February 2024 were retrospectively reviewed. Patients were grouped according to the presence or absence of subclinical inflammation, defined as elevated CRP levels during attack-free periods at more than 75% of follow-up visits. The clinical and genetic results of the two groups were compared.
Results: 572 FMF patients were included in the study, 288 (50.3%) of whom were female. Mean age was 168 ± 60 months. Subclinical inflammation was found in 15.6% of patients (n=89). Patients with subclinical inflammation had a significantly earlier age at diagnosis (p=0.038), longer duration of disease ($p<0.001$), more frequent attacks of fever (p=0.004) and arthritis ($p<0.001$), higher frequency of comorbid inflammatory diseases (p=0.027), and more frequent attacks per year ($p<0.001$). Independent predictors of subclinical inflammation included longer disease duration (OR=1.09, p=0.023), biallelic exon 10 mutations (OR=3.90, p=0.020), colchicine resistance (OR=2.60, p=0.048), arthritis (OR=7.06, $p<0.001$), and higher disease severity scores (ISSF) (OR=5.67, $p<0.001$). Maximum tolerated dose escalation of colchicine controlled inflammation in 45% of cases (n=40), while 55% (n=49) required biologics. Of those treated with biologics, 87.7% (n=43) achieved normalisation of inflammatory markers.
Conclusion: In paediatric FMF patients, subclinical inflammation can be seen with appropriate treatment doses of colchicine. Earlier age at diagnosis, carrying a biallelic exon 10 mutation, presence of arthritis, and higher ISSF scores seem to be related with subclinical inflammation. Increasing colchicine to the maximum tolerated dose is effective in almost half of these cases. Anti-IL-1 treatments are effective in those who are resistant to colchicine.
Disclosure
None declared

P044

Clinical course and treatment indications in mefv heterozygous children without fmf phenotype: a single-center experience

P. Esmeray Şenol[1], N. Belder[2], Ç. Yıldız[2], N. Karaçayır[2], M. Kutlar Tanıdır[2], B. Küçükali[2], D. Gezgin Yıldırım[2], S. Bakkaloğlu[2]
[1]Pediatric rheumatology, Mersin City Training and Research Hospital, Mersin, [2]Pediatric rheumatology, Gazi university, Ankara, Türkiye
Correspondence: P. Esmeray Şenol
Pediatric Rheumatology, **23(2):** P044

Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease in childhood. Although FMF is typically associated with the presence of two pathogenic variants in the MEFV gene, a diagnosis can also be established in the presence of a single pathogenic variant if characteristic clinical features are present. The diagnosis of FMF is primarily based on clinical findings, with genetic analysis serving as a supportive tool. However, the management of individuals who carry only a single MEFV mutation but do not exhibit clinical features of FMF remains controversial. Therefore, defining the long-term clinical course and treatment indications in MEFV heterozygous individuals without FMF phenotype is a significant unmet need in clinical practice.
Objectives: This study aims to evaluate the clinical course, laboratory features, and reasons for initiating treatment in pediatric patients who are heterozygous for MEFV mutations and do not present with FMF clinical findings at baseline.
Methods: We retrospectively reviewed the medical records of 116 pediatric patients with heterozygous MEFV mutations who were asymptomatic for FMF at initial presentation and followed at our center between 2015 and 2024. Demographic data, family history, presenting complaints, genetic findings, laboratory parameters, and follow-up data were analyzed. The primary outcome was the indication for initiating colchicine or other anti-inflammatory treatment during follow-up. *Group 1* comprised patients who, despite being asymptomatic for FMF at baseline, required the initiation of colchicine or other anti-inflammatory treatment during the follow-up period due to the development of clinical symptoms or persistent laboratory abnormalities. *Group 2* consisted of patients who remained untreated throughout the entire follow-up duration, as they did not exhibit any

clinical or laboratory indications warranting treatment. The decision to initiate treatment was made by the treating physician based on a comprehensive assessment of the patient's clinical presentation, laboratory findings, and family history, in accordance with established clinical guidelines.
Results: The median age of the 116 patients included in the study was 13.3 years (min: 3.7; max: 24.3), and the mean follow-up duration was 3.1 years. The most common presenting complaints were abdominal pain (34.5%), fever (13.8%), and family history (8.6%). The most frequent MEFV mutations identified were M694V/- (47.4%), V726A/- (15.5%), and E148Q/- (14.7%). A positive family history was present in 63.8% of patients, most commonly FMF (34.5%) and FMF+amyloidosis (3.4%). During follow-up, 51.7% of patients were diagnosed with FMF and treatment was initiated, while 48.3% continued to be monitored without treatment. The most common reasons for initiating treatment were recurrent attacks, persistent elevation of acute phase reactants, and a strong family history of severe FMF/Amyloidosis. A comparison of the clinical and genetic characteristics between Group 1 (patients who required treatment) and Group 2 (patients who remained untreated) revealed several notable differences. Patients who required treatment had significantly higher baseline ESR (26.9 vs. 16.2 mm/h, p=0.009) and CRP (22.1 vs. 7.8 mg/L, p=0.005) values compared to the untreated group. Among the 116 patients, the most frequent mutation was M694V/- in both groups. However, the compound heterozygous M694V/E148Q mutation was significantly more common in the treated group (9.8% vs. 0%, p=0.049).
Conclusion: A significant proportion of MEFV heterozygous children without FMF phenotype may develop clinical or laboratory indications for treatment during follow-up. Family history, persistent subclinical inflammation, and specific mutation types are prominent predictors of treatment initiation. Early identification of high-risk patients and proactive management may be critical to prevent long-term complications.
Disclosure
None declared

P045

Lung-only involvement in sting-associated vasculopathy with onset in infancy: a diagnostic pitfall in the absence of cutaneous vasculitis

R. M. Kisla Ekinci[1], U. Cay[2], D. Kor[3], H. A. Telefon[4], F. Ekinci[4], O. Ozgur Horoz[4], D. Yildizdas[4]
[1]Pediatric Rheumatology, [2]Pediatric Infectious Diseases, [3]Pediatric Metabolism, [4]Pediatric Intensive Care, Cukurova University Faculty of Medicine, Adana, Türkiye
Correspondence: R. M. Kisla Ekinci
Pediatric Rheumatology, **23(2):** P045

Introduction: STING-associated vasculopathy with onset in infancy (SAVI) is a type 1 interferonopathy, characteristically represents with unprovoked fever episodes and systemic inflammation along with skin and lung inflammation. Lung involvement is encountered in nearly %75 of patients with SAVI, mostly interstitial lung disease, resultant from non-specific fibrosis. there is arising information on patients only manifesting as interstitial lung disease (ILD) without any skin lesions, which makes the diagnosis more difficult and broadening the differential diagnosis of the disease to the ILD spectrum.
Objectives: We aimed to present our experience with a case of SAVI syndrome without cutaneous vasculitis.
Methods: Case presentation
Results: A 10-months old male patient, born to nonconsanguineous parents, was admitted to our hospital with cough and respiratory distress. His past medical history indicated that respiratory distress and tachypnea was present since birth and treated with antimicrobial agents at different occasions. He had a pediatric intensive care unit (PICU) hospitalization when he was 5 months old, lasting for 4-months in another medical center. Initial physical examination revealed hypotonia, pallor, bilateral crackles, tachypnea, and retractions.
High resolution thorax computerized tomography (HRCT) showed large, consolidated areas with air bronchograms, prominent in the lower lobes, compatible with infection along with ground-glass opacities and white circles reveal microcystic appearance in peripheral zones, suggestive for ILD.
At 14 months of age, whole exome sequencing revealed a heterozygote c.461A>G (p.Asn154Ser) variant in *STING1* gene (NM_198282.4) and a heterozygote c.2020G>C (p.Met680Ile) variant in *MEFV* gene (*NM_000243.3)*. Baricitinib was commenced at 3 mg/g per day, in three divided doses, but did not lead to any improvement in respiratory symptoms. Therefore, we aimed to suppress other inflammatory pathway, nuclear factor kappa B (NFKB) and initiated intravenous tocilizumab at a dosage of 12 mg/kg during the 3rd week of baricitinib. However, the patient deteriorated and deceased 1 months later. Parental testing confirmed that the variant was de-novo.
Conclusion: SAVI syndrome should be considered in differential diagnosis of ILD in every age, even in the absence of skin involvement. Consent to published had been obtained.
Disclosure
None declared

References

1. Liu Y, Jesus AA, Marrero B, et al. Activated STING in a vascular and pulmonary syndrome. N Engl J Med. 2014 Aug 7;371(6):507-518.
2. Frémond ML, Hadchouel A, Berteloot L, et al. Overview of STING-Associated Vasculopathy with Onset in Infancy (SAVI) Among 21 Patients. J Allergy Clin Immunol Pract 2021;9:803-18.e11.

P046

Efficacy of colchicine treatment in children with periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome

R. Kasem Ali Sliman, M. Hamad Saied
Pediatrics, Carmel medical center, Haifa, Israel
Correspondence: R. Kasem Ali Sliman
Pediatric Rheumatology, **23(2):** P046

Introduction: PFAPA syndrome is the most common periodic fever disorder in children, characterized by recurrent episodes of fever associated with cervical adenitis, pharyngitis, and aphthous stomatitis. Growing evidence suggests a connection between PFAPA and Familial Mediterranean Fever (FMF), with both having associations with IL-1β pathways. Colchicine, a standard treatment for FMF, may potentially benefit PFAPA patients, but limited evidence exists on its efficacy for preventing recurrent PFAPA episodes.
Objectives: To evaluate the efficacy of colchicine prophylaxis in children diagnosed with PFAPA syndrome by comparing attack frequency in colchicine-treated patients versus standard care controls.
Methods: We conducted a retrospective analysis of 55 PFAPA patients (15 in the colchicine group and 40 in the control group). Demographics, clinical characteristics, FMF genetic profiles, and attack frequency before and after intervention were collected. The primary outcome was the time interval between fever episodes. Statistical significance was set at P<0.05.
Results: Both groups were comparable regarding age at diagnosis (5.33 [3.71-6.96] vs. 4.63 [3.94-5.32] years, P=0.4), age of symptom onset (3.00 [2.02-4.57] vs 2.59 [2.16-3.03] years, P=0.42), and duration of fever before diagnosis (3.75 [2.93-4.57] vs 4.345 [3.90-4.99] days, P=0.14). The colchicine group demonstrated a significant increase in the time between attacks after treatment (83.00 [58.56-107.44] days) compared to pre-treatment intervals (27.92 [24.68-31.15] days, P=0.002). MEFV mutations were more prevalent in the colchicine group (58.33% vs 26.32%, P<0.05), with heterozygous M694V (5/11) and V726A (4/11) being most common. Within genetic subgroups, patients with mutations receiving colchicine experienced shorter fever duration (3.25 [2.66-3.84] days) compared to controls (4.45 [3.00-4.00] days, P<0.05. Notably, both genetically positive and negative patients responded favorably to colchicine treatment, although the magnitude of improvement was greater in those with MEFV mutations.
Conclusion
Conclusion: Colchicine prophylaxis significantly extended the interval between fever episodes in all PFAPA patients, with enhanced efficacy in those with MEFV gene mutations. The nearly three-fold increase in attack-free intervals in genetically positive patients demonstrates that genetic testing may be an important factor in predicting treatment response. These findings suggest colchicine as an effective

prophylactic treatment for all PFAPA patients, especially those with specific FMF genetic profiles, potentially transforming the management approach from episodic symptom control to sustained prevention in this challenging pediatric autoinflammatory condition.

Disclosure

None declared

P048

A retrospective study observing the role of serum ace, chitotriosidase and soluble CD25 as biomarkers in paediatric sarcoidosis

R. Lethem, S. Cuyx, S. Lacassagne
Great Ormond Street Hospital for Children, London, United Kingdom
Correspondence: R. Lethem
Pediatric Rheumatology, **23(2):** P048

Introduction: Paediatric sarcoidosis is a multisystem granulomatous inflammatory disease.[1] Several biomarkers to inform disease management in paediatric sarcoidosis have been researched, though their application can be limited.[2] Little is known of sarcoidosis biomarkers in children, and adult data is often used as a proxy.[3]
Objectives: This retrospective study observed three biomarkers, prominent within the adult literature (serum angiotensin-converting enzyme (ACE), chitotriosidase (CTO) and soluble CD25 (sCD25)), to assess their role in paediatric sarcoidosis.
Methods: Electronic notes of patients in a large UK paediatric rheumatology centre over a ten year period (Apr 2015– Apr 2025) were accessed. Data were collected on patients with biopsy-proven sarcoidosis that had at least one simultaneous measurement of serum ACE, CTO and sCD25. Clinician determination of the child's clinical status (flare versus non-flare) was correlated.
Results: Twenty-six simultaneous measurements of serum ACE, CTO and sCD25 in 14 patients were identified. A flare was reported in 7 of the 26 measurements. In cases of flare, absolute values were significantly raised for both CTO (p=0.004; mean 680 [0-150nmol/hr/ml], IQR 1788) and sCD25 (p<0.001; mean 8023 [0-2500pg/ml], IQR 10873). Whilst mean serum ACE was raised in cases of flare, this was not significant (p=0.093). Further, a significantly higher proportion of measurements of CTO (p=0.002) and sCD25 (p<0.001) were above the upper limit of normal in cases of flare; this was not true for ACE (p=0.069).
When combining biomarkers, measurements were elevated in cases of flare most significantly using a minimum of two biomarkers (p<0.001) compared to a minimum of one biomarker (p=0.026) and when combining all three biomarkers (p=0.014), respectively.
Sensitivity and specificity analyses suggested CTO alone was highly specific but had low sensitivity. ACE had a sensitivity of 71% and specificity of 73%. Combining CTO with sCD25 had optimal combined sensitivity and specificity (71% and 95% respectively).
Conclusion: These preliminary data support the use of combining CTO and sCD25 biomarkers in children for the purpose of disease monitoring in sarcoidosis, whilst inclusion of serum ACE may also be beneficial if used in combination with at least one other. Measurement of serum ACE alone was not a reliable biomarker.
Few publications have addressed the area of sarcoidosis biomarkers in children. Whilst this study is limited by small sample size, and the retrospective design may be prone to bias, the results may serve as a promising start in understanding the role of biomarkers in the management of paediatric sarcoidosis.

Disclosure

None declared

References

1. Chiu B, Chan J, Das S, Alshamma Z, Sergi C. Pediatric Sarcoidosis: A Review with Emphasis on Early Onset and High-Risk Sarcoidosis and Diagnostic Challenges. Diagnostics (Basel). 2019;25;9(4):160.
2. Bazewicz M, Heissigerova J, Pavesio C, Willermain F, Skrzypecki J. Ocular sarcoidosis in adults and children: update on clinical manifestation and diagnosis. J Ophthalmic Inflamm Infect. 2023;13(1):41
3. Nott K, Nott V, Lever E, Deakin C, Galloway J, Fisher C, Compeyrot-Lacassagne S. Pediatric Sarcoidosis: Retrospective Analysis of Biopsy-Proven Patients. J Rheumatol. 2023;50(7):924-933.

P049

Hyperinflammatory syndromes in the pediatric intensive care unit

I. de la Vega Morán[1], J. Mayordomo-Colunga[2], S. Murias Loza[3], A. Vivanco-Allende[2], V. Courel del Río[3], R. Fernández Montes[2], E. Pardo Campo[3], A. Concha-Torre[2], J. Rodríguez Suárez[3] on behalf of Select an option…
[1]Faculty of Medicine and Health Sciences, University of Oviedo, [2]Pediatric Intensive Care Unit, [3]Pediatric Rheumatology Unit, University Hospital Central of Asturias, Oviedo, Spain
Correspondence: S. Murias Loza
Pediatric Rheumatology, **23(2):** P049

Introduction: Hyperinflammatory syndromes are characterized by an uncontrolled release of cytokines. They include pediatric multisystem inflammatory syndrome associated with SARS-CoV-2 (MIS-C), hemophagocytic lymphohistiocytosis (HLH) including macrophage activation syndrome (MAS) and primary HLH, and other hyperinflammatory entities such as Kawasaki Disease (KD) or systemic-onset JIA (SoJIA)
Objectives: To differentiate the clinical and laboratory findings among MIS-C, HLH, and other hyperinflammatory syndromes in children admitted to the Pediatric Intensive Care Unit of a tertiary hospital
Methods: A descriptive, observational, and retrospective study was conducted in pediatric patients with suspected hyperinflammatory syndrome, admitted between October 2019 and 2024. Those cases with underlying diagnosis of sepsis or malignancies were excluded. Demographic, clinical, laboratory, and treatment variables were collected. Comparisons between groups were made using the Chi-square test for qualitative variables, and Student's t-test and ANOVA for quantitative variables with a normal distribution. For non-normally distributed variables, the Mann-Whitney U test and Kruskal-Wallis test were used. Data are shown as media (SD) and a p value < 0.05 was considered significant. Given that the MIS-C group was the largest and most distinctive due to its COVID-19–related etiopathogenesis, additional comparisons were made between this group and the other two combined
Results: A total of 20 patients were included in the study (mean age: 126.2 ± 60 months, 65% male). The sample comprised 10 patients diagnosed with multisystem inflammatory syndrome in children (MIS-C); 4 with hemophagocytic lymphohistiocytosis (HLH) including 1 case of Chédiak-Higashi syndrome and 3 secondary MAS; and 6 with other hyperinflammatory syndromes (3 KD, 1 SoJIA, and 2 undifferentiated). All patients presented with high-grade fever and elevated inflammatory markers: C-reactive protein (CRP) 29.5 ± 25.9 mg/dL, erythrocyte sedimentation rate (ESR) 71 ± 41 mm/h, and ferritin 694 [IQR: 492–1027] ng/mL. Clinically, the MIS-C group demonstrated a significantly higher frequency of cutaneous rash (p = 0.006) and acute respiratory distress syndrome (ARDS) (p = 0.025) compared to the other groups. Laboratory findings revealed that patients with MIS-C exhibited more pronounced lymphopenia (p = 0.006) and elevated NT-proBNP levels (p = 0.050), whereas HLH patients showed significantly lower neutrophil counts (p = 0.030), hypofibrinogenemia (p < 0.001), and higher triglyceride levels (p = 0.052). All patients received corticosteroid therapy; 16 were treated with intravenous immunoglobulins, and 3 required additional immunomodulatory treatment. One patient in the MIS-C group died
Conclusion: These syndromes share common hyperinflammatory features. However, MIS-C patients more frequently developed rash, ARDS, lymphopenia, and cardiac involvement, whereas HLH cases more often presented with neutropenia, hypofibrinogenemia, and hypertriglyceridemia

Disclosure

None declared

References

1. Carol HA, Mayer AS, Zhang MS, Dang V, Varghese J, Martinez Z, et al. Hyperferritinemia Screening to Aid Identification and Differentiation of Patients with Hyperinflammatory Disorders. J. Clin. Immunol. 2025;45:4.
2. Diorio C, Teachey DT, Canna SW. Cytokine Storm Syndromes in Pediatric Patients. J Allergy Clin Immunol Pract. 2023;11:1636-44

P050

Peripheral monocyte and dendritic cell distribution during and between flares in PFAPA syndrome

H. S. Kose, A. Simsek, M. A. Kızmaz, T. Bozkurt, F. Budak, S. S. Kilic

Bursa Uludag University, Bursa, Türkiye
Correspondence: S. S. Kilic
Pediatric Rheumatology, **23(2):** P050

Introduction: Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA) syndrome is an autoinflammatory disease characterized by recurrent fever, mouth ulcers, sore throat, and swollen lymph nodes.
Objectives: In this study, we aimed to evaluate monocyte and dendritic cell groups, which are sources of proinflammatory cytokines during febrile flare-ups and asymptomatic periods, comparing them with healthy controls.
Methods: Nineteen patients and 14 healthy controls were enrolled in the study. Serum immunoglobulin levels (IgG, IgM, and IgA) were measured nephelometrically during febrile and afebrile periods. Lymphocyte subsets were analyzed using flow cytometry.
Results: The study included 19 PFAPA patients, of whom 13 were male (68.4%), and 14 healthy controls. The median follow-up duration was 16 months (±12). During febrile attacks, mean sedimentation rate (26.36 ± 2.87) mm/h, CRP (71.95 ± 11.87) mg/dl, serum amyloid A (SAA) (629.26 ± 126.13) mg/dl and fibrinogen (369.05 ± 21.23) mg/dl were found to be significantly higher than in afebrile attacks and healthy controls (p <0.001, p< 0.001, p <0.001, p <0.003, respectively). There was a significant increase in the mean absolute counts of classical monocytes (885.4±86.97) (p<0.001), intermediate monocytes (116.2±14.9) (p=0.174), and non-classical monocytes (49.2±13.6) (p<0.001) compared to afebrile periods and healthy controls. The mean dendritic cell counts also increased significantly during febrile episodes: myeloid dendritic cells: 12,787.42 ± 5,500.82 (p<0.001), plasmacytoid dendritic cells: 543.52 ± 103.25 (p <0.001).
Conclusion: The study reveals that classical and intermediate monocytes, plasmacytoid dendritic cells (pDC), and conventional dendritic cells (cDC), which exhibit significant inflammatory properties, play a vital role in the activation process. Moreover, the notable increase in myeloid and plasmacytoid dendritic cells suggests a collaborative interaction between innate and adaptive immunity in PFAPA. These findings underscore the critical importance of innate immune activation during febrile episodes in PFAPA.
Disclosure
None declared

P051

The Addi score for assessing damage in autoinflammatory diseases: data from the eurofever registry

S. La Bella[1,2], G. Badino[1,3], M. Neri[4], A. Porreca[5,6], A. Insalaco[7], J. Frenkel[8], R. Caorsi[1,3], M. Gattorno[1] on behalf of the EuroFever registry and PReS Autoinflammatory WP for PReStaR
[1]UOC Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, Genova, [2]Paediatric Rheumatology Unit, "G. D'Annunzio" University of Chieti-Pescara, Chieti, [3]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), Università degli Studi di Genova, Genova, [4]Pediatric Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, [5]Department of Human Sciences and Promotion of the Quality of Life, San Raffaele University, [6]Unit of Clinical and Molecular Epidemiology, IRCCS San Raffaele, [7]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Roma, Italy, [8]Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands
Correspondence: S. La Bella
Pediatric Rheumatology, **23(2):** P051

Introduction: The Autoinflammatory Disease Damage Index (ADDI) is a validated and reliable tool used to quantify damage in patients with autoinflammatory diseases (AIDs). Currently, it has been validated in CAPS, FMF, MKD, and TRAPS [1, 2].
Objectives: This study aims to characterize the spectrum of damage in patients with AIDs and to highlight disease-specific relevant damage items not included in the ADDI.
Methods: The ADDI score, which ranges from 0 (no damage) to 27 (maximum damage), was applied to patients with the ten most prevalent diseases in the Eurofever registry at the time of enrolment. Patients were classified based on the presence or absence of damage. In addition, other clinical manifestations and laboratory data were evaluated to identify potential items for inclusion in future damage assessment tools.
Results: A total of 3211 patients with AIDs were assessed. The ten most prevalent diseases were: Behçet's disease (n=267), CAPS (n=131), CRMO (n=494), DADA2 (n=96), FMF (n=1484), MKD (n=100), PAPA syndrome (n=48), SURF (n=230), TRAPS (n=104), and undefined AID (n=257).
Overall, given the young age at enrolment, highest in PAPA with a median of 19.6 years [11.7; 31.9], the extent of damage was low, with the highest observed in CAPS and DADA2 (median ADDI of 1 [0.0; 3.0]).
Among the diseases for which the ADDI was validated, FMF showed the lowest frequency of damage (338, 22.8%), whereas CAPS had the highest (77, 58.8%), followed by MKD (38, 38%) and TRAPS (27, 26%).
In CAPS, damage was predominantly due to hearing loss (37, 28.2%), while in TRAPS it was mainly related to renal involvement (11, 10.6%), particularly persistent proteinuria and renal amyloidosis. Growth failure was the leading cause of damage in FMF (192, 12.9%), MKD (17, 17%), SURF (52, 22.6%), and undefined AIDs (61, 23.7%). Musculoskeletal damage was most prevalent in CRMO (162, 32.8%) and PAPA syndrome (11, 22.9%), mainly due to chronic musculoskeletal pain.
In Behçet's disease, 105 (39.3%) had documented damage, primarily due to ocular involvement (43, 16.1%), including vision loss and blindness (39, 14.6%).
A significant proportion of patients with undefined AIDs had some degree of damage (134, 52.1%), mainly due to growth failure and renal involvement (47, 18.3%), particularly persistent proteinuria. Similarly, in DADA2, damage was relevant and detected in 50 (52.1%) patients, primarily related to neurological involvement (22, 22.9%), especially affecting the central nervous system (18, 18.8%).
Regarding items not included in the ADDI but persistent and relevant for damage we identified the following ones:
DADA2: peripheral neuropathy in 8 (8.9%), aplastic anemia in 4 (4.2%), and gastrointestinal perforation or tumors in 3 (3.1%)
PAPA syndrome: muscular atrophy in 4 (8.3%)
TRAPS: intestinal obstruction in 4 (3.8%)
CAPS: patellar overgrowth in 4 (3.1%)
MKD: camptodactyly in 3 (3%).
Conclusion: The ADDI is effective in assessing damage in validated AIDs and highlights key damage domains across other autoinflammatory diseases. Additional recurrent manifestations suggest the need to refine and expand damage indices to better capture disease burden in non-validated conditions. In the EuroFever cohort, damage was generally mild, also due to the young age at enrolment.
Trial registration identifying number: NA
Disclosure
None declared

References

1. ter Haar NM et al, Ann Rheum Dis 2017
2. ter Haar NM et al, Ann Rheum Dis 2021

P053

Clinical course of two patients with savi treated with IFNAR1 blocking antibody anifrolumab

S. Palmeri[1,2], S. M. Orsi[1,2], V. Natoli[1,2], P. Bocca[2], R. Papa[2], S. Volpi[1,2], R. Caorsi[1,2], M. Gattorno[2]
[1]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, [2]Rheumatology and Autoinflammatory diseases Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: S. Palmeri
Pediatric Rheumatology, **23(2):** P053

Introduction: STING-associated vasculopathy with onset in infancy (SAVI) is a rare monogenic autoinflammatory disease caused by gain-of-function mutations in *STING1*, leading to constitutive activation of the type I interferon (IFN-I) pathway. This persistent signaling causes systemic inflammation, cutaneous vasculopathy, and interstitial lung disease. Jak inhibitors efficacy, especially on lung disease progression, might be limited, with a considerable increase in infection risks. Anifrolumab, a monoclonal antibody targeting the IFN-I receptor (IFNAR),

offers a promising alternative by selectively blocking IFN-I signaling. Few reports describe anifrolumab use in SAVI, but data remain limited in term of long-term efficacy or monotherapy potential.(1-3)
Objectives: To describe the clinical course of 2 SAVI patients treated with anifrolumab followed at IRCCS Istituto G. Gaslini of Genoa (Italy).
Methods: Patients' records were collected. Blood tests and type I interferon (IFN) scores were monitored before and after anifrolumab initiation. Written informed consent was obtained for data collection and publication.
Results: The first patient is a 20-year-old European female with disease onset at 8 months, carrying a de novo heterozygous P.Val155Met mutation in *STING1*. Clinical features included vesiculopapular skin lesions progressing to pustular and scarring forms, nail dystrophy, pulmonary involvement (ground-glass opacities), and renal involvement. Azathioprine, and etanercept were ineffective. Ruxolitinib was initially beneficial but later combined with mycophenolate mofetil due to incomplete disease control. Anifrolumab was initiated at 150 mg/2 weeks at the age of 19, combined with ruxolitinib (0.5 mg/kg/day), leading to a marked reduction in the type I IFN score after administration. One month after starting anifrolumab, the patient developed a mild papular rash on the trunk and face, prompting an increase of anifrolumab to 300 mg and gradual tapering with discontinuation of ruxolitinib. Five months after initiation, the patient developed hand dactylitis, requiring reintroduction of ruxolitinib at 0.2 mg/kg/day. The second patient is a 17-year-old European female carrying the *STING1* mutation p.Arg281His. At the age of 3 months, she presented with respiratory distress and developed severe chronic respiratory failure in interstitial lung disease, requiring continuous oxygen therapy. Following the development of pulmonary aspergillosis under mycophenolate mofetil and ruxolitinib, both drugs were sequentially discontinued. Anifrolumab was then initiated at 150 mg, leading to a marked reduction in the interferon score after the second dose.
Conclusion: We treated two patients with SAVI using anifrolumab—one with a milder phenotype and one with severe interstitial lung disease. The treatment appears promising, though incomplete type I interferon blockade or IFN-independent manifestations may require combination therapy.
Disclosure
S. Palmeri: None declared, S. M. Orsi: None declared, V. Natoli: None declared, P. Bocca: None declared, R. Papa: None declared, S. Volpi Consultant with: Boehringer, Speaker Bureau with: Speaker fee from SOBI, R. Caorsi Consultant with: SOBI, M. Gattorno Consultant with: Novartis, Sobi, Fresenius Kabi, Kiniksa, Speaker Bureau with: Novartis, Sobi, Fresenius Kabi, Kiniksa

References
1. Mansilla-Polo, M. et al, JAMA dermat 2024
2. Kretzschmar G. et al. JoCI 2024
3. Alehashemi S. et al. A&R 2025

P054

Study of overall mortality in patients with systemic autoinflammatory diseases in France

T. Julie[1], K. P. Isabelle[1,2], on behalf of FAI2R, D. CLEMENCE[3], on behalf of BNDMR
[1]94270, Bicêtre university hospital, Kremlin bicetre, [2]91190, University of Paris-Saclay, Faculty of Medecine, GIF SUR YVETTE, [3]75000, Banque Nationale de Données Maladies Rares (BNDMR), APHP, Innovation and Data department (I&D)., Paris, France
Correspondence: K. P. Isabelle
Pediatric Rheumatology, **23(2):** P054

Introduction: Systemic autoinflammatory diseases (SAIDs) are there is no data on overall mortality or life expectancy for these patients.
Objectives: The objective of this study is to obtain comprehensive mortality data in patients with FMF, MKD, CAPS and TRAPS, to compare them with each other and to relate them to general mortality data in France by age group.
Methods: We used data of patients with FMF, CAPS, TRAPS and MKD, included in the French National Rare Disease Registry (BNDMR). Patient's data originated from rare disease centers that are members of the FAI2R network, after study approval by the BNDMR institutional review board. Inclusion criteria were affected patients with confirmed diagnosis and with data collected between 01/01/2010 and 12/31/2023; healthy carriers were excluded. Dates of death were those entered in BAMARA and enriched with national publicly individual death data (INSEE), with verification of their coherence.
Results: After exclusion of patients whose diagnosis was uncertain and those who refused the reuse of their data we obtained a total of 1944 patients : 62 with MKD, 192 with CAPS, 1595 with FMF and 95 with TRAPS. Respective prevalence for these SAIDS were evaluated in 2022 as 0.9 per million for MKD, 2.5 per million for CAPS, 20.9 per million for FMF and 1.3 per million for TRAPS. A total of 31 deaths was observed during the period of observation, in which respectively : 24 patients with FMF, 2 with MKD, 2 with TRAPS and 3 with CAPS. The number of deaths observed in the FMF and MKD cohort was greater than the number of deaths expected according to INSEE life expectancy tables in France in a population of the same age and sex and followed over the same period, with respectively 11 and 0 expected deaths. It is the first study of mortality in rare SAIDs in France. It is a powerful study since it is based on a large database: the BNDMR cohort. However, it is exposed to some limitations, notably limited patients' follow-up and the small sample size.
Conclusion: Our analysis revealed low mortality in the CAPS and TRAPS cohorts. The mortality rate in patients with FMF and MKD is high compared to other cohorts and data from the French general population. An in-depth analysis of the causes of these deaths could perhaps make it possible to better prevent them.
Disclosure
None declared

P056

Neutrophil extracellular trap formation and inflammatory profiles in pediatric autoinflammatory diseases — a comparative study of fmf and surf across disease phases

K. Fidan[1], Y. Bayindir[2], A. Atak Yucel[3], D. Unal[2], Y. Bilginer[2], B. Celikel Acar[4], S. E. Baskin[5], S. Ozen[2], H. O. Soylemezoglu[1]
[1]Department of Pediatric Nephrology, Gazi University, [2]Department of Pediatric Rhematology, Hacettepe University, [3]Department of Immunology, Gazi University, [4]Department of Pediatric Rhematology, Ankara City Hospital, [5]Department of Pediatric Nephrology and Rheumatology, Baskent University, Ankara, Türkiye
Correspondence: Y. Bayindir
Pediatric Rheumatology, **23(2):** P056

Introduction: NETosis, the release of neutrophil extracellular traps, has emerged as a key player in the pathogenesis of autoinflammatory disorders. Yet, its role in pediatric conditions such as Familial Mediterranean Fever (FMF) and Syndrome of Undifferentiated Recurrent Fever (SURF) remains underexplored.
Objectives: This study offers a comparative assessment of NET formation during attack and remission phases, aiming to elucidate its relationship with systemic inflammation and potential utility as a disease activity marker.
Methods: This cross-sectional study included pediatric patients diagnosed with FMF or SURF, along with healthy controls. Participants were categorized into four groups: FMF attack (n=45), SURF attack (n=15), FMF remission (n=15), and healthy controls (n=17). NET formation was measured using a fluorescence-based assay following neutrophil isolation. C-reactive protein (CRP), white blood cell count (WBC), and other laboratory markers were analyzed in parallel.
Results: A total of 92 participants were included across four groups. NET levels differed significantly among groups ($p<0.001$), with the highest mean ranks observed in the FMF attack (59.37) and SURF attack (58.57) groups, followed by controls (27.71) and remission (17.13). Post hoc analysis confirmed statistically significant differences between most pairwise comparisons. NET, CRP, and WBC levels were significantly elevated during attack phases compared to remission and control groups ($p<0.001$); however, no significant difference was found between FMF and SURF attacks for NET ($p=0.950$) or CRP ($p=0.597$). Correlation analyses revealed a strong positive correlation between NET levels and CRP ($r=0.686$, $p<0.001$), and moderate correlations with alpha-1 antitrypsin (AAT) ($r=0.483$) and WBC ($r=0.417$). AAT and CRP were also positively correlated ($r=0.394$, $p<0.001$). No significant differences in NET, AAT, or CRP levels were observed across FMF mutation subgroups.

Conclusion: NET formation is significantly elevated during inflammatory attacks in pediatric FMF and SURF, aligning with classical inflammatory markers such as CRP and WBC. The strong correlation between NETosis and CRP suggests that NETs may serve as a reliable indicator of disease activity. These findings support the contribution of NETosis to the inflammatory burden in autoinflammatory syndromes.
Disclosure
None declared

P057

Early-onset interstitial lung disease in a child with sting-associated vasculopathy with onset in infancy

Y. S. Stepaniuk[1], O. A. Oshlianska[2]
[1]National Specialized Children's Hospital «Ohmatdyt» of the Ministry of the Health of Ukraine, Kyiv, [2]Department of pediatrics, neonatology, pediatric infectious diseases, immunology and allergology, Shupyk National Healthcare University of Ukraine, Kyiv, Kyiv, Ukraine
Correspondence: Y. S. Stepaniuk
Pediatric Rheumatology, **23(2):** P057

Introduction: According to ACR (2021), genetic testing for STING-associated vasculopathy with onset in infancy (SAVI) is recommended in cases of unexplained systemic inflammation, fever, rash and musculoskeletal, neurological, or pulmonary involvement. In younger children, suspicion is raised by intracranial calcifications, lupus-like symptoms, while in older children, it may present as a combination of arthritis and myositis.
Objectives: To analyze reasons for delayed SAVI diagnosis based on a case of early-onset interstitial lung disease (ILD).
Methods: Retrospective analysis of clinical data from a child with ILD.
Results: A boy, the 4th child of 5 siblings. Family history revealed lung involvement in close relatives, initially diagnosed as tuberculosis. From birth, he presented with anemia, skin rashes and recurrent infections. At 5 y.o., he developed dyspnea. CT showed interstitial changes and mediastinal lymph nodes enlargement; spirometry revealed restrictive changes; high inflammatory markers: ESR 58 mm/h, CRP 48 mg/L. Infections (herpesviruses, intracellular, fungal, tuberculosis) and immunodeficiencies (incl. HIV) were ruled out. By 5.5 y.o., chest deformity and finger clubbing developed. Extensive differential diagnosis excluded α−1 antitrypsin deficiency, cystic fibrosis, allergic and connective tissue diseases. Hamman-Rich syndrome was suspected, and systemic corticosteroids (CS) initiated. At 6 y.o., lung biopsy revealed hemosiderosis, lymphohistiocytic infiltrate, and vasculitis; lymph node - reactive hyperplasia; skin biopsy - dyskeratosis. Hydroxychloroquine was added. By 6.5 y.o., nephrolithiasis appeared. Autoimmune markers (ANA, anti-dsDNA, ANCA) were negative. By 8 y.o., respiratory symptoms worsened, and pulmonary hypertension developed. Brain MRI showed no changes. At 11 y.o., synovitis appeared; by 12 y.o., papular rashes recurred on the face and over joints (repeated biopsy was performed to exclude sarcoidosis: lichenification, acanthosis, dermal edema, basal vacuolization, collagen disorganization). Methotrexate was prescribed. At 13 y.o., severe growth retardation was noted (19 kg, 117 cm). Due to lung fibrosis progression, methotrexate was replaced with mycophenolate mofetil. Genetic testing (INVITAE, USA) revealed a pathogenic TMEM173 mutation (c.842G>A (p.Arg281Gln)), establishing the SAVI diagnosis. JAK inhibitors initiated, with CS tapering. Among 4 siblings, one asymptomatic sibling was identified as a carrier.
Conclusion: This case demonstrates an atypical, slowly progressive SAVI course, without overt vasculitis. Systemic inflammation was evident on biopsy but nonspecific. Lack of physician awareness and limited genetic testing access led to an 8-year diagnostic delay. Incorporating early genetic testing into pediatric ILD protocols, per the 2023 guidelines on the diagnostic workup of childhood ILD, is crucial. Consent to published had been obtained.
Disclosure
None declared

P058

Colchicine efficacy on oral ulcers caused by behçet's spectrum disorders including idiopathic recurrent aphthous stomatitis, PFAPA, and behçet's disease

Z. Aydin, F. Haslak
Pediatric Rheumatology, Istanbul Medeniyet University, Istanbul, Türkiye
Correspondence: Z. Aydin
Pediatric Rheumatology, **23(2):** P058

Introduction: Recurrent aphthous stomatitis (RAS) is a common oral mucosal disorder characterized by painful ulcers in pediatric patients. Significant genetic commonalities among RAS, periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome (PFAPA), and Behçet's disease (BD) suggest shared underlying pathophysiological mechanisms. Consequently, these disorders have been proposed to constitute a unified clinical spectrum termed "Behçet Spectrum Disorders (BSD)."
Objectives: Given the scarcity of objective data regarding the efficacy of colchicine in pediatric BSD-related RAS, this study aimed to evaluate clinical and laboratory changes in patients before and after colchicine treatment.
Methods: In this retrospective study, a total of 317 patients with RAS were evaluated between December 2019 and March 2024. Only patients with complete data were included in the study. Of these, 186 were classified as having BSD-related RAS, while 131 were excluded due to underlying conditions such as micronutrient deficiencies, autoinflammatory diseases, gastrointestinal disorders, chronic infections, immunodeficiencies, or hematologic disorders. The included patients were classified into three subgroups: Behçet's disease -associated RAS (BARAS), idiopathic-RAS (IRAS), and PFAPA-associated RAS (PFARAS). Clinical and laboratory parameters were assessed before and after colchicine treatment.
Results: Among the 186 patients classified as BSD-related RAS (81 males, 105 females), the median age at symptom onset was 5 (0.5–16.5) years. Minor aphthae were the most common ulcer type, observed in 82.8% of patients, while major aphthae were detected in 17.2%. Following colchicine treatment in all patients, the frequency and duration of oral ulcers significantly decreased ($p<0.001$). Both patient-/family-reported and physician-reported visual analog scale scores showed a substantial decrease after treatment ($p<0.001$). Laboratory assessments conducted during the asymptomatic period before and after colchicine therapy revealed a significant reduction in erythrocyte sedimentation rate and leukocyte count ($p<0.001$, $p=0.018$, respectively).
Conclusion: These findings demonstrate a substantial reduction in both clinical symptoms and laboratory markers following colchicine treatment, supporting its effectiveness as a therapeutic option for BSD-related RAS.
Disclosure
None declared

References

1. Koberová R, Merglová V, Radochová V. Recurrent aphthous stomatitis in children: a practical guideline for paediatric practitioners. ACTA MEDICA. 2020;63(4):145-9.
2. Manthiram K, Preite S, Dedeoglu F, Demir S, Ozen S, Edwards KM, et al. Common genetic susceptibility loci link PFAPA syndrome, Behçet's disease, and recurrent aphthous stomatitis. Proceedings of the National Academy of Sciences. 2020;117(25):14405-11.
3. Sánchez J, Conejero C, Conejero R. Recurrent aphthous stomatitis. Actas Dermo-Sifiliográficas (English Edition). 2020;111(6):471-80.
4. Scully C, Hodgson T, Lachmann H. Auto-inflammatory syndromes and oral health. Oral diseases. 2008;14(8):690-9.

P059

X-linked lymphoproliferative syndrome type 1 presenting with recurrent fever and unilateral inflammatory neck mass

A. Barmpakou[1], Z. Khan[1], H. Schmid[2], P. Torpiano[3], A. Bamford[2], O. Kul Cinar[1]
[1]Paediatric Rheumatology, [2]Paediatric Infectious Diseases, [3]Paediatric Immunology, Great Ormond Street Hospital, London, United Kingdom
Correspondence: A. Barmpakou
Pediatric Rheumatology, **23(2):** P059

Introduction: X-linked lymphoproliferative type1 (XLP1) disorder is a rare primary immunodeficiency caused by a mutation in the SH2D1A gene that results in B-cell lymphoproliferation and manifests with

various phenotypes including hemophagocytic lymphohistiocytosis, lymphomas and dysgammaglobulinemias.
Objectives: To present a case report of X-linked lymphoproliferative type1(XLP1) disorder.
Methods: 5 year-old boy's case with X-linked lymphoproliferative type1(XLP1) disorder.
Results: A 5-year-old boy presented with unilateral inflammatory neck mass and recurrent fever. Infective screen including EBV serology was negative. Ultrasound neck showed left posterior cervical lymphadenopathy. A prolonged course of antibiotics were prescribed with no response and progressive enlargement of the lymphadenopathy and continuation of fever. Patient had a 13-year-old half brother who had been treated with Burkitt's lymphoma at the age of 6.
Excisional lymph node biopsy showed necrotising lymphadenopathy and histopathology was suggestive of autoimmune/lymphoproliferative conditions without evidence of malignancy.
Rheumatology referral was done; however,autoimmune screening was negative.
The patient remained symptomatic in the next 6 months with recurrent fevers and progressive enlargement of the left cervical mass. CT head, neck and sinuses showed progression with erosive inflammatory mass causing erosion of the left mastoid and petrous temporal bone.
Head and neck MRI showed non-occlusive left sigmoid thrombophlebitis and left petrous segment internal carotid artery narrowing secondary to inflammatory changes in the temporal bone. PET scan showed increased uptake in the lateral cervical lymph nodes.
Further immunology investigations revealed low SLAM-Associated Protein (SAP) expression. Genetic testing showed that he was hemizygous for the SH2D1A c.137+2T>C pathogenic variant that confirmed XLP1. Repeat biopsies (skull, left cervical lymph node, left ear canal, left mastoid bone) confirmed Burkitt's lymphoma and the patient is further managed by haematology team.
Conclusion: XLP1 immunodeficiency can present with different clinical phenotypes and needs to be included in the differential diagnosis of patients with unexplained prolonged/recurrent fevers and necrotising lymphadenopathy with a negative autoimmune screening. Consent to published had been obtained.
Disclosure
None declared

P060

Predictors of invasive mycoses in patients with immune-mediated inflammatory diseases requiring intensive care

I. Avrusin[1], N. Abramova[2], A. Milevich[1], O. Kozlova[3], Y. Aleksandrovich[2], M. Kostik[1]
[1]Department of Hospital Pediatrics, [2]Department of Anesthesiology, Resuscitation and Emergency Pediatrics, Saint Petersburg State Pediatric Medical University, [3]Department of Clinical Mycology, North- Western State Medical University Named after I.I. Mechnikov, Saint Petersburg, Russian Federation
Correspondence: I. Avrusin
Pediatric Rheumatology, **23(2):** P060

Introduction: Invasive mycosis is one of the serious complications in patients with immune-mediated inflammatory diseases receiving intensive care. Identification of predictors of their development can optimize diagnostics and timely prescription of appropriate treatment, which can reduce mortality and improve the prognosis in this group of patients.
Objectives: To identify independent clinical and laboratory predictors of invasive mycosis in patients with immune-mediated inflammatory diseases requiring intensive care.
Methods: A retrospective analysis of data from 51 patients with systemic immune-mediated inflammatory diseases (systemic rheumatic diseases and generalized infections) hospitalized in the intensive care unit (ICU) was performed. Of these, 6 patients (11.8%) had invasive mycosis. Data from the first 7 days of stay in the ICU were taken into account. For statistical processing, the STATISTICA statistical software package, version 10.0 (StatSoft Inc., USA) was used.
Results: Invasive mycosis developed in 6 (11.8%) patients with systemic rheumatic diseases (SRD): 4 with systemic lupus erythematosus (SLE), 1 with systemic juvenile idiopathic arthritis, and 1 with systemic vasculitis. At the same time, invasive mycosis was not recorded in any patient with sepsis (p=0.022).
The main types of mycoses were invasive aspergillosis (5 cases) and pneumocystis pneumonia (1 case), one patient was diagnosed with a combination of aspergillosis and invasive candidiasis.
Patients who developed invasive mycosis were older (16 years 4 months vs. 8 years 11 months, p=0.003), more often received immunosuppressive therapy (66.7% vs. 22.5%), longer stayed in ICU (51 days vs. 6 days, p=0.007), and had much higher level of mortality (67% vs. 9%, p=0.014).
During the dynamic observation of patients condition in the ICU, the following key changes were identified: hypoalbuminemia, hypercreatininemia, arterial hypotension, impaired consciousness (less than 8 points according to the Glasgow scale) and worsening organ dysfunction (>6 points according to the pSOFA scale).
These data show an increase in complications in the group of patients with invasive mycoses.
When analyzing the risk factors associated with the development of invasive mycoses, the following independent predictors were identified:Older age.
1. Systemic rheumatic disease.
2. Intensive immunosuppressive therapy.
3. Long time before admission to the ICU.
4. Long stay in the ICU (more than two weeks).

Conclusion: Invasive mycoses are a significant problem in patients with immune-mediated inflammatory diseases hospitalized in ICU. Clinical and laboratory predictors of their development were identified, and can be used to optimize the diagnosis, prevention and treatment of these complications, what can reduce mortality and increase the effectiveness of therapy.
Disclosure
None declared

P061

Infection associated hyperinflammation: retrospective observational data from a tertiary referal centre in Eastern India

J. N. Bathia, R. Singh, A. Nandi, C. R. P. Goud, P. Pal
Pediatric Rheumatology, Institute of Child Health, Kolkata, India
Correspondence: J. N. Bathia
Pediatric Rheumatology, **23(2):** P061

Introduction: Hyperinflammatory states are a group similar yet distinct conditions occurring due to various etiologies. All lead to an increase in proinflammatory cytokines. Macrophage Activation Syndrome; primary hemophagocytic lymphohistiocytosis (HLH) have distinct diagnostic criteria.
No clearcut guideline defines infection associated secondary HLH, hence HLH 2004 criteria are often used in proxy. Other terminologies used under the umbrella of hyperinflammation include cytokine release syndrome (CRS), cytokine storm syndrome (CSS) and cytokine shock syndrome.
Infection as a cause of hyperinflammation is now being increasingly recognized. It has been seen to occur in association with various pathogens like *Salmonella typhi,* scrub typhus, dengue fever, Ebstein Barr virus, adenovirus, influenza etc. Notably, infection associated hypercytokinemia became more widely known and found acceptance with the general medical fraternity following the recent pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection.
Objectives: The aim of this study is to note the demographic profile, clinical features, laboratory investigations, therapy and outcome of hyperinflammatory state secondary to infections
Methods: It is a retrospective observational study on patients with hyperinflammation due to infections encountered from January,2023 to December,2024
Results: 27 had hyperinflammation of whom 15 patients fulfilled HLH 2004 criteria. 20 were males, 7 were females. Infections noted were: Salmonella typhi (n=8), scrub typhus (n=4), adenovirus (n=3), dengue (n=5), pneumonia with no isolated organism (n=3), Epsteinbarr virus (n=1) (EBV), mycoplasma (n=1), influenza b (n=2) Median age was 72 months. All had fever. Median day of fever at admission: 6 days, at hyperinflammation: 8 days. 17 had encephalopathy, 18 had

hepatomegaly, 16 had splenomegaly, 4 had pleural effusion, 2 had pericardial effusion, 8 had oedema, 7 had ascites, 2 had bleeding manifestations, 1 had pancreatitis. Median investigations were hemoglobin 8.8gm/dl, absolute neutrophil count 2,960/cmm, platelets 66,000/cmm, ferritin 5,799.5ng/ml triglyceride 265mg/dl, alanine transaminase 138.5 U/L, aspartate transaminase 280U/L, albumin 3.1 gm/L, C-reactive protein(CRP) 131 mg/l, 5 had normal CRP. All required dexamethasone, 21 received only short course of dexamethasone (median 5days), 3 were additionally upgraded to methylprednisolone, 3 also required anakinra. 3 very severe dengue patients succumbed rapidly, rest were successfully discharged.
Conclusion: High index of suspicion is required for diagnosing hyperinflammatatory states in early stage. Falling trends in blood counts along with rising ferritin, transaminitis, falling albumin should be looked out for. Criteria for HLH may not be always be fulfilled. CRP also may not rise in all. Early identification and timely initiation of immunosuppresants leads to better outcome.
Disclosure
None declared

P064

Rates of infections in children and adolescents with rheumatic diseases and association with therapies: analysis of german nationwide health insurance data

M. Freudenhammer[1], J. Klotsche[2], N. Grösch[2], F. Milatz[2], M. Hufnagel[1], K. Minden[2,3]
[1]Department of Pediatrics and Adolescent Medicine, University Medical Center Freiburg,, Freiburg, [2]Programme area Epidemiology and Health Services Research, Deutsches Rheumaforschungszentrum, [3]Department of Pediatric Respiratory Medicine, Charité – Universitätsmedizin Berlin, Berlin, Germany
Correspondence: M. Freudenhammer
Pediatric Rheumatology, **23(2):** P064

Introduction: Infections might be more frequent in children and adolescents with rheumatic diseases compared to the general population due to disease-inherent immune dysregulation or required medication, but studies upon this topic are scarce and show conflicting results.
Objectives: Compare rates of selected infections, antibiotic therapies and hospitalization because of infection among children and adolescents with different rheumatic diseases and matched controls using nationwide health insurance data.
Methods: Nationwide data from the statutory BARMER health insurance company for 2018-2023 were analyzed. The study included individuals aged 0-18 years with an ICD-10-GM diagnosis of juvenile idiopathic arthritis (JIA), juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (jDM) or chronic non-bacterial osteomyelitis (CNBO) in at least two quarters. Rates of selected infections, identified by ICD-10-GM codes (all infectious and parasitic diseases, 41 individual infections), hospitalization for infection, and annual antibiotic prescription rates (identified by Anatomical Therapeutical Chemical [ATC] code) were assessed and compared to sex- and age-matched controls. Incidence rates of infections, antimicrobial therapies and hospitalizations were calculated. Poisson regression models were used in order to assess the association of infections with rheumatic diseases as well as treatments.
Results: In the study period 2018-2023, 7796 observation years of patients with JIA, 124 of patients with jSLE, 91 of patients with jDM and 38 of patients with CNBO were recorded. Rates of several infections as well as antimicrobial therapies and hospitalization due to infections were higher in patients with JIA, jSLE and jDM compared to their matched controls. The most common infections were infections of the upper respiratory tract like tonsillopharyngitis (8.8/100 JIA patient years (py) vs. 6.4/100py in matched controls) or acute bronchitis (7.0/100py vs. 5.6/100py). Risk ratio was also increased for some bacterial infections such as pyelonephritis (RR 3,1 [1,7-5,7]) or opportunistic infections like herpes zoster (RR 3,4 [2,1-5,5]). Rates of hospitalization due to infection were 1.7/100py in JIA, 3.2/100py in SLE, 2.2/100py in jDM, and 0/100py in CNBO. Frequency of antibiotic therapies were 15/100py, 19/100py, 25/100py and 13/100py CNBO. In JIA patients, risk of antimicrobial therapy and hospitalization was already increased in patients without treatment (RR 1.2 [1.1-1.3] and RR 2.6 [1.9-3.3]) and was further increased by therapy with glucocorticoids (RR 1.5 [1.2-1.7] and RR 2.4 [1.6-3.8]), while therapy with c- and/or bDMARDs had no effect on hospitalization rates.
Conclusion: Patients with JIA, jSLE and JDM seek medical attention for infections more frequently, are more often hospitalized and receive more antibiotics than age-matched controls. In JIA, this was the case even for patients without GC or DMARDS, however, rates of hospitalized infections were overall low. Particularly GC treatment increases the risk for several infections including antimicrobial treatment and hospitalization significantly.
Disclosure
None declared

P065

Safety, immunogenicity and efficacy of the shingrix vaccine in immunocompromised varicella zoster virus naïve pediatric patients

M. Hamad Saied[1], L. Khoury[1], M. jansen[2], N. el Bied[2], J. van Montfrans[2], B. Vastert[2], S. de Roock[2], J. Swart[2], E. van Nieuwenhove[2], A. van Royen[2]
[1]Carmel medical center, haifa, Israel, [2]Department of Paediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands
Correspondence: M. Hamad Saied
Pediatric Rheumatology, **23(2):** P065

Introduction: Pediatric patients with autoimmune and inflammatory diseases often require immunosuppressive therapy, which increases their susceptibility to infections, including varicella-zoster virus (VZV). While the live attenuated varicella vaccine is contraindicated in most immunocompromised children, the recombinant subunit vaccine, Shingrix, may offer an alternative preventive strategy. However, data on its safety, immunogenicity, and efficacy in pediatric VZV-naïve patients remain limited.
Objectives: This study aimed to assess the safety, immunogenicity, and efficacy of the Shingrix vaccine administered to VZV-naïve pediatric patients receiving immunosuppressive therapy.
Methods: We conducted a monocenter, real-world retrospective cohort study at the Pediatric Rheumatology Department of Wilhelmina Children's Hospital, Netherlands. Ten pediatric patients (median age: 2 years 11 months) on immunosuppressive treatment who received the Shingrix vaccine were identified. Safety was evaluated based on adverse events recorded within three months post-vaccination. Immunogenicity was assessed by measuring VZV IgG antibody levels pre- and post-vaccination. Efficacy was determined by the incidence of breakthrough varicella infections.
Results: Two severe adverse events occurred in a single patient, both at least partially attributable to concurrent viral infections. Nine of ten patients developed positive VZV IgG antibodies post-vaccination. One patient who received only a single dose remained seronegative. Breakthrough varicella infections were observed in two patients, both presenting with mild disease.
Conclusion: Shingrix demonstrated an acceptable safety profile in immunocompromised pediatric patients and elicited a humoral immune response in most cases. The vaccine appeared to provide protection against varicella, although mild breakthrough infections were observed. Prospective studies with larger cohorts and longer follow-ups are warranted to confirm its long-term efficacy and optimal vaccination strategies in this vulnerable population.
Disclosure
None declared

P066

Phenotypic differences of t helper subpopulations in patients with inflammatory diseases as a guide for personalized therapy

J. Schlecht[1], J. Klaus[2,3], J. Weiss[3,4], A. Viardot[3,5], E. Tiessen[3,4], V. Hall[3,4], A. Rasche[3], E.-M. Jacobsen[1], A. Janda[1]
[1]Department of Pediatric and Adolescent Medicine, [2]Department of Gastroenterology, [3]Center for Personalized Medicine, [4]Department of Dermatology, [5]Department of Rheumatology, University Ulm, Ulm, Germany
Correspondence: A. Janda
Pediatric Rheumatology, **23(2):** P066

Introduction: There is currently no standardized approach for selecting the most suitable biologic disease-modifying antirheumatic drugs (bDMARDs) for Crohn's disease (CD), ulcerative colitis (UC), or psoriatic arthritis (PsA). Immunophenotyping of peripheral T-lymphocytes holds promise for enabling personalized therapy and systematic treatment monitoring.
Objectives: Here, we present preliminary data from a single center participating in a multicentric project at the Centers for Personalized Medicine (Inflammation) in Baden-Württemberg.
Methods: We analyzed activated Th1 and Th17 cells via flow cytometry in 29 CD, 26 UC, and 38 PsA patients at baseline (t0), 3 months (t1), 6 months (t2), and 12 months (t3) after initiating bDMARD therapy. Disease activity was assessed using clinical scores. Patients were classified into four immunophenotypes[$]: Th1-dominant (>2.2% Th1, <0.6% Th17), Th17-dominant (<2.2% Th1, >0.6% Th17), Th1/Th17-high (>2.2% Th1, >0.6% Th17), and Th1/Th17-low (<2.2% Th1, <0.6% Th17). Cut-offs were based on 50 healthy controls.
Results: bDMARD therapy reduced activated Th1 and Th17 cells, with a more pronounced decline in Th1. At t0, Th17 levels were significantly elevated across all diseases. No correlation was found between disease activity and cell population changes. A quarter of patients fell into a dominant immunophenotype, but no associations were observed between bDMARD type, immune changes, and disease activity.
Conclusion: The small sample size limits conclusions. However, the reduction in activated Th1 and Th17 cells and elevated Th17 levels at t2 suggest immunophenotyping could aid personalized therapy and monitoring. A pediatric study is underway to explore this further in younger age group.
Disclosure
None declared

References

1. Miyagawa, I., S. Nakayamada, K. Nakano, S. Kubo, S. Iwata, Y. Miyazaki, M. Yoshikawa, H. Yoshinari and Y. Tanaka (2019). "Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in psoriatic arthritis." Rheumatology 58(2): 336-344

P067

Is eosinophilia an underrecognized feature in pediatric rheumatology?

A. Doğru, B. Baser Taskin, S. D. Arik, N. Aktay Ayaz
Pediatric Rheumatology, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye
Correspondence: S. D. Arik
Pediatric Rheumatology, **23(2):** P067

Introduction: Eosinophilia is typically associated with allergic conditions and parasitic infections; however, its significance in autoimmune and autoinflammatory diseases remains poorly understood. Pediatric rheumatic disorders may exhibit eosinophilic responses due to underlying immune dysregulation, but data on its prevalence and clinical relevance in this population are limited.
Objectives: To determine the frequency, severity, and clinical context of eosinophilia in pediatric patients with rheumatic diseases, and to explore potential associations with disease activity, comorbidities, and treatment.
Methods: Pediatric patients with eosinophilia (≥500/μL) were retrospectively identified from electronic medical records at a tertiary pediatric rheumatology center. Eosinophilia was classified as mild (500–999/μL), moderate (1000–1499/μL), or severe (≥1500/μL) based on absolute eosinophil counts.
Results: Eosinophilia was observed in 106 of 1,810 screened patients (44 females, 62 males). Diagnoses included recurrent fever syndromes (n=60), JIA (n=17), CNO (n=5), vasculitis (n=13, including 1 EGPA), SLE (n=2), JDM (n=3), MIS-C (n=2), scleroderma (n=1), Sjögren's syndrome (n=1), IgG4-related disease (n=1), ADA2 deficiency (n=1), and sarcoidosis (n=2). MEFV mutations were detected in 44 patients (exon 10) and 8 (exon 2). Eosinophilia was noted before diagnosis in 12 patients, at diagnosis in 14, and post-diagnosis in 80. During eosinophilia, 12 patients had concurrent infections, and 39 had active disease. Allergy consultations were performed in 8 patients: 6 had asthma, 2 had seasonal allergic rhinitis. Inflammatory bowel disease was noted in 3 patients (1 ulcerative colitis, 2 Crohn's). The pattern of eosinophilia was single in 46 patients, intermittent in 54, and persistent in 6. Among those with persistent eosinophilia, 2 had FMF, 1 JIA, 1 Behçet's disease, one sarcoidosis, and 1 EGPA; 2 also had asthma. Eosinophilia severity was mild in 76 patients, moderate in 18, and severe in 12. The median peak eosinophil count was 800/μL (500–14,000), and the median eosinophil percentage was 8% (2.9–41.3%). Eosinophil levels were elevated a median of 2 times per patient (1–17 times) (Table 1). At the time of eosinophilia, 88 patients were receiving treatment, including corticosteroids (n = 12). Frequently used medications included colchicine (n=58), methotrexate (n=19), biologics (n=23), and other medications, such as sulfasalazine, mycophenolate mofetil, and symptomatic treatments (Table 2).
Conclusion: Eosinophilia is not uncommon among pediatric patients with rheumatologic diseases and may occur independently of classical allergic triggers. It can present prior to diagnosis, during active disease, or under treatment, suggesting a potential link to immune activation.
Disclosure
None declared

Reference

1. Yilmaz D, Sahin E. All-cause mortality and related factors in patients with varying degrees of peripheral blood eosinophilia. Medicine (Baltimore). 2024 May 31;103(22):e38359. doi: https://doi.org/10.1097/MD.0000000000038359. PMID: 39259127; PMCID: PMC11142823.

P068

Changes in proinflammatory cytokine responses in a patient with a TBK1-truncated mutation

B. S. Demir[1,2], A. Pac Kisaarslan[3], S. Ozdemir Cicek[3], M. Ahmad Houran[1,2], M. Asan[1,4], S. Erdem[1,2], H. Bas[5], B. S. Cetin[6], H. Gumus[7], E. Unal[8], E. W. Hsieh[9], H. Canatan[1,2], A. Eken[1,2,10]
[1]Department of Medical Biology, Erciyes University Faculty of Medicine, [2]GENKOK Genome and Stem Cell Centre, Erciyes University, [3]Department of Pediatric Rheumatology, Erciyes University Faculty of Medicine, [4]Department of Molecular Biology and Genetics, Erciyes University Gevher Nesibe Genome and Stem Cell Institutee, Kayseri, [5]Intergen Genetics and Rare Diseases Diagnosis Center, Ankara, [6]Department of Pediatric Infection, [7]Department of Pediatric Neurology, Erciyes University Faculty of Medicine, [8]Department of Nursery, Hasan Kalyoncu University Faculty of Health Sciences Medical Point Hospital, Kayseri, Türkiye, [9]Department of Immunology and Microbiology, University of Colorado Anschutz Medical Campus Faculty of Medicine, Denver, United States, [10]Department of Immunology and Microbiology, University of Colorado Anschutz Medical Campus Faculty of Medicine, Denver, Türkiye
Correspondence: B. S. Demir
Pediatric Rheumatology, **23(2):** P068

Introduction: The protein TBK1 functions as a main pathway mediator of canonical NFκB signaling which activates antiviral responses and Type I Interferons. Within the AKT pathway TBK1 serves as an essential factor for cell survival and proliferation. Research reveals that TBK1 destroys autophagy events in cancer cells simultaneously with its role in inflammatory processes. T cell-specific autoimmunity develops along with altered cellular homeostasis when TBK1 demonstrates elevated activities.
Objectives: The aim of our study was to investigate inflammatory responses in a patient with chronic polyarthritis who developed necrotizing encephalitis with a TBK1 truncating mutation in exons 4 and 5.
Methods: Peripheral Blood Mononuclear Cells (PBMCs) were isolated from blood of the Juvenile Idiopathic Arthritis (JIA) patient with exon4/5 deletion together with healthy controls. Upon stimulation with Poly I:C (10 μg/mL for 10 hours and anti-CD3/CD28 (10 μg/mL for 72 hours), activation status of cells was measured by using phospho-flow staining to evaluate STAT1 and AKT and NFκB. Via real-time qPCR, levels of *STING* and *cGAS* and Type I interferons (IFN-α and IFN-β) as well as proinflammatory cytokines were measured. LEGENDplex™ Human Inflammation Panel 1 was used to measure the contents of the supernatant solutions.
Results: The Truncated-*TBK1* defect has affected cell viability following α-CD3/CD28 activation. Additionally, IL-6 and IL-18 levels

have increased with stimulation. Furthermore, a decrease has been observed in the levels of IFN-γ, MCP-1, and IL-12p70, which are critical in anti-viral immunity.
Conclusion: The patients affected by TBK-1 deficiency mount impaired anti viral responses. The current novel TBK1 variant appears to explain elevated IL-6/IL-18 levels and biologics blocking IL-6 and IL-18 may be considered for the treatment for this and patients with similar TBK1 variants.
Disclosure
None declared

References
1. J. Taft et al., "Human TBK1 deficiency leads to autoinflammation driven by TNF-induced cell death," Cell, vol. 184, no. 17, pp. 4447-4463.e20, Aug. 2021, doi: https://doi.org/10.1016/j.cell.2021.07.026.
2. N. D. Sun et al., "TBK1 and IKKε protect target cells from IFNγ-mediated T cell killing via an inflammatory apoptotic mechanism," Aug. 08, 2024. doi: https://doi.org/10.1101/2024.08.06.606693.
3. B. R. tenOever, S.-L. Ng, M. A. Chua, S. M. McWhirter, A. García-Sastre, and T. Maniatis, "Multiple Functions of the IKK-Related Kinase IKKε in Interferon-Mediated Antiviral Immunity," Science (1979), vol. 315, no. 5816, pp. 1274–1278, Mar. 2007, doi: https://doi.org/10.1126/science.1136567.

P069
Gene expression signatures in patients with il-1β activation disorders
D. Suri, V. Joshi, P. Suku, J. Ahmed, S. Sharma, M. Dhaliwal, R. Pilania, V. Pandiarajan , A. Rawat, S. Singh
Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India
Correspondence: D. Suri
Pediatric Rheumatology, **23(2):** P069

Introduction: Patients with inflammasomopathies show specific gene expression which may aid in diagnosis, assessing treatment response and help differentiate IL-1β driven diseases from other inflammatory or autoimmune conditions.
Objectives: To study the gene expression profiles of inflammasomes (NLRP3, AIM2, NLRC4, NLRP12 and CASPASE-1) in patients with IL-1β activation disorder, including those with NLRP3-related disorders and MVK deficiency, and to compare these profiles with healthy controls.
Methods: Patients with NLRP3-related disorders, MVK deficiency, and healthy controls were enrolled in this study. mRNA expression levels of inflammasomes (NLRP3, AIM2, NLRC4, NLRP12 and CASPASE-1) were analyzed using SyBr green chemistry, and expression levels were quantified using the delta Ct method with GAPDH as a housekeeping gene. Relative gene expression was calculated as fold change compared to healthy controls.
Results: Four patients with pathogenic variants in the *NLRP3* gene, three patients with Hyper IgD Syndrome (HIDS), and ten healthy controls (n = 10) were enrolled in the study. Of the 4 patients with NLRP3 variants, 3 exhibited increased NLRP3 gene expression, suggesting a gain-of-function mechanism. In contrast, only 1 of the 3 patients with HIDS showed elevated NLRP3 expression. AIM2 gene expression was variable in both patient groups, whereas NLRP12 expression was decreased in 3 patients with NLRP3-related disorders.Notably, 2 patients with HIDS demonstrated elevated NLRC4 gene expression (fold changes: 377.95 and 15.49), a finding not observed in the NLRP3-related group.
Conclusion: These results suggest that while NLRP3-related disorders primarily involve upregulation of NLRP3, MVK deficiency is associated with broader activation of the inflammasome pathway, underscoring distinct molecular mechanisms underlying the two conditions. It highlights distinct gene expression profiles of inflammasomes in patients with IL-1β activation disorder which could serve as a potential tool for distinguishing it from other genetic etiologies. Further validation with larger sample size are needed to validate these findings and develop gene expression-based diagnostic assays for inflammasomopathies
Trial registration identifying number: Not applicable
Disclosure
None declared

References
1. Alehashemi S, Goldbach-Mansky R. Human Autoinflammatory Diseases Mediated byNLR P3-, Pyrin-, NLRP1-, and NLRC4-Inflammasome Dysregulation Updates on Diagnosis,Treatment, and the Respective Roles of IL-1 and IL-18. Front Immunol. 2020 Aug 25;11:1840.
2. De Pieri C, Vuch J, De Martino E, Bianco AM, Ronfani L, Athanasakis E, et al.Genetic profiling of autoinflammatory disorders in patients with periodic fever: a prospective study. Pediatr Rheumatol. 2015 Dec;13(1):11.

P070
Genotype targeted management for children with monogenic autoimmune phenotype
D. B. Pandya, on behalf of Dr Nitin Trivedi, Dr Nayan Kalawadia, Dr Hitesh Bhambhani, Dr Ankur Kothari, Dr Manjari Aggarwal, Dr Amit Chitaliya, Dr Vaibhav Shah, Dr Vinod Bhadukia, Dr Sameer Dhami, Dr Rushika Gadani, Dr Nilam Thacker, Dr Manish Mehta, Dr Vishak Kachhy
Pediatric Rheumatology, Dev Pediatric Rheumatology & Immunology Center, Ahmedabad, India
Correspondence: D. B. Pandya
Pediatric Rheumatology, **23(2):** P070

Introduction: Inborn errors of immunity (IEI) present clinically as increased susceptibility to infections, autoimmunity, autoinflammation, allergy, bone marrow failure, and/or malignancy.
Objectives: To study autoimmune manifestations and genotype-targeted management options for IEI children with autoimmune phenotype.
Methods: We have gathered a data of 14 children with a diagnosis of IEI with predominant autoimmune diseases, seen by us between August 2023 to April 2025. We have analysed their phenotype, immunotype, genotype and tried to see the response of genotype-targeted treatment options in some of the refractory autoimmune manifestations.
Results: Mean age of onset was 4.2 years. Male-female ratio was 2.5:1. Average delay between the onset of symptoms and the genetic diagnosis was 4.3 years. The commonest autoimmune manifestations were Lupus, Arthritis, Cytopenia/s, Enteropathy, Vasculitis, Interstitial Lung Disease and Endocrinopathy. Uncommon manifestations included granulomatous inflammation & primary sclerosing cholangitis. Few patients presented with overlapping phenotype. Immunoglobulin levels were normal in 4 patients, low in 3 patients, high in 2 patients and not available in 5 patients. Three patients were having low B cells and/or T cells. Out of 14 children, 4 were in clinical remission off glucocorticoids(GC) while rest of the 10 patients were either remained refractory to conventional agents or partially responded or having flare or were not able to wean GC prior to a genotype. Genetic tests revealed pathogenic variants in 8 patients which included LRBA,RAG1,CTLA4,RELA,C1Q,COPA,STXBP2, WAS and one patient had a likely pathogenic variant in RUNX1. Rest of the 5 patients had VUS in PSMB8, FCGR2B, DOC8, ADAMS17 & MMP2, but except for MMP2, each VUS variant was matching with their respective phenotype. Four children (RELA,STXBP2,FCGR2B, ADAMS17) were in clinical remission off GC prior to a genotype, did not require any change but we have chosen the best possible agent in 2 children (TNFi for RELA & ADAMS17) in case of any flare. Out of 10 non-responding patients, two (LRBA & CTLA4 - Abatacept) could not afford the medications, one was lost on follow up (DOC8),one died (WAS) and one was having genotype-phenotype mismatch (MMP2). Five patients (Sirolimus-RAG1, FFP-C1Q, Tofacitinib-COPA, RUNX1, & PSMB8) were given genotype-targeted treatments. Three patients (COPA,RUNX1 & PSMB8) achieved clinical remission off GC and 2 patients showed significant improvement.
Conclusion: We should always keep a high index of suspicion of IEI when there is an early-age of onset (< 5 years), poly-autoimmunity, refractory autoimmune manifestations & overlaping features of autoinflammation, allergy, lympho-proliferation and susceptibility to infections/malignancy. Genotype may guide us to choose the best possible agent which might work better for some refratory autoimmune manifestations until the definitive therapy becomes available.
Disclosure
None declared

P071

IFIH1 gene mutation as a cause of severe hyperinflammation – case report

D. Gensor[1], Z. Bystricanova[2], E. Fronkova[3], M. Jesenak[1,4,5] on behalf of -
[1]Department of Pediatrics and Adolescent Medicine, Jessenius Faculty of Medicine of Comenius University Bratislava,, University Hospital Martin, Martin, [2]Department of Pediatrics and Adolescent Medicine, Children University Hospital Banska Bystrica, Banska Bystrica, Slovakia, [3]Department of Molecular Genetics,, Childhood Leukaemia Investigation Prague, Praque, Czech Republic, [4]3. Department of Clinical Immunology and Allergology, [5]2. Department of Pneumology and Phthisiology,, University Hospital Martin, Martin, Slovakia
Correspondence: D. Gensor
Pediatric Rheumatology, **23(2):** P071

Introduction: Aicardi Goutieres Syndrome (AGS) belongs to the spectrum of rare primary immunodeficiencies, i.e. congenital immune disorders, which, depending on the type of genetic mutation, represent a heterogeneous group of diseases manifested by involvement of the CNS, immune system and skin. Aicardi-Goutieres syndrome-7 (AGS7) is an autosomal dominant autoinflammatory disease, characterized by severe neurological damage. The disease manifests itself in early childhood with delayed psychomotor development, axial hypotonia and spasticity. Typical is the MRI finding of calcifications present in the area of the basal ganglia, cerebral atrophy and white matter abnormalities.
Objectives: CASE REPORT
The authors present a case report of a 7-month-old infant, initially hospitalized for severe intracerebral haemorrhage during SARS-CoV-2 infection, followed by the development of a hyperinflammatory state of Multisystem inflammatory syndrome in children (MIS-C). Despite combined immunosuppressive therapy, the patient continues to have a febrile condition accompanied by worsening neurological findings in terms of quadruparesis progression, bulbar syndrome and dystonias.
Methods: The dominant clinical and laboratory finding is hyperinflammation (expressed by the elevation of CRP, serum amyloid A, ferritin…), which after excluding infectious, metabolic and paraneoplastic causes, leads to the indication of genetic testing focused on autoinflammatory diseases with confirmation of the IFIH1 gene mutation: NM_022168.4 c.1806A>Tp.E602D. Mutation in this gene is typical for Aicardi-Goutieres syndrome type 7 (AGS7).
Results: Based on the international EULAR/ACR recommendations for the treatment of diseases from the type I interferonopathy spectrum, the patient was treated with a non-selective Janus kinase inhibitor (JAKi) – baricitinib (dose 4 mg/kg/per day), with a significant effect especially on the neurological condition and thus improving the patient's quality of life.
Conclusion: Aicardi-Goutieres syndrome (AGS) belongs to the spectrum of rare primary immunodeficiencies. In the context of differential diagnosis, it is important to exclude other causes of hyperinflammation. Genetic testing is essential for the final diagnosis.
Despite the severity of the disease, early confirmation of the diagnosis and targeted treatment leads to an improvement in neurological symptomatology and the management of often fatal hyperinflammation. Consent to published had been obtained.
Keywords: hyperinflammation, Aicardi- Goutieres syndrome, baricitinib
Disclosure
None declared

P072

Combination of selective iga deficiency and rheumatic diseases in children: single center cohort study

M. Kaleda, I. Nikishina, E. Salyanova
Pediatrics, V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P072

Introduction: Selective immunoglobulin A deficiency (sIgAD) is one of the most common primary immunodeficiency. It has previously been suggested to be associated with a variety of concomitant autoimmune diseases.
Objectives: to investigate combination of sIgAD and rheumatic diseases in children based on the data from the single pediatric rheumatological center
Methods: Patients were admitted at the Pediatric rheumatology Department during 2024 year. Serum immunoglobulin concentrations were determined by nephelometry method. The definition developed by the Pan American Group on Immunodeficiency and the European Society for Immunodeficiency was used, which defines the sIgAD as the level of <0.07 g/L with normal IgM and IgG levels in individuals ≥4 years of age.
Results: Immunoglobulin A deficiency was detected in 124 (7.8%) of 1617 patients. 47 of them were identified as patients with sIgAD (3%), 64 had secondary hypogammaglobulinemia, 13 – combined immunodeficiency. The median level of IgA in patients with sIgAD consists 0.037 [0.026; 0.046] g/L, in patients with secondary hypogammaglobulinemia – 0.059 [0.05;0.065] g/L (p=0.043). The ratio boys:girls in patients with sIgAD was 1:1.5 (in patients with secondary hypogammaglobulinemia – 1:2.8). The median age at the time of assessment was 8.9 [5.85;13.35] y.o. The median age at the onset of RD – 3.8 [2.0; 7.0] y.o. 42 patients had juvenile idiopathic arthritis (JIA) (29 – polyarthritis, 11 – oligoarthritis, 2 – systemic JIA), 2 – systemic lupus erythematosus, 2 – systemic sclerosis, 1 – juvenile dermatomyositis. 6 patients with JIA had uveitis. ANA were found in 46.8% of patients. 5 patients had concomitant diseases: 1 - idiopathic urticaria, 2 - glomerulonephritis, 1 - Gilbert's syndrome, 1 - hypothyroidism. 2 girls with sIgAD and JIA were monozygotic twins. 19 patients (40.4%) had family history of autoimmune diseases, 9 from them had relatives with psoriasis. Recurrent infections were recorded in 3 patients only (6.4%).
Conclusion: The prevalence of sIgAD in our cohort of children with rheumatic diseases is relatively high (3.0%). There are more boys among patients with sIgAD than with secondary immunodeficiency. Patients with sIgAD have an earlier age of onset and lower level of immunoglobulin A than those with secondary immunodeficiency. Patients with sIgAD often have family history of autoimmune diseases. The frequency of infections in our cohort of patients with sIgAD turned out to be quite low.
Disclosure
None declared

P073

Expanding the spectrum of aire-related autoimmunity: a case of primary sjögren's syndrome in early childhood

J. B. Lima[1], B. P. Correia[2,3], M. Rodrigues[4], A. Martins[5], R. Campanilho-Marques[2,3], F. O. Ramos[2,3]
[1]Paediatrics Department, Unidade Local de Saúde de Santo António (ULSSA), Porto, [2]Paediatric Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde de Santa Maria (ULSSM), [3]Faculdade de Medicina, Universidade de Lisboa, [4]Department of Medical Genetics, [5]Paediatri Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde de Santa Maria (ULSSM), Lisboa, Portugal
Correspondence: J. B. Lima
Pediatric Rheumatology, **23(2):** P073

Introduction: Sjögren's syndrome (SS) is a chronic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, though its molecular pathogenesis remains unclear. The autoimmune regulator gene (AIRE) is crucial for central immune tolerance, and its dysfunction predisposes to autoimmunity, including SS. In AIRE-deficient mice, early lacrimal gland inflammation and signalling changes mimic SS, but in humans, this association is rarely reported.
Objectives: We describe a paediatric case of a primary SS most likely due to a heterozygous variant in AIRE gene.
Methods: Case-report
Results: We report a 4-year-old girl with no relevant past medical history and a family history of systemic lupus erythematosus (maternal grandmother), referred for bilateral submandibular swelling persisting for over a year, associated with intermittent parotid gland enlargement and episodes of unexplained high fever (~39ºC, 1–2 days/month). She also reported xerostomia, with no ocular symptoms. Physical examination revealed elastic, non-tender submandibular

swellings (~3.5 cm). Laboratory workup was mostly unremarkable, except for a positive ANA (1:320) and elevated serum amyloid A (max 37 mg/L). ENA panel, anti-dsDNA, and rheumatoid factor were negative. IgG4 and ACE levels were normal. Cryoglobulinemia, monoclonal component (free light chain ratio), hepatitis C and HIV were excluded. Ultrasound revealed enlarged parotid and submandibular glands with heterogeneous echotexture and poorly defined hypoechoic areas, suggestive of chronic inflammation. Normal ophthalmologic evaluation. Submandibular biopsy showed dense B- and T-cell infiltration forming seven lymphoid aggregates (>50 cells) with germinal centres; focus score was 2.1, compatible with SS. No evidence of IgG4-related disease or lymphoma. Given the early onset and systemic features, genetic testing was performed and identified a heterozygous variant of uncertain significance (VUS) in the AIRE gene: c.816G>T (p.Arg272Ser), which has not been previously described in the literature. Pathogenic AIRE mutations have been reported in bothautosomal dominant and recessive forms of autoimmune polyendocrine syndrome type 1 (APS-1). Cytokine profiling and familial segregation studies are pending. Treatment with hydroxychloroquine was initiated, with clinical improvement.

Conclusion: This case highlights a rare paediatric primary SS likely associated with a previously undescribed AIRE gene variant, pending further clarification via familial segregation studies. It supports the hypothesis that AIRE dysfunction may contribute to early-onset autoimmunity beyond classical APS-1. Findings from AIRE-deficient mouse models reinforce a potential pathophysiological link with salivary gland inflammation. Further studies are needed to clarify the role of AIRE variants in isolated autoimmune phenotypes such as SS. Consent to published had been obtained.

Disclosure

None declared

P075

Beyond the gut: is serum calprotectin clinically useful in pediatric inflammatory diseases?

M. Jelusic[1], M. Sestan[1], D. Grguric[1], A. Loncar Vrancic[2], D. Rogic[2], M. Frkovic[1]

[1]University of Zagreb, School of Medicine, University Hospital Centre Zagreb, Department of Paediatrics, [2]Department of Laboratory Diagnostics, University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, Croatia

Correspondence: M. Sestan

Pediatric Rheumatology, **23(2):** P075

Introduction: Calprotectin is a proinflammatory protein primarily secreted by neutrophils, serving as a sensitive marker of inflammation, especially in conditions involving neutrophil activation. While fecal calprotectin is widely used in gastrointestinal diagnostics, serum calprotectin is emerging as a marker for systemic inflammatory diseases.

Objectives: This study aimed to compare serum calprotectin levels in children with systemic juvenile idiopathic arthritis (sJIA), polyarticular juvenile idiopathic arthritis (pJIA), childhood-onset systemic lupus erythematosus (cSLE), IgA vasculitis (IgAV), inflammatory bowel disease (IBD), and IL-1-mediated autoinflammatory diseases (AID) to assess its role as a diagnostic and discriminative marker of inflammation.

Methods: This prospective study included 185 children in seven groups: 31 with sJIA, 62 with pJIA, 18 with cSLE, 33 with IgAV, 15 with IBD, 6 with AID, and 20 healthy controls. Serum calprotectin was measured using a turbidimetric assay (GCAL®, Gentian AS, Norway). Differences between groups were analyzed with the Kruskal-Wallis test ($p<0.05$).

Results: Median serum calprotectin levels (µg/ml) were: sJIA: 2.30 (0.50–110.61), pJIA: 1.19 (0.30–19.27), cSLE: 1.39 (0.31–6.29), IgAV: 3.45 (0.80–18.55), IBD: 1.62 (0.40–5.80), AID: 1.26 (0.56–232.5), and Controls: 1.00 (0.57–1.43). Children with sJIA and IgAV had significantly higher levels than controls ($p<0.001$). Significant differences were also found between sJIA and pJIA ($p=0.002$), pJIA and IgAV ($p<0.001$), cSLE and IgAV ($p=0.005$), and IBD and IgAV ($p=0.02$). Serum calprotectin levels by disease activity: sJIA (active): 9.47 (2.22–110.61) µg/ml vs. remission: 1.08 (0.50–2.06) µg/ml, pJIA (active): 2.5 (0.30–19.27) µg/ml vs. remission: 1.03 (0.40–4.71) µg/ml, cSLE (active): 3.77 (1.00–6.29) µg/ml vs. remission: 1.21 (0.31–3.54) µg/ml, IgAV (active): 5.27 (1.77–18.55) µg/ml vs. remission: 2.81 (0.80–5.34) µg/ml. Active phases of sJIA, pJIA, and cSLE had significantly higher serum calprotectin levels than their respective remission phases. In contrast, no significant difference was found between active and remission phases in IgAV. Active disease patients had higher calprotectin than controls, while remission patients had levels similar to controls, except in IgAV, where calprotectin remained elevated even in clinical remission.

Conclusion: Serum calprotectin is a useful biomarker for diagnosing and monitoring systemic inflammation in pediatric patients. It differentiates between active and remission phases in sJIA, pJIA, and cSLE. In IgAV, calprotectin remains elevated in clinical remission, suggesting residual inflammation. These findings highlight its potential as a diagnostic and monitoring tool in pediatric inflammatory diseases, though further studies are needed for broader clinical use. This work was supported by the Croatian Science Foundation under project number HRZZ-IP-2024-05-6848.

Disclosure

None declared

P076

Predictors of outcome in macrophage activation syndrome: a retrospective study from a tertiary care hospital in India

A. Sheref Mohammed[1], T. Bindal[1], A. Patteri[2], T. Singla[1], R. Lodha[1], A. Datt Upadhyay[3], N. Bagri[1]

[1]PAEDIATRICS, [2]ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, NEW DELHI, India, [3]RESEARCH UNIT, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, NEW DELHI, India

Correspondence: A. Sheref Mohammed

Pediatric Rheumatology, **23(2):** P076

Introduction: Macrophage Activation Syndrome (MAS) is a severe, life-threatening hyperinflammatory condition associated with various rheumatic diseases. Identifying predictors of adverse outcomes is crucial for early risk stratification and timely intervention.

Objectives: This study aims to determine the clinical and laboratory factors associated with mortality in children diagnosed with MAS at a tertiary care hospital in India.

Methods: This retrospective study included children diagnosed with MAS based on PRINTO 2016 criteria, admitted between 2018 and 2024. Patient data were extracted from medical records. The primary outcome was survival at discharge. Predictor variables included demographics like age, gender, underlying illness, duration of symptoms, organ involvement (CNS, myocarditis, ARDS, AKI, shock), laboratory parameters (hemogram, liver enzymes, ferritin, fibrinogen, triglycerides), treatment modality (IVIG/methylprednisolone pulse) and time to initiation. Univariate and multivariate analyses were performed to compare the outcome and predictor variables. Firth's penalized logistic regression was used for multivariate analysis to address small sample size, using the variables gender, duration of illness, clinical foci of infection, ARDS, CNS involvement, platelet count at admission, AST and ALT peak. ROC curve analysis assessed the performance of regression model.

Results: A total of 41 children with 46 episodes of MAS having a median age (IQR) of 11.5 (7,13) years at presentation were included in the study. The most common underlying conditions were systemic-onset JIA (56.1%) and SLE (36.5%). Mortality was 28% in our cohort (n=13). Forty-seven percent of our cohort had a clinical focus of infection simultaneously. Univariate analysis showed presence of shock, AKI, ARDS, myocarditis, longer duration of symptoms and lower levels of AST and ALT enzyme levels were associated with increased risk of mortality with p- value <0.05. Multivariate analysis identified acute respiratory distress syndrome (ARDS) as the strongest predictor of mortality (OR = 3.375, 95% CI : 1.103, 10.33, p = 0.03) while other laboratory markers failed to show any association with mortality. The model couldn't fit other multi organ involvement as they were perfect predictors of mortality. Firth's logistic regression improved model stability, and ROC analysis (AUC = 0.9059) demonstrated excellent predictive capability.

Conclusion: MAS remains a critical pediatric emergency with a high mortality risk. Early recognition and aggressive treatment remains the key for survival. Presence of ARDS and multi organ failure were

associated with increased odds of mortality. Early identification of these might improve the outcome. No reliable laboratory markers for early detection of an impending stormy clinical course could be identified from our cohort. Further prospective studies are warranted to validate these findings and identification of potential biomarkers to optimize risk stratification in pediatric MAS.

Disclosure

None declared

Reference

1. Ravelli A, Minoia F, Davì S, Horne A, Bovis F, Pistorio A, et al. 2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A European League Against Rheumatism/American College of Rheumatology/Pediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis. 2016 Mar;75(3):481–9.

P078

Significance and role of hyperferritinemia screening in pediatric patients

F. Lucioni[1], M. Rossano[1], F. Vianello[1], F. Di Stasio[1], S. Lanni[1], G. Chidini[2], G. Montini[3,4], F. Salvini[5], M. Fumagalli[4,6], M. Aloi[4,7], C. V. Agostoni[1,4], G. Filocamo[1,4], F. S. Minoia[1]

[1]Pediatric Immuno-Rhematology Unit, [2]Pediatric Intensive Care Unit, [3]Pediatric Nephrology and Dyalisis Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, [4]University of Milan, [5]Pediatric Emergency Care Unit, [6]Neonatal Intensive Care Unit, [7]Pediatric Gastroeneterology, Hepatology and Cystic Fibrosis Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Correspondence: F. Lucioni

Pediatric Rheumatology, **23(2):** P078

Introduction: Hyperferritinemia is a key biomarker in the diagnosis of a broad spectrum of life-threatening cytokine storms, including hemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS), and hyperinflammatory conditions, as Still's disease (SD). However, marked ferritin elevation may also be caused by a wide variety of other complex pediatric conditions, which differential is essential in clinical care.

Objectives: To investigate the underlying etiology of markedly elevated ferritin levels in a tertiary-level pediatric center

Methods: Data of patients evaluated in our center from 2020 to 2024 with at least 1 value greater than 1000 ng/ml were retrospectively reviewed. For each episode of hyperferritinemia, the highest value of serum ferritin available was selected and concomitant other laboratory parameters were collected, together with demographic data, diagnosis and outcomes.

Results: We identified 169 episodes of ferritin > 1000 ng/ml, with a median value of 1785 ng/ml (range: 1007-75313 ng/ml). A total of 149 patients were included with a median age of 9.0 years (IQR, 3.0–14.0), 60% males.

Hyperferritinemia was related to inflammatory conditions in 36% of patients (24% HLH/MAS, 12% rheumatologic diseases), infections (25%), hemoglobinopathies (18%), malignancies (1%) and an heterogenous group of other conditions (30%). Among rheumatic patients, most had SD (67%) and multisystem inflammatory syndrome in children (24%), followed by systemic lupus erythematosus, juvenile dermatomyositis and ANCA-associated vasculitis (5%). Interestingly, within the "other" group hyperferritinemia was observed mainly in hemolytic uremic syndromes (HUS) (29%), chronic renal insufficiency (20%) and hepatological diseases (18%), followed by DRESS and myocarditis/pericarditis (6%)

The median ferritin in the MAS/HLH group was significantly higher (3793 ng/ml, IQR 1655-13513) than in the rheumatic group (1700 ng/ml, IQR 1111-3753) and in the other conditions (1491 ng/ml, IQR 1189-2674).

Most episodes (80%) required hospitalization (with a median length of 13.0 days). Intensive care (ICU) admission was required in 27% of cases. Four patients (2%) died (1 EBV-HLH, 2 severe liver insufficiencies and 1 sepsis in HUS), with a median ferritin of 14119 ng/ml (range 1420–51300 ng/ml).

Conclusion: Marked elevated ferritin is a sensitive critical biomarker for the detection of potentially deadly inflammatory conditions such as MAS/HLH. However, a sizable number of patients presented hyperferritinemia in the context of other pediatric disorders, suggesting the need of implementing a diagnostic rule to assist physicians in the early differential of hyperferritinemic conditions.

Disclosure

F. Lucioni: None declared, M. Rossano: None declared, F. Vianello: None declared, F. Di Stasio: None declared, S. Lanni: None declared, G. Chidini: None declared, G. Montini: None declared, F. Salvini: None declared, M. Fumagalli: None declared, M. Aloi: None declared, C. Agostoni: None declared, G. Filocamo: None declared, F. Minoia Consultant with: SOBI/NOVARTIS

P079

D-dimer levels and clinical correlates in macrophage activation syndrome: a retrospective evaluation

K. Ulu[1], B. Sözeri[2]

[1]Pediatric Rheumatology, Sancaktepe Training and Research Hospital, [2]Pediatric Rheumatology, Ümraniye Training and Research Hospital, İstanbul, Türkiye

Correspondence: K. Ulu

Pediatric Rheumatology, **23(2):** P079

Introduction: Macrophage activation syndrome (MAS) is a life-threatening condition characterized by excessive immune activation and hyperinflammation. Key laboratory indicators of MAS include cytopenia, elevated ferritin levels, liver dysfunction, and coagulopathy. D-dimer, a by-product of fibrin breakdown, is often found at elevated levels in MAS patients, indicating systemic inflammation and activation of the coagulation cascade. However, the relationship between D-dimer levels and patterns of specific organ involvement in MAS has not yet been thoroughly investigated.

Objectives: This study aims to assess the correlation between D-dimer concentrations and organ involvement in MAS, as well as their association with other laboratory parameters that indicate disease severity.

Methods: This is a retrospective study conducted at a single center.

Results: The study involved 92 patients with MAS, comprising 41 with systemic juvenile idiopathic arthritis (sJIA) and 51 with multisystem inflammatory syndrome in children (MIS-C). Among the participants, 52 were female and 40 were male, with a mean age at diagnosis of 99.1 ± 64.4 months. The median duration of fever was 7 (4-14) days. The mean D-dimer level was measured at 3,307 ± 1,269 ng/mL. Among the patients in our cohort, rash was observed in 60 patients (65.2%), lymphadenopathy in 28 (30.4%), hepatomegaly in 25 (27.2%), splenomegaly in 21 (22.8%), and cardiac findings in 18 patients (19.6%). Significant correlations were identified between D-dimer levels and AST (Rho = 0.268), LDH (Rho = 0.306), and ferritin (Rho = 0.332) levels. D-dimer levels of 3650 or higher showed 72% sensitivity and 68% specificity for hepatomegaly (AUC: 0.690, p = 0.028). A weak but statistically significant regression relationship was observed between D-dimer levels and cardiac findings ($\beta = 0.18$, $R^2 = 0.04$, $p = 0.041$). Steroids were used in 64.1% of the patients, and anakinra in 59.8%. A total of 21 patients (22.8%) required inotropic support, and mortality was observed in 3 cases (3.3%).

Conclusion: Our findings suggest that D-dimer levels are moderately correlated with key indicators of disease severity in MAS, including AST, LDH, and ferritin. Additionally, elevated D-dimer levels may serve as a potential marker for hepatomegaly and cardiac involvement. These results highlight the utility of D-dimer as a supportive biomarker in the clinical assessment of MAS.

Disclosure

None declared

References

1. Bounds EJ, Kok SJ. D Dimer. 2023 Aug 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 28613718.
2. Ravelli A, Grom AA, Behrens EM, Cron RQ. Macrophage activation syndrome as part of systemic juvenile idiopathic arthritis: diagnosis, genetics, pathophysiology and treatment. Genes Immun. 2012 Jun;13(4):289-98. doi: https://doi.org/10.1038/gene.2012.3.

P080

Clinical and laboratory indicators for improvement and tapering of treatment in macrophage activation syndrome associated with systemic juvenile idiopathic arthritis: a multicenter retrospective observational study

K. Nishimura[1], M. Mizuta[2], S. Hattori[1], A. Ohara[1], H. Irabu[3], Y. Hayashi[3], Y. Aida[2], M. Shimizu[4], S. Kawabe[4], K. Akamine[5], U. Kaneko[6], T. Ebato[7], Y. Sugita[8], K. Hashimoto[9], N. Itoh[10], R. Yasuoka[11], H. Wakiguchi[12,13], J. Yasumura[14], Y. Yamasaki[15], Y. Nakagishi[2], H. Umebayashi[16], N. Okamoto[8,17], N. Iwata[4], T. Yasumi[18], M. Shimizu[3]

[1]Department of Pediatrics, Yokohama City University Graduate School of Medicine, Yokohama, [2]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kobe, [3]Department of Pediatrics, Perinatal and Maternal Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, [4]Department of Infection and Immunology, Allergy and Immunology Center, Aichi Children's Health and Medical Center, Aichi, [5]Department of Nephrology and Rheumatology, Tokyo Metropolitan Children's Medical Center, Fuchu, [6]Department of Pediatrics, Niigata University Graduate School of Medical and Dental Sciences, Niigata, [7]Department of Pediatrics, Kitasato University, Sagamihara, [8]Department of Pediatrics, School of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, [9]Department of Pediatrics, Nagasaki University School of Biomedical Sciences, Nagasaki, [10]Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Fukui, [11]Department of Pediatrics, Hamamatsu University School of Medicine, Hamamatsu, [12]Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Ube, [13]Division of General Pediatrics and Emergency Medicine, Department of Pediatrics, Oita University Faculty of Medicine, Yufu, [14]Department of Pediatrics, Hiroshima Prefectural Hospital Organization Futabanosato Prefectural Hospital, Hiroshima, [15]Department of Pediatrics, Kagoshima University Hospital, Kagoshima, [16]Department of Rheumatism, Infectious Disease, Miyagi Children's Hospital, Miyagi, [17]Department of Pediatrics, Osaka Rosai Hospital, Sakai, [18]Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan

Correspondence: K. Nishimura

Pediatric Rheumatology, **23(2):** P080

Introduction: Macrophage activation syndrome (MAS) is a life-threatening complication of systemic juvenile idiopathic arthritis (sJIA). Early diagnosis and intervention are crucial, and the diagnosis is based on the criteria. In contrast, data regarding indicators for improvement and tapering of treatment in MAS are limited.

Objectives: The aim of this study is to explore the clinical and laboratory indicators for improvement and tapering of treatment in MAS with sJIA.

Methods: This retrospective study included MAS episodes from 2016 to 2023 in patients with sJIA. Fourteen pediatric rheumatology centers across Japan contributed data. MAS was diagnosed based on the criteria proposed by Ravelli et al. Patients not fulfilling all the criteria but clinically considered to have MAS were defined as possible MAS, based on Delphi consensus among all members. Data on clinical features, laboratory findings, and treatments were retrospectively extracted. The earliest date on which any of the following occurred was defined as the date of MAS improvement: tapering of glucocorticoids (GCs), switching from dexamethasone palmitate (DEX-p) or methylprednisolone pulse therapy (MPT) to prednisolone (PSL), transition from continuous intravenous infusion (civ) of cyclosporine A (CyA) to oral administration, CyA discontinuation, or biologics administration.

Results: Forty-eight patients (29 female, 60.4%) and 51 episodes were analyzed. Median age at MAS onset was 8.8 years (range, 0.3–24.4), and median duration from sJIA onset to MAS onset was 0.2 years (range, 0–19.3). MAS criteria were fulfilled in 84.3% of the episodes. Background treatments included GCs: PSL (n=20), MPT (n=11), and DEX-p (n=2); CyA: oral (n=7) and civ (n=2); and biologics: naïve (n=24), tocilizumab (TCZ, n=17), and canakinumab (CAN, n=10). First-line MAS treatments were DEX-p (n=39), MPT to PSL (n=5), MPT to DEX-p (n=4), and PSL (n=3). CyA was administered as civ (n=24) and oral (n=10). Plasma exchange (n=2) and etoposide (n=1) were used. Treatment modifications that defined MAS improvement were DEX-p reduction (n=26), switch to PSL (n=9), PSL reduction (n=3), CyA switch to oral (n=4), CyA discontinuation (n=1), and biologics administration (n=9). On the improvement date, clinical and laboratory findings were as follows: afebrile 48/50 cases (96.0%), no systemic symptoms other than fever in 38/44 (86.4%), platelet count >18.1 x10^3/μL in 38/51 (74.5%), ferritin ≤684 ng/mL in 31/51 (60.8%), AST ≤48 IU/mL in 29/51 (56.9%), TG ≤156 mg/dL in 15/42 (35.7%), and fibrinogen >360 mg/dL in 4/48 (8.3%).

Conclusion: Absence of systemic symptoms and increased platelet count were suggested to be practical clinical indicators of MAS improvement and treatment tapering decisions.

Disclosure

None declared

P081

Variations of lymphocyte subpopulations in macrophage activation syndrome associated still's disease: possible role of B cells, NK cells, and CD38$^+$HLA-DR$^+$CD8$^+$ T cells as a biomarker for the diagnosis of macrophage activation syndrome

M. Hatano[1], S. Kaneko[1], F. Miyaoka[1], A. Shimbo[1], H. Irabu[1], Y. Akutsu[1], Y. Hayashi[2], M. Shimizu[2], M. Mori[3]

[1]Department of Pediatrics and Developmental Biology, [2]Department of Pediatrics, Perinatal and Maternal Medicine, [3]Joint Research Department of Lifelong Immunotherapy, Institute of Science Tokyo, Tokyo, Japan

Correspondence: M. Hatano

Pediatric Rheumatology, **23(2):** P081

Introduction: Early diagnosis of macrophage activation syndrome (MAS) is critically important. However, it remains challenging because clinical manifestations of active phase of Still's disease (SD) and MAS often overlap and also specific diagnostic biomarkers are still lacking. Recently, increase of activated CD8$^+$ T cells co-expressing CD38 and HLA-DR (CD38$^+$ HLA-DR$^+$ CD8$^+$ T cells) have been proposed as a characteristic feature with potential diagnostic value in primary or Epstein Barr Virus-associated hemophagocytic lymphohistiocytosis, However, its utility in MAS associated with SD has not been sufficiently investigated.

Objectives: This study aimed to identify some lymphocyte subpopulations as a useful diagnostic biomarker for MAS complicating SD and evaluating their diagnostic performance in differentiating MAS from active phase of SD.

Methods: Peripheral blood mononuclear cells were isolated from whole blood samples of patients with active SD (n = 18), MAS (n = 8), and disease controls (n = 13). Lymphocyte subsets were analyzed using multicolor flow cytometry. Markers that showed significant differences among the groups were further assessed by receiver operating characteristic (ROC) curve analysis to evaluate their sensitivity and specificity for distinguishing MAS from active SD. Serum or plasma levels of IL-18, CXCL9, soluble TNF receptor II, and IL-6 were quantified by Enzyme-linked immuno-sorbent assay. Correlation between cytokine levels and immune cell subsets was analyzed.

Results: In MAS patients, there was a marked reduction in NK cells, naïve B cells, and memory B cells, along with a significant increase in CD38$^+$HLA-DR$^+$CD8$^+$ T cells compared with active SD. ROC analysis revealed area under the curve values, sensitivity and specificity of B cells, NK cell, and CD38$^+$HLA-DR$^+$CD8$^+$ T cells were 0.83/0.63/0.94, 0.81/0.63/0.94, 0.83/1.00/0.61. Furthermore, the combination of these three markers yielded an AUC of 0.97, with a sensitivity of 0.88 and specificity of 1.00. A positive correlation between IL-18 and memory T cells and a negative correlation between IL-18 and NK cells, and a weak positive correlation between CD38$^+$HLA-DR$^+$CD8$^+$ T cells and CXCL9 were observed.

Conclusion: A marked reduction of NK cells, naïve B cells, and memory B cells, along with a significant increase in CD38$^+$HLA-DR$^+$CD8$^+$ T cells were characteristic in MAS. The combination of B cells, NK cells, and CD38$^+$HLA-DR$^+$CD8$^+$ T cells demonstrated high diagnostic accuracy and may serve as a valuable tool to improve MAS detection in clinical practice.

Disclosure

M. Hatano: None declared, S. Kaneko: None declared, F. Miyaoka: None declared, A. Shimbo: None declared, H. Irabu: None declared, Y. Akutsu: None declared, Y. Hayashi: None declared, M. Shimizu Grant/Research Support with: Medical and Biological Laboratories Co., Ltd, M. Mori Grant/Research Support with: AbbVie GK, Ayumi Pharmaceutical

Corporation, Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organization, Nippon Kayaku Co., Ltd., UCB Japan Co. Ltd., Asahi Kasei Corp.

P082

Clinical and laboratory features of macrophage activation syndrome associated with systemic juvenile idiopathic arthritis receiving tocilizumab and canakinumab

M. Mizuta[1], K. Nishimura[2], S. Hattori[2], A. Ohara[2], Y. Hayashi[3], H. Irabu[4], Y. Aida[1], M. Shimizu[5], S. Kawabe[5], K. Akamine[6], U. Kaneko[7], T. Ebato[8], Y. Sugita[9], K. Hashimoto[10], N. Itoh[11], R. Yasuoka[12], H. Wakiguchi[13,14], J. Yasumura[15], Y. Yamasaki[16], Y. Nakagishi[1], H. Umebayashi[17], N. Okamoto[9,18], N. Iwata[5], T. Yasumi[19], M. Shimizu[3]

[1]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kobe, [2]Department of Pediatrics, Yokohama City University Graduate School of Medicine, Yokohama, [3]Department of Pediatrics and Development Biology, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, [4]Department of Pediatrics, Perinatal and Maternal Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, [5]Department of Infection and Immunology, Allergy and Immunology Center,, Aichi Children's Health and Medical Center, Aichi, [6]Department of Nephrology and Rheumatology, Tokyo Metropolitan Children's Medical Center, Fuchu, [7]Department of Pediatrics, Niigata University Graduate School of Medical and Dental Sciences, Niigata, [8]Department of Pediatrics, Kitasato University, Sagamihara, [9]Department of Pediatrics, School of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, [10]Department of Pediatrics, Nagasaki University School of Biomedical Sciences, Nagasaki, [11]Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Fukui, [12]Department of Pediatrics, Hamamatsu University School of Medicine, Hamamatsu, [13]Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Ube, [14]Division of General Pediatrics and Emergency Medicine, Department of Pediatrics, Oita University Faculty of Medicine, Yufu, [15]Department of Pediatrics, Hiroshima Prefectural Hospital Organization Futabanosato Prefectural Hospital, Hiroshima, [16]Department of Pediatrics, Kagoshima University Hospital, Kagoshima, [17]Department of Rheumatism, Infectious Disease, Miyagi Children's Hospital, Miyagi, [18]Department of Pediatrics, OsakaRosai Hospital, Sakai, [19]Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan

Correspondence: M. Mizuta

Pediatric Rheumatology, **23(2):** P082

Introduction: Macrophage activation syndrome (MAS) can still occur in sJIA patients receiving tocilizumab (TCZ) or canakinumab (CAN). Previous reports showed that TCZ and CAN mask the clinical features of MAS, making early diagnosis difficult compared to MAS in biologics (Bio) naïve sJIA patients. Despite these observations, detailed comparative data and the specific clinical differences among them remain fully unknown.
Objectives: The aim of this study is to investigate the clinical and laboratory features of MAS in patients with sJIA receiving TCZ and CAN.
Methods: A total of 14 pediatric rheumatology centers in Japan participated in a study that involved the collection of MAS episodes in patients diagnosed with sJIA and who had received treatment with or without TCZ or CAN. The diagnosis of MAS was based on the criteria proposed by Ravelli A, et al. Patients who did not fulfil all the diagnostic criteria but were clinically considered to have MAS by the attending physician were categorized as possible MAS. A total of 63 episodes of MAS were evaluated according to clinical features, disease courses, laboratory data, and treatment plans. Furthermore, we compared the timing of MAS onset and the point of therapeutic intervention (TI) which means full-blown MAS among the three groups: Bio naïve, TCZ, and CAN groups. These points were determined according to Delphi method of all members.
Results: Thirty MAS episodes in Bio naïve group, 21 episodes in TCZ group, and 12 episodes in CAN group were included in this study. Possible MAS episodes were 1 in Bio naïve, 6 in TCZ, and 3 in CAN group. The incidence of no fever in MAS was 3% in Bio naïve, 66% in TCZ, and 25% in CAN group. Duration from onset to MAS was 4.3 years in TCZ group, and 6.8 years in CAN group. Serum ferritin and CRP, D-dimer levels were significantly decreased in TCZ and CAN group compared to Bio naïve group at MAS onset and TI. AST levels were significantly elevated in TCZ group compared to Bio naïve and CAN group at MAS onset. Platelet counts has no significance among three groups at onset and TI.
Conclusion: MAS in sJIA patients receiving TCZ or CAN often lacks the typical clinical features. Despite showing lower ferritin levels compared to Bio naïve-MAS, sJIA patients receiving TCZ or CAN may have a potential risk for developing MAS.
Disclosure
None declared

P083

Descriptive study of primary versus rheumatologic and infectious secondary hemophagocytic lymphohistiocytosis in pediatric population. value of cholesterol in disease monitoring

M. I. Menjívar Chavarría[1], J. Calzada-Hernández[2], A. Deyà[3], J. M. Mosquera[2], J. Antón [4], L. Alsina [5]

[1]Pediatrics, [2]Pediatric rheumatology, [3]Pediatric immunoallergy, [4]Head of department of pediatric rheumatology, [5]Head of the department of pediatric immunoallergy, Hospital Sant Joan de Déu, Barcelona, Spain

Correspondence: M. I. Menjívar Chavarría

Pediatric Rheumatology, **23(2):** P083

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome, either primary (F-HLH) or secondary to infections or autoimmune diseases, including macrophage activation syndrome (MAS). It is well known that increased triglycerides are prevalent in patients with HLH and is used as one of the diagnostic criteria by the International Society of Histiocytes. However, lipoprotein cholesterol levels have been rarely studied in HLH.
Objectives: 1) To analyze the clinical and laboratory features of pediatric patients with HLH: primary (F-HLH), MAS, and infection-associated HLH (HLH-NOS); 2) To correlate lipid profile with disease activity.
Methods: Retrospective observational study of patients ≤18 years diagnosed with HLH and treated at our center between 2000 and 2023.
Results: A total of 41 patients were included: F-HLH (A) (n=7), MAS (B) (n=27), and HLH-NOS (C) (n=7). Both F-HLH and HLH-NOS presented an early age (years) of onset (A=1.3; B=9.7; C=1.2 *(p=0.043)*; and absence of relevant history prior to HLH (A=100%; B=55.6%; C=100%; *p=0.012*).At diagnosis, F-HLH showed higher rates of hepatomegaly (A=100%; B=37%; C=28.6%; *p=0.007*), splenomegaly (A=100%; B=40.7%; C=85.7%; *p=0.005*), and more severe pancytopenia: hemoglobin (g/dL) (A=8.3; B=10.8; C=8.4; *p=0.002*), platelets (x10^6/mm^3) (A=30; B=141; C=65; *p<0.000*), leukocytes (x10^6/mm^3) (A=2.9; B=9.0; C=3.9; *p=0.008*), neutrophils (x10^6/mm^3) (A=1.0; B=5.8; C=1.2; *p=0.007*), hypertriglyceridemia (mg/dL) (A=401; B=186; C=207; *p*=0.018), elevated AST (U/L) (A=474; B=110; C=99; *p=0.030*), and impaired cytotoxicity (A=83.3%; B=25%; C=20%; *p=0.035*). MAS patients had a more frequent personal history of autoimmunity (B=48.1%; *p=0.007*), arthralgia (B=59.3%; *p*=0.005), and arthritis (B=37%; *p=0.032*). Low HDL cholesterol levels at admission were found in 51.2% of patients (A=3/3; B=13/16; C=2/2; *p=0.037*), and at diagnosis in 65.8% (A=3/3; B=16/22; C=2/2; *p=0.114*). Ferritin/HDL ratio showed a significant inverse correlation (r = - 0.356; *p < 0.001*), persisting throughout HLH episodes in all three groups.
Conclusion: Three distinct clinical-laboratory profiles were identified across pediatric HLH types. HDL cholesterol may serve as a useful biomarker for HLH activity monitoring, inversely correlated with ferritin values
Disclosure
None declared

P085

Ultrasonographic evaluation of exertional leg pain in patients with familial mediterranean fever: a silent component of the disease?

B. Küçükali, Ç. Yıldız, B. Acun, N. Karaçayır, M. Kutlar, N. Belder, K. Ahmadova, D. G. Yıldırım, S. A. Bakkaloğlu

Department of Pediatric Rheumatology, Gazi University, Ankara, Türkiye

Correspondence: B. Küçükali

Pediatric Rheumatology, **23(2):** P085

Introduction: Exertional leg pain (ELP) is a common finding in patients with Familial Mediterranean Fever (FMF). Although its pathophysiology has not been fully elucidated, the most widely accepted hypothesis is that it represents a silent enthesopathy.
Objectives: The aim of this study is to investigate the radiological manifestations and clinical significance of ELP in patients with FMF through ultrasonographic evaluation of lower extremity joints and tendons
Methods: Patients diagnosed with FMF and followed in our clinic between June and September 2024, who were found to carry homozygous or compound heterozygous pathogenic variants in the MEFV gene, were included in the study. Patients with comorbid musculoskeletal diseases, active professional athletes, and those with a follow-up period of less than one year were excluded. All included patients underwent bilateral ultrasonographic (USG) examination of the hip, knee, and ankle joints, as well as assessment and thickness measurements of the patellar tendon, Achilles tendon, and plantar fascia. USG images were obtained by a single blinded investigator and evaluated according to the OMERACT pediatric USG guidelines.
Results: A total of 50 patients were included in the study, comprising 25 FMF patients with ELP and 25 without. No significant differences were observed in demographic characteristics, MEFV variants, disease activity, or treatment regimens between groups. Joint USG revealed grade 1 synovial effusion in nine patients—seven of whom were in the ELP group—synovial hypertrophy in three patients, and loss of the normal fibrillar tendon structure in one patient. Among those with synovial effusion, 6 patients (67%) had elevated acute phase reactants and active disease. The Achilles tendon was found to be significantly thicker in the ELP group compared to those without ELP (right and left median values: 0.50 and 0.42 cm vs. 0.39 and 0.36 cm, p=0.003 and p=0.009, respectively). This difference remained significant even after adjusting for factors known to affect tendon thickness, such as age and sex, using a multivariate linear regression model (B= 0.065, p=0.007). No differences were observed between the groups in other tendon or plantar fascia thickness measurements.
Conclusion: Although the pathophysiology of ELP in FMF remains unclear, this study suggests that it may be associated with increased Achilles tendon thickness. This finding may indicate subclinical enthesopathy and highlight the potential need for further investigation and treatment modification. Moreover, synovial effusion may be present in FMF patients even in the absence of symptoms or physical examination findings and is generally associated with increased disease activity.
Disclosure
None declared

References

1. Bruyn GA, Iagnocco A, Naredo E, Balint PV, Gutierrez M, Hammer HB, et al. OMERACT definitions for ultrasonographic pathologies and elementary lesions of rheumatic disorders 15 years on. The Journal of rheumatology 2019;46(10):1388-93.
2. Eshed I, Rosman Y, Livneh A, Kedem R, Langevitz P, Ben-Zvi I, et al. Exertional leg pain in familial Mediterranean fever: a manifestation of an underlying enthesopathy and a marker of more severe disease. Arthritis & rheumatology 2014;66(11):3221-6.
3. Kushnir T, Eshed I, Heled Y, Livneh A, Langevitz P, Zvi IB, et al. Exertional muscle pain in familial Mediterranean fever patients evaluated by MRI and 31P magnetic resonance spectroscopy. Clinical Radiology 2013;68(4):371-5.

P087

The contribution of salivary gland ultrasonography to the classification criteria in juvenile sjögren disease: diagnostic value and predictive performance of a weighted scoring model

S. Türkmen, B. Sözeri
Department of Pediatric Rheumatology, Ümraniye Training and Research Hospital, İstanbul, Türkiye
Correspondence: S. Türkmen
Pediatric Rheumatology, **23(2):** P087

Introduction: Juvenile Sjögren's disease (jSjD) is a rare and diagnostically challenging autoimmune condition that lacks pediatric-specific classification criteria.
Objectives: This study evaluated the diagnostic utility of salivary gland ultrasonography (US)—not currently included in the 2016 ACR/EULAR criteria—in jSjD, and assessed its performance within a weighted scoring model (WS) incorporating conventional parameters.
Methods: Seventeen patients diagnosed with jSjD between 2017 and 2024 were retrospectively analyzed. All underwent B-mode parotid US scored using the OMERACT system. Diagnostic parameters included anti-SSA (Ro) positivity, Schirmer test (≤5 mm/5 min), labial salivary gland biopsy with focus score ≥1, and salivary gland US score ≥1. The WS (range 0–8) was calculated as:

$$WS = (\text{anti–SSA positivity} \times 3) + (\text{labial salivary gland biopsy positivity} \times 3) + (\text{Schirmer test positivity} \times 1) + (\text{parotid gland ultra sound positivity} \times 1)$$

ROC analyses evaluated the WS's ability to predict patients exceeding the ACR/EULAR threshold (>4 points), and the predictive value of US alone in identifying patients with ≥2 conventional criteria (Composite Score ≥2). WS and the classic model (excluding US) were compared by AUC and diagnostic metrics.
Results: Among 17 patients (94.1% female, n=16), salivary gland US score ≥1 was present in 64.7% (n=11), Schirmer test was positive in 41.2% (n=7), anti-SSA was positive in 35.3% (n=6), and biopsy was positive in 88.2% (n=15). The median US score was 1.0 (IQR: 0.0–2.0), median biopsy focus score was 2.0 (IQR: 1.0–2.0), and median WS was 4.0 (IQR: 4.0–5.0). The WS yielded an AUC of 0.72 for predicting ACR/EULAR positivity, indicating an acceptable level of discriminative performance. US alone showed strong alignment with classification components (AUC: 0.84 for Composite Score ≥2). ROC comparison revealed similar overall performance between WS and the classic model (AUC: 0.85 vs. 0.87; p = 0.76). However, WS had superior specificity (92% vs. 77%) and PPV (86% vs. 73%), enhancing its diagnostic value in borderline cases.
Conclusion: Although adding US to the classification model did not significantly increase overall AUC, it improved specificity and PPV. Its strong concordance with core criteria, noninvasive nature, and feasibility in pediatric settings support salivary gland US as a promising adjunct to jSjD classification—potentially substituting more impractical tests such as unstimulated salivary flow rate and ocular staining score. However, prospective validation in larger, multicenter pediatric cohorts is essential before its integration into formal classification systems.
Keywords: Classification criteria, Juvenile Sjögren, salivary gland ultrasonography
Disclosure
None declared

P089

The role of PET/CT in evaluating rheumatologic conditions in children with fever of unknown origin - a multicenter study

N. Berlak[1], L. Christodoulou[2], G. Amarilyo[3], O. Scheuerman[1], I. Tirosh[2], A. Kalter[4], A. Carmi[4], E. Forer[5], E. Kristal[6], Y. Levinsky[3,7]
[1]Pediatric B, Schneider children's medical center of Israel, Petah Tikva, [2]Pediatric rheumatology, Tel Hashomer, Ramat Gan, [3]Pediatric rheumatology, [4]Pediatric A, Schneider children's medical center of Israel, Petah Tikva, [5]Pediatric rheumatology, [6]Pediatric immunology, Soroka Medical Center, Beer Sheva, [7]Faculty of medicine, Tel Aviv universitiy, Tel Aviv, Israel
Correspondence: Y. Levinsky *Pediatric Rheumatology*, **23(2):** P089

Introduction: Fever of Unknown Origin (FUO) is a relatively common clinical challenge that is frequently referred for evaluation by pediatric rheumatologists. In many cases, it is necessary to rule out other medical conditions before establishing a rheumatologic diagnosis. 18F-FDG PET/CT is a valuable diagnostic tool that may help identify the fever's source. However, its use in children involves risks, including radiation exposure and the need for sedation.
Objectives: To assess the contribution of PET/CT to FUO diagnosis in hospitalized children, and to identify rheumatologic conditions that are either detected through the evaluation or excluded by it. In addition, to identify predictive factors for its diagnostic utility.
Methods: A retrospective cohort study reviewing medical records of children (0-18 years) diagnosed with FUO who underwent PET/CT

between 2010 and 2024 in three Israeli medical centers. Clinical and laboratory data were collected, and cases where PET/CT led to a diagnosis were compared to those where it did not.
Results: Among 113 cases, PET/CT contributed to diagnosis in 52 (46%). The majority of diagnoses identified by PET/CT were infectious (53.8%), whereas in cases where PET/CT did not aid in diagnosis, rheumatologic diseases were predominant (66.6%). Of all cases, 21% were ultimately diagnoses with a rheumatologic condition, the most frequent was systemic JIA. Immunodeficiency, low hemoglobin, and low albumin were more frequent in cases where PET/CT was diagnostic, while rash and arthritis were more common in cases where PET/CT did not contribute.
Conclusion: PET/CT is an effective diagnostic tool for FUO in children, aiding diagnosis in 46% of cases. Of all cases, 21% were ultimately diagnoses with a rheumatologic condition. However, most were diagnosed without direct findings on the PET/CT, which primarily served to rule out other conditions. Predictive factors for its utility are reported. In appropriate clinical scenarios, PET/CT should be considered as part of the FUO workup in pediatric patients.
Disclosure
None declared

P090

Behçet's syndrome: distinct features in 344 pediatric and adult patients in a non-endemic region

R. Machado[1], T. Souza[2], M. França[1], V. Matias[3], S. Farhat[1], C. Siqueira[3], M. C. Santos[3], L. Steuer[1], L. Forero[1], R. Macedo[4], T. Freitas[4], B. Bayeh[4], C. Ejnisman[4], P. Araujo[4], R. Cordeiro[4], F. Specian[4], V. Balbi[1], N. Aikawa[1,4], K. Kozu[1], C. Silva[1], L. Campos[1], A. Elias[1], H. Giardini[4]
[1]Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, [2]Faculdade de Medicina, Universidade de Brasília, Brasília, [3]Pediatric Rheumatology Unit, Faculdade de Ciências Médicas da Santa Casa de São Paulo, [4]Division of Rheumatology, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil
Correspondence: A. Elias
Pediatric Rheumatology, **23(2):** P090

Introduction: Behçet's syndrome (BS) is a chronic inflammatory disorder characterized by a heterogeneous clinical presentation, occurring primarily in young adults and very rarely in children and adolescents. In addition, there are few studies that compared childhood-onset BS (cBS) and adult-onset BS (aBS), especially in non-endemic regions.
Objectives: Therefore, the objectives of the present study were to evaluate demographic, clinical and therapeutic data in cBS and aBS.
Methods: Medical records of 344 patients [99 cBS (≤ 18 years-old) and 245 aBS] from three tertiary Brazilian Rheumatology centers were reviewed in order to compare clinical and therapeutic features. cBS and aBS were classified according to International Study Group and/or the International Criteria for Behçet's Disease.
Results: The median age at diagnosis was 11(0.5-17) years in cBS and 30(18-76) years in aBS. The median follow-up time was significantly reduced in cBS compared to aBD [7(0-23) vs. 10(0-27) years, p=0.014], with similar female sex in both groups (56% vs. 62%, p=0.14). Classification criteria were fulfilled in 82% of cBS and 100% of aBS patients. Fever (30% vs. 15%, p=0.002), gastrointestinal involvement (55% vs. 14%, p=0.003), and a family history of autoimmune diseases (22% vs. 16%, p=0.001) were significantly higher in cBS compared to aBS. In contrast, genital ulcers (67% vs. 81%, p=0.01), cutaneous lesions (47% vs. 68%, p=0.001), including pseudofolliculitis (34% vs. 53%, p=0.001) and erythema nodosum (24% vs. 36%, p=0.03), uveitis (32% vs. 44%, p=0.03), corticosteroids (68% vs. 88%, p<0.001), azathioprine (56% vs. 70%, p=0.01), cyclosporine (9% vs. 22%, p=0.004), cyclophosphamide (19% vs. 34%, p=0.001), and intravenous immunoglobulin use (9% vs. 18%, p=0.03) were significantly lower in the former group. Frequencies of oral and cutaneous ulcers, articular or central nervous system involvement, retinal vasculitis, colchicine, mycophenolate mofetil, and methotrexate use were similar in both groups (p>0.05).
Conclusion: cBS was rarely observed in our non-endemic region, potentially due to under recognition, as it often presented with non-specific symptoms such as fever and gastrointestinal involvement. The broader spectrum of symptoms in aBS patients might account for the more extensive use of immunosuppressive agents.
Disclosure
None declared

P091

Prognosis of juvenile idiopathic arthritis (remission and relapse rates) – slovak real-life data

B. Balažiová, A. Kušíková, T. Dallos
Department of Paediatrics, Comenius University Medical School in Bratislava, National Institute for Children's Diseases (NÚDCH), Bratislava, Slovakia
Correspondence: B. Balažiová
Pediatric Rheumatology, **23(2):** P091

Introduction: The prognosis of juvenile idiopathic arthritis (JIA) differs between JIA categories and may be affected by other factors, including local treatment practices and accessibility of biologic treatment.
Objectives: To evaluate key prognostic indicators including clinical remission on medication (CRM), clinical remission off medication (CR), and relapse rate across JIA categories.
Methods: Clinical and laboratory data from 216 Slovak JIA patients examined at our tertiary paediatric rheumatology centre between September 2021 and February 2024 were analysed retrospectively. Statistical analyses were performed using NCSS 11 Statistical Software.
Results: CRM within 2 years of initiating immunosuppressive therapy (IST) was achieved in 89% of patients, with no significant differences among JIA subtypes. Among patients with follow-up beyond 3 and 5 years, CR was documented in 24.5% and 47.5%, respectively. A relapsing course was observed in 53.4%. Oligoarticular and systemic JIA had significantly higher CR rates within 3 years from start of IST (32.6% and 50%, respectively) as compared to psoriatic, undifferentiated and enthesitis-related forms (each 0%; p=0.0004). Negative predictors of CR included a greater number of active joints and higher physician's global assessment of disease activity at disease onset and delayed initiation of treatment (p=0.03, p=0.013 and p=0.032, respectively). In non-systemic JIA, elevated baseline CRP and immunoglobulin G levels were associated with failure to achieve CR within 5 years (p=0.0026 and p=0.007) and with early relapse (p=0.01 and p=0.00003). Uveitis was detected in 13% and resulted in permanent ocular damage in 35.7% of the cases. Additionally, uveitis and positive antinuclear antibodies were negative predictors of CR within 5 years (p=0.005 and 0.04) and were linked to early relapse (p=0.003 a p=0.04).
Conclusion: Overall, JIA patients exhibit a favourable prognosis, with a majority achieving remission on treatment. Oligoarticular and systemic subtypes have the most favourable long-term outcomes. Delay in treatment initiation is a negative, but potentially influenceable, prognostic factor.
Disclosure
None declared

P092

Impact of biologic agent accessibility and insurance coverage on juvenile idiopathic arthritis outcomes: a comparative study from turkey and india within the pres sister hospital initiative

B. Küçükali[1], S. Mohan[2], Ç. Yıldız[1], J. S. Oswal[2], S. A. Bakkaloğlu[1]
[1]Department of Pediatric Rheumatology, Gazi University, Ankara, Türkiye, [2]Department of Clinical Immunology and Rheumatology, Bharati Vidyapeeth Medical College and Bharati Hospital, Pune, India
Correspondence: B. Küçükali
Pediatric Rheumatology, **23(2):** P092

Introduction: Biological treatments have changed the landscape regarding juvenile idiopathic arthritis (JIA) outcomes. However, accessibility of these medications remains challenging in various parts of the world, particularly due to their high costs.
Objectives: We investigated the impact of two different healthcare systems on JIA disease courses and outcomes.
Methods: JIA patients who presented to two tertiary healthcare institutions in Turkey and India between January 2014 and January 2025, with a minimum of one-year of follow-up, were enrolled in the study. Systemic JIA (sJIA) patients were excluded, as the management and prognosis of sJIA differ from other subtypes. Data on treatment,

disease activity, and JIA-related complications at six months and one year after diagnosis, and thereafter where available, were obtained retrospectively from medical charts.
Results: A total of 180 patients were enrolled —129 from Turkey and 51 from India. Clinical characteristics were similar, except for RF and ACPA positivity and the polyarticular subtype, which were more frequent in the Indian cohort. Biological disease-modifying anti-rheumatic drugs (bDMARDs), particularly etanercept, were prescribed significantly more often in the Turkish cohort (p=0,006 and p=0,001, respectively). In contrast, systemic corticosteroid use at the six-month and one-year evaluations was significantly higher in the Indian cohort. Initial remission was achieved more rapidly in the Turkish cohort (p=0,010), while the number of patients with active joint and elevated acute phase reactants was consistently higher in the Indian cohort throughout all follow-up periods., The number of patients with chronic joint involvement and uveitis did not differ between cohorts. Only one child from Indian cohort required wheelchair use.
Conclusion: The availability and accessibility to the bDMARDs are of paramount importance in ensuring optimal care for JIA patients. Universal healthcare coverage facilitated early initiation and sustained use of bDMARDs, leading to more rapid control of disease activity and inflammation. In contrast, when bDMARDs were unavailable or not reimbursed, physicians relied more heavily on prolonged systemic corticosteroid use. Interestingly, despite poor initial disease activity control in Indian cohort, JIA-related complications such as chronic joint involvement and uveitis did not significantly differ between the two cohorts, possibly due to ethnic and disease characteristic differences, and the limited number of patients with complications. Future studies should prospectively evaluate the impact of treatment strategies, including stepwise approaches, prior authorization policies, and disparities in healthcare access, on clinical outcomes.
Disclosure
None declared

P093

Long term comorbidity patterns in juvenile idiopathic arthritis

C. Zinterl[1,2,3], B. P. Correia[1,2,3], A. Silva[1,2], M. Antunes[4], F. Araújo[5], H. Assunção[6], S. Azevedo[7], M. Cabral[8], M. J Cadório[9], M. Conde[10], S. Dinis[11], M. D Lopes[12], P. Estanqueiro[13], M. Faria[14], A. R Fonseca[15], V. Fraga[16], C. Furtado[17], J. Lagoas-Gomes[18], A. F Mourão[19,20], P. Nero[21], P. Pinto[22], M. P Ferreira[23], G. Sequeira[24], I. Santos[25], J. Silva-Dinis[26], A. R Vieira[27], P. C Reis[1], R. Campanilho-Marques[1,2,3], F. Oliveira-Ramos[1,2,3]
[1]Pediatric Rheumatology Unit, Rheumatology and Pediatric Department, Unidade Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa (CAML), **[2]**Rheumatology Department, Unidade Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa (CAML), **[3]**Rheumatology Research Unit, Instituto de Medicina Molecular (iMM), Faculdade de Medicina, Universidade de Lisboa, CAML, **[4]**Centro de Estatística e Aplicações, Faculdade de Ciências, Universidade de Lisboa (CEAUL), **[5]**Hospital Ortopédico de Sant´Ana, Lisbon, **[6]**Centro Hospitalar Trás-os-Montes e Alto Douro, H. Vila Real, Vila Real, **[7]**Hospital Infante D. Pedro – Aveiro, Aveiro, **[8]**Hospital Fernando Fonseca – Serviço de Pediatria, Lisbon, **[9]**Hospital da Universidade de Coimbra, Coimbra, **[10]**Unid. Reuma. Pediátrica – Hosp. Dona Estefânia, Lisbon, **[11]**Hospital Sousa Martins – ULS Guarda, Guarda, **[12]**Rheumatologia, Unidade Local de Saúde São João, Oporto, **[13]**Unidade de Reumatologia Pediátrica HP CHUC, Coimbra, **[14]**Hospital Central do Funchal, Funchal, **[15]**Unidade Local de Saúde Entre Douro e Vouga, Santa Maria da Feira, **[16]**Hospital Garcia de Orta, Lisbon, **[17]**Hospital do Divino Espírito Santo, Ponta Delgada, **[18]**Unidade de Reumatologia Centro Hospitalar Tâmega Sousa, Guilhufe, **[19]**Unidade Local de Saúde Lisboa Ocidental, **[20]**Comprehensive Health Research Centre, Nova Medical School, **[21]**Hospital CUF Descobertas, Lisbon, **[22]**Hospital de Vila Nova de Gaia, Vila Nova de Gaia, **[23]**Unidade Local de Saúde do Alto Minho, Ponte de Lima, **[24]**Centro Hospitalar do Algarve – Unidade Faro, Faro, **[25]**Unidade Local Saúde Tondela Viseu, Viseu, **[26]**Reumatologia, Unidade Local de Saúde São José, **[27]**Instituto Português de Reumatologia, Lisbon, Portugal
Correspondence: B. P. Correia
Pediatric Rheumatology, **23(2):** P093

Introduction: Patients with Juvenile idiopathic arthritis (JIA) suffer considerable morbidity due to articular and extra-articular manifestations, including ocular, non-articular musculoskeletal, endocrine, cutaneous sequelae, and secondary amyloidosis, which can lead to serious impairment of their physical function and health-related quality of life [1]. To date, little is known about the prevalence and incidence rate of comorbidities in long term JIA.
Objectives: To assess the prevalence and incidence rates of key comorbidities in JIA patients reaching adulthood and its possible association with specific demographic and clinical characteristics.
Methods: This is a national multicentric retrospective observational cohort study. Data on sociodemographic, clinical features and comorbidities were collected from patients with JIA according to the 2001 revised International League of Associations for Rheumatology (ILAR) criteria, registered in the Rheumatic Diseases Portuguese Register (Reuma.pt), who were at least 18 years old at the time of data extraction. Comorbidities included cardiovascular disease, arterial hypertension, dyslipidaemia, diabetes, thyroid disease, amyloidosis, inflammatory bowel disease, allergy and asthma, osteoporosis, psychiatric disease, and autoimmune disease.
Due to small frequencies of some comorbidities these were clustered into wider groups, namely cardiovascular disease, which included ischemic heart disease, cardiac failure, arrhythmia, pericarditis, peripheral arterial disease, ischemic stroke, and valvular disease; as well as autoimmune disease, which included type 1 diabetes mellitus, Graves and Hashimoto's thyroiditis, vitiligo, myasthenia gravis, multiple sclerosis, coeliac disease, and autoimmune hepatitis. We did not consider extra-articular manifestations of JIA, such as psoriasis or uveitis.
Incidence rates of comorbidities were calculated as the number of new events per 1,000 person-years with 95% CI and prevalence was defined using frequencies.
Results: This study included 924 patients, of which 557 (60.3%) were female with a median [IQR] age of 29.7 [21.2] years. Median age at disease onset was 11.5 [7.8] years, median disease duration was 20.6 [19.7] years and median diagnostic delay was 1.0 [4.7] year. The most frequent category of JIA was undifferentiated JIA (n=293, 31.7%), followed by rheumatoid factor-negative polyarticular JIA (n=191, 20.7%). Most patients were prescribed conventional synthetic DMARDs (csDMARDs; 668, 72.2%) and biologic DMARDs (bDMARDs; 504, 54.7%).
The comorbidities with the highest incidence rate were autoimmune diseases (6.3/1,000 person-years), followed by arterial hypertension (6.1/1,000 person-years) and dyslipidaemia (4.6/1,000 person-years). The incidence of malignancy was 0.6/1000 person-years.
The most prevalent comorbidities were hypertension (n=95, 10%), psychiatric disease (n=60, 6%) and osteoporosis (n=54, 5.6%).
Biologic DMARD therapy in these patients was associated with a decreased risk of developing cardiovascular disease (OR 0.48, p=0.03), arterial hypertension (OR 0.39, p<0.001), dyslipidaemia (OR 0.49, p=0.01), thyroid disease (OR 0.16, p=0.01), amyloidosis (OR 0.12, p=0.049), anaemia (OR 0.21, p=0.02), inflammatory bowel disease (OR 0.31, p<0.001), autoimmune diseases (OR 0.13, p<0.001, osteoporosis (OR 0.39, p=0.003), psychiatric disease (OR 0.3, p<0.001), asthma and allergy (OR 0.19, p<0.001).
No significant association between therapy with bDMARDs and development of malignancy or infections was found.
Conclusion: JIA patients commonly experience comorbidities in the long term, with hypertension being the most frequent. Biologic DMARD treatment seems to be associated with a decreased risk of developing comorbidities. These findings underscore the importance of careful management and monitoring of comorbidities in JIA patients.
Disclosure
None declared

Reference

1. Ramos FO, Rodrigues A, Martins FM, Melo AT, Aguiar F, Brites L, et al. Health-related quality of life and disability in adults with juvenile

P094

Comparative assessment of cardiovascular risk in a large cohort of juvenile systemic lupus erythematosus and juvenile dermatomyositis

J. Li, S. Doddi, T. Mailoo, C. Ciurtin

Centre for Adolescent Rheumatology, University College London, London, United Kingdom
Correspondence: C. Ciurtin
Pediatric Rheumatology, **23(2):** P094

Introduction: Juvenile systemic lupus erythematosus (JSLE) and juvenile dermatomyositis (JDM) are associated with chronic inflammation that can accelerate atherosclerosis. There is no specific guidance regarding the best way to stratify adolescents/young adults (AYA) based on cardiovascular disease (CVD)-risk for personalised management.
Objectives: To evaluate the performance of validated CVD-risk scores in JSLE/JDM, comparing risk prediction with long-term atherosclerotic burden indicators.
Methods: A retrospective cohort analysis of 155 AYA with JSLE (n=76) and JDM (n=79) using descriptive statistics/regression analysis was conducted. CVD-risk was assessed at last follow-up using Framingham Risk Score (FRS), Pooled Cohort Equations (ASCVD), QRISK3, and the validated Pathobiological Determinants of Atherosclerosis in Youth (PDAY) score.
Results: AYA with JSLE vs. JDM were 84% vs.72% females (P=0.08), 60% vs. 29% Non-White (P<0.001), with age at last follow-up of 22.3±5.4 vs.18.3±5.5 years (P<0.001), and median age at disease onset 13.0 (11-16) and 7.5 (5-10) years (P<0.001). At last assessment, AYA with JSLE had more hypertension (13% vs. 3%, P=0.02), and higher total cholesterol (P=0.01) and LDL-cholesterol (P=0.02) levels compared to AYA with JDM, while there were no differences in BMI, smoking or diabetes prevalence. The cumulative dose of steroids was higher in JSLE vs. JDM (P<0.001). The PDAY score was the only one with adequate performance, stratifying 43.5% and 32.8% of JSLE patients as 'high' and 'very high' risk, respectively, while only 15% of AYA with JDM were classified as 'high' risk (P<0.001). PDAY scores remained significantly higher in JSLE vs. JDM after adjusting for age/disease duration (P<0.001). PDAY did not correlate with FRS, ASCVD or QRISK3 scores in either cohorts. When last visit was dichotomized by any major flare, AYA with active JSLE or damage (PedSDI>1) had higher PDAY score (mean 11 vs. 7, P=0.004, and mean 10 vs. 6, P=0.02), respectively. In a multivariable logistic model, four independent predictors of high CVD-risk were identified in JSLE: older age (OR ~1.5 per 5-year increase, P=0.03), longer disease duration (OR ~1.4 per 5-year increase, P=0.04), higher LDL level (OR ~2.0 per 1 mmol/L increase, P=0.02), and presence of active JSLE (OR ~3.3 for any BILAG A vs. no BILAG A flare at last visit, P=0.01). Too few AYA with JDM had high CVD-risk for robust modeling. However, all were males (N=12), one was an ex-smoker and N=9 had low HDL-cholesterol during active disease. None of the typical JDM disease features (muscle enzyme levels, MMT8, skin disease scores) showed an association with PDAY, supporting that traditional factors drove the high CVD-risk observed in JDM.
Conclusion: Traditional 10-year CVD-risk assessments, including FRS, ASCVD, and QRISK3, consistently classified all AYA with JSLE/JDM as low risk, while PDAY score was the only one useful for risk stratification in AYA with JSLE/JDM. This study is the first to highlight higher CVD-risk in JSLE vs. JDM, after adjustement for age/disease duration, as well as disease-related factors driving high CVD-risk in JSLE compared to traditional ones in JDM.
Disclosure
None declared

P096

Dynamic predictors of lethal outcome in children with immune-mediated inflammatory diseases hospitalized in intensive care unit: first week data

I. Avrusin[1], N. Abramova[2], O. Kozlova[3], L. Firsova[4], Y. Aleksandrovich[2], M. Kostik[1]
[1]Department of Hospital Pediatrics, [2]Department of Anesthesiology, Resuscitation and Emergency Pediatrics, Saint Petersburg State Pediatric Medical University, [3]Department of Clinical Mycology, North- Western State Medical University Named after I.I. Mechnikov, [4]Department of Propaedeutics of Childhood Diseases with a Course in General Child Care, Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russian Federation
Correspondence: I. Avrusin
Pediatric Rheumatology, **23(2):** P096

Introduction: Systemic immune-mediated inflammatory diseases can be quite severe and even lethal. Involvement of multiple systems and organs' failure requires admission to intensive care unit (ICU) and urgent treatment.
Objectives: To find dynamic predictors (of the 1st week) of fatal outcome in children with immune-mediated inflammatory diseases hospitalized in ICU.
Methods: 51 children (23 boys, 28 girls) aged 7 months to 17 years with immune-mediated inflammatory diseases were involved in the retrospective study: MIS-C (n=18), systemic rheumatic diseases (n=24) and generalized infections (n=9). All patients were admitted to ICU of the clinic of St. Petersburg State Pediatric Medical University from 2007 to 2023. Two groups were formed: died (n=13), and recovered (n=38). Complex examination was performed: description of clinical picture, laboratory tests, counting SOFA score, Glasgow Coma Scale. To assess hemophagocytosis, HLH-2004 criteria, criteria of MAS for systemic JIA, EULAR/ACR/PRINTO criteria and HScore calculation were used. Also, type of treatment was described. For statistical analysis, STATISTICA software package, version 10.0 (StatSoft Inc., St. Tulsa, OK, USA) was used.
Results: The main 1st day predictors were signs of hemophagocytosis, such as cytopenia (WBC ≤$3.1x10^9$/l (p˂0.001), platelets ≤$168x10^9$/l (p˂0.001)), diuresis ≤ 1.5ml/kg/h (p=0.002), saturation without O_2 support ≤ 92% (p=0.003), K^+> 4.7 mmol/l (p˂0.001), albumin ≤ 30 g/l (p=0.007), creatinine > 74 mcmol/l (p=0.023), pH ≤7.36 (p=0.003), $HCO3^-$ ≤22.2 (p=0.006), Glasgow Coma Scale score ≤ 13 (p=0.019), SOFA score > 2 (p=0.002), and need in O_2 therapy (p=0.02), mechanical ventilation (MV) (p=0.032), biological disease-modifying antirheumatic drugs (bDMAD) (p=0.015), fresh frozen plasma (FFP) transfusions (p=0.021).
3rd day predictors were, as follows: WBC ≤ $4.0x10^9$/l (p˂0.001), platelets ≤ $63x10^9$/l (p˂0.001), hemoglobin ≤ 87 g/l (p˂0.001), CRP > 129 mg/l (p=0.009), triglycerides > 2.45 mmol/l (p=0.039), albumin ≤ 28 g/l (p˂0.001), creatinine > 83.5 mcmol/l (p=0.002), pH ≤ 7.38 (p=0.004), Glasgow Coma Scale ≤ 10 (p˂0.001), SOFA > 2 (p˂0.001), and need in MV (p˂0.001), intravenous immunoglobulin (IVIG) (p=0.018), and blood transfusion (p=0.003).
On the 5th day the main predictors were CRP > 28 mg/l (p˂0.001), triglycerides > 2.3 mmol/l (p=0.029), creatinine> 58 mcmol/l (p=0.009), fibrinogen > 3.3 g/l (p˂0.001), compliance with the EULAR/ACR/PRINTO 2016 criteria for macrophage activation syndrome (MAS) (p=0.015), Glasgow coma scale score ≤ 14 (p=0.002), SOFA > 2 (p˂0.001), and need in MV (p=0.002), vasopressive (p=0.038) and anticoagulant (p=0.003) therapy, blood and FFP transfusion (p=0.009, p=0.021).
Predictors of the 7th day were CRP > 19.1 mg/l (p˂0.001), albumin ≤ 35 g/l (p=0.018), total protein ≤ 55 g/l (p˂0.001), compliance with the EULAR/ACR/PRINTO 2016 criteria for MAS (p=0.015), Glasgow Coma Scale score ≤ 12 (p=0.002), SOFA > 3 (p˂0.001), and need for MV (p=0.003), bDMAD (p=0.034), and anticoagulant therapy (p=0.008).
Conclusion: The hemaphagocytosis signs, tendency to acidosis, progressive decrease in the Glasgow Coma Scale, and an increase in the SOFA index, persistent high CRP, can be used as markers of an unfavorable outcome in patients with immune-mediated inflammatory diseases.
Disclosure
None declared

P097

Determinants of a successful transition in paediatric rheumatology

H. M. Narberhaus[1], S. Tatsis[2], I. Foeldvari[3]
[1]Semmelweis University, Asklepios Medical School, [2]Marienkrankenhaus Hamburg, Rheumatology Outpatient Clinic, [3]Hamburg Centre for Paediatric and Adolescent Rheumatology, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P097

Introduction: Adolescents with chronic rheumatologic diseases often get lost to follow-up during the transition process from paediatric to adult rheumatology care, even if a care in a transition clinic is part of the transition pathway. Several studies looked at reasons, why patients get lost or succeed during transition in centers with socialized medicine.

Objectives: The aim of this study was to identify factors for a successful transition into the adult care.
Methods: A retrospective analysis of medical records of patients was conducted in a single centre, at the Hamburg Centre for Paediatric and Adolescent Rheumatology, who entered the transitions program between December 2014 and December 2023. Only patients, who received a disease modifying agent (DMARD) during the disease course, were offered to participate in the transition program. Patients, who left the program on purpose, where excluded from the analysis. In the transition clinic a paediatric and an adult rheumatologist was present at the same time during the clinic visits. There are two visits (T1 und T2) with both specialist in the paediatric office and the third visit is at the adult rheumatologist office (T3). A transition was considered successful, if the patient reached T3. Demographic and clinical parameters as quality-of-life measures were reviewed.
Results: 547 cases could be included in the analysis, 359 (65,6%) had a successful transition to adult care. Patients with uveitis had a success rate of 96%, patients receiving DMARDs a success rate of 74,7%. Patients who received a combination of conventional DMARDs and biologic DMARDs had 91,2% success rate. Patients without medication at the first transition appointment had a transition rate of 56,6%. Patients with joint count of mean 4.5 or higher had a success rate of 65,6%.
Conclusion: A higher level of disease activity, presence of uveitis and the presence of DMARD treatment appear to positive factor for a successful transition. These date suggests that patients with no positive factors for transition need more closer support to succeed.
Disclosure
H. Narberhaus: None declared, S. Tatsis Grant/Research Support with: BMS, Abbvie, Pfizer, Sandoz, Biogen, Kanssen, Hexal, Mylan, Chugai, Lilly, Novartis, I. Foeldvari: None declared

P098

Severe infectious after rituximab therapy in pediatric and adult patients with refractory autoimmune rheumatic diseases

K. T. Kozu[1], N. E. Aikawa[1,2], L. Parente[2], E. Figueiredo[2], F. H. Souza[2], R. Miossi[2], S. Shinjo[3], L. M. Campos[1], A. M. Elias[1], V. Balbi[1], R. Machado[1], P. Palmeira[1], M. Carneiro-Sampaio[1], E. Bonfa[2], C. A. Silva[1,2]
[1]Reumatologia Pediátrica, Instituto da Criança e Adolescente -ICr, [2]Reumatologia, [3]Reumatologia Pediátrica, HCFMUSP, São Paulo, Brazil
Correspondence: K. T. Kozu
Pediatric Rheumatology, **23(2):** P098

Introduction: Rituximab treatment (RTXt) is an effective treatment for refractory autoimmune rheumatic diseases (ARDs). Severe infections (SI) were reported in 18-24%[1] of pediatric and in 1.7-24%[2] of adult patients under RTX. Pediatric data are limited, as no prior study has compared pediatric and adult ARD populations to identify factors associated with SI under RTXt.
Objectives: To compare the clinical characteristics, and laboratory features of SI between pediatric and adult ARD patients, and to identify factors associated with SI during RTXt.
Methods: This cross-sectional study was conducted at a tertiary center in Brazil. Pediatric ARD (pARD, <18 years old) and adult ARD (aARD) patients who received at least one RTXt cycle were retrospectively reviewed. Demographic data, SI occurrence (defined as requiring hospitalization or death), immunoglobulin G (IgG) levels [classified as low (<600mg/dL) or adequate (>600mg/dL)], and concurrent immunosuppressive drugs (ISD) were collected at baseline and six months post-RTX initiation.
Results: pARD included 18 patients: c-SLE (n=8), JDM (n=4), Rosai-Dorfman disease (n=2), JIA (n=1), CAPS (n=1), Sjögren's disease (n=1) and primary central nervous system vasculitis (n=1). Mean age of pARD patients was 15.2 years (IQR=14.7-16.6). SI occurred in pARD patients (n=4/18, 22%), including two JDM who had severe infections associated to infected calcinosis. JDM was significantly more frequent in those with SI compared to those without it (75% vs. 7%, p=0.019). Prednisone and immunosuppressive use were similar between the groups (p>0.05). Baseline IgG levels were similar in pARD with and without SI [1754.5(1411.7-1918.5) vs. 1425 (1064.7-1588.7) mg/dL, p=0.620], but six months post-RTXt, levels were non-significantly in the former group [796(778-814) vs. 1309.5(1013.5-1463.2) mg/dL, p=0.131]. The aARD group (n=87) comprised 48 SLE and 39 systemic autoimmune myopathies. The SI rates (22.2% vs. 13.8%, p=0.469), and mortality rates (11.1% vs. 18.3%, p=0.732) were not significantly different between the groups. Low IgG levels were more frequently observed in pARD (16.7% vs. 2.3%, p=0.035), but not at six months post-RTXt (12.5% vs. 6%, p=0.311). Prednisone use before RTXt was more common in pARD (100% vs. 89%, p=0.028). Intravenous immunoglobulin (IVIG) use before and during RTXt was significantly higher in pARD (61% vs. 16%, p=0.0001). Other clinical and treatment outcomes were similar in both groups.
Conclusion: This study identifies higher SI in pARD patients under RTXt, with associated mortality in JDM cases. SI and mortality rates were similar between the groups, and pARD had lower baseline IgG levels and greater IVIG use. These findings highlight the need for close monitoring of infections in pARD patients on RTXt and suggest potential differences in immunological vulnerability between these two populations
Trial registration identifying number: This study was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (#2022/13837-5) to KK, PP & MC-S; #2022/12925-8 to NEA & CAS.
Disclosure
None declared

References

1. Labrosse R, Barmettler S, Derfalvi B,et al. Rituximab-induced hypogammaglobulinemia and infection risk in pediatric patients. J Allergy Clin Immunol. 2021;148(2):523-532.e8.
2. Shi Y, Wu Y, Ren Y, Jiang Y, Chen Y. Infection risks of rituximab versus non-rituximab treatment for rheumatoid arthritis: A systematic review and meta-analysis. Int J Rheum Dis. 2019;22(8):1361-1370

P099

Unmet information needs impact transition competence: infotrans interim findings

K. Minden[1,2], F. Milatz[2,3], S. Schalm[4], M. Niewerth[2], G. Erbis[5], I. Foeldvari[6], S. Hansmann[7], A. Maier[8], C. Reiser[5,9], E. Seipelt[10], S. Tatsis[11], A. Wörner[12], K. Mönkemöller[13], J. Klotsche[2]
[1]Charite Universitätsmedizin Berlin, [2]Deutsches Rheumaforschungszentrum Berlin, [3]Charite Universitätsmedizin Berlin, Berlin, [4]Rheumatologie im Zentrum, Munich, [5]Universitätsklinikum Tübingen, Tübingen, [6]Hamburger Zentrum Kinder- und Jugendrheumatologie, Hamburg, Germany, [7]Universitätsklinikum Tübingen, Tübingen, Gabon, [8]St. Josef Stift Sendenhorst, Sendenhorst, Germany, [9]LKH Bregenz, Bregenz, Austria, [10]Immanuel Krankenhaus Berlin, Berlin, [11]Kath. Marienkrankenhaus Hamburg, Hamburg, Germany, [12]Universitäts-Kinderspital beider Basel, Basel, Switzerland, [13]Kliniken der Stadt Köln, Köln, Germany
Correspondence: K. Minden
Pediatric Rheumatology, **23(2):** P099

Introduction: In Germany, various support measures have been established to facilitate the transition of young people with juvenile rheumatic musculoskeletal diseases. These include an interactive website by the German Rheumatism League (www.mein-rheuma-wird-erwachsen.de), transition peers, camps, and transition clinics at paediatric rheumatology centers. The InfoTrans project explored young people's use of these resources, their satisfaction with transitional care, and the development of their transition competence.
Objectives: To investigate the development of transition competence in adolescents with juvenile idiopathic arthritis (JIA) receiving pediatric rheumatology care in Germany, and to identify factors associated with transition competence and satisfaction with care.
Methods: Longitudinal data from the National Paediatric Rheumatologic Database (NPRD) collected between 2022 and 2023 were analysed for adolescents aged ≥16 years with juvenile idiopathic arthritis (JIA). Transition competence and satisfaction with care were assessed using the validated Transitions-KompAZ instrument[1]. Participants also reported on their information-seeking behaviour and awareness of support services. Changes in transition competence and satisfaction over time, as well as associated factors, were analysed by generalized linear models.
Results: Transition data with one-year follow-up were available for 617 adolescents with JIA from 48 centers (72% female; mean age 17.0 ± 1.5 years).

Diagnoses included oligoarthritis (38%), RF-negative or RF-positive polyarthritis (31%), enthesitis-related arthritis (17%), and psoriatic arthritis (8%).
One in four participants sought information beyond clinical consultations, and nearly 30% were aware of the German Rheumatism League's website. About 25% reported unmet information needs - ranging from 12% for self-help services to 36% for the long-term disease course. Only 6% expressed dissatisfaction with their transitional care.
At the follow-up, the transition competence scores (range: 0–33) were significantly better (22.7±6.4 to 24.5±6.0, p<0.001), while satisfaction with preparation for the transfer to adult care (range: 0–20) had declined (18.9±7.6 to 15.9±7.7, p<0.001). Awareness of the website "mein-rheuma-wird-erwachsen.de" and higher satisfaction with care were associated with transition competence at follow-up (β=1.98, p<0.001, and β=0.19, p=0.02, respectively). Unmet information needs were negatively associated with both transition competence (β=–0.50, p<0.001) and satisfaction with care at follow-up (β=–0.43, p=0.002). Additionally, unmet needs for transitional services were associated with lower satisfaction with transitional care (β=–1.36, p=0.009).
Conclusion: Young people with JIA often experience information gaps, which are linked to reduced transition competence and satisfaction with care. Targeted efforts to address these gaps are essential for improving transitional care and outcomes.
Disclosure
K. Minden Grant/Research Support with: The InfoTrans project was funded by the Innovation Fund of the Federal Joint Committee (G-BA), grant number 01VSF20012., F. Milatz: None declared, S. Schalm: None declared, M. Niewerth: None declared, G. Erbis: None declared, I. Foeldvari: None declared, S. Hansmann: None declared, A. Maier: None declared, C. Reiser: None declared, E. Seipelt: None declared, S. Tatsis: None declared, A. Wörner: None declared, K. Mönkemöller: None declared, J. Klotsche: None declared

Reference

1. Haney H, Klotsche J, Niewerth M, et al. Assessing Competencies, Needs, and Satisfaction With the Transition From Pediatric to Adult Health Care in Rheumatology: Development and Validation of the Transition-KompAZ. J Rheumatol. 2024 Oct 1;51(10):1023-1032.

P100

Temporomandibular joint involvement in juvenile idiopathic arthritis: assessing the predictive role of inflammatory biomarkers in the population-based nordic jia cohort

K. Lindberg Larsen[1,2], P. Stoustrup[3], T. Klit Pedersen[3,4], C. Kessel[5], D. Foell[5], L. Berntson[6], A. Fasth[7], M. Ekelund[6,8], H. Nilsson[9], C. Myrup[10], S. Kreiborg[11,12], E. Nordal[13,14], V. Rypdal[13,14], J. Halbig[15], M. Rygg[16,17], E. Dalen Arnstad[16,18], T. Herlin[1,2], M. Glerup[1,2] on behalf of The Nordic Study Group of Pediatric Rheumatology (NoSPeR)
[1]Department of Pediatrics, Aarhus University Hospital, [2]Department of Clinical Medicine, Health, [3]Sections of Orthodontics, Department of Dentistry and Oral Health, Aarhus University, [4]Department of Oral and Maxillofacial Surgery, Aarhus University Hospital, Aarhus, Denmark, [5]Department of Pediatric Rheumatology and Immunology, University Hospital Münster, Münster, Germany, [6]Department of Women's and Children's Health, Uppsala University, Uppsala, [7]Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, [8]Department of Pediatrics, Ryhov County Hospital, Jönköping, [9]Section 3, Department of Orofacial Pain and Jaw Function, Faculty of Odontology, Malmö University, Malmö, Sweden, [10]Department of Pediatrics, Rigshospitalet, Copenhagen University Hospital, [11]Department of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, [12]Department of Oral and Maxillofacial Surgery, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, [13]Department of Pediatrics, University Hospital of North Norway, [14]Department of Clinical Medicine, UiT The Arctic University of Norway, [15]Public Dental Health Competence Centre of Northern Norway (TkNN), Tromsø, [16]Department of Clinical and Molecular Medicine, NTNU - Norwegian University of Science and Technology, [17]Department of Pediatrics, St. Olavs Hospital, Trondheim, [18]Department of Pediatrics, Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway
Correspondence: K. Lindberg Larsen
Pediatric Rheumatology, **23(2):** P100

Introduction: Diagnosing TMJ arthritis in patients with JIA is challenging due to presentation with only subtle symptoms. The role of inflammatory biomarkers in TMJ arthritis is not well described.
Objectives: To evaluate serum biomarkers obtained early in the disease course as predictors for involvement of the temporomandibular joint (TMJ) at long-term follow-up (FU).
Methods: Patients from the population-based Nordic JIA cohort study were recruited close to disease onset from defined regions in the Nordic countries between 1997-2000. Clinical data and serum biomarkers were obtained at baseline 6 (−1/+2) months from disease onset. At 17-year FU, a full-face cone-beam computed tomography (CBCT) was performed. S100 proteins, and 14 other inflammatory biomarkers (cytokines, chemokines) were determined by multiplexed bead array assay. We estimated both univariate and multivariate logistic regression models on binary outcomes of CBCT-verified TMJ involvement as explanatory variables. Computing receiver operating characteristics (ROC) to illustrate the area under the curve (AUC) for the prediction of TMJ involvement at 17-yr FU was used.
Results: A full-face CBCT scan at 17-yr FU was performed for 245/420 eligible patients of which 129 patients had baseline biomarkers available. TMJ involvement (erosions and/or condylar deformity) in the left and/or right TMJ was observed in 69 patients (53.5%) and 60 patients showed no TMJ abnormality.
Baseline serum levels of IL-18 and S100A9 were significantly higher for patients showing TMJ involvement at 17-yr FU (p values 0.019 and 0.003, respectively) compared to patients without TMJ involvement.
We found that significant levels of AUC were obtained for baseline levels of IL-18 and S100A9, as well as for ESR, number of active and cumulative joints at the baseline visit. Nested multivariate logistic regression models were compared in analysis of variance. We compared a clinical model (with the variables subcategories, gender, age, joint counts, ESR/CRP) and a combined clinical and biomarker model (clinical variables as above plus 16 biomarkers obtained at baseline: IL-1ß, IL-4, IL-6, IL-10, IL-12, IL-13, IL-17A, IL-18, TNFα, MMP-3; CCL-2, sCD25, GM-CSF, MPO, S100A9, S100A12). We found that the biomarkers increased the explanatory value predicting TMJ involvement at 17-yr FU (AUC increased from 0.67 to 0.78), however, not significantly.
Conclusion: Biomarkers of inflammation obtained early after JIA onset may complement the characterization of disease activity and may contribute to future models predicting long-term TMJ involvement.
Disclosure
K. Lindberg Larsen: None declared, P. Stoustrup: None declared, T. Klit Pedersen: None declared, C. Kessel Grant/Research Support with: Novartis and Sobi, D. Foell Grant/Research Support with: Novartis, Sobi and BionTech, L. Berntson: None declared, A. Fasth: None declared, M. Ekelund: None declared, H. Nilsson: None declared, C. Myrup: None declared, S. Kreiborg: None declared, E. Nordal: None declared, V. Rypdal: None declared, J. Halbig: None declared, M. Rygg: None declared, E. Dalen Arnstad: None declared, T. Herlin: None declared, M. Glerup: None declared

P101

What does transitional care look like for young people with chronic pain: a uk survey of healthcare professionals working in paediatric and adolescent rheumatology

L. Huckerby[1,2], V. Cuthbert[1], S. Johnson[3,4], J. Ford[5], J. E. McDonagh (Retired)[1,6,7], R. R. Lee[6]
[1]Department of Paediatric Rheumatology, Royal Manchester Children's NHS Foundation Trust, Manchester, [2]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, [3]Walton Centre NHS Foundation Trust, [4]Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, [5]Bath Centre for Pain Services, Bath, [6]Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, [7]National Institute for Health Research Biomedical Research Centre, Manchester University Hospital NHS Trust, Manchester, United Kingdom
Correspondence: L. Huckerby
Pediatric Rheumatology, **23(2):** P101

Introduction:
Chronic musculoskeletal pain affects up to 25% of children and young people[1]. A large proportion of young people (up to 40%) with chronic pain will have unresolved pain which continues into adulthood[2,3].

Therefore transitional care, which is the process of supporting the young person to build skills to manage their condition, including into adulthood, is essential.
There is a lack of published evidence about current approaches to transitional care for young people with chronic pain[4].
Objectives:
To explore healthcare professionals' (HCP) perspectives on clinical approaches to transitional care for young people with chronic pain in UK tertiary paediatric and adolescent rheumatology centres.
Methods:
An online survey was developed, then piloted and modified with feedback from three paediatric and adolescent rheumatology centres in the UK. The survey was then distributed via snowball sampling and emailed to known contacts at all UK paediatric and adolescent rheumatology centres (n=17). The survey included questions on type of transitional care provided, pain assessment, pain education, and arrangements for transfer to adult services. Responses were analysed using descriptive analyses (for numerical and categorical data collected) and thematic analysis (for qualitative free-text response questions).
Results:
22 participants from 10 tertiary paediatric and adolescent rheumatology centres in the UK provided data.
The survey was completed by 6 physiotherapists, 2 occupational therapists, 2 psychologists, 2 specialist nurses and 10 doctors.
7 of 22 (32%) of HCP reported that transitional care is either not provided in clinic (5 of 22) or they were unsure (2 of 22).
70% of HCP reported that young people were not always given the opportunity to be seen independently (including for part of) clinic visits.
10/22 (45%) of HCP thought that the HEEADSSS adolescent psychosocial screening template was used in their department for young people with JIA and 7/22 (31%) for young people with chronic pain.
15 of 22 (68%) of HCP reported transferring young people with chronic pain to the GP, 15 referred to an adult pain clinic, 4 to adult rheumatology, 6 referred to a young adult pain clinic and 2 were unsure. 2 HCP noted that referral to adult pain/rheumatology services may not be accepted or available and therefore these young people remain under primary care.
Where multiple responses from centres were captured, differences within centres were apparent in terms of how pain is assessed, pain education strategies used and where young people are transferred to in adult services.
Conclusion:
Findings highlight that there is a wide range of current approaches to transitional care for young people with chronic pain both between and within paediatric and adolescent rheumatology services in the UK, reflecting a need for organisations to have an agreed transitional care policy as recommended by NICE and international (EULAR/PReS) guidance[5,6].
Disclosure
None declared

References
1. Chambers CT et al. Pain 2024.
2. Walker LS et al. Pain 2010.
3. Kashikar-Zuck S et al. Pain 2019.
4. Huckerby L, McDonagh JE, Lee RR. Rheumatol Adv Pract 2023.
5. NICE guidance 2016 https://www.nice.org.uk/guidance/ng43
6. EULAR Foster HE *et al. Annals Rheum Dis* 2017.

P103

Radiographic assessment of measurable osteoarticular damage in juvenile idiopathic arthritis (Jia) patients transitioning to adult care

M. Klanjscek[1], L. De Nardi[2,3], A. Pin[4], L. Cereser[5,6], A. Taddio[1,4], A. Tommasini[1,4], A. Zabotti[5], S. Pastore[4]
[1]University of Trieste, Trieste, [2]Bambino Gesù Children's Hospital, [3]Tor Vergata University, Rome, [4]Institute for Maternal and Child Health IRCCS Burlo Garofolo, Trieste, [5]University Hospital S. Maria della Misericordia, [6]University of Udine, Udine, Italy
Correspondence: M. Klanjscek
Pediatric Rheumatology, **23(2):** P103

Introduction: Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatic disease, causing chronic joint inflammation and potential damage. While conventional radiography is the gold standard for detecting structural damage, interpreting scans in children is challenging due to skeletal immaturity. Routine radiographic monitoring is less common in JIA than in adult rheumatoid arthritis, partly based on the belief that damage is infrequent. However, recent studies indicate significant damage rates, particularly in certain JIA subtypes. Evidence suggests anti-TNFα agents may better prevent damage than methotrexate (MTX) in polyarticular cases. Critically, joint outcomes in JIA patients transitioning to adult rheumatology care have not been quantified.
Objectives: This study's primary aim was to quantify radiographic damage in a cohort of JIA patients after physeal closure and assess associations with childhood treatments. The secondary aim was to explore correlations between radiographic damage and clinical/laboratory variables.
Methods: This cross-sectional study, conducted from January to October 2023, included 30 patients with JIA (83.3% female) transitioning to adult care. Hands/wrists, knees, and pelvis radiographs were assessed using Larsen and modified Sharp/Van der Heijde scores. Clinical, laboratory, and treatment data were collected retrospectively. The Juvenile Arthritis Damage Index (JADI) was also applied. Fisher's test and Pearson correlation in R explored potential associations.
Results: No significant clinical differences were found between patients with and without radiographic damage, except for higher clinical hip involvement in the damaged group. Osteophytosis (71.4%) was the most common radiographic finding, followed by joint space narrowing (28.6%) and erosions/juxta-articular osteoporosis (14.3%). Of 14 patients with radiographic damage, 6 had positive scores on Larsen or Sharp/Van der Heijde scores. The hips were the most frequently affected joints on radiographs (9 patients), followed by the carpus (6) and knees (3). No substantial link was found between radiographic damage and MTX therapy duration, treatment with biologics, previous arthrocentesis, or cumulative months of active illness, but there was a mild inverse correlation with the JADI-A score.
Conclusion: This study found that up to 50% of patients with JIA exhibit radiographic damage after physeal closure. Notably, many presented only with osteophytosis, often missed by standard damage scores like Larsen and Sharp/Van der Heijde. Furthermore, the observed inverse correlation between JADI-A and the measures of radiographic damage underscores the poor agreement between different assessment tools. This highlights the limitations of current scoring methods and the need for revised approaches, although the clinical significance of osteophytosis, potentially reflecting mechanical stress rather than inflammation, warrants further study.
Disclosure
None declared

P104

Temporomandibular joint arthritis in juvenile idiopathic arthritis: clinical characteristics, imaging findings, and long-term outcomes in a longitudinal cohort

M. Bizjak[1], M. Zajc Avramovic [1], N. Emersic[1], G. Markelj[1], D. Vozlic[2], M. Knez[2], Z. Kovacic[2], A. Vesnaver[2], A. Gazikalovic[3], D. Kljucevsek[3], T. Avcin[1], N. Toplak[1]
[1]Department of Allergology, Rheumatology and Clinical Immunology, UCH Ljubljana, UMC Ljubljana, [2]Department of Surgery, UMC Ljubljana, [3]Department of Radiology, UCH Ljubljana, UMC Ljubljana, Ljubljana, Slovenia
Correspondence: M. Bizjak
Pediatric Rheumatology, **23(2):** P104

Introduction: Temporomandibular joint (TMJ) involvement has been increasingly reported in patients with juvenile idiopathic arthrits (JIA) and can lead to severe complications.
Objectives: To describe the clinical course and long-term outcome of patients with JIA-associated TMJ arthritis, treated at a tertiary care hospital.
Methods: We conducted a retrospective analysis of 36 patients with JIA and TMJ arthritis, who were treated at the Department of allergology, rheumatology and clinical immunology, University Children's

Hospital, University Medical Centre Ljubljana since 2017, with a median follow-up duration of 9.3 years (range 0.3–16.9). Demographic, clinical, imaging, and treatment data were reviewed.
Results: Of the 36 patients, 7 (19%) were male. The most common JIA subtypes were polyarticular (33%) and extended oligoarticular (28%). Median age at JIA diagnosis was 8.0 years (range 1.4–17.7), and median age at onset of TMJ signs and/or symptoms was 12.5 years (range 7.5–17.7). Signs and/or symptoms of TMJ arthritis were present at JIA diagnosis in 15 patients (42%), and in others they developed a median of 6 years later. Bilateral TMJ involvement was seen in 72%. The most frequent presenting symptom was pain with mandibular movement (64%), while 28% of patients reported no symptoms. On clinical examination, TMJ tenderness (64%) was the most common finding, followed by decreased mouth opening (39%), jaw deformity (micro- and/or retrognathia; 25%), mouth opening deviation (22%), mandibular deviation >3 mm (17%), and facial assymetry (11%).
Initial MRI revealed inflammatory changes in 28% of patients, combined inflammatory and structural changes in 67%, and isolated structural damage in 6%. At diagnosis of TMJ arthritis, 5 patients on methotrexate required additional biologic DMARDs; 2 patients switched bDMARDs. 18 patients were started on methotrexate, of whom 13 required escalation to biologic therapy. Nine patients were started directly on bDMARDs. Two patients did not receive systemic treatment for TMJ involvement. Five patients (14%) received intra-articular corticosteroid injections. Surgical intervention was required in 5 patients (3 total alloplastic joint replacements, 2 orthognathic surgeries), with surgeries planned for 5 additional patients.
Conclusion: Despite advances in the treatment of JIA, TMJ arthritis remains a significant cause of structural joint damage and long-term complications.
Disclosure
None declared

P105

Evaluation of the general characteristics of patients consulted to pediatric rheumatology from the pediatric intensive care unit

N. Kara Çanlıoğlu[1], H. C. Tuğrul[2], E. Tunce[1], S. Atamyıldız Uçar[1], G. Atay[3], S. Erdoğan[3], B. Sözeri[1]
[1]Pediatric Rheumatology, Ümraniye Training and Research Hospital, Istanbul, [2]Pediatric Intensive Care Unit, Van Training and Research Hospital, Van, [3]Pediatric Intensive Care Unit, Ümraniye Training and Research Hospital, Istanbul, Türkiye
Correspondence: Atamyıldız Uçar
Pediatric Rheumatology, **23(2):** P105

Introduction: Critically ill children with systemic inflammatory conditions may require specialized care by pediatric rheumatologists. Understanding the profile of patients consulted to pediatric rheumatology from the Pediatric Intensive Care Unit (PICU) can guide early recognition and appropriate treatment.
Objectives: This study aims to evaluate the demographic and clinical characteristics, treatment approaches, and outcomes of patients who were admitted to the PICU and consulted to pediatric rheumatology.
Methods: A retrospective review was conducted of patients admitted to the PICU of Ümraniye Training and Research Hospital between January 2016 and January 2025 and consulted to the pediatric rheumatology department. Data on age, gender, diagnosis, treatment, and survival status were collected from medical records.
Results: A total of 148 patients were evaluated. The mean age was 8.2 years (range 0–18); 67 were male and 81 female. At the time of PICU admission, 26 patients had an established primary rheumatologic diagnosis, including 7 cases of macrophage activation syndrome (MAS) secondary to systemic juvenile idiopathic arthritis (sJIA), 8 with systemic lupus erythematosus (SLE) experiencing disease flares, 1 with familial Mediterranean fever (FMF) presenting with ileus, 1 with interferonopathy (SPENCD) complicated by infections, and 9 with various forms of vasculitis manifesting as hypertension and altered mental status. Consistent with previous reports, SLE emerged as the most common rheumatologic condition requiring intensive care among pediatric patients, typically due to disease exacerbation or severe infectious complications [1], which aligns with our own findings.
Fourteen patients were diagnosed with a rheumatologic disease during their ICU stay, including sJIA (n=3), vasculitis (n=7), Tumor Necrosis Factor Receptor–Associated Periodic Syndrome (n=2), and SLE (n=2). Among 56 patients with prolonged fever, myocarditis, cytopenias, or elevated liver enzymes, 26 were diagnosed with multisystem inflammatory syndrome in children (MIS-C), and 30 with MAS secondary to infections or malignancies. The most frequent non-rheumatologic consult reasons were encephalitis/meningitis, viral myocarditis, and pneumonia with pleural effusion.
The mean ICU stay was 22.3 days. Plasmapheresis was used in 73 patients, hemodiafiltration in 24, mechanical ventilation in 64. Pulse steroid therapy was administered to 85 patients, IVIG to 101, and biologics to 66 (Anakinra in 58; 44.5%).
Overall mortality was 23% (35 patients). Mortality was 10% in MAS secondary to sJIA, 6.2% in vasculitis, and 44% in SLE. Among MIS-C patients, mortality was 11.5%; among secondary MAS cases, 41%. Of 36 patients with a primary rheumatologic diagnosis, 6 died (16.6%).
Conclusion: Rheumatologic diseases in critically ill children can lead to high mortality. Early diagnosis and prompt pediatric rheumatology consultation are essential for improving outcomes.
Disclosure
None declared

Reference

1. Al-Mayouf SM, Fallatah R, Al-Twajery M, Alayed T, Alsonbul A. Outcome of children with systemic rheumatic diseases admitted to pediatric intensive care unit: An experience of a tertiary hospital. Int J Pediatr Adolesc Med. 2019 Dec;6(4):142-145.

P106

Early assesment of efficacy of biologic treatment for children with multiple epiphyseal dysplasia course with osteoarthritis

A. Kozhevnikov[1,2], E. Melchenko[1], V. Kenis[1]
[1]H. Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, [2]St. Petersburg State Pediatric Medical University, State Budgetary Healthcare Institution Children's, Saint-Petersburg, Russian Federation
Correspondence: A. Kozhevnikov
Pediatric Rheumatology, **23(2):** P106

Introduction: Multiple epiphyseal dysplasia (MED) are a clinically and genetically heterogeneous group of skeletal dysplasia mainly involving the epiphyses of the long bones. One of the most common and severe outcomes of MED is the development of dislocation of the hip at the stage of osteoarthritis (OA). Clinical and instrumental manifestations of OA in children with MED may mimic of juvenile idiopathic arthritis (JIA). Prolonged uses of nonsteroidal anti-inflammatory drugs (NSAIDs) don't usually prevent of dislocation of the hip and reduce inflammatory. The effects of disease-modifying antirheumatic drugs (DMARDs) on the course of MED in children have not been studied.
Objectives: The aim of this preliminary study was evaluated the efficacy of DMARDs in children with MED course with hip OA.
Methods: The study included 12 children with MED (6 children – MED type 1, COMP gene mut; 6 children – MED type 4, SLC26A2 gene mut; mean age 9,5 ± 1,0 years 66,7% girls). 8 children treated with methotrexate, 4 – biologic agents. All children had clinical and MRI sings of hip OA and suffering from severe pain (≥60 mm on a 100 mm visual analog scale) which requiring daily NSAIDs administration. The average follow-up of DMARDs was 12 [8; 16] months.
Results: The analysis revealed that all children who were treated with methotrexate at a dose of 15 mg/m^2/week more than 6 months regularly felt hip pain and the saved needed for NSAIDs. All children continued MRI signs of OA. Biologics therapy (BT) had better clinical outcomes. Two children with MED type 1 and one with MED type 4 which received etanercept (0.8mg/kg/week) and one with MED type 4 with tofacitinib (10 mg/day) had reducing of painful and need NSAIDs. After 6 months of BT three children (two with MED type 1 treated etanercept and one with MED type 4 with tofacitinib) had decrease MRI signs of OA. This fact was the basis for the continued use of BT. Treatment of methotrexate was stopped due to inefficacy. Analysis of instrumental picture showed that DMARDs including biological agents

didn't changes on course of bone changes in MED. However, during the follow-up of BT where were no cases of dislocation hip among children.
Conclusion: BT in children with MED can be considered as one of the way to suppressed of OA activity and preventing the development of dislocation of hip. However to confirm data of this research needed a large number of children with MED.
Disclosure
None declared

References
1. Markova T, Kenis V, Melchenko E, Alieva A, Nagornova T, Orlova A, Ogorodova N, Shchagina O, Polyakov A, Dadali E, Kutsev S. Clinical and Genetic Characteristics of Multiple Epiphyseal Dysplasia Type 4. Genes (Basel). 2022 Aug 24;13(9):1512.
2. Sakamoto Y, Yamamoto T, Kajino Y, Kabata T, Tsuchiya H, Miyake N, Iwamoto Y, Matsumoto N, Ikegawa S. Multiple epiphyseal dysplasia mimicking osteoarthritis due to acetabular dysplasia: A report of a familial case with a COMP mutation. J Orthop Sci. 2017 Sep;22(5):967-971.
3. Osipova D.V., Markova T.V., Kenis V.M., Melchenko E.V., Nagornova T.S., Nikishina I.P., Zakharova E.Yu., Dadali E.L., Kutsev S.I. Differential diagnosis of juvenile idiopathic arthritis and multiple epiphyseal dysplasia: Experience of multidisciplinary interaction. Rheumatology Science and Practice. 2023;61(5):608-617. (In Russ.)

P107

Challenges in pediatric chronic nonbacterial osteomyelitis of the mandible: a multicenter retrospective study on biopsy, diagnostic delay and antibiotic use

A. Theobold[1], H. Morbach[2], H. Lausmann[3], C. Van Quekelberghe[4], F. Weller-Heinemann[5], A. Schnabel[6], K. Tenbrock[7], T. Keller[8], M. Laaths[9], H. Girschick[10], A. Skrabl-Baumgartner[11], A. Mráz[12], J. Kümmerle-Deschner[1], C. Reiser[1,12]
[1]Pediatric Rheumatology, Faculty of medicine and University Hospital, Tübingen, [2]Pediatric Rheumatology and Immunology, Children's Hospital, University of Würzburg, Würzburg, [3]Pediatric Rheumatology, Children's Hospital St. Marien gGmbH, Landshut, [4]Pediatric Rheumatology, Clementine Kinderhospital, Frankfurt am Main, [5]Department of Pediatrics, Prof.-Hess-Kinderklinik, Bremen, [6]Department of Pediatrics, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, [7]Dept of Pediatrics, Pediatric Rheumatology, RWTH Aachen University, Aachen, [8]Department of Pediatrics, KJF Klinik Josefinum, Augsburg, [9]Department of Pediatrics, Klinikum St. Marien, Amberg, [10]Department of Pediatrics, Vivantes Clinic Friedrichshain, Berlin, Germany, [11]Department of Pediatrics, Medical University Graz, Graz, [12]Department of Pediatrics, Landeskrankenhaus Bregenz, Bregenz, Austria
Correspondence: A. Theobold
Pediatric Rheumatology, **23(2):** P107

Introduction: Differentiating between bacterial infection and chronic non-bacterial osteomyelitis can be challenging, especially when the mandible is the only site affected.
Objectives: This study aimed to characterize a cohort of patients with CNO of the mandible, focusing on the diagnostic process.
Methods: This retrospective multicenter study included pediatric patients from 12 centers in Germany and Austria who had confirmed CNO/CRMO over the past 10 years. The diagnosis was based on histology and imaging and the disease onset occurred between 1 and 18 years of age. All patients had unilateral or bilateral mandibular involvement.
Results: Thirty-five patients were included. Of these, 63% were female, and 51% developed multifocal disease during the course of illness. The mean age at diagnosis was 10.2 ± 2.3 years, with an average diagnostic delay of 12.7 ± 13.7 months. At diagnosis, 37% presented with a multifocal disease course.
Mandibular biopsy was performed in 21 out of 35 patients — 15 using an intraoral approach, four extraorally, and in two cases the approach was undocumented. PCR testing was conducted in seven patients, with two testing positive. Bacterial cultures were obtained in 16 cases, with bacterial growth detected in 11. The most frequently identified bacteria were *Streptococcus viridans* and *Actinomyces spp*. (6/11 each).
Antibiotics were administered to 25 of 35 patients for a median duration of 18 days (range 4–233). The most prescribed antibiotic classes were penicillins (n=15), cephalosporins (n=6), and lincosamides (n=7). Other types were used less frequently or were not specified (n=8). During antibiotic therapy, three children experienced deterioration, six showed short-term improvement followed by MRI findings, and ten showed no change. Four children showed a sustained improvement, most likely due to concomitant treatment with NSAIDs. No information on improvement was available in one case. All patients required further treatment according to current guidelines to reach remission.
The delay in diagnosis tended to be longer in those who underwent biopsy (10.4 vs. 5.0 months, p=0.059). No significant differences were found regarding sex (p=0.942), multifocal presentation before biopsy (p=0.623), or antibiotic therapy (p=0.264). However, antibiotic use was significantly more frequent in patients who had undergone biopsy (90.5% vs. 42.9%, p=0.0056).
Conclusion: In summary, mandibular biopsy in children with CNO is associated with diagnostic delay and a significantly higher rate of antibiotic therapy. Other factors, such as sex, multifocal disease at diagnosis (before biopsy), or antibiotic use, did not significantly impact diagnostic delay. The microbiological results presented are consistent with those reported by Gaal et al (1). These findings highlight the diagnostic challenges in mandibular CNO and emphasize the importance of interpreting biopsy results with caution, especially when bacterial colonization may be misleading.
Disclosure
None declared

Reference
1. Gaal A, Basiaga ML, Zhao Y, Egbert M. Pediatric chronic nonbacterial osteomyelitis of the mandible: Seattle Children's hospital 22-patient experience. Pediatr Rheumatol Online J. 2020;18(1):4.

P108

Chronic recurrent multifocal osteomyelitis (crmo): two-year post-diagnosis outcomes in a prospectively identified inception cohort from the united kingdom and republic of Ireland

D. T. Chia[1], S. Sayers[1], A. P. Toms[2], A. Sanghrajka[3], A. V. Ramanan[4], O. G. Killeen[5], C. Ilea[6], C. E. Pain[7], S. Compeyrot-Lacassagne[8], K. Bailey[9], N. Martin[10], K. Armon[1,11], C. Suo[1]
[1]Department of Paediatrics, University of Cambridge, Cambridge, [2]Department of Radiology, [3]Department of Trauma and Orthopaedics, Norfolk and Norwich University Hospitals, Norwich, [4]Department of Paediatric Rheumatology, Bristol Royal Hospital for Children, Bristol, United Kingdom, [5]National Centre for Paediatric Rheumatology, Children's Health Ireland, Dublin, Ireland, [6]Department of Paediatrics, Royal National Orthopaedic Hospital, London, [7]Department of Rheumatology, Alder Hey Children's Hospital, Liverpool, [8]Department of Rheumatology, Great Ormond Street Hospital, London, [9]Department of Paediatric Rheumatology, Oxford University Hospitals, Oxford, [10]National Centre for Paediatric Rheumatology, Royal Hospital for Children, Glasgow, [11]Department of Paediatric Rheumatology, Cambridge University Hospitals, Cambridge, United Kingdom
Correspondence: D. T. Chia
Pediatric Rheumatology, **23(2):** P108

Introduction: Chronic Recurrent Multifocal Osteomyelitis (CRMO), also known as Chronic Non-Bacterial Osteomyelitis, is a rare autoinflammatory bone disorder primarily affecting children and adolescents. Data on short- to medium-term clinical outcomes remain limited to retrospective cohorts, commonly from specialist referral centres.
Objectives: To evaluate two-year clinical outcomes in a prospectively identified national cohort of patients diagnosed with CRMO across the United Kingdom (UK) and the Republic of Ireland (ROI).
Methods: A national prospective surveillance study was conducted between October 2020 to November 2022. Those under 16 years of age with a new diagnosis of CRMO were identified through monthly surveys sent via the British Paediatric Surveillance Unit and the British Society for Children's Orthopaedic Surgery to all paediatric consultants and paediatric orthopaedic consultants in the UK and ROI. Reporting clinicians completed standardised questionnaires at diagnosis (baseline), one-, and two-year follow-ups.

Results: During the 25-month surveillance period, 187 children and young people with confirmed CRMO were identified, with 6 patients reclassified later due to a change in diagnosis. Complete one- and two-year follow-up data were available for 153 of the remaining 181 patients (84.5%). The disease course reported at both year one and year two was similar with approximately a third in each category: 'Continuous', 'relapsing/remitting' and 'one-off episode'.
Over the two-year period, 75% were treated with NSAIDs and/or bisphosphonates only. Biologics were used in 15/146 (10.3%) of patients. Of these, 9/146 (6.2%) had an additional diagnosis and 12/146 (8.2%) were treated with TNF-alpha inhibitors.
At the two-year follow-up, 47.3% were off medications. Among those still on medication, 41.8% received NSAIDs, 17.1% bisphosphonates, 2.1% corticosteroids, 7.5% methotrexate, and 6.8% biologics. No significant difference in outcomes was observed between pamidronate and zoledronate.
Functional outcomes improved from presentation to two-year follow up: the proportion of patients reporting normal mobility increased from 68% to 79%, and full-time school attendance rose from 89% to 93%. CRMO-related hospital admissions declined from 37.1% to 2.7%. Similarly, emergency department attendances decreased from 62.8% to 1.3%. Reported complications over two years included fractures in 4.7% and bone deformities in 6.1%.
Conclusion: This is the first national inception cohort followed for two years. Most patients improved clinically, with reduced healthcare use, better mobility, and school attendance. Nearly half required no medication at two years; however, almost two-thirds had relapsing/remitting or persistent disease. Findings support favourable CRMO outcomes with current treatments, though a subset of patients require more intensive therapy.
Disclosure
None declared

P109

Scurvy mimicking chronic non-bacterial osteomyelitis in children with neurodevelopmental or behavioral conditions

D. Rouhani[1], Ö. Satirer[2], O. Buzoianu[2], S. Mikula[1], C. Reiser[2,3]
[1]Rheumatology Outpatient Clinic, St. Anna Children's Hospital, Vienna, Austria, [2]Autoinflammation
Reference Center Tübingen, University Hospital Tübingen, Tübingen, Germany, [3]State Hospital Bregenz, Bregenz, Austria
Correspondence: D. Rouhani
Pediatric Rheumatology, **23(2):** P109

Introduction: Chronic non-bacterial osteomyelitis (CNO) is a rare autoinflammatory bone disorder characterized by prolonged musculoskeletal pain and sterile bone inflammation. Its diagnosis relies on clinical presentation and imaging findings, often supported by whole-body MRI. Among these, scurvy—a rare but serious consequence of vitamin C deficiency—represents an important and well-recognized differential diagnosis, as also highlighted in current guidelines. Nevertheless, it remains underdiagnosed, particularly in at-risk pediatric populations.
Objectives: We present three pediatric cases in which scurvy closely resembled CNO in both imaging and clinical features. All affected children had underlying neurodevelopmental or neurological disorders, emphasizing the critical role of thorough nutritional assessment in children presenting with bone pain and imaging abnormalities suggestive of CNO.
Methods: This study presents a descriptive case series of three pediatric patients in two institutions. Clinical data were obtained from patient charts, including symptoms at presentation, diagnostic workup, therapeutic interventions, and short-term outcomes.
Results: Three children were referred for evaluation of persistent musculoskeletal pain and functional impairment. Two had autism spectrum disorder (ASD) and one had leukodystrophy. In the two most recent cases (diagnosed in 2024 and 2025), whole-body MRI revealed multifocal bone marrow edema and metaphyseal changes suggestive of CNO. In all three patients, a detailed dietary history revealed extremely selective food intake with little to no consumption of fresh fruits or vegetables. Clinical examination showed typical skin and gingiva manifestations. Laboratory testing confirmed severe vitamin C deficiency, with serum ascorbic acid levels below 0.5 mg/L. Following daily oral vitamin C supplementation, all patients experienced marked clinical improvement, and follow-up MRI showed resolution of bone lesions within six to twelve months. Non-steroidal anti-inflammatory drugs (NSAIDs) were administered occasionally for symptom relief.
Conclusion: Scurvy remains a relevant differential diagnosis in high-income countries, especially in children with neurodevelopmental or behavioral conditions that predispose to extreme dietary selectivity. Bone pain and MRI findings can resemble CNO, leading to misdiagnosis. In contrast to CNO, scurvy responds rapidly and completely to vitamin C supplementation, though imaging changes may lag behind clinical improvement. The presence of dermatological and intraoral signs, combined with restrictive eating, should prompt nutritional evaluation. In children with chronic musculoskeletal symptoms—particularly those with ASD, developmental delay, or neurological disorders—nutritional deficiencies must be considered. Early recognition and treatment are essential to avoid unnecessary interventions and ensure recovery. These cases highlight the need for interdisciplinary collaboration in assessing children with unexplained bone pain.
Disclosure
None declared

P110

Validation of the eular/acr classification criteria for chronic nonbacterial osteomyelitis in a pediatric cohort

D. Unal[1], Y. Demir Yigit[2], O. Basaran[1], A. Elcin Yildiz[3], Y. Bayindir[1], V. Cam[1], H. Ercan Emreol[1], M. O. Erkan[1], O. Necipoglu Banak[1], E. Sag[1], Y. Bilginer[1], U. Aydingoz[3], S. Ozen[1]
[1]Pediatric Rheumatology, Hacettepe University, [2]Pediatric Rheumatology, Firat University, [3]Department of Radiology, Hacettepe University, Ankara, Türkiye
Correspondence: D. Unal
Pediatric Rheumatology, **23(2):** P110

Introduction: Chronic nonbacterial osteomyelitis (CNO) is a rare autoinflammatory bone disorder primarily affecting children and adolescents. An international consensus group developed the EULAR/ACR Classification Criteria in order to define a homogeneous group of patients diagnosed with CNO.
Objectives: This study aims to validate these criteria in a diverse pediatric cohort and compare their performance with the Jansson and Roderick diagnostic criteria.
Methods: A retrospective evaluation was conducted on 78 pediatric CNO patients and 99 mimickers in Hacettepe University department of pediatric Rheumatology from 2020 to 2024. Demographic, clinical, laboratory, and imaging data were analyzed, and the sensitivity, specificity, and predictive values of the EULAR/ACR criteria were assessed. Statistical comparisons were made against the Jansson and Roderick criteria.
Results: The EULAR/ACR criteria demonstrated high accuracy, with a sensitivity of 92.68% and specificity of 97.89%, outperforming the Jansson criteria (sensitivity: 88.46%, specificity: 72.73%) and aligning closely with the Roderick criteria (sensitivity: 96.15%, specificity: 96.97%). Key distinguishing features included multifocal and symmetric lesions, frequent involvement of high-scoring anatomical sites (e.g., clavicle and mandible), and the absence of exclusion criteria such as fever and markedly elevated inflammatory markers.
Conclusion: The newly validated EULAR/ACR classification criteria for pediatric CNO demonstrated high specificity and good sensitivity in our cohort. Their application facilitates the identification of homogeneous patient populations, aiding in research consistency and the development of standardized approaches to CNO classification and management.
Disclosure
None declared

References

1. Jansson A, Renner ED, Ramser J, Mayer A, Haban M, Meindl A, et al. Classification of non-bacterial osteitis: retrospective study of clinical, immunological and genetic aspects in 89 patients. Rheumatology (Oxford). 2007;46(1):154-60.

2. Roderick MR, Shah R, Rogers V, Finn A, Ramanan AV. Chronic recurrent multifocal osteomyelitis (CRMO) - advancing the diagnosis. Pediatr Rheumatol Online J. 2016;14(1):47.
3. Zhao Y, Oliver MS, Schnabel A, Wu EY, Wang Z, Marino A, et al. EULAR/ACR classification criteria for paediatric chronic nonbacterial osteomyelitis (CNO). Annals of the Rheumatic Diseases. 2025.

P111

Clinical and imaging evolution in pediatric chronic non-bacterial osteomyelitis: insights from serial whole-body MRI

K. Chiotopoulou[1], K. Liontou[1], S. Proutzos[2], A. Chira[1], K. Kourtesi[1], O. Papakonstantinou[2], L. Fotis[1]
[1]3rd Department of Pediatrics, [2]Department of Radiology, ATTIKON General Hospital, National and Kapodistrian University of Athens, Athens, Greece
Correspondence: L. Fotis
Pediatric Rheumatology, **23(2):** P111

Introduction: While whole-body magnetic resonance imaging (WBMRI) is central to diagnosing Chronic Non-Bacterial Osteomyelitis (CNO), longitudinal imaging data and predictors of treatment intensity remain limited.
Objectives: This study aimed to describe the clinical characteristics, treatment outcomes, and MRI-based prognostic indicators in children with CNO.
Methods: We conducted a retrospective study of pediatric patients diagnosed with CNO in our center. Out of 52 total patients, 23 had available follow-up WBMRI and were included in this analysis. Demographic, clinical, therapeutic, and imaging data were reviewed, including lesion counts on both initial and follow-up MRIs.
Results: Among the 23 patients (12 females, 11 males), median age at diagnosis was 11 years (range 3.8–14.7), with a 12-month diagnostic delay (range 0.4–99.5). The median interval between MRIs was 13.1 months (range 2.9–67.1). All patients were symptomatic at baseline. Median lesion count decreased from 6(range 1–21) to 4 (range 0–15). Despite clinical improvement (69.6% asymptomatic), only 1 patient (4.3%) achieved full remission (symptom- and lesion-free). Subclinical inflammation persisted in 65.2%.
Eleven patients (48%) received only NSAIDs; 12 escalated to second-line therapy. Among them, 2 received biologics only, 2 DMARDs only, and others various combinations. Biologic users had higher baseline lesions (12 vs 5, p=0.06). A threshold of ≥10 lesions predicted biologic and bisphosphonate use (sensitivity 71%, specificity 88%, AUC 0.81). No treatment subgroup showed statistically superior lesion reduction.
Lesion reduction was greater with biologics (–5.4) vs NSAIDs (–1.0), with this difference approaching statistical significance (p=0.076). A similar trend was observed in bisphosphonates (–4.3 vs –1.0), though not statistically significant (p = 0.53). No difference was found between biologics and bisphosphonates (–5.4 vs –4.3) (p=1.0).
Conclusion: Serial whole-body MRI provides essential insights into disease progression and therapeutic response to CNO. A lesion count ≥10 at baseline may guide early treatment escalation. Among patients receiving second-line therapy beyond NSAIDs, lesion reduction was greater in those treated with biologic agents or bisphosphonates compared to NSAIDs only, although differences did not reach statistical significance.
MRI often detects persistent inflammation despite clinical remission, reinforcing its role in long-term disease monitoring and therapeutic decision-making.
Disclosure
None declared

References

1. Jansson AF, Müller I, Glaser C, Bachmann CJ, Blum WF, Koitschev A, Horger M, Hufnagel M. Long-term clinical course of chronic nonbacterial osteomyelitis and association with radiologic findings. *J Rheumatol*. 2015;42(8):1478–1485. doi:https://doi.org/10.3899/jrheum.141026
2. Kaut S, Van den Wyngaert I, Christiaens D, Jansen S, Van Eygen K, Vanhoenacker F, François G. Chronic nonbacterial osteomyelitis in children: a multicentre Belgian cohort of 30 children. *Pediatr Rheumatol*. 2022;20(1):98. doi:https://doi.org/10.1186/s12969-022-00698-3

P112

Grisel syndrome in pediatric rheumatic diseases: a rarely recognized complication

L. Koru, F. Haslak
Pediatric Rheumatology, Istanbul Medeniyet University, Istanbul, Türkiye
Correspondence: L. Koru
Pediatric Rheumatology, **23(2):** P112

Introduction: Grisel syndrome (GS) is a rare condition of non-traumatic atlantoaxial subluxation following infections or head and neck surgery in childhood. However, it may also develop due to inflammatory arthritis.
Objectives: We aimed to discuss two cases: one involving a patient with juvenile idiopathic arthritis (JIA) and another with familial Mediterranean fever (FMF), both of whom presented with torticollis and were subsequently diagnosed with GS.
Methods: Case 1: A 4.5-year-old girl presented with 3-month right knee swelling and 2-week progressive neck pain and torticollis. There was no history of infection, trauma, or surgery. Physical exam showed restricted cervical motion and right knee effusion. Laboratory tests revealed mildly elevated inflammatory markers (C-reactive protein (CRP): 7.5 mg/L, erythrocyte sedimentation rate (ESR: 39 mm/h)) and antinuclear antibody (ANA) positivity. Magnetic resonance imaging (MRI) revealed synovitis in the knee and atlantoaxial subluxation with joint effusion. Despite no visual symptoms, ophthalmologic screening showed bilateral anterior uveitis. The patient was diagnosed with ANA-positive oligoarticular JIA and treated with oral corticosteroids, methotrexate, topical ophthalmic drops, and a soft cervical collar.
Case 2: An 8-year-old girl with a known diagnosis of FMF presented with a 20-day history of neck pain exacerbated by movement. There was no history of infection or trauma. Despite regular colchicine, she experienced attacks every three months. Physical examination was unremarkable except for restricted cervical motion. Laboratory tests showed elevated CRP (75 mg/L), ESR (89 mm/h), and SAA (226 mg/L). MRI demonstrated atlantoaxial subluxation accompanied by joint effusion. A cervical collar was applied and colchicine dose was increased. Clinical and radiological improvement was achieved within one month. Two years later, atlantoaxial subluxation accompanied by joint effusion was repeated. Anti-interleukin-1(IL-1) therapy was initiated.
Results: In Case 1, neck pain and torticollis resolved within one month after anti-inflammatory treatment and cervical collar use. Cervical and joint mobility normalized, with no recurrence during follow-up. In Case 2, improvement occurred after colchicine dose adjustment and conservative management. However, GS repeated two years later. After anti-IL-1 therapy initiation, the patient remained symptom-free for two years.
Conclusion: In both cases, atlantoaxial subluxation occured due to joint inflammation, and improvement was achieved with anti-inflammatory treatment and cervical collar use. Consent to published had been obtained.
Disclosure
None declared

References

1. Rinaldo A, Mondin V, Suárez C, Genden EM, Ferlito A. Grisel's syndrome in head and neck practice. Oral Oncol. 2005 Nov 1;41(10):966–70.
2. Bocciolini C, Dall'olio D, Cunsolo E, Cavazzuti PP, Laudadio P. Grisel's syndrome: a rare complication following adenoidectomy Una rara complicanza dopo adenoidectomia: la sindrome di Grisel. ACTA OTORHINOLARYNGOL ITAL. 2005;25:245–9.
3. Ortiz GL, Pratts I, Ramos E. Grisel's syndrome: An unusual cause of Torticollis. J Pediatr Rehabil Med. 2013;6(3):175–80.

P113

Autosomal dominant early-onset osteoporosis due to heterozygous wnt1 mutation: variable phenotypic expression across three generations

E. Freitas[1], B. Pedreira[2], I. N. Marques[3], I. Madureira[3], C. Henriques[3], M. P. Ramos[3], C. Limbert[4], M. Venâncio[5], M. Conde[3]

[1]Department of Pediatrics, Hospital de Dona Estefânia, ULS São José, Lisbon, [2]Department of Pediatrics, Hospital Nélio Mendonça, Funchal, [3]Unit of Pediatric Rheumatology, Department of Pediatrics, [4]Unit of Pediatric Endocrinology, Department of Pediatrics, [5]Department of Genetics, ULS São José, Hospital de Dona Estefânia, ULS São José, Lisbon, Portugal
Correspondence: M. Conde *Pediatric Rheumatology*, **23(2):** P113

Introduction: Early-onset osteoporosis in children is a rare condition characterized by skeletal fragility, low bone mass, and recurrent fractures. While growth is typically preserved, phenotypic variability has been observed. Mutations in the *WNT1* gene have been identified as a cause of an autosomal dominant form of the disease.
Objectives: To describe the clinical, radiological and genetic features of two sisters with early-onset osteoporosis due to a heterozygous WNT1 mutation, and the identification of the same mutation in other symptomatic family members.
Methods: Retrospective review of medical records including clinical presentation, laboratory work-up, imaging, and genetic testing.
Results: The index case, a girl now 8 years old, with growth deceleration since 18 months (height < 3rd percentile) and was first evaluated at 4.5 years for recurrent arthralgia in hands, knees, and feet from age 2, responsive to NSAIDs. Examination revealed generalized joint hypermobility and a positive Adams test, but no arthritis. Laboratory work-up showed vitamin D deficiency, with normal endocrine tests and negative inflammatory and autoimmune markers. Radiographs showed diffuse osteopenia and thoracic scoliosis. Genetic testing identified a likely pathogenic heterozygous WNT1 c.610G>T (p.Gly204*) mutation and a variant of uncertain significance in FBN2 (p.Arg126His). Baseline DXA showed a lumbar spine Z-score of –3.7. She started calcium/vitamin D suplementation and was initially treated with alendronate, stopped after 8 months due to gastroesophageal reflux. Zoledronic acid was initiated at age 7.
Her, now 13 year-old sister, had two low-impact fractures and, since age 9, daily plantar and calcaneal pain, worsened by weight-bearing and responsive to NSAIDs. Physical examination and laboratory work-up were unremarkable. Radiographs showed osteopenia. Genetic testing confirmed the same *WNT1* mutation. Baseline DXA revealed a lumbar spine Z-score of –3.8. She started calcium/vitamin D and alendronate, later switched to zoledronic acid at age 12. Both sisters wait follow-up DXA at 1 year of treatment.
Following their diagnoses, their previously asymptomatic father began experiencing foot fractures. A history of adolescent-onset fractures was also recalled in their paternal grandmother. Both carried the same *WNT1* mutation, confirming autosomal dominant inheritance.
Conclusion: This familial case of autosomal dominant early-onset osteoporosis across three generations linked to a heterozygous *WNT1* c.610G>T mutation, illustrates the phenotypic variability of this genetic disease. The growth failure in the younger sister remains unexplained and may represent a novel manifestation associated with disease, warranting further investigation. Consent to published had been obtained.
Disclosure
None declared

P114

Misdiagnosed osteoid osteoma: challenges in pediatric rheumatology

S. M. Orsi[1], S. Palmeri[1,2], L. Anfigeno[3], A. Consolaro[1,2], M. B. Michelis[4], A. Ravelli[5], M. B. Damasio[3], M. Gattorno[2], R. Caorsi[2]
[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Università degli Studi di Genova, [2]UOC Reumatologia e Malattie Autoinfiammatorie, [3]Pediatric Radiology Department, [4]Department of Pediatric Orthopedics, [5]Direzione Scientifica, UOC Servizio Sperimentazioni Cliniche pediatriche, IRCCS Istituto Giannina Gaslini, Genova, Italy
Correspondence: S. M. Orsi
Pediatric Rheumatology, **23(2):** P114

Introduction: Osteoid osteoma (OO) is a benign osteoblastic bone tumor that typically affects adolescents and young adults, more commonly males. It usually presents with nocturnal pain that responds well to NSAIDs. While most OOs are located in the metaphysis or diaphysis of long bones, atypical intra- or peri-articular localizations are not uncommon and can lead to diagnostic challenges due to atypical clinical and radiologic features. These atypical cases may mimic inflammatory arthropathies such as juvenile idiopathic arthritis (JIA), leading to diagnostic delay and inappropriate treatment.
Objectives: To describe a pediatric case series of OO with a focus on intra- and peri-articular localizations, clinical presentation, diagnostic pitfalls, and the role of imaging in differentiating OO from inflammatory arthritis.
Methods: We retrospectively reviewed clinical data from all patients diagnosed with OO at Istituto Giannina Gaslini (Genoa, Italy) between January 2015 and May 2024. Data collected included: age at onset, sex, site of lesion, symptoms at onset, inflammatory markers, imaging, misdiagnoses, time to diagnosis, treatment, and recurrences.
Results: A total of 11 patients were identified (3 males, 8 females; mean age 12.8 years). Lesions were located in the femur (5), humerus (2), vertebrae (2), tibia (1), and acetabulum (1). Eight patients had intra- or peri-articular localizations and presented with joint pain; of these, 3 had joint swelling and 4 had functional limitation. One patient had concomitant rheumatoid arthritis. All but one reported nocturnal pain. Inflammatory markers were elevated in only 2 cases. A total of 8 patients (72%) were initially misdiagnosed, with a mean diagnostic delay of 8.4 months, longer in intra/peri-articular cases. Misdiagnoses included post-traumatic arthritis, JIA, and scoliosis. MRI was often misleading due to bone edema, while CT was diagnostic in all cases. All patients were treated initially with NSAIDs and underwent radiofrequency or surgical ablation. One patient underwent an intra-articular steroid injection, with transient benefit. Only one patient experienced a recurrence.
Conclusion: Intra- and peri-articular OO can mimic inflammatory arthritis, often leading to diagnostic delay and inappropriate treatment. Atypical presentations, including joint swelling and lack of classic radiologic features, complicate the differential diagnosis with JIA. MRI may overestimate inflammatory findings, while CT remains the gold standard for diagnosis. OO should be considered in cases of persistent monoarthritis unresponsive to conventional treatment, especially when pain is nocturnal and imaging is inconclusive.
Disclosure
None declared

P115

Prevalence of low bone mineral density and developing a nomogram for its early identification in children with juvenile idiopathic arthritis

S. Kalsotra[1], N. K. Bagri[1], V. Jain[1], M. Jana[2], Y. Gupta[3], M. A. Khan[4], S. K. Das[4]
[1]Paediatrics, [2]Radiodiagnosis, [3]Endocrinology, [4]Biostatistics, AIIMS NEW DELHI, Delhi, India
Correspondence: S. Kalsotra
Pediatric Rheumatology, **23(2):** P115

Introduction: Juvenile idiopathic arthritis (JIA) affects bone health. Various factors in JIA, such as inflammation, disease activity, and limited mobility, contribute to low bone mineral density (BMD). Low BMD has a long-term implication in children with JIA, making them susceptible to fractures. There is a paucity of data on the prevalence and risk factors for low BMD in children with JIA. Though DXA is a preferred modality for identifying low BMD; however, given its accompanying radiation exposure, there is a need for guidance to optimize its rational use for identifying low BMD.
Objectives: To determine the prevalence and risk factors associated with low BMD in children with JIA. Using the factors associated with low BMD, we aim to develop a nomogram to predict the risk of osteoporosis in children with JIA.
Methods: This cross-sectional study was conducted at the Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi. All children diagnosed with JIA as per ILAR criteria were screened. Children aged 5-18 years with JIA and a disease more than one year were included. Children with a history of bisphosphonate intake, bone damage due to infection, trauma, and JIA with overlap syndrome were excluded. Demographic details, clinical assessments, and laboratory investigations were recorded. Disease activity and functional disability

were assessed using the cJADAS-10 and Steinbrocker, respectively. BMD was measured using DXA of the lumbar spine and left femoral neck, which was height-adjusted. Height adjustment ensures that children are evaluated based on their growth patterns. Low HA-BMD was defined as a Z-score ≤ - 2 SD at either of the two sites. Analysis was done using Stata 14.0 statistical software (Stata Corp, TX, USA). Stepwise multivariable logistic regression was done to identify factors associated with low HA-BMD.
Results: 101 children were enrolled in this study. The prevalence of low HA-BMD in our study population was 28.7% (29/101). On multivariable regression analysis, the higher cJADAS-10 score, Steinbrockers class, and systemic JIA were independently associated with low BMD. Using these factors, a nomogram to predict the probability of low BMD was developed. This nomogram quantifies the risk and predicts the likelihood of low BMD by assigning scores to each parameter and calculating a total score. The area under the ROC curve is 0.7883.
Conclusion: Significant children with JIA have low HA-BMD. Screening the children with identified risk factors might help in early identification and prevent long-term skeletal complications.
Disclosure
None declared

P116

Prognostic value of biomarkers of bone metabolism in assessing the risk of osteopenia in children with juvenile idiopathic arthritis

S. Samsonenko, S. Ilchenko, O. Makoviichuk
Dnipro State Medical University, Dnipro, Ukraine
Correspondence: S. Samsonenko
Pediatric Rheumatology, **23(2):** P116

Introduction: Juvenile idiopathic arthritis (JIA) continues to be a significant medical and social concern worldwide. One of its potential complications is the onset of osteopenic syndrome (OS), which may eventually progress to osteoporosis. Conventional laboratory diagnostic approaches often yield results within normal ranges for extended periods, making them ineffective for early detection of OS before clinical symptoms of bone metabolism impairment appear. Additionally, current imaging techniques used to measure bone mineral density (BMD) do not provide insights into the rate or nature of bone metabolic activity. Consequently, evaluating biochemical markers of bone turnover (BTMs) is a valuable complement for the early identification of OS in children with JIA.
Objectives: *was to determine the diagnostic value of bone metabolism markers for predicting the risk of osteopenic syndrome in children with JIA.*
Methods: A total of 50 children with juvenile idiopathic arthritis (JIA), aged between 5 and 18 years, were included in the study. In addition to standard clinical laboratory tests, specific analyses were conducted to measure serum levels of 25-hydroxyvitamin D (25(OH)D), osteocalcin, and the bone resorption marker β-CrossLaps (β-CTX) using enzyme-linked immunosorbent assay (ELISA). Instrumental diagnostics involved evaluating bone mineral density (BMD) with the use of a Sunlight Omnisense 9000 ultrasonic densitometer.
Results: A total of 42% of children with juvenile idiopathic arthritis (JIA) were found to have osteopenic syndrome (OS) of varying severity. Analysis of serum 25(OH)D levels, a key diagnostic marker for OS, showed significantly lower concentrations in children with OS compared to those without (17.5 [15.7; 23.6] vs. 34.1 [22.8; 39.2] ng/mL; $p<0.05$). Osteocalcin levels were also markedly reduced in the OS group (6.7 [3.9; 11.5] vs. 14.9 [9.2; 20.9] ng/mL; $p<0.05$), whereas the bone resorption marker β-Cross Laps was significantly elevated (1.83 [1.48; 2.27] vs. 0.95 [0.78; 1.52] ng/mL; $p<0.05$).
Correlation analysis revealed a positive relationship between osteocalcin levels and both the densitometry Z-score ($r = 0.44$, $p<0.05$) and serum 25(OH)D ($r = 0.60$, $p<0.05$), along with negative correlations with disease activity ($r = -0.88$, $p<0.05$) and the number of active joints ($r = -0.29$, $p<0.05$). Similarly, β-Cross Laps levels negatively correlated with both Z-score ($r = -0.42$, $p<0.05$) and 25(OH)D ($r = -0.40$, $p<0.05$).
ROC analysis identified optimal diagnostic thresholds for OS risk in JIA patients: β-Cross Laps levels above 1.7 ng/mL (sensitivity 61.9%, specificity 89.7%, diagnostic efficiency 78.0%) and osteocalcin levels below 8.7 ng/mL (sensitivity 66.7%, specificity 75.9%, diagnostic efficiency 72.0%).
Conclusion: In children with juvenile idiopathic arthritis and osteopenic syndrome, there was a significant increase in the level of β-Cross Laps and a decrease in osteocalcin in the blood serum, which correlated with densitometry indices, 25(OH)D level and disease activity. Certain threshold values for β-Cross Laps (>1.7 ng/ml) and osteocalcin (<8.7 ng/ml) can serve as markers for early diagnosis of the risk of developing osteopenia in children.
Disclosure
None declared

P117

Use of molecular genetic tests to determine etiology in patients with limited joint mobility

F. M. Bedel, A. Adrovic
Erzurum City Hospital, Erzurum, Türkiye
Correspondence: A. Adrovic
Pediatric Rheumatology, **23(2):** P117

Introduction: Although rheumatologic diseases are mostly responsible for the joint pain and limited range of motion (ROM) in childhood, rare congenital bone and cartilage disorders can also be the etiological cause. These rare diseases represent a heterogeneous group including Stickler Syndrome, Kneest Syndrome, Progressive Pseudo-Rheumatoid Dysplasia, Congenital Contractural Arachnodactyly, and microdeletion syndromes.
Objectives: The aim was to perform further investigation for underlying genetic conditions in children with joint complaints and dismorphic features.
Methods: A total of 8 (2 females, 6 males) subjects who were referred to pediatric genetics due to joint pain and limited ROM and dismorphic features were included. All of them were previously evaluated by the pediatric rheumatologist and none underlying rheumatologic disease was registered. In one family, fitrst the pediatric patient has been identified (patient no.2). Furtherly, 3 adult family members were detected (patients no. 3,4,5). Whole exome sequencing (WES) was performed in 7 and chromosomal microarray test was performed in 1 patient.
Results: A patologic variant in fibrillin-2 gene (FBN2) was detected in 5 patients. In one patient, a variant in the
discoidin domain receptor tyrosine kinase 2 (DDR2) gene that we considered disease causative was detected. In a patient with chromosomal microarray test, 18p 11.32 deletion was registered.
All of the patients had musculoskeletal complaints (joint pain, limited ROM, joint swelling) and dismorphic features (microcephaly, hypertelorism, saddle nose, low set ears, etc). A patient with DDR2 mutation had additional mental-motor retardation while the one with 18p 11.32 deletion had puberty precocious.
Conclusion: In patients with joint findings and no pathology observed in rheumatological evaluation, genetic tests should be performed to determine the etiology by evaluating dysmorphic findings. Although single-gene diseases can be seen more frequently, it should not be forgotten that microdeletion syndromes can also be the cause in rare cases.
Disclosure
None declared

References

1. Huang Y, Fang X, Ma L, Zhang J, Wang C, Gao T, Peng D. FBN2 pathogenic mutation in congenital contractural arachnodactyly with severe skeletal manifestations. Mol Genet Metab Rep. 2025 Jan 22;42:101193. doi: https://doi.org/10.1016/j.ymgmr.2025.101193. PMID: 39911746; PMCID: PMC11795632.
2. Summers KM. Genetic models of fibrillinopathies. Genetics. 2024 Jan 3;226(1):iyad189. doi: https://doi.org/10.1093/genetics/iyad189. PMID: 37972149; PMCID: PMC11021029.
3. Uludağ Alkaya D, Kasapçopur Ö, Bursalı A, Adrovic A, Demir B, Aykut A, Tüysüz B. Specific early signs and long-term follow-up findings of progressive pseudorheumatoid dysplasia (PPRD) in the Turkish cohort. Rheumatology (Oxford). 2022 Aug 30;61(9):3693-3703. doi: https://doi.org/10.1093/rheumatology/keab926. PMID: 34919662.

P118

Diagnostic efficiency of 65-gene panel in patients with suspected monogenic autoinflammatory diseases. russian cohort results

M. Beketova[1], S. Salugina[1], E. Fedorov[1], I. Nikishina[1], A. Torgashina[1], E. Zakharova[2], N. Milovanova[2], A. Lila[1]
[1]V.A. Nasonova Research Institute of Rheumatology, [2]Research Center of Medical Genetics, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P118

Introduction: The spectrum of monogenic autoinflammatory diseases (mAIDs) is quite wide in clinical manifestations, which leads to difficulties in its differential diagnosis. Results of using a gene panel testing with different composition of studied genes is published by various centers.
Objectives: to present results of the application of genetic testing on 65-gene panel in patients (pts) with suspected mAIDs
Methods: 103 pts with suspected mAIDs, who were examined previously in V.A. Nasonova Research Institute of Rheumatology, underwent genetic analysis using NGS with 65-gene panel in Research Centre for Medical Genetics from Mar 2021 to June 2023. Median age 10 [0.7–14] yrs, 89% of them were children; M:F=1:1,2. Inclusion criteria were: presence of systemic inflammation signs, absence of response to previous therapy. The identified genetic variants were assessed using the ACMG criteria.
Results: Genetic mutations were detected in 37 patients (36%). Median age of the onset was 9[5-14], M:F=1:1,3. 31 monogenic (9 in gene MEFV, 4 – NOD2, 3 – NLRP3, 2 - TNFRSF1A, MVK, RAG1, NLRP1, ADA2, and 1 - IFIH1, NLRP12, UNC13D, RIPK1, IL36RN) and 6 digenic/oligogenic mutations (2 - MEFV/TNFRSF1A, 1 - MEFV/MVK/TNFAIP3, NOD2/MEFV, MEFV/NLRP12, SH2D1A/TNFAIP3) were detected. According to the ACMG criteria, 16 cases (43%) were classified as pathogenic or likely pathogenic variants (6 – MEFV, 3 – MVK, 2 – RAG1, ADA2, NOD2, 1 – IL36RN). Variants of uncertain significance were detected in 46% cases (including 5 cases of p.K695R in gene MEFV), benign/likely benign – 32%. The most frequent symptoms were fever (89%; periodic fever 72%), arthralgia (65%; arthritis 35%), skin lesions (60%), CNS involvement (27%), myalgia (27%) and lymphadenopathy (24%). Other symptoms were not so common. Laboratory inflammatory activity was presented in 86%. Median CRP was 44 [15.35–115.35] mg/L.
Conclusion: Molecular genetic testing with 65-gene panel was positive in a third of patients with suspected monogenic AIDs in the Russian cohort. 43% identified variants were pathogenic or likely pathogenic, accordingly, the diagnostic efficiency was 15%. However, despite the fact that the expansion of the gene panel leads to greater diagnostic value and diversity, the most frequently genetic variants were from the group of main mAIDs (FMF, TRAPS, CAPS, MKD, syndrome Blau). Nonetheless, autoinflammatory phenotype patients with negative gene panel result require further testing, including WES/WGS, to detect rarer causes of the condition.
Disclosure
None declared

Reference

1. Le Goueff A, Smits G, Delaunoy M, Vandernoot I, Vandergheynst F. Genetic testing in autoinflammatory diseases - past, current and future perspectives. Eur J Intern Med. 2022;106:71-79. doi: https://doi.org/10.1016/j.ejim.2022.08.020

P119

MAN1B1 mutations and glycosylation disorder: a new cause of monogenic lupus?

P. Morán Álvarez[1], M. Freppel[1], J. Sormani[1], H. Reumaux[2], N. Pottier[3], J. Claise[4], F. Huet[4], M. Nallet-Amate[4], M. Jouret[1], M. Tusseau[1], A. Belot[1]
[1]Hospices Civils de Lyon, Lyon, [2]Pediatric Rheumatology, [3]CHU Lille, Lille, [4]CHU Dijon, Dijon, France
Correspondence: P. Morán Álvarez
Pediatric Rheumatology, **23(2):** P119

Introduction: Monogenic lupus, a specific form of lupus caused by single-gene mutations, has been reported to be associated with a broad range of metabolic disorders, including prolidase deficiency, chronic granulomatous disease and congenital disorders of glycosylation (CDG). While CDG-associated monogenic lupus has already been described, this association has been exclusively linked to *MAN2B1* mutations.
Objectives: To describe the first two cases of monogenic lupus associated with CDG caused by the same homozygous c.1833_1834del (p.Asp613fs) mutation in the *MAN1B1* gene.
Methods: Genetic, clinical and laboratory data, as well as therapeutic strategies, were retrospectively collected from two patients with MAN1B1-CDG who developed lupus.
Results: Patient 1, a 6-year-old female firstborn child of non-consanguineous parents, with genetically confirmed MAN1B1-CDG (homozygous frameshift mutation c.1833_1834del, p.Asp613fs), characterized by developmental delay and characteristic facial dysmorphisms, developed lupus symptoms. She presented with chilblains and malar rash in the presence of ANA, anti-dsDNA, and anti-Rib-P. She exhibited elevated type-I interferon signature (IS) at 50.9 (nv <2.3). Isoelectric focusing of transferin confirmed the diagnosis. A treatment with hydroxychloroquine (HCQ) was started, with positive response.
Patient 2, a 7-year-old female of Sudanese origin born to consanguineous parents, with a diagnosis of MAN1B1-CDG presented with severe multisystem involvement, including pancytopenia, diffuse alveolar hemorrhage, nephritis (24h-proteinuria of 1 g) and neurological manifestations (white matter hyperintensities). Laboratory findings revealed positive ANA, anti-dsDNA, anti-Sm, anti-Ro, anti-La, anti-C1q, RF with low C3 and C4 levels. She also showed elevated IS (13.6) and the same *MAN1B1* mutation. She required intensive care and multiple immunosuppressive therapies (glucocorticoids, HCQ, cyclophosphamide, mycophenolate, plasma exchange, extracorporeal membrane oxygenation and anti-CD20) resulting in favorable clinical and biochemical response.
Conclusion: This report highlights the novel association between MAN1B1-CDG and monogenic lupus. α1,2-mannosidase participates in the retrograde transport of misfolded proteins from the Golgi to the endoplasmic reticulum by interacting with the gamma subunit of coat protein complex I (COPI). COPI mediates STING retrieval from the Golgi, a crucial negative regulatory mechanism under homeostatic conditions. MAN1B1 deficiency may impair COPI function, leading to STING accumulation and overactivation of the type-I IFN pathway, contributing to autoimmune dysregulation and lupus development. Further research is necessary to elucidate the precise mechanisms linking *MAN1B1* mutations to SLE.
Disclosure
None declared

References

1. Han Y, Zhou Y, Pan J et al. MAN2B1 in immune system-related diseases, neurodegenerative disorders and cancers: functions beyond α-mannosidosis. *Expert Rev Mol Med*. 2025
2. Pan S, Cheng X, Sifers RN. Golgi-situated endoplasmic reticulum α−1, 2-mannosidase contributes to the retrieval of ERAD substrates through a direct interaction with γ-COP. *MBoC*. 2013

P120

Human beta 2 defensin levels in patients with immunoglobulin a vasculitis

D. Alkan[1], R. B. Us[2], A. Alkaya[1], A. Sen[1], T. Gundogdu[1], B. Demirbas[1], C. Dinler Yarasir[1], N. G. Kocamaz[1], E. Arslanoglu Aydin[1], E. N. Sunar Yayla[1], P. N. Akpınar Tekgöz[1], E. Baglan[1], S. Ozdel[1]
[1]Paediatric Rheumatology, [2]Biochemistry, Etlik Integrated Health Campus, Ankara, Türkiye
Correspondence: D. Alkan *Pediatric Rheumatology*, **23(2):** P120

Introduction: Immunoglobulin A vasculitis (IgAV), is the commonest form of systemic vasculitis in children. It may affect various systems but oftenly presents with palpable purpura in addition to gastrointestinal system, musculoskeletal system or genitourinary system (1).
Human Beta Defensin-2 (hBD-2) is the first inducible anti-microbial peptide (2) which is primarily synthesized in the gastrointestinal tract (3) elevated through inflammation both in acute infection and other diseases such as cystic fibrosis (4).

Objectives: Our primary objective is to determine whether hBD-2 levels differ between children with IgAV and healthy controls. Our secondary aim was to compare hBD-2 levels in children with IgAV with gastrointestinal (GI) and/or genitourinary (GU) involvement and those with skin and joint involvement only.
Methods: The study included 45 children diagnosed with IgAV who presented to our pediatric rheumatology clinic and 35 healthy controls. Blood samples for hBD-2 measurement were collected from patients prior to steroid administration, if used. Healthy controls had no infections and had not used antibiotics or steroids in the week prior to sampling. Patients with IgAV were divided into two groups according to steroid use and baseline laboratory parameters and hBD-2 levels were compared. Patients were also grouped by age (<10 and ≥10 years) to compare hBD-2 levels. Human Beta Defensin-2 ELISA kits were provided by E-Lab Science™. We used SPSS v28 for statistical analysis.
Results: IgAV onset was spontaneous in 8 patients (18.2%), while potential triggers included upper respiratory infections (URTI) (23, 52.3%), gastroenteritis (5, 11.4%), lymphadenitis or trauma (3 each, 6.8%), and skin infection or preseptal cellulitis (1 each, 2.3%). The hBD-2 levels of patients with IgAV (median:10410 pg/dl);min-max: 6410-55614 pg/dl) were higher than in healthy controls (median:8662 pg/dl; min-max: 5438-18303 pg/dl) (p=0.005). Among IgAV patients, hBD-2 levels were higher in patients who were 10 years or older (p=0.008). Additionally, hBD-2 levels were higher in patients with a history of URTI prior to the onset of the disease compared to those with spontaneous IgAV (p=0.015).
Conclusion: Patients with IgAV had higher blood hBD-2 levels than healthy controls. Furthermore hBD-2 levels in IgAV patients who are older than 10 years were higher. That age difference was not observed in the healthy control group. Despite the control group had a higher median age and patients who are older had higher hBD-2 levels, it's outstanding that we have found hBD-2 levels higher in IgAV group than the healthy control group. Additionally, patients who suffered from URTI had higher hBD-2 levels than the spontaneous group. Despite URTI is the most common predisposing factor in our study group, it only covered half of the cases. These results indicate that elevation of hBD-2 levels in IgAV patients doesn't necessarily correlate with age or infection alone, and it may serve as a marker for the disease.
Disclosure
None declared

References

1. Oni L, Sampath S. Childhood IgA Vasculitis (Henoch Schonlein Purpura)-Advances and Knowledge Gaps. Front Pediatr. 2019 Jun 27;7:257.doi: https://doi.org/10.3389/fped.2019.00257. ü2. Harder J. et al. A peptide antibiotic from human skin.Nature 1997;387:861.3. O'Neil DA. Regulation of expression of beta-defensins: endogenous enteric peptide antibiotics. Mol Immunol. 2003 Nov;40(7):445-50. doi: https://doi.org/10.1016/s0161-5890(03)00161-4.
2. Dalcin D et al. the Role of Human Beta-Defensin-2 in Pseudomonas aeruginosa Pulmonary Infection in Cystic Fibrosis Patients. Infect Dis Ther.2013 Dec;2(2):159-66. doi: https://doi.org/10.1007/s40121-013-0015-5.

P121

JIA T cells use cysteine instead of cystin porters to produce glutathione and control ferroptosis at the site of inflammation

C. Neullens[1], S. H. Subramanyam[1], J. V. Loosdregt[2], B. Vastert[2], K. Ohl[3], K. Tenbrock[1]
[1]Translational Pediatric Rheumatology, RWTH Aachen, Aachen, Germany, [2]UMC, Utrecht, Netherlands, [3]Immunology, RWTH Aachen, Aachen, Germany
Correspondence: K. Tenbrock *Pediatric Rheumatology*, **23(2):** P121

Introduction: Ferroptosis has been identified as a type of regulated cell death that is driven by lipid peroxidation. Cells have evolved various defense mechanisms to detoxify these toxic lipid peroxides. Especially T cells established a fine-tuned redox-balance as reactive oxygen species (ROS) are required to activate T cells, while too high amounts are deleterious for their function. We had shown that T cells in inflamed tissue have significantly enhanced mitochondrial ROS and therefore in need of antioxidant defense and dependent on mechanism to counteract ferroptosis.
Objectives: The aim of this work was to clarify the role of ferroptosis in JIA.
Methods: We analyzed CD4+ T cells from peripheral blood and from inflamed joints of these patients.
Ferroptosis-associated genes and proteins in CD4 T cells were analyzed by qRT-PCR and flow cytometry. Lipid peroxidation was induced in CD4 T cells by sulfasalazine and erastin and subsequent functional analysis was performed by in vitro assays. Synovial fluid and PBMC T cells from JIA patients were analyzed by flow cytometry
Results: The suppression of the extrinsic NRF2/SLC7A11 pathway induced lipid peroxidation in T cells. Induction of ferroptosis by sulfasalazine and erastin reduced inflammatory cytokine production in control T cells while not in JIA T cells. JIA T cells exhibited reduced NRF2 and SLC7A11 expression as well as reduced CD36 expression, which is the main transporter of lipid peroxides in tumor associated T cells, which undergo enhanced ferroptosis. Instead of SLC7A11 the Cysteine transporter ASCT1 is upregulated in synovial fluid T cells and blockade of this transporter reduces IFNy production.
Conclusion: Synovial fluid JIA T cells upregulate ASCT1 to import Cysteine and to compensate for negligible SLC7A11 expression and thus Cystine-import. Both can substitute for the production of Glutathione, which is the major antioxidative molecule. We thus identified a novel pathway in inflammatory T cells that prevents ferroptosis and cell death. Blocking Cysteine import might be a novel therapeutic opportunity in JIA.
Disclosure
None declared

P122

Precision therapy for rare pediatric immune-mediated diseases: development of a peptide-based biosensor system to detect aberrant jaks kinase activity

R. Franca[1], L. Pugnetti[3], N. Parmesan[2], A. Muzzo[1], P. Rispoli[1], S. Braidotti[4], A. Tommasini[1,4], S. Pastore[4], M. Zajc Avramovic [5,6], B. Jenko Bizjan[5,6], A. Taddio[1,4], T. Avcin[5,6], G. Stocco[1,3]
[1]Department of Medical, Surgical and Health Sciences, [2]PhD School in Personalized Medicine and Innovative Therapies, University of Trieste, [3]Department of Advanced Translational Diagnostics, [4]Department of Pediatrics, Institute for Maternal & Child Health (I.R.C.C.S) Burlo Garofolo, Trieste, Italy, [5]Department of Pediatrics, University of Ljubljana, [6]Department of Allergology, Rheumatology and Clinical Immunology, University Children's Hospital, University Medical Center Ljubljana, LJUBLJANA, Slovenia
Correspondence: R. Franca
Pediatric Rheumatology, **23(2):** P122

Introduction: The recent development of tyrosin kinase JAK inhibitors (JAKi) has brought an important change in the treatment of multiple immune-mediated disorders.
Objectives: The aim of the study is to develop a peptide-based biosensor system to detect aberrant JAK activity in primary cells from pediatric patients affected by these diseases among those enrolled in the INTERREG VI-A Italy - Slovenia"CONCERTO" project, and to screen *in vitro* and *a priori* the efficacy of JAK inhibitors (JAKi), providing integrative information to current diagnosis and monitoring of JAK-related diseases.
Methods: The biosensors, $P_{JAK2\text{-}S}$ and $P_{JAK2\text{-}L}$, are biotynilated peptide probes with sequences that include a tyrosine (Y) phosphorylation site specific for JAK2. Initial analysis was conducted on HEL and SET2 immortalized cell lines, which harbor the JAK2 V617F gain-of-function mutation. Activation/phosphorilation of JAK2 in whole cell lysates and immunoprecipiteted full-lenght JAK2 was analyzed in Western Blot. JAK2-mediated phosphorylation of biosensors was indirectly measured using a luminescent ADP detection kit, or directely assessed via fluorescence using a solid-phase ELISA assay with an anti phospho-Y primary antibody.
Results: We first provide evidence that $P_{JAK2\text{-}S}$ and $P_{JAK2\text{-}L}$ were suitable substrate sequences of JAK2 catalytic domain (JAK2-JH1). ADP was released when 2.5 ng/µl JAK2-JH1 was incubated with the peptide biosensors, achieving statistical significance for $P_{JAK2\text{-}S}$at 10 µM

and $P_{JAK2\text{-}L}$ at 20 µM (RLU basal phosphorylation of JAK2-JH1 *versus* 10 µM $P_{JAK2\text{-}S}$ or 20 µM $P_{JAK2\text{-}L}$ phosphorylation = median ± SEM = 21.0 ± 3.0 *versus* 190.3 ± 44.75 or 182.5 ± 18.06, respectively, both $p < 0.05$, two-way ANOVA, Bonferroni post-test). Notably, an increased in ADP detection could not be observed in the presence of $P_{PHOSPHO\text{-}JAK2\text{-}L}$, a phosphorilated form of $P_{JAK2\text{-}L}$, or with peptide probes specific for the ABL kinase. In the ELISA assay, the phosphorylation $P_{JAK2\text{-}L}$ and $P_{JAK2\text{-}S}$ could not be detected above the baseline level of whole cell lysates. Several efforts were made in the lysates-biosensors incubation step to optimize the ELISA results, includig changes in lysate amount (4µg *versus* 40µg), stringency of lysis buffer (TKB *versus* RIPA), time (1h *versus* 2 h) and temperature (25°C *versus* 37 °C)). $P_{JAK2\text{-}L}$ and $P_{JAK2\text{-}S}$ were exposed to full length JAK2, isolated from the whole cell lysates by immunoprecipitation. However, they were not phosphorylated above background levels in any experimental condition tested, despite the presence of active/phosphorilated JAK2 confirmed by Western Blot. Significantly higher fluorescence values than baseline were observed for $P_{PHOSPHO\text{-}JAK2}$, used as technical positive control for the ELISA assay ($P<0.0001$, Two-way ANOVA,Bonferroni's post-test).

Conclusion: $P_{JAK2\text{-}S}$ and $P_{JAK2\text{-}L}$ are suitable peptide sequences for monitoring the activity of JAK2-JH1 altought further optimization is needed for their use with full-length JAK2.

Trial registration identifying number: This work was carried out with the contribution of the project 'CONCERTO', CUP C93C22009370005, funded by the INTERREG VI-A Italy - Slovenia Programme 2021-2027

Disclosure

None declared

P125

Timed squat test as a functional outcome measure in childhood idiopathic inflammatory myopathies: correlation with CMAS, MMT8, and DAS

A. Alkandari[1], C. K. Lam[1], K. Peralta [1], Y. Goh[1,2], K. Chiu[1,3], J.-A. Marcuz[3], K. Whitney[1,3], B. M. Feldman [1,4,5]

[1]Division of Rheumatology, The Hospital for Sick Children, [2]SickKids Research Institute, Child Health Evaluative Sciences, [3]Department of Rehabilitation, The Hospital for Sick Children, [4] Department of Paediatrics, Faculty of Medicine, University of Toronto,, [5]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada

Correspondence: A. Alkandari

Pediatric Rheumatology,
23(2): P125

Introduction: Monitoring muscle strength and function in children with idiopathic inflammatory myopathies (IIM) is essential for effective disease management. While established tools such as the Childhood Myositis Assessment Scale (CMAS), Manual Muscle Testing (MMT-8), and Disease Activity Score (DAS) are widely used, functional performance measures like the timed squat test (TST) may offer practical, real-time insights into clinical status. This study evaluates the utility of the TST by comparing its results with CMAS, MMT-8, and DAS in children with IIM.

Objectives: To assess the potential of timed squat counts as a functional outcome measure in routine assessments of children with IIM, in relation to CMAS, MMT-8, and DAS.

Methods: A retrospective review was conducted on children with IIM at a tertiary center between June 1, 2018, and December 31, 2023. Generalized estimating equations (GEE) were used to model squat performance against CMAS, MMT-8, and DAS across all clinical visits. Additional analyses included baseline correlation matrices, standardized response mean (SRM) calculations in a 21-patient inception cohort (baseline to 6 months), and visualization of repeated measures using jittered scatter plots with LOESS curves.

Results: Eighty children with IIM were identified; six were excluded due to missing or non-applicable data. The final cohort included 66 with juvenile dermatomyositis (JDM), five with amyopathic JDM, two with overlap myositis, and one with necrotizing myopathy. The mean age at disease onset was 8.49 years, and 74% were female. Most (81%) were classified as having definite IIM, and 19% as probable. GEE modeling showed a significant positive association between squat counts and CMAS (estimate = 0.39, $p = 0.031$) and MMT-8 (estimate = 0.1, $p = 0.004$), and a significant negative association with DAS (estimate = −0.89, $p < 0.001$). Correlation matrices at baseline supported these findings. SRM analysis demonstrated TST responsiveness to clinical change over 6 months. Scatter plots showed consistent trends across visits: higher CMAS and MMT-8 scores correlated with better TST performance, while higher DAS scores were associated with reduced performance. The TST showed a floor effect in weaker patients but avoided the ceiling effect seen in CMAS and MMT-8 as strength improved.

Conclusion: The TST correlates significantly with CMAS, MMT-8, and DAS and is responsive to clinical change. Its simplicity and real-time applicability make it a useful tool for routine clinical monitoring in pediatric IIM.

Disclosure

None declared

P126

Clinical characteristics and prognostic factor in juvenile dermatomyositis: data of the spanish registry

C. Esquirol-Herrero[1], S. Carriquí-Arenas[1], J. M. Mosquera[1], E. Quesada-Masachs[2], M. López[2], D. Clemente [3], A. Boteanu[4], C. Udaondo[5], J. de Inocencio[6], J. C. Nieto[7], L. Riancho[8], E. Núñez[9], J. Sánchez-Manubens[1], M. J. Lirola[10], R. Roldán[11], M. Camacho[12], M. Martínez[13], M. Medrano[14], P. Alcañiz[15], J. Antón[1], E. Iglesias[1]

[1]Pediatric Rheumatology, Hospital Sant Joan de Déu, [2]Pediatric Rheumatology, Vall d'Hebron University Hospital, Barelona, [3]Pediatric Rheumatology, Niño Jesús Hospital, [4]Rheumatology, Ramón y Cajal University Hospital, [5]Pediatric Rheumatology, La Paz University Children's Hospital, [6]Pediatric Rheumatology, University Hospital 12 de octubre, [7]Rheumatology, Gregorio Marañón General University Hospital, Madrid, [8]Rheumatology, Valdecilla Hospital, Santander, [9]Pediatric Rheumatology, Regional University Hospital of Malaga, Málaga, [10]Pediatrics, Instituto Hispalense de Pediatría, Sevilla, [11]Pediatric Rheumatology, University Hospital Reina Sofía, Córdoba, [12]Pediatric Rheumatology, Virgen del Rocío University Hospital, Sevilla, [13]Rheumatology, Germans Trias i Pujol University Hospital, Badalona, [14]Rheumatology, Miguel Servet University Hospital, Zaragoza, [15]Pediatric Rheumatology, Virgen de la Arrixaca University Clinical Hospital, Murcia, Spain

Correspondence: C. Esquirol-Herrero *Pediatric Rheumatology*,
23(2): P126

Introduction: Juvenile Dermatomyositis (JDM) is the most common chronic idiopathic inflammatory myopathy in children. The diagnosis is clinical. Baseline laboratory and complementary studies trace the phenotype of these patients.

Objectives: The objective of this study was to describe epidemiological, clinical and laboratory characteristics at diagnosis of JDM patients included in the Spanish JDM registry, as well as to identify prognostic factors on these patients.

Methods: Retrospective review of clinical features, laboratory tests, and complementary studies at diagnosis of JDM patients included on the Spanish JDM registry. These data were analyzed to assess whether there was a relationship with the development of complications and time to disease inactivity.

Results: One hundred and sixteen patients from 17 Spanish paediatric rheumatology centres were included, 76 girls (65%). Median age at diagnosis was 7.3 years (Interquartile range (IQR) 4.5–10.2). All patients had pathognomonic skin lesions at the beginning of the disease. Muscle weakness was present in 86.2%. Median Childhood Muscle Assessment Scale was 34 (IQR 22–47). Twelve patients (34%) had dysphagia and 3,5% dysphonia. Anti-p155 was the most frequently detected myositis specific antibody, followed by anti-MDA5. Twenty-nine patients developed calcinosis and 4 presented with macrophage activation syndrome. 70% reached inactivity in a median time of 8.9 months (IQR 4.5–34.8). 41% relapsed after a median time of 14.4 months (IQR 8.6–22.8) of inactivity. Shorter time to treatment was associated with better prognosis (Hazard ratio (HR) = 0.95 per month of evolution, $p = 0.02$). Heliotrope rash at diagnosis correlates with higher risk of development complications.

Conclusion: We describe heliotrope rash as a risk factor for developing complications in our cohort of JDM patients, an easy-to-evaluate

clinical sign that could help us to identify the group of patients we should monitor closely for this complication.

Disclosure

None declared

P127

Novel use of anifrolumab in a young patient with jo-1-positive juvenile dermatomyositis shows rapid improvement of skin and muscle involvement

D. Windschall[1,2], S. Hardt[1], T. Hinze[1], F. Gohar[1]

[1]Clinic for Paediatric and Adolescent Rheumatology, St. Josef-Stift Hospital, Northwest German Center for Rheumatology, Sendenhorst, [2]Medical Faculty, University of Halle-Wittenberg, Halle, Germany

Correspondence: D. Windschall *Pediatric Rheumatology*, **23(2):** P127

Introduction: Anifrolumab is a monoclonal antibody targeting the type 1 interferon (IFN) receptor subunit 1. Experience of anifrolumab in patients with juvenile dermatomyositis (JDM) is limited, with a single published case reporting improvement with anifrolumab 300 mg/month in an adolescent with skin and muscle disease, without calcinosis cutis and without longitudinal IFN-signatures reported.(1)

Objectives: To report the change in disease activity and interferon-signature with off-label use of anifrolumab (150 mg/month) in an 8-year-old female with refractory muscle and skin involvement combined with calcinosis cutis.

Methods: The patient demographic and disease characteristics are reported. The disease activity (DA) scores including the childhood myositis assessment scale (CMAS, maximum 52) and the DA in JDM score (DAS20, range 0 (no activity)−20 (highest activity)) and change in IFN-signature (IFN, 6 gene expression panel of IF27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1, normal < 6.0, moderate activity 20,1-50,0) were collated over the disease course and six months anifrolumab treatment. Safety and adverse events were recorded.

Results: Jo-1 positive JDM was first diagnosed aged 4 years with Gottron's papules and myositis (MRI-diagnosed) present. Initial treatment included methylprednisolone pulse therapy, oral prednisolone and methotrexate. After six months, hydroxychloroquine was added and azathioprine replaced methotrexate, but were ineffective after 9 months treatment. Tofacitinib was initiated 16 months after diagnosis, with myositis initially improving significantly (CMAS 37 to 51 and DAS20 from 15 to 9) with minimal change in IFN: 6 to 9.4. Skin involvement remained refractory and calcinosis cutis developed 3.5 years after first presentation with a worsened CMAS=49 and stable DAS20=9. Addition of immunoglobulin therapy and a switch to baricitinib resulted in worsening of DA: CMAS=49.5, DAS20=11 and IFN=30.5. Off-label anifrolumab (150 mg/month) was then started, 4.5 years after initial diagnosis. Methotrexate and oral prednisolone were continued. After two doses of anifrolumab DA improved: CMAS=52, DAS20=9 (lowest since diagnosis) and the IFN-signature decreased to 17.3. Before the 5th dose, CMAS remained at 52, DAS20 improved further to 5. The vasculitis skin signs, Gottron's papules, skin erythema as well as myositis were no longer present, with minimal nailfold erythema remaining. No new calcinosis cutis lesions developed, whilst others appeared to be qualitatively healing after draining. The IFN-signature remained moderately elevated (48.8). No safety or adverse events were reported.

Conclusion: Skin and muscle involvement of JDM rapidly improved/normalised in this young patient with refractory disease after just two doses of anifrolumab 150 mg. No safety or adverse events occurred. The IFN-signature remained elevated despite clinical improvement. Larger prospective studies are required to confirm efficacy and safety in a paediatric population. In addition, longer-term follow-up is required for this promising therapy for JDM to ascertain the effect of anifrolumab on the course of calcinosis cutis lesions and association with IFN-signature. Consent to published had been obtained.

Disclosure

None declared

Reference

1. Leila H Shayegan et al. Improvement in dermatomyositis-associated muscle disease with anifrolumab, *British Journal of Dermatology*, 2025;ljaf064

P128

Evolving trends in myositis autoantibodies in an irish cohort: a seven-year retrospective review

D. Henderson[1], V. Tormey[2], O. G. Killeen[1]

[1]Rheumatology, Children's Health Ireland at Crumlin, Dublin, [2]Immunology, University Hospital Galway, Galway, Ireland

Correspondence: D. Henderson *Pediatric Rheumatology*, **23(2):** P128

Introduction: Juvenile dermatomyositis (JDM) is a rare, immune-mediated disorder that preferentially affects dermal and muscular tissues, presenting with proximal muscle weakness and skin involvement. Whilst pathogenesis is not completely understood, there appears to be a temporal association between infectious triggers and disease onset (1). JDM is a heterogeneous disease, with variable clinical phenotypes and treatment responses. Myositis specific antibodies (MSA) and myositis associated antibodies (MAA) are present in approximately 60% of cases and inform patient sub-stratification with disease phenotype, outcomes and differing treatment approaches (2).

Objectives: To characterise the patterns of MSA/MAA autoantibodies in a cohort of Irish patients over a seven-year period. Our secondary objective is to describe the influence of the SARS-COV-2 pandemic on the quantity and types of antibodies present.

Methods: A retrospective monocentric analysis of 265 myositis autoantibody requests between 2018 and 2024 was performed. Myositis autoantibodies were detected using laboratory techniques such as immunoblotting, reverse immunoprecipitation, and immunoprecipitation-immunodepletion. This was compared to a previously reported MSA/MAA autoantibody profile in our centre in 2017 (3).

Results: Between 2018 and 2024, 23.8% of requested tests were positive, with a total of 63 (n=27 MSA, n=46 MAA) positive myositis autoantibodies identified. The number of positive detections increased gradually, peaking in 2023 (n=25). The most frequently detected autoantibodies were anti-PM/Scl75 (n=16), Ro-52 (n=10), Ku (n=6), and anti-HMGCR (n=7). Anti-CN-1A antibodies, added to the immunoblotting panel in 2016, were identified in 7 cases. Anti-Mi-2 variants (α and β) were found in a total of 6 patients, while other autoantibodies such as TIF-1γ, NXP2, and Jo-1 appeared less frequently. No positive cases were recorded for MDA 5, SAE1, PL-12, EJ, or OJ autoantibodies during this period. 13 differing myositis autoantibodies were detected, compared to 9 in 2017.

Conclusion: The trends of myositis autoantibodies have evolved in our centre in the post pandemic period. Since 2018, we have not detected any positive MDA 5 autoantibodies, despite these previously accounting for 38% of those with positive result (3). In contrast, there has been an increase in detection of anti-PM/Scl75 and anti-HMGCR since 2022. These are typically associated with overlap syndromes and necrotising myopathy respectively. Future studies should further investigate the effect and role of the SARS-CoV-2 pandemic in myositis autoantibody profiles, disease phenotype and clinical course.

Disclosure

None declared

References

1. Sassetti C, Borrelli C, Mazuy M, Turrini I, Rigante D, Esposito S. The relationship between infectious agents and juvenile dermatomyositis: a narrative update from the pediatric perspective. Front Immunol. 2024;15:1377952.
2. Tansley SL, Simou S, Shaddick G, Betteridge ZE, Almeida B, Gunawardena H, et al. Autoantibodies in juvenile-onset myositis: Their diagnostic value and associated clinical phenotype in a large UK cohort. Journal of Autoimmunity. 2017;84:55-64.
3. MacMahon J, Tormey V, MacDermott E, Killeen O. A Profile of Myositis Autoantibodies in an Irish Cohort of Juvenile Dermatomyositis/Myositis Patients2017.

P129

Effects of hydroxychloroquine in children with juvenile dermatomyositis in Nepal: a retrospective study on the only pediatric rheumatology centre

D. Bhattarai[1], R. Baral[2], A. Pokharel[3], A. Neupane[4]

[1]Pediatric Immunology & Rheumatology, Advanced Centre for Immunology & Rheumatology, Kathmandu, [2]Pediatrics, Western Regional Hospital, Pokhara, [3]Otorhinolaryngology, Civil Hospital, [4]Pediatrics, Advanced Centre for Immunology & Rheumatology, Kathmandu, Nepal
Correspondence: D. Bhattarai
Pediatric Rheumatology, **23(2):** P129

Introduction: Juvenile dermatomyositis (JDM) contributes to more than 3/4th of all juvenile idiopathic inflammatory myositis. Treatment of JDM is multi-pronged, comprehensive, and challenging due to inadequacy of data, heterogeneity of disease, and complications. The literature on hydroxychloroquine (HCQ) in JDM is limited.
Objectives: To study the effect of HCQ in patients with JDM
Methods: Ours is a single center for pediatric rheumatology in Nepal. We analyzed all cases diagnosed with JDM in our center as per modified Bohan and Peter criteria between August 2020 and March 2025. Cross-sectional data on demographics, disease activity, drugs, and course were noted. Bivariate analysis and multivariate logistic regression analysis were performed.
Results: As per the registry, a total of 61 children were diagnosed with definite JDM. All patients had features of dermatitis and myositis at the time of diagnosis. All patients were of age below 16 at the time of diagnosis. 55 (90.1%) had clear information about the use of HCQ and further courses. All patients were commenced on corticosteroids and immunosuppressants irrespective of being on HCQ. 35 (63.6%) patients had taken HCQ whereas 20 (36.4%) patients never used HCQ during their treatment period. A significant association was found between the use of HCQ and the improvement of any rash (malar erythema, Gottron's rash, heliotrope rash, or shawl/V signs) (p=0.012), CHAQ (p=0.024), calcinosis (p=0.044) and proximal myopathy (p=0.016). In multivariate analysis, only those patients with skin rashes (p=0.009) and calcinosis (p=0.021) were found to have a significant association with HCQ therapy. We could not find any association of HCQ therapy with improvement on large or small joint arthritis, vasculitis, lipodystrophy, major organ involvement, or complications.
Conclusion: There is a paucity of literature on the effect of long-term treatment of HCQ in children with JDM. Patients with dermatitis and calcinotic presentations were found to have benefitted from HCQ therapy whereas this drug was not found to leave a significant impact on other aspects like myositis, arthritis, vasculitis, CHAQ, and multi-organic complications. Due to the presence of many possible confounding factors and biases, a causal association cannot be promulgated. However, this study may be an addition to the scarce HCQ literature on JDM. Further longitudinal data will help to ascertain the benefits of HCQ in patients with JDM.
Trial registration identifying number: Not applicable
Disclosure
None declared

Reference
1. None

P131

Nailfold capillaroscopy changes in active juvenile dermatomyositis: results of a two-center study

V. Podzolkova[1], I. Avrusin[2], M. Nikolaeva[3], E. Afonina[3], A. Nurseitova[2], K. Kravtsova[2], A. Malahova[2], M. Kostik[2], V. Chasnyk[2]
[1]Department of Children's Diseases, I.M. Sechenov First Moscow State Medical University, Moscow, [2]Department of Hospital Pediatrics, Saint Petersburg State Pediatric Medical University, Saint Petersburg, [3]Department of Pediatric Rheumatology №1, Clinic of Children's Diseases Sechenov's Center of Maternity and Childhood, Moscow, Russian Federation
Correspondence: I. Avrusin
Pediatric Rheumatology, **23(2):** P131

Introduction: Nailfold capillaroscopy (NFC) is a valuable diagnostic and monitoring tool for conditions involving microvascular inflammation. Juvenile dermatomyositis (JDM) is primarily characterized by microangiopathy affecting the vessels of the skin, muscles, and internal organs. Despite its pathophysiological relevance, the diagnostic utility of NFC in JDM remains insufficiently defined.
Objectives: To identify specific NFC patterns associated with active disease stage in patients with JDM.
Methods: This retrospective-prospective observational study included 49 children with confirmed JDM, followed at the clinics of Sechenov University and Saint Petersburg State Pediatric Medical University. Patients were stratified into two groups based on disease activity at the time of NFC: Group 1 – patients with active JDM; Group 2 – patients with inactive JDM. Disease activity was assessed using the modified Disease Activity Score (DASmod) (1). Demographic, clinical, laboratory, and instrumental data were collected and analyzed. NFC assessment was performed using standardized criteria originally developed for adult patients with systemic sclerosis and Raynaud's phenomenon (2). Statistical analysis was conducted using Windows v.13 (StatSoft). Spearman's rank correlation coefficient was used to assess the relationship between variables. The study was approved by the Local Ethics Committee of Sechenov University (protocol №08-25, dated 10.04.2025).
Results: The groups were comparable in major demographic and clinical characteristics. Both groups were predominantly female (Group 1: 65.4% girls vs. Group 2: 57.7% girls). Median age at disease onset was 6 years [IQR: 5–8], median disease duration before diagnosis was 3 months [IQR: 2–6], and before NFC – 40 months [IQR: 13–67]. The DASmod activity index at diagnosis did not differ significantly between the groups, with a median of 8 points [IQR: 6–9]. According to NFC findings in patients with active JDM, reduced capillary density (89.7% vs. 59.1%, $p < 0.001$), with a mean of 3.6 capillaries per linear mm compared to 6.4 in the inactive group ($p < 0.001$), as well as giant capillaries (74.1% vs. 9.1%, $p < 0.001$), hemorrhages (66.7% vs. 40.9%, p=0.015), and perivascular edema (74.1% vs. 13.6%, $p < 0.001$) were significantly more frequent. In addition, the apical loop width was markedly increased in this group: 65.10 µm [46.58–96.04] vs. 32.50 µm [26.43–44.20], $p < 0.001$. Disease activity correlated most strongly with the presence of giant capillaries ($r = 0.65$, $p < 0.05$), perivascular edema ($r = 0.60$, $p < 0.05$), and reduced capillary density ($r = 0.46$, $p < 0.05$) on NFC.
Conclusion: Reduced capillary density, presence of giant capillaries, and perivascular edema were significantly more common in children with active JDM. These findings suggest that NFC may serve as a potential method for evaluation of disease activity. Further research is planned to evaluate the diagnostic performance and predictive value of NFC in assessing disease activity in pediatric JDM.
Disclosure
None declared

References
1. Clairman, Hayyah et al. "Correlation of a Modified Disease Activity Score (DAS) with the Validated Original DAS in Patients with Juvenile Dermatomyositis." *The Journal of rheumatology* 48,1 (2021): 101-104. doi:https://doi.org/10.3899/jrheum.191255
2. Smith, Vanessa et al. "Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis." *Autoimmunity reviews* 19,3 (2020): 102458. doi:https://doi.org/10.1016/j.autrev.2020.102458

P132

Treatment options for juvenile idiopathic dermatomyositis with calcinosis: single centre experience

I. Nikishina, O. Kostareva, S. Arsenyeva, V. Matkava, M. Kaleda, A. Shapovalenko
Paediatric, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P132

Introduction: Calcinosis is a feared and difficult to manage complication of Juvenile Dermatomyositis (JDM).Biologics and JAK-inhibitors become promising options especially in refractory cases with complications although there are no special controlled studies and registered indications regarding their use.
Objectives: To describe real world data of long term managing of JDM pts with calcinosis.

Methods: Single center data of 67 pts(27/40% male,40/60% female) with Juvenile Idiopathic Inflammatory Myopathies(JIIM) who were observed in our clinic since 2020 to 2024 years.
Results: Our cohort includes 51 pts with JDM and 16 pts with overlap syndromes.Calcinosis was observed in 17/25%(11-JDM,5–overlap syndrome).The median age at onset for this category of pts was 6.92 y.o.(min-10mo; max-12y.o.).The median disease duration before establishing diagnosis–8 mo(min–1;max–88).17/100% pts had myopathic syndrome,14/88%-typical skin lesions,16/94% suffered from arthritis, the lung involvement-in 4/23%.Laboratory findings included positive ANA in 13/76%, level of CK was elevated in 7/41%. 17/100% pts received glucocorticoids and methotrexate(MTX),4 of them combined with hydroxychloroquine,2-mycophenolate mofetil,IVIG-11/64% pts. Due to refractory course of JIIM 9/17/53% were treated by Biologics and JAK-inhibitors(among them 1/9/11% pts with overlap syndrome). Spectrum of therapy included abatacept (4 pts–in 1-st line, 1–in 2-nd),rituximab (2 pts–in 1-st line),tofacitinib (2 pts–in 1-st line, 2–in 2-nd),upadacitinib(1 pt–in 3-rd line after inefficacy of abatacept and tofacitinib).Under the therapy we observed improvement of muscle force,relieve of myopathic syndrome,decrease of calcinosis in all cases. We observed a significant regression of calcifications in one patient under the upadacitinib after failures in the use of abatacept and tofacitinib sequentially, which was confirmed by the low-dose whole-body CT with dynamics after 1 year.
Conclusion: Despite the "off label" status of Biologics ang JAK-inhibitors for JIIM (JDM including),we satisfied with their good effectiveness and favorable safety profile for pts with calcinosis.The most impressive thing in our experience was the observation of a significant regression of calcifications in 16 y.o. boy as a result of the use of upadacitinib.
Disclosure
None declared

P133

Janus kinase inhibitors as a therapeutic option for juvenile idiopathic inflammatory myopathies: an experience of single center

I. Nikishina, O. Kostareva, S. Arsenyeva, V. Matkava, M. Kaleda, A. Shapovalenko
Paediatric, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P133

Introduction: Juvenile Idiopathic Inflammatory Myopathies (JIIM) is a rare autoimmune disease affecting children as idiopathic Juvenile Dermatomyositis (JDM) or part of overlap-syndrome. Despite of the absence of official Tofacitinib indication in JIIM patients (pts), it may be good option in severe course of disease.
Objectives: To analyze the efficacy and safety of Tofacitinib (TOFA) therapy in pts with JIIM.
Methods: The retrospective study since 2010 to 2024 years included 69 pts with JIIM. Among them 11/15.9% pts with JIIM received Tofacitinib.
Results: A total of 11 pts (8 females) were identified: 7 pts with JDM, 4 pts with overlap syndromes (JIA – 2, JIA+Sjogren's syndrome-2). The mean age at the onset was 9.2 years (min 1.25; max 16.5). All pts had myopathic syndrome, arthritis had 10 pts (91%), the typical rash - 9 pts (82%), lipodystrophy - 3 pts (27%). The lung involvement observed in 1 pts (12,5%). Calcinosis had 4 pts (36%). Levels of CK, ALT, AST and LDH were elevated in 10 pts (91%). ANA were positive in 10 pts (91%). Anti-RNP, anti-phospholipid antibodies were detected in 3 pts (27%). Nailfold capillaroscopic changes typical for JIIM had 2 pts (18%). Before TOFA all pts received corticosteroids (CS) and methotrexate, 6/11 (55%) - IVIG. TOFA was started due to insufficient efficacy of previous therapy (6 pts in 1-st line, 4 – in 2-nd after inefficacy of abatacept, infliximab; 1 – in 3-d line after inefficacy of rituximab, abatacept). The mean age at TOFA initiation was 12.8 years (min 4; max 17.8). The mean disease duration prior to treatment with TOFA was 45.5 month (min 1; max 107). The mean disease duration before biologic treatment was 27.2 month (min 1; max 70). 7 pts were analyzed repeatedly in 6 months. The mean duration of TOFA therapy was 9.4 month (min 4; max 18). TOFA therapy allowed to reduce the dose of CS to maintenance in all pts, decrease of myopathic and skin syndromes, arthritis in 6 pts, calcinosis in 2 pts, the lung involvement in 1 patient. 1 patient was switched to upadacitinib (due to secondary inefficiency by the 13th month of therapy with achievement of inactive status and calcification regression). Overall tolerance was good. Serious AE was not observed.
Conclusion: Our study demonstrated that TOFA is effective option in children with refractory JIIM and have the acceptable safety. Early initiation of target anti-inflammatory therapy (including Biologics and JAK-inhibitors) are important in reducing symptoms of refractory JIIM. Further studies are needed.
Disclosure
None declared

P134

Diagnostic significance of nailfold videocapillaroscopy in the early detection of oligosymptomatic juvenile dermatomyositis

N. Yudkina, A. Volkov, I. Nikishina
V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P134

Introduction: Establishing the diagnosis of juvenile dermatomyositis (jDM) in pediatric patients is particularly challenging in the absence of classical manifestations such as Gottron's papules or erythema, heliotrope rash, proximal muscle weakness, elevated creatine kinase (CK), or disease-specific autoantibodies. Nailfold videocapillaroscopy (NVC) is not currently included in international diagnostic criteria for jDM but may prove useful in clinically ambiguous or atypical presentations.
Objectives: To evaluate the role of NVC within the diagnostic workup of children with suspected onset of a systemic connective tissue disease.
Methods: We present two unrelated female patients aged 2 and 4 years, referred to pediatric rheumatology following dermatological evaluation for persistent facial erythema of unclear origin. Initial working diagnoses included contact or allergic dermatitis. Screening tests revealed positive antinuclear antibodies (ANA), raising suspicion of a systemic connective tissue disease, prompting referral to rheumatology. Both patients underwent comprehensive laboratory and instrumental evaluation, including NVC.
Results: Clinical examination revealed persistent, slightly elevated, non-pruritic, non-scaling facial erythema in both cases. Classic cutaneous and muscular features of jDM (Gottron's papules/erythema, heliotrope rash, periorbital edema, proximal muscle weakness) were absent. ANA titers exceeded 1:640 in both patients. Immunoblot testing for anti-dsDNA, Sm, RNP, Ro, La, nucleosomes, Scl-70, and centromere antibodies was negative. Complement levels (C3, C4), CBC, urinalysis, ESR, and CRP were within normal ranges. The older patient had mildly elevated CK-MB and LDH, with normal total CK, ALT, and AST. NVC was performed as an additional diagnostic tool. In both cases, capillaroscopic findings showed a non-specific but characteristic pattern frequently seen in inflammatory myopathies, particularly dermatomyositis. Key features included altered loop morphology, reduced capillary density, disorganization, microhemorrhages, giant and bushy capillaries. These findings supported a presumptive diagnosis of juvenile dermatomyositis and guided further clinical management.
Conclusion: 1) In the absence of typical clinical and laboratory markers, NVC may play a crucial role in the early diagnosis of jDM. 2) This method deserves consideration as an adjunctive diagnostic tool in atypical presentations of pediatric systemic rheumatic diseases. 3) Unusual or subtle cutaneous findings in ANA-positive children should be viewed as a potential indication for NVC. Consent to published had been obtained.
Disclosure
None declared

P136

Patient and public involvement (ppi) in myoscope: a study to bring a visual measure of disease activity into clinical practice to help children with dermatomyositis

L. Huckerby[1,2], C. Papadopoulou[3], E. Deja[4], A. Murray[5], G. Dinsdale[6], K. Roberts[7], M. Hadjittofi[7], J. S. Ainsworth[8], A. Vail[9], K. Kupiec[3], J. Fitzgerald[10], L. R. Wedderburn[3,11,12,13], C. E. Pain[1,14], C. Taylor[15], A. Herrick[5,6], L. J. McCann[1,14]

[1]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, [2]Department of Paediatric Rheumatology, Royal Manchester Children's NHS Foundation Trust, Manchester, [3]Department of Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, [4]Department of Public Health, Policy and Systems, University of Liverpool, Liverpool, [5]Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Science, University of Manchester, [6]Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester, [7]Department of Clinical Health Psychology, Alder Hey Children's Hospital, [8]University of Liverpool, Liverpool, [9]Centre for Biostatistics, University of Manchester, Manchester, [10]Experimental Arthritis Treatment Centre for Children, University of Liverpool, Liverpool, [11]NIHR Biomedical Research Centre, Great Ormond Street Hospital for Children NHS Foundation Trust, [12]Centre for Adolescent Rheumatology Versus Arthritis at UCL, Great Ormond Street Hospital NHS Foundation Trust and University College London Hospitals NHS Foundation Trust, [13]Infection Immunity and Inflammation Research and Teaching Department, University College London Great Ormond Street Institute of Child Health, London, [14]Department of Women and Children's Health, University of Liverpool, Liverpool, [15]University of Manchester, Manchester, United Kingdom
Correspondence: L. Huckerby
Pediatric Rheumatology, **23(2):** P136

Introduction:
Nailfold capillary changes in juvenile dermatomyositis (JDM) associate with biomarkers of vasculopathy and disease activity[1]. MYOSCOPE is investigating feasibility and benefits of using nailfold capillaroscopy (NFC) in clinic in patients with JDM. Here we describe the patient and public involvement (PPI) which informed (and continues to inform) study design and delivery.
Objectives:
1. To co-design the study in partnership with patients/families, to ensure that all relevant data are captured.
2. To assess whether NFC is acceptable to patients/families, helps them understand their disease better, and improves adherence to treatment.
Methods:
The study was co-designed with support of YourRheum (a group of 11-24 year olds with rheumatic disease), 'GenerationR Liverpool' (a network alliance of young people advisory groups which support paediatric health research) and a patient and parent lead, supported by our Patient and Family Coordinator. A new JDM advisory group was established to help further design the study, co-write materials and provide ongoing input (4 meetings over 2 years).
40 patients with JDM (≤18 years of age, any time point of disease) were recruited over 2 UK paediatric rheumatology centres. NFC was performed at clinic visits. Patients and carers were asked to complete age-appropriate questionnaires to explore feelings about NFC, with further evaluation through qualitative patient/family interviews.
Results:
Discussion at PPI focus groups led to a fundamental change in study design. Our initial intention was to compare NFC changes to novel biomarkers of vasculopathy. Through PPI work we appreciated the importance of a visual tool, which patients/carers thought would aid understanding of their disease, self-management and empowerment. We changed our study design to evaluate impact of NFC through patient questionnaires/interviews.
Age-appropriate information sheets, consent/assent forms and patient/carer questionnaires were co-written with our JDM advisory group. Allowing patients to have a copy of their NFC images, suggested during advisory groups, was added to the protocol. Our advisory group helped determine how images should be shown to patients, including examples of 'non-JDM' and JDM capillaries. A newsletter was produced as suggested after the mid-point PPI meeting.
Preliminary data after visit 1 from 71 patient/carer questionnaires suggested that 64/71 (90%) felt "really good" or "fantastic" about NFC. 56/71 (79%) felt visualising their NFC helped them understand how active (or inactive) their JDM was currently and helped them know if they needed medications 63/71 (89%).
Conclusion:
Co-design with PPI advocates ensured MYOSCOPE was acceptable and meaningful to patients/families, with further valuable opinions gathered through regular PPI meetings. Preliminary data from parent/carer questionnaires and qualitative interviews suggest an encouraging response to NFC performed in clinic.
Acknowledgements:
Funded by NIHR RfPB NIHR204944
Disclosure
None declared

Reference
1. Papadopoulou C, Hong Y, Krol P, Al Obaidi M, Pilkington C, Wedderburn LR, et al. The Vasculopathy of Juvenile Dermatomyositis: Endothelial Injury, Hypercoagulability, and Increased Arterial Stiffness. Arthritis Rheumatol. 2021;73(7):1253-1266

P137

Reduced CD4+ IFNG+ T cell response is associated with more severe clinical disease in juvenile dermatomyositis

N. M. L. Evans[1,2,3], L. R. Marshall[1], E. C. Rosser[3,4], C. T. Deakin[1,2,3,5], A. E. Syntakas[1,2,3], Q. Wu[1,6], D. Cancemi[1,2,3], M. L. G. Wilkinson[1,2,3], L. R. Wedderburn[1,2,3] on behalf of on behalf of the UK JDM Cohort and Biomarker Study
[1]Infection, Immunity and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, [2]NIHR Biomedical Research Centre at Great Ormond Street Hospital, [3]Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCL Hospital and Great Ormond Street Hospital, [4]Department of Ageing, Rheumatology and Regenerative Medicine, UCL Division of Medicine, London, United Kingdom, [5]School of Population Health, Faculty of Medicine and Health, University of New South Wales, Sydney, Australia, [6]Department of Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
Correspondence: N. M. L. Evans
Pediatric Rheumatology, **23(2):** P137

Introduction: Juvenile Dermatomyositis (JDM) is a rare, systemic autoimmune disorder, resulting in skin and muscle inflammation. JDM aetiology is not well understood, meaning treatment is not targeted to specific pathways in disease pathology, highlighting the need for further research. Dysregulation of Type I and Type II interferon (IFN) has been observed in JDM in blood and muscle and has previously been shown to be associated with more severe clinical disease in JDM and other autoimmune rheumatic conditions.
Objectives: The aim of this project is to investigate whether CD4+IFNγ+ T cell dysregulation can be identified in blood from JDM patients compared to age-matched healthy controls, and if so, whether this is associated with clinical disease activity.
Methods: Expression of IFNγ, IL-17 and IL-2 in CD4+ T cells in peripheral blood mononuclear cells (PBMC) of JDM patients, obtained from treatment-naïve (JDM Pre, n=15), and on-treatment (JDM On, n=29) patients and from age-matched healthy controls (HC, n=36) was assessed by flow cytometry, following stimulation with PMA/Ionomycin/Brefeldin A (P/I/B) for 4 hours. Clinical disease activity measures including Physician's global assessment of disease activity (PGA), determined using the physician Visual Analogue Scale, were obtained from the JDCBS database. Clinically inactive disease or active disease were defined using the Almeida et al amended PRINTO criteria (2015).
Results: Intracellular cytokine staining following P/I/B stimulation showed a significant decrease in the proportion of CD4+ IFNγ+ T cells in JDM Pre ($p<0.0001$) and JDM On ($p=0.0036$) patients compared to HC. JDM Pre patients had a trend to decreased proportion of CD4+IL-17+ T cells compared to HC. No significant differences between JDM and HC were observed in CD4+IL-2+ T cells. An abnormal Th17/Th1 ratio was observed between JDM patients and controls ($p=0.0001$). A significant recovery of CD4+IFNγ+ T cell frequency was seen in JDM patients on treatment in remission ($p=0.0069$), compared to JDM treatment-naive patients with active disease. Significant negative ($p=0.0314$) correlation was observed between PGA and CD4+IFNγ+ T cell frequency in JDM patients, suggesting that deficit of CD4+IFNγ+ Th1 cells is associated with more severe clinical disease.

Conclusion: Our findings show a lack of CD4+IFNγ+ T cell response in JDM patients compared to controls. Clinical data indicated that lack of CD4+IFNγ+ T cell response is associated with more severe clinical disease in JDM patients, and recovery of this population is seen in remission of clinical disease.
Disclosure
N. Evans: None declared, L. Marshall: None declared, E. Rosser: None declared, C. Deakin: None declared, A. Syntakas: None declared, Q. Wu: None declared, D. Cancemi: None declared, M. Wilkinson: None declared, L. Wedderburn Grant/Research Support with: Pfizer, Consultant with: Pfizer, Cabaletta

P139

Clinical profile of juvenile dermatomyositis patients with interstitial lung disease from a tertiary care center in India

R. Semwal, V. Pandiarajan, A. Dod, P. Nadig, S. Basu, R. Pilania, D. Suri, A. Rawat, S. Singh
Pediatric Clinical Immunology and Rheumatology Unit, Post Graduate Institute of Medical Education and Research, Chandigarh, India
Correspondence: R. Semwal
Pediatric Rheumatology, **23(2):** P139

Introduction: Idiopathic inflammatory myopathies (IIMs) are a group of rare and heterogeneous rheumatological diseases with systemic involvement. Juvenile dermatomyositis (JDMS) forms the most common subtype among IIMs. Interstitial Lung Disease (ILD) associated with anti-MDA5 positivity is the most common cause of mortality among IIMs.
Objectives: To describe the clinical profile of JDMS patients with ILD from a tertiary care center in North-West India.
Methods: We did a retrospective review of the medical records of pediatric patients diagnosed with JDMS and being followed up at a tertiary care center in North-West India. Prevalence of ILD and the risks associated were studied.
Results: A total of 172 patients diagnosed with JDMS were included. ILD was present in 21 (12.2%) patients in our cohort. Of these, 38.1% were males and 61.9% were female. Age of onset of symptoms was 9.8 years (IQR-4.4) with a delay in diagnosis of 7 months (IQR-14). Most of the patients were diagnosed with ILD at the time of diagnosis of JDMS. Fever and cutaneous symptoms like Gottron's papules were noted at onset in most patients (61.9%, 81% respectively). 16 out of 21 patients with ILD complained of proximal muscle weakness. Nail fold capillaroscopy showed abnormal findings in 42.9% patients with ILD. Most of the patients (16/21) had elevated liver enzymes. Autoantibodies associated with interstitial lung disease include anti-MDA5, anti-PmScl, and anti-Ku. 75% patients received pulse dose of corticosteroids followed by methotrexate injection (13/21) and additional Cyclophosphamide (45.5%) was administered in 8 patients (44.4%). 3 out of 21 children with ILD died with cause of death being attributed to Rapidly Progressive ILD (RP-ILD).
Conclusion: ILD is a major contributor to extramuscular morbidity and mortality in these patients. Risk factors for ILD include presence of fever and anti-MDA5 positivity. Early diagnosis and interventions such as intensive immunosuppression are imperative in the management of ILD.
Disclosure
None declared

P141

JAK inhibition in juvenile dermatomyositis: SIGLEC-1 as an in vitro biomarker and IFN-beta as promising therapeutic target

S. Veldkamp[1], M. Reugebrink[1], S. W. Evers[2], T. R. Moreau[3], V. Bondet[4], W. Armbrust[5], J. M. van den Berg[6], P. C. Hissink Muller[7], S. Kamphuis[8], E. Schatorjé[9], E. M. Delemarre[1], A. J. van der Kooi[2], B. Bader-Meunier[10], D. Duffy[4], M. P. Rodero[3], J. Raaphorst[2], A. van Royen-Kerkhof[11], M. H. Jansen[11], F. van Wijk[1]
[1]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, [2]Department of Neurology, Amsterdam University Medical Centres, location AMC, Amsterdam, Netherlands, [3]Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques UMR8601, CNRS, [4]Translational Immunology Unit, Université Paris Cité, Institut Pasteur, Paris, France, [5]Department of Paediatric Rheumatology and Immunology, University Medical Center Groningen, Groningen, [6]Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam University Medical Centres, location AMC, Emma Children's Hospital, Amsterdam, [7]Department of Paediatric Rheumatology, Leiden University Medical Centre, Willem Alexander Children's Hospital, Leiden, [8]Department of Paediatric Rheumatology, Erasmus University Medical Centre, Sophia Children's Hospital, Rotterdam, [9]Department of Paediatric Rheumatology, Radboud University Medical Centre, Amalia Children's Hospital, Nijmegen, Netherlands, [10]Paediatric Haematology-Immunology and Rheumatology Department, Necker-Enfants Malades Hospital, AP-HP, Paris, France, [11]Department of Paediatric Rheumatology and Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, Netherlands
Correspondence: S. Veldkamp
Pediatric Rheumatology, **23(2):** P141

Introduction: Juvenile Dermatomyositis (JDM) is characterized by a dysregulated type I interferon (IFN) pathway, making it an interesting choice of target. Janus kinase inhibitors (JAKi) are increasingly being used in JDM, although the optimal choice of JAKi remains unknown.
Objectives: To develop an in vitro model to study the inhibition of IFN-mediated responses in JDM using different JAKi and Siglec-1 (an IFN-induced monocyte marker) as read-out.
Methods: Healthy donor (HD) PBMCs were cultured for 18 hours with IFN-α, IFN-β, plasma from JDM patients, or plasma from HDs. Siglec-1 expression on CD14+ monocytes was analyzed using flow cytometry. Inhibitory assays involved pre-incubation with interferon-α/β receptor (IFNAR)-blocking antibody and with JAKi (filgotinib, tofacitinib, baricitinib, ruxolitinib, deucravacitinib) at concentrations of 0.1, 1.0 and 10.0 µM. Correlations between JDM plasma-induced Siglec-1 levels and clinical disease activity, measured by Physician's Global Assessment (PGA) scores, were analyzed. IFN-α and -β levels in the patient plasma were measured by an in-house developed Simoa assay and were correlated with plasma-induced Siglec-1 levels.
Results: Siglec-1 expression was induced by IFN-α and IFN-β, which could be prevented by IFNAR blockade and by various JAKi in a dose-dependent manner. IFN-β-mediated induction was more effectively inhibited by filgotinib, a JAK1 inhibitor, and less effectively by deucravacitinib, a TYK2 inhibitor, when compared to IFN-α-mediated induction, suggesting that IFN-β signaling may be more dependent on JAK1 than IFN-α. Co-culture with plasma from JDM patients induced Siglec-1 expression on healthy monocytes, which could be inhibited by JAKi and IFNAR blockade. Plasma-induced Siglec-1 levels correlated strongly with clinical disease activity ($rs = 0.99$, $p<0.001$) and with IFN-β plasma levels ($rs = 0.97$, $p<0.001$), but not with IFN-a plasma levels ($rs = 0.4$, $p = 0.4$).
Conclusion: Our data support Siglec-1 as a reliable in vitro marker for type I IFN activity and demonstrate the assay's potential for studying patient-specific IFN responses. Moreover, our findings point to IFN-β as the main driver of the type I IFN signature in JDM, highlighting it as a promising therapeutic target.
Disclosure
None declared

P142

Advances in juvenile dermatomyositis: biomarker and mri sensitivity, patient outcomes and steroid management in a dutch national prospective cohort

S. Veldkamp[1], L. van der Griend[2,3], E. Noppers[2], W. Armbrust[4], J. M. van den Berg[5], P. C. Hissink Muller[6], E. Hoppenreijs[7], S. Kamphuis[8], J. Wienke[1], F. van Wijk[1], A. van Royen-Kerkhof[2], M. H. Jansen[2]
[1]Center for Translational Immunology, University Medical Center Utrecht, [2]Department of Paediatric Rheumatology and Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, [3]Utrecht University, Utrecht, [4]Department of Paediatric Rheumatology and Immunology, University Medical Center Groningen, Groningen, [5]Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam University Medical Centres, location AMC, Emma Children's Hospital, Amsterdam, [6]Department of Paediatric Rheumatology, Leiden University Medical Centre, Willem Alexander Children's Hospital, Leiden, [7]Department of Paediatric Rheumatology, Radboud University Medical Centre, Amalia Children's Hospital, Nijmegen, [8]Department of Paediatric Rheumatology, Erasmus University Medical Centre, Sophia Children's Hospital, Rotterdam, Netherlands
Correspondence: S. Veldkamp
Pediatric Rheumatology, **23(2):** P142

Introduction: Juvenile Dermatomyositis (JDM) is a rare and heterogeneous immune-mediated disease with suboptimal treatment responses. Evaluating patient outcomes and the role of diagnostic tools in clinical practice can help refine disease management and improve care.
Objectives: The aim of this prospective study was to describe the characteristics and outcomes of the Dutch JDM population.
Methods: Demographics, clinical features, diagnostic test results, and medication use were prospectively evaluated at diagnosis and during follow-up visits in JDM patients diagnosed between 2007 and 2024 in the study-coordinating center and between 2015 and 2024 in five other tertiary referral hospitals.
Results: The incidence was established at 2.9 cases/million children/year. A total of 83 patients were included (65% female). The median age at diagnosis was 6.0 years (IQR 4–9). The duration between symptom onset and diagnosis was 3.0 months (IQR 1.3–5.9). Patients were followed for a median of 3.2 years (IQR 1.4–5.8) with a median number of visits of 11 (IQR 6-16). The most common features at diagnosis were proximal muscle weakness (94.9%) and Gottron's papules/sign (79.7%). Myositis-specific autoantibodies were detected in 56.0%, with TIF1-γ (18.7%) and NXP2 (17.3%) being the most prevalent. While CK was abnormal in only 73.1%, IFN-related biomarkers Galectin-9 and CXCL10 were elevated in 98.3% and 93.3% at diagnosis, respectively. Whole-body MRI showed muscle edema in 30/33 (90.9%) patients, whereas muscle biopsy was abnormal in 21/27 (77.8%) patients. Corticosteroids could be tapered to 0.2 mg/kg at 6 months in only 41.5%. Of all patients, 24 (28.9%) had a refractory disease course and 27 (32.5%) experienced one or more flares. Nearly half of all flares (20/43) occurred closely after steroid dose reduction or discontinuation. Calcinosis occurred in 12 patients (14.5%) and damage-related symptoms in 26.9%. At last follow-up, 28.9% of patients had clinically inactive disease without medication. No patient died.
Conclusion: This prospective cohort study provides the first comprehensive report on the Dutch JDM population, showing similarities to other cohorts in incidence, female/male ratio, age at diagnosis, and time to diagnosis. Our data highlight the superior diagnostic sensitivity of Galectin-9 and CXCL10 over CK, the high sensitivity of MRI, and the frequent occurrence of refractory disease and flares despite immunosuppressive treatment. Reliable predictors are needed to identify patients who can safely taper immunosuppressants versus those needing continued treatment, and who may benefit from targeted therapies initiated upfront.
Disclosure
None declared

P143

Intravenous immunoglobulin therapy in juvenile dermatomyositis: a multicenter retrospective evaluation of clinical practice

S. D. Arik[1], G. Kavrul Kayaalp[1], Ö. Akgün[1], A. Doğru[1], B. Başer Taşkın[1], B. Menentoğlu[1], A. Dudaklı[1], S. Türkmen[2], N. Z. Özaslan[3], N. Şahin[3], M. Çakan[4], B. Sözeri[2], N. Aktay Ayaz[1]
[1]Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, [2]Clinics of Pediatric Rheumatology, Umraniye Training and Research Hospital, [3]Clinics of Pediatric Rheumatology, Kocaeli University Kocaeli Faculty of Medicine, [4]Clinics of Pediatric Rheumatology, University of Health Sciences Zeynep Kamil Education and Research Hospital, Istanbul, Türkiye
Correspondence: S. D. Arik
Pediatric Rheumatology, **23(2):** P143

Introduction: Juvenile dermatomyositis (JDM) is the most prevalent subtype of juvenile idiopathic inflammatory myopathy and is characterized by a capillary vasculopathy primarily affecting muscle and cutaneous tissues. The therapeutic efficacy of intravenous immunoglobulin (IVIG) was initially demonstrated in a controlled clinical trial involving adult patients with dermatomyositis. However, to date, no randomized controlled trials have evaluated IVIG use in the pediatric JDM population.
Objectives: In this multicenter study, we aim to present and evaluate our collective clinical experiences with the use of IVIG in the management of JDM.
Methods: This multicenter retrospective study included patients diagnosed with JDM before age 18 who received IVIG treatment at any point during their disease course in four pediatric rheumatology centers. All patients fulfilled the Bohan and Peter diagnostic criteria and provided informed consent. Clinical, demographic, and laboratory data were collected from medical records. Indications for IVIG included refractoriness to standard therapies, severe skin or organ involvement, or calcinosis. Treatment responses were evaluated using PRINTO/ACR/EULAR juvenile dermatomyositis core set measures, including CMAS, MMT-8, Patient and Physician Global VAS scores, and serum CPK levels.
Results: A total of 29 patients with JDM were included in the study, of whom 18 (62.1%) were female. The median age at diagnosis was 5.54 years (IQR: 3.29–9.44), and the median disease follow-up duration was 3.74 years (IQR: 2.37–7.08). IVIG therapy was initiated at a median of 3.54 months (IQR: 0.18–18.95) after diagnosis, with a median treatment duration of 8.34 months (IQR: 5.55–22.25). All patients exhibited muscle weakness, myalgia, and skin involvement at diagnosis. Common mucocutaneous findings during the disease course included heliotrope rash (86.2%), Gottron's papules (82.8%), malar rash (82.8%), photosensitivity (62.1%), calcinosis (41.4%), Shawl sign (17.2%), lipodystrophy (17.2%), cutaneous ulcers (13.8%), and Raynaud's phenomenon (10.3%). Muscle strength and disease activity improved significantly throughout treatment. Median CMAS scores rose from 22 at diagnosis to 47 after IVIG and 51.5 at final follow-up. Patient VAS scores decreased from a median of 9 to 0, while physician VAS scores decreased from 8 to 2. Patients received a median of 6 IVIG infusions (IQR: 5.5–9), with most receiving 1 g/kg/month; 17.4% received 2 g/kg/month. Twenty-four patients (82.8%) continued corticosteroids during IVIG (median dose 1 mg/kg/day). Biologic therapy was administered to 12 patients (41.4%), with 6 already on biologics at IVIG initiation due to refractory disease. The most common indication was decreased muscle strength (55.17%), moderate disease activity at diagnosis (31.03%), calcinosis (20.68%), severe skin findings (13.79%), and interstitial lung disease (3.44%). During IVIG treatment, disease flare-ups occurred in 7 patients (24.1%); however,no adverse effect related to IVIG were reported in any case.
Conclusion: This multicenter retrospective study supports the use of IVIG in JDM, especially for patients with muscle weakness, moderate disease activity, or calcinosis. Significant improvements in CMAS and VAS scores were observed, with no adverse events reported. IVIG was often used alongside steroids and biologics, suggesting a beneficial role in refractory or severe cases within a multidisciplinary treatment approach.
Disclosure
None declared

P144

Differences in clinical presentation and interferon signature gene assay between patients with JDM and JDM overlap syndromes

S. Cuyx[1], H. Codes-Méndez[2], A. Barmpakou[1], E. Moraitis[1], S. Lacassagne[1], M. Al-Obaidi[1], C. Papadopoulou[1]
[1]Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [2]Rheumatology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
Correspondence: S. Cuyx
Pediatric Rheumatology, **23(2):** P144

Introduction: In juvenile dermatomyositis (JDM), upregulation of the interferon (IFN) signalling system has been described. Exploration of the IFN signature gene assay (ISGA) as a biomarker for disease activity is ongoing.
Objectives: To assess clinical and ISGA differences between patients with JDM and JDM overlap syndromes and the potential value of ISGA in differential diagnostics.
Methods: A retrospective study of patient records was conducted at the largest paediatric rheumatology centre in the UK. Data collection spanned the period from 03/2020 until 05/2024. IFN type I and II gene expression were assessed using quantitative RT-PCR. The expression of the following genes was measured: CXCL9, CXCL10, IFI27, IFI44L, IFIT1, IFNB1, IFNG, IL-18, RSAD2, SIGLEC1. Disease activity was measured using several validated scales (CMAS, MMT8, mDAS). Statistical analysis

included Mann Whitney U tests and Fisher's exact tests to differentiate between "pure" JDM and JDM overlap syndromes.
Results: A total of 74 patients, encompassing 157 study visits, were analysed. Of these, 15 patients had a JDM overlap syndrome with a total of 24 study visits between them.
Patients with JDM overlap were older (p<0.001) in years at diagnosis (median 8; IQR 9-11) versus those with JDM (median 6; IQR 3-8). The predominance of female patients was more pronounced (p=0.030) in the overlap group (F:M ratio 38:21 for JDM versus 14:1 for JDM overlap).
During their study visits, patients with JDM, when compared to those with JDM overlap, more often showed active pulmonary (p=0.019) and skeletal involvement (p=0.002), but there was no statistically significant difference regarding muscular or cutaneous involvement. CMAS, MMT8, and mDAS scores did not significantly differ between the two groups.
CK was higher (p=0.010) for JDM (median 121; IQR 76-201) versus JDM overlap (median 72; IQR 49-99), but there was no significant difference for ALT, AST, LDH, or ESR.
When correcting for multiple statistical tests, none of the IFN gene expression scores differed significantly between JDM and JDM overlap, neither for absolute values per gene nor for comparisons between normal versus elevated ISGA values.
Conclusion: The current study shows that patients with JDM overlap are older at diagnosis, more often female, have active pulmonary and skeletal involvement less often, and have lower CK when compared to those with "pure" JDM. While ISGA did not differ significantly between JDM and JDM overlap, previous work showed its potential as a biomarker and the association between specific gene expression signatures and clinical characteristics such as muscle, skin, respiratory, gastro-intestinal, and skeletal involvement.
The current study is limited by its retrospective nature and the convenience cohort being from a "real-life" clinical setting. Further studies with prospective inclusion and standardised measurement intervals could further elucidate and strengthen the use of the ISGA as a biomarker for diagnosis and follow-up.
Disclosure
None declared

P145

The impact of fatigue in juvenile dermatomyositis

S. Rosina[1], A. I. Rebollo-Giménez[2], L. Tarantola[3], C. Campone[3], V. Natoli[3], F. Bovis [4], A. Consolaro[1,3], A. Ravelli[3,5]
[1]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [2]Health Research Institute Gregorio Marañón (IiSGM), Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), [4]Department of Health Sciences (DISSAL), University of Genoa, [5]Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: S. Rosina
Pediatric Rheumatology, **23(2):** P145

Introduction: Fatigue is a key symptom of patients with juvenile dermatomyositis (JDM). However, although it can be very disabling and have a profound impact on quality of life (QoL), its assessment is not included in response criteria and is seldom incorporated in routine practice.
Objectives: To investigate the relationship between fatigue and clinical measures of disease activity and parent-reported outcomes (PROs).
Methods: The clinical charts of patients with JDM followed at study center from October 2016 to March 2025 were reviewed retrospectively. For each patient, the first available visit with complete data was retained. Physician-centered outcomes were retrieved, together with the main PROs. Fatigue was assessed through a 21-points 0-10 numeric rating scale (NRS) (0 = no fatigue; 10 = extreme fatigue). Baseline associations between fatigue scores and demographic and clinical variables as well as PROs were evaluated using Spearman's rank correlation test. Correlations >0.7, 0.4-07 and <0.4 were considered high, moderate, and low, respectively. Fatigue scores were also compared among different groups of patients using either U-Mann-Whitney or Kruskal-Wallis test.
Results: 49 patients (59.2% female) with a mean age at visit of 8.9 ± 5.0 years were included. 53.1% were ANA-positive, and 61.7% myositis-specific antibody-positive. Child's fatigue was reported by 69.4% of parents, with a median NRS value of 5 (IQR: 0-8). Moderate to strong correlations were demonstrated between fatigue scores and physician's global assessment of disease activity (r=0.71), parent's global assessment of child's well-being (r=0.77), MMT8 (r=−0.63), hybrid MMT/CMAS (r=−0.65), total DAS (r=0.69), JDMAI1 (r=0.75) and JDMAI2 (r=0.78). Correlations with functional ability and QoL measures were moderate to high (r=0.61-0.79), whilst correlations with skin measures, muscle enzymes and damage index were low (r=−0.16–0.37). Fatigue scores were higher in patients with active disease than in those with remission, as assessed by JDMAI1- and JDMAI2-based criteria and by parent's subjective judgement (p<0.0001). Median fatigue scores were also higher in patients with impaired physical function than in those with normal functionality (6.42 vs 0.60, p<0.0001), and in patients whose parents were not satisfied with their child's disease outcome than in those who were satisfied (6.25 vs 0.00, p<0.0001).
Conclusion: Fatigue is common in children with JDM, and is strongly associated with reduced QoL and impaired physical function, as well as with level of disease activity and parents' satisfaction with illness outcome. Based on its marked impact on patients' health status, fatigue should be considered for inclusion in composite disease activity scores and response criteria used in JDM. It may also represent a qualified therapeutic goal in the treat-to-target strategy for this disease.
Disclosure
None declared

P146

Serum IL-18 and CXCL-9 as biomarkers of interstitial lung disease associated with juvenile idiopathic inflammatory myopathies

S. Kittivisuit[1,2], Y. Hong[2], P. Brogan[2,3], D. Eleftheriou[2,3], C. Papadopoulou[3] on behalf of UK Juvenile Dermatomyositis Cohort and Biomarker Study (JDCBS) research group
[1]Department of Paediatrics, Prince of Songkla University, Hat Yai, Thailand, [2]Infection, Immunity and Inflammation Department, University College London Great Ormond Street Institute of Child Health, [3]Department of Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH), London, United Kingdom
Correspondence: S. Kittivisuit
Pediatric Rheumatology, **23(2):** P146

Introduction: Interstitial lung disease (ILD) is a potentially life-threatening complication and a major cause of mortality in patients with juvenile idiopathic inflammatory myopathies (JIIM). However, studies evaluating biomarkers associated with ILD are limited, and their findings remain inconsistent.
Objectives: This study aimed to investigate role of serum IL-18 and CXCL-9 as biomarkers of ILD in JIIM patients.
Methods: This study is part of the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland). We included 26 patients with ILD, 41 without ILD, all with available serum samples at diagnosis and/or follow-up. Serum samples at diagnosis were available from 15 ILD patients and 39 non-ILD patients. Additionally, samples from 25 healthy controls were included. Serum IL-18 and CXCL-9 levels were measured using U-PLEX Human Assays (Meso Scale Discovery, Maryland, US). Clinical data, muscle weakness scores, laboratory findings, and ILD-related information were comprehensively reviewed.
Results: Patients with ILD were significantly older at presentation than those without ILD (median age 11.1 [IQR 9.8–14.3] vs 8.3 [IQR 4.9–12.6] years; p = 0.003). While most patients in both groups were diagnosed with juvenile dermatomyositis, overlap syndromes were more common in the ILD group (30.8% vs 4.9%; p = 0.018). The ILD group had a higher prevalence of anti-MDA5 antibodies (30.8% vs 2.4%; p = 0.005) and higher serum IgG levels (16.4±4.5 vs 11.7±4.8 g/dL; p = 0.002). At diagnosis, serum IL-18 levels were significantly higher in the ILD group (median 20,583.6 [IQR 15,461.2–29,648.2] pg/mL) compared to the non-ILD group (7,832.2 [IQR 5,392.3–12,441.2] pg/mL; p < 0.001) and healthy controls (722.3 [IQR 419.5–863.4] pg/mL; p < 0.001). Serum CXCL9 levels were also significantly higher in the ILD

group compared to healthy controls (1,999.5 [IQR 791.8–8,915.0] vs 926.1 [IQR 454.6–1,515.9] pg/mL; $p = 0.032$) and trended higher than the non-ILD group (972.2 [IQR 585.5–2,480.4] pg/mL; $p = 0.137$). At 1-year follow-up, both serum IL-18 (4,158.0 [IQR 2,932.0–6,839.0] pg/mL; $p = 0.005$) and CXCL9 (634.8 [IQR 432.9–760.7] pg/mL; $p = 0.016$) significantly decreased from baseline. Serum IL-18 levels at diagnosis showed significant positive correlations with ferritin (r = 0.58), lactate dehydrogenase (r = 0.33), IgG levels (r = 0.45), IgA (r = 0.47), and significant negative correlations with FEV_1 % predicted (r = –0.51), FVC % predicted (r = –0.46), DLCO % predicted (r = –0.53), and KCO z-score (r = –0.88), all with $p < 0.05$.
Conclusion: Serum IL-18 and CXCL-9 may serve as potential biomarkers in juvenile idiopathic inflammatory myositis (JIIM) for both identifying the presence of ILD and monitoring treatment response.
Disclosure
None declared

P148

Single-centre experience with JAK inhibitors in the treatment of juvenile dermatomyositis

T. Hinze[1], F. Gohar[1], C. Hinze[2], D. Windschall[1,3]
[1]Clinic for Paediatric and Adolencent Rheumatology, St. Josef-Stift Hospital, Northwest German Center for Rheumatology, Sendenhorst, [2]Clinic for Paediatric Rheumatology and Immunology, University Hospital Muenster, Muenster, [3]University of Halle-Wittenberg, Germany, Halle, Germany
Correspondence: T. Hinze
Pediatric Rheumatology, **23(2):** P148

Introduction: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathie in childhood. Despite the availability of various effective treatments, some patients experience chronic disease and complications. Janus kinase (JAK) inhibitors have emerged as a promising therapeutic option for patients with JDM.
Objectives: The aim of this study was to evaluate the treatment response with JAK inhibitors in patients with JDM.
Methods: We retrospectively reviewed internal medical records from January 2020 to January 2025 to identify patients diagnosed with JDM who received JAK inhibitor therapy. Treatment response was assessed using the Childhood Myositis Assessment Score (CMAS), interferon score (IFS), and physician global assessment (PG). The IFS represents the expression of six type I interferon-stimulated genes measured by real-time PCR, with values above 5.3 considered elevated.
Results: Between January 2020 and January 2025, six patients with JDM were treated with JAK inhibitors at our centre. Antibody profiles included MDA5 (n=3), NXP2 (n=1), Jo-1 (n=1), and Mi2/TIF1γ (n=1). The median age at diagnosis was 12 years (range 4–16). All patients had received prior treatments and continued background therapies during JAK inhibitor use. One MDA5-positive patient had skin and lung involvement without muscle disease. Another MDA5-positive patient presented with severe vasculitis and digital necrosis. The NXP2-positive patient had extensive calcinosis but no active disease. Two patients (Jo-1 and Mi2/TIF1γ positive) had therapy-resistant skin disease. Median IFS decreased from 55.15 (range 2.9–155) at baseline to 23.0 (range 1.2–48.4) after 12–18 months of treatment. Median CMAS improved from 44 (range 26–52) to 49 (range 40–52), and PG scores declined from 9 (range 9–10) to 2.5 (range 1–7). The extensive calcinosis in the NXP2-positive patient improved markedly. Notably, the patients with MDA5 and NXP2 antibodies showed substantial improvement, whereas no response was observed in patients with refractory skin involvement.
Conclusion: JAK inhibitors appear to be an effective treatment for selected patients with JDM including patients with calcinosis cutis, particularly those with MDA5 or NXP2 antibodies. However, therapy-resistant skin involvement may not respond to JAK inhibition. Further studies are warranted to confirm these findings and refine patient selection.
Disclosure
T. Hinze Grant/Research Support with: Novartis-funded research projects, F. Gohar: None declared, C. Hinze: None declared, D. Windschall: None declared

P149

Early intravenous methylprednisolone pulse therapy provides clinical benefits in children with juvenile dermatomyositis

T. Nagakura[1], Y. Yamasaki[2], H. Wakiguchi[1], T. Ito[3], A. Nakamura[2], T. Mitsunobu[2], S. Takei[2]
[1]Department of Pediatrics, Oita University Faculty of Medicine, Yufu, [2]Department of Pediatrics, Kagoshima University Hospital, Kagoshima, [3]Department of Pediatrics, University of Occupational and Environmental Health, Kitakyusyu, Japan
Correspondence: T. Nagakura
Pediatric Rheumatology, **23(2):** P149

Introduction: The best goal for children with juvenile dermatomyositis (JDM) is to achieve clinical remission (CR) off medication; however, two-thirds of patients suffer from chronic or recurrent disease.
Objectives: To identify the benefits of early introduction of intravenous methylprednisolone (IVMP) pulse therapy in JDM.
Methods: This was a retrospective single-center study of patients with JDM from 1997 to 2016. Children aged ≤ 18 years who had definite, probable or possible JDM according to Bohan and Peter criteria were reviewed. For analysis, patients were divided into two groups based on whether they received IVMP pulse therapy within 6 months from disease onset (early IVMP), or not (non-early IVMP). CR off medication was defined as no evidence of active myositis or elevation of serum muscle enzymes for ≥ 6 months without any medication. The primary endpoint was the cumulative rate of CR off medication at 5 years after initial glucocorticoid (GC) treatment, and the secondary endpoints were the frequency of relapse and development of calcinosis.
Results: A total of 34 children (16 boys and 18 girls) with 25 definite, 7 probable and 2 possible JDM were analyzed. The median (interquartile range, IQR) duration of follow-up was 103.9 (56.5-146.7) months. The median (IQR) age at onset was 5.9 (2.7-8.4) years, and the median (IQR) disease duration before starting GC was 4.4 (2.0-9.8) months. Twenty-two (64.7%) patients started with IVMP (at least 2 courses), followed by the combination of oral GC and immunosuppresants; 13 (38.2%) patients received IVMP within the first 6 months (early IVMP group). On the other hand, 12 patients were initially treated with oral GC (1-2mg/kg/day). At baseline, there were no significant differences in demographics, clinical and laboratory parameters between the two groups, except for the disease duration before GC initiation; the median (IQR) disease duration was 3.1 (1.9-4.7) and 6.7 (3.0-11.7) months in the early IVMP and non-early IVMP groups, respectively (p = 0.049). A total of 18 (52.9%) patients achieved CR off medication at the last follow-up; and the median (IQR) time to achieve CR off medication was 62.4 (40.1-76.3) months. Kaplan-Meier analysis revealed that the cumulative rate of CR off medication at 5 years was significantly higher in patients with early IVMP (49.5%) than those with non-early IVMP (14.3%), (p = 0.008). About two-thirds of patients experienced relapses of disease: more frequently observed in patients with non-early IVMP (16/21, 76.2%) than those with early IVMP (6/13, 46.2%), (p = 0.075). No patients in the early IVMP group developed calcinosis while 9 of 21 (42.9%) patients in the non-early IVMP group did (p = 0.006).
Conclusion: Early initiation of IVMP pulse therapy is crucial not only for achieving CR off medication but for preventing calcinosis in children with JDM.
Disclosure
None declared

P150

Type i interferon signature is associated with disease activity and muscle outcomes in juvenile dermatomyositis

V. Natoli[1,2], F. Bovis[3], P. Bocca[2], S. Palmeri[1], S. M. Orsi[2], S. A. Stoian[1], D. Lemmi[1], A. I. Rebollo-Giménez[1,4], C. Campone[1], A. Consolaro[1,2], C. Malattia[1,2], R. Caorsi[1,2], R. Papa[2], M. Gattorno[2], A. Ravelli[1,5], S. Volpi[1,2], S. Rosina[2]
[1]Università degli Studi di Genova, Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), [2]IRCCS Istituto Giannina Gaslini, Paediatric Rheumatology and Autoinflammatory Diseases Unit, [3]Department of Health Sciences, University of Genoa, Genoa, Italy, [4]Hospital Universitario Príncipe de Asturias, Madrid, Spain, [5]IRCCS Istituto Giannina Gaslini, Direzione Scientifica, Genoa, Italy
Correspondence: V. Natoli
Pediatric Rheumatology, **23(2):** P150

Introduction: Type I interferons play a key role in the pathogenesis of juvenile dermatomyositis (JDM). Type I IFN-related gene signatures (IGS) have emerged as potential biomarkers of disease activity, but their association with clinical outcomes in JDM remains to be fully defined.
Objectives: To evaluate associations between IGS and clinical parameters, disease activity states, and remission status in JDM.
Methods: All available IGS measurements made in JDM patients followed at the Gaslini Institute (Genoa, Italy) between 2019 and 2025 were retrieved (N=101). After excluding repeated samples, 43 patients were included, of whom only the first available sample was analyzed. IGS was determined as previously described[1]. Correlations of IGS with Juvenile DermatoMyositis Activity Index (JDMAI) 1 and 2[2], physician global assessment (PhGA), MMT8, hybrid MMT/CMAS (hMC)[3], muscle and skin component of DAS, and 0-10 skin visual analog scale (VAS) were tested using Spearman's rank correlation. IGS were compared across JDMAI1- and JDMAI2-defined disease activity states[4], using the Kruskal-Wallis test and post-hoc comparisons. Mann-Whitney U test was used to compare IGS by the presence or absence of muscle and skin remission and complete clinical response, and by muscle enzyme status (normal vs elevated).
Results: IGS showed a moderate correlation with JDMAI1 (R=0.64, p<0.001), JDMAI2 (R=0.65, p<0.001), PhGA (r=0.61, p<0.001), MMT8 (R=−0.56, p<0.001) and hMC (R=−0.42, p=0.008), whilst no significant correlations were observed with skin VAS and skin DAS. IGS levels were significantly higher in patients classified as being in the state of high disease activity (HDA) than in those with inactive disease (ID) (median JDMAI1 3.5 vs 0.31, p=0.018; median JDMAI2 3.3 vs 0.3, p=0.0009) and low disease activity (LDA) (median JDMAI1 3.5 vs 0.3, p=0.017). IGS distinguished well patients with muscle remission vs those with active muscle disease (p=0.007), with complete clinical response vs no response (p=0.056), and with normal vs elevated muscle enzymes (p=0.020).
Conclusion: IGS levels were associated with higher global and muscle disease activity scores, but not with skin disease activity measures. IGS levels discriminated strongly between HDA and ID/LDA states, as well as between patients who experienced or did not experience muscle remission, complete clinical response, or had or did not have normal muscle enzymes. These observations support the potential role of IGS measurement as a biomarker for disease monitoring and for defining treatment targets in the treat-to-target strategy for JDM.
Disclosure
None declared

References
1. Tesser A et al. Type I interferon signature: a quantitative standardized method for clinical application. Clin Exp Immuno. 2025
2. Rosina S et al. Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis. Rheumatology (Oxford) 2019.
3. Varnier GC et al. Development and testing of a hybrid measure of muscle strength in juvenile dermatomyositis for use in routine care. Arthritis Care Res (Hoboken) 2018.
4. Rosina S et al. Defining criteria for disease activity states in juvenile dermatomyositis based on the Juvenile Dermatomyositis Activity Index. RMD Open 2024

P151

Characterisation of myositis-specific and myositis-associated antibodies in juvenile idiopathic inflammatory myositis: insights from a north indian cohort

V. Pandiarajan, S. Basu, P. L. Nadig, S. Sivagnanaganesan, A. Dod, R. Kumrah, R. Garg, P. Khalko, M. Sudhakar, R. Tyagi, M. Dhaliwal, S. Sharma, R. Pilania, D. Suri, A. Rawat, S. Singh
Postgraduate Institute of Medical Education and Research, Chandigarh, India
Correspondence: V. Pandiarajan
Pediatric Rheumatology, **23(2):** P151

Introduction: Myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) are important biomarkers for diagnosing, classifying, and predicting outcomes in juvenile idiopathic inflammatory myopathies (JIIM). These autoantibodies are increasingly recognised for their connection to specific clinical phenotypes, disease severity, and complications such as interstitial lung disease and calcinosis [1, 2]. However, reports on MSAs and MAAs in JIIM from India are limited, and awareness among paediatricians and rheumatologists is not widespread.
Objectives: This study aimed to examine the prevalence and clinical characteristics associated with MSA/MAA in a cohort of JIIM patients from North India.
Methods: We conducted a retrospective review of medical records from the Pediatric Rheumatology Clinic at a tertiary care referral centre in Chandigarh, North India, spanning the period from January 1992 to October 2024. We analysed clinical data from children diagnosed with juvenile idiopathic inflammatory myopathy (JIIM). Myositis-specific and myositis-associated autoantibody testing was performed using a 16-antigen immunoblot assay (Euroline Autoimmune Inflammatory Myopathies 16 Ag, Euroimmun, Lübeck, Germany). In our study, we included JIIM patients who tested positive for at least one myositis-specific or myositis-associated autoantibody at a level of 1+ or higher. Cases with two or more autoantibodies showing a positivity of 1+ or greater on the immunoblot were classified as having mixed positivity. We excluded trace-level positivity, particularly in treatment-naïve patients and those with multiple positive autoantibodies.
Results: In our cohort of 173 patients diagnosed with Juvenile Idiopathic Inflammatory Myopathy (JIIM), MSA/MAA testing was performed on 113 individuals. This group included patients with juvenile dermatomyositis (n=89), clinically amyopathic dermatomyositis (n=8), overlap myositis (n=13), and juvenile polymyositis (n=3). Autoantibodies were detected in 72.5% of these patients (82 out of 113). The most frequently identified antibody was anti-NXP2 (n=24), followed by anti-MDA5 (n=14), anti-TIF-1γ (n=12), and anti-Mi-2 (n=9). Children who tested positive for anti-NXP2 were diagnosed at a younger age, with a mean of 3.15 years (range: 1.2–11.88 years; p=0.015). They also exhibited more pronounced muscle weakness at disease onset (p=0.04) and showed persistent calcinosis during follow-up (p=0.004). Persistent skin involvement during follow-up was commonly observed in patients with anti-TIF1γ antibodies (p<0.001). In cases of anti-MDA5-positive juvenile dermatomyositis, there was a higher incidence of arthritis (p=0.001), inverse Gottron papules (p=0.003), skin ulcerations (p=0.065), oral ulcers (p=0.012), and interstitial lung disease (ILD) (p<0.001).
Conclusion: In North Indian children with JIIM, 72.5% show positivity for myositis-specific or myositis-associated autoantibodies when tested using a standardised 16-antigen myositis immunoblot assay. Anti-NXP2 emerges as the most frequently detected autoantibody, followed by anti-MDA5 and anti-TIF1γ. Anti-NXP2 is linked to an earlier age of onset and a higher prevalence of calcinosis, whereas anti-MDA5 is associated with interstitial lung disease and skin manifestations resembling type I interferonopathies.
Trial registration identifying number: Not applicable
Disclosure
None declared

References
1. Tansley SL, Simou S, Shaddick G, Betteridge ZE, Almeida B, Gunawardena H, et al. Autoantibodies in juvenile-onset myositis: Their diagnostic value and associated clinical phenotype in a large UK cohort. J Autoimmun. 2017;84:55–64.
2. Papadopoulou C, Chew C, Wilkinson MGL, McCann L, Wedderburn LR. Juvenile idiopathic inflammatory myositis: an update on pathophysiology and clinical care. Nat Rev Rheumatol. 2023;19(6):343–62.

P152

The effect of autoantibody negativity on clinical and prognosis in juvenile dermatomyositis

V. Gungorer[1], E. Kılıç Könte[2], G. Kılbaş[3], A. Uzun Bektaş[4], K. Uçak[5], B. Demirbaş[6], A. Günalp[2], P. Ö. Avar Aydın[7], N. Şahin[5], O. Köker[8], S. Özdel[6], K. Öztürk[9], M. Çakan[10], B. Kasap Demir[11], M. K. Gürgöze[12], S. Yüksel[13], S. E. Ünsal[4], Ö. Kasapçopur[2], B. Çelikel Acar[14]
[1]Pediatric Rheumatology, Health Science University, Gülhane Medical School, Gülhane Training and Research Hospital, Ankara, [2]Pediatric Rheumatology, İstanbul University, Cerrahpaşa Medical School, İstanbul, [3]Pediatric Rheumatology, Pamukkale University Medical School, Denizli, [4]Pediatric Rheumatology, Dokuz Eylül University Medical School, İzmir, [5]Pediatric Rheumatology, Kocaeli University Medical School, Kocaeli, [6]Pediatric Rheumatology, Etlik City Hospital, Ankara,

[7]Pediatric Rheumatology, Tekirdağ City Hospital, Tekirdağ, [8]Pediatric Rheumatology, Marmara University Medical School, [9]Göztepe Training and Research Hospital, Istanbul Medeniyet University, [10]Pediatric Rheumatology, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, İstanbul, [11]Pediatric Rheumatology, Izmir Katip Çelebi University Faculty of Medicine, İzmir, [12]Pediatric Rheumatology, Fırat University Medical School, Elazığ, [13]Pediatric Rheumatology, Çanakkale Onsekiz Mart University Medical School, Çanakkale, [14]Pediatric Rheumatology, Health Science University, Ankara Bilkent City Hospital, Ankara, Türkiye
Correspondence: V. Gungorer
Pediatric Rheumatology, **23(2):** P152

Introduction: Juvenile dermatomyositis (JDM) is the most common inflammatory myopathy in children. In 60-70% of patients, myositis specific autoantibodies (MSA) associated with clinical phenotypes and myositis-associated antibodies (MAA) are positive in the circulation. However, in some patients neither MSA nor MAA are detected.
Objectives: The aim of this study was to determine the clinical and prognostic characteristics of patients with JDM in whom autoantibodies were not detected and to determine their differences from JDM patients in whom autoantibodies were detected.
Methods: For this study, data from ten pediatric rheumatology centers in Türkiye were retrospectively analyzed. Patients <16 years of age and 0-17 years of age who were diagnosed with JDM and followed up for at least 6 months were included in the study. Patients were divided into two groups as those with positive and negative myositis-specific or myositis-related autoantibodies and clinical and prognostic differences between these two groups were evaluated.
Results: 83 (64.6%) of the patients were female. The mean age at symptom onset was 8.2±4.1 years. 79 patients (62.2%) had autoantibodies (66 have MSA, 17 MAA, 57 ANA) while 48 patients (37.8%) had no autoantibodies. The mean follow-up period was 58.0±46.7 months. When patients with and without autoantibodies were compared in terms of gender, age at onset of symptoms, age at diagnosis, parental consanguinity and presence of rheumatic diseases in the family, no significant difference was found between the two groups. There was no statistical difference between groups in terms of clinical findings at the time of diagnosis. However, heliotrope rash, Raynaud's phenomenon, lipodystrophy (p=0.024, p=0.001, p=0.027, respectively) and musculoskeletal involvement (p=0.032) were statistically significantly higher in the autoantibody positive group at follow up. While there was no difference between the two groups in terms of remission (p=0.132), the rate of drug-free remission was significantly higher in the autoantibody negative group (p=0.001).
Conclusion: In JDM, the pathogenesis of which is still not clearly understood, autoantibody negativity has been shown to favorably affect on prognosis, especially in long-term follow-up.
Disclosure
None declared

References

1. Kwiatkowska D, Reich A. The Significance of Autoantibodies in Juvenile Dermatomyositis. Biomed Res Int. 2021 Nov 19; 2021: 5513544. doi: https://doi.org/10.1155/2021/5513544.
2. Petty RE, Laxer Rm, Lindsley CB, Wedderburn LR. Juvenile Dermatomyositis. Textbook of Pediatric Rheumatology. 7th ed. Elsevier Health Sciences; 2015. p.351-83.
3. M. Pachman and A. M. Khojah, "Advances in juvenile dermatomyositis: myositis specific antibodies aid in understanding disease heterogeneity," The Journal of Pediatrics, vol. 195, pp. 16–27, 2018.
4. Tansle SL, Simou S, Shaddick G, Betteridge ZE, Almeida B, Gunawardena H, et al. Autoantibodies in juvenile-onset myositis: their diagnostic value and associated clinical phenotype in a large uK cohort. Journal of Autoimmunity. 2017; 84: 55-64.

P153

The use of tocilizumab in 11 patients with juvenile localized scleroderma – observations from 1 center

A. Gazda[1], B. Kołodziejczyk[1], O. Krasowicz-Towalska[1], J. Królikowska[1], P. Gietka[1], D. Labochka-Chyżyńska[1], M. Mańczak[2], K. Rząd[3], I. Sudoł-Szopińska[3], K. Rybak[1], K. Branicka[1], A. Kudlak[1]
[1]Clinic of Developmental Age Rheumatology, [2]Department of Gerontology and Public Health, [3]Department of Radiology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland
Correspondence: A. Gazda
Pediatric Rheumatology, **23(2):** P153

Introduction: Juvenile localized scleroderma (JLS) often leads to serious consequences in the musculoskeletal system with limb deformities, disability and significant cosmetic defects, especially in linear JLS of head and face. The treatment standards include local treatment, methotrexate (MTX), mycophenolate mofetile (MMF) and glucocorticosteroids (GCs), and biological drugs as a experimental treatment.
Objectives: 11 patients with JLS were treated in NIGRiR in Warsaw with tocilizumab (TOC) due to the severe course of JLS during the period 2020- 2025; 4 boys (36%) and 7 girls (64%). The median age at diagnosis was 4.3 years. In 3 patients (27%) limited deep JLS was diagnosed, in 1 (9%) "en coup de sabre" (EDCS), in 2 ECDS and progressive hemifacial atrophy PHA (18%), and in 5 cases (45%) mixed JLS. Previous treatments included MTX, MMF, Cyclosporin A, GCs or intravenous immunoglobulin. The median age for TOC initiation was 13.9 years. The time from diagnosis to the start of TOC treatment was 7.5 years. The median TOC treatment duration was 18 months (6- 38 m-ths).
Methods: In a retrospective analysis, the activity index mLOSSI, damage index LOSDI, motor function according to CHAQ and Physician Global Assessment (PGA) were assessed at the baseline, after 6, 12 months and at the 18-24 month period. In patients with ECDS once a year Magnetic Resonance (MR) of the facial skull was assessed: subcutaneous tissue narrowing, extent of the lesion and bone thickness were evaluated.
Results: A statistically significant improvement was achieved: after 6 months- reduction in LOSSi (p-0,012) and PGA (0,028); and after 12 months- mLOSSi (p-0,008) and PGA (p-0, 030). At the 18 to 24 month evaluation, improvement was no statistically significant, due to a decreased number of participants from 11 to 9 and a large range of values: from 1 to 17, no deterioration was observed. LOSDI scores remained stable; improvement in CHAQ recorded from the 6th month of observation showed no statistical significance. In MR patients with ECDS: in 2 cases progression of changes was halted; in 1 patient, there was progression in the extent of the lesion. TOC was well tolerated, with no SAE or serious infections observed; in 1 patient was discontinued due to leukopenia.
Conclusion: TOC treatment resulted in improvement or inhibition of disease progression (90%patients). A statistically significant improvement in mLOSSI and PGA was observed. LOSDI scores remained stable, no deterioration was observed. Treatment was well tolerated, only 1 patient had to discontinue the drug due to leukopenia.
Trial registration identifying number: Ethics committee 30.01.2025 nr KBT-1/5/2025
Disclosure
None declared

References

1. Zulian F. et al. Consensus-based recommendations for the management of juvenile localised scleroderma. Ann Rheum Dis. 2019 Aug;78(8):1019-1024. doi: https://doi.org/10.1136/annrheumdis-2018-214697. Epub 2019 Mar 2. PMID: 30826775; PMCID: PMC6691928.
2. Kelsey CE, Torok KS. The Localized Scleroderma Cutaneous Assessment Tool: responsiveness to change in a pediatric clinical population. J Am Acad Dermatol. 2013 Aug;69(2):214-20. doi: https://doi.org/10.1016/j.jaad.2013.02.007. Epub 2013 Apr 4. PMID: 23562760; PMCID: PMC3720681.
3. Sener S, Batu ED. Use of biologic drug in the treatment of localized scleroderma and systemic sclerosis in children: A scoping review. Semin Arthritis Rheum. 2025 Apr;71:152634. doi: https://doi.org/10.1016/j.semarthrit.2025.152634. Epub 2025 Jan 29. PMID: 39938346.

P154

A new fibrotic subtype of juvenile systemic sclerosis

F. Zulian[1], F. Tirelli[1], G. Mastrangelo[1], M. Binda[2], E. Zanatta[2], A. Meneghel[1]
[1]Department of Woman's and Child's Health, University Hospital of Padova, Pediatric Rheumatology Unit, [2]Department of Medicine-DIMED, University of Padova, Rheumatology Unit, Padova, Italy
Correspondence: A. Meneghel
Pediatric Rheumatology, **23(2):** P154

Introduction: Juvenile Systemic Sclerosis (JSSc) is a rare condition in childhood that encompasses a wide spectrum of clinical manifestations characterized by vascular and connective tissue abnormalities. According with the adult classification, four subtypes are usually considered: Diffuse (dcSSc), Limited (lcSSc), Sine Scleroderma (ssSSc) and Overlap syndrome (OS), when features of other connective tissue diseases are also present. The majority of patients with JSSc develop a broad spectrum of vascular manifestations, including Raynaud's phenomenon (RP), digital ulcers (DU) or vascular disease–related internal damage.
Objectives: To describe the clinical features and long-term outcome of a new JSSc subtype with no evident vascular component.
Methods: A prospective single center cohort study of consecutive children with jSSc, diagnosed according with the most recent classification criteria [1-3] and seen between january 2004 and December 2024, was conducted.Demographic, clinical, laboratory, autoantibody profile and treatment were captured following a harmonized protocol at six months interval time. The primary outcome was the achievement of disease Disease remission defined as good (remission with no or just symptomatic drugs), moderate (clinical remission on medication) or severe (death, end-stage organ failure, or rapidly progressing course). Statistical significance was considered for p-values <0.05. Statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).
Results: Forty-four patients, 68% female, with a mean age at 10.5 years (IQR 4.2-17) entered the study. Nineteen (43.2%) had dcSSc of whom 5 (11.4%), 1M, 4 F, never presented vascular manifestations. In this subgroup of patients, the skin involvement was predominant with mRSS ranging between 18 and 26 during the first six months since the disease onset. Internal organ involvement was present in four patients (pulmonary in 2, gastrointestinal in 4). All patients were ANA positive, none had SSc-specific autoantibodies and two had SSc-associated autoantibodies (Ro52, Pm-Scl75). Capillaroscopy abnormalities were detected in 4/5 patients (early > unspecific in two, active > late in two). All patients responded well to treatment with MTX in three, MMF/RTX in one and MMF alone in the other. After a mean follow-up of 7.8 years (range 2.7-12), the outcome was good in three patients and moderate in two (remission on medication for mild pulmonary disease). Indeed, the mRSS, at the last check, ranged between 0 (two patients), 2 (one patient) and 4 (two patients).
Conclusion: Our results suggested that, in addition to the established clinical phenotypes of jSSc, a new clinical entity characterized by the absence of vascular manifestations should be considered. We have termed this as Fibrotic Subtype (JSSc-FS). This subtype is characterized by predominant skin involvement, moderate internal organs abnormalities (namely pulmonary and gastrointestinal), absence of SSc-specific autoantibodies and good outcome. From a physiopathological point of view, JSSc-FS underlines the dual vascular/fibrosing nature of scleroderma, as described in adults [4]. Further studies are needed to confirm this preliminary observation and to clarify whether this represents a pediatric-only subtype.
Disclosure
None declared

Reference
1. van den Hoogen F, *Arthritis Rheum.* 2013;65(11):2737–47; Poormoghim H, et al. *Arthritis Rheum* 2000;43:444-51; Zulian F, et al., *Arthritis Rheum.* 2007;57(2):203-12; Allanore Y. Et al. *Arthritis Rheum* 2018;70:162–170

P155

Juvenile systemic sclerosis: clinical trajectories of 44 patients

A. Meneghel[1], F. Tirelli[1], G. Mastrangelo[1], B. Moccaldi[2], F. Vittadello[3], E. Zanatta[2], F. Zulian[1]
[1]Department of Woman's and Child's Health, University Hospital of Padova, Pediatric Rheumatology Unit, **[2]**Department of Medicine-DIMED, University of Padova, Rheumatology Unit, Padova, **[3]**Explora – Research and Statistical Analysis, Vigodarzere, Italy
Correspondence: A. Meneghel
Pediatric Rheumatology, **23(2):** P155

Introduction: Juvenile Systemic Sclerosis (JSSc) is a rare condition in childhood with a wide spectrum of clinical phenotypes characterized by vascular and connective tissue abnormalities. Although rare in pediatrics, juvenile systemic sclerosis (jSSc) is a severe and life-threatening condition that significantly impacts children's quality of life.
Objectives: To describe the clinical trajectories of a series of 44 patients followed at a single center.
Methods: A prospective single center cohort study of consecutive children with jSSc diagnosed according to actual classification criteria [1-3], between January 2004 and December 2024 was conducted.
Patients with JSSc, diagnosed according with the most recent classification criteria [1-3] and seen between january 2004 and December 2024, were evaluated. Demographic, clinical, imaging and laboratory data, autoantibody profile and treatment were collected at baseline and then every 6 months follow-up in a standardized format. Trajectories were defined, following the adult classification based on the skin involvement, in four subtypes: Diffuse, Limited, Sine Scleroderma and Overlap syndrome when specific skin and vascular changes are associated with other connective tissue diseases, namely dermatomyositis. Disease outcome at the last evaluation was categorized as good (remission with no or just symptomatic drugs), moderate (clinical remission on medication), severe (death, end-stage organ failure, progressing organs involvement).
Results: A total of 44 patients were included, 68% were female, the median age at onset was 10.5 years (IQR 4.2-17). Nineteen (43.2%) had diffuse cutaneous SSc (dcJSSc), 15 (34.1%) limited cutaneous SSc (lcJSSc), 5 (11.4%) overlap syndrome (OS), 5 (11.4%) sine scleroderma (ssJSSc).
Vascular involvement was present in 40 patients (Raynaud phenomenon 88.6%, digital ulcers 47.7%), pulmonary involvement in 43.2%, cardiac in 15.9%, gastrointestinal in 84.1%, renal in 4.5%. Pulmonary and cardiac involvement were significantly more frequent in dcSSc and ssSSc forms (p=0.05 and 0.001 respectively). All patients were ANA positive while scleroderma-specific autoantibodies were found in 54.5%: anti-topoisomerase 40.9%, anticentromere 6.8%, anti-RNA polymerase III 2.3%, anti-fibrillin 4.5%. Unlike in adults, we did not find any correlation between the presence of particular scleroderma-specific antibody and a specific organ involvement.
After a mean follow-up of 7.3 years (range 2-19), 34.1% of patients had a good, 38.6% moderate and 27.3% severe outcome. DcJSSc and ssJSSc subtypes presented a severe clinical course in 63.2% of patients that is significantly higher than in the other subtypes, all together (p=0.000).
Conclusion: Despite the innovative therapies introduced in the last decade, JSSc is a disease with a severe course and outcome in almost one third of patients and are significantly worse in the dcJSSc and ssJSSc subtypes. As in adults, the vascular phenotype is predominant and the SSc-specific autoantibodies are more represented in dcJSSc and lcJSSc subtypes. Conversely, no correlation was found between the presence of particular SSc-specific antibody and organ involvement.
Disclosure
None declared

Reference
1. van den Hoogen F, et al. Arthritis Rheum. 2013;65(11):2737–47; Poormoghim H, et al. *Arthritis Rheum* 2000;43:444-51; Zulian F, et al., *Arthritis Rheum.* 2007;57(2):203-12

P156

When occam's razor dulls: pansclerotic morphea amid complex comorbidities

A. Tavares[1], J. B. Lima[2], A. Bandeira[3], C. Garrido[4], S. Alves[5], C. Zilhão[5]
[1]Department of Pediatrics, Unidade Local de Saúde Gaia/Espinho, Vila Nova de Gaia, **[2]**Department of Pediatrics, **[3]**Hereditary Metabolic Diseases Reference Center, **[4]**Department of Pediatric Neurology, **[5]**Pediatric Rheumatology Unit, Centro Materno-Infantil do Norte, Oporto, Portugal
Correspondence: J. B. Lima
Pediatric Rheumatology, **23(2):** P156

Introduction: Pansclerotic morphea is a rare disabling subtype of localized scleroderma, with progressive fibrosis extending from the dermis to deeper tissues, including fascia, muscle, and bone.
Objectives: N/A

Methods: N/A
Results: A 17-year-old female of Romani origin, born to consanguineous parents, with previous diagnoses of medium-chain acyl-CoA dehydrogenase deficiency (MCAD) and dystroglycanopathy with longstanding tetraparesis and loss of independent ambulation since age 9. At 11, she was referred to pediatric rheumatology with sclero-atrophic skin lesions with a 2 months' evolution with increased limb stiffness and pain. There was no Raynaud's phenomenon or visceral involvement.
Examination revealed hypo- and hyperpigmented lesions on the trunk, abdomen, right upper limb, and lower limbs, with reduced tissue pliability, diffuse skin thickening, and scleroatrophic changes in both legs and feet. Fingers, toes, and face were spared. She had circumferential fibrosis of the lower limbs, 90° knee flexion contractures, limited elbows and wrists mobility and complete absence of ankle movement.
Laboratory findings showed elevated ESR (42 mm/h), hypergammaglobulinemia (2542 mg/dL), ANA 1:1280 (homogeneous), negative anti-dsDNA, anti-U1RNP, myositis-specific and systemic sclerosis antibodies, and increased muscle enzymes. MRI revealed global muscle atrophy with lipomatous involution, without bone involvement. Deep skin biopsy showed dermal/hypodermal fibrosis, adipocyte atrophy, and lymphoplasmacytic infiltrate, consistent with deep morphea.
Treatment included pulse corticosteroids followed by oral prednisolone and sc methotrexate, along with topical therapy and physiotherapy. At 6 months, a trophic ulcer infected with *Pseudomonas aeruginosa* required prolonged hospitalization and wound care. After 1 year, skin thickening had stabilized. At 6-year follow-up, inflammatory remission persisted, with no new lesions. However, overall joint mobility remained limited, influenced by the underlying neuromuscular disease. Laboratory parameters normalized, except for persistently elevated muscular enzymes. Methotrexate was maintained, and prednisolone—previously tapered to a minimal dose—was discontinued after 5 years.
Conclusion: This case highlights the rare coexistence of three severe conditions in a single patient. While no direct link has been established, their overlap emphasizes the need to consider multiple rare diagnoses in genetically vulnerable individuals. Functional improvement was difficult to assess due to baseline muscular impairment, and persistently elevated muscular enzymes raised uncertainty as to whether it reflected myopathy, disease activity, or methotrexate exposure. Despite the infectious complication, the patient achieved sustained improvement, underscoring the importance of multidisciplinary, individualized care in complex scenarios. Long-term functional prognosis remains poor due to the confluence of these rare conditions.
Disclosure
None declared

P157

More than what meets the eye: a not so obvious course

A. Batchu Prithvi, C. Govardhan, A. Ramanan
Paediatric Rheumatology, Bristol Royal Hospital for Children, Bristol, United Kingdom
Correspondence: A. Batchu Prithvi
Pediatric Rheumatology, **23(2):** P157

Introduction: Systemic sclerosis (SSc)is an autoimmune condition with visceral and skin fibrosis, vascular dysfunction and immune dysregulation. Cardiac manifestations in diffuse cutaneous form of juvenile SSc though rare can affect upto 3% of the children(1). Myocardial, pericardial, valvular or fibrosis of the conduction system constitute primary involvement(2). Whereas secondary can occur in the form pulmonary hypertension or secondary to interstitial lung disease or renal disease(2). Pericardial effusion in SSc is rare and can be asymptomatic and may portend a poor prognosis(3).
Objectives: To describe a young child with diffuse cutaneous SSc who developed massive pericardial effusion within 6 months of diagnosis
Methods: A descriptive case report for paediatric thieves market
Results: 6-year-old Caucasian girl, previously healthy presented with oedema of upper and lower limbs with progressive tightening of the skin. Examination-sclerodactyly, sclerotic skin involving symmetrically of both upper and limbs, anterior aspect of the chest. Modified Rodnan score-28/51. Baseline-normal full blood count and inflammatory markers. Anti-nuclear antibody and rheumatoid factor was positive. Systemic sclerosis antibody panel was negative. HRCT of chest and echocardiography were normal at the baseline. A clinical diagnosis of diffuse cutaneous systemic sclerosis was made. Treatment was commenced corticosteroids and mycophenolate mofetil. At 3 months, modified rodnan score remained unchanged hence received rituximab. At six months, she complained of left sided chest pain. Work up revealed massive pericardial effusion requiring a drain, no diastolic dysfunction or pulmonary hypertension. She received intravenous pulse methylprednisolone followed by oral weaning course. Planned for 6 cycles of intravenous cyclophosphamide.
Conclusion: Cardiac involvement although a rare in systemic sclerosis should be considered as a possibility. Clinicians should have a high index of suspicion and regular screening may be indicated as it could be clinically asymptomatic in small subgroup. Cardiac manifestation is to considered to be an important poor prognostic marker. Consent to published had been obtained.
Disclosure
None declared

References

1. Foeldvari I, Klotsche J, Torok KS, Kasapcopur O, Adrovic A, Stanevicha V, et al. Are diffuse and limited juvenile systemic sclerosis different in clinical presentation? Clinical characteristics of a juvenile systemic sclerosis cohort. J Scleroderma Relat Disord. 2019 Feb;4(1):49–61.
2. Lambova S. Cardiac manifestations in systemic sclerosis. World J Cardiol [Internet]. 2014 Sep 26 [cited 2025 May 13];6(9):993–1005. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4176808/. 3. Martini G, Vittadello F, Kasapçopur O, Magni Manzoni S, Corona F, Duarte-Salazar C, et al. Factors affecting survival in juvenile systemic sclerosis. Rheumatol Oxf Engl. 2009 Feb;48(2):119–22.

P159

Preliminary data of a monocentric study regarding the comparison of localized scleroderma assessment tools, teletermography and ultrasound in the evaluation of juvenile localized cutaneous scleroderma

C. Matucci Cerinic[1], S. La Bella[1], M. Virgilio[1], G. Viglizzo[2], L. Basso[3], M. Gattorno[1], C. Malattia[1]
[1]IRCCS Istituto Giannina Gaslini, Rheumatology and Autoinflammatory diseases; [2]IRCCS Istituto Giannina Gaslini, Dermatology department; [3]IRCCS Istituto Giannina Gaslini, Pediatric Radiology Department, Genoa, Italy
Correspondence: C. Matucci Cerinic
Pediatric Rheumatology, **23(2):** P159

Introduction: The assessment of disease activity in Juvenile Localized cutaneous scleroderma (JLS) is very often challenging due to the lack of standardized and reliable outcome measures. The clinical assessment is performed with the Localized Scleroderma Assessment Tool (LOSCAT) which consists in two parts, evaluating the disease activity (mLOSSI) and the damage (LOSDI) and with Infrared termography (IRT). More recently, also skin high frequency ultrasound (US) in the assessment of disease activity has been proposed.
Objectives: to compare the ability of LOSCAT, IRT and skin US to assess disease activity in JLS patients.
Methods: JLS patients followed at the Rheumatology Unit of the Istituto Gaslini Hospital were evaluated retro-prospectively. Patients were diagnosed according to 2006 Padua Classification criteria. A minimum follow-up of 6 months was required for inclusion. All patients were evaluated with LOSCAT, IRT (Lesions considered positive when warmer 0.5 °C than surrounding area or contralateral limb) and high frequency US (20 MHz probe, parameters of activity: increased hypodermal echogenicity or loss of dermo-hypodermal borders and increase of dermal and/or hypodermal vascularization, with signs of increased blood arterial or venous flow at color doppler with/without increased velocity > 2 cm/s).
Results: 7 patients were enrolled (4 male), with a mean age at disease onset of 7.4 years, and at enrolment of 11.95 years. 3 patients presented a circumscribed JLS, while 4 had a mixed type with linear and circumscribed JLS. All patients were off therapy at time of enrolment (in 2

cases therapies discontinued previously). 4 patients had an active disease at enrolment. All patients received an initial steroid course of 2mg/kg and methotrexate (MTX). Disease relapse on MTX therapy was documented in 2 patients, who were switched to mophetil micofenolate. A concordance between mLOSSI, IRT and US was found in 5 cases (71%). In 2 patients (28.6%) IRT and US showed a disease activity, with a negative mLOSSI, thus allowing therapy reintroduction/dose adjustment. In one patient mLOSSi reduced and IRT remained negative while US showed a disease activity. Specifically, the patients with a disease activity presented all an irregularity of the dermo- hypodermal junction and signs of an increased vascularization, with an increased peak velocity.
Conclusion: there was a good concordance in LOSCAT, IRT and high-frequency US in the assessment of disease activity, even if US and IRT were more efficient than LOSCAT alone in early detection of disease activity. Further studies on larger cohorts of patients are needed to confirm these preliminary findings obtained with three different outcome measures.
Disclosure
None declared

P160

Outcome measures for the assessment of cardiac involvement in juvenile systemic sclerosis: a scoping review

F. Tirelli[1], A. Leo[1], E. Marrani[2], B. Castaldi[3], A. Petaccia[4], P. Duong[5], S. Li[6], C. Pain[7], M. Twilt[8], N. Vasquez Canizares[9], F. Zulian[1]
[1]Pediatric Rheumatology, Department of Woman and Child Health, University Hospital of Padova, Padova, [2]Pediatric Rheumatology Unit, Meyer Children's Hospital IRCSS, Florence, [3]Pediatric Cardiology, Department of Woman and Child Health, University Hospital of Padova, Padova, [4]Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [5]Department of Cardiac Surgery and Cardiology, Alder Hey Children's Hospital, Liverpool, United Kingdom, [6]Hackensack Meridian School of Medicine, Joseph M. Sanzari Children's Hospital, Hackensack, United States, [7]Department of Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom, [8]Department of Pediatrics, Alberta Children's Hospital, Calgary, Canada, [9]Department of Pediatrics, Division of Pediatric Rheumatology, Children's Hospital at Montefiore/ Albert Einstein College of Medicine, Bronx, NY, United States
Correspondence: F. Tirelli
Pediatric Rheumatology, **23(2):** P160

Introduction: Juvenile Systemic Sclerosis (JSSc) is a rare condition in childhood that encompasses a range of disorders characterized by vascular and connective tissue abnormalities. Cardiac abnormalities, including arrythmias, cardiac fibrosis and heart failure, can be detected in up to 25% of children with jSSc and represent a leading cause of mortality; however, there are no definite standards for cardiac assessment in jSSc.
Objectives: To identify outcome measures used to assess cardiac involvement in SSc, as part of an international effort based on CARRA and PReS to establish consensus-based, organ-specific assessment standards for jSSc to be used in future studies[1].
Methods: Using the PRISMA-SCR framework, we conducted a scoping literature review to identify outcome measures for organ assessment in both pediatric and adult-onset systemic sclerosis (SSc). Articles were included if they met the following criteria: written in English, published after 1993, involved both adult and pediatric SSc patients, reported at least one SSc-specific outcome measure, and, in the case of series, included a minimum of 3 pediatric or 10 adult cases. Final data extraction was limited to original studies that provided detailed information on outcome measures and assessed these measures at least twice, enabling evaluation of changes over time.
Results: 24,849 articles from 4 databased were initially screened, resulting in 3,285 articles being identified for organ-specific review. Of these, 594 related to cardiac involvement were retrieved for full-text review, and 35 were ultimately extracted. Most studies were prospective (68.6%) or retrospective case series (25.7%), and the majority were single-center (77.1%), with only 8 being multicenter (22.9%). Adult patients were predominantly included (91.6%), with only 3 studies (8.6%) enrolling individuals under 18 years of age. Pulmonary hypertension was the most frequently investigated cardiac manifestation (88.6%), followed by myocardial dysfunction (42.9%), arrhythmias (40%), and other findings (20%) such as pericardial effusion, valvular disease, or coronary artery disease. Standard echocardiography was the most commonly used instrumental assessment (85.7%), followed by right heart catheterization (48.6%). Advanced echocardiography assessing global longitudinal strain (GLS) was employed in 17.1% of studies, whereas cardiac magnetic resonance imaging (CMR) was reported in only 3 studies (8.6%).
Conclusion: This review shows that most available research on cardiac involvement in systemic sclerosis focuses on adult populations, with a lack of data in pediatric patients. These findings emphasize the need for high-quality, pediatric-specific studies to develop standardized outcome measures to guide future research and improve clinical care in children with jSSc.
Disclosure
None declared

Reference
1. Canizares NV, et al. Pediatr Rheumatol Online J. 2025 May 2;23(1):46.

P161

Combining dermoscopy and infrared themography may increase accuracy in staging juvenile localized scleroderma (JLS)?

G. Martini[1], E. Zelin[2], Z. Fratton[2], F. Larotonda[1], E. Errichetti[2]
[1]Pediatrics, [2]Dermatology, Academic Hospital Santa Maria della Misericordia, Udine, Italy
Correspondence: G. Martini
Pediatric Rheumatology, **23(2):** P161

Introduction: JLS is characterized by an inflammatory phase followed by an atrophic phase. Staging JLS is crucial for treatment decisions and clinical accuracy can be increased by non-invasive imaging such as infrared thermography (IRT). IRT is reliable in assessing disease activity but may show "false positive" hyperthermia in severely atrophic lesions. Dermoscopy is a non-invasive method examination that has been demonstrated to be a useful in differential diagnosis of inflammatory skin diseases and Localized Scleroderma in adults.
Objectives: To evaluate whether combining dermoscopy and IRT can improve clinical staging of JLS, particularly in case IRT shows hyperthermia not consistent with clinical impression.
Methods: A cross-sectional study including consecutive patients with JLS between March 2024 and March 2025. Patients were evaluated in a blinded manner by a pediatric rheumatologist by clinical score LoSCAT and IRT and by a dermatologist by dermoscopy. Lesions were defined as "true active" or "true inactive" when there was agreement between LoSCAT and IRT, "false active" when clinically inactive, but IRT showed hypertermia. The expression of dermoscopic features (erythematous areas and linear vessels for inflammation, white fibrotic beams/white clouds, unfocused large purple vessels and pigmentary structures for sclerosis and atrophy) within the observed field was ordered quantitatively with score 0 to 4 according to the percentage of feature presence. Statistical analysis included Student's t-test, Mann-Whitney U test and Fisher exact test, as appropriate.
Results: 21 patients (15 F, 6 M) were included, 55 lesions were examined (18 trunk, 11 upper limbs, 20 lower limbs, 6 face). Seven patients had Linear scleroderma, 5 mixed subtype, 5 plaque morphea and 4 generalized morphea. Sixteen patients had received systemic treatment (MTX, MMF, corticosteroids), eight were still on therapy. Four lesions were "true active" while 21 were "false active". False active lesions had significantly higher LoSDI score (measuring subcutaneous/dermal atrophy and dyspigmentation) than true active/inactive ones (5.95 vs 4.44, $p<0.0001$). Total scores for sclerotic and atrophic dermoscopic findings were slightly higher in false compared with true inactive lesions (mean 4 vs 3.7, p n.s.), with greater differences for "unfocused large purple vessels" (mean score 0.95 vs 0.5 respectively, p n.s.), so the absence of this feature was associated with 50% probability of a true inactive lesion.
Conclusion: Although with the need of confirmation in a greater number of lesions our results suggest that a multidisciplinary approach combining dermoscopic analysis with clinical evaluation may help in identify false positive hyperthermia by IRT.

Disclosure
None declared

References
1. Martini G, Murray KJ, Howell KJ, Harper J et al. Juvenile onset localized scleroderma activity detection by infrared thermography. Rheumatology (Oxford). 2002;41: 1178–82.15.
2. Errichetti E, Lallas A, Apalla Z, Di Stefani A, Stinco G. Dermoscopy of Morphea and Cutaneous Lichen Sclerosus: Clinicopathological Correlation Study and Comparative Analysis Dermatology 2017;233:462–470.

P162

Three-dimensional magnetic resonance imaging reconstruction in quantification and monitoring of tissue damage in linear scleroderma of the head

A. Tel[1], E. Marrani[2], S. Pastore[3], A. Taddio[3], S. Della Paolera[4], G. Simonini[2], S. Sembronio[1], G. Martini[4]
[1]Maxillo-facial surgery, Academic Hospital Santa Maria della Misericordia, Udine, [2]Pediatric Rheumatology, Meyer's Children Hospital, Florence, [3]Pediatric Rheumatology, IRCCS Burlo GAROFOLO, Trieste, [4]Pediatrics, Academic Hospital Santa Maria della Misericordia, Udine, Italy
Correspondence: G. Martini
Pediatric Rheumatology, **23(2):** P162

Introduction: Juvenile Linear Scleroderma of the head (HJLS) is a rare disorder affecting face and scalp and may cause severe aesthetic sequelae and functional disability. The two subtypes are En Coup de Sabre (ECDS) involving front and scalp and Parry Romberg syndrome (PRS) affecting the lower part of the face. To date, no reliable tool has been validated for assessment and quantification of tissue damage in HJLS as clinical score LoSCAT and other methods such as Infrared Thermography and ultrasound have significant limitation when applied to face and scalp.
Objectives: To evaluate the reliability of 3-D reconstruction and processing softwares (Materialise Mimics and Materialise 3-matic) applied to Magnetic Resonance Imaging (MRI) to obtain a qualitative and quantitative analysis of adipose subcutaneous tissue thickness by colorimetric map and point sampling around the defect area. Second, our aim was to apply the part comparison analysis method to assess surface discrepancies between the volumetric reconstruction of the pathologic side and the overlapped mirrored healthy side.
Methods: This is a cross-sectional study involving patients with juvenile onset HJLS from three Paediatric Rheumatology centres in Italy. Craniofacial MRI was performed using 1.5T according to a shared standardized protocol in the different centres and 3-D reconstruction and analysis was performed by an expert maxillo-facial surgeon blinded to patients' clinical features. First, adipose subcutaneous tissue and skin segmentation was obtained from MRI images by selective thresholding, then mirroring and coregistration of affected and non-affected side was performed to analyze subcutaneous tissue thickness by colorimetric map and surface differences by part comparison analysis. This procedure identifies involved areas and subsequently allows to make point-by-point sampling of local thickness, according to patient features.
Results: Nine patients were included (6 ECDS, 3 PRS), with mean age 14.8 years (range 6.0 to 24.0) and mean age at disease diagnosis of 7.1 years (range 4.0 to 10), all but one received systemic treatment (Methotrexate, Mycophenolate mofetil, Prednisone, Abatacept, Tofacitinib). The mean LoSDI score (for subcutaneous/dermal atrophy and dyspigmentation) was 4.6 (range 2 to 8). The 3-D reconstruction analysis was possible on all the MRI performed at different centres and the blinded qualitative assessment clearly identified the affected areas by colorimetric map obtained after segmentation and mirroring. The point-by-point measures sampling of local thickness of subcutaneous tissue showed differences ranging from 0.25 to 2.4 mm between paired affected and non-affected areas.
Conclusion: 3-D reconstruction analysis of MRI appears a reliable and objective measure of tissue damage in patients with HJLS as it obtains a precise quantification of tissue loss. The sensitivity to change of this technique in monitoring the disease progression is ongoing in a prospective study.

Disclosure
None declared

P163

Scleroderma-like skin changes in a noncompliant adolescent with phenylketonuria: a diagnostic challenge

G. Oğuz, S. N. Tığrak, S. Ayduran, S. Türkuçar
Pediatric Rheumatology, Pamukkale University, Denizli, Türkiye
Correspondence: G. Oğuz
Pediatric Rheumatology, **23(2):** P163

Introduction: Phenylketonuria (PKU) is autosomal recessive disorder caused by phenylalanine hydroxylase deficiency, leading to accumulation of phenylalanine and its metabolites in blood and tissues. While neurodevelopmental impairment is wellknown, rare cases may also present with sclerodermatous skin changes due to metabolite deposition. Early dietary restriction is essential, though some cases may require additional therapy.
Objectives: to present a case of PKU with sclerodermatous skin changes
Methods: Case report
Results: A 17-year-old male with history of phenylketonuria(PKU) diagnosed at the age of one presented to pediatric rheumatology with progressive skin thickening, hardening of the extremities over the past four months. Notably, he had been non-compliant with the PKU diet for the preceding eight months. On physical examination, he exhibited restricted wrist extension, indurated skin extending from wrists to the elbows, while the skin over hands, feet appeared normal. Raynaud's phenomenon was absent.
A preliminary diagnosis of scleroderma was considered, and further investigations were initiated. Laboratory evaluation revealed positive ANA with nucleolar pattern at 1:100 titers, while extractable nuclear antigen panel negative. Nailfold capillaroscopy showed normal capillary density and morphology, with no signs of capillary dropout, dilatation, hemorrhage, arguing against a microangiopathy typically seen in systemic sclerosis. No evidence of pulmonary, cardiac, gastrointestinal system involvement was detected. Blood phenylalanine levels were elevated.
Skin biopsy demonstrated increased dermal collagen deposition without cellular infiltration, vasculitis, endothelial injury. Although some inflammatory changes were observed in subcutaneous tissue,there was no histological evidence supporting a connective tissue disease such as scleroderma or eosinophilic fasciitis.
Considering the clinical, laboratory, histopathological, radiological findings, the skin involvement was interpreted as scleroderma-like fibrosis related to PKU, rather than primary connective tissue disease. The patient was advised to resume a strict phenylalanine-restricted diet and is currently under regular follow-up.
Conclusion: Accumulation of these derivatives in the skin is probably responsible for the skin changes in PKU. These scleroderma-like changes in PKU have a predisposition for the proximal areas of the extremities, sparing the hands, feet, and are usually limited to the skin and subcutaneous tissue. However, the condition may cause joint contractures, deformity, and limb atrophy. We report a child with PKU who developed progressive sclerodermatous skin changes. The diagnosis of sclerodermatous changes was made based on clinical and skin biopsy specimen findings. Children with skin changes suggestive of scleroderma, especially in the presence of mental and motor retardation, should be investigated for the possibility of PKU.
Disclosure
None declared

P164

Differences in capillaroscopic patterns in children and adults with systemic sclerosis with similar clinical and immunological phenotype

N. Yudkina, A. Volkov, I. Nikishina
V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P164

Introduction: Systemic sclerosis (SSc) in juvenile and adult populations can demonstrate similar clinical and immunological characteristics, but the features of microcirculatory changes remain poorly understood.
Objectives: To compare capillaroscopic patterns in patients with juvenile and adult forms of SSc with comparable clinical and immunological phenotype.
Methods: Due to the rarity of the nosology, 8 patients with a reliable diagnosis of SSc, verified according to the ACR/EULAR 2013 criteria, were included. A total of 5 adults and 3 children. Eight patients underwent nailfold videocapillaroscopy (NVC) using an Olympus device with 200x magnification and analysis of shape, size, density, presence of bushy capillaries and hemorrhages. Patterns were assessed using the Cutolo classification.
Results: All patients had a similar clinical picture: Raynaud's syndrome, finger edema, sclerodactyly, digital scars/ulcers, interstitial lung disease. Anti-topoisomerase I antibodies (Scl-70) were detected in 8 cases, the presence of other autoantibodies was excluded based on the results of ANA immunoblot test. All patients underwent NVC for the first time 7±5 months after the first symptoms of SSc. In 3 of 5 adult patients with SSc, a late scleroderma pattern was determined: absence of dilated capillaries and hemorrhages, disorganization and avascular fields. In 2 of 5 patients with SSc over 18 years of age, the NVC changes were assessed as non-specific: there were isolated dilated capillaries and altered forms, and a decrease in density was visualized in some areas. All three patients with juvenile SSc had an active scleroderma pattern: giant capillaries and fresh numerous microhemorrhages with a moderate decrease in density.
Conclusion: Despite the clinical and immunological identity, patients with the juvenile form of SSc at the early stage of the disease showed changes in the microvascular bed that were different from those in adults: a predominantly active pattern with pronounced microangiopathy. The data obtained indicate possible differences in the pathogenesis or rate of microvascular remodeling between juvenile SSc and SSc in adults, which requires further study.
Disclosure
None declared

P165

Age of onset effect on the clinical manifestations of patients with juvenile systemic sclerosis

I. Foeldvari[1], J. Klotsche[2], K. Torok[3], O. Kasapcopur[3], A. Adrovic[3], B. Feldman[3], F. Sztajnbok[3], M. T. Terreri[3], A. P. Sakamoto[3], R. Khubchandani[3], J. Anton[3], G. Özomay Baykal[3], S. Johnson[3], D. Schonenberg-Meinema[3], V. Stanevicha[3], E. Alexeeva[3], M. Katsicas [3], S. Sawhney[3], V. Smith[3], S. Abu Al-Saoud[3], E. Al-Abadi[3], S. Appenzeller[3], T. Avcin [3], N. Cabrera[3], S. Hajek[3], S. O. Hetlevik[3], M. Kostik[3], T. Lehman[3], S. Li[3], H. Malcova[3], E. Marrani[3], C. Pain[3], A. Patwardhan[3], W.-A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], P. Costa Reis[3], M. Janarthanan [3], M. Moll[3], D. Nemcova [3], M. J. Santos[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], D. Eleftheriou[3], L. Harel[3], G. Horneff[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], J. M. López Benítez[3], K. Minden[2], S. Nielsen[3], F. Nuruzzaman[3], M. Sparchez[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, [2]German Rheumatism Research Center, Berlin, [3]jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P165

Introduction: Juvenile systemic sclerosis(jSSc) is a rare disease with a prevalence of 3 in 1 000 000 children. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world (1, 2). The jSScC collects data multinationally, including clinical manifestations, auto-antibodies profile and patient and physician reported outcomes. Disease presentation can be different in the prepubertal age in lot of diseases.
Objectives: Assess the differences in clinical presentation between patients with age of onset of disease under and over 9 years of age.
Methods: The jSScC enrols jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion (1, 2). We reviewed data from patients in the jSScC at the time of inclusion in the registry until 15th of December 2024.
Results: We studied 260 patients, 70% Caucasian, 80% female, in 41% (n=107) the age of onset was under 9 years (jSSc<9). The patients with jSSc<9 had a non-significant higher number of diffuse subset patients (74% versus 65%). The median disease duration was 4.2 in the jSSc<9 versus 1.9 years in jSSc>9. The female to male ratio was higher in jSSc <9 (4.6:1 versus 3.6:1). Regarding antibody pattern the only difference found between jSSc<9 and jSSc>9 was a significantly higher number of patients with anti-PM-Scl positivity (24% versus 10%; p=0.048). The jSSc<9 group had a more frequent history of ulceration (61% versus 46%, p value non significant (NS)) and higher number of calcinosis (25% versus 9%, p=0.021). The number of patients with pulmonary hypertension assessed by ultrasound was lower in the jSSc<9 group (3% versus 8%, p value NS). Renal involvement, mostly proteinuria, was lower in the jSSc<9 with 1% versus 4%, p value NS. Renal crisis was not reported. Number of patients with decreased Body Mass Index z score ≤2 was higher in the jSSc<9 group (19% versus 12%, p value NS). Tendon friction rub was less common in the jSSc<9 (2% versus 9%, p value NS). There was no difference in the assessed patient and physician related outcomes. The mean CHAQ was 0.5 in both groups.
Conclusion: In the currently in this largest jSSc cohort of the world patients in the jSSc<9 group seems for have slightly more severe disease. It is remarkable the significant higher number of patients with anti-PM-Scl antibodies in the jSSc<9 group.
Disclosure
None declared

References

1. Foeldvari I, Klotsche J, Torok KS, Kasapcopur O, Adrovic A, Stanevica V, et al. Characteristics of the first 80 patients at timepoint of first assessment included in the juvenile systemic sclerosis inception cohort. www.juvenilescleroderma.com. Journal of Scleroderma and Related Disorders. 2018;4(1–13).
2. Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Terreri MT, Sakamoto AP, et al. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.

P166

Patient and physician reported outcomes of juvenile systemic sclerosis patients significantly improve over 12 months observation period in the juvenile systemic scleroderma inception cohort

I. Foeldvari[1], J. Klotsche[2], O. Kasapcopur[3], A. Adrovic[3], B. Feldman[3], M. T. Terreri[3], A. P. Sakamoto[3], K. Torok[3], S. Johnson[3], J. Anton[3], G. Özomay Baykal[3], F. Sztajnbok[3], V. Stanevicha[3], M. Katsicas [3], R. Khubchandani[3], S. Appenzeller[3], T. Avcin [3], M. Kostik[3], E. Marrani[3], W.-A. Sifuentes-Giraldo[3], D. Schonenberg-Meinema[3], D. Nemcova [3], S. Abu Al-Saoud[3], E. Al-Abadi[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], P. Costa Reis[3], D. Eleftheriou[3], G. Horneff[3], M. Janarthanan [3], T. Kallinich[3], T. Lehman[3], K. Minden[2], M. Moll[3], S. Nielsen[3], C. Pain[3], A. Patwardhan[3], M. J. Santos[3], V. Smith[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, [2]German Rheumatism Research Center, Berlin, [3]jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P166

Introduction: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects data prospectively in jSSc, allowing the evaluation of the development of organ involvement and patient and physician reported outcomes in jSSc over time.
Objectives: Assess the differences in clinical presentation from patients who had 12 months follow up in the jSSc.
Methods: The jSScC cohort enrols jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion. We reviewed jSScC patient clinical data and patient and physician reported outcomes, who had 12 months follow up from the time of inclusion until 15th of December 2024.
Results: There were 150 patients with 12 months follow up included in the jSScC (79% Caucasian, 78% female). Diffuse subset occurred in 75% of the patients. Mean disease duration at the time of inclusion

in the cohort was 2.5 years. Median age of onset of Raynaud´s was 10 years old (YO) and median age of first non-Raynaud´s organ involvement was 10.6 YO. 92% of the patients were treated with DMARDs at time point 0 and 97% at tie point 12 months. There was a significant improvement in the mean modified Rodnan skin score (MRSS) in 12 months (12 vs 8; p=0.031); table 1). The MRSS decreased 10% or more in 47% and increased 10% or more in 25% of the patients. After 12 months 7 patients decreased FVC to < 80% and 4 patients decreased DLCO to <80%, but 6 patients improved FVC or DLCO to >80%, in the mean of the group no significant change. The number of patients with a 6 Minute Walk Test below the 10th percentile for age decreased from 67% to 45% (p=0.058). The number of patients with swollen joints decreased significantly from 16 to 7% (p=0.019). No changes were seen in cardiac, renal or gastrointestinal involvement. No renal crisis occurred. All assessed patient and 2 of the 3 physician reported outcomes improved significantly.
Conclusion: Skin and musculoskeletal clinical features improved over 12 months, with almost all patients on DMARDs, supporting the response of these features to therapy. It was promising that internal organ involvement, like cardiac, lung and gastrointestinal, did not significantly worsen after 12 months. The most striking observation is the improvement of all assessed patient and physician reported outcome measures over 12 months in this largest international cohort of jSSc patients.
Disclosure
None declared

P168

Anticentromere antibodies are occurring only in 6% of juvenile systemic sclerosis patients but correlate with more severe pulmonary involvement

I. Foeldvari[1], J. Klotsche[2], K. Torok[3], M. T. Terreri[3], S. Johnson[3], F. Sztajnbok[3], J. Anton[3], B. Feldman[3], R. Khubchandani[3], G. Özomay Baykal[3], D. Schonenberg-Meinema[3], E. Alexeeva[3], M. Katsicas [3], V. Smith[3], S. Abu Al-Saoud[3], S. Appenzeller[3], S. Hajek[3], S. O. Hetlevik[3], M. Kostik[3], S. Li[3], H. Malcova[3], E. Marrani[3], A. Patwardhan[3], W.-A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], E. Al-Abadi[3], T. Avcin [3], P. Costa Reis[3], T. Lehman[3], D. Nemcova [3], C. Pain[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], J. M. López Benítez[3], K. Minden[2], M. Moll[3], S. Nielsen[3], F. Nuruzzaman[3], M. J. Santos[3], S. Sawhney[3], M. Sparchez[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, [2]German Rheumatism Research Center, Berlin, [3]jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P168

Introduction: Juvenile systemic sclerosis (jSSc) is a rare disease with a prevalence of 3 in 1 000 000 children. In adult patients anticentromere antibodies correlate with the limited subtype. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects data multinational, including clinical presentation, auto-antibody profile and patient and physician reported outcomes.
Objectives: Assess the differences in clinical presentation between anticentromere antibody positive and negative patients in the jSSc.
Methods: The jSScC enrols jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion (1, 2). We reviewed, data of patients in jSScC at the time of inclusion in the registry, including clinical data and patient and physician reported outcomes until 15th of December 2024. Absence of results of anticentromere antibodies was an exclusion criterion.
Results: We analyzed 197 patients. 78% female, 66% Caucasian, 11 (6%) were anticentromere antibody positive (AC+). Diffuse subtype was present in 45% of the AC+ and in 68% of the AC- patients. There were no differences regarding median disease duration (2.5-2,8 years9 at registry entrance or ethnicity between the two groups. The onset of Raynaud´s was significantly earlier in the AC+ group (7.2 versus 10.1 years, p=0.042). Moreover, the median age of the first non-Raynaud organ involvement was significantly earlier in the AC+ (6.8 to 10.4 years, p=0.039). Anti-scl 70 positivity was not significantly different (18% in AC+ versus 29% in AC-).
The AC+ group (Table 1.) had more lung involvement. Decreased FVC <80% was seen in 63% of AC+ (5/8), compared to 27% of AC- patients (39/144) (p=0.032). DLCO < 80% occurred in 86% of the AC+ patients (6/7) and 29% of AC- (45/115) (p=0.027). Lung HRCT findings occurred in 88% of the AC+ (7/8) and in 43% of AC- patients (65/152) (p=0.015). The AC+ patients had significantly more decreased Body Mass Index of ≤ - 2 z score and calcinosis (p=0.044 and p=0.045, respectively). The history of ulceration was more frequent in the AC- group. The patient rated Raynaud activity in the last 7 days was significantly higher in the AC+ group.
Conclusion: jSSc patients with AC+ show different characteristics in the largest cohort of jSSc patients. The number of AC+ patients is significantly lower than in an adult systemic sclerosis population. Interestingly, the aC+ patients have a significantly lower age at onset of disease and higher pulmonary involvement. We need further data to reconfirm this unique observation.
Disclosure
None declared

References

1. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.
2. Foeldvari I, Klotsche J, Torok KS, Kasapcopur O, Adrovic A, Stanevica V, et al. Characteristics of the first 80 patients at timepoint of first assessment included in the juvenile systemic sclerosis inception cohort. www.juvenilescleroderma.com. Journal of Scleroderma and Related Disorders. 2018;4(1–13).

P169

Is gastroesophageal reflux a risk for interstitial lung disease in juvenile systemic sclerosis?

I. Foeldvari[1], J. Klotsche[2], K. Torok[3], O. Kasapcopur[3], A. Adrovic[3], B. Feldman[3], F. Sztajnbok[3], M. T. Terreri[3], A. P. Sakamoto[3], J. Anton[3], S. Johnson[3], R. Khubchandani[3], V. Stanevicha[3], G. Özomay Baykal[3], D. Schonenberg-Meinema[3], E. Al-Abadi[3], E. Alexeeva[3], M. Katsicas [3], S. Sawhney[3], V. Smith[3], S. Abu Al-Saoud[3], S. Appenzeller[3], T. Avcin [3], N. Cabrera[3], S. Hajek[3], S. O. Hetlevik[3], M. Kostik[3], T. Lehman[3], S. Li[3], H. Malcova[3], E. Marrani[3], C. Pain[3], A. Patwardhan[3], W.-A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], P. Costa Reis[3], M. Janarthanan [3], M. Moll[3], D. Nemcova [3], M. J. Santos[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], D. Eleftheriou[3], L. Harel[3], G. Horneff[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], J. M. López Benítez[3], K. Minden[2], S. Nielsen[3], F. Nuruzzaman[3], M. Sparchez[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, [2]German Rheumatism Research Center, Berlin, [3]jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P169

Introduction: Gastroesophageal involvement, particularly reflux, has been identified as a risk factor for development and progression of interstitial lung disease (ILD) in adult systemic sclerosis However, this association has not yet been extensively studied in juvenile systemic sclerosis (jSSc)(1, 2, 3). To further address this gap, the juvenile systemic scleroderma inception cohort(jSSclC) (4) including 279 patients provides an opportunity to investigate the potential link between these two manifestations in the paediatric population.
Objectives: To assess the risk of ILD in patients with and without gastroesophageal reflux (GR) in the jSSclC.
Methods: We analysed baseline clinical data from all patients enrolled in jSSclC till April 15th, 2025 and compared the clinical characteristics of patients with and without GR.
Results: We reviewed data of 279 patients: 93 (33%) had reported to have gastroesophageal reflux (GR+). Patients with GR+ were more frequently evaluated by barium swallow (32% versus 18%, p=0.006) and endoscopy (22% versus 5%, p=0.041). Approximately 70% of the patients had diffuse cutaneous subset. The Median age at onset of first non-Raynaud presentation was around 11 years. Patients with GR+ had more nailfold capillary changes (91% versus 71%, p=0.001) and telangiectasia (49% versus 30%, p=0.002) compared to GR negative (GR-) patients. GR+ patients were more likely to have lung

involvement than GR- patients with higher frequency had FVC<80% (p=0.05), DLCO<80% (p=0.001) and ILD as identified by high-resolution CT (p=0.004). The pulmonary function findings GR+ patients had more positive findings for ILD on high resolution CT of the lung as GR- patients (56% versus 37%, p=0.004). No significant differences were observed regarding autoantibody profile, cardiac, renal and musculoskeletal involvement between the groups.
Conclusion: GR+ had a significantly higher prevalence of ILD. Patients reported GR is correlating with an increased frequency of microvascular changes. This findings highlight the importance of assessing all patients for GR to enable timely management of reflux and potentially reduce occurrence/progression for ILD in jSSc. Further long-term studies are needed to prove our hypothesis and support targeted intervention strategies.
Disclosure
None declared

References
1. Ambartsumyan L, et al. Relationship Between Esophageal Abnormalities on Fluoroscopic Esophagram and Pulmonary Function Testing in Juvenile Systemic Sclerosis. Arthritis Care Res (Hoboken). 2019;71(11):1444–9.
2. Roth E, et al. Gastroesophageal reflux disease is associated with a more severe interstitial lung disease in systemic sclerosis in the EUSTAR cohort. Rheumatology (Oxford). 2025.
3. Li JC, et al. Pulmonary Nodules in Juvenile Systemic Sclerosis: A Case-Series from the National Registry for Childhood Onset Scleroderma (NRCOS). Diagnostics (Basel). 2023;13(12).
4. Foeldvari I, et al. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.

P170

Is anti-SCL70 positivity associated with a more severe disease in juvenile systemic scleroderma?

I. Foeldvari[1], J. Klotsche[2], K. Torok[3], O. Kasapcopur[3], A. Adrovic[3], B. Feldman[3], F. Sztajnbok[3], M. T. Terreri[3], A. P. Sakamoto[3], S. Johnson[3], J. Anton[3], R. Khubchandani[3], V. Stanevicha[3], G. Özomay Baykal[3], D. Schonenberg-Meinema[3], E. Alexeeva[3], M. Katsicas [3], S. Sawhney[3], V. Smith[3], S. Abu Al-Saoud[3], E. Al-Abadi[3], S. Appenzeller[3], T. Avcin [3], S. Hajek[3], S. O. Hetlevik[3], M. Kostik[3], T. Lehman[3], S. Li[3], H. Malcova[3], E. Marrani[3], A. Patwardhan[3], W.-A. Sifuentes-Giraldo[3], N. Vasquez-Canizares[3], N. Cabrera[3], P. Costa Reis[3], M. Janarthanan [3], D. Nemcova [3], C. Pain[3], M. J. Santos[3], C. Battagliotti[3], L. Berntson[3], B. Bica[3], J. Brunner[3], L. Harel[3], G. Horneff[3], D. Kaiser[3], T. Kallinich[3], D. Lazarevic[3], J. M. López Benítez[3], K. Minden[2], M. Moll[3], S. Nielsen[3], F. Nuruzzaman[3], M. Sparchez[3], Y. Uziel [3], N. Helmus[1]
[1]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, **[2]**German Rheumatism Research Center, Berlin, **[3]**jSSc collaborative group, Hamburg, Germany
Correspondence: I. Foeldvari
Pediatric Rheumatology, **23(2):** P170

Introduction: Juvenile systemic sclerosis(jSSc) is a rare disease with a prevalence of 3 in 1 000 000 children. In adult patients antic-scl 70 antibodies correlate with the diffuse subtype and a specific organ involvement pattern. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects multinational data including clinical presentation, antibody profile and patient and physician reported
Objectives: Assess the differences in clinical presentation between anti-Scl70 antibody positive and negative patients in the jSSc.
Methods: The jSScC enrols jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion (1, 2). We extracted the data at the time of inclusion in the registry from patients in the jSScC, including clinical manifestations and patient and physician reported outcomes until 15th of December 2024. Unknown antibody status for anti-Scl70 antibodies was an exclusion criteria.
Results: 260 patients from the cohort. 31% (n=80) were anti Scl-70 positive (antiScl70+). the anti-Scl70+ and anti-Scl70- group were similar regarding disease duration at time of inclusion (approximately 2.5 years), mean age at first non-Raynaud´s involvement (11 years of age), ethnicity, subtype of SSc and positive for anti-centromere antibodies. C-reactive protein (CRP) was elevated in 23% in the anti-Scl70+ group compared to 5% in the anti-Scl70- group (p <0.001). Anti-Scl70+ patients had less overlap features (18% versus 30%, p<0.001). Patients with anti-Scl70+ had higher rate of nailfold capillary changes (84% versus 74%, p=0.015), history of ulcerations (61% versus 47%, p=0.345) and telangiectasias (29% versus 40%, p=0.049). There were no differences regarding number of patients with decrease FVC<80%, DLCO<80% or positive HRCT findings for interstitial lung disease. Rate of pulmonary hypertension was 8% in anti-Scl70+ compared to 5% in anti-Scl70. No differences in cardiac, gastrointestinal or renal involvement were found. No renal crisis occurred. Patient rated the global disease damage significantly higher in the anti-Scl-70+ group (48 versus 30 (VAS 0-100), p=0.031) and the Raynaud activity (45 versus 20 (VAS 0-100),p=0.022).
Conclusion: Anti-Scl70+ patients have distinct features compared to anti-Scl- patients, but interstitial lung disease is not more common at inclusion in the registry, despite the higher rate of CRP elevation. Pediatric organ involvement pattern clearly differs from adults.
Disclosure
None declared

References
1. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.
2. Klotsche J, Torok KS, Kasapcopur O, Adrovic A, Stanevica V, et al. Characteristics of the first 80 patients at timepoint of first assessment included in the juvenile systemic sclerosis inception cohort. www.juvenilescleroderma.com. Journal of Scleroderma and Related Disorders. 2018;4(1–13).

P172

Clinical profile and outcomes of pediatric mixed connective tissue disease and overlap syndrome : a single center experience

N. Bagri[1], T. Singla[1], M. jana[2], A. Sinha[1], K. Jat[1], S. Gupta[3]
[1]Pediatrics, **[2]**Radiodiagnosis, **[3]**Pediatric Cardiology, All India Institute of Medical Sciences, Delhi, India
Correspondence: T. Singla
Pediatric Rheumatology, **23(2):** P172

Introduction: Pediatric MCTD and overlap syndrome are rare, comprising 2–3% of childhood rheumatic diseases, but is likely underreported due to overlapping features and diagnostic challenges.
Objectives: To describe the clinical, serological, radiological profiles and evaluate treatment outcomes of pediatric patients diagnosed with overlap syndromes and MCTD.
Methods: A retrospective chart review of children diagnosed with MCTD or overlap syndromes being followed in pediatric rheumatology clinic at a tertiary care hospital from May 2014 to April 2015 was done. MCTD was diagnosed based on the Kasukawa criteria, while children presenting with overlapping clinical features of at least two systemic rheumatic diseases were classified as overlap syndrome. Clinical manifestations, laboratory parameters including antibody profile and imaging findings, therapeutic details and outcome were analyzed. The present study did not disclose the identity of any patient nor was any intervention conducted solely for the purpose of this study (ethical waiver applied).
Results: Among the 16 children (14 girls) analyzed, 5 were diagnosed with MCTD and 11 had overlap syndrome. The median age at diagnosis was 12 years (range 11-14 years) and the median duration of symptoms was 36 months (range 24-96 months). Among overlap syndrome, 81.8% (n=9) had features of JDM and SSc, 9% (n=1) had features of JIA and JDM; and 9% (n=1) had features of JIA and SSc. Raynaud phenomenon was most common clinical feature reported in 88% (n=14). Other common clinical features seen were scleroderma 75% (n=12), arthritis 69% (n=11) and myositis 63% (n=10). Digital ischemic changes (gangrene and ulcers) and calcinosis cutis were seen in 31% (n=5) and 25% (n=4) patients, respectively. Serologically, ANA was positive (≥1:100 titres) in 88% (n=14) and Anti-U1 RNP antibodies were detected in 69% (n=11). 50% (n=6) children with overlap syndrome had U1RNP positivity despite not meeting MCTD criteria. High-resolution computed tomography (HRCT) of the chest revealed interstitial lung disease in 50% patients (n=8) out of which 7 had usual interstitial

pneumonia (UIP) pattern and 1 had non-specific interstitial pneumonia (NSIP) pattern. Echocardiography identified mild pulmonary arterial hypertension in 13% (n=2). Nailfold capillaroscopy demonstrated a scleroderma pattern in 69% patients (n=11). Corticosteroids were administered in 88% patients (n=14), including intravenous pulse therapy in 11 and oral corticosteroids in 14. Methotrexate was used in 69% patients (n=11), mycophenolate mofetil in 56% (n=9), and intravenous cyclophosphamide in 38% (n=6). Rituximab was given in 2 patients (13%) with severe or refractory disease. During 2 year follow-up, 11 patients (69%) had achieved clinical improvement or stabilization, 3 (19%) experienced disease flares, and 2 (13%) were lost to follow-up.
Conclusion: This cohort from a single centre describes 5 children with MCTD and 11 children with overlap syndrome. The distinction of these seemingly similar diseases may not be necessary for clinical care. The existing criteria may be revised for better understanding of these complex diseases.
Disclosure
None declared

P173

Early diagnosis of pediatric sjogren syndrome and off-label treatment with rituximab and belimumab

S. Pastore[1], A. Ballaben[2], L. Godina[1], E. Valencic[1], V. Boz[1], A. Tommasini[1,2], A. Taddio[1,2]
[1]I.R.C.C.S. Burlo Garofolo, [2]University of Trieste, Trieste, Italy
Correspondence: S. Pastore
Pediatric Rheumatology, **23(2):** P173

Introduction: We hereby discuss two cases of Sjogren syndrome, both in adolescent girls.
Objectives: none
Methods: none
Results: The first girl was brought to medical attention in 2022 when she was 13 years old, with a history of weight loss, asthenia and arthralgias. Blood tests showed leukopenia, elevation of ESR (36 mm/h), immunoglobulins (IgG 1704 mg/dL, IgA 426 mg/dL) and interferon-score (29.2). Autoimmunity panels showed high-titer positivity for ANA, anti-SSA-Ro60 and anti-SSB-La antibodies, and rheumatoid factor positivity. Further evaluations of ultrasound of parotids and salivary glands showed abnormal findings of hypoechogenic areas. A minor salivary glands biopsy confirmed the diagnosis of Sjogren syndrome, with a Focus Score of 8. Therapy with rituximab was immediately started, followed soon after by introduction of belimumab with good clinical response: ESSPRI and ESSDAI scores decreased from a peak of 5.7 and 5 respectively, to 3.3 and 1 at 6 months follow-up.
The second case is a 13-year-old girl, with recurrent Raynaud phenomenons, arthralgias and asthenia since december 2023. Laboratory tests showed mild thrombocytopenia, ESR elevation (25 mm/h) and marked Siglec-1 elevation and hypergammaglobulinemia (1843 mg/dL). Autoimmunity panels showed high-titer positivity for ANA, and positivity to rheumatoid factor, anti-U1RNP and anti-RNP70 antibodies. Ultrasound evaluation showed an enlargement of parotids and salivary glands with hypoechogenic areas. A minor salivary glands biopsy confirmed the diagnosis of Sjogren syndrome, with a Focus Score of 4. Treatment with rituximab followed by belimumab was also started and obtained a good clinical response: ESSPRI and ESSDAI scores decreased from a peak of 4.6 and 5 respectively, to 3.3 and 3 at a 3 months follow-up.
Conclusion: These two cases highlight some critical aspects of Sjogren syndrome (SS) in pediatric patients. The onset of disease must not be strictly linked to sicca syndrome symptoms, as the two girls only later developed mild xerostomia. Constitutional symptoms are more often present at the onset of disease, and an ultrasound evaluation of the parotids and salivary glands should be performed as soon as possible in the clinical suspect of SS. Minor salivary gland biopsy is minimally invasive and equally contributory to diagnosis. We have started two off-label drugs with the goal of halting disease progression and with excellent results at the last follow-up. It is important to increase awareness of Sjogren's syndrome even in the absence of parotid swelling, xerophthalmia and xerostomia, so that treatment can be introduced to slow or stop disease progression. Consent to published had been obtained.
Disclosure
None declared

P174

Key features of paediatric sjögren's disease: a portuguese cohort overview

B. Paulo Correia[1,2], J. B. Lima[3], C. Zinterl[1,2], A. L. Martins[1], P. C. Reis[1,2], C. Zilhão[4], S. Alves[4], R. Campanilho-Marques[1,2], F. O. Ramos[1,2]
[1]Paediatric Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde Santa Maria (ULSSM), Centro Académico de Medicina de Lisboa, [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisbon, [3]Paediatrics Department, [4]Paediatric Rheumatology Unit, Centro Materno Infantil do Norte, Unidade Local de Saúde de Santo António (ULSSA), Oporto, Portugal
Correspondence: B. Paulo Correia
Pediatric Rheumatology, **23(2):** P174

Introduction: Paediatric Sjögren's disease (pSjD) is a rare autoimmune condition presenting with diverse systemic manifestations, often leading to underdiagnosis. Its identification and classification are challenging due to the absence of specific paediatric criteria, often leading to reliance on clinical judgment and adult guidelines.
Objectives: This study aims to describe the clinical and laboratory features of paediatric SjD throughout the follow-up period, highlighting the need to increase awareness of this condition in clinical practice.
Methods: We conducted a retrospective study using data from patients followed in the Paediatric Rheumatology Units of two Portuguese university hospital centres, between January 2014 and March 2025. All patients were under 18 years of age at disease onset. Electronic medical records were reviewed to collect medical history and relevant investigations, and disease activity scores reported at the last visit.
Results: A total of 16 patients with pSjD were included, of whom 81.3% were female, with a mean disease onset age of 12.9 ± 3.8 years (range 3–17) and a mean disease duration of 6.2 ± 4.5 years at the last visit (mean follow-up 4.9 ± 4.8 years). Fifteen patients (93.8%) had primary SjD, and one had SjD associated with systemic lupus erythematosus (SLE). Recurrent parotid swelling was observed in 43.8% of patients at presentation, and 18.8% had persistent glandular enlargement. During follow-up, 81.3% reported dry mouth and 75.0% dry eyes. Other common manifestations included lymphadenopathy (68.8%), arthritis/arthralgia (43.8%), constitutional symptoms (37.5%), hematologic involvement (37.5%), and Raynaud's phenomenon (18.8%). Two patients (12.5%) had CNS manifestations (seizures and psychiatric symptoms). Hypergammaglobulinemia was present in 75%, with a median IgG of 2256 mg/dl (IQR 1272). All patients were ANA-positive, 93.8% had SSA/Ro and 56% had SSB/La antibodies, and 57.1% were rheumatoid factor (RF)-positive. Low C3 complement was present in 31.3% of patients. In our cohort, 62.5% (10/16) had a positive salivary gland ultrasound (OMERACT ≥2), 42.9% (6/14) a positive salivary gland biopsy (focus score ≥1), 54.5% (6/11) a positive Schirmer's test, and 28.6% (2/7) abnormal unstimulated sialometry. The median ESSDAI score at the last visit was 1.0 (IQR 1.0). Most patients (75%) were being treated with hydroxychloroquine, 25% with oral corticosteroids, 18.8% with rituximab, 6.3% with methotrexate, and 6.3% with etanercept, at the time of the last visit. Only 56.3% of patients fulfilled the 2016 EULAR/ACR criteria for adult SjD.
Conclusion: In this cohort of paediatric Sjögren's disease, sicca symptoms, parotitis, lymphadenopathy, and joint involvement were the most common features, alongside high rates of hypergammaglobulinemia and positivity for ANA and SSA/Ro antibodies. Thus, glandular and biological involvement appear to be prominent in children with SjD, with most patients achieving remission or low disease activity with systemic therapies.
Disclosure
None declared

P175

Ectopic calcifications - 3 cases of hyperphosphatemic familial tumoral calcinosis (HFTC)

C. Van Quekelberghe, C. Rietschel
Pediatric Rheumatology, Clementine Kinderhospital, Frankfurt am Main, Germany
Correspondence: C. Van Quekelberghe
Pediatric Rheumatology, **23(2):** P175

Introduction: In pediatrics, ectopic calcifications occur very rarely in systemic diseases such as juvenile dermatomyositis and systemic sclerosis, but also in the context of rare genetic diseases.
Objectives: Ectopic calcifications require careful differential diagnosis. A rare but important differential diagnosis is hyperphosphatemic familial tumorous calcinosis (HFTC), which is caused by mutations in the FGF23, GALNT3 or Klotho genes. These lead to impaired phosphate homeostasis with consecutive hyperphosphatemia and ectopic calcification.
Methods: Case report:
We report on three children who presented with atypical joint swelling. Patient 1, of Polish origin, developed swelling of the left elbow at the age of 9 years. After surgical removal and recurrence, further lesions appeared on the right elbow and the root of the nose.
Patient 2, daughter of consanguineous parents from Sri Lanka, developed pain in the left lower leg at the age of 8 years, imposing as hyperostosis in the area of the tibial diaphysis on X-ray. This was followed by development of a marked calcinosis of the left elbow at the age of 9 years. Her younger brother (patient 3) showed swelling of the metatarsophalangeal joint of the big toe at the age of 7 years.
Laboratory chemistry revealed persistent hyperphosphatemia with normal serum calcium and high tubular reabsorption of phosphate in all three patients. Inflammatory parameters were unremarkable. Radiologically, cloudy calcifications were seen in the area of the affected joints.
Results: Further investigation revealed a compound heterozygous mutation (patient 1) and a homozygous mutation (patients 2 and 3) in the GALNT3 gene, responsible for HFTC.
HFTC is inherited in an autosomal recessive manner and is characterized by chronically elevated phosphate levels, which can lead to ectopic calcifications. Low-phosphate diets, phosphate binders (e.g. Sevelamer) and drugs to increase phosphate excretion (e.g. nicotinamide, calcitonin) are available for treatment. Surgical removal of calcinosis is indicated in cases of functional limitations or pain, as there are high recurrence rates.
Our patients all received nutritional counselling in order to adhere to a low-phosphate diet. Patient 2 and 3 additionally received the phosphate binder Sevelamer, without significant reduction in phosphate levels. In an individual healing attempt patient 2 was treated with calcitonin (subcutaneous and intranasal) which proved to be very difficult due to the lack of an adequate administration and preparation form on the european market.
Currently, all 3 patients are symptom-free on a strict low-phosphate diet without further medications.
Conclusion: Our case reports emphasize the importance of early diagnosis of HFTC as therapeutic intervention (especially a low-phosphate diet) slows the progression of the disease and improves the patient's quality of life. Genetic testing should be considered in any combination of hyperphosphatemia, increased tubular reabsorption of phosphate (TRP) and ectopic calcifications. Consent to published had been obtained.
Disclosure
None declared

References
1. Hyperphosphatemic Familial Tumoral Calcinosis, M.Scott Ramnitz, GeneReviews® 2018 Feb 1.
2. Hyperphosphatemic Tumoral Calcinosis, V.Tiwari, StatPearls Publishing; 2025 Jan-NCBI Bookshelf

P176

Overcoming barriers to ana testing in pediatric populations in Africa

E. Ogbu[1,2], A. Migowa[3], R. Sahay[1], D. Sharma[1], P. Vega-Fernandez[1,2], M. Henrickson [1,2], E. Omalla[4], A. Faleye[5], W. Hamdi[6], H. Brunner[1,2]
[1]Cincinnati Children's Hospital Medical Center, [2]College of Medicine, University of Cincinnati, Cincinnati, United States, [3]Agha Khan University, [4]Paediatric Society of the African League Against Rheumatism, Nairobi, Kenya, [5]Lagos State University Teaching Hospital, Lagos, Nigeria, [6]Kassab Institute, Faculty of Medicine of Tunis, UR17SP04, Tunis El Manar University, Tunis, Tunisia
Correspondence: E. Ogbu
Pediatric Rheumatology, **23(2):** P176

Introduction: Timely diagnosis of children, adolescents and young adults with rheumatologic disorders remains a global challenge especially in lower resource countries and areas (LRCs). There are several LRCs on the African continent with limited access to antinuclear antibodies (ANA) testing necessary to support a diagnosis of several pediatric rheumatic disorders (PRD; % of patients with positive ANA) including systemic lupus erythematosus (100%), juvenile dermatomyositis (60-75%), and juvenile idiopathic arthritis (40-60%).
Objectives:
As the presence of ANA has near-ubiquitous utility in initially evaluating for a rheumatic condition, we aimed to understand physician perspectives on the barriers to ANA testing in pediatric populations across Africa, and the regional differences in barriers.
Methods:
Electronic REDCap surveys were sent to physicians within the Pediatric Society of the African League Against Rheumatism (PAFLAR). Surveys were sent via individual email links from January to March 2025. Dillman's methods for surveys were used to optimize survey response rates. Descriptive analysis was done and comparisons considering geographic region and the World Bank classification of economies based on Gross National Income per capita.
Results:
Response rate was 74% (38 of 50). Most respondents were attendings (89%), from Lower Middle-Income Countries (LMIC; 68%), and from North Africa (41%). All physicians had experience in treating PRDs, including 30% of respondents who lacked formal training in rheumatology. ANA testing was needed > 10 times a month (46%). The cost of ANA testing was high at $20–60/test (60%). Over 80% of respondents had little to no difficulty collecting and centrifuging venous blood for ANA testing. However, only 31% found it easy to ship samples to a lab within 1 - 2 days of sample collection. There was difficulty in processing ANA testing by ELISA which was worse in the Southern (100%), and West regions (83%) (p=0.03). Over 70% of respondents had difficulty receiving results of ANA testing quickly enough to support patient care which was worse with lower income countries and LMIC compared to others (p = 0.04); and in West and Central/East regions compared to others (p = 0.03). Even with local laboratories available, ANA testing was not readily available in public hospitals and so samples were often sent overseas.
Conclusion:
Our results provide highly desired quantitative evidence of the urgent need to improve access to affordable, and robust ANA testing in LRCs in Africa. Specifically, our results highlight critical barriers to ANA testing that will inform successful scaling of testing methods and future research and intervention efforts that would improve early diagnosis of rheumatic conditions in children, adolescents and young adults.
Disclosures
Supported by the Cincinnati Children's Hospital Medical Center Faculty International Research Excellence (FIRE) Award.
Disclosure
E. Ogbu Consultant with: Cartesian Therapeutics, A. Migowa: None declared, R. Sahay: None declared, D. Sharma: None declared, P. Vega-Fernandez: None declared, M. Henrickson : None declared, E. Omalla: None declared, A. Faleye: None declared, W. Hamdi: None declared, H. Brunner: None declared

P177

Neurodevelopment and screening for attention deficit hyperactivity disorder and autism spectrum disorder in children of mothers with rheumatic diseases

S. G. Rosiles De la Garza, C. E. López Cardona, A. D. J. Rangel Elizondo, A. V. Villarreal Treviño, F. García-Rodríguez, N. E. Rubio Perez[1] on behalf of Colaborativa de Investigación en Beneficio de la Reumatología Infantil (COLIBRI)
Universidad Autonoma de Nuevo Leon, Monterrey, Mexico
Correspondence: C. E. López Cardona
Pediatric Rheumatology, **23(2):** P177

Introduction: It is estimated that between 20% and 80% of the children of women with rheumatic diseases will experience some type of developmental disorder throughout their lives, including attention

deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). This incidence is higher than the general population, however, the existing evidence on long-term outcomes remains limited.
Objectives: To estimate the prevalence of neurodevelopmental screening abnormalities, ADHD, and ASD in children over 2 years old born to women with rheumatic diseases.
Methods: This is a cross-sectional, observational, and descriptive study. The "Ages & Stages Questionnaire - 5 (ASQ-5)", "M-CHAT", and the DSM-V criteria for ADHD were used to identify neurodevelopmental alterations, as well as warning signs for ASD and ADHD, respectively. Children aged between 2 and 5 years old born to mothers with rheumatic diseases diagnosed before or during pregnancy were included. The questionnaires were answered by the child's primary caregiver assisted by a trained health professional.
Results: The study included 42 children, with a median age of 48 months (IQR: 36–60), 19 (45.2%) were male, 11 (26.2%) were born prematurely, 11 (26.2%) had at least one comorbidity, and 35 (83.3%) received breastfeeding. About maternal diseases, 18 (43.9%) were inflammatory arthropathies (RA and PsA), and 23 (56.1%) were connective tissue disorders (SLE, Sjögren, APS, and DM).
About the ASQ-5 scores; 10 children (23.8%) showed a deficiency in at least one domain. The most frequently affected domains were communication (5, 11.9%), fine motor (4, 9.52%), and social skills (3, 7.14%). Regarding the risk of autism spectrum disorder, 37 children (88.09%) were classified as low risk, 4 (9.52%) as moderate risk, and 1 (2.38%) as high risk.
As for ADHD prevalence, 30 children (71.4%) did not meet the criteria for diagnosis, 7 (16.7%) presented with a hyperactive-predominant type, 3 (7.1%) with a combined subtype, and 2 (4.8%) with a predominantly inattentive type.
The age group between 54 and 60 months showed a higher frequency of communication deficits in the ASQ-5, although the differences were not statistically significant.
Conclusion: A notable proportion of children born to mothers with rheumatic diseases presented neurodevelopmental concerns, particularly in the domains of communication, fine motor, and social skills. While most children screened as low risk for ASD and did not meet criteria for ADHD, nearly one in four showed developmental delays, highlighting the importance of systematic follow-up. These findings underscore the need for multidisciplinary monitoring beyond infancy to identify and address potential neurodevelopmental issues early in life.
Disclosure
None declared

References

1. Yousef Yengej FA, van Royen-Kerkhof A, Derksen RHWM, Fritsch-Stork RDZE. The development of offspring from mothers with systemic lupus erythematosus. A systematic review. Autoimmun Rev. julio de 2017;16(7):701–11.
2. Vinet É, Bernatsky S. Outcomes in Children Born to Women with Rheumatic Diseases. Rheumatic Disease Clinics of North America. mayo de 2017;43(2):263–73.

P178

Sjögren's syndrome: a difficult entity to diagnose in childhood

M. Villaraviz Varela[1], P. Martínez Calabuig[2,3], M. I. Gonzalez Fernandez[4], B. Lopez Montesinos[4], M. Marti Masanet[4], L. Lacruz Perez[4], I. Calvo Penades[4]
[1]Department of Pediatrics, [2]Pediatric Rheumatology Unit, Hospital Universitario y Politecnico La Fe, [3]Rheumatology, Hospital General Universitario de Valencia, [4]Pediatric Rheumatology Unit, Health Research Institute Hospital La Fe (IIS La Fe), Hospital Universitario y Politecnico La Fe, Valencia, Spain
Correspondence: Calvo Penades
Pediatric Rheumatology, **23(2):** P178

Introduction: Sjögren's Syndrome (SS) is a chronic systemic autoimmune disease characterized by involvement of the salivary and lacrimal glands. Pediatric SS is rare and has a different presentation compared to adults, with extraglandular manifestations predominating and, less frequently, classic symptoms of sicca syndrome.
Objectives: To describe the patients registered with a suspected diagnosis of primary/secondary pediatric SS in a
Reference Pediatric Rheumatology unit, as well as to evaluate the classifying criteria of the ACR/EULAR (2016) and the pediatric diagnostic criteria proposed by Tomiita et al. in 2018.
Methods: A retrospective observational study was conducted at a pediatric rheumatology
Reference unit between 2008 and 2024. Databases were reviewed and demographic, clinical, analytical and therapeutic data were collected from patients with a suspected diagnosis of pediatric SS.
Results: Twelve patients with a diagnosis of SS were included. Half were female and 92% were Caucasian, with a median (min-max) age at symptom onset of 8 (3-12) years. Association with other pathology in 17%: juvenile idiopathic arthritis (n=1) and systemic lupus erythematosus (n=1).The main manifestations at the beginning were musculoskeletal (67%), followed by ocular (17%), recurrent parotitis (17%), livedo reticularis (17%) and Raynaud's phenomenon (17%).During the course of the disease, a higher percentage of patients developed the typical sicca syndrome symptoms (xerophthalmia in 58% and xerostomia in 25%). However, the predominant manifestations during follow-up were musculoskeletal (83%), with renal involvement also being important (25%).At the serological level, ANA antibody positivity was the most frequent (92%), followed by anti-Ro antibodies (75%) and to a lesser extent, rheumatoid factor (42%) and anti-La (33%).In terms of treatment, most patients received hydroxychloroquine (83%), while 42% were treated with systemic corticosteroids and 33% with DMARDs, depending on clinical features. Regarding the criteria, only 42% of the patients met the 2016 ACR/EULAR classification criteria. Diagnostic criteria of Tomiita et al. (2018) were met by 83%, classified as: definite (33%), probable (25) and possible (25%).
Conclusion: As reported in the literature, musculoskeletal symptoms were the most common initial manifestation in our series (67%). Recurrent parotitis, a distinctive feature in children, occured at younger age at onset. Clinical presentations were heterogeneous, with renal involvement observed in three patients. Over time, the prevalence of ocular and oral dryness increased.
The varied presentation of pediatric SS complicates diagnosis and underscores the need for clinical suspicion. In this context, we support the classification into possible, probable, and definite SS proposed by Tomiita et al., which better reflects pediatric cases. The ACR/EULAR classification criteria are less applicable in children due to the lower frequency of sicca symptoms, highlighting the need for pediatric-specific diagnostic criteria.
Disclosure of Interest
M. Villaraviz Varela: None declared, P. Martínez Calabuig: None declared, M. I. Gonzalez Fernandez: None declared, B. Lopez Montesinos: None declared, M. Marti Masanet: None declared, L. Lacruz Perez: None declared, I. Calvo Penades Speaker Bureau with: GSK, Pfizer, Novartis, Abbvie, Sobi.

P179

Preliminary data from first russian registry of patients with fibrodysplasia ossificans progressiva

I. Nikishina[1], S. Arsenyeva[1], V. Matkava[1], A. Polyakov[2], A. Borovikov[2], I. Sermyagina[2], E. Gasymov[3], V. Kenis[4], M. Kostik[5], A. Arefieva[1], G. Torosyan[6], S. Rodionovskaya[6], O. Inozemtseva[1], L. Blank[3]
[1]Paediatric, V.A. Nasonova Scientific Research Institute of Rheumatology, [2]Research Centre for Medical Genetics, [3]Radiology, V.A. Nasonova Scientific Research Institute of Rheumatology, [4]Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Moscow, [5]Hospital Pediatry Department of Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, [6]Federal Scientific and Clinical Center for Children and Adolescents of the Federal Medical and Biological Agency, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P179

Introduction: Fibrodysplasia ossificans progressiva(FOP)is an ultrarare(<1:1 million)monogenic condition which caused by a mutation in the ACVR1 gene and provoked appearance of multiple heterotopic ossification(HO).Due to its rarity there is no big data about this

condition in real-world clinical practice.In Russian Federation a FOP Registry was launched since 2021 year.
Objectives: To analyze the demographic, clinical and imaging features of patients with FOP, and the spectrum of therapeutic options in prospective study.
Methods: Among all our historical cohort FOP patients(N=59)39 pts were included in FOP Registry.Routine rheumatological assessment, imaging was performed in all pts. Low-dose whole-body computed tomography was done in 32/82% pts.HO volume was calculated separately for each body region and summarized.The CAJIS, CHAQ used for functional status assessment.
Results: In 39 pts(22 male/17 female) the diagnosis was verified by "classic" phenotype:malformed great toes-39/100%pts;malformed thumbs-11/28%;abnormalities of cervical spine, peripheral osteochondromas and multiple HO in 39/100% pts.Genetic test was done in 39/100% pts and confirmed typical(p.Arg206His)–37 pts or ultra-rare mutation(n=2).FOP was misdiagnosed as Grizel's syndrome,Buschke's scleredema, abscess, multiple calcinates. In 21/54% biopsy was done. FOP was verified by rheumatologist 18/46%,in 12 cases–by orthopedists, 6–oncologists,3-geneticists. In male the mean age of first symptoms was earlier than in female(2.1 y.o.(0;12) in compare to 3.6 y.o.(0;18).The mean age at diagnose verification in male patients was 4.9 y.o.(0;14); in female pts-8.4 y.o.(0;36). Flare-up triggers were traumas in 22/56% pts, vaccination in 8/21%, intramuscular injections in 11/28%, dental treatment in 4/10%,massage in 13/33%.The mean HO volume was 297,13 cm^3 and depends on the age:in group 0-5 y.o. the mean HO volume was 57.1 cm^3(2;12.1);6-10 y.o.–103.9 cm^3(1.2;346);11-15 y.o.–222 cm^3(49.7;359);>16 y.o.–659.7 cm^3(9.2;1416).Hearing impairment was detected in 8/40% from 20 who had audiogram examination.The mean CAJIS was 8.5(0;22).The mean CHAQ was 1.7(0.5;2,8). Synovitis of large joints revealed in 35(90%) pts.Pts had ankylosis of the facet joints and vertebral bodies by the type of syndesmophytes(30/77% of cervical spine, 25/64% of thoracic spine). Among 25 pts older than 10 years 16/64% pts had bilateral sacroiliitis. All pts used different medicines(NSAIDs-39/100%, corticosteroids oral–23/59%, intravenous–14/36%; bisphosphonates-10/26%).Tofacitinib received 35/90% pts for the flare-up prevention.Pathogenic drug, which are blocking the pathway "chonrogenesis-osteogenesis" palovarotene was administered in 12/30% pts as combined therapy and 1–in monotherapy.By now we have only preliminary data of it using.
Conclusion: It's crucial to increase awareness about FOP among specialist to avoid unnecessary manipulations and for better diagnostics.It seems that early manifestation of the disease in males provokes more severe course.We identify that HO volume increases according the age and correlates with disease duration.Combination of palovarotene and TOFA can be considered as a new encouraging strategy but need to further investigations.No doubt that FOP should be recognize as rheumatic disease.
Disclosure
None declared

P180

Referral patterns in childhood onset sjögren disease

M. L. Basiaga[1], A. Thatayatikom[2], S. M. Lieberman[3], E. Marrani[4], E. Kilic Konte[5], S. Sahin[5], J. M. Mosquera Angarita[6], J. E. Orrock[7], J. Lai[8], E. B. Treemarcki[9], S. M. Stern[9]
[1]Department of Pediatric and Adolescent Medicine, Division of Pediatric Rheumatology, Mayo Clinic, Rochester, [2]Division of Pediatric Rheumatology, Advent Health for Children, Orlando, [3]Stead Family Department of Pediatrics, Division of Pediatric Rheumatology, University of Iowa, Iowa City, United States, [4]Pediatric Rheumatology Unit, ERN ReCONNET Center-Meyer Children's Hospital-IRCCS, Firenze, Italy, [5]Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa, Istanbul, Türkiye, [6]Department of Pediatric Rheumatology, Hospital Sant Joan de Déu, Barcelona, Spain, [7]Department of Pediatrics, Division of Pediatric Rheumatology, The University of Texas at Austin Dell Medical School, Austin, [8]Department of Pediatrics, Division of Pediatric Rheumatology, Texas Children's Hospital, Baylor College of Medicine, Houston, [9]Department of Pediatrics, Division of Pediatric Rheumatology, University of Utah, Salt Lake City, United States
Correspondence: M. L. Basiaga
Pediatric Rheumatology, **23(2):** P180

Introduction: Sjögren disease (SjD) is an uncommon yet likely underrecognized disease in children. Understanding referral patterns to rheumatology and symptoms at onset can inform efforts to improve disease recognition and timely diagnosis.
Objectives: Describe referal patterns in childhood onset SjD and analyze the impact on disease activity and symptom duration at diagnosis.
Methods: The Childhood Onset Sjögren disease Outcomes Network (CHOSON) is an international collaboration of pediatric rheumatologists collecting longitudinal observational data on children under 18 years of age diagnosed with, or suspected of having, SjD. The enrollment visit includes demographic and clinical data. As an observational convenience sample, there was random missing data for some variables.
Results: A total of 70 patients (74% female) with a diagnosis of SjD from nine centers were included. Analyzing baseline data from the enrollment visit, nearly half, 49%, were referred to rheumatology from primary care followed by 24% from otolaryngology and 20% from a variety of specialties. No patients were referred from oral medicine. Symptom duration at diagnosis was available for 41 patients; 24% (n=10) reported less than one year of symptoms, 68% (n=28) reported 1-5 years of symptoms, and 7% (n=3) greater than five years of symptoms. No statistically significant differences in symptom duration were seen by referring specialty, though all patients referred by dermatology, infectious diseases, and oncology were referred in the first year of symptoms. Extended symptom duration at the time of SjD diagnosis was strongly associated with higher baseline visit EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) pain domain (p=0.04), fatigue domain (p=0.007), and composite score (p=0.01), but not dryness domain (p=0.07) [Figure 1].
Conclusion: Most children diagnosed with SjD are referred to rheumatology from a primary care provider. The majority of children report 1-5 years of symptoms at the time of SjD diagnosis. The longer symptom duration before disease diagnosis was strongly associated with higher patient reported disease burden. Interestingly, no children in our cohort were referred from oral medicine providers despite reports of xerostomia and excessive dental caries in several. Future efforts to increase disease awareness should consider focusing on oral medicine and dental providers.
Disclosure
None declared

P181

A phase 3, randomized, placebo-controlled study to assess the safety and efficacy of garetosmab in fibrodysplasia ossificans progressiva: baseline characteristics of patients in the optima study

R. Papa[1], S. Rhee[2], P. Delai[3], K. Zhang[4], M. Zhou[2], K.-C. Chan[2], R. Pordy[2], R. Keen[5]
[1]Rheumatology and Autoinflammatory Diseases Unit, IRCCS Istituto Giannina Gaslini, Genova, Italy, [2]Regeneron Pharmaceuticals, Inc., Terrytown, United States, [3]Hospital Israelita Albert Einstein, Instituto de Ensino e Pesquisa, São Paulo, Brazil, [4]Department of Endocrinology, Tongji Hospital, Shanghai Tongji University, Shanghai, China, [5]Centre for Metabolic Bone Disease, Rheumatology, Royal National Orthopedic Hospital NHS Trust, Middlesex, United Kingdom
Correspondence: R. Papa
Pediatric Rheumatology, **23(2):** P181

Introduction: Fibrodysplasia ossificans progressiva (FOP) is an ultrarare, severely disabling disease characterized by progressive multifocal heterotopic ossification (HO) formation of extra skeletal tissue, caused by heterozygous missense mutations in the gene encoding activin A receptor type 1 (ACVR1). The phase 2 LUMINA-1 study demonstrated clinical benefit of garetosmab, an investigational fully human monoclonal antibody that selectively binds activin A and blocks ACVR1 signaling, in patients with FOP. In LUMINA-1, all patients experienced ≥1 adverse event; most (86%) were not serious. Five deaths occurred, though considered unrelated, causality was not ruled out.
Objectives: To describe the baseline characteristics of participants in the phase 3 OPTIMA trial (NCT05394116).
Methods: OPTIMA was a phase 3, randomized, multi-center, parallel-group, placebocontrolled study in adult patients with active FOP caused by any FOP-causing variant of ACVR1. Patients included in the

trial were randomized 1:1:1 to receive garetosmab 10 mg/kg, 3 mg/kg, or placebo intravenously every 4 weeks. Primary endpoints were number of new HO lesions at Week 56, assessed by a total body low-dose computed tomography scan during screening, at Week 28, and at Week 56, and safety from baseline to Week 56. Secondary endpoints included number of clinicianassessed flare ups through Week 56, occurrence of new HO lesions (yes/no) at Week 56, patient-reported flare-ups (yes/no) through Week 56, and total volume of new HO lesions at Week 56.
Results: A total of 63 patients were enrolled in the study. Mean (SD) age was 26.6 (6.8) years, and 56 (88.9%) of patients carried the classic R2O6H mutation. Overall, 38 (60.3%) patients were female, and 42 (66.7%) were White. Mean (SD) weight was 59.1 (15.3) kg, with a median (interquartile range) body mass index of 20.5 (18.1–27.1) kg/m^2. At enrollment, patients experienced symptoms of disease activity for a mean (SD) duration of 24.8 (9.0) years. Thirteen (20.6%) patients received prior medication for FOP symptom management. Overall, 25 (39.7%) patients experienced a flare up in the 12 months prior to study entry, and mean (SD) total Cumulative Analogue Joint Function Scale (CAJIS) score was 12.5 (4.3).
Conclusion: Based on the duration of FOP and baseline CAJIS scores, patients enrolled in OPTIMA had a substantial burden of disease, and the majority had evidence of the classic R206H mutation.
Trial registration identifying number: NCT05394116: A Study to Assess Safety, Tolerability and Efficacy of Garetosmab Versus Placebo Administered Intravenously (IV) in Adult Participants With Fibrodysplasia Ossificans Progressiva (FOP) (OPTIMA)
Disclosure
R. Papa: None declared, S. Rhee Shareholder with: Regeneron Pharmaceuticals, Inc., Employee with: Regeneron Pharmaceuticals, Inc., P. Delai: None declared, K. Zhang: None declared, M. Zhou Shareholder with: Regeneron Pharmaceuticals, Inc., Employee with: Regeneron Pharmaceuticals, Inc., K.-C. Chan Shareholder with: Regeneron Pharmaceuticals, Inc., Employee with: Regeneron Pharmaceuticals, Inc., R. Pordy Shareholder with: Regeneron Pharmaceuticals, Inc., Employee with: Regeneron Pharmaceuticals, Inc., R. Keen: None declared

P182

Increased salivary gland inflammation in pediatric-onset sjögren's disease: a histopathological comparison with adult patients

F. Riccio[1], M. Neri [2], M. Mellone [1], I. Cozzolino [1], J. Ferro [2], V. G. Vellone [2], C. E. Boschetti[1], G. Colella [1], N. Laffi [2], P. Buono [3], E. Tirri[4], R. Franco[1], M. Gattorno[2], F. Ciccia[1], C. Malattia[2], S. Gandolfo[4]
[1]University of Campania "Luigi Vanvitelli", Naples, [2]Giannina Gaslini IRCCS Institute, Genoa, [3]Directorate-General for Health, Campania Region, [4]Ospedale del Mare, Naples, Italy
Correspondence: M. Gattorno
Pediatric Rheumatology, **23(2):** P182

Introduction: Pediatric Sjögren's disease (pSjD) is increasingly recognized as a distinct clinical entity, characterized by differences in both presentation and serological profile compared to the adult form. While classic sicca symptoms such as xerophthalmia and xerostomia are less common in children, parotid gland enlargement and cutaneous manifestations are more frequently observed. From a serological perspective, pediatric patients tend to show lower rates of ANA and anti-SSA/SSB positivity, but higher Rheumatoid Factor (RF) levels [1]. Given the limited histopathological data available in pSjD, we undertook this study with the hypothesis that the heightened disease activity commonly observed in children would correspond to more severe structural changes in the salivary glands.
Objectives: To investigate and compare the histopathological features of minor salivary gland biopsies in pediatric and adult patients with Sjögren's disease (SjD).
Methods: This study included 18 children with pSjD followed at a single Italian pediatric rheumatology center and 37 adult SjD patients assessed at an Italian adult rheumatology unit. All biopsy specimens were evaluated by an experienced pathologist at each center according to EULAR guidelines for the standardized histological assessment of salivary gland tissue [2]. Immunohistochemical analyses were conducted using CD3, CD20, CD21, Bcl6.
Results: The surface area of biopsy samples did not differ significantly between the two groups (p = 0.551). Pediatric patients exhibited significantly higher focus scores (p = 0.0227) and a greater prevalence of ectopic germinal centers, as shown by increased CD21 (52.94% vs. 16.22%, p = 0.0058) and Bcl6 expression (47.06% vs. 8.11%, p = 0.0011). Lymphoepithelial lesions were more frequently detected in pediatric cases (55.56% vs. 18.92%, p = 0.0065), as was fibrosis (66.67% vs. 29.73%, p = 0.031). No significant differences emerged regarding glandular atrophy (p = 0.687) or ductal dilatation (p = 0.128). Interestingly, within the pediatric cohort, patients with prepubertal disease onset showed a higher frequency of germinal centers than those with postpubertal onset, as well as lymphoepithelial lesions (p<0.05).
Conclusion: This study represents the first direct comparison of minor salivary gland histopathology between pediatric and adult patients with Sjögren's disease. The findings reveal more intense inflammatory histopathological activity in children, mirroring the observed higher disease activity in clinical features in these patients. Moreover, the higher frequency of ectopic germinal centers and lymphoepithelial lesions observed in prepubertal patients may suggest the involvement of an age-dependent immunopathological mechanism driving early-onset pSjD. These insights reinforce the relevance of salivary gland biopsy in both diagnosis and prognostic evaluation, and underscore the importance of early recognition and close monitoring of pediatric patients.
Disclosure
None declared

References
1. Riccio F, et al. POS0767 Annals of the Rheumatic Diseases 2024;83:1178.
2. Fisher BA, et al. Ann Rheum Dis 2017;76:1161–1168.

P184

Association of arthritis and uveitis - is it always idiopathic arthritis or not? rare case of rosah syndrome

S. Arsenyeva[1], I. Nikishina[1], V. Matkava[1], T. Markova[2], A. Panova[3], O. Borodacheva[1]
[1]Paediatric, V.A. Nasonova Scientific Research Institute of Rheumatology, [2]Research Centre for Medical Genetics, [3]Moscow Helmholtz Research Institute of Eye Diseases, Moscow, Russian Federation
Correspondence: S. Arsenyeva
Pediatric Rheumatology, **23(2):** P184

Introduction: Retinal dystrophy, optic nerve oedema, splenomegaly, anhidrosis and migraine headache (ROSAH) syndrome is an autosomal dominant autoinflammatory disease caused by pathogenic variants in ALPK1 (1). Patients with ROSAH syndrome usually have vision loss but also can have autoinflammatory features, such as arthritis and fever. In most patients the variant Thr237Met of ALPK1 was found, one patient has Tyr254Cys variant, and six patients have new Ser277Phe variant.
Objectives: To describe a clinical case of newly diagnosed ROSAH syndrome with ultrarare variant Tyr254Cys which was recognized because of unusual course of Juvenile Idiopathic Arthritis (JIA) combined with anterior bilateral uveitis.
Methods: Case report: From birth our patient has hyperkeratosis and face erythema and was observed by dermatologist from 3 months age with congenital ichthyosis. Also he has anhidrosis, brittle nails. At the age of 4 months mother noticed swelling of the hands joints and knee without pain and local hyperthermia. At the age of 1 year movement restrictions in the hands joints appeared with the inability to clench the hand into a fist, so mucopolysaccharidosis was excluded. However, for 2 years he was under the supervision of a dermatologist. Also, he has multiple dental caries, recurrent fever, headache, episodic malaise. At the age of 2.5 years a geneticist examined him and paid attention to the deformation of the chest ("foveated chest") and hand joints and recommended to visit the rheumatologist.
Results: Patient admitted to rheumatological department at 3 y.o., chronic erosive arthritis of the joints of the hands and feet was detected by X-ray and MRI. RF, anti-CCP, ANA, HLAB27 were negative, CRP was normal. Despite the presence of arthritis, we proposed genetic pathology due to early onset of the disease and severe hands joints deformities like advanced RF-positive JIA without pain and local

hyperthermia. It was unexpected that the ophthalmologist revealed bilateral acute anterior uveitis, local glucocorticoid therapy was prescribed with positive effect. Later tofacitinib was administered. We performed whole exome sequencing and revealed pathogenic variant in the gene ALPK1 p.Tyr254Cys. His parents don't have ALPK1 mutation. Patient has a normal sized spleen and he's never had cytopenia, on the contrary, he has leukocytosis (from 12X10^9/L to 18X10^9/L) without any connection with inflammatory flare or infection. After diagnosis verification we continued tofacitinib treatment and completely stop local steroids in 5 months after starting the tofacitinib.
Conclusion: ROSAH syndrome is a new autoinflammatory disease and should be taken in consideration in case of severe oculopathy and atypical arthritis. This condition is probably underdiagnosed and need for broader awareness of the disease to facilitate early diagnosis and start treatment before irreversible complications development. The anti-inflammatory effect of JAK-inhibitors Tofacitinib seems to be the good option for treatment of ROSAH syndrome and help to control the intraocular inflammation and prevent retinal degeneration. Future studies are needed. Consent to published had been obtained.
Disclosure
None declared

Reference
1 Huryn LA, Kozycki CT, Serpen JY, Zein WM, Ullah E, Iannaccone A, Williams LB, Sobrin L, Brooks BP, Sen HN, Hufnagel RB, Kastner DL, Kodati S. Ophthalmic Manifestations of ROSAH (Retinal Dystrophy, Optic Nerve Edema, Splenomegaly, Anhidrosis, and Headache) Syndrome, an Inherited NF κB-Mediated Autoinflammatory Disease with Retinal Dystrophy. Ophthalmology. 2023 Apr;130(4):423-432. doi: https://doi.org/10.1016/j.ophtha.2022.10.026. Epub 2022 Nov 2. PMID: 36332842; PMCID: PMC10038920.

P185

Correlation between monocyte expression of siglec-1 and serum levels of antinuclear antibodies in pediatric rheumatological disorders and autoimmune thyroiditis

E. Valencic[1,2], V. Boz[1], L. Donna[2], A. Tesser[1], G. Tornese[1,2], S. Pastore[1], M. Fabris[3,4], A. Tommasini[1,2], A. Taddio[1,2]
[1]Department of Paediatrics, Institute for Maternal and Child Health IRCCS "Burlo Garofolo", [2]Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, [3]Department of Medicine (DMED), University of Udine, [4]Department of Laboratory Medicine, Azienda Sanitaria Universitaria Friuli Centrale (ASU FC), Udine, Italy
Correspondence: V. Boz
Pediatric Rheumatology, **23(2):** P185

Introduction: Siglec-1 expression on peripheral monocytes is an indirect measure of type I interferon inflammation used in rheumatology. Interferon-driven rheumatic diseases like lupus and Sjogren's disease often feature antinuclear antibodies (ANA), whose production is promoted by interferon. However, it is unknown if interferon inflammation also characterizes other conditions with ANA, such as oligoarticular juvenile idiopathic arthritis (JIA) or autoimmune thyroiditis.
Objectives: To analyze the correlation between antinuclear antibody titers and Siglec-1 expression in subjects referred to a pediatric rheumatology clinic.
Methods: Observational study with two groups: a convenience sample of patients referred to pediatric rheumatology evaluated for ANA and Siglec-1 based on clinical indication; a cohort with autoimmune thyroiditis enrolled in a study aimed at identifying early Sjogren's signs. ANA were measured by immunofluorescence (1 point/dilution increment). Siglec-1 was measured by flow cytometry (percentage of positive monocytes). Correlation used linear regression; p<0.05 was significant.
Results: 125 samples with ANA and Siglec-1 data were included. In the connective tissue disease group (34 samples overall, including 18 SLE, 5 pSS, 10 UCTD, and 1 interferonopathy), a moderate correlation between Siglec-1 and ANA was observed (r^2=0.14, p=0.027). No correlation was seen in oligoarticular arthritis (12 patients) (r2=0, p=0.9), while a good correlation was observed in the polyarticular arthritis group (17 patients, incl. JPsA and SPA) (r2=0.26, p=0.035). In the thyroiditis group (17 patients), a clear correlation was observed (r2=0.58,p=0.0006). No correlation was found in the other groups (55 subjects: 22 with autoinflammatory diseases, 6 infections, 8 cytopenias, 9 PIDs). Results suggest that the significance of ANA positivity differs between conditions. In oligoarticular JIA, ANA positivity isn't typically associated with interferon inflammation, but it tends to be in polyarticular arthritis. High levels of Siglec-1 in oligoarticular JIA were observed only in two cases that had a post-pubertal onset. Polyarticular cases included some patients with extended oligoarticular arthritis who exhibited both ANA and increased Siglec-1. Even if previous measures were not available, we may hypothesize that combined ANA and Siglec-1 positivity might help predict oligo-extended evolution in JIA. ANA/Siglec-1 co-positivity in autoimmune thyroiditis might identify a group at risk of rheumatic comorbidities; follow-up is needed.
Conclusion: Concomitant Siglec-1 evaluation can help clarify the meaning of positive ANA in various rheumatic conditions.
Disclosure
None declared

P186

New competitions for rheumatologists: progressive pseudorheumatoid dysplasia

V. Matkava[1], I. Nikishina[2], S. Arsenyeva[2], T. Markova[3], O. Kostareva[1]
[1]Paediatric, V.A. Nasonova Research Institute of Rheumatology, [2]Paediatric, V.A. Nasonova Scientific Research Institute of Rheumatology, [3]Research Centre for Medical Genetics, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P186

Introduction: Progressive pseudorheumatoid dysplasia (PPD), also known as spondyloepiphyseal dysplasia tarda with progressive arthropathy, is a rare autosomal recessive genetic disorder caused by mutations in the CCN6 (WISP3) gene. This condition primarily affects the cartilage and bone, leading to progressive joint stiffness, pain, and enlargement, often mimicking juvenile idiopathic arthritis. Treatment of these patients is a difficult challenge and requires new approaches.
Objectives: To describe single center case series of PPD and analyze the main clinical features and treatment options.
Methods: Among patients examined in our center with huge variety of genetic conditions, including different types of spondyloepiphyseal dysplasias, we identified 5 patients (pts) with PPD. Genetic tests performed in all pts. Full spectrum of Imaging was done in all pts, X-Ray, US and MRI including in 100%, CT on demand.
Results: In 5 pts (3 male/2 female) were verified as haven PPD. Genetic testing was done in all pts and confirmed mutation in CCN6 (WISP3) gene. The average age of onset was 4,2 y.o. (from 3 to 5 years). All pts had diagnostic delay from 5 to 13 years. In all pts PPD manifested in early childhood, with symptoms including gait abnormalities, joint contractures, and progressive skeletal deformities. Current clinical features present by symmetric hypertrophy of interphalangeal joints as key symptom with previous pain and stiffness, progressive kyphoscoliosis, short stature, wadding gait. Radiological findings included enlargement epiphyses, platyspondyly, short and wide femoral necks. Two pts were with extremely hard disability and used additional mobility support and wheelchair. Laboratory assessment found positive HLA-B27 in 1 pt, elevated CRP in 1 pt. Routine rheumatological examination detected signs of arthritis in all pts, confirmed by ultrasound or MRI, especially in wrists and hip joints. Due to severe pain syndrome all pts receive NSAIDs; 3 pts with polyarthritis, progressive structural damage (bilateral hip osteonecrosis) received Biologics (etanercept in 2 pts) or tofacitinib (1 pt) as 1-st line therapy. Because of 12-year diagnostic delay of PPD one pt was treated by 4 lines of Biologics (etanercept, adalimumab, upadacitinib, secukinumab) due to «refractory» course of disease and now he receives tofacitinib as 5-th line. In fact we noticed that his functional status is much better than in other pts without any anti-inflammatory treatment.
Conclusion: Early recognition of PPD clinical features is essential for providing appropriate management and support. When identifying suspicious features of the polyarthritis phenotype, a genetic examination is necessary. The rheumatologist`s skills can be useful in managing patients with PPD, and reducing the symptoms of joints inflammation by Biologics may prevent their destruction.

Disclosure
None declared

P187

Juvenile idiopathic arthritis associated with rare type of congenital insensitivity to pain: small case series

V. Matkava[1], I. Nikishina[1], S. Arsenyeva[1], T. Markova[2], T. Pachkoria[1], A. Shapovalenko[1]
[1]Paediatric, V.A. Nasonova Scientific Research Institute of Rheumatology, [2]Research Centre for Medical Genetics, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P187

Introduction: Congenital insensitivity to pain (CIP) represents a group of rare hereditary disorders characterized by inability to perceive pain while preserving other sensory modalities. This condition has 6 subtypes, associated with more than 10 genes (most commonly NTRK1) and leads to complications including Charcot arthropathies. Rheumatologists could observed these patients because of mimicking to JIA.
Objectives: To describe a small case series of 4 patients (pts) with ultra-rare CIP subtype which was recognized because of unusual course of Juvenile Idiopathic Arthritis (JIA).
Methods: Among patients examined in our center with huge variety of rheumatic conditions, we identified 4 male pts with CIP. Genetic tests performed in all pts. Full spectrum of Imaging was done in all pts, X-Ray, US and MRI including in 100%,CT on demand.
Results: All pts (11, 13, 15 and 16 y.o.) was admitted to our clinic with polyarticular type of JIA and suffered from progression of functional impairment and disability. 3 pts had recurrent episodes of autotraumatization and self-injuries in early childhood. All pts have generalized joint hypermobility (Ehlers-Danlos syndrome was initially considered). 3 pts had diagnostic arthroscopy due to severe arthritis of left knee which revealed osteochondritis dissecans of lateral condyle of left femur. We identified arthritis of large joints and multiple osteitis (by whole-body MRI) which allowed us to established JIA in all pts (in 3 pts – associated with chronic non-bacterial osteomyelitis). HLA-B27 was negative in all pts. All pts were treated with long-term NSAIDs course with repeated intraarticular corticosteroids injections (II) without significant effect, 1 pt received methotrexate. We noticed that all pts have reduced numbers of fungiform papillae, 3 pts had anosmia, hypogeusia, neuropathic joints. Due to refractory course of JIA and untypical features genetic test was done and confirmed mutation in SCN9A gene in 3 pts (ultra-rare CIP IID type), NTRK1 gene in 1 pt (CIP with anhidrosis (CIPA)). First pt with CIP IID (16 y.o.) was treated by etanercept (ETA) but after history of sepsis and developing psoriasis de novo therapy was switched to tofacitinib (TOFA) with good efficacy. 13 y.o. boy was treated by ETA, TOFA with partially response, we administered secukinumab and observed decreasing joint swelling. 15 y.o. boy was treated by ETA with decreasing left knee swelling. Patient with CIPA was treated by bisphosphonates with development flu-like syndrome and ETA without any positive effect. We administered TOFA with good response predominantly of knees and ankles.
Conclusion: The combination of unusual phenotype with extreme joint hypermobility, the presence of destructive changes, osteitis and a sign of pain insensitivity requires vigilance in recognizing CIP. Therapeutic approaches in such patients are comparable to patients with JIA but need clinical suspicion regardless methotrexate due to predisposition of patients with CIP to septic conditions.
Disclosure of Interest
None declared

P188

Artificial intelligence in adult and paediatric rheumatology practice and research: pilot results from an international survey

A. I. Rebollo Giménez[1], S. La Bella [2], K. Aouad[3], L. Gupta[4,5,6,7], D. Cangelosi [8], T. Hugle[9], J. Knitza [10], N. Ruperto[11,12], V. Venerito[13], A. El Maghraoui[14], A. Alongi[12], W. Bautista-Molano[15], D. Bayraktar[16,17], T. Davergne[18], D. Dey[19], I. Hmamouchi[20], A. M. Hoens[17,21], L. Li[21], A. Migowa[22], E. M. Treemarcki[23], N. Ziade[24], T. Kragstrup[25,26], D. Benavent[27]
[1]Hospital General Universitario Gregorio Marañón, Health Research Institute Gregorio Marañón (IiSGM), Madrid, Spain, [2]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [3]Department of Rheumatology, Saint George Hospital University Medical Center, Saint George University of Beirut, Beirut, Lebanon, [4]Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, [5]School of Infection, Inflammation and Immunology, College of Medicine and Health, Birmingham, [6]Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester, [7] Francis Crick Institute, London, United Kingdom, [8]Unità di Bioinformatica Clinica, Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [9]Department of Rheumatology, University Hospital Lausanne (CHUV) and University of Lausanne, Lausanne, Switzerland, [10]Institute for Digital Medicine, University Hospital Gießen-Marburg, Philipps University, Marburg, Germany, [11]Pediatric Rheumatology, Fondazione IRCCS San Gerardo dei Tintori, [12]Università Milano Bicocca, Milan, [13]Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", Bari, Italy, [14]Rheumatology Office, Mohamed V University, Rabat, Morocco, [15]Rheumatology Section, University Hospital Fundacion Santa Fe de Bogotá, School of Medicine Universidad El Bosque, Bogotá, Colombia, [16]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Izmir Katip Celebi University, Izmir, Tunisia, [17]Arthritis Research Canada, Vancouver, British Columbia, Canada, [18]Department of rehabilitation, Team METHODS, CRESS UMR 1153, University of Paris Cité, France, [19]Rheumatology Unit Department of Medicine and Therapeutics, rle bu Teaching Hospital, University of Ghana Medical School, Accra, Ghana, [20]Health Sciences Research Center (CReSS).Faculty of Medicine, International University of Rabat, Rabat, Morocco, [21]Department of Physical Therapy, University of British Columbia, British Columbia, Canada, [22]Aga Khan University Medical College East Africa, Nairobi, Kenya, [23]Department of Pediatrics, Division of Pediatric Rheumatology, University of Utah Health, Utah, United States, [24]Department of Rheumatology, Saint-Joseph University and Hotel-Dieu de France, Beirut, Lebanon, [25]Department of Biomedicine, Aarhus University, Aarhus C, [26]Rheumatology Sector, Medical Diagnostic Center, Silkeborg Regional Hospital, Silkeborg, Denmark, [27]Rheumatology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain
Correspondence: A. I. Rebollo Giménez
Pediatric Rheumatology, **23(2):** P188

Introduction: Artificial intelligence (AI) is transforming rheumatology care, with innovative tools now empowering physicians and health professionals (HPRs).
Objectives: Our survey examines how adult and pediatric rheumatologists, and HPRs currently perceive and utilize AI tools in rheumatology clinical and research environments, by identifying their experiences, concerns, and unmet needs.
Methods: An international, cross-continental online survey following CROSS & CHERRIES frameworks was shared in March 2025 to gather perspectives from the adult and paediatric rheumatology community. The questionnaire included 27 questions, both multiple-choice and open-ended, in four sections: sample characteristics, AI usage and applications, opinions and concerns, and expectations for AI implementation in clinical practice and research.
Results: By early May 2025, a total of 263 respondents (63.5% female) from 43 countries completed the survey, including rheumatologists, paediatric rheumatologists, and HPRs. Median age of responders was 38 [IQR 32–48.5] years; only a minority of participants primarily worked in paediatric rheumatology (52, 19.8%),as HPRs (24, 9.1%),or mainly in research rather than clinical practice (54, 20.5%).
Most respondents (220, 83.7%) reported using large language models (LLMs)for medical purposes, commonly for text editing (176, 66.9%),brainstorming (137, 52.1%),summarizing papers (133, 50.6%), and manuscript writing assistance (115, 43.7%);only 30 (11.4%) respondents had never used LLMs.Attitudes towards AI were predominantly positive, with 204 (81.4%)expressing optimism regarding AI's efficacy and safety.However, up to 151 (58.1%) participants emphasized the need for strict AI regulation in medicine.
AI literacy was highly valued, with 214 (81.6%) rating it as very or extremely important, with 92 (35.5%) having or having had

subscriptions to AI models/tools. Respondents favoured LLM use for practical tasks:email drafting (191, 72.9%), copy-editing (191, 74%), generating manuscript sections (136, 51.9%), and facilitating
Reference access (157, 59.9%). Substantial support existed for integrating AI into peer review, assisting reviewers (118, 45%) and editors(112, 42.7%). Respondents indicated AI's greatest future impact in research (212, 80.6%), diagnosis (183, 69.6%), and administrative tasks (177, 67.3%).
Key concerns included ethical issues (176, 67.2%),lack of trust in AI-generated decisions (181, 69.1%),and insufficient training (156, 59.5%). Respondents supported AI integration into rheumatology practice, with only 5(1.9%) not recommending AI tools to colleagues.
Conclusion: Pilot results suggest the rheumatology community is recognizing AI's transformative potential whilst acknowledging the need for appropriate governance frameworks. AI tools are widely used and positively perceived by rheumatology and pediatric rheumatology professionals.However, concerns about ethics, trust, and training highlight the need for clear guidance and targeted education to support safe integration into clinical and research practice.
Disclosure
None declared

References
1. Knitza J,el al. Nat Rev Rheumatol. 2024
2. Holzer M-T, el al.Ther Adv Musculoskelet Dis 2024
3. La Bella S, el al. Curr Opin Rheumatol. 2025

P189

Functional subtype classification in juvenile idiopathic arthritis via pedobarographic analysis: a pilot study using dimensionality reduction and machine learning clustering

A. Yekdaneh[1,2], N. Arman[3], A. Albayrak[2,4], I. Donmez[5], N. Aktay Ayaz[6]
[1]Vocational School of Health Services Physiotherapy English Program, Fenerbahce University, [2]Institute of Graduate Studies Physiotherapy and Rehabilitation Doctorate Program, [3] Faculty of Health Sciences Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpaşa, [4]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Istanbul Kent University, [5]Institute of Graduate Studies, Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpaşa, [6]Department of Pediatrics, Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Türkiye
Correspondence: A. Yekdaneh
Pediatric Rheumatology, **23(2):** P189

Introduction: Juvenile Idiopathic Arthritis (JIA) affects lower limb function and gait, leading to abnormal load distribution and reduced mobility (1). Traditional assessments provide limited biomechanical insight (2). Pedobarography combined with computional methods, offers objective, high-resolution foot pressure analysis.
Objectives: This pilot study aimed to classify functional subtypes in JIA using dimensionality reduction and machine learning clustering, and to identify high risk patients based on plantar pressure profiles.
Methods: Ten JIA patients underwent pedobarographic, anthropometric and functional assessments, including the 30 Second Sit to Stand (30SST) and 6 Minute Walk Test (6MWT). Principal Component Analysis (PCA) reduced dimensionality and K-means clustering, an unsupervised machine learning algorithm, identified three functional subgroups based on the principal components. Clusters were visualized via 2D PCA projection. Random Forest regression revealed key predictors of functional performance. Statistical tests examined differences by age, sex, and Body Mass Index (BMI).
Results: PCA reduced dataset complexity, with the first two components explaining over 70% of total variance. K-means clustering identified three functional subtypes among 10 JIA patients. Cluster 0 (n: 2) included the tallest and heaviest patients with the best functional outcomes (mean (mn) 6MWT: 592 m; 30SST: 16.5 reps). Cluster 1 (n: 4) had intermediate anthropometric and plantar pressure profiles (mn 6MWT: 564.7 m). Cluster 2 (n: 3) showed shorter stature, elevated plantar pressures (mn left plantar max: 1833), and lowest performance (mn 6MWT: 460 m). Key cluster separation variables included left arch and hallux pressures, sex, and medial right foot loading. Random Forest analysis identified height and right foot lift-off speed as key predictors of functional performance. Age moderately correlated with 6MWT; sex and BMI showed no significant differences.
Conclusion: This pilot study demonstrates that dimensionality reduction and machine learning clustering can identify functional subtypes in JIA using the pedobarographic data. The identification of a subgroup with elevated plantar pressures and poor functional capacity scores highlights the potential of computational tools for early risk stratification and personalized rehabilitation. Using cluster analysis for underlying the functional impariments are exploratory in the present study. Validation of these methods should be pursued in larger, multi-center cohorts to confirm their generalizability and clinical applicability.
This study was funded by TUSEB B R&D Projects Support Program, Project number: 12075.
Disclosure
None declared

References
1. Woolnough L, et al. Juvenile idiopathic arthritis, gait characteristics and relation to function. Gait Posture. 2021.
2. Fairburn PS, et al. The use of multidisciplinary assessment and scientific measurement advanced juvenile idiopathic arthritis can categorise gait deviations to guide treatment. Arch Dis Child. 2002.

P190

Immediate effects of posture training in children and adolescents with juvenile idiopathic arthritis and familial Mediterranean fever: a pilot study using 3D wearable motion capture

A. Albayrak[1,2], S. Ozbal[3], R. B. Sarikaya[4], H. Argunsah[4], A. Yekdaneh[1,5], I. Donmez[6], N. Arman[7], N. Aktay Ayaz[8]
[1]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [2]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [3]Biomedical Engineering Doctorate Program, Acıbadem Mehmet Ali Aydınlar University, Graduate School of Natural and Applied Sciences,, [4]Department of Biomedical Engineering, Acıbadem Mehmet Ali Aydınlar University, Faculty of Engineering and Natural Sciences, [5]Physiotherapy English Program, Fenerbahçe University, Vocational School of Health Services, [6]Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [7]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [8]Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Department of Pediatrics, Istanbul, Türkiye
Correspondence: A. Albayrak
Pediatric Rheumatology, **23(2):** P190

Introduction: In childhood rheumatic diseases, problems such as joint pain, fatigue, joint stiffness and decreased muscle strength often manifest as asymmetrical movement patterns, postural misalignments, and gait abnormalities (1). Early postural correction and motor retraining are essential to prevent long-term biomechanical dysfunctions.
Objectives: This pilot study aimed to investigate the immediate effects of a single session of posture training on dynamic balance, postural alignment, joint kinematics, center of mass (COM) displacement, and movement symmetry during walking in patients with Juvenile Idiopathic Arthritis and Familial Mediterranean Fever using 3D motion analysis.
Methods: The study included 4 patients with JIA (2 females, 2 males) and 3 patients with FMF (3 males), aged between 9 and 18 years. Full-body kinematic data during walking were recorded and analyzed using XSens MVN (Xsens Technologies BV, Netherlands®) before and after posture training. Each postural training session incorporated visual biofeedback through avatar visualization and employed metaphor-based instructions grounded in motor learning principles to explain the key
Reference points of correct posture to the patient. To improve posture, a collaborative discussion was held with the patient to identify inadequacies and determine necessary corrections. Outcome metrics included trunk lean, COM sway, shoulder symmetry and joint range of

motion (ROM). Within-subject comparisons were conducted to evaluate pre- to post-training changes.
Results: After training, trunk lateral bending decreased by 142.9% (from 0.14° ± 0.68 to −0.06° ± 1.32), and trunk flexion shifted toward a more upright posture. COM sway in the mediolateral direction increased by 64.3% (from 0.14 ± 0.08 m to 0.23 ± 0.24 m) and shoulder height asymmetry remained consistent. In terms of joint kinematics, hip ROM increased slightly by 2.7% (from 6.93° ± 3.46 to 7.12° ± 2.21), knee ROM increased by 1.8% (from 11.99° ± 3.99 to 12.21° ± 5.10), and ankle ROM increased by 2.9% (from 11.26° ± 3.16 to 11.59° ± 2.64).
Conclusion: A single session of posture training with real-time feedback can yield measurable improvements in alignment, movement control, and mobility in patients with JIA and FMF. Wearable motion capture offers a powerful tool for individualized assessment and awareness. Active engagement in observing and understanding body movement increases motivation and autonomy. These short-term improvements support the feasibility of early, feedback-driven posture interventions in pediatric rheumatology and justify further longitudinal studies in larger cohorts.
This study was funded by TUSEB B R&D Projects Support Program, Project number: 12075.
Disclosure
None declared

Reference
1. Woolnough L, et al. Juvenile idiopathic arthritis, gait characteristics and relation to function. Gait Posture, 2021

P191

Strong back, strong steps: a pilot study exploring lumbar extensor strength and locomotor function in Jia

I. Dönmez[1], N. Arman[2], A. Yekdaneh[3,4], A. Albayrak[3,5], Y. Acıkgoz[1], F. Cakmak[6], N. Aktay Ayaz[7]
[1]Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [2]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [3]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [4]Physiotherapy English Program, Fenerbahçe University, Vocational School of Health Services, [5]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [6]Department of Pediatric Rheumatology, Istanbul Basaksehir Cam ve Sakura City Hospital, [7]Department of Pediatrics, Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Türkiye
Correspondence: I. Dönmez
Pediatric Rheumatology, **23(2):** P191

Introduction: In Juvenile idiopathic arthritis (JIA), due to the involvement of the musculoskleteal system, muscle weakness, walking speed, and slower stair descent-ascent skills were observed compared to their healthy peers (1,2).
Objectives: The aim of this study was to investigate the relationship between lumbar extensor muscle strength and locomotor function in children with JIA.
Methods: 19 children (10 girls, 9 boys) diagnosed with JIA were included in the study. Lumbar extensor muscle strength was assessed using the K-Bubble device (Kinvent Physio, France). Measurements were taken in a supine position with the knees flexed at 135°, during which participants were asked to compress the device placed under the lumbar region. Locomotor function was evaluated using the 10-Step Stair Ascent-Descent Test (10SST), the 6-Minute Walk Test (6MWT), and gait analysis via the Digitsole Pro System. The relationship between variables was analyzed using the Spearman Correlation Test.
Results: The mean age, height, and weight of the participants were 10.11±1.94 years, 138.88±11.94 cm, and 34.78±9.31 kg, respectively. The mean of the Lumbar extensor peak force and average force values was 12.29±4.34 kg and 8.39±4.21 kg. Lumbar extensor peak force and average force values showed significant correlations with the 10SST, 6MWT, and step length ($p<0.05$). Additionally, lumbar extensor fatigue index was significantly correlated with cadence ($p<0.05$).
Conclusion: The results of this study highlight the significant relationship between lumbar extensor muscle strength and various locomotor functions, emphasizing the critical role of trunk muscle strength in children with JIA. The observed correlation between lumbar extensor fatigue and cadence suggests that muscular endurance may have a substantial impact on gait dynamics. These findings imply that incorporating trunk strengthening exercises into the rehabilitation programs of children with JIA may contribute to improvements in locomotor performance. However, given the limited sample size, further research with a larger cohort is necessary to confirm and expand upon these findings.
Disclosure
None declared

References
1. Thatayatikom, A., et al. (2023). Juvenile Idiopathic Arthritis. In StatPearls. StatPearls Publishing.
2. Vincent, H. K., et al. (2022). Gait parameters, functional performance and physical activity in active and inactive Juvenile Idiopathic Arthritis. Gait & posture.

P192

"Gaining control when so much is unknown/uncertain" – initial feedback from caregivers testing a rheumatological chatbot

K. Kupiec[1,2], P. Livermore[2,3] on behalf of IMPACT Study Steering Group
[1]Great Ormond Street Hospital NHS Foundation Trust, [2]Infection, Immunity, and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, [3]NIHR GOSH BRC, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom
Correspondence: K. Kupiec
Pediatric Rheumatology, **23(2):** P192

Introduction: Adjusting to a 'new normal' when a child or young person (CYP) is diagnosed with a rheumatological condition is difficult for the CYP as well as the wider family. It is known that CYP with rheumatological conditions are 15% to 65% more likely to have a mental health disorder [1]. Moreover, research has shown that 82% of caregivers reported that their child's diagnosis had an impact on their own mental health [2].
Objectives: The IMPACT study is a UK wide study to design, develop and test a technology intervention to support parents of CYP with rheumatological conditions [3]. The study follows Experience Based Co-Design methodology where the patients and families help shape the study from design through to dissemination. Understanding their viewpoints is critical to ensure the technology created is useful and usable by caregivers.
Methods: The chatbot has been co-created with families and is currently being tested by caregivers. A mixed-method approach is used for this project. Quantitative data is collected by using the Net Promoter Scale (NPS) which rates how likely parents are to recommend the intervention to a friend and the UX-Lite which measures functionality. Qualitative data is obtained via feedback collected from the chatbot directly and from virtual drop-in sessions that were offered to caregivers.
Results: A total of 27 caregivers (85.2% female, M_{age}= 42.78, SD = 5.75) participated in the first stage of user testing. The NPS increased from a 8/10 rating after one week of user testing to a 10/10 rating at Week 12. The UX-Lite showed that caregivers rated the chatbot's ease of use highly with a mean score of 5 (out of 5) and a score of 4/5 in relation to the overall features having met their needs. Qualitative data has shown that caregivers see the chatbot as a "fantastic tool for worried parents with a million questions."
Conclusion: Evidence suggests that a family approach is needed to support caregivers and CYP with rheumatological conditions as well as the wider family to improve health outcomes for the child, and increase family functioning [4]. We are hoping that the chatbot will be a supportive tool to improve psycho-social well-being of families living with rheumatological conditions.
Disclosure
None declared

References
1. Davis AM, Rubinstein TB, Rodriguez M, Knight AM. Mental health care for youth with rheumatologic diseases–bridging the gap. Pediatric Rheumatology. 2017 Dec;15:1-8. https://doi.org/10.1186/s12969-017-0214-9

2. Livermore P, Ainsworth S, Beesley R, Douglas S, Earle E, Wilson D, Woolley L, Clinch J. 'The current mental health status of children and young people with JIA, and their wider family': a charity partner collaboration survey. Pediatric Rheumatology. 2023 Oct 6;21(1):111. https://doi.org/10.1186/s12969-023-00898-5
3. Livermore P, Kupiec K, Wedderburn LR, Knight A, Solebo AL, Shafran R, et al. Designing, developing, and testing a chatbot for parents and caregivers of children and young people with rheumatological conditions (the IMPACT study): protocol for a co-designed proof-of-concept study. JMIR research protocols. 2024 Apr 3;13(1):e57238. https://doi.org/10.2196/57238
4. Lobst EA, Nabors LA, Brunner HI, Precht B. Pain, fatigue, family functioning, and attitude toward illness in children with juvenile rheumatic diseases. Journal of Developmental and Physical Disabilities. 2007 Apr;19:135-44. https://doi.org/10.1007/s10882-006-9028-2

P193

Design and validation of educational audiovisual material on exercise for patients with Juvenile idiopathic arthritis

M. M. Rodríguez Reyes[1], I. D. P. Peláez Ballestas[1], A. V. Villarreal Treviño [1], F. García Rodríguez[1], A. C. Méndez Silva [1], L. D. C. Reynoso Medina [1], C. E. López Cardona[1], Z. I. García Murillo [1], F. A. Vásquez Triminio[1], N. E. Rubio Pérez[1] on behalf of Colaborativa de Investigación en Beneficio de la Reumatología Infantil (COLIBRI)
[1]Pediatria, Hospital Universitario "Dr. José Eluterio González", Nuevo Leon, Mexico
Correspondence: M. M. Rodríguez Reyes
Pediatric Rheumatology, **23(2):** P193

Introduction: It is known that JIA can lead to both short- and long-term disability, making supervised physical activity and physiotherapy essential for managing associated complications such as contractures, deformities, and chronic pain. A qualitative study conducted at our center from March to June 2023 found that up to 60% of patients did not engage in exercise due to their health condition, fatigue, fear, pain, as well as lack of time and additional costs; therefore, they preferred to exercise at home. (1,2)
Objectives: To design and validate educational audiovisual material focused on exercise for patients with Juvenile Idiopathic Arthritis
Methods: Sequential mixed-methods study with a qualitative-quantitative approach aimed at developing and validating educational audiovisual material about exercise for patients with JIA. Demographic data, disease activity (JADAS), treatment, and functional status (CHAQ) were collected. The study was conducted during the years 2024–2025. The design and content of the videos were developed with the support of a rehabilitation physician with expertise in pediatrics. The audiovisual production was carried out with the assistance of a professional audiovisual designer. Subsequently, with guidance from a methodology expert and based on UNICEF's guidelines for validating audiovisual materials, validation tools were developed. These included questions related to appearance, comprehension, acceptance, and engagement.
Two focus groups were formed, comprising JIA patients aged 6–12 and 13–18, along with their caregivers. The videos were screened, and participants completed the audiovisual material evaluation instrument to finalize the validation process. Two rounds of revisions were carried out.
Results: A total of 30 patients of both sexes were included, with a mean age of 11.71 ± 3.15 years and a confirmed diagnosis of JIA.
Two videos were created, each composed of five shorts on "joint care." These shorts were developed using animations and had a duration of 1–2 minutes each. After two rounds of revisions, the material was validated, meeting the criteria for appearance, comprehension, acceptance, and engagement.
Although differing opinions were noted among experts during the initial stages of design and validation, patient feedback demonstrated high levels of effectiveness (>80%).
Conclusion: The study successfully designed and validated educational audiovisual material on exercise for children with JIA, achieving high levels of acceptance and effectiveness among patients and their caregivers. This represents a valuable tool for promoting physical activity and preventing complications associated with the disease.

Disclosure
None declared

Reference
1. 2022 ANA KAREN LEOS LEIJA - Tesis terminada.pdf [Internet]. [citado 20 de octubre 2024]. Disponible http://eprints.uanl.mx/26599/1/2022%20ANA%20KAREN%20LEOS%20LEIJA%20%20Tesis%20terminada.pdf. Full Text PDF [Internet]. [citado 20 de octubre de 2024]. Disponible en: https://www.researchgate.net/publication/374748341_Artritis_idiopatica_juvenil_una_enfermedad_limitante/fulltext/652d2bb36725c324010c55c0/Artritis-idiopatica-juvenil-una-enfermedad-limitante.pdf

P194

Position statement on the establishment of telemedicine for rheumatoid arthritis, oligoarticular and polyarticular juvenile idiopathic arthritis, and systemic lupus erythematosus

T. Miyamae[1], A. Abe[2], Y. Inoue[3], S. Iwata[4], A. Kawakami[5], S.-Y. Kawashiri[5], T. Kishi[1], R. Sakai[1,6], K.-E. Sada[7], T. Sato[8], E. Tanaka[1], K. Taneda[9], K. Nishida[10], F. Nonaka[5], K. Yamazaki[11], H. Furuya[9,12,13], H. Yamada[9,13], Y. Kawahito[14] on behalf of Japan Research Group of the Ministry of Health, Labour, and Welfare for Research Conducive to the Visualization and Societal Implementation of Unmet Medical Needs in Rheumatic Diseases from the Patient's Standpoint (24FE0401)
[1]Tokyo Women's Medical University School of Medicine, Tokyo, [2]Niigata Rheumatic Center, Shibata, [3]Graduate School of Medicine, Chiba University, Chiba, [4]Wakayama Medical University, Wakayama, [5]Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, [6]Meiji Pharmaceutical University, Kiyose, [7]Kochi Medical School, Kochi University, Nankoku, [8]Shiga University of Medical Science, Shiga, [9]Medii, inc., Tokyo, [10]Locomotive Pain Center, Okayama University Hospital, Okayama, [11]St. Marianna University School of Medicine, Kawasaki, Japan, [12]TANAAKK INC., New York, United States, [13]Japanese Telemedicine and Telecare Association, Takasaki, [14]Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan
Correspondence: T. Miyamae
Pediatric Rheumatology, **23(2):** P194

Introduction: Telemedicine offers a potential solution to address regional disparities in access to specialized rheumatology care and to promote equitable distribution of expert services.
Objectives: This study aimed to develop a position statement for establishing telemedicine services for rheumatoid arthritis (RA), oligoarticular and polyarticular juvenile idiopathic arthritis (JIA), and systemic lupus erythematosus (SLE).
Methods: In developing this position statement, we conducted three main studies: (1) a scoping review on the implementation of telemedicine in rheumatology, including EULAR Points to Consider; (2) a Google Forms–based survey of healthcare professionals via national rheumatology associations; and (3) development of online care models for representative rheumatic diseases, followed by a health economic simulation.
Results: The scoping review identified three randomized controlled trials and three observational studies. Telemedicine was found not to compromise patient outcomes and was associated with reduced visit frequency and lower healthcare costs. In light of these findings, establishing robust quality metrics for telemedicine services was emphasized to ensure patient safety and continuity of care.
Survey results indicated that 77.5% of internal medicine, 58.6% of orthopedic, and 76.6% of pediatric respondents reported having patients traveling more than one hour to access care. This highlights a significant burden of travel, particularly in pediatric care, where physician shortages and regional disparities are most pronounced. More than half of providers expressed interest in online medical care: 67.0% in internal medicine, 54.1% in orthopedics, and 81.2% in pediatrics, reflecting a growing recognition of telemedicine's potential to improve access.
Regarding criteria for stable disease activity, 71.9% of pediatric providers agreed with defining JIA stability as sustained remission without glucocorticoids and with stable symptoms. For SLE, agreement with defining stability as remission maintained with a daily dose of ≤5 mg of prednisolone—or ≤0.15 mg/kg/day or ≤5 mg/day in pediatric patients—was reported by 75.6% of pediatricians. These findings

indicate a broad consensus across specialties on reasonable benchmarks for disease stability when considering remote management.
Based on these findings, a hybrid care model was proposed, incorporating bi-monthly online consultations supplemented by in-person visits every six months. An economic simulation showed that specialized centers might experience a reduction in revenue due to limited opportunities to perform laboratory and imaging tests during online consultations. These factors must be considered when designing sustainable telemedicine systems for chronic disease management.
Conclusion: This position statement and future research agendas were developed based on the above findings. Telemedicine, including online consultations, is expected to promote equitable access to expert rheumatology care in Japan and is strongly recommended for active implementation.
Disclosure
T. Miyamae: None declared, A. Abe: None declared, Y. Inoue: None declared, S. Iwata: None declared, A. Kawakami Grant/Research Support with: AbbVie GK, AYUMI Pharmaceutical Corporation, ONO PHARMACEUTICAL CO., LTD., Gilead Sciences, Inc., Celltrion Healthcare Japan K.K., Taisho Pharmaceutical Co., Ltd., Daiichi Sankyo Company, Limited, Boehringer Ingelheim Japan, Inc., Neopharma Japan Co., Ltd., Bristol-Myers Squibb K.K, Speaker Bureau with: Asahi Kasei Pharma Corporation, AbbVie GK, Eisai Co., Ltd., ONO PHARMACEUTICAL CO., LTD., Taisho Pharmaceutical Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Boehringer Ingelheim Japan, Inc., Pfizer Japan Inc., S.-Y. Kawashiri Speaker Bureau with: Asahi Kasei Pharma Corporation, Astellas Pharma Inc., AbbVie GK, Eisai Co., Ltd., ONO PHARMACEUTICAL CO., LTD., Eli Lilly Japan K.K., T. Kishi: None declared, R. Sakai: None declared, K.-E. Sada: None declared, T. Sato: None declared, E. Tanaka Speaker Bureau with: Asahi Kasei Pharma Corporation, Astellas Pharma Inc., AbbVie GK, Eisai Co., Ltd., Chugai Pharmaceutical Co., Ltd., Pfizer Japan Inc., K. Taneda: None declared, K. Nishida Grant/Research Support with: AbbVie GK, Chugai Pharmaceutical Co., Ltd., Speaker Bureau with: Asahi Kasei Pharma Corporation, AYUMI Pharmaceutical Corporation, Eisai Co., Ltd., ONO PHARMACEUTICAL CO., LTD., Daiichi Sankyo Company, Limited, Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Pfizer Japan Inc., Janssen Pharmaceutical K.K., F. Nonaka Speaker Bureau with: Sumitomo Pharma Co., Ltd., Eli Lilly Japan K.K., K. Yamazaki: None declared, H. Furuya Employee with: TANAAKK INC, H. Yamada Employee with: Medii, Inc., Y. Kawahito Grant/Research Support with: AbbVie GK, Eisai Co., Ltd., Chugai Pharmaceutical Co., Ltd., Speaker Bureau with: Asahi Kasei Pharma Corporation, Astellas Pharma Inc., Eisai Co., Ltd., GlaxoSmithKline K.K, Daiichi Sankyo Company, Limited, Chugai Pharmaceutical Co., Ltd., Boehringer Ingelheim Japan, Inc., Bristol-Myers Squibb K.K., Janssen Pharmaceutical K.K., UCB Japan Co., Ltd.

Reference
1. de Thurah A, Bosch P, Marques A, et al. 2022 EULAR points to consider for remote care in rheumatic and musculoskeletal diseases. Ann Rheum Dis. 2022;81:1065-71.

P195

Heart rate patterns as indicators of physical fitness in juvenile idiopathic arthritis: insights from a preliminary study

Y. Açıkgöz[1], N. Arman[2], A. Yekdaneh[3,4], A. Albayrak[3,5], I. donmez[1], N. Aktay Ayaz[6]
[1]Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [2]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [3]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [4]Physiotherapy English Program, Fenerbahçe University, Vocational School of Health Services, [5]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [6]Department of Pediatrics, Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, İstanbul, Türkiye
Correspondence: Y. Açıkgöz
Pediatric Rheumatology, **23(2):** P195

Introduction: Physical inactivity in children and adolescents is a global public health problem(1). Juvenile Idiopathic Arthritis (JIA) is characterized not only by joint inflammation but also by limitations in physical function and aerobic performance(2). Pedometric data such as step count are widely used to assess activity, whereas heart rate (HR) has not yet been fully investigated as a marker of physical fitness in pediatric rheumatology(3).
Objectives: This study aimed to investigate whether temporal HR patterns can discriminate between children with JIA and their healthy peers and provide predictive insight into underlying fitness levels.
Methods: 30 children aged 12–18 years with JIA and 24 healthy adolescents using Android-based mobile phones were included. Participants received smartwatches from four different brands and were trained in their usage and data management. The Pedi@ctivity mobile application developed by our team was synchronized with the Google Fit application on the Pedi@ctivity web platform for remote monitoring. Daily metrics (step count, movement speed, and heart rate) of participants were recorded for seven consecutive days from these watches. Step counts during the winter school period were recorded and analyzed remotely. Statistical analysis with SPSS Version 28.0., cluster analysis using only heart rate data further separated participants into two distinct groups corresponding to their clinical classification.
Results: Children with JIA exhibited consistently higher daily heart rate values compared to healthy controls, with statistically significant group differences on Monday (p=0.029), and non-significant differences on the remaining days (Tuesday to Sunday, p>0.05). Notably, Thursday was the only day showing similar group means. In the healthy control group, step count was significantly and inversely correlated with heart rate on Friday (r=−0.84, p=0.001), suggesting superior cardiovascular efficiency on days of peak activity. While similar negative trends were observed on Monday (r=−0.66, p=0.074) and Wednesday (r=0.27, p=0.430), with no statistical significance. K-means clustering based solely on heart rate data revealed two distinct physiological profiles: Cluster 0 (n=9) exhibited lower and more stable heart rates (66–75 bpm), comprising 6 healthy children and 3 with JIA, while Cluster 1 (n=3) showed markedly elevated and more variable HR (80–92 bpm), including 2 JIA and 1 healthy participant. Although clusters did not perfectly correspond to clinical groups, they reflected meaningful differences in cardiovascular efficiency.
Conclusion: The results suggest that HR monitoring using smartwatches, when combined with activity measurements, may be a valuable noninvasive biomarker for estimating physical fitness in children with JIA, with high and variable HR responses reflecting reduced cardiorespiratory efficiency. These findings support the continued exploration of HR analytics as a non-invasive clinical tool for assessing and monitoring physiological adaptation in children with JIA.
This study was supported by the TUBITAK 1001-Scientific and Technological Research Projects Support Program 121E690.
Disclosure
None declared

References
1. Guthold, et al. (2020). Global trends in insufficient physical activity among adolescents:A pooled analysis of 298 population-based surveys with 1.6 million participants. The Lancet Child & Adolescent Health
2. Pella, et al. (2023). Cardiorespiratory fitness assessed with cardiopulmonary exercise testing in patients with juvenile idiopathic arthritis:a systematic review and meta-analysis. Rheumatology
3. Nørgaard et. al. Accelerometry-based monitoring of daily physical activity in children with juvenile idiopathic arthritis. Scand J Rheumatol 2016

P196

Closed-loop artificial intelligence model 'Maverik' to aid in the diagnosis of chronic nonbacterial osteomyelitis in childhood: a national multicenter performance evaluation in Turkey

E. Aliyev[1,2], Y. Ugur[3], V. Cam[1], P. Garipcin[4], E. Tunce[5], E. K. Konte[6], A. Dudakli[7], Y. Bayindir[1], R. Isguder[8], E. Ozcelik[9], E. Arslanoglu[10], R. M. K. Ekinci[11], H. K. Zora[12], Z. Aydin[13], M. Cakan[14], S. Sener[15], N. Karacayir[16], O. Baba[17], T. Kasap[18], S. Demir[19], B. B. Yucel[20], M. K. Gurgoze[21], H. A. Dundar[22], H. E. Sonmez[23], O. Koker[24], S. Ayduran[25], S. Turkucar[25], S. Yuksel[18], M. Kalyoncu[17], S. A. Bakkaloglu[16], K. Ozturk[13], S. S. Kilic[12], S. Ozdel[10], B. C. Acar[9], B. Bora[8], E. Unsal[8], N. A. Ayaz[7], O. Kasapcopur[6], B. Sozeri[5], A. P. Kisaarslan[4], O. Basaran[1], Y. Bilginer[1], S. Ozen[1]

[1]Pediatric Rheumatology, Hacettepe University, [2]SEMBA Informatics Ltd. Co., [3]Keytech Co., Ankara, [4]Pediatric Rheumatology, Erciyes University, Kayseri, [5]Pediatric Rheumatology, Umraniye Training and Research Hospital, University of Health Sciences, [6]Pediatric Rheumatology, Istanbul University-Cerrahpasa, [7]Pediatric Rheumatology, Istanbul University, Istanbul, [8]Pediatric Rheumatology, Dokuz Eylul University, Izmir, [9]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Ankara Bilkent City Hospital, [10]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Etlik City Hospital, Ankara, [11]Pediatric Rheumatology, Cukurova University, Adana, [12]Pediatric Rheumatology, Uludag University, Bursa, [13]Pediatric Rheumatology, Istanbul Medeniyet University, Goztepe Suleyman Yalcin City Hospital, [14]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Zeynep Kamil Research and Training Hospital, Istanbul, [15]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Adana City Hospital, Adana, [16]Pediatric Rheumatology, Gazi University, Ankara, [17]Pediatric Rheumatology, Karadeniz Technical University, Trabzon, [18]Pediatric Rheumatology, Canakkale On Sekiz Mart University, Canakkale, [19]Pediatric Rheumatology, Eskisehir Osmangazi University, Eskisehir, [20]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Samsun Research and Training Hospital, Samsun, [21]Pediatric Rheumatology, Firat University, Elazig, [22]Pediatric Rheumatology, Republic of Turkey, Ministry of Health, Behçet Uz Research and Training Hospital, Izmir, [23]Pediatric Rheumatology, Kocaeli University, Kocaeli, [24]Pediatric Rheumatology, Marmara University, Istanbul, [25]Pediatric Rheumatology, Pamukkale University, Denizli, Türkiye
Correspondence: E. Aliyev
Pediatric Rheumatology, **23(2):** P196

Introduction: Childhood-onset Chronic Non-bacterial Osteomyelitis (CNO) is an inflammatory bone disease that has become better defined in the last two decades. It is frequently encountered in Pediatric Rheumatology practice. However, the disease is still poorly understood and often confused with malignancy and growing pains, so it can easily be missed in daily practice.
Objectives: We aimed to evaluate the performance of 'Maverik', a computer-based physician-friendly model for a diagnostic tool using closed-loop Artificial Intelligence (AI) by testing it on real patient data with national multicenter participation.
Methods: The study included data from 395 patients from 23 Pediatric Rheumatology centers, and 13 cities in Turkey.
Training of the Model: The model is based on the Python software language, the Tensorflow AI library, and the Recurrent Neural Network and has 12 inner layers and 1024 neurons. To train the model, 83 cases of CNO, 9 cases of growth pain, 9 cases of bone tumors (5 Ewing's Sarcoma and 2 Osteosarcoma, 2 Osteid Osteoma), 9 cases of Juvenile Idiopathic Arthritis (JIA) (5 oligo-JIA, three poly-JIA, 1 Crohn's related Arthritis) and 30 healthy control data were used. During the model's training, the number of data points was increased with the duplication method, and two different pediatric rheumatologists checked that it reflected the real data in the separation. The model was registered by the Turkish Patent and Trademark Office with the name 'Maverik' as a 'Utility Model' with the number 2025-X8XXX, 'Physician Friendly Closed Circuit Artificial Intelligence Software for the Evaluation of Medical Data in Childhood Chronic Non-bacterial Osteomyelitis Disease'.
Evaluation of Model Performance: Laboratory, clinical, sociodemographic, and clinical data of the cases and written details of imaging reports were digitized as 1 (abnormal), 0 (normal range), and −1 (abnormal). Duplication of real data was avoided to avoid 'overfitting' the model.
Results: Maverik processed data input of 395 patients from 23 centers in 0.042 seconds and produced output with a technical margin of error of 0.028. The model adopted a 70-100% prediction interval to recognize CNOs. Accordingly, the model recognized CNO patients with an average prediction rate of 0.7937. Interestingly, it gave a 'missing data-possible CNO' warning for 47 of the 65 outputs (72.31%). This output was the model's interpretation and was not previously taught. Indeed, all forty-seven outputs had at least one input violation. Despite this, the model correctly recognized 368 outputs (93.17%).
Conclusion: Our study is the first in the literature to develop an AI model as a CNO diagnostic tool, analyze real patient data with multicenter participation, evaluate it, and demonstrate its performance in daily practice. This study shows that the model can help clinicians in the diagnostic stage and differential diagnosis of CNO disease and avoids 'overfitting' by continuing to train itself with real data.

Disclosure
None declared

References
1. Winter, E., et al., *Expert consensus recommendations for the diagnosis and treatment of chronic non-bacterial osteitis (CNO) in adults.* Annals of the Rheumatic Diseases, 2025.
2. McMaster, C., et al., *Artificial Intelligence and Deep Learning for Rheumatologists.* Arthritis Rheumatol, 2022. 74(12): p. 1893–1905.

P197

AI-based flare prediction in Juvenile idiopathic arthritis using simulated symptom data: a machine learning approach

M. T. Karadoğan[1], T. Güzel[1], F. Çakmak[1]
[1]Pediatric Rheumatology Department, Basaksehir Cam And Sakura City Hospital, Istanbul, Türkiye
Correspondence: M. T. Karadoğan
Pediatric Rheumatology, **23(2):** P197

Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory condition with unpredictable disease flares, which can result in joint damage and long-term morbidity. Timely identification of impending flares can improve treatment responsiveness and patient outcomes. With the increasing use of mobile health tools, artificial intelligence (AI) provides new opportunities to interpret subtle trends in daily patient-reported symptoms.
Objectives: To evaluate the feasibility of a machine learning model in predicting disease flares using simulated, daily patient-reported symptom data from virtual JIA patients.
Methods: A synthetic dataset of 100 virtual JIA patients was generated, each reporting daily scores for pain, fatigue, morning stiffness, and joint swelling across 180 days. Flares were defined based on clinical threshold combinations of these symptoms. All values were simulated using Gaussian distributions informed by typical clinical observations. A Random Forest classifier was trained on 80% of the dataset and tested on the remaining 20%. To address the highly imbalanced flare distribution (flare rate ~0.07%), the Synthetic Minority Oversampling Technique (SMOTE) was applied to the training data. The selected features were chosen for their relevance in clinical practice (e.g., JADAS components) and for their feasibility in self-reporting via mobile platforms. Laboratory markers such as ESR and CRP were intentionally excluded, as they are not routinely available in daily monitoring scenarios.
Results: The machine learning model achieved an F1-score of 0.81 for detecting flare days in the unseen test set. Precision and recall metrics also demonstrated acceptable performance. Feature importance analysis showed that pain and morning stiffness were the most influential predictors of flare occurrence.
Conclusion: This proof-of-concept study demonstrates that AI models can effectively detect flare risk using only daily patient-reported symptoms, even without clinical or laboratory input. With further validation on real-world data, this approach may support early, remote flare detection and improve digital disease management in children with JIA. Scientific writing assistance was supported by OpenAI's ChatGPT (GPT-4-turbo, May 2024), while model development was performed using traditional machine learning tools.
Disclosure
None declared

References
1. Consolaro A, Ruperto N, Bazso A, et al. Development and validation of a composite disease activity score for juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)*. 2009;61(5):658–666.
2. Guzman J, Oen K, Tucker LB, et al. The outcomes of juvenile idiopathic arthritis in children managed with contemporary treatments: results from the ReACCh-Out cohort. *Ann Rheum Dis*. 2015;74(10):1854–1860.
3. Miotto R, Wang F, Wang S, Jiang X, Dudley JT. Deep learning for healthcare: review, opportunities and challenges. *Brief Bioinform*. 2018;19(6):1236–1246.
4. Sarker IH, Ehsan M, Rahman MA, et al. A Comprehensive Review on Machine Learning in Healthcare Industry: Classification, Restrictions, Opportunities, and Challenges. *Healthcare*. 2025;13(5):4405. https://doi.org/10.3390/electronics13224405.

P198

Plasma proteomic profiles separate surf patients from FMF and PFAPA: preliminary data from the persaids project

F. Penco[1], M. Bartolucci[2], C. Lavarello[2], S. Palmeri[1,3], D. Foll[4], S. Ozen[5], S. Volpi[1,3], R. Caorsi[1], R. Papa[1], G. Fiorito[6], P. Uva[6], I. Ceccherini[7], C. Speziani[7], S. Fühner[4], M. Gattorno[1], A. Petretto[2]
[1]UOC Reumatologia e Malattie Autoinfiammatorie, [2]Core Facilities - Proteomics and Metabolomics, IRCCS Giannina Gaslini, [3]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-infantili (DINOGMI), Università degli Studi di Genova, Genova, Italy, [4]Pediatric rheumatology and immunology, University of Munster, Munster, Germany, [5]Rheumatology, Hacettepe University Hospital, Ankara, Türkiye, [6]Bioinformatica e Intelligenza Artificiale, [7]UOSD Aggregation Area for Research Laboratories, IRCCS Giannina Gaslini, Genova, Italy
Correspondence: R. Caorsi
Pediatric Rheumatology, **23(2):** P198

Introduction: Syndrome of Undifferentiated Recurrent Fever (SURF) is an emerging group of patients displaying recurrent inflammatory episodes. Although very similar to Familial Mediterranean Fever (FMF) clinical presentation, they do not share their genotype, being negative for mutation in the MEFV gene or in other genes related to autoinflammatory diseases. Furthermore, SURF enter in differential diagnosis with the most common multifactorial recurrent fever, namely PFAPA syndrome.
Objectives: Our aim is to evaluate the differences in the expression of plasma proteins in patients with SURF compared with healthy subjects, FMF and PFAPA patients to clusterize and better understand the mechanisms underlying these disorders.
Methods: Plasma samples from 15 SURF, 20 FMF, and 9 PFAPA patients, along with 22 age-matched healthy donors, were analyzed using high-resolution mass spectrometry-based proteomics. The analyses were performed in Data- Independent Acquisition (DIA) mode using an Orbitrap Exploris 480 mass spectrometer coupled with the Evosep One chromatography system.
Results: We identified 485 proteins; T-tests were conducted to identify differentially expressed proteins. For the significantly modulated proteins, a functional enrichment analysis was performed using Gene Ontology annotations to uncover the biological processes that vary across the conditions. This analysis aimed to identify proteins associated with the disease and to reveal potential novel biomarkers. Our findings indicate that protein expression profiles are differentially enriched depending on the specific conditions analyzed, providing insights into disease mechanisms and potential diagnostic targets.
Conclusion: In this study, we explored how a high-resolution plasma proteomics approach can enhance our understanding of SURF as a distinct clinical entity. Specifically, SURF proteomics shows similarities with FMF but exhibits significant differences compared to PFAPA. The comprehensive characterization of a broad spectrum of proteins, coupled with functional enrichment analysis, provides valuable insights into the biological processes underlying these distinct pathologies. This approach offers the potential to identify novel biomarkers and improve our understanding of genetically undefined disorders.
Disclosure
None declared

References

1. This work was supported by ERA PerMed (PerSAIDs Consortium) funded from the European Union's Horizon 2020 research and innovation programme (grant agreement No. 779282).
2. Papa R, Rusmini M, Volpi S, Caorsi R, Picco P, Grossi A, et al. Next generation sequencing panel in undifferentiated autoinflammatory diseases identifies patients with colchicine-responder recurrent fevers. Rheumatology. 2020 Feb 1;59(2):344–60.
3. Luu I, Nation J, Page N, Carvalho D, Magit A, Jiang W, et al. Undifferentiated recurrent fevers in pediatrics are clinically distinct from PFAPA syndrome but retain an IL-1 signature. Clin Immunol. 2021 May;226:108,697.80
4. Batth TS, Tollenaere MX, Rüther P, Gonzalez-Franquesa A, Prabhakar BS, Bekker-Jensen S, Deshmukh AS, Olsen JV. Protein Aggregation Capture on Microparticles Enables Multipurpose Proteomics Sample Preparation. Mol Cell Proteomics. 2019 May;18(5):1027–1035. https://doi.org/10.1074/mcp.TIR118.001270. Epub 2019 Mar 4. PMID: 30,833,379; PMCID: PMC6495262.

P199

AI Knows the difference: simulating how machine learning distinguishes FMF attacks from respiratory infections

T. Güzel, M. T. Karadoğan, F. Çakmak
Pediatric Rheumatology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye
Correspondence: T. Güzel
Pediatric Rheumatology, **23(2):** P199

Introduction: FMF is a monogenic autoinflammatory disease characterized by episodic fever and serosal inflammation. Clinically, its manifestations can mimic other inflammatory conditions, notably respiratory infections (e.g., Rhinovirus), leading to diagnostic uncertainty. This study builds upon prior work predicting FMF attacks and introduces a comparative group to assess whether AI can distinguish FMF flares from URIs.
Objectives: Using an artificial intelligence tool, it was aimed to enable patients to differentiate between FMF attack and URIs.
Methods: A synthetic dataset of 938 daily records was generated, including: 800 healthy days, 38 FMF attack days, 100 URI days
The dataset was curated to reflect real-world clinical variation while preserving intergroup discriminability.
Six clinically relevant features were included: Body temperature (°C), Abdominal pain score (0–9 scale), C-reactive protein (CRP, mg/L), Erythrocyte sedimentation rate (ESR, mm/h), Leukocyte count (10^9/L), Colchicine dose (mg/day)
A Random Forest classifier was employed due to its robustness and interpretability in medical datasets. The data was split into 80% training and 20% test sets using stratified sampling. All features were standardized prior to model fitting. Performance metrics included accuracy, precision, recall, F1-score, and confusion matrix analysis.
In this study, OpenAI's ChatGPT-4o application was used.

Results: On the test set, the model achieved:

- Overall accuracy: 100%
- FMF Attack – Precision: 100%, Recall: 100%, F1-score: 100%
- Infection – Precision: 100%, Recall: 100%, F1-score: 100%

The most influential features for class separation were:
- Abdominal pain (absent in URI cases, prominent in FMF)
- CRP, ESR, leukocyte count (elevated in both FMF and URI but with distinct profiles)
- Temperature and colchicine dose had secondary discriminative value.

Conclusion: This study shows that AI models can effectively distinguish FMF flares from respiratory infections using routine clinical features in a simulated environment. With real-world validation, this approach could support clinicians in timely and accurate differential diagnosis of autoinflammatory versus infectious presentations, ultimately improving patient outcomes.
Disclosure
None declared

Reference

1. Ozen S, Bilginer Y. A clinical guide to autoinflammatory diseases: Familial mediterranean fever and next-of-kin. Nature Reviews Rheumatology. 2013 Nov 19;10(3):135–47. doi:https://doi.org/10.1038/nrrheum.2013.174

P200

Addressing symptoms of burnout amongst pediatric rheumatology fellows: a quality improvement project

G. Mastrangelo[1], M. J. Dushnicky[1,2], E. Itzkovitz[1], R. M. Laxer[1], D. M. Levy[1], S. M. Tse[1]
[1]Division of Rheumatology, Department of Pediatrics, The Hospital for Sick Children, Toronto, [2]Division of Rheumatology, Department of Pediatrics, McMaster University, Hamilton, Canada
Correspondence: G. Mastrangelo
Pediatric Rheumatology, **23(2):** P200

Introduction: Up to 40% of rheumatology fellows and 55% of pediatricians in the United States have experienced at least one symptom of burnout, representing higher rates compared to age-matched controls.[1,2] Physician burnout leads to lower job satisfaction, higher rates of

mental health issues, and decreased efficiency at work.[3] Literature on wellness and burnout among pediatric rheumatologists is scarce leading to little awareness and few strategies aimed at reducing burnout.[4]
Objectives: Using quality improvement methodology, we aimed to reduce burnout symptoms among pediatric rheumatology fellows in a tertiary academic hospital as measured by the Maslach Burnout Inventory (MBI)[5] by 20% over 6 months.
Methods: Baseline MBI was sent to three pediatric rheumatology fellows enrolled in 2023-2024 academic year to determine the degree of burnout symptoms. The MBI reports scores in three categories: emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA), with higher scores equating to higher risk of burnout. A stakeholder group was formed, including eight pediatric rheumatology fellows, and engaged colleagues including allied health team members and staff physicians within the Division of Pediatric Rheumatology. The workgroup identified key and modifiable contributors to burnout within the workplace. Processes were implemented and modified using multiple plan, do, study, act (PDSA) cycles. Wellness sessions were run by the study leads fellows and faculty and implemented with attendance and post-session feedback obtained to guide subsequent PDSA cycles. The MBI was followed at the 0, 3, and 6-month mark to assess success of these strategies.
Results: A baseline MBI was completed by 3/12 pediatric rheumatology fellows as an audit. Average scores were EE = 15.7/36 (moderate), DP = 10.0/20 (moderate), and PA = 13.0/32 (low). Each wellness session represented a new PDSA cycle. Attendance at sessions, and a Likert scale survey on satisfaction with the session were collected as process measures. Five PDSA cycles were completed from January to June 2024. The initial cycle highlighted that there was no process in place to address symptoms of burnout. Implementation strategies included "Treats and Talks" focused sessions during protected educational time, social events among fellows and external events including fellows' families. Six-month MBI scores showed improvement in all MBI domains with EE = 10.8/36 (low), DP = 4.6/12 (low), and PA = 8.8/32 (low), a decrease of 31%, 54%, and 32% respectively.
Conclusion: Our study has revealed a baseline risk of burnout amongst pediatric rheumatology fellows at our tertiary academic hospital. With a quality improvement-based approach we have implemented change strategies that show reduced risk of burnout, as measured by the MBI at 6 months. Ongoing change ideas will be focused on the sustainability of these changes.
Disclosure
None declared

References

1. McGoldrick J, Dey M, Sharma D, et al. An evaluation of burnout among US rheumatology fellows: a national survey. *J Rheumatol*. 2023;50:1185–90.
2. Dyrbye LN, West CP, Satele D, et al. Burnout among U.S. medical students, residents, and early career physicians relative to the general U.S. population. *Acad Med*. 2014;89:443–51.
3. Yates SW. Physician stress and burnout. *Am J Med*. 2020;133:160–4.
4. Cook K, Rouster-Stevens K, Mehta J, et al. Wellness and burnout among pediatric rheumatologists in North America—a 2024 CARRA study [abstract]. *Arthritis Rheumatol*. 2024;76(Suppl 9).
5. Maslach C, Jackson SE, Leiter MP. Maslach Burnout Inventory manual. 4th ed. Menlo Park (CA): Mind Garden, Inc.; 2016.

P201

Prevalence of autoimmune comorbidities in Juvenile idiopathic arthritis: a retrospective single-center cohort study

A. Čengić[1], V. Selmanović[1], S. Hasanbegović[2], A. Hadžimuratović[1], M. Konaković[1]
[1]Allergology, rheumatology and clinical immunology, [2]Endocrinology, Clinical Center University Sarajevo, Sarajevo, Bosnia and Herzegovina
Correspondence: A. Čengić
Pediatric Rheumatology, **23(2):** P201

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. and is characterized by persistent joint inflammation with onset before the age of 16. It is a complex disease in which both genetic and environmental factors play an important role. As an autoimmune disorder, JIA is often associated with a broader spectrum of immune dysregulation, which may predispose affected individuals to additional autoimmune comorbidities such as: autoimmune thyroid disease (commonly Hashimoto's thyroiditis-HT), celiac disease (CD), and insulin-dependent diabetes mellitus (IDDM). Early recognition of such comorbidities is crucial, as they may influence both the clinical course and the management strategies of JIA.
Objectives: This study aimed to assess the frequency of coexisting autoimmune conditions- HT, CD, and IDDM among pediatric patients diagnosed with JIA. To date, the occurrence of these comorbidities within this specific patient population has not been systematically investigated in Bosnia and Herzegovina.
Methods: The retrospective study included pediatric patients diagnosed with JIA according to the International League of Associations for Rheumatology Classification. who were consecutively diagnosed at the tertiary pediatric rheumatology center in Bosnia and Herzegovina between January 2018 and December 2023. Data were obtained through a review of medical records. Laboratory results used to assess comorbidities included: for HT- thyroid-stimulating hormone (TSH), free thyroxine (fT4), and anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies. For diagnosing CD- total serum IgA, tissue transglutaminase IgA antibodies (tTG-IgA), endomysial antibodies (EMA) and duodenal biopsy. IDDM: fasting glucose levels, HbA1c, and presence of diabetes-associated autoantibodies (GAD, IAA, IA-2).
Results: A total of 143 children were included in the study, with 56% being female and 44% male. The mean age of the participants was 9.2 ± 4.6 years, with the youngest patient being 1 year old and the oldest 16 years. HT was diagnosed in 14 patients, accounting for 10% of the cohort. CD was identified in 5 patients, representing 3% of the sample. One patient (0.7%) had a diagnosis of coexisting IDDM.
Conclusion: The prevalence of HT and CD among children with JIA in our cohort is higher than that reported in the general pediatric population. These findings highlight the importance of routine screening for autoimmune comorbidities in children with JIA to ensure early diagnosis and integrated management. Further prospective studies are needed to confirm these associations and develop optimal care pathways.
Disclosure
None declared

References

1. Petty RE, Southwood TR, Manners P, et al. International league of associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31:390–392
2. van Straalen JW, de Roock S, Giancane G et al. Paediatric Rheumatology International Trials Organisation (PRINTO). Prevalence of familial autoimmune diseases in juvenile idiopathic arthritis: results from the international Pharmachild registry. Pediatr Rheumatol Online J. 2022 Nov 18;20(1):103. https://doi.org/10.1186/s12969-022-00762-y. PMID: 36,401,230; PMCID: PMC9673358.
3. Sapountzi E, Tsinopoulou VR, Kotanidou EP, Giza S, Galli-Tsinopoulou A. Coexistence of Autoimmune Thyroiditis and Juvenile Idiopathic Arthritis. Cureus. 2023; 15(8):e44384.
4. Poddighe D, Romano M, Dossybayeva K, Abdukhakimova D, Galiyeva D, Demirkaya E. Celiac Disease in Juvenile Idiopathic Arthritis and Other Pediatric Rheumatic Disorders. *J Clin Med*. 2022;11(4):1089

P202

Parents and physicians do not always agree in identifying joints with active arthritis. data from a large multinational study

A. Amodio[1,2], M. Burrone[1], S. M. Orsi[1], F. Ridella[1], S. La Bella[1], J. Lasagna[1], S. ALMAYOUF[3], Y. Boyko[4], J. E. Davidson[5], M. Gattorno[1], N. Ruperto[6], A. Ravelli[1], A. Consolaro[1]
[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Università degli Studi di Genova, Genova, [2]Dipartimento della Donna, del Bambino e di Chirurgia Generale e Specialistica, Università degli Studi della Campania "Luigi Vanvitelli", Napoli, Italy, [3]King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia, [4]Western Ukrainian Specialized Children's Medical Centre, Lviv, Ukraine, [5]The Royal Hospital for Children, Glasgow, United Kingdom, [6]Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy
Correspondence: A. Amodio
Pediatric Rheumatology, **23(2):** P202

Introduction: Patient's self assessment (or parent's proxy assessment) has gained increasing importance in chronic diseases in recent years. This is due both to the widespread use of telemedicine and to the evidence that including patient's perception in the evaluation of the disease course may improve the outcome of the disease. The count of joints with active arthritis is an essential outcome measure in Juvenile Idiopathic Arthritis (JIA), used alone or as part of composite scores and criteria for inactive disease (ID) to summarize providers' appraisal of disease activity. Patient's self-assessment or parents' proxy evaluation of joints with active arthritis might be an important outcome measure of JIA disease course for both telemonitoring and routine assessment.
Objectives: To measure the agreement between parents and physicians in identifying joints with active arthritis and to assess factors affecting the agreement variability.
Methods: Patients' data were obtained from a large multinational dataset of subjects enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis (EPOCA) study (1). Briefly, the EPOCA study is a survey conducted by the Paediatric Rheumatology International Trials Organisation (PRINTO) between 2011 and 2016, involving 9081 JIA patients from 130 paediatric rheumatology centres in 49 countries, grouped into eight geographical areas. Parent/child reported outcomes were collected with the juvenile arthritis multidimensional assessment report (JAMAR). The proxy- and self-assessment of joint inflammatory signs was obtained by asking the parent or the patient to rate the presence of pain or swelling in the following joints or joint groups: shoulders, elbows, wrists, small hand joints, hips, knees, ankles, and small foot joints. The agreement between parents and physicians was calculated by Cohen's Kappa analysis in each joint, by adapting the rheumatological exam to the joints or joint groups listed in the JAMAR. The mean Kappa coefficient of the joints was then compared among eight geographic areas, three levels of socioeconomic status (low, average, and high), and three levels of education (elementary, high school, and degree) of the parent filling the JAMAR. Kappa results were interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.
Results: A total of 9,081 visits had all the evaluations available for the tested tools in the EPOCA dataset. Kappa coefficient was in the fair range for the shoulder (lowest Kappa at 0.22), hip, and toes and in the moderate range in elbow, wrist, fingers (highest Kappa at 0.50), knees and ankles. Highest mean Kappa was observed in Eastern Europe (0.46) and lowest in North America (0.25) (Figure). Mean Kappa coefficients were similar in the different levels of parent's education, ranging from 0.40 (elementary) to 0.42 (degree); mean Kappa coefficients was higher in patients with high socioeconomic status 0.46 and lower in in patients with average socioeconomic status (0.38)
Conclusion: Agreement between parents and physicians in identifying active joints was fair to moderate, with important variability among different joints. The agreement remained stable among different levels of parents' education, but it showed remarkable variability after grouping by geographic areas.
Disclosure
None declared

Reference
1. Consolaro A. Lancet Child Adolesc Health. 2019

P203

Discordance between physician ratings in juvenile idiopathic arthritis patients with inactive disease: comparison of multicenter versus single-center cohorts

A. I. Rebollo Giménez[1,2], S. Rosina[3], F. Ridella[4], S. M. Orsi [5], E. Aldera[6,7], M. Burrone[3,6], V. Natoli[3,6], A. Consolaro [3,6], E. Naredo [8], A. Ravelli[9]
[1]Department of Rheumatology, Gregorio Marañón University Hospital, Gregorio Marañón Health Research Institute (IiSGM), [2]Universidad Autónoma de Madrid, Madrid, Spain, [3]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, [4]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DINOGMI),, [5] Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DINOGMI), [6]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DINOGMI), Università degli Studi di Genova, Genoa, [7]Paediatric Unit, Paediatric Unit, Asti, Italy, [8]Department of Rheumatology and Joint and Bone Research Unit, Fundación Jiménez Díaz University Hospital, Health Research Institute Fundación Jiménez Díaz (IIS-FJT, UAM), Madrid, Spain, [9]Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: A. I. Rebollo Giménez
Pediatric Rheumatology, **23(2):** P203

Introduction: Concern was raised by the recent observation of a wide variability in physician global assessment (PhGA) scores across pediatric rheumatologists. Some studies have highlighted the tendency of some clinicians not to mark their PhGA at zero when no active joints are detected, and even when all the other inactive disease (ID) criteria are met. However, it is still unclear whether training improves the concordance between clinicians in rating the PhGA in juvenile idiopathic arthritis (JIA) patients with ID.
Objectives: To compare the frequency of visits in which the physician provided a PhGA > 0 despite the absence of joints with active arthritis between two multicenter patient samples and one cohort of patients assessed in a single pediatric rheumatology center with a long tradition in clinimetric assessments.
Methods: Data were extracted from three cross-sectional datasets: the first included 9081 patients enrolled in a multinational study of the epidemiology, treatment and outcome of JIA (EPOCA dataset); the second comprised 563 patients with systemic JIA who were part of a multicenter study aimed to develop and validate the systemic JADAS (sJADAS) and its cutoffs; the third was a single-center dataset composed of 394 patients followed at the Gaslini Institute (Gaslini dataset). For the purposes of the study, only patients with an active joint count = 0 were evaluated in each dataset. The state of ID was established using the 2004 or 2011 Wallace criteria. UpSet plots were generated to visualize combinations of ID criteria.
Results: A PhGA > 0 and the elevation of acute phase reactants (APR) were the most frequent reasons for not meeting the ID definition in patients with no active joints. The proportion of patients who had a PhGA > 0 with all the other ID criteria met was lower in the Gaslini dataset (5.1%) than in the EPOCA and sJADAS datasets (14.8% and 13.7%, respectively). As compared with the two multicenter cohorts, the Gaslini cohort also had a lower frequency of patients with a PhGA > 0 plus one or more of the other ID criteria not met, and with a PhGA > 0 plus the other ID criteria met or not met. The percentage of patients who did not meet ID criteria because of isolated elevation of APR was lower in the EPOCA dataset (10.8%) than in the sJADAS and Gaslini datasets (19% and 18.8%, respectively). The frequency of patients who had a PhGA > 0 plus elevated APR, but all other ID criteria met was higher in the sJADAS dataset (19.6%) than in the EPOCA and Gaslini datasets (5.5% and 2.7%, respectively).
Conclusion: Our study confirms the previous observation that a sizeable proportion of physicians provide a PhGA > 0 in patients who are found not to have clinical evidence of inflammation in any joint. However, this disparity was less pronounced in patients evaluated in a single center with tradition and expertise in making clinimetric assessments. This observation suggests that regular application and training may increase the consistency of the PhGA. An important finding of our study is that a sizeable proportion of patients did not meet the ID definition due the isolated increase of APR.
Disclosure
None declared

Reference
1. Alongi A, et al; Pediatric Rheumatology International Trials Organization (PRINTO). Drivers of non-zero physician global scores during periods of inactive disease in juvenile idiopathic arthritis. RMD Open. 2022 Mar;8(1):e002042.

P204

A comparative study of headache prevalence in children with Juvenile idiopathic arthritis and healthy controls

A. Dudaklı[1], B. Menentoğlu[1], S. D. Arık[1], G. Kavrul Kayaalp[1], C. Baykan[2], A. Doğru[1], B. Başer Taşkın[1], P. Prencuva Akyürek[1], Ö. Akgün[1], M. A. Kılıç[3], E. Pempegül Yıldız[3], N. Aktay Ayaz[1]

[1]Pediatric Rheumatology, Istanbul University Faculty of Medicine, Istanbul, [2]Department of Pediatrics, Artvin Yusufeli State Hospital, Artvin, [3]Pediatric Neurology, Istanbul University Faculty of Medicine, Istanbul, Türkiye
Correspondence: A. Dudaklı
Pediatric Rheumatology, **23(2):** P204

Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease among pediatric population. Chronic inflammation, medications and physical limitations can have a negative impact on not only somatic but also neurological and psychosocial health in children with JIA. While several studies have investigated primary headache disorders in patients with rheumatoid arthritis, data remain limited in the pediatric population, particularly among those with JIA (1,2).
Objectives: This preliminary study aims to compare the prevalence of primary headache disorders between JIA patients and healthy controls (HC).
Methods: A questionnaire including demographic information, disease characteristics and symptoms of primary headache disorders was administered to JIA patients and age- and sex-matched HC. Individuals with headache symtoms were evaluated by a pediatric neurologist. Participants with secondary headache disorders were excluded from the study. Primary headache types were classified according to the criteria outlined in the International Classification of Headache Disorders, 3rd edition (ICHD-3). The data obtained from the questions were analyzed using IBM SPSS Statistics.
Results: Fourty three JIA patients and 45 HCs were questioned. In the JIA group, 24 (55.8%) were female and 19 (44.2%) were male. Likewise 24 (53,3%) female and 21 (46,7%) male individuals included in healthy control group. The mean age was 13 (±3.4) years in the JIA group and 12 (±2.1) years in the HC group. Among JIA group, 16 (%37,2) patients complained of headaches. Three of the patients were diagnosed with migraine according to ICHD-3 criteria and the remaining 13 patients were diagnosed with tension-type headache. Three (6,7%) patients found to have headache in HC. Two of them were diagnosed with migraine and one with tension-type headache. Cluster type headache was not found in both JIA and HC groups. There was significant difference of headache prevelance between JIA and HC (p<0,001). In the JIA group, no significant association was found between gender or biologic DMARD use and the presence of headache (p=0.18, p=0.8, respectively). When the JADAS27 score was compared, no significant difference was found between patients with and without headache, both at the time of diagnosis and at the last visit (p=0.38, p=0.09, respectively).
Conclusion: The higher prevalence of primary headaches in patients with JIA compared to HC underscores the importance of systematic headache assessment during routine clinical follow-up, which may enable early recognition and management, thereby improving overall quality of life.
Disclosure
None declared

References

1. Tian D, Zhao X, Ning Z, Gong Z, Wu J, Wang X. Migraine and risk of rheumatoid arthritis: A systematic review and meta-analysis of observational studies. *Heliyon*. 2023;9(8):e18430. Published 2023 Jul 19. doi:https://doi.org/10.1016/j.heliyon.2023.e18430
2. Uluduz D, Tavsanli ME, Uygunoğlu U, et al. Primary headaches in pediatric patients with chronic rheumatic disease. *Brain Dev*. 2014;36(10):884-891. doi: https://doi.org/10.1016/j.braindev.2014.01.009

P205

Is juvenile arthritis associated with lower physical activity levels among U.S. children? a cross-sectional analysis of the national survey of children's health (2016–2021)

C. Y. Tamashiro, W. D. Soulsby
University of California San Francisco (UCSF), San Francisco, United States
Correspondence: C. Y. Tamashiro
Pediatric Rheumatology, **23(2):** P205

Introduction: Juvenile arthritis (JA) is characterized by joint pain, stiffness, and decreased mobility, potentially affecting participation in physical activity (PA)[1]. The CDC and WHO recommend that children engage in at least 60 minutes of PA daily. While research in PA level and JIA has been conducted in European countries like Germany and the Netherlands, limited data exists in the U.S. [2,3]. It remains unclear whether children with arthritis in the U.S. meet PA guidelines or how achieving these recommendations impacts their overall health outcomes.
Objectives: To assess whether a current diagnosis of arthritis is associated with lower PA levels among a nationally representative sample of U.S. children and adolescents.
Methods: This cross-sectional study assessed adherence to daily PA recommendations among U.S. children with JA compared to peers without JA, using 2016–2021 National Survey of Children's Health (NSCH) data, a nationally representative survey that investigates health of pediatric population in the U.S. Univariable and multivariable logistic regression models examined the association between JA and meeting daily PA recommendations. A sensitivity analysis using ordinal logistic regression assessed PA frequency ("0 days," "1–3," "4–6," "daily"). Models were adjusted for potential confounders.
Results: Children with JA were less likely to meet daily PA recommendations than peers without arthritis (13.5% vs. 17.0%; p = 0.05), and had higher rates of obesity (23.3% vs. 13.9%; p < 0.001), physical limitations, pain (69.9% vs. 10.3%; p < 0.001), and comorbidities (55.2% vs. 30.6%; p < 0.001). However, in adjusted analyses, arthritis was not significantly associated with meeting PA guidelines (aOR = 1.34; 95% CI: 0.78–2.32; p = 0.29). Similarly, arthritis was not significantly associated with PA level in ordinal logistic regression (aOR = 1.17; 95% CI: 0.81–1.69; p = 0.41). Female sex, older age, presence of mental health conditions, and obesity (aOR for ≥95th percentile = 0.64; 95% CI: 0.52–0.78), were negatively associated with PA. Sports participation was strongly associated with meeting guidelines for PA (aOR = 1.58; 95% CI: 1.44–1.74; p < 0.001).
Conclusion: Children and adolescents with and without arthritis demonstrated low adherence to the CDC and WHO-recommended PA levels. Overall, arthritis was not found to be a statistically significant predictor of PA levels in unadjusted or adjusted analyses. These findings might suggest that while arthritis poses challenges, it may not be a key independent barrier to PA. Efforts to increase PA should address modifiable barriers like obesity and mental health, and promote sports participation, especially among older children with JA.
Disclosure
None declared

References

1. Klepper SE. Exercise and fitness in children with arthritis: evidence of benefits for exercise and physical activity. Arthritis Rheum. 2003;49(3):435–43. https://doi.org/10.1002/art.11055
2. Milatz F, Hansmann S, Klotsche J, et al. Level and correlates of physical activity among children and adolescents with juvenile idiopathic arthritis compared to controls: results from a German nationwide prospective observational cohort study. Pediatr Rheumatol. 2024;22:39. https://doi.org/10.1186/s12969-024-00976-2
3. Bos GJ, Lelieveld OT, Armbrust W, Sauer PJ, Geertzen JH, Dijkstra PU. Physical activity in children with Juvenile Idiopathic Arthritis compared to controls. Pediatr Rheumatol. 2016;14(1):42. https://doi.org/10.1186/s12969-016-0102-8

P206

Assessing attention and timing impairments in juvenile idiopathic arthritis using the MOXO-CPT

Ç. Yıldız, N. Karaçayır, D. Gezgin Yıldırım, S. A. Bakkaloğlu
Pediatric Rheumatology, Gazi University Faculty of Medicine, Ankara, Türkiye
Correspondence: Ç. Yıldız
Pediatric Rheumatology, **23(2):** P206

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood (1). Beyond musculoskeletal symptoms, chronic inflammation, fatigue, pain, and long-term treatment may impact attention, executive functions, and information processing speed in patients with JIA (2, 3). Both conventional and biological disease-modifying antirheumatic drugs (cDMARDs, bDMARDs)

may have an impact on cognitive performance (4). The MOXO-Continuous Performance Test (MOXO-CPT) is a valuable tool for assessing attention and timing abilities (5).
Objectives: This study aims to evaluate attention and executive functions in children with JIA using the MOXO-CPT.
Methods: Thirty-four children with JIA (per ILAR criteria) without neurodevelopmental or psychiatric comorbidities were evaluated. MOXO-CPT was administered by a trained clinician to assess attention, timing, impulsivity, and hyperactivity. Demographic, clinical, laboratory, and treatment data were collected. The effects of disease activity, inflammation markers, and treatment modalities (NSAIDs, cDMARDs, bDMARDs, corticosteroids, subcutaneous formulations) on cognitive outcomes were analyzed ($p < 0.05$).
Results: Among 34 patients, 67% were female, and 76.5% had oligoarticular JIA. ANA positivity was 41.2%. The mean age at diagnosis was 8.13 years; mean age at testing was 13.57. The weakest performance was seen in timing (Table 1). Males had lower attention scores, though not statistically significant ($p = 0.055$). Elevated CRP, ESR, and ANA positivity were not linked to cognitive scores. NSAID use was associated with significantly lower impulsivity ($p = 0.012$), whereas cDMARDs, bDMARDs, and corticosteroids were associated with reduced attention ($p = 0.009, 0.012, 0.009$). Subcutaneous formulations correlated with lower hyperactivity ($p = 0.031$). Patients with inactive disease had better attention ($p = 0.009$). Longer disease duration correlated with poorer timing performance ($r = -0.521$, $p = 0.002$) (Table 2).
Conclusion: Juvenile idiopathic arthritis is the most common rheumatic disease in childhood. Our study demonstrated that both disease activity and treatment modalities may influence cognitive functions. In particular, reduced attention performance in patients with active disease highlights the importance of achieving early remission. The use of methotrexate and biological agents may negatively affect attention, while patients receiving treatment in subcutaneous injection form were found to exhibit lower hyperactivity scores. Additionally, longer disease duration was associated with marked impairments in timing abilities. These findings underscore the importance of incorporating neurocognitive assessments into the management of JIA and suggest that further studies are warranted to explore the cognitive impact of treatment strategies and the potential benefits of achieving and maintaining remission.
Disclosure
None declared

P207

Factors associated with flares in patients with non-systemic juvenile idiopathic arthritis

D. Sarısoy, F. Aydın, Ö. Taş, O. Bahçeci, B. Öksüz Aydın, Z. B. Özçakar
Ankara University School of Medicine, Ankara, Türkiye
Correspondence: D. Sarısoy
Pediatric Rheumatology, **23(2):** P207

Introduction: Juvenile idiopathic arthritis (JIA) is a common childhood rheumatic disease involving a heterogeneous patient group. While some patients benefit from standard anti-rheumatic therapies and remain in remission, others require long-term and intensive treatment for relapsing courses. Therefore, identifying factors associated with flares is crucial for disease management.
Objectives: The aim of this study was to determine the factors associated with flares in patients with non-systemic JIA.
Methods: The medical records of non-systemic JIA patients followed up at our clinic between December 2015 and December 2024 were retrospectively reviewed. Only patients who were followed up for at least six months were included in the study. Remission status of the patients was evaluated according to the Wallace criteria. Patients were grouped according to their flare status and the clinical results of the groups were compared.
Results: 142 JIA patients were included in the study, 91 (64%) of whom were female. Median (IQR) age was 6 (8) months. 58.4 % (n=83) of the patients were oligoarticular JIA, 16.9 % (n=24) were polyarticular JIA, and 22.5 % (n=32) were enthesitis-related arthritis. The median (IQR) follow-up time of the patients was 67.5 (64.25) months. 73 (51%) patients experienced at least one flare during the follow-up period, while 69 (49%) patients did not experience any flare. When patients who had flared and those who had not were compared, it was found that female gender was significantly more frequent ($p = 0.007$), age at diagnosis was earlier ($p = 0.01$), and the number of joints involved at diagnosis was higher ($p = 0.01$) in patients with flares. Also, the frequency of patients with oligo-JIA (p=0.005) and JADAS scores were higher at diagnosis ($p = 0.014$) in the same group. Furthermore, ankle, elbow, metacarpophalangeal (MCP) and temporomandibular joint (TMJ) involvement, as well as uveitis, were significantly more common ($p<0.05$) and ANA positivity was also more frequent ($p = 0.01$) in the flare group.
Conclusion: Half of the patients with JIA experience at least one flare during follow-up. Female gender, earlier age at diagnosis, higher number of joints involved, elevated JADAS scores at onset, oligoarticular subtype, specific joint involvement (ankle, elbow, MCP, TMJ), uveitis, and ANA positivity were significantly associated with flare. These findings may help identify patients at higher risk for disease flare and guide closer monitoring and management strategies.
Disclosure
None declared

P208

Is obesity associated with time to diagnosis and disease severity in Juvenile psoriatic arthritis?

E. Broden-Barbareau[1], on behalf of CAPs PIs, A. Cox[1], on behalf of CAPS PIs, H. Lythgoe[2], on behalf of CAPS PIs, C. Ciurtin[3], on behalf of CAPS PIs, A. Chieng[2], on behalf of CAPS PIs, G. Cleary[4], on behalf of CAPS PIs, F. McErlane[5], on behalf of CAPS PIs, K. Hyrich[1,6], S. Shoop-Worrall[1], on behalf of CAPS PIs on behalf of CAPS PIs
[1]Children and Young Person's Rheumatology Research Programme, Centre for Musculoskeletal Research, The University of Manchester, [2]Paediatric Rheumatology and Adolescent Rheumatology, Royal Manchester Children's Hospital, Manchester, [3]Department of Ageing, Rheumatology and Regenerative Medicine, Division of Medicine, University College London, London, [4]Alder Hey Children's Hospital, Liverpool, [5]Great North Children's Hospital and Newcastle University, Newcastle, [6]NIHR Manchester Biomedical Research Centre, Manchester Foundation NHS Trust, Manchester, United Kingdom
Correspondence: E. Broden-Barbareau
Pediatric Rheumatology, **23(2):** P208

Introduction: Obesity is linked to delays in diagnosis, lower rates of minimal disease activity and poorer treatment response in adult-onset psoriatic arthritis, but its role in juvenile psoriatic arthritis (JPsA) is unclear.
Objectives: To examine the associations between obesity and JPsA features at initial presentation to paediatric rheumatology.
Methods: Children were recruited to the Childhood Arthritis Prospective Study, a UK multicentre JIA inception cohort, between 2001–2019. Participants selected had a physician's diagnosis of JPsA within one year of initial presentation to paediatric rheumatology. Demographic, clinical and patient-reported outcome data were collected at initial presentation.
Standardised BMI-z-scores at initial presentation were calculated using World Health Organization
Reference data and classified as 'underweight', 'healthy', 'overweight', or 'obese'.
Differences in JPsA features were compared between healthy and obese BMI-z-score groups descriptively and using Kruskal-Wallis (continuous variables) and Chi-squared tests (categorical variables).
Results: Among 111 children with JPsA, 48 (60.0%) had a healthy BMI, 18 (22.5%) were overweight, and 14 (17.5%) were obese. The proportion of overweight children exceeded the national average reported between 2001-2019 (11.5-15.5%), though the obesity rate was representative of national trends (14.0–18.5%).
Compared to children with healthy-weight-BMI, those with obese-range BMI had an older age of symptom onset (11.2 years, IQR: 10.2 to 14.6vs. 6.0 years, IQR: 2.7 to 11.2, p=0.010), and longer disease duration to diagnosis (6.6, IQR: 2.4 to 28.9vs. 5.1, IQR: 2.7 to 11.3, p=0.100), respectively.
Clinically, compared with children with healthy-weight-BMI, those with obese-range BMI had a higher ESR (26.0, IQR: 17.0 to 46.0 vs.10.0, IQR: 5.0 to 23.0, p=0.015). alongside clinically significant increases in

active joint counts (4.0, IQR: 1.0 to 10.0 vs.3.0, IQR: 2.0 to 5.0), limited joint counts (2.0, IQR: 1.0 to 9.0 vs.1.0, IQR: 1.0 to 3.0), proportion of individuals with psoriasis (54.6% vs.37.8%, p=0.200), and nail abnormalities (20.0% vs.12.2%, p=0.700), respectively.
Patient-reported outcomes were worse in the obese-range BMI compared with the healthy-BMI group: parental global score (5.2cm, IQR: 1.8 to 7.6 vs. 1.8cm, IQR: 0.1 to 4.1, p=0.050); pain (5.4cm, IQR: 2.0 to 8.2 vs. 2.0cm, IQR: 0.4 to 3.5, p=0.050); and CHAQ scores (1.4, IQR: 0.3 to 1.9 vs. 0.31, IQR: 0.13 to 0.63, p=0.130), respectively.
Conclusion: In JPsA, obesity is associated with later symptom onset, increased inflammation, and worse wellbeing and pain. A larger sample size is needed to confirm these findings. This highlights the importance of holistic and developmentally appropriate care, including proactive weight management and early intervention strategies for young people living with JPsA.
Disclosure
None declared

P209

Factors affecting systemic steroid use in the first three months in children with Juvenile idiopathic arthritis

E. Kucuk[1], K. Ozturk[1]
[1]Pediatric Rheumatology, Istanbul Medeniyet University, Istanbul, Türkiye
Correspondence: E. Kucuk
Pediatric Rheumatology, **23(2):** P209

Introduction: Variables such as disease subtypes, age of onset, systemic findings, and laboratory parameters significantly affect both clinical course and treatment strategies of Juvenile Idiopathic Arthritis (JIA).
Objectives: Glucocorticoid therapy is frequently used to control disease activity in the early stages. This study aimed to determine the factors affecting the use of steroid therapy in patients with JIA in the first three months following diagnosis.
Methods: This retrospective study included patients with JIA whose diagnoses were made in our center. Patients with a diagnosis of systemic JIA, those receiving intra-articular steroid treatment, those who were non-compliant with treatment, and those who did not attend follow-up regularly were excluded. JIA was diagnosed according to the International League for Rheumatology (ILAR) criteria. Disease activity was evaluated with the Juvenile Idiopathic Arthritis Disease Activity Score-71 (JADAS-71).
Results: This study included 161 patients (female/male =1.14). The number of patients receiving systemic steroids in the first three months was 109 (67.7%). Ankle (p=0.001) and wrist involvement (p=0.039), number of joints involved (p<0.001), C-reactive protein (p<0.001) erythrocyte sedimentation rate (ESR) (p<0.001), anti-nuclear antibody (ANA) positivity (p=0.001), and JADAS-71 scores (p<0.001) were significantly higher in the steroid group. In contrast, age at diagnosis (p=0.020) and the presence of sacroiliitis (p=0.006) were significantly lower in the steroid group. High JADAS-71 scores (OR: 1.45, 95% CI: 1.032-2.047, p=0.032) and younger age at JIA onset (OR: 0.88, 95% CI: 0.790-0.986, p=0.027) were found to be strongly associated with steroid needing. Rheumatoid factor (RF)-positive polyarticular JIA subtype (p=0.012), ankle (p=0.001) and foot proximal interphalangeal (PIF) joint involvement (p=0.015), number of joints involved (p=0.003), ESR (p<0, 001), ANA (p<0.001) and RF positivity (p=0.003), JADAS-71 scores (p<0.001) and use of conventional synthetic disease-modifying antirheumatic drugs (cDMARDs) (p=0.001), younger age onset (p=0.013) were associated with increasing steroid dosage. Furthermore, those with sacroiliitis tended to need lower dosage of steroids (p=0.002).
Conclusion: This study showed that systemic steroid use in the first three months in children with JIA increased with high JADAS-71 scores, hand and ankle involvement, elevated ESR, ANA, and RF positivity, whereas it decreased with older age at disease onset and presence of sacroiliitis. Therefore, individualization of treatment approaches according to clinical subtype and laboratory findings is critical to ensure effective control of inflammation, while reducing unnecessary steroid exposure and minimizing the risk of steroid-related complications such as Cushing's syndrome.
Disclosure
None declared

References

1. Bhardwaj U, Bagri N, Lodha R, Kabra S, Velpandian T, Pandey R. Efficacy of Pulse Dexamethasone in non-systemic Juvenile Idiopathic Arthritis: a double-blind randomised controlled trial. *Rheumatology.* 2021. https://doi.org/10.1093/rheumatology/keab914.
2. Ersoy G, Ergüven M, Yıldız M. Factors Associated with the Development of Adrenal Insufficiency in Patients with Juvenile Idiopathic Arthritis Who Received Systemic Corticosteroids. *The Journal of Pediatric Research.* 2023 https://doi.org/10.4274/jpr.galenos.2022.04207.

P210

An altered immunometabolic profile characterizes b cells of patients with oligoarticular- and polyarticular-juvenile idiopathic arthritis

E. Marasco, A. Aquilani, A. Ariolli, G. Tarantino, M. I. Petrone, R. Nicolai, I. Caiello, S. Barresi, S. Magni Manzoni, F. De Benedetti
Rheumatology Unit, Ospedale Pediatrico Bambino Gesù, Rome, Italy
Correspondence: E. Marasco
Pediatric Rheumatology, **23(2):** P210

Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common form of chronic arthritis in childhood. An hyperactivation of B cells characterizes patients with oligo- and poly-articular JIA (1) and we have showed that switched memory B cells are expanded in these patients (2). Our preliminary data showed that B cells of JIA patients exhibit changes in the immunoglobulin repertoire with a lower frequency of somatic hypermutation, suggesting an extrafollicular activation of B cells.
Objectives: We aimed to investigate the signalosome and transcriptomic profile of B cells in patients with JIA.
Methods: We enrolled patients with a diagnosis of oligoarticular and polyarticular JIA (n=15) and age matched controls (n=15). Intracellular levels of phospho-proteins (Syk, BLNK, ERK1-2, BTK, PLC g) and surface levels of CD22 were evaluated by flow cytometry. Calcium mobilization after anti-Ig stimulation was evaluated with Indo-1 by flow cytometry. Bulk-RNA seq was performed on sorted naïve B cells of patients and controls activated with anti-Ig, rhCD40L and IL-21 (n=4 for each group).
Results: We first analyzed the basal expression and phosphorylation levels of key proteins involved in regulation of B cell signaling. We observed a higher frequency of phosphorylation of BLNK and lower surface expression of CD22 in naïve B cells. Upon activation with an anti-Ig, naïve B cells showed higher phosphorylation of BTK but not PLCγ. Upon in vitro stimulation of BCR, we observed that naïve B cells of patients with JIA showed a faster calcium response to BCR activation, with a shorter peak time compared to controls. We then investigated the transcriptomic profile of naïve B cells. After quality controls, gene annotation to the
Reference genome, counting and filtering for low expression genes, we identified 13161 genes. We performed a PCA analysis: the first 2 components explained 84.5% of the total variance and the two groups of samples separated on the PCA plot, indicating differences in gene expression between the two groups. We identified 372 differentially regulated genes (DEGs) between patients and controls with the algorithm DESeq2. We performed on our set of DEGs over-representation analysis (ORA) and gene set enrichment analysis (GSEA). Both analyses confirmed that most of the DEGs were related to immune signaling of the TNF family and of NFkB, and genes involved in the metabolisms of amino acids and protein synthesis. We also identified two differentially regulated long non coding RNAs (lnRNAs), regulating respectively amino acid metabolisms and expression of CIITA, a gene that is important for antigen presentation.
Conclusion: Our data show that naïve B cells of JIA patients exhibit an increased phosphorylation of BLNK together with a reduced expression of CD22. Upon BCR activation, naïve B cells respond more promptly with faster calcium mobilization. Transcriptomic analysis of activated naïve B cells showed a differential expression of genes related to immune signaling of the TNF family and of NFkB, antigen presentation and protein synthesis. These latter pathways are controlled by mTOR, a crucial switch in regulating differentiation towards the extrafollicular pathway, suggesting a relationship between B cell activation outcome and metabolism in B cells of patients with JIA.

Disclosure
None declared

References
1. Barnes MG, Arthritis Rheum. 2009
2. Marasco E, Arthritis Rheumatol. 2018

P211

Real-world experience of tofacitinib as treatment for juvenile idiopathic arthritis – a retrospective, multi-centre study

E. S. Sen[1,2], S. Ali[3], O. Aragon[4], S. Cooray[5], J. Fisher[6], L. Hakoun[7], H. Lythgoe[7], A. Vahed[8], E. Willis[7]
[1]Department of Paediatric Rheumatology, Great North Children's Hospital, [2]Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, [3]School of Pharmacy, Liverpool John Moores University, [4]Pharmacy Department, Alder Hey Children's Hospital NHS Foundation Trust, Liverpool, [5]Department of Paediatric Rheumatology, Addenbrooke's Hospital, Cambridge, [6]Department of Paediatric Rheumatology, Alder Hey Children's Hospital NHS Foundation Trust, Liverpool, [7]Department of Paediatric and Adolescent Rheumatology, Royal Manchester Children's Hospital, Manchester, [8]Faculty of Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom
Correspondence: E. S. Sen
Pediatric Rheumatology, **23(2):** P211

Introduction: Tofacitinib has been shown to be effective at treating juvenile idiopathic arthritis (JIA) in a randomised controlled trial[1]. In the UK, tofacitinib is recommended to treat polyarticular-course JIA and juvenile psoriatic arthritis in cases resistant to at least one disease-modifying anti-rheumatic drug (DMARD), such as methotrexate (MTX), and for whom a TNFα inhibitor is not suitable or does not control disease adequately[2].
Objectives: This study aims to assess the real-world effectiveness of tofacitinib in treating JIA.
Methods: Patients (≤ 18 years) with JIA, who received tofacitinib between October 2021 and January 2025 with ≥ 3 months' follow-up were identified at 4 Paediatric Rheumatology centres in the UK. Data were collected retrospectively from electronic patient records. Baseline data included patient demographics, JIA categories, and previous and concomitant medications. The active joint count (AJC), side effects and any decision to stop tofacitinib were recorded at 3-monthly follow-up.
Results: Data were collated from 46 patients (65% female), with a median disease duration of 3.4 years (Q1 2.4, Q3 7.6). The main categories of JIA were rheumatoid factor (RF)-negative polyarticular in 16 (35%), extended oligoarticular in 8 (17%), RF-positive polyarticular in 8 (17%) and systemic in 6 (13%). The median number of previous conventional synthetic or biologic DMARDs was 2.5 (range 1-6). Needle anxiety was an indication for starting tofacitinib in 16 (35%) patients. Twenty-five patients were on concomitant DMARDs of whom 20 (80%) were taking MTX. The median AJC changed from 3 (range 0-31) at baseline to 1 (range 0-40) at 3 months. Of 41 patients who were on tofacitinib with data at both 0 and 3 months, the AJC remained at 0 or decreased in 32 (78%). However, it increased in 7 (17%) and was unchanged in 2 (5%). Tofacitinib was stopped in 19 (41%) patients at a median of 6 months, in most cases (16/19, 84%) due to inadequate control of arthritis. Termination of tofacitinib due to inefficacy was not associated with the number of previously-failed DMARDs, the AJC at baseline, JIA category or use of a concomitant DMARD. The commonest side effects were skin and upper respiratory tract infections. One patient developed new uveitis while on tofacitinib.
Conclusion: As an oral drug, tofacitinib offers an alternative treatment option for children and young people who have struggled with injected DMARDs. These patients may benefit from its use earlier in the JIA treatment pathway. Although 16 (35%) patients stopped tofacitinib due to inefficacy, others achieved disease control despite prior inadequate response to 2 or more DMARDs. Further biomarker research may help to target tofacitinib to those patients most likely to respond.
Disclosure
None declared

References
1. Ruperto N, et al. Tofacitinib in juvenile idiopathic arthritis: a double-blind, placebo-controlled, withdrawal phase 3 randomised trial. Lancet. 2021;398:1984–96.
2. National Institute for Health and Care Excellence. Tofacitinib for treating juvenile idiopathic arthritis. Technology appraisal guidance [TA735]. London: NICE; 2021.

P212

Characterization of mir22hg expression and role in oligoarticular juvenile idiopathic arthritis patients at disease onset

F. Briasco[1], S. Pelassa[1], F. Raggi[1], C. Rossi[1], C. Artale[1], S. M. Orsi[2], F. Orso[3,4], D. Taverna[4], M. Gattorno[1], A. Consolaro[1], M. C. Bosco[1]
[1]Unit of Rheumatology and Autoinflammatory Diseases, Department of Pediatric Sciences, IRCCS G. Gaslini Institute, [2]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health,, University of Genova, Genova, [3]Department of Molecular Biotechnology and Health Sciences, Molecular Biotechnology Center "Guido Tarone", Torino, [4]Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy
Correspondence: F. Briasco
Pediatric Rheumatology, **23(2):** P212

Introduction: Oligoarticular Juvenile Idiopathic Arthritis (OJIA), the most common form of pediatric rheumatic disease, is characterized by joint immune cell infiltration and synoviocyte proliferation, causing inflammation and cartilage erosion. While most patients achieve remission, others experience a severe, treatment-refractory course with joint damage and functional impairment. Understanding the molecular mechanisms underlying OJIA development and progression may provide early biomarkers and therapeutic targets.Recent studies suggest that the long non-coding RNA, MIR22HG, plays a role in adult arthritis, showing potential as a biomarker and therapeutic target. However, its expression and function in OJIA remain unexplored.
Objectives: This study investigates MIR22HG expression in peripheral blood (PB)- and synovial fluid (SF)-derived cells from new-onset OJIA patients, its correlation with patient clinical parameters at 1 year of follow up and functional role.
Methods: PB and SF mononuclear cells (PBMC, SFMC) from 30 OJIA patients were collected at onset, and CD14+ monocyte (Mn) and CD14- lymphocyte subsets were isolated. PBMCs from 25 age/gender-mached controls were analyzed in parallel. Fibroblast-like synoviocytes (FLS) were isolated from SF of 6 patients Cells were phenotypically characterized, and MIR22HG expression analyzed by RT-qPCR.
Results: MIR22HG expression was significantly higher in CD14+ than in CD14- cells from patient PBMCs and SFMCs and control PBMCs. However, OJIA patients showed lower MIR22HG levels than controls in PBMC subsets with good discriminatory power and expression correlation with clinical course at follow up. FLS exhibited an inflammatory synovial sublining phenotype and expressed MIR22HG. To asses MIR22HG function, siRNA-mediated silencing was performed in THP-1 human monocytic and FLS cell lines. Silencing increased apoptosis, IL-6 and IL-1β secretion in THP-1 cells, and IL-6 and IL-8 in FLS.
Conclusion: These findings suggest that MIR22HG has a protective role on inflammation by modulating Mn and FLS viability and activities. Its downregulation in OJIA represents a molecular mechanism promoting inflammatory processes, thus highlighting MIR22HG potential as an early biomarker of disease progression and therapeutic target.
Disclosure
None declared

P213

Moderate or intense physical activity is associated with a better perception of disease and well-being in adolescents and young adults with Juvenile idiopathic arthritis

F. Laborie[1], A. Combier[1], J. Wipff[1], M. Thomas[1], A. Loisel[2], H. Lefèvre[2], G. Touanga[1], P. Quartier[3], Y. Allanore[1], S. Hecquet[1]
[1]Rheumatology, [2]Médecine de L'adolescent - Maison de Solenn, Cochin Hospital, [3]Immunology - Rheumatology, Necker Hospital, Paris, France
Correspondence: S. Hecquet
Pediatric Rheumatology, **23(2):** P213

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children, leading to significant disability. In children and adolescents, some evidence indicates a benefit of physical activity on strength, stiffness, mobility, and pain. However, limited data are available regarding adolescents' physical activity and its impact on disease activity and patient well-being.
Objectives: The objective of our study was to assess physical activity and its impact on the well-being of adolescent and young adult patients with JIA.
Methods: A questionnaire was sent by email to patients from a retrospective monocentric cohort of JIA patients during their transition to adult rheumatology. This anonymous questionnaire simultaneously evaluated disease activity, patients' perception of the impact of the disease (using the Rheumatoid Arthritis Impact of Disease [RAID] score (6)), functional ability (using the Health Assessment Questionnaire (HAQ) patients' well-being (using the WHO-5 score), and physical activity (using the International Physical Activity Questionnaire or IPAQ).
Results: In total, 98 patients (70 females [71%]) responded to the questionnaire. Among them, 34 patients (35%) had a polyarticular form, 13 patients (13%) had enthesitis-related arthritis, 9 patients (9.2%) had an oligoarticular form, 4 patients (4.1%) had a form associated with psoriasis, and 38 patients (39.2%) were unclassified.The mean disease visual analog scale (VAS) was 3.67/10 and did not differ according to the JIA subtype. Morning stiffness lasting longer than 30 minutes and nocturnal awakenings were reported by 37 patients (38%) and 28 patients (29%), respectively. The mean Health Assessment Questionnaire (HAQ) score was 0.542/3, the mean WHO-5 score was 59.4/100, and the mean RAID score was 3.04/10. According to the IPAQ score, low, moderate, and high levels of physical activity were reported in 7/59 patients (11.9%), 28/59 patients (47.5%), and 18/59 patients (30.5%), respectively. RAID and HAQ scores were significantly higher in patients with low physical activity compared with those with moderate and high physical activity. The WHO5 score was significantly higher in patients with high physical activity. The HAQ score was inversely correlated with low physical activity ($p = 0.04$; $r=-0.3$).
Conclusion: This study, conducted in a monocentric cohort of 98 patients with JIA transitioning to adulthood, shows that 11.9% of patients reported low levels of physical activity compared to 27.5% in the global adult population (according to a WHO study) (7) and 21% in a French interministerial study of 1,280 civil servants. Our study suggests that our patients are not more sedentary than the general adult population. The results also show a significant link between physical activity and better quality of life and well-being. Active patients reported greater personal satisfaction and fewer functional limitations than sedentary patients. These findings highlight the importance of promoting physical activity in this population, not only to improve well-being, but also to improve patients' perceptions of the impact of their disease.
Disclosure
None declared

P214

Predicting clinical response to adalimumab in juvenile idiopathic arthritis with a multidimensional model integrating disease activity and pharmacokinetics

G. Tarantino[1], A. Di Deo[2], R. Simeoli[3], S. Magni-Manzoni[1], E. Marasco[1], A. Aquilani[1], R. Nicolai[1], M. I. Petrone[1], C. Rossi[3], C. Dionisi Vici[3], B. M. Goffredo[3], O. Della Pasqua[2], F. De Benedetti[1]
[1]Rheumatology Department, Bambino Gesù Children's Hospital IRCCS, Rome, Italy, [2]University College of London, Clinical Pharmacology & Therapeutics Group, London, United Kingdom, [3]Division of Metabolic Diseases, Bambino Gesù Children's Hospital IRCCS, Rome, Italy
Correspondence: G. Tarantino
Pediatric Rheumatology, **23(2):** P214

Introduction: Adalimumab, a fully human TNF-inhibitor, has revolutionized treatment of patients with juvenile idiopathic arthritis. The development of antidrug antibodies (AAA) has been reported in several paediatric inflammatory conditions. Most children treated with adalimumab respond within several months, but a minority of these may show loss of response (LOR) after continued exposure.
Objectives: The study describes clinical features in a single-centre cohort of JIA patients treated with adalimumab, grouped according to frequency (1W vs 2W), dose of drug administration (20 vs 40 mg) and disease activity (from inactive to high according to ACR-JADAS score). Subsequently, we investigated correlation between adalimumab levels and antidrug antibodies titres and the predictive covariates of clinical response.
Methods: Records of patients were retrospectively reviewed to identify patients with dosage of adalimumab and AAA in a 5-years-period. Clinical and demographic parameters were collected. Indirect E-max response model was created.
Results: From June 2019 to January 2024, we collected 445 samples in 110 patients (a median of 4 for each child). The majority of patient had ANA-positive oligoarthritis (55.4%) followed by RF- negative polyarthritis (24.5%). The median age at disease onset was 3.7 years. About 40% switched from drug originator to biosimilar. Pharmacokinetic analysis showed a moderately variable time-profile both of adalimumab concentration and ADA titres. Drug clearance was affected by 2 covariates: ADA titres (power increased 12%) and weight (allometric effect + 0.85 Kg/h). We observed a complete clinical response (CID) after only 3 months follow-up in 65% of children, who maintain remission also at 6 and 24 months. In the first 12 month of therapy, higher clinical inflammation at baseline is related to greater pharmacodynamic effect and better clinical response. The predicted adalimumab concentration (Css), at the same drug dose, were on average lower in patients with mild and high disease activity score. After 3 and 6 months of follow-up, the percentage of children with HDA was smaller in the upper drug exposition quantile than in lower one. However, the model did not predict (prediction rate 95%) long-term relapses (> 24 months).
Conclusion: This targeted risk analysis on the effect of ADA on the clinical incidence of loss of response has very important impact in our clinical practise. Our findings, together with target adalimumab ranges based on exposure-clinical response relationships, highlights the need of further pharmacological investigation to establish model-based personalized treatment approaches. The monitoring of the immunogenicity of the drug will therefore be implemented and will become the subject of future studies.
Disclosure
None declared

References

1. Marino A. Anti-adalimumab antibodies in a cohort of patients with juvenile idiopathic arthritis: incidence and clinical correlations. Clin Rheumatol 2018.
2. Bartelds G.M. Development of antidrug antibodies against adalimumab and association with disease activity and treatment failure during long-term follow-up. JAMA 2011.

P216

Ethnic variations in the course and treatment of juvenile idiopathic arthritis in the circumpolar region: a comparative analysis of Sakha and Russian pediatric cohorts

S. Boeskorova[1,2], M. Afonskaya[2], V. Argunova[2], P. Sleptsova[2], L. Leontieva[1,3], T. Burtseva[1,3], I. Avrusin[4], A. Yakovlev[4], M. Kostik[4]
[1]Medical Institute, North-Eastern Federal University named after M.K. Ammosov, [2]Republican Hospital No. 1 - M.E. Nikolaev National Center of Medicine, [3]Yakut Science Center for Complex Medical Problems, Yakutsk, [4]Department of Hospital Pediatrics, Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russian Federation
Correspondence: I. Avrusin
Pediatric Rheumatology, **23(2):** P216

Introduction: An indigenous population, Sakha, living in the extreme conditions of the North and the Arctic, has a unique profile of morbidities.
Objectives: This study aimed to investigate ethnic-specific manifestations of juvenile idiopathic arthritis (JIA) among indigenous children of the Republic of Sakha (Yakutia), in comparison with their Caucasian (Russian) counterparts residing in the same region, to support the development of personalized diagnostic and treatment approaches.
Methods: The single-center cohort retrospective study included data from the medical history of all patients (n=225) diagnosed with JIA

who underwent examination and treatment at the Cardiorheumatology Department of the Pediatric Center of the Republican Hospital No. 1-the M.E. Nikolaev National Center of Medicine from 2016 to 2023. Routine clinical and laboratory tests and ongoing therapy were evaluated.
Results: Children of Sakha ethnicity exhibited a later onset of juvenile idiopathic arthritis (JIA) with a predominance of the enthesitis-related arthritis (ERA) category (51.2% vs. 18.3%, P = 0.0002), enthesitis (19% vs. 2.0%, P = 0.003), sacroiliitis (23.8% vs. 2.0%, P = 0.0003), and HLA-B27 positivity (46.3% vs. 14.6%, P = 0.00005). Among Sakha children, the overall rate of biologic DMARD initiation was relatively high (41.7%), particularly within the ERA category (52.3% vs. 33.3%, P = 0.0003); however, the initiation of biologic therapy occurred significantly later compared to Russian patients. Despite this, the remission rate among Sakha children was significantly lower (29.2% vs. 72.2%, P = 0.002), as was the overall probability of achieving remission (Log-Rank test, P = 0.005), independent of JIA category (P = 0.008). Moreover, Sakha children had a 64.4% reduced likelihood of achieving remission with the first biologic DMARD compared to their Russian counterparts (HR = 0.36, 95% CI: 0.18–0.71, P = 0.004).
Conclusion: Significant differences in the clinical course and treatment response of JIA were observed between children of Sakha ethnicity and their Caucasian counterparts. These findings underscore the importance of incorporating ethnic background into personalized approaches for the management of JIA.
Disclosure
None declared

P217

Prevention of methotrexate side effects with prophylactic ondansetron in children with Juvenile idiopathic arthritis: final results of the OPT-Jia trial

G. Chédeville[1], H. Schmeling[2], J.-P. Proulx-Gauthier[3], M. Batthish[4], J. J. De Bruycker[5], B. M. Feldman[6], R. A. Berard[7], R. Bolaria[8], A. Chhabra[9], L. S. Lim[10], A. M. Huber[11], M. Berkowitz[12], T. Loughin[12], J. Guzman[13] on behalf of OPT-JIA Investigators
[1]Pediatrics, McGill University, Montreal, [2]Pediatrics, U of Calgary, Calgary, [3]Pediatrics, CHU de Quebec-Universite Laval, Quebec, [4]Pediatrics, McMaster University, Hamilton, [5]Pediatrics, Universite de Montreal, Montreal, [6]Pediatrics, U of Toronto, Toronto, [7]Pediatrics, Western University, London, [8]Pediatrics, UBC, Victoria, [9]Pediatrics, UBC, Penticton, [10]Pediatrics, U of Manitoba, Winnipeg, [11]Pediatrics, Dalhousie University, Halifax, [12]Statistics, Simon Fraser U, Burnaby, [13]Pediatrics, UBC, Vancouver, Canada
Correspondence: J. Guzman
Pediatric Rheumatology, **23(2):** P217

Introduction: About 50% of children with Juvenile Idiopathic Arthritis (JIA) starting methotrexate (MTX) experience intolerance, manifested by severe nausea and vomiting, abdominal pain, headaches, and refusal to take the medication.
Objectives: To evaluate if prophylactic weekly premedication with ondansetron prevents MTX intolerance, compared to as needed use.
Methods: In this block-randomized pragmatic controlled trial nested in the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) Registry, children 4-16y starting MTX for the first time were assigned to 1) routine premedication with oral ondansetron from the very first dose of MTX (intervention), or 2) ondansetron used only after developing nausea/vomiting (control). Ondansetron was prescribed as 3 weekly weight-based doses starting one hour before MTX. The primary trial endpoint was the proportion of children on MTX with good tolerance one year after starting MTX, estimated using Kaplan Meier survival analysis. Intolerance was defined as a Methotrexate Intolerance Severity Score (MISS) ≥6 points. Secondary endpoints assessed MTX intolerance, attainment of inactive disease (Wallace criteria), starting biologic DMARDs, and mean quality of life (QoL, 0 to 100) and MISS scores at 6m.
Results: Trial enrollment was stopped early for futility by the Data and Safety Committee in December 2023 and study follow-up was completed in January 2025. Of 68 children assessed for eligibility, 55 were randomized to intervention (n=23) or control (n=32). In the intention to treat analysis, the Kaplan Meier estimate of remaining on MTX with good tolerance by one year was 55.9% with prophylactic ondansetron, versus 65.3% with as needed ondansetron (p=0.59 by log rank test). MTX Intolerance at any time (35.1% vs 31.5%, p=0.84), attainment of inactive disease (60.9% vs 73.5%, p=0.46), starting biologic DMARDs (53.8% vs 59.4%, p=0.40), and mean QoL scores at 6 m (73.7 vs 80.5, p=0.30 by t-test) and MISS scores (5.0 vs 1.7, p=0.21) were similar in both groups. A per protocol analysis, which excluded 4 patients with poor adherence to study medications, reported similar results.
Conclusion: Prescription of prophylactic ondansetron to prevent MTX intolerance did not result on more patients remaining on MTX with good tolerance one year after starting the medication. Secondary outcomes showed no clear benefit of prophylactic ondansetron.
Trial registration identifying number: ClinicalTrials.gov: NCT04169828
Study funded by a competitive research grant from The Arthritis Society, Canada.
Disclosure
None declared

P218

Adoption of new treatment options in non-systemic juvenile idiopathic arthritis (Jia) in clinical practice

H. C. Lamers, J. F. Swart , S. Roock, de, A. Royen, van-Kerkhof, van, M. H. Jansen, E. Nieuwenhove, van, B. Vastert
Department of Pediatric Immunology and Rheumatology, University Medical Center Utrecht, Wilhelmina Children's Hospital,, Utrecht, Netherlands
Correspondence: J. F. Swart
Pediatric Rheumatology, **23(2):** P218

Introduction: The recent development of biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) has expanded the possibilities of pharmacological treatment for patients with juvenile idiopathic arthritis (JIA).
Objectives: The objective of this study is to evaluate trends in initial prescriptions for targeted therapies in patients aged 0-18 years with non-systemic JIA in clinical practice. We also identified the approval dates and key regulatory changes for each medication.
Methods: A retrospective cohort study was conducted using prescription records from the Wilhelmina Children's Hospital, the largest pediatric rheumatology center in the Netherlands, analyzing data from April 2011 to September 2024. The market introduction of targeted therapies for JIA were extracted from the European Medicines Agency (EMA) database.
Results: Over a 12-year period, 11 targeted therapies (N=714) and 3 csDMARDs (N=726) were analysed among 703 patients. TNF-alpha inhibitors accounted for the largest proportion of bDMARDs and tsDMARDs, comprising 78.2%. The prescription of bDMARDs and tsDMARDs increased, from a relative proportion of 32.2% in 2012 to 87.5% in 2024. The prescription of JAK inhibitors rose from 1.6% in 2020 to 22.0% in 2024.
Conclusion: This study provides a comprehensive overview of the implementation of targeted therapies in non-systemic JIA over the past decade, highlighting the gradual integration of these therapies into clinical practice. While TNF-alpha inhibitors remain the most commonly prescribed, there has been a significant rise in the prescription of JAK inhibitors and other new therapies. Factors such as route of administration, patient comfort, costs and treatment efficacy may influence the adoption of these DMARDs. The findings highlight the need for continued research to identify factors for successful implementation of these therapies in clinical practice.
Disclosure
None declared

References

1. Martini A, Lovell DJ, Albani S, Brunner HI, Hyrich KL, Thompson SD, et al. Juvenile idiopathic arthritis. Nat Rev Dis Primers [Internet]. 2022 Dec 1.
2. Prakken B, Albani S, Martini A. Juvenile idiopathic arthritis. Lancet [Internet]. 2011.

3. Weiss JE, Ilowite NT. Juvenile idiopathic arthritis. Pediatr Clin North Am [Internet]. 2005.
4. Cimaz R, Maioli G, Calabrese G. Current and emerging biologics for the treatment of juvenile idiopathic arthritis. Expert Opin Biol Ther [Internet]. 2020 Jul 2.
5. Yue X, Huang B, Hincapie AL, Wigle PR, Qiu T, Li Y, et al. Prescribing Patterns and Impact of Factors Associated with Time to Initial Biologic Therapy among Children with Non-systemic Juvenile Idiopathic Arthritis. Paediatr Drugs [Internet]. 2021 Mar 1.
6. Grazziotin LR, Currie G, Twilt M, Ijzerman MJ, Kip MMA, Koffijberg H, et al. Real-world data reveals the complexity of disease modifying anti-rheumatic drug treatment patterns in juvenile idiopathic arthritis: an observational study. Pediatr Rheumatol Online J [Internet]. 2022 Dec

P219

What proportion of children with Juvenile idiopathic arthritis have persistent disease in adulthood: a systematic literature review

J. Rawlinson-Smith[1], R. Keerio[1], J. Humphreys[1,2], K. Hyrich[1,2,3], L. Kearsley-Fleet[1]
[1]Centre for Epidemiology Versus Arthritis, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, University of Manchester, [2]Kellgren Centre for Rheumatology, Manchester Royal Infirmary, [3]NIHR Manchester Biomedical Research Centre, Manchester University Hospitals NHS Trust, Manchester, United Kingdom
Correspondence: J. Rawlinson-Smith
Pediatric Rheumatology, **23(2):** P219

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children; in some cases it persists well into adulthood.
Objectives: To describe studies of persistent disease in adults with JIA.
Methods: Searches were conducted on 16th December 2024 in MEDLINE, Embase and PubMed. Observational studies that measured outcomes in adults aged ≥18 years with a diagnosis of JIA were included. Primary outcome of interest was persistent arthritis in adulthood (proportion or percentage). Secondary outcomes included disease activity measures. Studies investigating outcomes in any ILAR subtype of JIA were included. There were no restrictions based on the context, setting, publication date, or number of participants. Risk of bias was assessed using the Quality In Prognosis Studies (QUIPS) tool, modified for prognosis studies of overall prognosis.
Results: Twenty studies published between 2000 and 2024 involving a combined total of 5123 individuals with JIA were included. Sixteen studies defined JIA using the 2001 ILAR criteria for JIA, two used the 1977 EULAR criteria for juvenile chronic arthritis, and two used the outdated term juvenile rheumatoid arthritis. Sample sizes ranged from 43 to 666 participants with JIA at the time of follow-up. Median age of study participants at last follow-up ranged from 19 to 39 years. Global representation was limited: 17 studies were conducted in Europe, the others in Canada, India, and Turkey. Nineteen studies reported disease activity, and one reported healthcare utilisation. The proportion of people with JIA that had persistent disease in adulthood ranged from 34% to 80%. There was inconsistency in definitions used for remission or inactive disease; these included Wallace criteria for clinical remission, definitions based on Disease Activity Score (DAS; typically used for adults with rheumatoid arthritis), Juvenile Arthritis Disease Activity Score (JADAS), and Physician's Global Assessment, as well as various other author-defined criteria. Overall, risk of bias was deemed to be moderate to high. Most (16/20) studies enrolled children and followed them up into adulthood, whereas three studies enrolled only adults with JIA, and one longitudinal study excluded people who were lost to follow-up before adulthood. Due to the observational and long-term nature of these studies, partial participation rates and loss to follow-up were key factors for the potential introduction of selection bias and attrition bias.
Conclusion: This systematic literature review found there is substantial variation in the reported proportion of children with JIA who have persistent disease in adulthood, likely due to heterogeneity in outcome definitions. At least a third of children with JIA appear to have persistent disease into adulthood.
Disclosure
None declared

P220

Semaphorin 5a as a new protein involved in the pathogenesis of Juvenile idiopathic arthritis

J. Roszkiewicz[1], K. Wyka [2], E. Smolewska[1]
[1]Department of Pediatric Cardiology and Rheumatology, [2]Department of Pediatrics, Oncology and Hematology, Medical University of Lodz, Łódź, Poland
Correspondence: J. Roszkiewicz
Pediatric Rheumatology, **23(2):** P220

Introduction: Although Juvenile Idiopathic Arthritis (JIA) is the most common form of autoimmune-driven arthritis in paediatric population, due to the lack of universal diagnostic markers and heterogeneity of the disease many patients face a significant delay when establishing the diagnosis. As angiogenesis and inflammation are the major mechanisms leading to pannus formation, the key molecules participating in both processes are promising therapeutic targets. Whereas the role of vascular endothelial growth factor (VEGF) and its soluble receptors (sVEGFR-1, sVEGFR-2) has been described in JIA, the reports on novel angiogenesis markers in JIA are scarce. Semaphorin 5 A (SEMA5A), a member of the immune semaphorins family, is involved in various physiological and pathological processes, including both angiogenesis and immune response. Although there are reports on SEMA5A overexpression in the serum, synovial membrane and synovial fluid of rheumatoid arthritis (RA) patients, no study has assessed the impact of this protein on the pathogenesis of JIA.
Objectives: The aim of our study was to compare the serum concentration of SEMA5A and VEGF in newly-diagnosed JIA patients and sex-and-age-matched healthy controls.
Methods: 35 JIA patients and 35 sex-and-age matched healthy controls were enrolled to the study. Serum concentrations of SEMA5A and VEGF-A were established using ELISA method.
Results: The serum concentration of SEMA5A was elevated in JIA patients in comparison to healthy controls with the median value 2,04 (IQR 12,41) in JIA patients and 1,34 (IQR 1,79) in healthy controls (p=0.002). The difference was particularly prominent in oligoartucalar JIA, where median SEMA5A concentration equalled 1,76 ng/ml (IQR 1,56) in comparison to 0,33 ng/ml (IQR 1,34) in sex-and-age-matched healthy controls (p=0.001). SEMA5A concentration correlated strongly with VEGF-A concentration (r= 0,807, p<0.001) and differed significantly in subgroups of different synovial membrane Power-Doppler ultrasound inflammatory activity (p=0.018).
Conclusion: Although our findings need to be repeated on larger groups of JIA patients, SEMA5A is a promising marker of JIA, linked to pathological angiogenesis of synovial membrane in this entity. Moreover, it may be useful as a target of innovative treatment strategies in the nearest future.
Disclosure
None declared

P221

Effect of SLC19A1 polymorphisms on methotrexate treatment in juvenile idiopathic arthritis patients

K. Aslan[1], F. A. M. A. Abdullah[2], S. D. Temtek[2], F. İpekten[3], A. Y. Bülbül[4], E. Kayhan[4], E. Esen[5], C. Arslanoğlu[6], S. Ö. Çiçek[4], A. P. Kısaarslan[4], H. Canatan[1]
[1]Department of Medical Biology, School of Medicine and Betül-Ziya Eren Genome and Stem Cell Center, [2]2.Department of Medical Biology, Institute of Health Sciences, Erciyes University, [3]Department of Biostatistics and Medical Informatics, Adıyaman University, [4]Division of Pediatric Rheumatology, Department of Pediatrics, Erciyes University, Kayseri, [5]Ankara Bilkent City Hospital Division of Pediatric Rheumatology, University of Health Sciences, Ankara, [6]Kocaeli City Hospital Division of Pediatric Rheumatology, University of Health Sciences, Kocaeli, Türkiye
Correspondence: S. Ö. Çiçek
Pediatric Rheumatology, **23(2):** P221

Introduction: Background: Juvenile Idiopathic Arthritis (JIA) is a chronic rheumatic disease affecting children. The most common subtype in Türkiye is oligoarticular JIA. Methotrexate (MTX) is the most common drug used in the treatment of the disease, but in some patients, MTX and Biological Disease Modifying Antirheumatic Drugs (bDMARDs) are administered together due to inadequate treatment

with MTX. The SLC19A1 gene encodes a protein involved in the transport of folates into cells. Point mutations in the SLC19A1 gene and changes resulting in downregulation of its message are the main factors involved in resistance to antifolate compounds.
Objectives: Aim: Our study aimed to reveal the relationship between polymorphisms in the SLC19A1 gene and treatment response of JIA patients receiving MTX alone or bDMARD treatment together with MTX.
Methods: Methods: Genomic DNA was isolated from peripheral blood samples of 192 JIA patients. A 230 bp SLC19A1 gene was amplified by conventional Polymerase Chain Reaction. Using this amplicon, genotyping (GA, GG, AA) was determined by performing RFLP with Hha I restriction enzyme digestion.
Results: Results: The study included 192 JIA patients. Of these, 76 were treated with MTX, and 116 were treated with bDMARDs in addition to MTX. 53 (69.7%) of those receiving MTX and 76 (65.5%) of those receiving bDMARDs were female. While 38 (50%) of the patients in the MTX group had persistent oligoarticular JIA, 38 (32.8%) of the patients in the bDMARDs group had RF negative polyarticular JIA. The number of joints affected was significantly higher in the bDMARDs group (5-20) compared to the MTX group (3-14) ($p<0.0019$). No difference was found in GG, GA and AA alleles between the two groups. Laboratory tests showed that WBC count was 7.485/mm^3 (1.378-19.4) in the MTX + bDMARDs group, higher than in the MTX alone group, 6.545/mm^3 (3.370-17.430) ($p=0.044$). When patients were compared in terms of genetic alleles they carried, there was no difference in clinical and laboratory findings between allelic groups in co-dominant and recessive models, while the frequency of uveitis in the recessive model was significantly higher in GG allele carriers 9 (25.0%) compared to GA/AA allele carriers 19 (12.2%) ($p=0.049$).
Conclusion: Discussion: Although no significant difference was observed between the allele type carried by the patients and clinical laboratory findings, a significant relationship was found between the incidence of uveitis, WBC count, and the number of joints involved and the allele type. Increasing the sample size of the study may be an important step in revealing the relationship between allele type and treatment response.
Disclosure
None declared

P222

Overlapping shadows: juvenile idiopathic arthritis look-alikes in pediatric hip disorders – a 10-year review

K. Uçak[1], F. Temez[2], C. Erdemir[2], K. Memişoğlu[2]
[1]Department of Pediatric Rheumatology,, [2]Department of Orthopedics and Traumatology, Kocaeli University, Faculty of Medicine,, Kocaeli, Türkiye
Correspondence: K. Uçak
Pediatric Rheumatology, **23(2):** P222

Introduction: Slipped capital femoral epiphysis (SCFE) is a rare pediatric hip disorder characterized by displacement of the proximal femoral epiphysis from the femoral neck. It is believed to be associated with mechanical, endocrine, and metabolic changes that weaken the growth plate during adolescence. Diagnosis is typically made using anteroposterior and frog-leg lateral radiographs, while advanced imaging may be necessary to assess complications. Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood. SCFE often presents with hip pain and limping, symptoms that may mimic JIA. Therefore, in patients with JIA who develop new-onset unilateral hip pain and limited range of motion, SCFE should be considered in the differential diagnosis.
Objectives: This retrospective study aimed to contribute to the literature by examining the demographic, clinical and surgical data of patients under the age of 18 diagnosed with SCFE between 2014 and 2024. The relationship with JIA was also examined.
Methods: In this retrospective study, clinical, laboratory and imaging data of children under 18 years of age diagnosed with SCFE between 2014 and 2024 were examined. Ethical approval was obtained, and demographic information, surgical methods and complications of the patients were analyzed for association with JIA.
Results: Of the 25 SCFE patients included in the study, 56% were male and 44% were female, and the median age was 13 years. SCFE was seen as 48% left, 28% right, and 24% bilateral. Obesity was detected in 48% of the patients, and the most common surgical method was in situ fixation (64%). No significant relationship was found between obesity and trauma history and complications. Also, no JIA patients were detected during the long-term follow-up of patients diagnosed with SCFE.
Conclusion: SCFE is a disease with high morbidity in children presenting with hip pain. In acute and chronic conditions, a detailed history and physical examination are necessary for accurate diagnosis. This approach guides the treatment process and facilitates timely referral to a specialist, providing important scientific contributions on the etiology and prognosis of SCFE. It should definitely be kept in mind in presentations with hip pain and limping.
Trial registration identifying number: Numbered E-80418770-020-558335, 2024/94 was discussed by the Kocaeli University Non-Interventional Ethics Committee at the meeting dated 2024/03.36 GOKAEK on February 15, 2023 and the ethics committee approval was received. Patient consents were also obtained.
Disclosure
None declared

References

1. Mathew, S.E.; Larson, A.N. Natural History of Slipped Capital Femoral Epiphysis. J. Pediatr. Orth.op. 2019, 39, S23–S27.
2. Perry, D.C.; Metcalfe, D.; Costa, M.L.; Van Staa, T. A Nationwide Cohort Study of Slipped Capital Femoral Epiphysis. Arch. Dis. Child. 2017, 102, 1132–1136.
3. Loder, R.T.; Schneble, C.A. Seasonal Variation in Slipped Capital Femoral Epiphysis: New Findings Using a National Children's Hospital Database. J. Pediatr. Orthop. 2019, 39, e44–e49.
4. Tosounidis T, Stengel D, Kontakis G, Scott B, Templeton P, Giannoudis PV. Prognostic significance of stability in slipped upper femoral epiphysis: a systematic review and meta-analysis. J Pediatr. 2010 Oct;157(4):674–80, 680. e1. https://doi.org/10.1016/j.jpeds.2010.04.018. PMID: 20,605,166.

P223

Measles immunity status in children with rheumatological conditions on biologic disease-modifying antirheumatic drugs

L. Abdelgadir, O. Busari, K. Haslam
Paediatrics Rheumatology, Leeds children's Hospital, Leeds, United Kingdom
Correspondence: L. Abdelgadir
Pediatric Rheumatology, **23(2):** P223

Introduction: Following the increase in measles cases, United Kingdom Health Security Agency (UKHSA) updated national measles guidelines to identify individuals who may lose or not maintain adequate antibody levels from past exposure or vaccination, and includes patients receiving or within 6 months of completing biological therapies. This recommends IVIG in patients on biologics at risk of severe measles, if within a specified timeframe of exposure and immunity is not known.
Revised European League Against Rheumatism (EULAR) guidance on immunisation has enabled us to offer booster MMR vaccine on certain bDMARDs where applicable, if their immunity wanes.
The preliminary data was presented as poster at the British Society of Rheumatology (BSR) Conference. This updated version includes data from five additional patients.
Objectives: To assess the measles immunity status in our cohort of Paediatric Rheumatology patients on bDMARDs and to determine any waning of immunity.
Methods: Patients under the care of the Leeds Children's Hospital Rheumatology team who were receiving bDMARD therapy were identified. Measles immunity status was assessed using standard IgG serological testing as part of routine care. All collected data were recorded in Microsoft Excel and stored securely.
Results: This audit presented data collected between April 2024 and April 2025. A total of 76 patients underwent measles IgG testing; 66% were aged between 11 and 17 years. The majority (87%) were diagnosed with Juvenile Idiopathic Arthritis, and 75% were receiving Adalimumab.

The median duration of bDMARD treatment was 2.5 years, ranging from 1 to 10 years.
Sixty-one patients (86%) had received at least two doses of the MMR vaccine, of whom 59 (91%) tested IgG positive. Five patients with negative serology had previously received 2 MMR doses. Two patients who were initially IgG positive later tested negative after 4 and 9 years on bDMARDs, respectively. In three additional patients, prior IgG status could not be confirmed due to missing pre-treatment data. Among 8 patients who had received only one MMR dose, 88% were IgG positive. All three unvaccinated patients were IgG negative.
Conclusion: Most fully vaccinated patients on bDMARDs maintained their immunity despite bDMARD therapy. However, we identified waning of immunity in two patients who received 2 MMR vaccine doses on bDMARDs. This finding highlighted that clinicians should consider re-evaluating serological status when prevalence and risk of measles is increased and not to rely on vaccination history alone, Booster doses should be considered in patients with negative serology based on EULAR guidelines.
Disclosure
None declared

References
1. National Measles Guidelines. Ref: UKHSA Publication Gateway Number GOV-16999
2. Jansen MHA, Rondaan C, Legger GE, et al. EULAR/PRES recommendations for vaccination of paediatric patients with autoimmune inflammatory rheumatic diseases: update 2021. *Annals of Rheumatic Disease* 2023;82:35–47.

P224
Intra-articular corticosteroid injections may suffice in older children with Juvenile idiopathic arthritis: a single-center study
K. Liontou, K. Chiotopoulou, K. Kourtesi, M. Mpakirtzoglou, A. Chira, L. Fotis
3rd Department of Pediatrics, National and Kapodistrian University of Athens, Athens, Greece
Correspondence: L. Fotis
Pediatric Rheumatology, **23(2):** P224

Introduction: Juvenile Idiopathic Arthritis (JIA) is a heterogeneous disease where intra-articular corticosteroid injections (IACIs) are frequently used as initial therapy. At diagnosis, the necessity of immediate initiation of systemic treatment in all children, particularly older ones, remains a critical question.
Objectives: This study aimed to analyze the therapeutic management and joint involvement patterns among newly diagnosed JIA patients.
Methods: We retrospectively reviewed 109 patients newly diagnosed with JIA who underwent at least one IACI at the time of initial diagnosis at our center. Patients who received IACIs after the initiation of systemic therapy were excluded. All IACIs were performed under ultrasound guidance using Triamcinolone Acetonide or Triamcinolone Hexacetonide.Patients were classified into three groups based on therapeutic management:(1) those treated exclusively with IACIs without systemic therapy,(2) those who initiated systemic therapy within 30 days of the IACI (immediate group), and (3) those who initiated systemic therapy more than 30 days after the IACI (delayed group). Demographic data, joint involvement patterns, and treatment timelines were recorded. Descriptive statistics were calculated. Group comparisons for age at diagnosis were performed using the Kruskal-Wallis and Mann-Whitney U tests. For patients treated exclusively with IACIs, follow-up duration was assessed up to April 30, 2025.
Results: The median age at diagnosis was 4.3 years (range 0.9–16.0). 73 (67.0%) were females and 36 (33.0%) were males. Thirty-three patients (30.3%) were treated exclusively with IACIs, 56 (51.4%) initiated systemic therapy within 30 days, and 20 (18.3%) initiated systemic therapy after more than 30 days. The median age at diagnosis differed significantly between groups ($p = 0.0032$), with the IACIs-only group being older (median: 5.83 years) than those in the immediate (3.34 years, $p = 0.0067$) and delayed groups (3.10 years, $p = 0.0159$). No significant difference was observed between the immediate and delayed groups ($p = 1.000$). In the IACI-only group, the median follow-up was 20.2 months (range: 4.5–48.3 months) without the need for systemic therapy. Joint involvement analysis revealed that 25/33 patients (75.8%) in the IACI-only group had monoarticular disease, most commonly involving the knee. The median number of IACIs in this group was 1 (range: 1–3). Among patients in the delayed group, the median time from IACI to systemic treatment initiation was 143 days (range: 31–1004).
Conclusion: A significant proportion of JIA patients, especially older children with limited joint involvement, achieved disease control with intra-articular corticosteroid injections alone. Extended follow-up confirms that many of these patients remained stable without systemic treatment for prolonged periods. In many cases multiple injections were sufficient to maintain control without systemic therapy in some cases. Careful patient stratification at diagnosis may allow for delayed or even avoided systemic therapy in selected cases, optimizing treatment strategies in JIA.
Disclosure
None declared

References
1. Li S, Zhang W, Lin Y. Application of intra-articular corticosteroid injection in juvenile idiopathic arthritis. Frontiers in Pediatrics. 2022 Mar 29;10. https://doi.org/10.3389/fped.2022.822009
2. Rubin S, Ohana O, Goldberg O, Peled O, Gendler Y, Habot-Wilner Z, et al. The efficacy and safety of intra-articular injection of triamcinolone acetonide versus triamcinolone hexacetonide for treatment of juvenile idiopathic arthritis. Pediatric Rheumatology. 2022 Jan 29;20(1). https://doi.org/10.1186/s12969-022-00666-x

P225
Multidimensional assessment of damage at transition in JIA
L. Scagnellato[1], C. Giraudo[2], A. Meneghel[3], A. Michielin[2], M. Lorenzin[1], G. Cozzi[1], F. Zulian[3], A. Doria[1], R. Ramonda[1]
[1]Rheumatology - Department of Medicine DIMED, [2]Imaging Diagnostics - DSCTV, [3]UOSD Paediatric Rheumatology - Woman and Child Health Department, University Hospital of Padova, Padova, Italy
Correspondence: L. Scagnellato
Pediatric Rheumatology, **23(2):** P225

Introduction: Since Juvenile Idiopathic Arthritis (JIA) can persist into adulthood, these patients should be efficiently transitioned from paediatric to adult rheumatology services. Adult rheumatologists should evaluate not only the current disease activity but also consider the patient's long medical history and accumulated damage.
Objectives: The study aims to describe the outcomes and multisystem damage in a newly established cohort of patients with non-systemic JIA referred to the University Hospital of Padova. The assessment includes not only joint damage but also reproductive and ocular health.
Methods: At the transfer visit from peadiatric to adult rheumatology services, patients are prospectively enrolled and disease activity and damage are clinically scored by JADAS10-CRP, DAS28 and JADI. Multidimensional assessments include blood tests, magnetic resonance imaging (MRI) of the most affected joint through time, gynaecological or andrological referral. The MRI protocol includes T1, T2, STIR, PETRA, and DIXON sequences that have been blindly scored by a trained radiologist. The radiological score is an adapted version of the JAMRIS score for the knee in JIA without contrast enhancement. Gynaecological evaluation includes clinical evaluation, blood hormone levels and transaddominal ultrasound scan.
Results: The cohort consists of 82 patients transferred to our unit between 2017 and 2024, mostly females presenting with ANA positive oligoarticular JIA and treated with DMARDs. Almost 30% of patients had active disease with a median JADAS10CRP 8.5 (IQR 5.7). Among 50 patients with sufficient follow up time, nearly one-third relapsed within 3 years. The primary risk factor for relapse was a previous history of monoarthritis, independent of other disease characteristics, including ANA positive early onset classification. Among 82 patients, 57% (47) had JADI score >0. However no predictors for JADI A or JADI E could be identified among clinical and treatment variables, except for uveitis for JADI E. 19 patients (23.3%) underwent joint surgery before transition and 10% of patients had complicated uveitis. 22 patients underwent MRI of the most affected joint – mostly the knee-,

diplaying at least 1 lesion in 21/22 cases. Residual joint effusion was found in 77% of cases, synovial thickening in 63%, bone marrow oedema in 40%, bone erosions in 22%. These lesions were found in clinically active but also in clinically inactive patients (12 patients), suggesting high rates of subclinical synovitis. Fitted models for MRI damage prediction could not find any significant result. 17 female patients underwent gynaecological evaluation finding high rates of dysmenorrhoea (71%) and polycystic ovary morphology (12%).
Conclusion: Patients transitioning from paediatric to adult rheumatology services exhibit high rates of residual joint activity and damage in their most affected joints. These findings emphasize the need for careful therapy management and highlight the risks of therapy reduction in this population.
Disclosure
None declared

P226

Isolated tarsitis in Juvenile idiopathic arthritis: a distinct clinical subset?

L. Tobias[1,2], M. H. Saied [3,4,5], L. Harel[6], Y. Butbul Aviel[4,7], N. Assalia[8]
[1]Pediatric Rheumatology, Lady Davis Carmel Medical Center, [2]Pediatric Rheumatology, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, [3]Department of Pediatrics, Lady Davis Carmel Medical Center, [4]Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, [5]Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, University Medical Center, Utrecht, Netherlands, [6]Pediatric Rheumatology Unit, Schneider Children's Medical Center, Tel-Aviv University, Petach Tikva, [7]Pediatric Rheumatology Service, Ruth Rappaport Children's Hospital, Rambam Health Care Campus, Haifa, [8]Pediatric Rheumatology Unit, Schneider Children's Medical Center, Tel-Aviv University, Petach Tikva, Israel
Correspondence: M. H. Saied
Pediatric Rheumatology, **23(2):** P226

Introduction: Juvenile Idiopathic Arthritis (JIA) is a common chronic autoimmune disorder in children, affecting 16 to 150 per 100,000. It is classified into seven subtypes, with oligoarthritis being the most common. While foot involvement, particularly in the ankle, is common, the involvement of the tarsal bones and midfoot in pediatric patients has been less studied. Tarsitis refers to the inflammation of the tarsal joints and overlying structures, including the subtalar, tarsometatarsal, and naviculocuneiform joints, which can significantly impact mobility and foot function. Tarsitis has never been discussed as a sole joint involvement in JIA. This study focuses on a cohort with isolated tarsitis in JIA.
Objectives: This study aims to explore epidemiology, clinical manifestations, diagnostic modalities, and management implications of tarsitis as the sole clinical presentation in pediatric JIA.
Methods: We conducted a retrospective review of medical records from 2004 to 2024 of children with JIA at three large Israeli tertiary medical centers. Only patients with tarsitis were included, except for concurrent ankle involvement on the same side. Data collected included demographics, clinical history, laboratory results, and treatment modalities. Tarsitis diagnosis was based on clinical and radiological findings.
Results: Out of 36 patients with tarsal inflammation during JIA disease follow up, 10 had sole midfoot involvement. All presented with limp and dorsal foot swelling, with a mean age at symptom onset of 7.2 ± 3.75 years. Ninety percent were female. Six patients (60%) tested positive for ANA, and one was RF positive. The majority were diagnosed with Polyarticular JIA (60%), the latter were Enthesitis-related arthritis (ERA). 80% of patients received methotrexate as 1 st line therapy, and 60% required second-line therapy, primarily with anti-TNF agents. Inactive disease was achieved in 70% within a mean of 8.9 ± 11.2 months.
Conclusion: Tarsitis is not a common presenting symptom in pediatric populations and is often associated with the ERA subset. In our cohort, the majority had Polyarticular JIA, and most required biological therapy for remission, suggesting a poorer prognosis for midfoot involvement compared to standard Polyarticular JIA cohort.
Disclosure
None declared

References

1. Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369(9563):767–78. https://doi.org/10.1016/S0140-6736(07)60363-8.
2. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, He X, Maldonado-Cocco J, Orozco-Alcala J, Prieur AM, Suarez-Almazor ME, Woo P, International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390–2.
3. Thierry S, Fautrel B, Lemelle I, Guillemin F. Prevalence and incidence of juvenile idiopathic arthritis: a systematic review. Joint Bone Spine. 2014;81(2):112–7. https://doi.org/10.1016/j.jbspin.2013.09.003.
4. Kurup H, Vasukutty N. Midfoot arthritis—current concepts review. J Clin Orthop Trauma. 2020;11(3):399–405. https://doi.org/10.1016/j.jcot.2020.03.002.
5. Phatak S, Mohindra N, Zanwar A, Aggarwal A. Prominent midfoot involvement in children with enthesitis-related arthritis category of juvenile idiopathic arthritis. Clin Rheumatol. 2017;36(8):1737–45. https://doi.org/10.1007/s10067-017-3733-3.

P227

A single scottish centre retrospective audit of biologic use in JIA between 2015 and 2025

L. Paterson-Brown, A. Weaver, A. Fell, E. Carson, N. Martin
Paediatric Rheumatology, Royal Hospital for Children, Glasgow, United Kingdom
Correspondence: L. Paterson-Brown
Pediatric Rheumatology, **23(2):** P227

Introduction: There is growing opinion that juvenile idiopathic arthritis (JIA) management should prioritise early aggressive treatment to achieve remission(1,2). We audited our time to starting biologic drugs for JIA and reviewed how this has changed over 10 years.
Objectives: To assess whether patients met the Scottish Paediatric and Adolescent Rheumatology Network (SPARN) target for all JIA patients with persistently active arthritis 6 months after diagnosis to have started a biologic. Secondary objectives were time to biologic and time to zero active joints. We also compared data between early (0-6 months), intermediate (7-12 months) and late (>12 months) biologic start.
Methods: Retrospective data collection. Inclusion criteria were JIA diagnosis and biologic naïve. Exclusion criteria were still's disease, non JIA diagnosis and <3 months since starting biologic. When analysing time to zero active joints, data were removed for patients with zero active joints on starting biologic. These patients had reached zero active joints following previous treatment with DMARD/corticosteroids, or started biologic therapy for uveitis.
Results: SPARN target was met by 97% (35/36) patients in 2015 and 93% (99/107) in 2025. In 2015 initial biologics used were Etanercept (n=26), Adalimumab (n=5), Infliximab (n=2), Tocilizumab (n=2), Abatacept (n=1). In 2025 Adalimumab (n=43), Etanercept (n=41), Infliximab (n=12), Tocilizumab (n=6), Secukinumab (n=3), Rituximab (n=1) and Tofacitinib (n=1). Median time from symptom onset to diagnosis was 3 months in both groups (IQR 2015=5, 2025=6.75). Median time from symptom onset to biologic was 20 months in 2015 (IQR=26) and reduced to 14 months in 2025 (IQR=19.75, p=0.21). Median time from diagnosis to biologic in 2015 was 15 months (IQR=20) and reduced to 7 months in 2025 (IQR=14, p=0.009). Median time from biologic start to zero active joints was 4 months in 2015 (IQR=4.5) and 3 months (IQR=4) in 2025. Percentage responder and median time to zero active joints from symptom onset were 100% and 3 months (early), 75% and 2.5 months (intermediate) and 76.5% and 5 months (late) in 2015 and 86.7% and 4 months (early), 75% and 3 months (intermediate) and 85.4% and 3 months (late) in 2025.
Conclusion: Over 90% of our patients met the SPARN biologic target in both cohorts, this has not improved between 2015 to 2025. Time from symptom onset to diagnosis has not changed between cohorts but our patients are starting biologics sooner with significantly shorter time from diagnosis to first biologic. In this retrospective cohort we did not see a correlation between time to starting first biologic and successful response based on achieving zero active joints on that drug.

Disclosure
None declared

References
Huang B et al. Timing matters: real-world effectiveness of early combination of biologic and conventional synthetic disease-modifying antirheumatic drugs for treating newly diagnosed polyarticular course juvenile idiopathic arthritis. RMD Open. 2020 Jan;6(1):e001091. doi: https://doi.org/10.1136/rmdopen-2019-001091. PMID: 32396520; PMCID: PMC7003379.
Wallace CA et al. Trial of early aggressive therapy in polyarticular juvenile idiopathic arthritis. Arthritis Rheum. 2012 Jun;64(6):2012-21. doi: https://doi.org/10.1002/art.34343. Epub 2011 Dec 19. PMID: 22183975; PMCID: PMC3319524.

P228

Evaluation of ana staining patterns and titers in patients with Juvenile idiopathic arthritis

L. Koru, K. Ozturk
Pediatric Rheumatology, Istanbul Medeniyet University, Istanbul, Türkiye
Correspondence: L. Koru
Pediatric Rheumatology, **23(2):** P228

Introduction: Antinuclear antibody (ANA) test is utilized in Juvenile Idiopathic Arthritis (JIA) patients in terms of predicting complications. However, whether ANA staining patterns and titers are associated with clinical features, disease subtypes and activities remains unclear.
Objectives: In this study, we aimed to investigate the relationship between ANA staining patterns and titers with clinical and laboratory parameters such as age, gender, JIA subtype, number of joints involved and inflammatory markers in patients diagnosed with JIA and positive ANA test.
Methods: The study included patients who were evaluated as JIA according to International League Against Rheumatology (ILAR) criteria during routine outpatient clinic visits between January and March 2025 and whose ANA test was positive with a titer of 1/100 and above. ANA test was performed by indirect immunofluorescence method (IIF) and staining patterns were evaluated with AC codes according to the *International Consensus on ANA Patterns (ICAP)* classification.
Results: The study included 50 patients (Female: n=35 (68.6%)). The mean age at diagnosis was 8.73 ± 4.58 years. Of the patients, 78% (n=39) had oligoarticular JIA, 12% (n=6) had enthesitis-associated arthritis (ERA), 2% (n=1) had psoriatic arthritis, 6% (n=3) had Rheumatoid Factor (RF) negative polyatricular JIA and 2% (n=1) had RF positive polyarticular JIA. The most common ANA nuclear staining patterns were AC-1 (n=32, 64%), AC-4/5 (n=11, 22%) and AC-2 (n=5, 10%). ANA cytoplasmic staining pattern (AC-15-17) was detected in only 2 (4%) patients. In the oligoarticular JIA subtype, the most common staining pattern was AC-1 (87.5%) and in the ERA subtype, the most common staining pattern was AC-4/5 (66.7%) (p= 0.019). AC-1 staining pattern was significantly higher in patients with a younger age at diagnosis (p=0.003). When ANA staining titer was compared with JIA subtypes it was shown that while the patients with oligoarticular JIA tend to have a titer of 1/100-1/320, a titer of ≥1/1000 was significantly higher in the patients with ERA (p=0.009).
Conclusion: Our unique findnigs show that while oligoarticular JIA subtype was associated with AC-1 staining pattern, low-intermediate ANA titer and younger age at diagnosis, ERA subtype was associated with AC-4/5 staining pattern, higher ANA titer and older age at diagnosis. It was concluded that staining pattern and titer levels may be associated with JIA subtypes.
Disclosure
None declared

References
AndradeLEC,DamoiseauxJ,VerganiDetal.Antinuclearantibod- ies (ANA) as a criterion for classification and diagnosis of systemic autoimmune diseases. J Transl Autoimmun 2022;5:100145.
Bossuyt X, De Langhe E, Borghi MO et al. Understanding and interpreting antinuclear antibody tests in systemic rheumatic dis- eases. Nat Rev Rheumatol 2020;16:715–26.
BredaL,NozziM,DeSanctisSetal.Laboratorytestsinthediag- nosis and follow-up of pediatric rheumatic diseases: an update. Semin Arthritis Rheum 2010;40:53–72.

P229

Impact of anti-adalimumab antibodies in pediatric rheumatic diseases: a retrospective study

M. Zajc Avramovic[1,2], G. Markelj[1,2], N. Emersic[1,2], N. Toplak[1,2], A. Koren Jeverica[1,2], S. Cucnik[3,4], T. Avcin[1,2]
[1]University Medical Center Ljubljana, Children's Hospital, [2]Medical Faculty, University of Ljubljana, [3]Department for Rheumatology, University Medical Center Ljubljana, [4]Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia
Correspondence: M. Zajc Avramovic
Pediatric Rheumatology, **23(2):** P229

Introduction: Adalimumab (ADA) has significantly improved the management of pediatric rheumatic diseases. However, the development of anti-adalimumab antibodies (anti-ADA) can lead to reduced drug efficacy and treatment failure.
Objectives: To evaluate the clinical impact of anti-ADA in children with rheumatic diseases treated with adalimumab.
Methods: All measurements of serum adalimumab concentration (s-ADA) and anti-ADA in children with rheumatic diseases, treated at the Department of Allergology, Rheumatology, and Clinical Immunology, Pediatric Clinic, University Medical Center Ljubljana, Slovenia, from 2017 to 2024, were retrospectively reviewed. Clinical, laboratory, and treatment data were collected from the Registry of Children with Immune-Mediated Diseases. s-ADA was measured first in all patients, with anti-ADA testing performed only in those with s-ADA below the threshold (<0.5 mcg/mL).
Results: A total of 156 s-ADA measurements were performed in 94 patients, 33% of whom were female. The average age at measurement was 14.0 years (range: 2.0–21.6 years). s-ADA levels were below the laboratory threshold in 28 measurements (17.9%). Of these, anti-ADA was not detected in 7 cases (25%), suggesting non-adherence to therapy. Anti-ADA was positive in 19 patients (15 female), with serum concentrations ranging from 4 to >1000 ng/mL. Most patients had juvenile idiopathic arthritis (16/19, 84,2 %, 5 of these with uveitis), 1 had idiopathic uveitis and 2 had sarcoidosis (both with uveitis). Altogether, 42 % of patients had the manifestation of uveitis (8/19). Further clinical data were available for 18 patients. Additional immunosuppressive therapy was used in 83.3% (methotrexate in 12 patients, mycophenolate mofetil in 2, leflunomide in 1). Five patients (27%) were receiving adalimumab at extended intervals due to sustained remission (4) or personal reasons (1). Anti-ADA was tested due to disease flares in 88.9% (16/18) of patients, with antibodies first detected an average of 27.5 months (range: 3.9–97.6 months) after starting adalimumab. In 77.8% (14/18) of patients, ADA was discontinued due to anti-ADA. In 4 patients, ADA was continued (2 with increased dosage, 2 with unchanged dosage), and subsequent measurements showed no detectable anti-ADA. In 75% (3/4) of these cases, anti-ADA concentrations were below 10 ng/mL when they were first positive.
Conclusion: Anti-ADA may contribute to rheumatic disease flares, particularly when therapy is taken on extended intervals or irregularly. Additional immunosuppressive therapy did not prevent anti-ADA formation. In some cases with low antibody concentrations, anti-ADA became undetectable with continued therapy. One-quarter of patients had unmeasurable s-ADA without anti-ADA, indicating non-adherence to adalimumab therapy.
Disclosure
None declared

P230

Tarsitis as a distinct yet undefined feature of Jia

N. Assalia[1], L. Tobias[2], Y. Levinsky[1], L. Harel[1], G. Amarilyo[1], Y. A. Butbul[2], M. Hamad Said[3]
[1]Rheumatology Unit, Schneider children's medical center, Petah Tekvah, [2]Pediatric Rheumatology Unit, Rambam medical center, [3]Pediatrics, Carmel nedical center, Haifa, Israel
Correspondence: N. Assalia
Pediatric Rheumatology, **23(2):** P230

Introduction: Tarsitis is defined as inflammation of intertarsal joints, overlying tendons, entheses and soft tissue. While ankle joints involvement is common in juvenile idiopathic arthritis (JIA), tarsitis is less frequently observed and often under-recognized particularly in paediatrics. this under recognition may delay appropriate management and contribute to long term functional impairment.
Objectives: The aim of this study is to investigate the manifestation of tarsitis among JIA patients in terms of epidemiology, clinical manifestations and treatment response.
Methods: We conducted a multicentre retrospective cohort study in 3 tertiary university medical centres at Israel. every patient with tarsitis involvement as part of JIA according to ILAR criteria was included, exclusion criteria were tarsitis as part of infectious aetiology, inflammatory bowel disease or reactive arthritis. Tarsitis diagnosis was based on clinical and/or radiological findings. They were classified based on tarsitis involvement as isolated manifestation of JIA or as part of broader pattern of joint involvement.
Results: A total of 36 patients with tarsitis were included. the first group included 10 patients who had isolated tarsitis, while the second group comprised 26 patients in whom tarsitis was one of several joints involved in the course of the disease**.** the mean age at tarsitis onset was 6.5 years old. 66.6% were female. 66.6% tested positive for ANA. Polyarticular JIA was the most prevalent subtype (47.2%), with enthesitis related arthritis (ERA) being the second most diagnosed 25%.
The majority received methotrexate as first line Disease-modifying antirheumatic drugs (DMARD) 86%, of them 78% required second-line therapy, mostly anti-TNF. Inactive disease was achieved in 81% within a mean of 8.7 months. mean duration of follow up was 71.4 months. No statistically significant difference was observed between the two groups.
Conclusion: Tarsitis may occur as an isolated manifestation in JIA and show a potential involvement across different JIA subtypes, contrary to earlier reports indicating a higher prevalence of tarsitis in the ERA subtype. The vast majority didn't respond to MTX and required biological therapy for remission. These findings may indicate a less favourable prognosis and may justify the consideration of early escalation of therapy and therefore, the tarsal joint warrants greater clinical attention and recognition.
Disclosure
None declared

P231

An international delphi survey towards a new classification criteria for Juvenile idiopathic arthritis

A. Alongi[1], H. Brunner[2], A. Ravelli[3,4], T. Avcin[5], M. W. Beresford[6,7], R. Burgos-Vargas[8,9], R. Cuttica[10], R. Khubchandani[11], R. M. Laxer[12,13], S. Ozen[14], R. E. Petty[15,16], C. A. Wallace[17,18], N. M. Wulffraat[19,20], S. Magni-Manzoni[21], M. Jelusic[22], A. Consolaro[4], J. Anton[23], G. Horneff[24], M. Glerup[25], G. Filocamo[26], G. Simonini[27,28], A. Civino[29], A. Remesal[30], S. Scala[31], A. Pistorio[32], D. J. Lovell[2], A. Martini[3,4], N. Ruperto[33,34] on behalf of For the Pediatric Rheumatology International Trials Organization (PRINTO) and the Pediatric Rheumatology Collaborative Study Group
1Università Milano Bicocca, Milan, Italy, ***2***Cincinnati Children's Hospital Medical Center, Cincinnati, OH, United States, ***3***Università degli Studi di Genova, ***4***IRCCS Istituto Giannina Gaslini, Genoa, Italy, ***5***University Children's Hospital, Ljubljana, Slovenia, ***6***Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, ***7***Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom, ***8***Hospital General de México and Faculty of Medicine, ***9***Universidad Nacional Autónoma de México, Mexico City, Mexico, ***10***Hospital Pedro de Elizalde, Buenos Aires, Argentina, ***11***Jaslok Hospital and Research Centre, Mumbai, India, ***12***The Hospital for Sick Children, ***13***University of Toronto, Toronto, Canada, ***14***Hacettepe University, Ankara, Türkiye, ***15***British Columbia Children's Hospital, ***16***University of British Columbia, Vancouver, Canada, ***17***Seattle Children's Hospital, ***18***University of Washington, Seattle, United States, ***19***Wilhelmina Children's Hospital, ***20***University Medical Center Utrecht, Utrecht, Netherlands, ***21***IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, ***22***University Hospital Centre Zagreb, Zagreb, Croatia, ***23***Hospital Sant Joan de Déu, Barcelona, Spain, ***24***Department of General Paediatrics, Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, ***25***Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark, ***26***Pediatric Immunorheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, ***27***ERN ReCONNET center, Meyer Children's Hospital IRCCS, ***28***NEUROFARBA Department, University of Florence, Florence, ***29***Department of Pediatric Immunology and Rheumatology, Vito Fazzi Hospital, Lecce, Italy, ***30***Hospital Universitario La Paz, Madrid, Spain, ***31*** Clinica Pediatrica e Reumatologia, IRCCS Istituto Giannina Gaslini, ***32***Servizio di Epidemiologia e Biostatistica, IRCCS Istituto Giannina Gaslini, Genoa, ***33***Department of Medicine, Università Milano Bicocca, Milan, ***34***Reumatologia Pediatrica, IRCCS San Gerardo dei Tintori, Monza, Italy
Correspondence: N. Ruperto
Pediatric Rheumatology, **23(2):** P231

Introduction: To improve the current classification criteria for juvenile idiopathic arthritis (JIA), a multi-step initiative coordinated by PRINTO was launched in 2015, with a consensus process that culminated in the proposal of the preliminary PRINTO JIA classification criteria. The steps included a large-scale prospective data collection of patients with new-onset JIA and the ongoing validation of evidence-based criteria. To initiate the validation phase, an international Delphi survey was conducted among pediatric rheumatologists to identify the most relevant categories and candidate variables for subsequent data collection.
Objectives: To identify consensus-based categories and variable sets for the evidence-based revision of JIA classification criteria.
Methods: An invitation to participate in two Delphi rounds was sent to PRINTO/PRCSG membership starting in 2020.
In Round 1, participants evaluated each ILAR category along with 'Early Onset ANA Positive Arthritis', indicating whether to retain or discard it, and suggesting revised names. They also listed variables used in practice to diagnose each category.
In Round 2, participants re-evaluated each category for retention and ranked the top three preferred names and the ten most useful variables for the category-specific diagnosis among those identified in Round 1. Based on the ranking, a median score for each variable was calculated. Variables falling above the 75th percentile of the score were identified for each category.
Results: 434 physicians responded in Round 1 and 884 in Round 2. Votes to retain the ILAR categories were 236 (73%) for Systemic arthritis, 218 (70%) for Oligoarthritis, 209 (69%) for Polyarthritis Rheumatoid Factor (RF) negative, 276 (92%) for Polyarthritis RF positive, 188 (66%) for Psoriatic arthritis, 225 (78%) for Enthesitis-related arthritis (ERA), 183 (67%) for Early-onset ANA-positive JIA, and 142 (53%) for Other arthritis.
Top ranking labels for each new category were 'Juvenile-onset Still disease', 'Oligoarticular JIA', 'Juvenile polyarthritis', 'JIA RF positive or anti-CCP positive', 'Juvenile psoriatic arthritis', 'Early onset spondyloarthritis', 'ANA positive juvenile arthritis' and 'Unclassified JIA'.
The variables identified as most useful for the diagnosis (in the top quartile of the score) were 15 for Systemic arthritis, 31 for Oligoarthritis, 33 for Polyarthritis RF negative, 33 for Polyarthritis RF positive, 45 for ERA, 26 for Psoriatic arthritis, 27 for Early-onset ANA-positive JIA and 19 for Other arthritis.
Conclusion: The study yielded consensus-based categories to be considered in the new classification criteria and identified candidate variables to be included in the ongoing step of the project, namely the evidence-based validation of new classification criteria for JIA based on real new-onset patients' data.
Disclosure
A. Alongi: None declared, H. Brunner: None declared, A. Ravelli: None declared, T. Avcin: None declared, M. Beresford: None declared, R. Burgos-Vargas: None declared, R. Cuttica: None declared, R. Khubchandani: None declared, R. Laxer: None declared, S. Ozen Speaker Bureau with: Novartis, SOBI, Pfizer, R. Petty: None declared, C. Wallace: None declared, N. Wulffraat: None declared, S. Magni-Manzoni: None declared, M. Jelusic: None declared, A. Consolaro: None declared, J. Anton: None declared, G. Horneff: None declared, M. Glerup: None declared, G. Filocamo: None declared, G. Simonini: None declared, A. Civino: None declared, A. Remesal: None declared, S. Scala: None declared, A. Pistorio: None declared, D. Lovell: None declared, A. Martini: None declared, N. Ruperto: None declared

References
Martini A, Ravelli A, Avcin T, Beresford MW, Burgos-Vargas R, Cuttica R, Ilowite NT, Khubchandani R, Laxer RM, Lovell DJ, Petty RE, Wallace CA, Wulffraat N, Pistorio A, Ruperto N, for the Paediatric Rheumatology International Trials Organisation (PRINTO). Toward new classification criteria for juvenile idiopathic arthritis. First steps, the Paediatric Rheumatology International Trials Organisation international consensus. J Rheumatol 2019;46:190-197.

P232

Longitudinal effectiveness of abatacept in juvenile idiopathic arthritis (jia): results from an ongoing registry

N. Ruperto[1], H. I. Brunner[2], J. Huggins[3], E. Alexeeva[4], C. Correll[5], J. Bohnsack[6], S. Tarvin[7], G. Simonini[8], T. Griffin[9], A. Zeft[10], G. Horneff[11], P. Quartier[12], I. Orban[13], H. Walters[14], V. Stanevica[15], J. Patel[16], A. M. Huber[17], M. Rosenkranz[18], D. Kingsbury[19], R. Scuccimarri[20], G. Vega Cornejo[21], J. F. Swart[22], R. Carroll[23], T. Sherrard[2], C. Pallotti[24], C. Malattia[25], D. J. Lovell[2], A. Martini[26], on behalf of PRINTO and PRCSG Coordinating Centers
[1]Università degli Studi Milano-Bicocca, Milan, Italy, [2]Cincinnati Children's Hospital Medical Center, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [4]National Medical Research Center for Children's Health Federal State Autonomous Institution of the Russian Federation Ministry of Health and I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russian Federation, [5]University of Minnesota, Minneapolis, [6]University of Utah, Salt Lake City, [7]Riley Hospital for Children, Indianapolis, United States, [8]Azienda Ospedaliera Universitaria Meyer Istituto di Ricovero e Cura a Carattere Scientifico, Firenze, Italy, [9]Atrium Health Levine Children's Hospital, Charlotte, [10]Cleveland Clinic, Cleveland, United States, [11]Asklepios Klinik, Sankt Augustin, Germany, [12]Hôpital Necker-Enfants Malades, Paris, France, [13]Department of Rheumatology and Clinical Immunology of Semmelweis University, Budapest, Hungary, [14]Northwell, New Hyde Park, United States, [15]Riga Stradiņš University, Riga, Latvia, [16]Children's Hospital of Georgia, Augusta University, Augusta, United States, [17]IWK Health Centre and Dalhousie University, Halifax, Canada, [18]University of Pittsburgh, Pittsburgh, [19]Randall Children's Hospital at Legacy Emanuel, Portland, United States, [20]McGill University Health Centre, Montreal, Canada, [21]Clinica de reumatología Guadalajara, Guadalajara, Mexico, [22]Wilhelmina Children's Hospital/UMC Utrecht, Utrecht, Netherlands, [23]Bristol Myers Squibb, London, United Kingdom, [24]Istituto G. Gaslini, Servizio di Sperimentazioni Cliniche Pediatriche, [25]Istituto G. Gaslini, Pediatria II Reumatologia and University of Genova, [26]Istituto G. Gaslini Pediatria II Reumatologia and University of Genova, Genova, Italy
Correspondence: N. Ruperto
Pediatric Rheumatology, **23(2):** P232

Introduction: Abatacept is a selective T-cell costimulation modulator approved for use in JIA. Efficacy and safety of abatacept in patients (pts) with JIA has been demonstrated previously in 2 Phase 3 trials[1,2] and earlier results from this Phase 4 abatacept JIA registry (NCT01357668).[3]
Objectives: To determine real-world longitudinal safety and effectiveness of intravenous (IV) and subcutaneous (SC) abatacept in pts with JIA.
Methods: By protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group and Pediatric Rheumatology International Trial Organization enrolled pts meeting the International League of Associations for Rheumatology criteria for 1 of the categories of JIA and currently taking or starting IV or SC abatacept. Planned duration of follow-up (FU) is 10 years; data were collected up to March 31, 2024. Effectiveness was assessed at day of entry into registry (baseline [BL]), 3 and 6 months, and 1, 2, 3, 4, and 5 years. Safety data were collected at each visit.
Results: Of the 740 pts enrolled, 701 were included in the analysis (476 IV, 225 SC); 561/701 (80%) were female. At BL, median age was 13.6 years, and 28 (4%) pts were aged 2–5 years; JIA disease duration was 4.5 years. Median abatacept treatment duration was 6.1 months and number of active joints was 1.0 (mean 2.7). JIA categories were Systemic (2%), Oligo (25%), Polyarthritis rheumatoid factor (RF)-negative (48%), Polyarthritis RF-positive (10%), Psoriatic (5%), Enthesitis-related (4%), and Undifferentiated (6%). Total abatacept exposure was 1513.2 pt-years with a mean/median duration of abatacept treatment of 25.9/19.7 months. At 1-year FU, pts had low Physician Global Disease Activity (mean 1.2, SE 0.08), low Juvenile Arthritis Multidimensional Assessment Report combined scores (mean 3.7, SE 0.20), and improvement in the number of joints with active arthritis (mean 1.5, SE 0.16) compared with BL. A higher percentage of pts achieved clinically inactive disease after 1 year of FU compared with BL (46% vs 32%). This trend continued despite low numbers of pts with 4 and 5 years of FU. There were 11 serious infections reported (incidence rate [IR] 0.52/100 pt-years of FU, 95% CI: 0.26, 0.92; IR 0.73/100 pt-years on treatment, 95% CI: 0.36, 1.30). There were 17 autoimmune events (IR 0.80/100 pt-years of FU, 95% CI: 0.46, 1.28; IR 1.12/100 pt-years on treatment, 95% CI: 0.65, 1.80). There were 2 adverse event malignancies (n = 1 each medulloblastoma, T-cell lymphoma). No cases of tuberculosis were reported. There was 1 unrelated death (pre-existing cardiac complications).
Conclusion: In this real-world JIA cohort, abatacept was safe and well tolerated with no new safety risks identified. This longitudinal analysis further supports the persistent effectiveness of abatacept in pts with JIA.
Trial registration identifying number: NCT01357668
Disclosure
N. Ruperto Grant/Research Support with: Bristol Myers Squibb, Consultant with: Consulting fees: AbbVie, AClaris, AlfaSigma, Amgen, AstraZeneca, Aurinia, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Genentech Roche, Guidepoint, Idorsia, Janssen, Novartis, Pfizer, Sanofi, Takeda; Participation on a Data Safety Monitoring Board or Advisory Board: Amgen, H. Brunner Grant/Research Support with: Writing support; no monetary value: Bristol Myers Squibb, J. Huggins: None declared, E. Alexeeva: None declared, C. Correll: None declared, J. Bohnsack Grant/Research Support with: Bristol Myers Squibb, Jannsen, Pfizer (payments made to my institution), S. Tarvin Grant/Research Support with: Amgen, Arthritis Foundation, AbbVie, Roche, Pfizer, UCB, Rheumatology Research Alliance, Childhood Arthritis Rheumatology Research Alliance (paid to institution); Support for attending meetings and/or travel: Childhood Arthritis Rheumatology Research Alliance; Equipment for Grant Contract work (Remarkable tablet): Childhood Arthritis Rheumatology Research Alliance; Leadership or fiduciary role in other board, society, committee or advocacy group: American Academy of Pediatrics (payment to me), Childhood Arthritis Rheumatology Research Alliance (grant to institution), CureJM Clinical Care Network (unpaid), Consultant with: CureJM (Medical Advisory Board Member), Speaker Bureau with: American College of Rheumatology, American Board of Pediatrics (honoraria paid to me), G. Simonini: None declared, T. Griffin: None declared, A. Zeft: None declared, G. Horneff Grant/Research Support with: Pfizer, Novartis, Roche, Janssen; Support for attending meetings and/or travel: Sobi, Consultant with: Sanofi, Novartis, Speaker Bureau with: AbbVie, Bayer, GSK, Novartis, P. Quartier Consultant with: AbbVie, Chugai-Roche, Eli Lilly, Novartis, Pfizer, Sobi (consultant, speaker/honoraria [includes speakers bureau, symposia, and expert witness]); Sanofi (advisor or review panel member, consultant), I. Orban: None declared, H. Walters: None declared, V. Stanevica: None declared, J. Patel: None declared, A. Huber: None declared, M. Rosenkranz: None declared, D. Kingsbury: None declared, R. Scuccimarri Grant/Research Support with: Bristol Meyers Squibb (involvement in patient registry), G. Vega Cornejo: None declared, J. Swart Grant/Research Support with: Pfizer (research grant payment to institution), Consultant with: Pfizer (payment to institution); Participation on a Data Safety Monitoring Board or Advisory Board: Bristol Myers Squibb (payment to institution); Leadership or fiduciary role in other board, society, committee or advocacy group: ERN-RITA coordinator (payment to institution), PRES-council member (unpaid), Speaker Bureau with: Pfizer (payment to institution), R. Carroll Shareholder with: Bristol Myers Squibb, Employee with: Bristol Myers Squibb, T. Sherrard: None declared, C. Pallotti: None declared, C. Malattia: None declared, D. Lovell Grant/Research Support with: Bristol Meyers Squibb (supporting study, analysis publication cost, Coordinating Center Contract [to my institution for this study]), Consultant with: Pfizer, Jannsen Pharmaceuticals (consultant for JIA studies to my institution); Participation on a Data Safety Monitoring Board or Advisory Board: NIAMS-NIH DSMB member, NIAID-NIH DSMB member (payment to me), A. Martini Consultant with: Pfizer

References
1. Brunner HI, Tzaribachev N, Vega-Cornejo G, et al. Subcutaneous abatacept in patients with polyarticular-course juvenile idiopathic arthritis: results from a phase III open-label study. *Arthritis Rheumatol* 2018;70(7): 1144-54. 2. Ruperto N, Lovell DJ, Quartier P, et al. Abatacept in children with juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled withdrawal trial. *Lancet* 2008;372(9636): 383–91. 3. Lovell DJ, Tzaribachev N, Henrickson M, et al. Safety and effectiveness of abatacept in juvenile idiopathic arthritis: results from the PRINTO/PRCSG registry. *Rheumatology (Oxford, England)* 2024;63(Si2): SI195-SI206.

P233

Investigation of biopsychosocial characteristics according to the pain catastrophizing status reported by parents in patients diagnosed with adolescent Jia: a pilot study

O. Tüfekçi[1], A. Barlak[1], S. Buran[1], E. Aliyev[2], M. O. Erkan[2], Y. Bilginer[2], E. Ünal[1], S. Özen[2]
[1]Faculty of Physical Therapy and Rehabilitation, [2]Department of Pediatrics, Division of Rheumatology, Hacettepe University, Ankara, Türkiye
Correspondence: S. Buran
Pediatric Rheumatology, **23(2):** P233

Introduction: Juvenile idiopathic arthritis (JIA) is the main rheumatologic disease reported in the pediatric group. It has been reported that parents' thoughts and feelings about pain (pain cognitions) in the disease management of their children diagnosed with JIA may play a role in treatment compliance (1, 2). Especially considering that this situation may also affect children's compliance with treatment, the importance of identifying and managing parents' pain catastrophizing is emphasized in improving treatment outcomes (2, 3).
Objectives: This pilot study aimed to examine the biopsychosocial characteristics of patients diagnosed with adolescent JIA according to parent-reported pain catastrophizing.
Methods: In this study, 40 cases (21 girls, 19 boys) diagnosed with adolescent JIA who were followed up with routine controls were included. Demographic information of the patient and their parents was recorded. For adolescent patients; Pain catastrophizing status was assessed by Pain Catastrophizing Scale for Children (PCS-C), disease activity by Juvenile Arthritis Disease Activity Score in 27 joints (JADAS-27), activities of daily living by Childhood Health Assessment Questionnaire (CHAQ), participation by Child and Adolescent Scale of Participation (CASP) and biopsychosocial status by Juvenile Arthritis Biopsychosocial-Questionnaire-Child (JAB-Q-C), for parents, pain catastrophizing status Pain Catastrophizing Scale for Parents (PCS-P), biopsychosocial status "Juvenile Arthritis Biopsychosocial-Questionnaire-Parents" (JAB-Q-P). According to the PCS-P score, the participants were classified into two groups within the study: low pain catastrophizing with a score range of 0-24 (Group 1) and high pain catastrophizing with a score of 25-48 (Group 2). The characteristics of the groups were compared with "The Mann-Whitney U test." The relationships between the scales were examined using Spearman correlation analysis.
Results: The demographic characteristics of the parents who reported low and high levels of pain catastrophizing and the patients were similar (p>0.05). While there was no difference between the adolescent cases according to the pain catastrophizing status of the parents (p>0.05), the JAB-Q-P scores of the parents were better in favor of Group 1 (p<0.05). A moderate correlation was found between PCS-P and JABQ-P scores.
Conclusion: In this pilot study, it was observed that the parents with high pain catastrophizing status had worse biopsychosocial status. However, it was determined that the adolescent cases were not affected at the same rate by parents' pain catastrophizing status. The results obtained from the study were interpreted to suggest that parents' pain catastrophizing status should be evaluated in the disease management of patients diagnosed with adolescent JIA, and parents' education should be provided on this issue. It was decided to continue the study to interpret the results with more patients.
Disclosure
None declared

References
Brandelli YN, Chambers CT, Tutelman PR, Stinson JN, Huber AM, Wilson JP. Parent pain cognitions and treatment adherence in juvenile idiopathic arthritis. *J Pediatr Psychol*. 2019;44(9):1111–9.
Şener S, Karaca NB, Kaşlı K, Özçadırcı A, Batu ED, Başaran Ö, et al. Comparison of biopsychosocial characteristics of children with juvenile idiopathic arthritis according to common disease subtypes. *Turk Arch Pediatr*. 2023;58(6):625–30.
Şentürk İA, Ünal E, Tarakçıoğlu MC, Kepekçi M, Yıldız EP. Preliminary validation of the Turkish version of the pain catastrophizing scale for children and parents (PCS-C and PCS-P) in primary childhood headache. *Agri*. 2022;34(4):278–91.

P234

Personalising adalimumab therapy in patients with juvenile idiopathic arthritis: definition of cut-off concentration for therapeutic drug monitoring and impact of the FCGR3A RS396991 genetic variant

P. Dalla Zuanna[1,2,3], D. Curci[1], M. Klanjscek[2,4], G. Pauli[2], M. Lucafò[5], R. Franca[2], A. Fabretto[1], A. Tommasini[2,4], A. Taddio[2,4], A. Arbo[4], S. Pastore[4], G. Stocco[1,2]
[1]Diagnostica avanzata traslazionale, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, [2]Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, [3]Clinical and Experimental Pharmacology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, aviano, [4]Institute for Maternal and Child Health, IRCCS Burlo Garofolo, [5]Department of Life Sciences, University of Trieste, Trieste, Italy
Correspondence: P. Dalla Zuanna
Pediatric Rheumatology, **23(2):** P234

Introduction: Adalimumab (ADM) is an effective therapeutic choice in juvenile idiopathic arthritis (JIA). However, many patients do not respond to therapy or lose response over time due to a pharmacokinetic (PK) failure. Knowing a cut-off of adalimumab levels for therapeutic drug monitoring (TDM) and genetic variants that impact the PK of adalimumab can reduce the rate of therapeutic failures (1,2).
Objectives: To confirm the association between serum adalimumab levels and anti-adalimumab antibodies (AAA) appearance with clinical remission and disease activity in JIA patients, to calculate a cut-off for TDM and to evaluate the effect of the *FCGR3A* rs396991 on adalimumab levels, ADA appearance, clinical remission and disease activity.
Methods: JIA patients (age < 16y at diagnosis) treated with adalimumab for more than 2 months (6 months for correlations with remission) were considered. Clinical remission was evaluated according to Wallace criteria (3). Disease activity was assessed using JADAS27 clinical score. adalimumab was quantified in serum using a lateral flow assay while an ELISA kit was used to detect AAA. Genetic analyses were conducted using TaqMan assay. Statistical analyses were performed using software R. The association between continuous-categorical, continuous-continuous and categorical-categorical variables was assessed respectively by the Kruskal-Wallis, Spearman's and Chi-squared test. ROC curve was constructed for adalimumab levels to determine the optimal therapeutic cut-off.
Results: Fourty-seven patients, for a total of 134 samples (median age 11.96 years, 33 female, median therapy duration 21.3 months) were enrolled. adalimumab levels were higher in patients in clinical remission (p=0.033, median 6.8 mg/L (IQR: 12.7) vs 13.5 mg/L (IQR: 12)) and inversely correlated with JADAS27 (p=0.015, r=−0.21). The cut-off for adalimumab levels associated with remission is 6.9 mg/L (ROC AUC=61.6%, specificity=53.1%, sensitivity=75.0%). Regarding pharmacogenetics, adalimumab levels tended to be lower in patients carrying the *FCGR3A* rs396991 variant, in both the additive, recessive and dominant models (p=0.080, 0.058 and 0.081 respectively).
Conclusion: Adalimumab levels are correlated with clinical remission and JADAS27, with a cut-off of 6.9 mg/L that could be considered for dose adjustment. Furthermore, the *FCGR3A* rs396991 presented a trend with reduced adalimumab levels. After validation by further studies, adalimumab levels and the *FCGR3A* rs396991 could be proposed as pharmacological determinants useful to personalize adalimumab therapy in patients with JIA.

Disclosure
None declared

References
Dehoorne JL, Groth H, Carlé E, De Schrijver I, Sys C, Delbeke P, et al. Defining a therapeutic range for adalimumab serum concentrations in the management of pediatric noninfectious uveitis, a step towards personalized treatment. Pediatr Rheumatol. 2023 Dec 20;21(1):148.
Tutuncu Z, Kavanaugh A, Zvaifler N, Corr M, Deutsch R, Boyle D. Fcγ receptor type IIIA polymorphisms influence treatment outcomes in patients with inflammatory arthritis treated with tumor necrosis factor α–blocking agents. Arthritis & Rheumatism. 2005 Sep;52(9):2693–6.
Wallace CA, Ruperto N, Giannini E, Childhood Arthritis and Rheumatology Research Alliance, Pediatric Rheumatology International Trials Organization, Pediatric Rheumatology Collaborative Study Group. Preliminary criteria for clinical remission for select categories of juvenile idiopathic arthritis. J Rheumatol. 2004 Nov;31(11):2290–4.

P235

The impact of the covid-19 pandemic on new onset juvenile idiopathic arthritis in Canada and The Netherlands

R. Quilty[1], A. Cheng[1], D. Marshall[2], S. Vastert[3], J. Swart[3], S. Benseler[4,5], R. S. M. Yeung[1], on behalf of the UCAN CAN-DU consortium
[1]Pediatric Rheumatology, The Hospital for Sick Children, Toronto, [2]Community Health Sciences, University of Calgary, Calgary, Canada, [3]Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [4]Pediatric Rheumatology, Alberta Children's Hospital Research Institute, Calgary, Canada, [5]Children's Health Ireland, Dublin, Ireland
Correspondence: R. Quilty
Pediatric Rheumatology, **23(2):** P235

Introduction: Healthcare delivery changed dramatically during the COVID-19 pandemic, impacting care. Gaps remain in our understanding of the impact on juvenile idiopathic arthritis (JIA) management in different countries.
Objectives: To study the impact of the COVID-19 pandemic on JIA presentation at pediatric rheumatology centers in Canada and the Netherlands.
Methods: Consecutive patients enrolled in UCAN CAN-DU, an international, prospective observational study of children with JIA in Canada and the Netherlands. This study focused on the subgroup of children with treatment naïve new onset JIA, whose baseline clinic visit was from October 1, 2018, to May 31, 2024. Three intervals were compared: pre-pandemic (Oct 1, 2018–Feb 28, 2020), intra-pandemic (Mar 1, 2020–Dec 31, 2023), and post-pandemic (Jan 1–May 31, 2024). Comparisons were also made between countries within each interval. Assessed variables included demographics, clinical features including disease activity indices, patient-reported outcomes, and time from symptom onset to diagnosis. Descriptive and comparative analyses were completed.
Results: A total of 593 patients (303 in Canada, 290 in the Netherlands) were included: 76 pre-pandemic, 478 intra-pandemic, and 39 post-pandemic. Overall, 60.5% were female, median age at diagnosis was 9.4 years (IQR 3.9–13.2), and oligoarticular JIA was the most common subtype (53.3%). Median time from symptom onset to diagnosis was 134 days (IQR 61–327), with no significant differences across intervals. The following measures of disease activity were significantly higher in the pandemic time period compared to post-pandemic time with a higher median active joint count (AJC) (2, IQR 1-5), clinical juvenile arthritis disease activity score (cJADAS)10 (10, IQR 5.7-14.9), and physician global assessment (PGA) (3, IQR 2-4.5) compared to a median AJC of 1 (IQR 1-2), cJADAS10 of 7 (IQR 4.5-8.5), and PGA 2 (IQR 1-4.3) during the post-pandemic period. During the pandemic, Dutch centers had shorter median time to diagnosis (110.5 days, IQR 58–241) compared to 125 days (IQR 61-301) in Canada.
Conclusion: The UCAN CAN-DU study allowed evaluation of the impact of the COVID-19 pandemic on JIA diagnosis in Canada and the Netherlands. It was clear that disease activity was higher during the pandemic than post-pandemic. The Netherlands had shorter time to diagnosis during the pandemic, likely reflecting national differences in in-person care policies—which were more restricted in Canada. These results have potentially important implications for epidemic related health care policy guidelines for children with chronic diseases.
Disclosure
None declared

P236

Global variations in AI-generated information on juvenile idiopathic arthritis

S. La Bella[1,2], D. Bayraktar[3,4], A. Porreca[5,6], L. C. Li[4,7], M. Attanasi[8], E. Aliyev[9], A. Migowa[10], C. Scott[11], D. R. Thakare[12], Y. Bayindir[9], A. Consolaro[1], B. Feldman[13,14], S. Ozen[9]
[1]UOC Rheumatology and Autoinflammatory Diseases, IRCCS Istituto Giannina Gaslini, Genova, [2]Paediatric Rheumatology Unit, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, [3]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir Katip Celebi University, Izmir, Türkiye, [4]Arthritis Research Canada - British Columbia, Vancouver, Canada, [5]Department of Human Sciences and Promotion of the Quality of Life, San Raffaele University, [6]Unit of Clinical and Molecular Epidemiology, IRCCS San Raffaele, Roma, Italy, [7]Department of Physical Therapy, University of British Columbia, Vancouver, Canada, [8]Department of Paediatrics, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy, [9]Faculty of Medicine, Department of Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye, [10]Department of Paediatrics and Child Health, Aga Khan University, Nairobi, Kenya, [11]Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Canada, [12]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, [13]Department of Rheumatology, The Hospital for Sick Children, [14]Child Health Evaluative Sciences, Research Institute, The Hospital for Sick Children, Toronto, Canada
Correspondence: S. La Bella
Pediatric Rheumatology, **23(2):** P236

Introduction: Several studies assessed the performance of large language models (LLMs) in answering medical questions. However, little is known about regional differences in their behavior. It is unclear if the same questions prompted from different parts of the world result in responses with similar readability, text organization, and accuracy.
Objectives: We aimed to evaluate similarities and variations across responses generated by a broadly used LLM (ChatGPT 4o) to validated questions about oligoarticular juvenile idiopathic arthritis (oJIA) across five different countries representing different regions of the world.
Methods: The ten PICOs related to the oJIA treatment on the 2021 ACR recommendations (1, 2) were simultaneously prompted in English to ChatGPT 4o from Canada, India, Italy, Kenya and Türkiye. Readability was assessed with the Flesch Reading Ease Score (FRES), distinctiveness of terms through the Term Frequency Inverse Document Frequency (TF-IDF) analysis. Co-occurrence networks (CONs) detailed the relationships between terms. Three independent experts rated the adherence of the responses to the recommendations using a Likert-like scale. Agreement within experts was assessed with the Cohen's Kappa.
Results: The 50 responses provided by ChatGPT had a median of 454 [352-556] words, 20 [16-27] sentences, and 43 [26-54] percent of passive sentences. No differences were observed across countries in terms of words, sentences, and percentage of passive sentences. The readability was low. All the responses were difficult (25, 50%) or very difficult (25, 50%) to read, with a median FRES of 30 [24-34]. There was a variation in the readability based on the question, with often similar behaviour within countries. Experts determined that the majority of responses were mostly or fully adherent to the 2021 ACR recommendations. Responses mostly or fully adherent to recommendations ranged from 26/50 (52%, rater 1) to 42/50 (84%, rater 3). No response was considered not adherent at all, and accuracy was similar across different countries. Inter-rater agreement on the adherence of LLM-generated responses was generally weak (Kappa values mostly below 0.40), highlighting the challenges of consistently evaluating AI-generated medical information. The TF-IDF analysis showed that the distinctiveness of terminology in LLM-generated responses varied across countries, with scores ranging from 0.60 to 0.85. CONs detailed how regional differences can influence responses from the LLM: Canada focused on broad-spectrum treatment; India strongly prioritized

methotrexate as a primary systemic treatment; Italy emphasized intra-articular corticosteroid treatments and the role of uveitis; Kenya focused on intra-articular therapies and their short- and long-term efficacy; Türkiye highlighted diversity in DMARDs and their therapeutic combinations with intra-articular options.
Conclusion: While regional factors may influence the way LLMs present information across different countries, the overall adherence of responses to the recommendations remains satisfactory, even with variations depending on the expert, with promising applications in healthcare settings. However, the low readability, the variability highlighted by the experts in evaluating AI's accuracy, and differences in emphasis and terminology depending on the questions across diverse countries suggest the importance of critical evaluation of LLM outputs.
Trial registration identifying number: Not applicable.
Disclosure
None declared

References
Onel et al, Arthritis Rheumatol 2022
Onel et al, Arthritis Rheumatol 2022

P237

Effects of an 8-week online yoga intervention on physical activity and motivation in patients with juvenile idiopathic arthritis: preliminary results from a pilot study

S. Y. Cetin[1], S. N. Arman[2], A. Yekdaneh[3,4], S. Caglayan[5], N. Aktay Ayaz[6]
[1]Department of Physiotherapy and Rehabilitation, Akdeniz University, Antalya, [2]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpaşa, [3]Vocational School of Health Services Physiotherapy English Program, Fenerbahce University, [4]2Institute of Graduate Studies Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpaşa, İstanbul, [5]Department of Pediatric Rheumatology, Antalya Training and Research Hospital, Antalya, [6]Department of Pediatric Rheumatology, İstanbul University, İstanbul, Türkiye
Correspondence: S. Y. Cetin
Pediatric Rheumatology, **23(2):** P237

Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic condition that limits physical activity and impacts motivational levels in children. Yoga, as a mind-body intervention, may help improve physical engagement and motivation, particularly in non-traditional exercise programs as a complementary method.
Objectives: This pilot study aimed to investigate the effect of an 8-week online yoga intervention on physical activity levels and motivation for physical activity in children diagnosed with JIA.
Methods: Fourteen children diagnosed with JIA (mean age: 11.9 years) participated in a structured online yoga program delivered via 'Google Meet'. The intervention consisted of two sessions per week over eight weeks (16 sessions total). Physical activity was assessed using the Physical Activity Questionnaire for Children/Adolescents (PAQC/A), and motivation levels were measured using a standardized motivation scale. Both assessments were conducted at baseline (t0) and post-intervention (t1). PAQC/A scores were further classified into two categories to reflect physical activity adequacy: scores ≥2.5 for girls and ≥2.7 for boys were categorized as "good" physical activity level, while lower scores were categorized as "poor." Statistical analyses were conducted using paired samples t-tests to evaluate changes in physical activity and motivation scores before and after the intervention.
Results: There was a statistically significant improvement in both physical activity and motivation scores following the yoga intervention. The mean PAQC/A score increased from 2.50 (±0.83) at t0 to 2.85 (±0.74) at t1 ($p = 0.008$). Motivation scores increased from 54.14 (±10.52) to 56.64 (±11.78) ($p = 0.013$). At baseline, 5 children (35.7%) were classified as having "good" physical activity levels, while 9 (64.3%) were "poor." After the intervention, 10 children (71.4%) were classified as "good," and only 4 (28.6%) remained in the "poor" category. PAQC/A scores improved in 9 participants (64.3%), and motivation scores improved in 7 participants (50%).
Conclusion: The 8-week online yoga intervention significantly enhanced physical activity levels and motivation in children with JIA. The increase in the number of children classified as having "good" physical activity post-intervention further supports the effectiveness of the yoga program. These findings suggest that remote yoga interventions are a feasible and beneficial addition to supportive care strategies in pediatric rheumatology as a complementary method.
Disclosure
None declared

P238

Distinct gut microbiota in untreated oligoarticular Juvenile idiopathic arthritis

S. Yüksel[1], E. Dönmez [2], A. U. Özsoy[3], D. Şener Okur[4]
[1]Pediatric Rheumatology, Çanakkale Onsekiz Mart University, Çanakkale, [2]Pediatrics, Pamukkale University, Denizli, [3]Diagen Biotechnological Systems Health Services, Istanbul, [4]Pediatric Infectious Diseases, Pamukkale University, Denizli, Türkiye
Correspondence: S. Yüksel
Pediatric Rheumatology, **23(2):** P238

Introduction: Oligoarticular Juvenile Idiopathic Arthritis (JIA) is the most common chronic rheumatic disease in childhood, with a multifactorial etiology. Emerging evidence suggests that intestinal dysbiosis may play a crucial role in modulating immune responses and contributing to JIA pathogenesis.
Objectives: This study aimed to comprehensively characterize and compare fecal microbiota composition, diversity, and specific bacterial alterations in treatment-naïve children diagnosed with oligoarticular JIA against healthy pediatric controls, while acknowledging potential confounding factors such as age.
Methods: This prospective, single-center comparative study enrolled 25 treatment-naïve children (median age 150 months; 6 months-16 years) with oligoarticular JIA and 25 healthy control children (median age 50 months; 0-18 years). A significant difference in median age between groups was noted (p=0.0001). Demographic data, clinical parameters including Body Mass Index (BMI) and Juvenile Arthritis Disease Activity Score (JADAS), were recorded. Fecal samples were collected, and genomic DNA was extracted. The V3-V4 region of the 16S rRNA gene was sequenced. Bioinformatics analyses (QIIME 2, DADA2, SILVA database) assessed alpha diversity (Chao1, Shannon, Simpson, Pielou's evenness) and beta diversity (Jaccard distance, PERMANOVA). Differential abundance analysis was performed using ANCOM-BC. The potential influence of age on key microbial findings was considered during interpretation. Ethical approval (Pamukkale University, E-60116787-020-299011, 29.11.2022) and parental consent were obtained.
Results: Despite the age difference, distinct microbial patterns emerged. Alpha diversity (Chao1 index) was significantly higher in JIA patients ($p<0.004$). Beta diversity (Jaccard distance, PERMANOVA) showed a significant difference in microbial community structure (p=0.002). ANCOM-BC analysis at the genus level identified a significant increase in *Catenibacterium* (LFC 1.58), *Family XIII AD3011 group* (LFC 0.79), *Howardella* (LFC 1.10), *Holdemanella* (LFC 1.73), *Megasphaera* (LFC 1.32), and *Akkermansia* (LFC 1.28) in JIA patients. Conversely, *Lactococcus* (LFC −0.93), *Rothia* (LFC −1.43), *Clostridium sensu stricto 1* (LFC −1.40), and *Lactobacillus* (LFC −1.63) were significantly decreased. Descriptively, *Oscillibacter* and *Alistipes* were more abundant, while *Faecalibacterium* was less abundant in JIA patients; this trend for *Faecalibacterium* and the increase in *Akkermansia* persisted even when considering the age disparity by exploratory sub-analysis excluding younger controls.
Conclusion: Children with oligoarticular JIA exhibit distinct fecal microbiota profiles compared to healthy controls, even when considering the observed age difference as a study limitation. The increase in potentially pro-inflammatory genera like *Akkermansia* and *Megasphaera*, and a decrease in beneficial genera like *Lactobacillus* and *Faecalibacterium*, suggest intestinal dysbiosis in JIA. While these findings are significant, the age disparity underscores the need for future studies with rigorously age-matched cohorts to definitively separate disease-specific microbial shifts from age-related variations and to further elucidate the role of the gut microbiome in JIA pathogenesis.
Disclosure
None declared

P239

Experience with janus kinase inhibitors in refractory Juvenile idiopathic arthritis patients: a single-center real-world study

S. Atamyıldız Uçar, E. Tunce, N. Kara Çanlıoğlu, B. Sözeri
Pediatric Rheumatology, University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Türkiye
Correspondence: S. Atamyıldız Uçar
Pediatric Rheumatology, **23(2):** P239

Introduction: Juvenile idiopathic arthritis (JIA) is a heterogeneous chronic inflammatory disorder in children, and a subset of patients remains refractory despite multiple biologic treatments. Janus kinase inhibitors (JAKi) have emerged as a promising therapeutic option for difficult-to-treat cases.
Objectives: To evaluate the effectiveness of JAKi in refractory JIA patients.
Methods: This cross-sectional study included a total of 27 refractory JIA patients who were initiated on JAKi (tofacitinib and/or upadacitinib) at a referral pediatric rheumatology center. JIA patients were categorized according to the ILAR criteria. Demographic, clinical and laboratory data, as well as treatment choices and switches, were recorded.
Results: Among the patients, 21 (77.8%) were female. The median age at diagnosis was 10.2 (IQR,5.4-11.9) years, and the median age at initiation of DMARD was 10.4 (IQR,5.4-12) years. The median age at initiation of biologic agents was 11.1 (IQR,7.8-14.5) years. Based on JIA subtypes, 14 (51.9%) had RF-negative polyarticular JIA, 5 (18.5%) had enthesitis-related arthritis, 4 (14.8%) had oligoarticular JIA, 2 (7.4%) had RF-positive polyarticular JIA, and 2 (7.4%) had juvenile psoriatic arthritis. The first-line biologic agents included etanercept in 19 (70.4%), adalimumab in 6 (22.2%), and infliximab in 2 (7.4%). JAKi were used as fourth-line (range, 2^{nd}–7^{th}) treatment. Except 2 patients, all had failed at least one anti-TNF therapy in addition to either tocilizumab or secukinumab. The median age at JAKi initiation was 15.6 (IQR,13-16.8) years. Tofacitinib was the first-choice in 24 patients (88.9%), while upadacitinib was preferred in 3 patients (11.1%).
17 (62.9%) patients experienced treatment failure with the initial JAK inhibitor. Of these, seven were switched to another JAKi—six to upadacitinib and one to tofacitinib. Among the switched patients, four are currently continuing JAKi, whereas the treatment of three has been switched to other biologic agents.
During follow-up, uveitis was observed in only two patients, both of whom had been diagnosed with uveitis prior to initiation of JAKi. In both cases, tofacitinib was initiated due to uveitis-related symptoms. One patient required a treatment switch due to uveitis reactivation, while the other continued to receive tofacitinib with sustained remission of uveitis symptoms. At the last visit, 14 patients (54.1%) were still on JAKi. All patients demonstrated full adherence to oral JAKi, and no difficulties in compliance were reported during the follow-up period.
Conclusion: This study highlights the promising effectiveness of JAKi in patients with treatment-resistant JIA. Approximately half of the patients who had failed at least three biologic therapies continued JAKi due to observed clinical benefit. However, larger randomized controlled trials are needed to validate these findings and to assess the long-term safety profile of these therapies.
Disclosure
None declared

P240

How do we define flare in Juvenile idiopathic arthritis?

M. Burrone[1], S. M. Orsi[1], A. Amodio[2], V. Rypdal[3,4], F. O. Ramos[5,6], J. Guzman[7], J. Swart[8], A. Ravelli[1,9], M. Gattorno[10], A. Consolaro[1,10]
[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Università degli Studi di Genova, Genova, [2]Università degli studi della Campania "Luigi Vanvitelli", Napoli, Italy, [3]Department of Pediatrics, University Hospital of North Norway, [4]Department of Clinical Medicine, UIT the Arctic University of Norway, Tromsø, Denmark, [5]Rheumatology and Pediatric Department, University Hospital Santa Maria, [6]Faculdade de Medicina, Universidade de Lisboa, lisboa, Portugal, [7]Department of Pediatrics, University of British Columbia, Vancouver, Canada, [8]Department of Pediatric Immunology and Rheumatology, Wilhelmina Children's Hospital, Utrecht, Netherlands, [9]Scientific Direction, UOC Servizio Sperimentazioni Cliniche pediatriche, [10]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genova, Italy
Correspondence: S. M. Orsi
Pediatric Rheumatology, **23(2):** P240

Introduction: Assessing disease activity in juvenile idiopathic arthritis (JIA) is essential for both clinical practice and research. While cutoffs to define disease activity states in oligoarticular and RF-negative polyarticular JIA were published in 2021 and later validated for other subtypes, a standardized definition according to the International League of Associations for Rheumatology (ILAR) classification of disease flare remains lacking. This limits comparability across studies and may influence treatment decisions. A preliminary flare based on the six core response variables (CRVs) was proposed by Brunner et al. in 2002, but it was only preliminary validated and it was not adopted in all trials. This highlights the urgent need for a wildly accepted flare definition.
Objectives: To describe the definitions of disease flare used in JIA clinical trials and highlight the heterogeneity across studies.
Methods: A literature search of ClinicalTrials.gov and PubMed was conducted to identify JIA trials reporting a definition of flare. Trials initiated between May 1997 and January 2025 were considered. Trials without a clearly stated flare definition were excluded. A descriptive analysis was performed to assess the frequency and characteristics of definitions used.
Results: 38 JIA trials were identified; 10 were excluded due to the absence of a flare definition. Among the 28 included studies, the most adopted definition (16/28, 57%) was the PRINTO/PRCSG criteria developed by Brunner et al., defining flare as a ≥30% worsening in at least three of the six core set variables (CRVs), without ≥30% improvement in any CRV, and requiring at least two active joints, with the
Reference point being the end of phase 1. Five trials (18%) defined flare as the reappearance of active disease after a previously inactive joint count. Four studies (14%) adopted a definition of flare based on the juvenile arthritis disease activity score (JADAS): a patient previously in inactive disease was considered to experience a flare if he/she had a JADAS above the thresholds for minimal disease activity (2 studies) or for moderate disease activity (2 studies). Other definitions included worsening of CHAQ, ESR, and AJC, or the need to intensify treatment.
Conclusion: The analysis confirms significant heterogeneity in how flare is defined across JIA trials. While the PRINTO/PRCSG definition is most common, it has notable limitations, including its validation in a small population and the discontinuation of follow-up once flare criteria were met. Additionally, the
Reference visit for comparison is not consistently defined. While JADAS-based definitions offer a simplified tool, optimal cutoffs for flare detection remain undefined. The results of this survey highlight the need for an evidence-based definition of flare in JIA.
Disclosure
None declared

P241

Cytological analysis of synovial fluid in patients with Juvenile idiopathic arthritis

S. Djordjevic[1,2], M. Vitomirac[2], M. Cazic[3], H. Petrovic[1], D. Lazarevic[4,5], D. Novakovic[6], G. Susic[1]
[1]Division of Pediatric Rheumatology, University Children's Hospital, [2]Faculty of Medicine, University of Belgrade, [3]Immunology laboratory, University Children's Hospital, Belgrade, [4]Department of Pediatric Rheumatology, Clinic of Pediatrics, University Clinical Center Nis, [5]Faculty of Medicine, University of Nis, Nis, [6]Division of Pediatric Rheumatology, Institute of Rheumatology, Belgrade, Serbia
Correspondence: S. Djordjevic
Pediatric Rheumatology, **23(2):** P241

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease in children and is considered a diagnosis of exclusion. Cytological analysis of synovial fluid (SF) plays an important role in the differential diagnosis of arthritis.
Objectives: To assess the association between the clinical and laboratory characteristics of JIA and the cytological findings of SF.

Methods: This was a retrospective cross-sectional study conducted between February 2022 and December 2024. The study included all patients who were ultimately diagnosed with juvenile idiopathic arthritis (JIA) and who had undergone diagnostic arthrocentesis at presentation. Patients were excluded if they had received anti-inflammatory therapy prior to arthrocentesis, if an adequate amount of synovial fluid for cytological analysis was not obtained, or if the joint puncture was traumatic.
The following data were collected for all patients: sex, age at the time of arthrocentesis, disease duration prior to arthrocentesis, JIA subtype, antinuclear antibody (ANA) and rheumatoid factor (RF) status, presence of HLA-B27 antigen, presence of systemic inflammation, and associated anterior uveitis.
Results: A total of 61 patients were included (47 female, 14 male). The median age at arthrocentesis was 6.3 years (range: 1.5–17 years), and the median disease duration was 97 days (range: 7–1,481 days). Among them, 38 (62.30%) had oligoarticular JIA, 13 (21.31%) polyarticular, 5 (8.20%) enthesitis-related arthritis (ERA), 3 (4.92%) undifferentiated, and 2 (3.28%) systemic JIA (sJIA). None of the patients had psoriatic arthritis.
The median white blood cell (WBC) count in synovial fluid was 7,056/mm^3 (range: 991–67,200/mm^3). WBC counts differed significantly among the oligoarticular, polyarticular, and ERA subtypes ($\chi^2(2) = 18.966$, $p = 0.001$), with the highest values observed in the ERA subgroup. Male patients had a significantly higher WBC count than female patients (median: 11,927.5 vs. 5,712/mm^3; $U = 198$, $p = 0.025$).
No statistically significant correlation was observed between WBC count in synovial fluid and age at arthrocentesis ($r(61) = 0.221$, $p = 0.088$) or disease duration prior to arthrocentesis ($r(61) = -0.041$, $p = 0.753$). Patients with a positive HLA-B27 antigen had a significantly higher absolute neutrophil count (median: 6,543.6/mm^3; range: 247.0–25,401.6/mm^3) compared to HLA-B27-negative patients (median: 2,016.0/mm^3; range: 0–63,840.0/mm^3) ($U = 164.0$, $p = 0.008$).
Conclusion: Cytological findings in synovial fluid vary according to the clinical subtype of JIA and may partially overlap with those observed in other forms of arthritis and arthropathies. When patients with sJIA and undifferentiated JIA are excluded, the highest WBC and granulocyte counts are seen in ERA. The higher WBC count observed in male patients may reflect the higher prevalence of males within the ERA subgroup.
Disclosure
None declared

References

1. Martinez Del Val E, Rodriguez Martinez A, Sanchez Becerra V, Cruz Rojo J, Enriquez Merayo E, Barral Mena E, et al. Characteristics of synovial fluid in patients with juvenile idiopatic arthritis. An Pediatr (Engl Ed). 2019; 91(4):244-250.
2. Brannan SR, Jerrard DA. Synovial fluid analysis. J Emerg Med. 2006;30(3):331-339.

P243

Enhancing Juvenile idiopathic arthritis management through co-designed devices: insights from a feasibility study

U. Ankeny[1], C. Dunbar[2], N. Dulake[1], J. Langley[1], D. P. Hawley[2]
[1]Lab4Living, Sheffield Hallam University, [2]Rheumatology, Sheffield Children's Hospital, Sheffield, United Kingdom
Correspondence: U. Ankeny
Pediatric Rheumatology, **23(2):** P243

Introduction: Juvenile Idiopathic Arthritis (JIA) is the most common childhood rheumatic disease, causing pain, joint inflammation and stiffness requiring daily self-management[1]. Existing studies highlight significant impacts across emotional, physical, social, psychological, and educational wellbeing. Despite this, JIA remains largely invisible in the technology space, with available products often designed for adults or perceived by children and young people (CYP) as stigmatising or failing to respond to their unique needs[2-5].
This feasibility study builds on prior co-design work and a successful proof-of-concept study[6], trialling a suite of three co-designed technologies, collectively called 'JIA Toolbox', developed in response to needs identified by CYP, parents, healthcare professionals and teachers.
Objectives: To assess the effectiveness of the improved 'JIA Toolbox' in supporting CYP's self-management, particularly regarding independence and functional ability.
To obtain real-world feedback to guide future development.
To gather contemporary insights into daily experiences of managing JIA.
Methods: 'JIA Toolbox' comprises three co-designed prototype devices: P1: A wearable pain management device, P2: A motivational physiotherapy tool and P3: A school-based communication aid.
25 CYP (aged 7–16) with JIA, their parents and teachers used 'JIA Toolbox' over a 16-week period in a self-directed manner. Initial training was provided. Data collection included baseline, intervention, and post-intervention self-reported diaries, interviews, and prototype usage data.
Results: Preliminary analysis indicates 85–95% of participants found one or more tools beneficial. Reported improvements included better pain management, enhanced adherence to physiotherapy, improved classroom communication, and greater independence. Usage varied by individual need, reflecting the fluctuating nature of JIA.
P 1
was the most widely used, described as helpful for "aching and stiffness" due to its soothing effects. One participant noted regret at not bringing it to school during a flare.
P 2
supported physiotherapy adherence, with one participant progressing from non-adherence to regular stretching, reportedly leading to functional improvements. The gamification element was positively received.
P 3
's impact was influenced by classroom confidence and school support. Where used, CYP "did not feel embarrassed asking for help", improving communication with teachers, enabling stronger relationships and understanding of the condition
Battery life emerged as a consistent area for improvement across devices.
Conclusion: This feasibility study suggests the 'JIA Toolbox' is a suite of beneficial tools to support self-management for CYP with JIA. It also underscores the value of addressing the less visible aspects of the condition, such as disbelief in schools or physiotherapy motivation. These findings suggest potential applicability beyond JIA as these needs are not specific to JIA. Next steps include further device development based on this study data, and applying for a larger funding grant to carry out a multi-site pilot study.
Disclosure
None declared

Reference

1. References available upon request

P244

Difficult-to-treat subgroup in the single-centre cohort of paediatric still's disease

A. Kozáková, Š. Fingerhutová, P. Šeferna, K. Šingelová, P. Doležalová, N. Husáková
Department of Pediatrics and Inherited Metabolic Disorders, General University Hospital in Prague, Prague, Czech Republic
Correspondence: A. Kozáková
Pediatric Rheumatology, **23(2):** P244

Introduction: Difficult-to-treat (D2T) subgroup of Still's disease is characterised by failure to respond to IL-1 and IL-6 blockade, severe or recurrent macrophage activation syndrome (MAS) and lung disease (LD).
Objectives: Review of the presentation and disease outcomes of D2T paediatric Still's disease (SJIA) patients on the background of the SJIA cohort.
Methods: Retrospective electronic record review (2005-2020) and prospective (2021-2024) data collection on patients with SJIA.
Results: 66 patients (39 girls) fulfilling SJIA ILAR and/or PRINTO criteria were identified. Mean follow-up (F/U) time was 6.2±4.3 years, age at diagnosis 7.4±4.7 years. Initial systemic manifestation score (SMS) was 4.4 (SD 1.7). MAS developed in 25/66 (38%) patients, in 18/66 (27%)

at SJIA onset. D2T disease was identified in 12/66 (18.2%) patients: Severe/recurrent MAS=6 (LD in 5), therapy failure=5 (one MAS episode in 3), LD with one MAS episode=1. MAS progressed to severe organ involvement in 4 cases: liver and respiratory failure (2 each), gut failure (3), CNS (seizures, coma,1). In one patient pulmonary hypertension (PH) developed. From 7 patients with LD 4 carried HLA-DRB1*15. During MAS, median (IQR) values of selected biomarkers were: Ferritin: 6,329 µg/L (3,674–18,524), IL-18: 15,437 pg/mL (9,904–20,006), CXCL-9: 26,789 pg/mL (1,016–124,985), CXCL-10: 7,375 pg/mL (2,109.88–20,183.75), S100A8/9: 26.12 µg/mL (18.31–28.24), S100A12: 237.8 ng/mL (4.6–752.4). 59 patients were treated with anakinra (28 first-line,16 as monotherapy). Canakinumab was used in 17 patients as a 2nd or 3rd line biologic, 21 received tocilizumab,11 had TNF inhibitor, 2 abatacept. Haematopoietic stem cell transplantation (HSCT) was performed in 3 D2T patients (1 autologous), 5 received emapalumab for MAS, one was also treated with MAS825. 9/12 (75%) D2T patients received 3 or more different biologics. Other agents used included JAKi (n=8), cyclosporin A (n=14), etoposide (n=2), mycophenolate mofetil (n=3), cyclophosphamide (n=1). CID without CS at 6 months was achieved in 32/66 (48.5%) patients (none from D2T). At the last F/U 49/66 (74.2%) had CID without CS, 30 (45.5%) were in full remission. From 12 D2T patients 2 died aged 4.5 (acute pneumonia) and 6 years (heart failure due to PH), both 3 years from SJIA onset. One patient is in full remission, 3 remain active after >5 years of therapy. From 6 patients who reached CID on therapy, 2 developed IBD.

Conclusion: Despite major advances in SJIA therapy, management of D2T subgroup remains a challenge. All 5/12 D2T patients with unfavourable outcome (active or dead) received all available therapies including experimental ones in 3. Our take-home message has been an earlier consideration of allo-HSCT in patients combining recurrent MAS and cardiopulmonary involvement.

Acknowledgments

Supported by the Czech Health Research Council (AZV CR) grant NU21-05-00522

Disclosure

A. Kozáková Grant/Research Support with: Sobi, Š. Fingerhutová Grant/Research Support with: Sobi, Speaker Bureau with: Novartis, Sobi, P. Šeferna Grant/Research Support with: Pfizer, Sobi, K. Šingelová Grant/Research Support with: Sobi, Pfizer, Speaker Bureau with: GSK, P. Doležalová Speaker Bureau with: Novartis, Sobi, Pfizer, Medac, N. Husáková: None declared

P245

Systemic juvenile idiopathic arthritis- fifteen-year experience from a tertiary centre at bristol, United Kingdom

A. Batchu Prithvi, C. Govardhan, B. Aladaileh, A. Ramanan

Paediatric Rheumatology, Bristol Royal Hospital for Children, Bristol, United Kingdom

Correspondence: A. Batchu Prithvi

Pediatric Rheumatology, **23(2):** P245

Introduction: Systemic juvenile idiopathic arthritis (sJIA) is a chronic disease that results in significant morbidity and mortality in children. (1) Improved understanding of the pathophysiology of sJIA has led to recent therapeutic advances including a growing evidence base for the earlier use of IL-1 or IL-6 blockade.(2) We aim to describe our experience of sJIA over a period of 15 years which includes clinical presentation, therapeutic interventions and the heterogeneity around the use of biologics spanning over this period, and the clinical outcomes at different time points over the course of the disease.

Objectives: To describe the clinical, laboratory features, treatment and long term outcomes of children with sJIA.

Methods: Children with a diagnosis of sJIA treated at Bristol Royal Hospital for children from 2010 to 2025 were included. Electronic medical records were reviewed retrospectively. Details regarding patient demographics, clinical features, laboratory parameters, treatment and outcomes were recorded. Patients were categorized as monocyclic, polycyclic and persistent depending on the disease course. Data was analyzed using descriptive statistics.

Results: A total of 80 children diagnosed with sJIA-29 (36.25%) monocyclic, 12(15%) polycyclic, 39(48.75%) were persistent. The mean age of diagnosis 7.6 (0.8-16) years. 43(53.75%) were females. Apart from fever (in 100%), other common presentations included rash 67(83.8%), arthritis 54(67.5%), splenomegaly 23(28.8%). Median(IQR) laboratory investigations at diagnosis included haemoglobin 98gm/L(85-112), white cell count 18*10^9(10-26), platelets 411 *10^9(288-549), C-reactive protein 121mg/L(63-195), ESR 75mm/hr(25-136),D-dimer 3089ng/mL(1359-6106), LDH 501U/L(345-902), fibrinogen 5.2ng/mL(3.4-6.4), ferritin 1443mcg/L(459-4415), triglycerides 1.5mmol/L(1-2.3), ALT 26 U/L(12-65). Treatment received primarily was variable over the 15 year span and included combination of corticosteroids, disease modifying anti-rheumatic drug, IL-1 and IL-6 blockade. IL-1/IL-6 blocker therapy initiated in 15(18.8%) within 3 months of diagnosis and 39(48.7%) by the end of 1 year. Maximum disease inactivity off treatment was achieved in the monocyclic group(80.8%). Disease activity controlled on treatment was achieved in 62.5% in polycyclic and 56.4% in persistent group. At the end of 5 years, 5/8 in polycyclic and 6/30 in persistent achieved clinical remission off treatment.

Conclusion: sJIA is a disease with the variable course that determines the outcome. Based on our study, it has been observed that children in persistent category required combination of therapies to keep the disease under control.

Disclosure

None declared

References

1. Singh-Grewal D, Schneider R, Bayer N, Feldman BM. Predictors of disease course and remission in systemic juvenile idiopathic arthritis: significance of early clinical and laboratory features. Arthritis Rheum. 2006 May;54(5):1595–601.
2. Foley CM, McKenna D, Gallagher K, McLellan K, Alkhdher H, Lacassagne S, et al. Systemic juvenile idiopathic arthritis: The Great Ormond Street Hospital experience (2005-2021). Front Pediatr. 2023;11:1218312.

P246

Pro-kind Sjia: real-world treatment strategies and outcomes in systemic Juvenile idiopathic arthritis

C. Hinze[1], A. Klein[2], G. Horneff[2], M. Hufnagel[3], K. Vollbach[4], P. Oommen[5], T. Kallinich[6], J.-P. Haas[7], J. Kümmerle-Deschner[8], K. Mönkemöller[9], A. Hospach[10], R. Trauzeddel[11], F. Dressler[12], D. Windschall[13], I. Foeldvari[14], R. Berendes[15], D. Foell[1], K. Tenbrock[4], J. Klotsche[16], K. Minden[16] on behalf of the German PRO-KIND Rheuma Study Group

[1]Klinik für Pädiatrische Rheumatologie und Immunologie, Universitätsklinikum Münster, Münster, [2]Klinik für Kinder- und Jugendmedizin, Asklepios Kinderklinik, Sankt Augustin, [3]Klinik für Allgemeine Kinder- und Jugendmedizin, Universitätsklinikum Freiburg, Freiburg, [4]Klinik für Kinder- und Jugendmedizin, Uniklinik RWTH Aachen, Aachen, [5]Klinik für Kind-Onkologie, -Hämatologie und Klinische Immunologie,, Universitätsklinikum Düsseldorf, Düsseldorf, [6]Klinik für Pädiatrie mit Schwerpunkt Pneumologie, Immunologie und Intensivmedizin, Charité – Universitätsmedizin Berlin, Berlin, [7]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, [8]Zentrum für Kinder- und Jugendrheumatologie, Universitätsklinikum Tübingen, Tübingen, [9]Klinik für Kinder- und Jugendmedizin, Kliniken Köln, Köln, [10]Pädiatrie 2 - Allgemeine und Spezielle Pädiatrie, Klinikum Stuttgart, Stuttgart, [11]Kinder- und Jugendmedizin, Helios Klinikum Berlin-Buch, Berlin, [12]Kinderheilkunde, Päd. Pneumologie, Allergologie und Neonatologie, Medizinische Hochschule Hannover, Hannover, [13]Klinik für Kinder- und Jugendrheumatologie, St. Josef-Stift Sendenhorst, Sendenhorst, [14]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, [15]Zentrum für Kinder- und Jugendrheumatologie, Kinderkrankenhaus St. Marien, Landshut, [16]Kinder- und Jugendrheumatologie, Deutsches Rheuma-Forschungszentrum, Berlin, Germany

Correspondence: C. Hinze

Pediatric Rheumatology, **23(2):** P246

Introduction: Systemic juvenile idiopathic arthritis (SJIA) is a severe inflammatory condition carrying a risk of severe morbidity, including macrophage activation syndrome (MAS). Early and effective treatment is considered critical for improving outcomes. The German multicenter PRO-Kind initiative provides real-world data on SJIA management, enabling evaluation of treatment strategies, disease burden, and outcomes in routine care.

Objectives: This study aims to describe baseline characteristics, therapeutic approaches, and disease course of SJIA patients within the PRO-Kind inception cohort. We sought to assess how early interventions align with international treatment goals and to identify limitations in current data collection regarding early treatment dynamics.
Methods: Data from the nationwide, prospective PRO-Kind SJIA registry were analyzed. Clinical features, laboratory findings, treatment modalities, disease activity (using cJADAS-10), and MAS occurrence were evaluated. Descriptive statistics were applied to characterize the cohort, with focus on antirheumatic medication use and achievement of long-term treatment goals.
Results: Sixty-four patients with new-onset SJIA were assessed. At baseline, patients exhibited a high burden of systemic and articular symptoms, along with marked laboratory abnormalities. Interleukin-1 inhibitors were frequently used early in the disease course (e.g., anakinra in 35.9% and canakinumabin 20.3% [n=64]), with canakinumab and tocilizumab being the most common biologics administered during follow-up (e.g., at 12 months canakinumab in 32.3% and toclizumab in 25.8% of patients with follow-up data available at that time point [n=31]). Over time, a substantial reduction in disease activity was observed both globally and at the individual level. Seventy-four to 88% of patients achieved formulated long-term treatment targets of inactive disease at 6 months and 12 months, respectively. However, the dataset lacked detailed information on early response and initial treatment modifications due to limited temporal resolution in data capture. MAS was present at baseline in 9/64 patients (14%) and occurred in 4 more patients during follow-up (6%), i.e., cumulatively in 20% of patients, further underscoring the severity of SJIA.
Conclusion: The PRO-Kind SJIA registry reflects high initial disease burden and supports early use of IL-1 blockade in routine care. While many patients achieve long-term disease control, assessing early treatment response remains challenging due to data limitations. Future analyses incorporating detailed biomarker and molecular data from the PRO-Kind add-on module may improve early stratification and therapy monitoring in SJIA.
Disclosure
None declared

P247

Don't miss the biceps tendon: a new clue to articular involvement in systemic Juvenile idiopathic arthritis

E. Barbieri[1], L. Rossi-Semerano[2], P. Dusser-Benesty[2], I. Konè-Paut[2], F. Anselmi[2]
[1]University of Naples "Federico II", Naples, Italy, [2]Department of Pediatric Rheumatology and CEREMAIA, Bicêtre University Hospital, France, France
Correspondence: E. Barbieri
Pediatric Rheumatology, **23(2):** P247

Introduction: Tenosynovitis is a recognized but often overlooked feature of systemic Juvenile Idiopathic Arthritis (sJIA). Regarding musculoskeletal or joint and tendon involvement, most literature has focused on large joint synovitis or tenosynovitis of the lower limbs, while inflammation of the long biceps tendon (LBT) remains poorly described (1), particularly in pediatric patients. This lack of attention may lead to underdiagnosis of LBT involvement.
Objectives: To assess the clinical and imaging involvement of LBT in sJIA. Secondarily, to explore whether LBT involvement is associated with a specific phenotype of the disease.
Methods: We retrospectively analyzed data from patients with sJIA followed at Bicêtre Hospital (France) between 1999 and 2023, and prospectively collected data from 2023 onward, with systematic assessment of ultrasound-detected LBT involvement. Patients were included if clinical or imaging evidence (ultrasound [US] and/or Magnetic Resonance Imaging [MRI]) of LBT involvement was available at disease onset or during flare-ups. Clinical, laboratory, and imaging data were collected at baseline and during the follow-up. US and MRI were performed based on clinical suspicion, particularly in cases of shoulder pain or reduced mobility. Imaging findings were reviewed using standardized pediatric definitions of tenosynovitis (2). Associations between LBT involvement and clinical phenotype (articular or systemic) were evaluated.
Results: Out of 48 patients with sJIA, 33 were included in the analysis (15 excluded due to missing baseline data). Fourteen out of 33 patients (42%) showed evidence of LBT involvement, based on either clinical findings or imaging. Among these, 11/14 presented clinical signs. Eight patients (5 symptomatic) out of 14 underwent US examination, which was positive in 7 cases. For the remaining patient, no specific mention of LBT investigation was reported on US. MRI was performed only in 2 symptomatic patients and confirmed LBT tenosynovitis in both cases. Regarding the prospective analysis, among the eight newly diagnosed patients who underwent systematic US examination of the LBT, five (62.5%) showed LBT involvement (including two asymptomatic cases). In our cohort, two distinct ultrasound patterns were highlighted: typical tenosynovitis and bicipital synovial cyst. Notably, only 1/14 patients with LBT involvement developed Macrophage Activation Syndrome (MAS) (7% vs 93% without MAS, $p<0.05$), suggesting a potential inverse association between LBT involvement and MAS development.
Conclusion: LBT involvement may be an underrecognized marker of joint-predominant sJIA, particularly in patients without biological features of MAS. Its presence could help delineate a less inflammatory, more articular subtype of the disease. Given its frequency and diagnostic implications, we advocate for routine US assessment of the LBT in sJIA patients, even in those lacking overt arthritis, shoulder pain or systemic symptoms.
Disclosure
None declared

References

1. Shimizu M, Yokoyama T, Wada T, Yachie A. Bicipital synovial cyst in systemic-onset juvenile idiopathic arthritis. J Pediatr. 2010 Jul;157(1):168. doi: https://doi.org/10.1016/j.jpeds.2010.02.014. Epub 2010 Mar 24. PMID: 20338579.
2. Collado P, Martire MV, Lanni S, De Lucia O, Balint P, Guillaume-Czitrom S, Hernandez-Diaz C, Sande NK, Magni-Manzoni S, Malattia C, Rossi-Semerano L, Roth J, Ting T, Vega-Fernandez P, Windschall D, D'Agostino MA, Naredo E; OMERACT Ultrasound Group. OMERACT International Consensus for Ultrasound Definitions of Tenosynovitis in Juvenile Idiopathic Arthritis: Systematic Literature Review and Delphi Process. Arthritis Care Res (Hoboken). 2023 Nov;75(11):2277-2284. doi: https://doi.org/10.1002/acr.25159. Epub 2023 Jun 26. PMID: 37221153.

P248

Factors driving therapeutic decision-making in still's disease: when to start and when to stop? data from the metaphor project worldwide survey

F. Baldo[1], G. Rogani[2], C. Bracaglia[3], D. Foell[4], M. Gattorno[5], M. Jelusic[6], J. Anton[7], P. Brogan[8], S. Canna[9], R. Cron[10], F. De Benedetti[3], A. Grom[11], M. Heshin Bekenstein[12], A. Horne[13], R. Khubchandani[14], M. Mizuta[15], S. Ozen[16], P. Quartier[17], A. Ravelli[5], M. Shimizu[18], G. Schulert[11], R. Sinha[19], C. Scott[20], N. Ruperto[21], J. Swart[2], B. Fautrel[22], S. Vastert[2], F. Minoia[23] on behalf of PReS MAS/sJIA Working Party
[1]PAediatric Rheumatology Unit, ASST-G.Pini-Cto, Milano, Italy, [2]Univeristy Medical Center, Utrecht, Netherlands, [3]IRCCS Ospedale Pediatrico Bambin Gesù, Rome, Italy, [4]University Hospital Muenster, Muenster, Germany, [5] IRCCS Giannina Gaslini, Genova, Italy, [6]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia, [7]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [8]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [9]Children's Hospital of Philadelphia, Philadelphia, [10]University of Alabama at Birmingham, Birmingham, [11]Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [12]Dana Dwek Children's Hospital, Tel Aviv Medical Center, Tel Aviv, Israel, [13]Karolinska Institute, Sollentuna, Sweden, [14]SRCC Childrens Hospital, Mumbai, India, [15]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kanazawa, Japan, [16]Department of Pediatrics, Hacettepe University, Ankara, Türkiye, [17]Université Paris-Cite, IMAGINE Institute, Necker Children's Hospital, Paris, France, [18]Tokyo Medical and Dental University, Tokyo, Japan, [19]Systemic JIA Foundation, Cincinnati, United States, [20] Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Canada, [21]Fondazione IRCCS San Gerardo dei Tintori, Università degli Studi Milano-Bicocca, Monza, Italy, [22]Department of Rheumatology, AP-HP, Pitié-Salpêtrière Hospital, Sorbonne University, Paris, France,

[23]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy
Correspondence: F. Baldo
Pediatric Rheumatology, **23(2):** P248

Introduction: Despite continuous improvement in care and the recent update of international recommendations, relevant discrepancies in the diagnostic and treatment approach to Still's disease (SD) may still exist, in particular in the timing and factors influencing treatment start and withdraw.
Objectives: The study was aimed to explore current global treatment strategies for SD, focusing on parameters driving the decision-making process at treatment start and at withdrawal
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize treatment in SD and macrophage activation syndrome, a global survey on SD treatment was developed based. Topics were selected by 22 experts, including 1 patient representative and 1 adult rheumatologist. The survey included demographic data, clinical practice insights, a patient-led section on unmet needs. International physicians part of the PReS/PRINTO network and adult rheumatologists involved in SD care were invited to complete the anonymous online survey (Dec 3, 2024–Feb 14, 2025).
Results: A total of 206 responses, mainly from pediatric rheumatologists (91%) from 56 countries were collected. Infectious tests performed at SD onset included TB, EBV, and blood cultures (80%), parvovirus, HBV, HCV, and SARS-CoV-2 (50%). Most physicians performed peripheral blood smears (85%), while 54% bone marrow aspiration, 38% immunophenotyping and 17% bone marrow biopsy. Imaging was commonly performed, with chest X-ray, abdominal ultrasound, and echocardiography as the most frequent investigations (~80%). Among biomarkers, ferritin was almost always tested, while IL-18 (25%), S100 proteins (19%), and HLA-DRB1*15 (17%) were less frequently assessed. Before starting glucocorticoids (GCs) 68% of clinicians deemed certain investigations mandatory: bone marrow aspiration (74%), blood coltures and TB screening (50%), chest-abdomen CT scan and bone marrow biopsy (~20%).
Beginning of steroid tapering was guided mostly by clinical and laboratory parameters: acute phase reactants (95%) and ferritin (87%) reduction, fever resolution (82%, ≥1 week: 37%; ≥72h: 29%; ≥2 weeks: 16%), arthritis improvement (75%), steroid side effects (42%); 29% and 25% requires normalization of acute phase reactants and ferritin, respectively, to start GCs tapering. More than half of physicians took patient/parent-reported outcomes (51% global VAS, 35% pain VAS) in consideration. Steroid discontinuation required at least 4-6 weeks of inactive disease for 40% of participants, and ≥3 months for 34%. Biologics withdrawal was considered after at least 6 months (35%), 1 year (35%) and 3 months (36%) of inactive disease. Patient reported outcomes and laboratory parameters driving biologics withdrawal were similar to ones influencing steroid tapering.
Conclusion: A considerable heterogeneity in clinical practice still exist, in particular in timing and factors guiding treatment tapering and withdrawal. Fostering harmonization of management of SD is essential to ensure consistent and optimal care for patients across different clinical settings
Disclosure
None declared

P249

Different perspectives between physicians and patients on treatment priorities and challenges in still's disease

G. B. Beretta[1], L. Pereira[2], G. Rogani[3], F. Baldo[4], C. Bracaglia[5], D. Foell[6], M. Gattorno[7], M. Jelusic[8], S. Vastert[3], R. Sinha[2], F. Minoia[1] on behalf of PReS MAS/sJIA Working Party and the Systemic JIA Foundation
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [2]Systemic JIA Foundation, Cincinnati, United States, [3]University Medical Center, Utrecht, Netherlands, [4]ASST Gaetano Pini, Milan, [5]IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [6]University Hospital, Muenster, Germany, [7]IRCCS Giannina Gaslini, Genoa, Italy, [8]University Hospital Centre, Zagreb, Croatia
Correspondence: G. B. Beretta
Pediatric Rheumatology, **23(2):** P249

Introduction: Despite therapeutic advances, major concerns and disparities persist in the care of Still's Disease (SD). Capturing both patient/caregiver and physician perspectives is essential to optimize patient-centered care.
Objectives: This real-life study aims to assess and compare the perspective of physicians and patients/caregivers regarding treatment goals, challenges, and unmet needs related to the treatment of SD.
Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize SD and Macrophage Activation Syndrome (MAS) management, 2 surveys, 1 addressed to physicians and 1 to patients/caregivers, were developed by a core team, involving physicians and patients representatives. The physician survey was forwarded through the PReS/PRINTO network, while the patient survey via the Systemic JIA Foundation to all their members. Responses were analyzed using chi-square tests to assess group differences.
Results: 197 physicians and 139 patients/caregivers participated. Most patient respondents were parents or legal guardians (94%), primarily from the United States (64%) and Europe (19%). Physicians were mainly pediatric rheumatologists (90%), from 56 countries worldwide. Regarding treatment goals, both groups prioritized complete symptom control (84% vs 79%, p=0.28) and achieving a quality of life similar to peers (63% vs 73%, p=0.44). However, patients considered pain control a key objective more often than physicians (43% vs 13%, p< 0.001), whereas physicians placed greater emphasis on glucocorticoid reduction (79% vs 54%, p< 0.001).
In terms of glucocorticoid-related concerns, mood changes were predominantly reported by patients (65% vs 14%, p<0.001), whereas physicians were more concerned about osteoporosis (66% vs 32%, p< 0.001), glucose intolerance (52% vs 27%, p< 0.001), and hypertension (51% vs 37%, p=0.02). Both groups highlighted growth delay and infection risk as shared concerns.Regarding fears at treatment initiation, both groups were concerned about treatment failure (82% patients vs 66% physicians, p=0.001) and adverse events (77% vs 72%, p=0.27). However, physicians were more worried about treatment duration (57% vs 21%, p< 0.001), while patients emphasized infection risk (52% vs 27%, p< 0.001) and lack of clear information about the treatment (34% vs 23%, p=0.03).As for future challenges, both groups stressed the need to reduce the burden of glucocorticoid use (68% patients vs 59% physicians, p=0.10). Physicians more frequently cited the inability to prevent MAS (52% vs 40%, p=0.03), while patients highlighted limited physician expertise (57% vs 15%, p< 0.001) and lack of access to psychological support (33% vs 10%, p< 0.001) as major unmet needs.
Conclusion: Besides shared perspectives, patients and physicians show relevant differences in prioritizing treatment outcomes and concerns in SD. Including patient priorities early in the disease course is essential to advancing truly patient-centered care.
Disclosure
G. B. Beretta: None declared, L. Pereira: None declared, G. Rogani: None declared, F. Baldo: None declared, C. Bracaglia: None declared, D. Foell: None declared, M. Gattorno Grant/Research Support with: Novartis, Consultant with: SOBI, Novartis, Speaker Bureau with: Fresenius-Kabi, SOBI, Novartis, M. Jelusic: None declared, S. Vastert Grant/Research Support with: SOBI, Consultant with: SOBI, Novartis, Speaker Bureau with: SOBI, Novartis, R. Sinha: None declared, F. Minoia: None declared

P250

Refractory systemic Juvenile idiopathic arthritis: a single-center retrospective study

M. Kaleda, I. Nikishina
Pediatric, V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P250

Introduction: Modern therapy of systemic juvenile idiopathic arthritis (sJIA), based on early administration of IL6 or IL1 inhibitors, have improved the prognosis in most patients. Despite this, there are still patients with a refractory course of the disease.
Objectives: to analyze all cases of refractory sJIA in our clinical practice.

Methods: Our retrospective study included all patients, completing criteria of refractory sJIA*, in our pediatric department for the last 10 years.
Results: We observed 23 patients (14 girls), who fulfilled the criteria of refractory sJIA. The median age at onset was 24 [IQR 18; 46] months. The number of systemic manifestations at onset was 6 [5;6], the number of active joints – 14 [IQR 6;24], CRP – 122.5 [IQR 63.25; 170.0] mg/l. 21.7% patients had polycyclic, 78.2% – persistent disease course. All patients received steroids. Among DMARDs only 4 patients received methotrexate alone, 10 – methotrexate and cyclosporine, 8–3 DMARDs (as 3rd mycophenolate mofetil (2), cyclophosphamide (3), leflunomide (2), sulfasalazine (1). 1 patient had a history of 5 DMARDs (methotrexate, mycophenolate mofetil, cyclophosphamide, cyclosporine, leflunomide). 79.2% of patients received from 2 to 6 biologics. All patients received tocilizumab, 11 – canakinumab, 2 – anakinra, 4 – infliximab, 6 – etanercept, 4 – adalimumab, 5 – abatacept, 4 – rituximab, 3 – sarilumab. The reasons for substitution therapy were anaphylactic reactions on tocilizumab (8 patients), other cases – loss of efficacy. 5 patients received tofacitinib. 16 patients had episodes of macrophage activation syndrome (MAS): 6 – one-time episode, 5 – twice, 4–3 times, 1 patient – 4 episodes. 9 patients had MAS at onset, 13 – under biologics therapy (1 on anakinra, 3 – canakinumab, 1 – rituximab, 10 – tocilizumab, 1 – adalimumab). 8 patients developed the lung disease associated with sJIA (sJIA-LD), 3 of them had respiratory symptoms at onset. 7 patients with sJIA-LD had the history of MAS: 3 at onset, 4 – recurring MAS. The median of disease duration at the time of sJIA-LD verification was 4.0 years [IQR 2.5; 6.25]. 12 patients (52.2%) had progression of functional disability due to destructive polyarthritis. 8 patients had a history of septicemia. 4 patients died due to the development of multiple organ failure, 2 as a result of sJIA-LD, 1 with MAS, 1 – amyloidosis.
Conclusion: Early age at onset, MAS at onset, infusion reactions to tocilizumab increases the risk of developing refractory sJIA with difficulties of choosing therapy, the risk of developing sJIA-LD and progression of functional disability. We found that different clinical phenotypes of refractory sJIA can be observed in the same patient during the course of the disease.
Disclosure
None declared

Reference
1. Schulert G, Vastert SJ, Grom AA. The 4th NextGen therapies for SJIA and MAS: part 2 phenotypes of refractory SJIA and the landscape for clinical trials in refractory SJIA. Pediatr Rheumatol Online J. 2024 Jan 5;21(Suppl 1):87. doi: https://doi.org/10.1186/s12969-023-00865-0

P251

Distinct roles of serum free and total interleukin 18 level as a biomarker for still's disease and macrophage activation syndrome

M. Shimizu[1], M. Hatano[2], S. Kaneko[2], F. Miyaoka[2], A. Shimbo[2], H. Irabu[2], Y. Akutsu[2], Y. Hayashi[1], M. Mori[3]
[1]Department of Pediatrics, Perinatal and Maternal Medicine, [2]Department of Pediatrics and Developmental Biology, [3]Joint Research Department of Lifelong Immunotherapy, Institute of Science Tokyo, Tokyo, Japan
Correspondence: M. Shimizu
Pediatric Rheumatology, **23(2):** P251

Introduction: Overproduction of interleukin (IL)−18 is closely related to the pathogenesis of Still's disease (SD). We previously reported serum total IL-18 levels were extremely elevated and were useful for the diagnosis, monitoring of disease activity and the prediction of macrophage activation syndrome (MAS) development in SD patients. Recent reports showed that increase of free IL-18 in blood is causatively involved in the development of MAS. Furthermore, serum free IL-18 levels could predict susceptibility to MAS as well as serum total IL-18 levels. However, it is still unknown the role of serum free IL-18 levels as a biomarker for Still's disease and MAS.
Objectives: This study aimed to clarify the role of serum free IL-18 levels as a biomarker for Still's disease and MAS.
Methods: Fiftythree patients with SD including 41 patients with systemic juvenile idiopathic arthritis (s-JIA) and 12 patients with adult onset SD (AOSD), 17 patients with MAS including 12 patients with s-JIA associated MAS and 5 patients with AOSD associated MAS, 22 patients with other inflammatory diseases including 13 patients with Kawasaki disease, 7 patients with vasculitis, 1 patient with rheumatic fever and 1 patient with reactive arthritis and 13 healthy controls (HC), were studied. Serum levels of free IL-18, total IL-18 and CXCL9 were quantified using enzyme-linked immunosorbent assay. The results were compared with the clinical features of Still's disease and MAS.
Results: Serum free IL-18 levels were significantly elevated in patients with SD compared to HC. Furthermore, Serum free IL-18 levels were significantly elevated in patients with MAS compared to SD, other inflammatory diseases and HC. However, there was no significant difference of serum free IL-18 levels between SD and other inflammatory diseases. Serum total IL-18 levels were significantly elevated in patients with SD compared to other inflammatory diseases and HC. Furthermore, Serum total IL-18 levels were significantly elevated in patients with MAS compared to SD, other inflammatory diseases and HC. Serum free IL-18 levels increased earlier as MAS developed compared to serum CXCL9 levels.
Conclusion: Serum free and total IL-18 levels have distinct roles as a biomarker for SD and MAS. Serum free IL-18 levels may represent a sensitive indicator of disease activity for assessing the transition to MAS from acute phase. In contrast, serum total IL-18 levels may be a useful marker for the diagnosis of SD and the differentiation SD from other inflammatory diseases.
Disclosure
M. Shimizu Grant/Research Support with: Medical and Biological Laboratories Co., Ltd, M. Hatano: None declared, S. Kaneko: None declared, F. Miyaoka: None declared, A. Shimbo: None declared, H. Irabu: None declared, Y. Akutsu: None declared, Y. Hayashi: None declared, M. Mori Grant/Research Support with: AbbVie GK, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organization, Nippon Kayaku Co., Ltd., UCB Japan Co. Ltd., Asahi Kasei Corp.

P252

Outcome of patients with pericardial effusion in systemic onset Juvinile idiopathic arthritis

R. Singh, A. Nandi, R. P. Goud, J. N. Bathia, P. Pal
Pediatric rheumatology, Institue of Child Health, Kolkata, India
Correspondence: R. Singh
Pediatric Rheumatology, **23(2):** P251

Introduction: Pericardial effusion (PCE) is a common finding in various autoimmune and rheumatologic disorders. Studies have indicated that its presence correlates with higher morbidity rates in paediatric patients with systemic lupus erythematosus and Kawasaki disease. However, there is limited research on the outcomes of children with systemic juvenile idiopathic arthritis (SJIA) and PCE. We conducted a retrospective observational study to delineate the characteristics of children admitted with SJIA and PCE and to assess the association of PCE on their clinical outcomes.
Objectives: To determine if the presence of a pericardial effusion is associated with adverse outcomes amongst children with SJIA.
Methods: A single centre, retrospective observational study was conducted and data from hospital admissions and f/u OPD patients, between June 2023 and December 2024, were obtained. 52 patients diagnosed as SJIA on basis of ILAR Criteria were enrolled. Pericardial effusion was the primary predictor variable; the outcomes of interest were time taken for remission, additional need for Biologics (Tocilizumab), incidence of macrophage activation syndrome (MAS) and death after diagnosis.
Results: A total of 52 patients diagnosed with systemic juvenile idiopathic arthritis (SJIA) were enrolled in the study, of whom 3 (5.8%) had pericardial effusion (PCE).
These three patients showed only partial response to steroids and required Tocilizumab to control inflammation.
Overall, 13 patients (25%) presented with or developed macrophage activation syndrome (MAS), including all three with PCE—one at disease onset and two during the course of illness.
2 of the 3 PCE patients (66%) died despite treatment, while 1 achieved remission following a combination of pulse steroids, Tocilizumab, and Cyclosporin.

In total, there were 4 deaths (6%) during the study period, with half of them occurring in patients with PCE.
Compared to the 49 patients without PCE, those with PCE had significantly higher rates of MAS (100% vs. 20%), biologic therapy requirement (100% vs. 28%), polyserositis (100% vs. 4%), and mortality (66% vs. 4%), highlighting the severity and poor prognosis associated with PCE in SJIA.
Conclusion: Pericardial effusion is rare complication in SJIA but is associated with significant morbidity and mortality and its presence may be a marker of disease severity and a poor prognostic sign. Children with SJIA may benefit from early screening echocardiography and treatment intensification with Biologics if pericardial effusion is diagnosed early.
Disclosure
None declared

P253

Emapalumab's role in a severe and treatment-resistant paediatric macrophage activation syndrome

R. Pereira Da Costa[1,2], M. Lima[3], S. Guedes[3], A. Claro[3], A. Dias Curado[3], F. Prata[3], I. Esteves[3], R. Campanilho-Marques[1,2,4], J. G. Marques[3], F. Oliveira Ramos[1,2,4]
[1]Rheumatology Department, Unidade Local de Saúde Santa Maria, [2]Faculdade de Medicina, Universidade de Lisboa, [3]Paediatrics Department, [4]Paediatric Rheumatology Unit, Unidade Local de Saúde Santa Maria, Lisbon, Portugal
Correspondence: F. Oliveira Ramos
Pediatric Rheumatology, **23(2):** P253

Introduction: Macrophage activation syndrome (MAS), a subset of haemophagocytic lymphohistiocytosis (HLH), is a life-threatening condition characterized by systemic hyperinflammation and haemophagocytosis. MAS management includes immunomodulation. Emapalumab is an IFNγ directed antibody approved for refractory HLH in the USA, but not in Europe.
Objectives: -
Methods: -
Results: We report on a 15-year-old girl with a severe and highly refractory MAS. She presented a 5-day history of fever (>39ºC), odynophagia and an erythematous macular rash accompanying the fever spikes. She was hospitalized and empiric antibiotics were started. After 9 days, she was admitted to the ICU for ventilatory and vasopressor support. She had *de novo* pancytopenia, hypofibrinogenemia and elevated AST, ALT, LDH, triglycerides, soluble CD25, serum calprotectin and ferritin (highest 357976ng/ml). Imaging showed hepatosplenomegaly. An infectious screening and immune profile was negative. Myelogram and bone biopsy showed a hypocellular marrow with haemophagocytosis. An exome-based gene panel for inherited immune dysregulation disorders (576 genes associated with HLH, autoinflammatory syndromes and immunodeficiencies) did not identify pathogenic variants.
She was treated with 5 daily IV pulses of methylprednisolone 1 g, followed by oral methylprednisolone 1mg/kg/day, anakinra (IV, max 100 mg q6h) and cyclosporine (max 150 mg q12h). Despite an initial response, an infectious complication led to worsening of MAS. Cyclosporine was suspended due to drug induced microangiopathy, and anakinra reduced to 100 mg q12h due to hepatotoxicity. She was retreated with methylprednisolone pulses and 2 IV immunoglobulin perfusions. However, pancytopenia persisted, requiring erythrocyte transfusions and G-CSF. On the 41st day of admission, with a ferritin level of 71233ng/ml, emapalumab was started. She received ten 3-day spaced treatments, with progressive and sustained improvement, allowing for tapering of steroids and anakinra, and discharge. She is clinically stable with 8 months of follow-up, on canakinumab (switched from anakinra due to a local reaction) maintenance treatment for 4 months and reducing steroids.
Conclusion: This case highlights the diagnostic and management challenges of MAS and supports the role of IFN-γ inhibition in the treatment of severe and resistant disease. It describes a severe and prolonged episode of MAS—lasting over 2 and a half months—as the inaugural manifestation of a likely underlying Still's disease. Diagnosis was initially obscured by the intensity of the hyperinflammatory state, with an exceptionally high ferritin level. MAS was refractory to high-dose corticosteroids, cyclosporin, and IL-1 blockade, with partial and transient responses. Emapalumab—used for the first time in Portugal—after 2 and a half months of uncontrolled severe disease, was associated with a rapid and sustained clinical and laboratory remission. Consent to published had been obtained.
Disclosure
None declared

P254

A retrospective cohort study on the safety and efficacy of sulfasalazine in Juvenile idiopathic arthritis

A. D'hont[1], B. Ogunjimi[2,3], R. Joos[2,3]
[1]Division of Paediatrics, [2]Division of Paediatric Rheumatology, Antwerp University Hospital, [3]Division of Paediatric Rheumatology, Ziekenhuis aan de Stroom, Antwerp, Belgium
Correspondence: A. D'hont
Pediatric Rheumatology, **23(2):** P254

Introduction: Sulfasalazine (SSZ) is a commonly used disease-modifying antirheumatic drug for juvenile idiopathic arthritis (JIA) that is primarily recommended within the group of juvenile spondyloarthropathies, although its effectiveness appears more pronounced for peripheral arthritis rather than the axial component and current treatment guidelines increasingly limit its role in the management of JIA.
Objectives: This retrospective cohort study aimed to evaluate the efficacy, tolerability and predictive factors of SSZ response in children with JIA, focusing on the impact of ILAR and PRINTO classifications and specific clinical characteristics.
Methods: This is a retrospective review of 70 children (≤16 years) with JIA treated with SSZ. Efficacy was assessed by rates of inactive disease, remission and clinical remission off medication. Tolerability was evaluated by the incidence and nature of adverse events. Univariate and multivariate logistic regression analyses were used to identify predictors of SSZ remission, including ILAR and PRINTO categories, axial disease and hip involvement.
Results: SSZ induced inactive disease in 70% of patients and remission in 47.1%, with 12.9% achieving clinical remission off medication. Adverse events occurred in 24.3% of patients, leading to SSZ cessation in 20%, primarily involving abdominal complaints. Univariate logistic regression analysis showed no significant differences in remission rates between ILAR and PRINTO subgroups. However, patients with persistent oligoarthritis had a significantly increased likelihood of remission (OR 4.7) compared to the overall cohort. The absence of axial disease (OR 3.7) and hip involvement (OR 2.8) were significant predictors of remission. Multivariate analysis confirmed the association between the absence of axial disease and remission.
Conclusion: This multicenter retrospective study reinforces the efficacy of SSZ in JIA. Sulfasalazine demonstrated acceptable tolerability in this cohort. Clinical characteristics, such as the absence of axial disease and hip involvement, appear to be more significant predictors of treatment response than ILAR or PRINTO classifications. Given the observed lower likelihood of remission in patients with axial disease, all of whom had sacroiliitis in this cohort, a more rapid transition to biologicals may be warranted in such cases. SSZ appears to be a viable treatment option, especially for persistent oligoarthritis, however cautious interpretation is warranted due to the retrospective design. Future research should focus on elucidating the risk of severe drug-induced hypersensitivity reactions and identifying genetic markers that predict predisposition to these reactions.
Disclosure
None declared

P255

Clinical and laboratory predictors of biologic therapy use in enthesitis-related arthritis and Juvenile psoriatic arthritis

B. Menentoğlu[1], S. Atamyıldız Uçar[2], Z. Özaslan[3], E. Tunce[2], A. Dudaklı[1], T. Güzel[4], S. D. Arık[1], G. Kavrul Kayaalp[1], Ö. Akgün[1], A. Tanatar[5], F. G. Demirkan[6], F. Çakmak[4], M. Çakan[7], H. E. Sönmez[3], B. Sözeri[2], N. Aktay Ayaz[1]

[1]Pediatric Rheumatology, Istanbul University Faculty of Medicine, [2]Pediatric Rheumatology, Ümraniye Training and Research Hospital, Istanbul, [3]Pediatric Rheumatology, Kocaeli University Faculty of Medicine, Kocaeli, [4]Pediatric Rheumatology, Başakşehir Çam and Sakura State Hospital, [5]Pediatric Rheumatology, Marmara University, [6]Pediatric Rheumatology, Kanuni Sultan Süleyman Training and Research Hospital, [7]Pediatric Rheumatology, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Istanbul, Türkiye
Correspondence: B. Menentoğlu
Pediatric Rheumatology, **23(2):** P255

Introduction: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are heterogeneous subtypes of juvenile spondyloarthropathies with variable courses and treatment responses. While early identification of optimal therapy is key to preventing joint damage, predictive clinical and laboratory markers for biologic therapy remain unclear.
Objectives: We aimed to evaluate the relationship between disease characteristics and treatment strategies in patients diagnosed with ERA and JPsA.
Methods: This retrospective, multicenter study included patients diagnosed with ERA or JPsA according to the ILAR 2001 classification criteria.Demographic characteristics, clinical features, and laboratory findings were collected through a detailed review of medical records. Disease activity was assessed using the Juvenile Spondyloarthritis Disease Activity Index (JSpADA) for patients with axial involvement, and the Juvenile Arthritis Disease Activity Score-27 (JADAS-27) for those without axial involvement.
Results: Of the patients included in the study, 73.8% were diagnosed with enthesitis-related arthritis (ERA) (n=124), and 26.2% with juvenile psoriatic arthritis (JPsA) (n=44). The median age at diagnosis was 13 years (IQR: 10–15) in the ERA group and 12.5 years (IQR: 10.23–13.32) in the JPsA group. The median follow-up duration was 2.7 years (IQR: 1.62–3.89) in ERA and 2.66 years (IQR: 1.95–4.66) in JPsA. Male predominance was observed in the ERA group (68.5%) compared to the JPsA group (50%). Biological therapy was required in 46.7% of patients with ERA (n=58), with etanercept being the most commonly used agent (72.4%). Among JPsA patients, 47.7% (n=21) received biological treatment, most frequently adalimumab (80.9%). When factors associated with the need for biological therapy were evaluated, the following variables were significantly associated with biologic use in the ERA group: higher number of affected joints at diagnosis (higher number of affected joints at diagnosis (median [IQR 25–75]: 3 [2-4] vs 2 [2-3], p= 0.005), presence of hip involvement at diagnosis (39.7 % vs. 19.7%, p=0.015), steroid use at diagnosis (56.9% vs.19.7%, p<0.001), elevated baseline C-reactive protein levels (median [IQR 25–75]: 7.9 [1.46-19.25] vs 1.51 [0.5-5.85], p=0.001), elevated baseline erythrocyte sedimentation rate (median [IQR 25–75]: 22.5 [10.5-35.25] vs 12.5 [4-25.25], p=0.004), and HLA-B27 positivity (58.7% vs. 41.3%, p=0.009). In the JPsA group, female sex was significantly associated with the use of biological therapy (66.7% vs. 34.8%, p=0.035), whereas no significant associations were observed for the other clinical or laboratory parameters. In both groups, no significant association was found between baseline disease activity, assessed by JADAS and/or JSpADA; sacroiliac joint involvement; dactylitis; or enthesitis, and the requirement for biological treatment.
Conclusion: Certain clinical and laboratory features at diagnosis were associated with biologic use in ERA, including higher inflammatory markers, higher joint counts, and hip involvement. Female gender was predictive in the JPsA group. These findings may contribute treatment planning by highlighting features potentially associated with the need for biologic therapy; however, further prospective studies are required to better understand and confirm these observations.
Disclosure
None declared

P257

Validation of axial Juvenile spondyloarthropathy criteria in turkish juvenile spondyloarthropathy patients

D. Unal, C. A. Tatar, E. Sag, Y. Bayindir, E. Aliyev, V. Cam, H. Ercan Emreol, M. O. Erkan, O. Basaran, Y. Bilginer, S. Ozen
Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye
Correspondence: D. Unal
Pediatric Rheumatology, **23(2):** P257

Introduction: Juvenile spondyloarthritis (JSpA) is s a heterogeneous group of disease. An international consensus group developed the axial juvenile SpA (AxJSpA) classification criteria for this purpose, defining a homogeneous group of patients diagnosed with jSpA and experiencing axial symptoms before the age of 18 years.
Objectives: To validate this new set of criteria in our pediatric SpA patients.
Methods: This study was held in Hacettepe University Department of Pediatric Rheumatology. Juvenile SpA patients suspected of axial disease diagnosed and followed at the same center between 2005 and 2024 were included. Patients who had other etiologies for axial symptoms including chronic nonbacterial osteomyelitis, mechanical back pain- overuse injuries, amplified pain/growing pains, and SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis) served as control group.
Results: 123 JSpA patients and 74 controls were included in this study. The sensitivity/specificity of the new criteria were 61%/77% with an area under curve value of 0.75 (95% CI: 0.68-0.83) in our cohort. Among different criteria sets, European Spondyloarthropathy Study Group (ESSG) criteria was the most sensitive (sensitivity/specificity 91%/68%), ASAS-peripheral criteria (Assesment in SpondyloArthritis Internaitonal Society) was the most specific (sensitivity/specificity 67%/84%) in our cohort when compared to ASAS-axial (sensitivity/specificity 74%/65%), ILAR (International League of Association for Rheumatology) (sensitivity/specificity 85%/81%) and ILAR+SI (sacroiliitis) (sensitivity/specificity 67%/74%) criteria.
Conclusion: The area under the curve of the new AxJSpA criteria was similar to the original report; however, both sensitivity and specificity were lower in our cohort, possibly due to factors such as earlier disease presentation and a lower prevalence of chronic structural changes on MRI.
Disclosure
None declared

References

1. Rudwaleit M, Landewé R, van der Heijde D, Listing J, Brandt J, Braun J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. Ann Rheum Dis. 2009;68(6):770-6.
2. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011;70(1):25-31.
3. Weiss PF, Brandon TG, Aggarwal A, Burgos-Vargas R, Colbert RA, Horneff G, et al. Classification Criteria for Axial Disease in Youth with Juvenile Spondyloarthritis. Arthritis Rheumatol. 2024.
4. Petty RE, Southwood TR, Baum J, Bhettay E, Glass DN, Manners P, et al. Revision of the proposed classification criteria for juvenile idiopathic arthritis: Durban, 1997. J Rheumatol. 1998;25(10):1991-4.
5. Dougados M, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum. 1991;34(10):1218-27.

P258

Juvenile vs. Adult-onset spondyloarthritis: uncovering similarities and differences

M. Kalçık Unan[1], N. Z. Özaslan[2], G. Dilek [1], N. Şahin[2], H. E. Sönmez[2], K. Nas[3]
[1]Department of Physical Therapy and Rehabilitation, and Division of Rheumatology, Sakarya University, Sakarya, [2]Department of Pediatrics, Division of Pediatric Rheumatology, Kocaeli University, Kocaeli, [3]DDepartment of Physical Medicine and Rehabilitation, Division of Immunology, Rheumatology, and Algology, Sakarya University, Sakarya, Türkiye
Correspondence: N. Z. Özaslan
Pediatric Rheumatology, **23(2):** P258

Introduction: Spondyloarthritis (SpA) refers to chronic inflammatory rheumatic diseases with spinal and joint involvement, which can manifest in both childhood and adulthood.
Objectives: This study aims to evaluate the similarities and differences between enthesitis-related arthritis (ERA), a pediatric counterpart to ankylosing spondylitis (AS), and AS.
Methods: A cross-sectional study was conducted at a pediatric rheumatology center and an adult rheumatology center. Demographics and clinical characteristics were compared between patients with AS and ERA.
Results: A total of 200 patients (101 children, 99 adults) were evaluated. Peripheral arthritis was more common in ERA (54.5%) than AS (21.2%, p<;0.001), while sacroiliitis, axial involvement, and morning stiffness were more frequent in AS. Hip and heel pain were more common in ERA, while neck pain and uveitis were more frequent in AS. Non-steroidal anti-inflammatory drugs were the most common initial treatment (99% vs. 91.9%, p=0.01). ERA patients used corticosteroids (35.6% vs. 11.1%, p<0.001) and DMARDs (87.1% vs. 60.6%, p<0.001) more often, with no significant difference in biological agent use. The median follow-up was 18 months for children and 72 months for adults. At the last follow-up, 24.8% of ERA patients were medication-free, while no AS patients were off medication. Radiographic progression was less frequent in ERA (10.9% vs. 54.5%, p=0.001).
Conclusion: More scientific evidence is needed about the characteristics of ERA, which is currently considered more in the context of Juvenile SpA, that distinguishes it from adults, and our study is an observational cohort study that sheds light on this need. Although ERA and AS show differences and similarities, further large-scale studies with inflammatory biomarkers are needed to determine whether they are distinct diseases or part of a disease spectrum.
Disclosure
None declared

References

1. Martini A, Ravelli A, Avcin T, Beresford MW, Burgos-Vargas R, Cuttica R, Ilowite NT, Khubchandani R, Laxer RM, Lovell DJ et al: Toward New Classification Criteria for Juvenil Idiopathic Arthritis: First Steps, Pediatric Rheumatology International Trials Organization International Consensus. J Rheumatol 2019, 46(2):190-197.
2. Lancas SHS, Furlan MZB, Fernandes TAP, Drumond SGL, Magalhaes CS: Presentation of enthesitis-related arthritis and juvenile-onset spondyloarthritis: a cross-sectional study in pediatric and adult clinic. Adv Rheumatol 2024, 64(1):39.
3. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, Landewe RBM, Van den Bosch FE, Boteva B, Bremander A et al: ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis 2023, 82(1):19-34.

P259

Comparing composite disease outcome measures versus MD global in era: a cross-sectional correlation study

N. Rajpal[1], M. Agarwal[1], S. Sawhney[1], P. Chugh[2]
[1]Division of Paediatric Rheumatology, Department of Paediatrics, [2]Department of Research, Sir Ganaga Ram Hospital, New Delhi, India
Correspondence: N. Rajpal
Pediatric Rheumatology, **23(2):** P259

Introduction: ERA involves the axial skeleton, peripheral joints and has extra articular manifestations. MD Global is a widely used gold standard to assess disease activity and there a few validated composite scores as well.
Objectives: 1. To assess the correlation between MD Global and composite disease activity indices: BASDAI, ASDAS-CRP, JSpADA, and Patient Global in ERA
2. To compare these across active and inactive disease state
3. Further analysis for axial and non-axial involvement.
Methods: This cross-sectional study included 50 children (<18 years) with ERA (ILAR criteria) seen February–April 2025. Demographic, clinical, and treatment data were collected. Disease activity assessed using JSpADA, BASDAI, ASDAS-CRP, PT Global, and MD Global. Spearman's correlation tested associations between measures. Patients categorized as active (MD Global > 0) or inactive, with subgroup analysis of axial (n=10) vs. non-axial (n=20) among active cases. Group differences assessed using the Mann–Whitney U test.
Results:
- Mean age 14.4 ± 3.5 years, disease onset: 10.4 ± 2.5 years, and mean disease duration: 4.0 ± 3.3 years; 90% males.
- Active disease in 60% (n=30), axial involvement 33%, enthesitis 23.3%, extra-articular features 10%.
- DMARDs 94% (methotrexate: n = 45), biologics 66% (adalimumab: 27; etanercept: 6), NSAIDs 10%, and small molecules 14%.
- MD Global showed strong correlations with BASDAI (ρ = 0.732), ASDAS (ρ = 0.800), JSpADA (ρ = 0.800), and PT Global (ρ = 0.701), all $p < 0.001$. Inter-measure correlation was highest between BASDAI and PT Global (ρ = 0.882).
- Disease activity scores were significantly higher in active compared to inactive patients: BASDAI (2.89 vs. 1.06), ASDAS (2.74 vs. 0.70), JSpADA (2.90 vs. 0.63), and PT Global (4.68 vs. 1.80).
- Mann-Whitney U tests showed a significant difference only in JSpADA scores between axial and non-axial groups (U = 51.0, $p = 0.031$), while differences in others statistically not significant.
Conclusion: ERA involves diverse manifestations, often beyond joint inflammation with entheseal, eye, gastrointestinal or skin involvement. While there is no fully validated composite outcome measure, MD Global is widely used in clinical practice as an integrative outcome measure. In our study, we found that:
- MD Global correlated strongly with all commonly used outcome measures and with each other.
- All measures discriminated between active and inactive disease and maintained inter measure correlation.
- JSpADA was the only index to significantly differentiate axial from non-axial disease, likely due to its greater axial weightage as compared to others
- Thus, although our cohort is small, it is observed that MD Global gives a robust and comprehensive clinical measure. All outcome measures correlated well with the gold standard. JSpADA offers added sensitivity in axial ERA as compared to other measures.
Disclosure
None declared

P260

Juvenile arthritis in children with inflammatory bowel disease

Y. Stepaniuk[1], O. A. Oshlianska[2]
[1]National Specialized Children's Hospital «Okhmatdyt» of the Ministry of the Health of Ukraine, [2]Department of pediatrics, pediatric infectious diseases, immunology and allergology, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine
Correspondence: O. A. Oshlianska
Pediatric Rheumatology, **23(2):** P260

Introduction: Inflammatory bowel diseases (IBD), as systemic autoimmune disorders, can extend beyond the gastrointestinal (GI) tract. According to previous studies, up to 30% of cases present with extraintestinal manifestations (EIM).
Objectives: To investigate the frequency and structure of EIM at the onset of IBD in Ukrainian children.
Methods: A retrospective analysis of 333 pediatric IBD cases (146 Crohn's disease (CD), 187 ulcerative colitis (UC)) aged 3–17 years, diagnosed at NSCH "Okhmatdyt" and SI «UCMC of NAMS of Ukraine» between 2020–2024. Diagnoses were based on ESPGHAN 2014 criteria and confirmed morphologically. Comparative analysis with data from 207 patients with juvenile idiopathic arthritis (JIA) receiving biologic therapy was conducted (diagnosed by ILAR 2001 criteria).
Results: Boys predominated among the examined IBD patients (186/147), 62.76% were over 10 y.o. Diagnostic delay ranged from 1 to 72 mos. GI symptoms predominated (77.5%), mainly abdominal pain (69%). Night symptoms were more common in UC (14.4% vs 4.8%, p<0.01), while fever and fatigue - in CD (11.6% vs 5.9% and 74.6% vs 40.6%, respectively). EIM included skin lesions (10.8%), mucosal involvement (1.8%), ocular symptoms (1.5%), and anemia (31.8%). Arthritis was observed at disease onset in 34 IBD patients (10.2%), more often in CD (17.8% vs 4.3%), predominantly peripheral arthritis; 8.7% had arthralgia. Two cases showed asymmetric polyarthritis affecting hips, knees, and ankles. Oligoarthritis mainly involved large

joints of the lower limbs, one patient had shoulder monoarthritis. Three children diagnosed with IBD had a prior diagnosis of JIA up to two years before GI symptoms appeared. Axial skeleton involvement was not documented, likely reflecting underassessment. Among 207 JIA patients receiving biologics, 18 (8.6%) developed verified IBD during follow-up, 15 of whom had enthesitis-related arthritis (ERA) with spine and sacroiliac joint involvement.
Conclusion: Approximately 1/3 of pediatric IBD patients exhibit EIM at onset, most commonly joint, skin, and hematologic involvement. Due to the lower detection rate of arthritis in Ukrainian IBD patients compared to international data, mandatory IBD screening (fecal calprotectin) should be integrated into clinical protocols for patients with undifferentiated fever, erythema nodosum, and newly diagnosed JIA, especially in ERA cases.
Disclosure
None declared

P261

Reliability and validity of the ankylosing spondylitis performance index in patients with enthesitis-related arthritis: a pilot study

S. Buran[1], O. Tüfekçi[2], A. Barlak[2], H. Ercan-Emreol[3], E. Aliyev[3], S. Aydın[3], Y. Bilginer[3], E. Karabulut[4], E. Ünal[1], S. Özen[3]
[1]Department of Heart and Respiratory Physiotherapy and Rehabilitation, Hacettepe University Faculty of Physical Therapy and Rehabilitation, [2]Department of Basic Physiotherapy and Rehabilitation, Hacettepe University Institute of Health Sciences, [3]Department of Pediatrics, Division of Rheumatology, [4]Department of Biostatistics, Hacettepe University Faculty of Medicine, Ankara, Türkiye
Correspondence: S. Buran
Pediatric Rheumatology, **23(2):** P261

Introduction: Enthesitis-related arthritis (ERA) is a subtype of juvenile idiopathic arthritis characterized by enthesitis and arthritis (1). The Ankylosing Spondylitis Performance Index (ASPI) is an objective physical performance test composed of a combination of three reliable tasks—bending (picking up six pencils), putting on socks, and getting up from the floor—derived from the Bath Ankylosing Spondylitis Functional Index (BASFI) (2). Self-reported questionnaires are more commonly used to assess ERA patients, whereas performance-based objective measurements are less frequently utilized.
Objectives: This pilot study aimed to evaluate the ASPI's test–retest reliability, construct validity, and minimal detectable change in assessing physical function in patients with ERA.
Methods: The study included thirteen individuals (four girls, nine boys) diagnosed with ERA. Demographic data were recorded, and the following assessments were conducted: disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), spinal mobility using the Bath Ankylosing Spondylitis Metrology Index (BASMI), functional status using the Childhood Health Assessment Questionnaire (CHAQ), ASPI, and BASFI, and biopsychosocial status using the modified version of the Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Qm). The ASPI was re-administered one hour after the initial assessments. The ASPI's test–retest reliability was analyzed using intraclass correlation coefficient (ICC) estimates and their 95% confidence intervals (CIs), based on a two-way random effects model with absolute agreement. Construct validity was evaluated using correlation analysis, and the minimal detectable change was determined by calculating the standard error of measurement (SEM) and the minimal detectable change at 95% confidence (MDC95). In addition, the Bland–Altman method was used to assess the level of agreement between the first and second ASPI measurements.
Results: The mean age of the participants with ERA was 14.69 ± 2.95 years. The ASPI measurements demonstrated moderate to excellent reliability regarding ICC values (ICC = 0.683–0.980). The highest reliability was observed in the time component of the 'getting up from the floor' task (ICC = 0.980), while the lowest was in the effort score of the 'putting on socks' task (ICC = 0.683). Statistically significant differences were observed in all ASPI parameters between the first and second trials ($p < 0.05$). The SEM values ranged from 0.17 to 1.85, and the MDC95 values ranged from 0.48 to 5.13, indicating acceptable measurement error levels. Agreement between the first and second ASPI measurements, as assessed by Bland–Altman plots, revealed a mean bias of 0.3 repetitions for forward bending (95% limits of agreement: −2.9 to 3.4), 1.5 repetitions for putting on socks (95% limits of agreement: −1.9 to 5.3), and 0.1 repetitions for rising from the floor (95% limits of agreement: −0.1 to 0.7). In the construct validity analyses of the ASPI, moderate to high significant correlations were found between test parameters and related clinical measures ($p < 0.05$).
Conclusion: The data obtained from this pilot study indicate that the ASPI is a potentially reliable and valid test for objectively assessing physical function in individuals with ERA. In light of this potential, it was concluded that the study should be continued until an adequate sample size is reached.
Trial registration identifying number: NCT06383195
Disclosure
None declared

References
Petty RE, Southwood TR, Manners P, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390-392.
van Weely SF, Dekker J, Steultjens MP, et al. Objective evaluation of physical functioning after tumor necrosis factor inhibitory therapy in patients with ankylosing spondylitis: a selection of 3 feasible performance-based tests. J Rheumatol. 2015;42(4):623-629.

P262

A comparative analysis of pediatric-onset and adult-onset spondyloarthropathy

U. Gul[1], B. Sulu[2], N. Akay[1], E. Kilic Konte[1], E. Aslan[1], A. Gunalp[1], M. Yildiz[1], S. Sahin[1], K. Barut[1], S. Ugurlu[2], O. Kasapcopur[1]
[1]Department of Pediatric Rheumatology, [2]Department of Rheumatology, Istanbul University-Cerrahpasa, Istanbul, Türkiye
Correspondence: U. Gul
Pediatric Rheumatology, **23(2):** P262

Introduction: The term spondyloarthropathy (SpA) encompasses a group of heterogeneous HLA-B27-related inflammatory diseases characterized by the involvement of axial skeletal and peripheral joints. In addition to joint involvement, enthesitis, nail changes, dactylitis, psoriasis, uveitis, and inflammatory bowel diseases may also be SpA-related findings (1). SpA can occur in a wide age range, but the highest incidence is in late adolescence and early adulthood (2).
Objectives: Although they share similar pathologic mechanisms and clinical features, adult-onset and juvenile-onset spondyloarthropathies differ significantly in terms of associated features, patterns of involvement, presenting symptoms, and treatment modalities. We aimed to reveal the differences between these two onset stages and identify the distinguishing features.
Methods: The medical records of 163 pediatric and 165 adult patients from our clinics were retrospectively reviewed. Data on demographic characteristics, medical history, presenting symptoms, family history, test results, joint involvement during follow-up, and treatment regimens were collected and analyzed.
Results: The study included 163 pediatric (67.5% male) and 165 adult (59.4% male) patients (p=0.128). The median age at diagnosis was 13(10-15) years in children and 32(25-40) years in adults. Follow-up was significantly longer in adult patients than in pediatric patients (37 and 49 months, respectively)(p=0.000).
Presentation with peripheral arthritis was 57.7% (94/163) in children versus 17% (28/165) in adults (p=0.000). The rate of sacroiliitis at presentation was 98.8% (163/165) in adults compared to 61.3% (100/163) in children (p=0.000).
Acute phase reactant positivity was similar at initial evaluation. HLA-B27 positivity was significantly higher in adults than in pediatric patients (58.7% vs. 46.3% p=0.036).
AAA was more common in pediatric patients (12.9% vs. 1.2% p=0.000), while uveitis was more common in adults (18.2% vs. 3.6% p=0.000). The most common musculoskeletal system involvements in pediatric patients were sacroiliitis (69.3%), enthesitis (42.3%), and ankle involvement (36.8%). In adults, sacroiliitis (98.8%) was most common, followed by hip (44.2%) and enthesitis (28.5%).
In terms of initial treatment, systemic steroid (p=0.000) and cDMARD (p=0.000) use were significantly more frequent in pediatric patients.

In adults, the use of NSAIDs as initial treatment was more frequent (p=0.000). bDMARDs were added to the treatment earlier in pediatric patients (p=0.000).
Conclusion: Children presented more frequently with peripheral arthritis and enthesitis, whereas adults had predominantly axial involvement. While HLA-B27 positivity was higher in adults, AAA was significantly more common in pediatric patients. However, uveitis was more common in adults. Treatment options differed significantly between groups, with pediatric patients more commonly receiving steroids, cDMARDs, and bDMARDs started earlier in the disease.
Disclosure
None declared

References
Yıldız M, Haşlak F, Adroviç A, Şahin S, Barut K, Kasapçopur Ö. Juvenile spondyloartropathies. Eur J Rheumatol. 2021;9(1):42-49.
Colbert RA. Classification of juvenile spondyloarthritis: Enthesitis-related arthritis and beyond. Nat Rev Rheumatol. 2010;6(8):477-85.

P263

Evaluation of inflammatory bowel disease in patients with Juvenile spondyloarthropathy: a single centre multidisciplinary study

U. Gul[1], I. Ulkersoy[2], A. Tunc[3], S. Ozyildirim[3], N. Akay[1], N. Kologlu Ates[2], O. Tin[2], E. Kilic Konte[1], E. Aslan[1], A. Gunalp[1], A. Kalyoncu Ucar[4], M. Yildiz[1], N. Kepil[5], K. Barut[1], S. Sahin[1], S. Kuruoglu[4], O. F. Beser[2], O. Kasapcopur[1]
[1]Department of Pediatric Rheumatology, [2]Department of Pediatric Gastroenterology, Hepatology and Nutrition, [3]Department of Pediatrics, [4]Department of Pediatric Radiology, [5]Department of Pathology, Istanbul University-Cerrahpasa, Istanbul, Türkiye
Correspondence: U. Gul
Pediatric Rheumatology, **23(2):** P263

Introduction: Juvenile spondyloarthropathies (JSpA) are a group of diseases associated with peripheral joint involvement, axial skeleton involvement, enthesitis, and HLA-B27 positivity(1). In spondyloarthropathies, in addition to classic musculoskeletal involvement, extra-articular findings such as dactylitis, nail changes, psoriasis, acute anterior uveitis, and inflammatory bowel disease (IBD) may also be observed(2).
Symptoms associated with spondyloarthropathies can significantly impact disease progression and lead to significant morbidity and mortality. In particular, symptoms related to IBD (chronic abdominal pain, bloody/mucous diarrhea, weight loss, etc.) affect both the patient's quality of life and the treatment approach. Therefore, early diagnosis of IBD that may accompany joint involvement is essential in patients with spondyloarthropathies.
Objectives: This study was designed to investigate the relationship between FCP levels and endoscopic/histological findings of intestinal inflammation in patients with JSpA. We aimed to determine how FCP concentrations and IBD diagnosis can be predicted based on demographic, clinical, laboratory, imaging, and treatment characteristics.
Methods: A total of 81 JSpA patients were included in the study.
FCP levels were measured, and patients with elevated FCP levels (>100 mcg/g) or ≥2 IBD-related symptoms (chronic diarrhea, weight loss, abdominal pain, bloody or mucus-containing stool) underwent ileocolonoscopy, histopathological evaluation, and radiological assessment (abdominal ultrasound for patients <5 years of age) with MR enterography.
Results: A total of 81 JSpA patients (71.6% male) with an average age of 15.1 years were included in the study. Of these 81 patients, 23 (23.5%) had elevated FCP levels and 6 (7.4%) had symptoms associated with IBD, and all 23 patients underwent ileo-colonoscopy examination and histopathological evaluation. Of these 23 patients, 10 were diagnosed with both macroscopic and microscopic colitis (10/23, 43.5%; 10/81, 12.3%), and 4 with microscopic colitis alone (4/23, 17.4%; 4/81, 4.9%). while the histopathological evaluation of the remaining 9 patients (9/23, 39%; 9/81, 11.1%) was normal. A significant proportion of JSpA patients with elevated FCP levels presented without clinical symptoms of IBD (n=18/81, 22.2%). All 19 patients with positive FCP test results had a history of sacroiliitis confirmed by MRI (p-value: 0.001). No statistically significant differences between the FCP-positive (19/81) and FCP-negative (62/81) groups regarding CRP, ESR, PLT values, and JSPADAI/JADAS-27 scores were found.
Conclusion: Since the results of ileo-colonoscopy in patients with elevated FCP levels confirmed findings associated with EBH, the FCP test can be used for screening for silent EBH, but it should be supported by ileo-colonoscopy examination and histopathological evaluation. These findings suggest that the FCP test and gastrointestinal symptom monitoring should be considered in the early diagnosis and management of EBH in JSpA patients.
Disclosure
None declared

References
1. Adrovic A, Barut K, Sahin S, Kasapcopur O. Juvenile spondyloarthropathies. Curr Rheumatol Rep. 2016;18(8):55.
2. Yıldız M, Haşlak F, Adroviç A, Şahin S, Barut K, Kasapçopur Ö. Juvenile spondyloartropathies. Eur J Rheumatol. 2021;9(1):42-49.

P264

Tear proteomic analysis in uveitis associated with behçet's disease: preliminary results

B. Oksel[1], M. Kasap[2], B. Y. Tuğan[3], A. Cefle[4], G. Akpınar[2], A. Yazıcı[4], L. Karabaş[3], N. Şahin[1], N. Yüksel[3], H. E. Sönmez[1]
[1]Department of Pediatric Rheumatology, [2]Department of Medical Biology, [3]Department of Ophthalmology, [4]Faculty of Medicine, Department of Internal Medicine, Kocaeli University, Kocaeli, Türkiye
Correspondence: B. Oksel
Pediatric Rheumatology, **23(2):** P264

Introduction: Behçet's disease (BD) is a multisystem inflammatory disorder with an incompletely understood pathogenesis. Ocular involvement occurs in 25–75% of patients and, if left untreated, may lead to blindness. The most common ocular manifestation is uveitis, typically presenting as bilateral, recurrent, and non-granulomatous panuveitis. In 10-year retrospective records of patients with Behçet's uveitis, approximately one-third had severe visual impairment at onset, with notable delays in diagnosis. Early and appropriate initiation of immunomodulatory treatment is essential. If uveitis development can be predicted, treatment may be initiated earlier to prevent complications. However, no reliable biomarker currently exists to identify patients at risk.
Objectives: To identify potential protein biomarkers predictive of uveitis risk by analyzing proteomic alterations in tear samples of Behçet's patients with and without uveitis.
Methods: Fourteen Behçet's patients (7 with uveitis, 7 without), followed in rheumatology clinics, were included. Tear samples were collected using Schirmer's test paper and stored at −80°C. Tear proteins were extracted and separated using Bradford and SDS-PAGE methods, followed by comparative analysis. Differentially expressed proteins were excised from gels and analyzed via LC-MS/MS. Bioinformatic analysis was conducted using the STRING database.
Results: Proteomic analysis revealed 61 proteins with differential expression between the groups: 36 were upregulated and 25 downregulated in uveitis samples. Among the upregulated proteins, mucin-1, guanine nucleotide-binding protein, histone H1, and inter-alpha-trypsin inhibitor heavy chain showed the highest increases (up to 1000-fold). Other upregulated proteins exhibited 2–6.4-fold increases. Among the downregulated proteins, ganglioside GM2 activator, immunoglobulin lambda, and V-type proton ATPase subunit G1 demonstrated >1000-fold decreases, while the remainder had approximately 4-fold decreases. Bioinformatic analysis indicated that these proteins are mainly involved in peptidase regulation, endopeptidase inhibition, enzyme inhibition, and signaling pathways.
Conclusion: Although it remains uncertain whether tear protein expression changes reflect disease pathogenesis or chronic inflammation, the identification of tear-based biomarkers may provide insights into uveitis development in Behçet's disease. These findings may support earlier diagnosis and contribute to the development of targeted therapies.
Disclosure
None declared

References

1. Ksiaa, I., Abroug, N., Kechida, M., Zina, S., Jelliti, B., Khochtali, S., Attia, S., & Khairallah, M. (2019). Eye and Behçet's disease. *Journal francais d'ophtalmologie*, *42*(4), e133–e146.
2. Zhong, Z., Su, G., & Yang, P. (2023). Risk factors, clinical features and treatment of Behçet's disease uveitis. *Progress in retinal and eye research*, *97*, 101216. https://doi.org/10.1016/j.preteyeres.2023.101216

P265

Juvenile idiopathic arthritis (JIA) with chronic anterior uveitis: long-term progression and classification insights from a national reuma.pt study

B. Paulo Correia[1,2], D. Vinha[3], S. Rosário[2], I. Leal[4,5], J. M. Dias[6], G. Sequeira[7], R. Sousa[8], I. Santos[9], J. Silva-Dinis[10], H. Assunção[11], L. Miranda[12], M. Cruz[13], M. S. Faria[14], F. Araújo[15,16], P. Nero[17], F. Albuquerque[18], M. D. Lopes[19], F. Costa[20], F. Farinha[21], C. Furtado[22], A. F. Mourão[23,24], M. Cabral[25], V. Fraga[26], S. F. Azevedo[27,28], J. Costa[29], A. R. Vieira[30], M. Conde[31], M. P. Ferreira[32], A. M. Rodrigues[24,33], R. Campanilho-Marques[1,2], F. O. Ramos[1,2]

[1]Paediatric Rheumatology Unit, Rheumatology and Paediatrics Department, Unidade Local de Saúde Santa Maria (ULSSM), Centro Académico de Medicina de Lisboa, [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, [3]School of Science and Technology, Nova University of Lisbon, [4]Ophthalmology Department, Unidade Local de Saúde Santa Maria (ULSSM), Centro Académico de Medicina de Lisboa, [5]Centro de Estudos das Ciências da Visão, Ophthalmology University Clinic, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisbon, [6]Rheumatology Unit, Unidade Local de Saúde do Médio Tejo, Torres Novas, [7]Rheumatology Department, Unidade Local de Saúde do Algarve, Faro, [8]Rheumatology Unit, Unidade Local de Saúde do Tâmega e Sousa, Penafiel, [9]Rheumatology Department, Unidade Local de Saúde de Viseu Dão-Lafões, Viseu, [10]Rheumatology Department, Unidade Local de Saúde de São José, Lisbon, [11]Rheumatology Department, Unidade Local de Saúde de Trás-os-Montes e Alto Douro, Vila Real, [12]Rheumatology Department, Hospital CUF Alvalade, Lisbon, [13]Rheumatology Clinic, Medical Clinics Caldas da Rainha, Caldas da Rainha, [14]Rheumatology Department, Hospital Central do Funchal, Funchal, [15]Rheumatology and Osteoporosis Unit, Hospital de Sant'Ana, SCML, [16]Rheumatology Department, Hospital CUF Cascais, Cascais, [17]Rheumatology Department, Hospital CUF Descobertas, Lisbon, [18]Rheumatology Department, Unidade Local de Saúde de Coimbra, Coimbra, [19]Rheumatology Department, Unidade Local de Saúde de São João, Oporto, [20]Rheumatology Department, Unidade Local de Saúde de Gaia/Espinho, Gaia, [21]Rheumatology Department, Unidade Local de Saúde – Lezíria, Hospital Distrital de Santarém, Santarém, [22]Rheumatology Department, Hospital do Divino Espírito Santo, Ponta Delgada, [23]Rheumatology Department, Unidade Local de Saúde de Lisboa Ocidental, Hospital Egas Moniz, [24]Comprehensive Health Research Centre (CHRC), Nova Medical School (NMS-FCM), Lisbon, [25]Paediatric Department, Hospital Prof. Doutor Fernando Fonseca, Amadora, [26]Rheumatology Department, Unidade Local de Saúde de Almada-Seixal, Almada, [27]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, [28]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, [29]Rheumatology Department, Hospital Lusíadas Braga, Braga, [30]Instituto Português de Reumatologia, [31]Paediatric Rheumatology Unit, Unidade Local de Saúde de São José, Hospital de Dona Estefânia, Lisbon, [32]Rheumatology Department, Unidade Local de Saúde do Alto Minho, Ponte de Lima, [33]Reuma.pt, Sociedade Portuguesa de Reumatologia, Lisbon, Portugal

Correspondence: B. Paulo Correia

Pediatric Rheumatology, **23(2):** P265

Introduction: Chronic anterior uveitis is the most common extra-articular manifestation of juvenile idiopathic arthritis (JIA). The PRINTO criteria suggest a unique JIA subtype in children at high risk of iridocyclitis. This study investigates whether chronic uveitis defines a distinct JIA subset with consistent characteristics into adulthood, independent of ANA status, sex, or age at onset.

Objectives: To identify clinical and laboratory factors associated with chronic or recurrent anterior uveitis in JIA patients during long-term follow-up and assess whether this subgroup constitutes a distinct disease entity that persists into adulthood.

Methods: A retrospective, national, multicentre study using data from the National Registry of Rheumatic Patients (Reuma.pt) was conducted. JIA patients aged ≥18 years at their last visit were included. Chronic or recurrent uveitis was defined as a single episode lasting >3 months with relapse within 3 months post-therapy, or repeated episodes with ≥3 months of inactivity between them. Patients with acute or no uveitis were grouped for analysis. Associations were analysed with appropriate statistical tests, and multiple comparisons were adjusted using the Holm-Bonferroni correction. A weighted logistic regression model was used for multivariate analysis.

Results: Among 778 patients with JIA, 63.8% were female, with a mean disease duration of 23.6 ± 3.1 years. Of these, 51 (6.6%) developed chronic or recurrent anterior uveitis during the follow-up period. No significant sex differences were observed between patients with and without uveitis ($p = 0.766$).

Compared to those without uveitis, patients with chronic or recurrent uveitis had a significantly earlier disease onset (median 4.7 *vs*. 10.1 years, $p < 0.001$), higher frequency of ANA positivity (62.7% *vs*. 31.0%, $p < 0.001$), and lower frequency of RF positivity (2.4% *vs*. 17.0%, $p = 0.025$). Persistent oligoarthritis was the most common JIA category in the uveitis group compared to those without (52.0% *vs*. 18.0%, $p < 0.001$). These patients were also more often treated with biologic DMARDs (62.7% *vs*. 44.7%, $p = 0.019$) and had more frequent treatment switches ($p < 0.001$).

In multivariate analysis, earlier age at onset (OR 0.93, 95% CI 0.89–0.97, $p < 0.001$), ANA positivity (OR 2.64, 95% CI 1.80–3.90, $p < 0.001$), RF negativity (OR 0.13, 95% CI 0.05–0.31, $p < 0.001$), and persistent oligoarthritis (OR 2.38, 95% CI 1.51–3.80, $p < 0.001$) remained independently associated with chronic uveitis.

Despite long-term follow-up, only 46.5% of patients with chronic uveitis met adult disease classification criteria, compared to 73.8% of those without uveitis ($p < 0.001$).

Conclusion: In long-term follow-up into adulthood, chronic anterior uveitis in JIA was associated with early onset, ANA positivity, RF negativity, and persistent oligoarthritis, but not with sex. These features remained consistent over time and defined a group of patients who rarely fulfilled adult classification criteria. This supports the concept of a unique childhood-onset disease that remains clinically distinct in adulthood.

Disclosure

None declared

P266

Paediatric uveitis - retrospective comparison of cataract surgery outcomes with or without intraocular lens implantation from two tertiary centres in the United Kingdom

C. Govardhan[1], A. Batchu Prithvi[1], B. Aladaileh [1], E. Cattermole[2], F. Abdelsattar[2], C. Guly[2], J. Choi[3], J. Keller[2], A. V Ramanan[1]

[1]Paediatric Rheumatology, Bristol Royal Hospital for Children, [2]Opthalmology, Bristol Eye Hospital, [3]Opthalmology, Sheffield Children's Hospital, Bristol, United Kingdom

Correspondence: C. Govardhan

Pediatric Rheumatology, **23(2):** P266

Introduction: Cataract is one of the most common and visually debilitating complications of paediatric uveitis, developing as a consequence of chronic inflammation and steroid use. Cataract surgery can be technically challenging in patients with uveitis, and the outcomes are less certain. (1) Inserting an intraocular lens (IOL) is controversial for paediatric uveitis patients, leading to variable practice across different institutions. This study compares the outcomes of cataract surgery associated with paediatric uveitis with or without IOL implantation.

Objectives: To compare outcomes in children with uveitis undergoing cataract surgery with and without intraocular lens implantation.

Methods: A retrospective comparison study was conducted at two centres, Bristol Eye Hospital (Centre 1-Cataract surgery with IOL implantation) and Sheffield Children's Hospital (Centre 2-Cataract surgery without IOL implantation). All children below 18 years of age with uveitis who underwent cataract surgery between year 2011 and 2024 were included. Pre and post operative outcomes from the two groups were compared, including best corrected visual acuity(BCVA), LogMAR lines of improvement, ocular inflammation and complications. Follow

up data upto 2 years post-surgery where available were recorded. Data was analysed using descriptive statistics.
Results: There were total 35 children (43 eyes) identified from both centres, 25 children (30 eyes) from centre-1 and 10 children (13 eyes) from centre 2. The median age at diagnosis in years was 5.5years(centre 1) and 5years (centre 2) and median age at surgery was 9 and 5 years with M:F=2:3 and 1.6:1 respectively. JIA was the most common etiology at both centres (60% and 90% respectively). Anterior uveitis was the most common subtype of uveitis at both centres (29 eyes, 9 eyes respectively). Median preoperative BCVA (IQR) was 0.84 (0.60-1.43) and 1.6 (0.92- 2.48) respectively. The median postoperative BCVA at 3 months, 12 months and 24 months at centre 1 was 0.20,0.2 and 0.10 and at centre 2 was 0.38, 0.50 and 0.15. Percentage of children with 2 or more lines of improvement at 3,12 and 24 months at centre 1 was 82.8%, 93.1% and 80.8% whereas at centre 2 was 84.6%, 75% and 81.8%. Surgical capsulotomy was required in 3 eyes (10%) by 24 months at centre 1. Active anterior chamber inflammation >1+ cells was recorded in 10(33%), 8(36.4%), 5(16.7%) in centre-1 and 1(7.7%), 2(15.4%), 1(7.7%) in centre-2 at 3,12 and 24 months.
Conclusion: Good visual improvement following cataract surgery in children with uveitis with and without IOL would support either of the practices. However, a caveat being that IOL insertion could potentially be associated with active inflammation.
Disclosure
None declared

Reference
1. Quiñones K, Cervantes-Castañeda RA, Hynes AY, Daoud YJ, Foster CS. Outcomes of cataract surgery in children with chronic uveitis. J Cataract Refract Surg. 2009 Apr;35(4):725–31.

P267

Transcriptiomics of tear rna from children with active and inactive chronic anterior uveitis

T. Do[1], B. Michalidas[1], M. Pavlenko[1], A. Duell[1], S. Angeles-Han[1,2], G. S. Schulert[1,2]
[1]Cincinnati Children's Hospital, [2]University of Cincinnati College of Medicine, Cincinnati, United States
Correspondence: G. S. Schulert
Pediatric Rheumatology, **23(2):** P267

Introduction: Chronic anterior uveitis (CAU) is a potentially sight-limiting complication of pediatric rheumatic diseases, including juvenile idiopathic arthritis. However, the underlying inflammatory biology of CAU in the eye is poorly understood, and there is a critical need for improved biomarkers for CAU development, progression, and damage.
Objectives: Our objective was to develop methods for RNA collection and transcriptional profiling from tear fluid of children with CAU.
Methods: Tear fluid was collected using Schirmer strips. CAU was graded as active (anterior chamber [AC] cell ≥0.5+) or inactive (AC=0) by Standardization of Uveitis Nomenclature (SUN) criteria. RNA was extracted from fresh or frozen absorbed Schirmer strips using three methods. MagMAX-96 Total RNA Isolation Kit was used after incubating with either 140uL of Lysis/Binding, or with 500uL Phosphate Buffered Saline (PBS). Alternatively, 500uL of TRIzol Reagent (ThermoFisher) was added to each tear strip, followed by RNA extraction. Samples with RNA Integrity Number (RIN)> 4 were selected for transcriptional profiling using the Ampliseq Transcriptome Panel on the Ion Torrent sequencing system. Sequencing data was processed and aligned using Ion Torrent, and differential gene expression for genes with mean reads per million > 5 was determined using AltAnalyze ($p<0.05$, fold change >2). Pathway analysis was performed using GO-Elite.
Results: For both RNA extraction methods using the MagMAX-96 Total RNA Isolation kit, the concentration of RNA was low and of poor quality. In contrast, for 32 samples that were extracted via TRIzol, RNA concentrations ranged from 6.9ng/uL – 69.8ng/uL with RIN numbers 1.0–7.8. We then performed Ampliseq Transcriptome profiling on 6 tear RNA samples from 4 patients with active CAU and 7 samples from 5 patients with inactive CAU. One patient with active CAU was excluded after sequencing for low read quality. The remaining samples were sequenced to a mean depth of 6.4 million reads (range 4.0-9.9 million) and we identified 11,595 genes with mean expression >5 RPM. Comparing active to inactive CAU, we found 113 significantly upregulated and 35 significantly downregulated genes. Among the most enriched gene pathways of upregulated genes in active CAU were laminin complex (z-score 13.3, adjusted p=0.026), extracellular matrix (z-score 7.6, adjusted p=0.003), and regulation of cell migration (z-score 5.1, adjusted p=0.09). The most significantly enriched gene pathway of downregulated genes in active CAU was immune system processes (z-score 6.2, adjusted p=0.0001), including IL7R, IRF5, NAIP, and NCF1. Among the marker genes for patients with inactive CAU was MAPILC3A, which encodes LCA3, expressed in the retinal pigment epithelium, which has a key role in blood-retinal barrier and retinal immune regulation.
Conclusion: This pilot work demonstrates our ability to obtain high-quality RNA suitable for transcriptomics from tear fluid of children with CAU. We also find that active CAU is associated with transcriptional activation in pathways associated with eye injury and blood-retinal barrier, including laminin complex, extracellular matrix, and cellular migration, as well as downregulation of inflammatory response genes.
Disclosure
T. Do: None declared, B. Michalidas: None declared, M. Pavlenko: None declared, A. Duell: None declared, S. Angeles-Han: None declared, G. Schulert Grant/Research Support with: IpiNovyx, Consultant with: Novartis, SOBI

P268

Comparing biomarkers associated with uveitis in tear fluid and blood samples of children with juvenile idiopathic arthritis: the pedia-u study

I. Maccora[1,2], M. Pavlenko[3], M. Altaye[4], H. I. Brunner[3,5], M. Chang[6], A. Cooper[7], S. Davidson[8], A. Duell[3], B. Gangwani[9], A. Hersh[10], G. N. Holland[11], C. D. Langefeld[12], M. Ierman[13], M. Lo[6], V. Miraldi Utz[14,15], S. Prahalad[16], G. Schulert[3,5], M. Quinlan-Waters[3], E. Stahl[17], E. Tsui[11], S. T. Angeles-Han[3,5]
[1]Rheumatology Division, ERN ReCoNNET Center, [2]Rheumatology Unit, ERN ReCoNNET, Meyer Children's Hospital IRCCS, Florence, Italy, [3]Rheumatology Division, [4]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, [5]Department of Pediatric, University of Cincinnati College of Medicine, Cincinnati, [6]Immunology Division, Boston Children's Hospital, Boston, [7]Rheumatology Division, Children's Mercy Hospital and University of Missouri-Kansas City, Kansas City, [8]Department of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, [9]Department of Ophthalmology, Boston Children's Hospital, Boston, [10]Pediatric Rheumatology, University of Utah School of Medicine, Salt lake City, [11]UCLA Jules Stein Eye Institute and the Department of Ophthalmology, UCLA David Geffen School of Medicine, Los Angeles, [12]14Department of Biostatistics and Data Science, Center for Precision Medicine, Wake Forest School of Medicine, Winston-Salem, [13]Rheumatology Division, lermanm@chop.edu, Philadelphia, [14]Abrahamson Pediatric Eye Institute, Cincinnati Children's Hospital Medical Center, [15]Department of Ophthalmology, University of Cincinnati College of Medicine, Cincinnati, [16]Department of Pediatric, Emory University School of Medicine, Atalanta, [17]Department of Ophthalmology, Children's Mercy Kansas City, UMKC School of Medicine, Kansas City, United States
Correspondence: I. Maccora
Pediatric Rheumatology, **23(2):** P268

Introduction: Chronic anterior uveitis (CAU) develops in 15-20% of juvenile idiopathic arthritis (JIA) cases. Early detection may prevent vision loss. However, known clinical risk factors do not accurately predict CAU. We and others report that 50% of the same protein biomarkers detected in tear fluid of patients overlapped in paired aqueous humor. Non-invasive biomarkers that reflect eye inflammation and are easily implemented in clinic may improve prediction of CAU and influence screening.
Objectives: We aim to compare inflammatory mediators in tear fluid and serum of children with JIA with and without CAU.
Methods: This prospective multicenter study enrolled JIA children without (JIA-no-U) and with CAU (JIA-U) ≥4 y/o. Serum was paired with tear fluid collected from both eyes using Schirmer strips during clinic visits. S100A8/A9 and A12 were measured by ELISA, and IL-8, CXCL-10 (IP-10), MCP-1, sICAM-1, APRIL and VEGF-A by Luminex assays

in all samples. We compared levels between JIA-no-U and JIA-U per sample type, then between serum and tear fluid where we calculated tear/blood ratios to assess the difference in abundance between both samples. As samples were collected from both eyes, we used a mixed model analysis with individuals and eyes as random effects. Data was transformed to a log scale prior to analysis.

Results: Forty-two patients (31 JIA-no-U, 11 JIA-U) contributed 84 tear (62 JIA-no-U, 22 JIA-U) and 20 serum samples (16 JIA-no-U, 4 JIA-U). Two JIA-no-U patients at time of collection later developed CAU but were grouped as JIA-U.

In serum, S100A12 (JIA-no-U LS mean 76,807.11 vs JIA-U LS mean 27,455.02, p=0.0027) and S100A8/A9 (JIA-no-U LS mean 5,608.29 vs JIA-U LS mean 2,217.52, p=0.0008) were elevated in JIA-no-U (Table 2). In tears, CXCL-10 (JIA-no-U LS means 5.1 vs JIA-U LS means 4.01, p=0.001) and MCP1 (JIA-no-U LS Means 2.18 vs JIA-U LS means 1.31, p= 0.0083) were elevated in JIA-no-U.

Comparing paired serum and tears levels in 19 patients, S100A12 (serum mean 4.67 vs tears mean 3.09, ratio 0.66 p<0.001) and sICAM-1 (4.24 vs 3.55, 0.83 p<0.001) were significantly elevated in serum. Conversely, CXCL10 (serum 0.09 vs tear 2.14, ratio 22.76 p<0.001), APRIL (1.88 vs 3.55, 1.86 p<0.001), and VEGF (2.2 vs 2.69, 1.22 p<0.003) were elevated in tear fluid. MCP-1 and S100A8/9 were similar in both samples (21.06 vs 0.86, 0.811 p=0.292 and 3.54 vs 3.66, 0.393 p=0.393 respectively).

Conclusion: We newly compare levels of tear and blood-based biomarkers in children with JIA with and without CAU. Differences in S100 proteins in serum may reflect systemic inflammation. CXCL10, APRIL and VEGF were highly enriched in tear fluid, while MCP-1 and S100 proteins were similar in both samples. These tear-based biomarkers may reflect damage from inflammation, allowing an influx of inflammatory mediators into the eye. Importantly, biomarkers reported in JIA and JIA-U were detected in both sample types. Elevated baseline S100A12 in JIA children who develop CAU has been noted, as well as VEGF in cystoid macular edema. Tear and blood-based biomarkers are easily measured in various clinical settings. may complement known CAU risk factors, and improve screening. Our future studies consider disease activity and topical and systemic treatment.

Trial registration identifying number: N/A

Disclosure

None declared

P269

Best outcome measures to use in a 12-month clinical trial in Juvenile idiopathic arthritis associated anterior uveitis

I. Foeldvari[1], S. T. Angeles-Han[2], A. G. Brost [3], J. de Boer[4], J. Díaz-Cascajosa [5], M. Glerup [6], H. Ingels [3], V. Koopman-Kalinina Ayuso[7], I. Maccora [8], E. Nordal [9], S. Gabriele[10], A. Solebo [11], J. F. Swart[12], C. L. L. I. van Meerwijk[13], J. Anton [5]

[1]Hamburg Centre for Pediatric and Adolescent Rheumatology, Hamburg, Germany, [2]Department of Pediatrics and Department of Ophthalmology, Cincinnati Children's Hospital Medical Center, Cincinnati, United States, [3]Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, [4]University Medical Center Utrecht, Utrecht, Netherlands, [5]Hospital Sant Joan de Déu, Barcelona, Spain, [6]Aarhus University Hospital, Aarhus, Denmark, [7]Universitair Medisch Centrum Utrecht, Utrecht, Netherlands, [8]University of Florence, Florence, Italy, [9]University Hospital of North Norway, UiT The Arctic University of Norway, Tromsø, Norway, [10]ERN-ReCONNET Center, Meyer Children's Hospital IRCCS, Florence, Italy, [11]Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [12]Wilhelmina Children's Hospital/UMC Utrecht, Utrecht, [13]University Medical Center Groningen, Groningen, Netherlands

Correspondence: I. Foeldvari

Pediatric Rheumatology, **23(2):** P269

Introduction: JIA associated anterior uveitis (JIAU) is the most common extraarticular manifestation of JIA. There are no published proposed outcome measures for a 12-month trial.

Objectives: To develop outcome measures for use in a 12-month clinical trial

Methods: The Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC) is an international multidisciplinary group including paediatric rheumatologists and ophthalmologists with academic interest in JIAU and patient representatives. At our last meeting, 01/25 in Barcelona, Spain, we had presentations regarding outcome measures used in Phase III trials or in publications. This was followed by a consensus meeting where nominal group technique was used with 15 to 16 voters per subject. Consensus required 80% agreement.

Results: The inclusion criterion is: Active anterior uveitis defined as anterior chamber (AC) grade ≥1+ according to SUN criteria[1] at two consecutive visits.

We propose primary and secondary outcome measures:

Primary outcome measures of improvement:

Reduction of cell number in the AC (by a blinded assessor) 15/15

A two step reduction or grade 0 in the worst eye 16/16

Secondary outcome measures:

- Inactive disease according to the published MIWGUC definition* [2] 16/16
- Remission of JIAU on or off medication** 16/16
- Best corrected visual acuity in each affected eye 16/16
- Quality of life: EYE-Q 16/16
- New occurrence of damage *** 16/16
- Need for topical or systemic steroids 16/16
- Adverse events (MEDDRA dictionary) 16/16
- Active joint count 16/16
- Physician global disease activity VAS 15/15

Flare: exploratory measure

Conclusion: Based on a global consensus meeting of rheumatologists and ophthalmologists with expertise in uveitis, we propose outcome measures for use in a 12-month drug trial in JIAU. Validation is needed in a prospective trial.

Disclosure

None declared

References

1. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol. 2005 Sep;140(3):509–16.
2. Foeldvari I, Klotsche J, Simonini G, Edelsten C, Angeles-Han ST, Bangsgaard R, de Boer J, Brumm G, Torrent RB, Constantin T, DeLibero C, Diaz J, Gerloni VM, Guedes M, Heiligenhaus A, Kotaniemi K, Leinonen S, Minden K, Miranda V, Miserocchi E, Nielsen S, Niewerth M, Pontikaki I, de Vicuna CG, Zilhao C, Yeh S, Anton J. Proposal for a definition for response to treatment, inactive disease and damage for JIA associated uveitis based on the validation of a uveitis related JIA outcome measures from the Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC). Pediatr Rheumatol Online J. 2019 Oct 1;17(1):66.

P270

Economic burden of Juvenile idiopathic arthritis (JIA)-associated uveitis: results from the icon jia inception cohort

J. Klotsche[1], K. Minden[1,2], M. Niewerth[1], C. Tappeiner[3,4], A. Heiligenhaus[4,5]

[1]Epidemiologie, Deutsches Rheuma-Forschungszentrum, Leibniz Institut, [2]Abteilung für Rheumatologie und klinische Immunologie, Charité - Universitätsmedizin Berlin, Berlin, Germany, [3]Augenabteilung, Pallas Kliniken, Olten, Switzerland, [4]Universität Duisburg-Essen, Essen, [5]Augenzentrum am St. Franziskus Hospital, Münster, Germany

Correspondence: J. Klotsche

Pediatric Rheumatology, **23(2):** P270

Introduction: There is little data available on the economic burden of JIA-associated uveitis (JIAU) in comparison to JIA patients without uveitis.

Objectives: This study analyzes the direct and indirect costs of medical care and the costs for the families of affected children.

Methods: In the multicenter prospective observational study ICON, a total of 953 patients with newly diagnosed JIA (diagnosis within 12 months before enrolment) were included in the cohort and regularly examined by pediatric rheumatologists (3 monthly within the first year and then every 6-months). Patients with new-onset uveitis were additionally examined by ophthalmologists (3 monthly within the first year and then every 6-months). Clinical data, laboratory parameters and medical costs and expenses were collected from 128 patients

with new-onset uveitis by parents (cost diary) and compared with JIA patients without uveitis (n=128 controls matched for age, JIA category, disease duration, gender). The standardized valuation rates from a societal perspective according to Bock at al. 2015 were used to calculate the costs; the year 2021 formed the basis for calculating the medication costs.

Results: The proportion of girls in patients with uveitis or controls was 75%, 56% were diagnosed with persistent oligoarthritis and 23% with seronegative polyarthritis, the mean age at onset of uveitis was 4.6 years. The mean total direct and indirect annual costs for JIAU (M±SD, 8334±7066€) were significantly higher (p<0.001) compared to the control group without uveitis (M±SD, 3219±5207€), especially for patients with uveitis-related complications (n=52; M±SD 10000±7797€) or patients with performed eye surgeries (n=8; M±SD 15,700±9142€). Drug therapy, in particular disease-modifying drugs (DMARD; M±SD, 5187±5560€ versus 2395±4786€), utilization of medical services (M±SD, 685±814€ versus 284±335€) and inpatient stays (M±SD, 1180±2378€ versus 155±533€) caused significantly higher costs in JIAU patients (each, p<0.001). Indirect costs due to days absent from work (1003±2375 versus 262±573, p<0.001) and financial burden on families (281±604 versus 149±272, *p*=0.018) were significantly increased due to uveitis compared to JIA patients without uveitis.

Conclusion: JIA-associated uveitis is associated with a significant financial burden. Especially DMARD, uveitis-related complications and secondary eye surgery are relevant cost factors.

Disclosure

None declared

P271

The impact of autoimmune uveitis on the quality of life in children

O. A. Oshlianska[1,2], I. Shevchenko[1]

[1]Pediatrics, Neonatology, Pediatric Infectious Diseases, Immunology, and Allergology, P. L. Shupyk National University of Health Care of Ukraine, [2]Pediatric, State Institution "All-Ukrainian Center for Motherhood and Childhood of the National Academy of Medical Sciences of Ukraine", Kyiv, Ukraine

Correspondence: O. A. Oshlianska

Pediatric Rheumatology, **23(2):** P271

Introduction: Severe ocular involvement significantly affects the quality of life in children. However, it remains unclear how much ocular complications worsen the condition of patients with systemic diseases, particularly those with juvenile idiopathic arthritis (JIA).

Objectives: To conduct a comparative study of the visual involvement influence quality of life indicators using standardized scales in children with JIA associated uveitis (JIA-U), idiopathic uveitis (IU) and JIA without uveitis.

Methods: A total of 70 patients aged 3–18 years were examined and divided into three groups: 33 children with JIA without uveitis, 26 children with JIA-U, and 11 children with IU. Girls comprised 65.0% of the cohort. All patients underwent ophthalmologic and general clinical examinations. In patients with JIA, disease activity was assessed using the JADAS-27 score. Quality of life was evaluated using the Childhood Health Assessment Questionnaire (CHAQ), the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25), and the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire.

Results: Anterior uveitis was present in all cases. The frequency of intermediate uveitis was comparable across groups (15.38% in JIA-U and 18.18% in IU). Bilateral ocular involvement was observed in 57.59% of patients with JIA-U and in 64.54% of patients with IU. The frequency of ocular complications was similar between the groups. Arthritis activity was comparable between JIA patients with and without uveitis (JADAS-27 scores: 9.7±2.4 vs. 9.4±2.5, respectively). Assessment of quality of life demonstrated significant impairment in patients with ocular involvement, with more severe deterioration observed in children with JIA-U (NEI VFQ-25: 3.319±0.4 vs. 3.3±0.6 for IU; DASH: 3.619±0.4 vs. 3.909±0.5 for IU).

The CHAQ "uveitis" domain did not show significant differences between patients with and without arthritis. The CHAQ "joint" domain scores were comparable between JIA patients without uveitis (2.070±0.3) and those with uveitis (2.108±0.3). Correlation analysis revealed that systemic inflammatory markers (ESR and CRP) did not significantly affect quality of life. However, persistent ocular damage was strongly associated with quality of life impairment (band keratopathy r=0.677, cataract r=0.55, optic nerve and macular edema r=0.503). A decrease in serum vitamin D levels negatively impacted quality of life (r=−0.508). Anemia did not significantly influence quality of life according to CHAQ scores.

Conclusion: Currently, autoimmune uveitis has a relatively reduced impact on the quality of life in children. The NEI VFQ-25 questionnaire was more sensitive in detecting the effect of uveitis on quality of life, while the DASH questionnaire proved useful for assessing the impact of visual impairment on fine motor skills, physical activity, and social interaction.

Disclosure

None declared

P273

Baricitinib in paediatric rheumatology: real-world safety experience from a UK tertiary centre

A. Barmpakou, O. Kul Cinar, S. Compeyrot-Lacassagne, E. Moraitis, M. Al Obaidi, P. Brogan, D. Eleftheriou, C. Papadopoulou

Paediatric Rheumatology, Great Ormond Street Hospital, London, United Kingdom

Correspondence: A. Barmpakou

Pediatric Rheumatology, **23(2):** P273

Introduction: Baricitinib,a Janus kinase(JAK) inhibitor,has been investigated as a potential treatment for monogenic interferonopathies and other autoinflammatory disorders.By inhibiting JAK1 and JAK2,baricitinib may downregulate excessive interferon signaling,thereby alleviating inflammatory manifestations.However,treatment with JAK inhibitors may be associated with adverse effects,including abdominal pain,dyslipidaemia,headache,increased susceptibility to infections,nausea,skin reactions,neutropenia,thrombocytosis and herpes zoster.

Objectives: To evaluate the safety and tolerability of baricitinib in a cohort of paediatric patients with rheumatological conditions.

Methods: We conducted a retrospective study at Great Ormond Street Hospital,a tertiary paediatric rheumatology centre in London,UK to assess adverse effects associated with baricitinib treatment.The cohort included 37 patients with various rheumatological diagnoses who received baricitinib between 2017 and 2025.

Results: Among the 37 patients,16(43%) were diagnosed with monogenic interferonopathies or other autoinflammatory conditions:3 with SAVI,1 with CANDLE syndrome,3 with IRAK-4 deficiency(NASA syndrome),1 with Blau syndrome and 8 with unclassified interferonopathies.Three patients(8%) were diagnosed with juvenile dermatomyositis(JDM) with overlap features;3(8%) had soJIA;1(3%) had JIA-associated uveitis;1(3%) had haploinsufficiency of A20;12(32%) had isolated JDM and 1(3%) had acute COVID-19 with a complex genetic background.

Severe lower respiratory tract infections occurred in 4 patients(11%),two of whom required intensive care unit admission. One of these patients developed pleural effusions requiring VATS and necrotizing Staphylococcus aureus pneumonia, leading to discontinuation of baricitinib.

Baricitinib was discontinued in three patients(8%) due to parental decision.In another four patients(11%),the medication was discontinued by the clinical team due to lack of efficacy.Two patients discontinued treatment due to severe anaemia.

Positive urinary BK/JC virus PCR was detected in 6 patients(16%) without clinical evidence of renal disease; 5 patients(13.5%) had transient viraemia.Laboratory abnormalities included transient leukopenia(n=11,30%),lymphopenia(n=13,35%) and neutropenia(n=7,18%).Transient transaminitis was observed in 3 patients(8%),while no cases of renal dysfunction were reported.Moreover,one patient developed cutaneous mastocytosis.

The dose of baricitinib varied from 2 mg OD(in the patient with JIA-associated uveitis) to 10 mg BD as per NHS commissioning policy for baricitinib use in monogenic interferonopathies.

Conclusion: Baricitinib represents a novel and promising therapeutic option in the management of paediatric rheumatological conditions driven by type I interferon dysregulation.While adverse

effects—including some potentially severe infections and cytopenias—were observed,the majority were transient and manageable. Overall,baricitinib demonstrated an acceptable safety profile in this diverse cohort,supporting its continued consideration in carefully monitored clinical settings.

Disclosure
None declared

Reference
1. https://www.england.nhs.uk/publication/baricitinib-for-use-in-monogenic-interferonopathies-adults-and-children-2-years-and-over/July 2021

P274

Healthcare professionals' decision making around methotrexate in paediatric rheumatology: qualitative study

D. Ghio[1], A. Ledwith[1], F. McErlane[2], C. Pain[3], H. Lythgoe[4], J. Brooks[1]
[1]University of Manchester, Manchester, [2]Newcastle Upon Thyne Hospitals NHS Foundation Trust, Newcastle, [3]Alder Hey, Liverpool, [4]Royal Manchester Children's Hospital, Manchester, United Kingdom
Correspondence: A. Ledwith
Pediatric Rheumatology, **23(2):** P274

Introduction: Methotrexate is considered the gold standard first line treatment for many inflammatory rheumatological diseases with onset in childhood. Methotrexate can be an effective treatment for inflammatory disease (with JIA responses between 65 and 90%) but more than half of the children who take it experience a well-known phenomenon of "methotrexate intolerance". Methotrexate intolerance includes a range of distressing physical and/or behavioural symptoms and is the most common reason for discontinuing the treatment or not taking it as prescribed. The information needed to facilitate shared decision making around methotrexate intolerance is poorly understood.
Objectives: To explore how healthcare professionals (paediatric rheumatologists and specialist nurses) explore and mitigate methotrexate intolerance, focussing on the information needed to inform shared decision making.
Methods: 10 UK-based paediatric healthcare professionals took part in a qualitative study. Interview questions were informed by a decision-making framework exploring why and how methotrexate decision are made in paediatric rheumatology clinics. Data were collected through semi-structured interviews and thematically analysed through template analysis, allowing development of inductive themes, whilst also considering a priori themes developed from the shared decision-making literature.
Results: Healthcare professionals believe methotrexate is a useful treatment, but we identified clear differences in the approach to methotrexate intolerance. Nausea was reported to be the most common side effect reported by patients and/or discussed in clinic. Participants reported prioritising patient quality of life in communication and decision making around next steps. There were discrepancies between reported approaches to management.
Managing psychological and behavioural side effects. There were differences in how healthcare professionals dealt with and communicated about anticipatory symptoms and behavioural symptoms related to methotrexate.
Decisions on when to stop or withhold treatment. Decision making around monitoring was unclear, for example, the optimal response to elevated alanine aminotransferase (ALT) levels was identified as requiring more guidance.
Focusing on holistic care including quality of life – there is inconsistency around the exploration and mitigation of methotrexate intolerance of overall quality of life.
Conclusion: There is presently no clear guidance relating to the facilitation of shared decision-making around methotrexate treatment in paediatric rheumatology. Treatment plans can vary and there is little guidance for healthcare professionals attempting to use a shared decision-making approach around methotrexate and methotrexate intolerance. This work further supports the need for novel tools to aid shared decision-making and clinical communication relating to methotrexate intolerance.

Disclosure
None declared

P275

Influenza vaccination rates and the use of live attenuated intranasal influenza vaccine (LAIV) and inactivated intramuscular vaccine (IIM) in children on immune modulating rheumatology medications (IMRM) in two centres

A. Fell[1], I. Kelly[2], A. Cruickshank[2], E. Carson[1]
[1]Paediatric Rheumatology, NHS Greater Glasgow and Clyde, Glasgow, [2]Paediatric Rheumatology, NHS Lothian, Edinburgh, United Kingdom
Correspondence: A. Fell
Pediatric Rheumatology, **23(2):** P275

Introduction: WHO(1) recommends a flu vaccine coverage rate of 75% in at-risk groups, there is no recent data on rates in children on IMRM in the UK.
PRES recommends IIM (2) as no data available on mucosal vaccines. Within the UK, LAIV is recommended on csDMARDs (3).
LAIV has been shown to be more protective than IIM (4), and as it is pain free it can increase vaccination rates (5).
Objectives: IMRM Patients in 2 health boards were audited in the Flu 24/25 season to
Establish confirmed uptake rates, compared to national averages
To show use of LAIV by medications
Compile LAIV side effects
Compare Flu positivity rates, versus national age group
Methods: Between September 2024 and March 2025, All children over 2 years until 18 are offered free seasonal flu vaccine, with children from 6 months in at risk groups also offered. Vaccination is centrally recorded. Glasgow holds lists of patients on IMRM. During this period A&E, Outpatient, inpatient and helpline notes were checked for reports of coryzal symptoms or side effects from vaccination. Respiratory swab results were obtained from microbiology's central database. Edinburgh reviewed all patients attending Paediatric Rheumatology clinics between the start of January 2025 and end March 2025.
Results: A total of 346 patients were identified, Glasgow having ⅔ of the group. 193 were vaccinated. Overall vaccination rate was 55.7% slightly lower than the under 18 national average of 59.5%, the 5-11 age group was most divergent at 55.9% compared to 68.1%, over 12 rate matched national average.
Of 41 who were given LAIV, no side effects were reported.
9 were pre IMRM start, 17 were on csDMARDS of MMF, leflunomide, colchicine, MTX, however 15 were Biologics or tsDMARDs (4 Adalimumab + DMARD, 2 Etanercept, 2 Etanercept +DMARD, 2 Infliximab +DMARD, 4 Rituximab, 1 Tofacitinib + DMARD). Of the 151 given IIM, 17 could have been offered LAIV.
National under 18 flu swab positivity rate was 13%, in the group overall rate was 23% (8.7% in those vaccinated and 43.7% in those unvaccinated).
Conclusion: Vaccination rates in children were below WHO recommendations and lagged behind the general population, a quality improvement (QI) project to increase uptake is required. LAIV was tolerated in this cohort, it's safe inadvertent use in biologics and tsDMARDs may allow painless vaccination in this group, however, a QI to improve appropriate administration is needed. Flu positivity rates were higher in patients on IMRM.

Disclosure
None declared

References
1. WHO. Prevention and control of influenza pandemics and annual epidemics. 2003(FIFTY-SIXTH WORLD HEALTH ASSEMBLY).
2. Jansen MHA, Rondaan C, Legger GE, Minden K, Uziel Y, Toplak N, et al. EULAR/PRES recommendations for vaccination of paediatric patients with autoimmune inflammatory rheumatic diseases: update 2021. Ann Rheum Dis 2023;82(1):35–47.
3. UK Health Security Agency. Contraindications and special considerations. In: Ramsey M, editor. Immunisation against infectious disease London: UK Health Security Agency; 2017. p. Chapter 6, page 5.

4. Bagga S, Krishnan A, Dar L. Revisiting live attenuated influenza vaccine efficacy among children in developing countries. Vaccine 2023;41(5):1009–1017.
5. Merckx J, McCormack D, Quach C. Improving influenza vaccination in chronically ill children using a tertiary-care based vaccination clinic: Is there a role for the live-attenuated influenza vaccine (LAIV)? Vaccine 2016;34(6):750–756.

P276

Disease recapture rates after withdrawal of biological treatment due to remission in juvenile idiopathic arthritis

A. Tanatar[1], S. Çağlayan[2], B. Sözeri[2], N. A. Ayaz[1]
[1]Istanbul University Faculty of Medicine, [2]Umraniye Training and Research Hospital, Istanbul, Türkiye
Correspondence: A. Tanatar
Pediatric Rheumatology, **23(2):** P276

Introduction: Children with juvenile idiopathic arthritis (JIA) frequently experience a flare after treatment is discontinued due to remission, but the consequences of these flares are not well defined.
Objectives: This study aims to evaluate whether patients started on treatment for disease flare after their biological treatment was discontinued due to remission and then reached inactive disease again.
Methods: The medical charts of children with JIA who had their biologics discontinued due to remission but then flared and their medication(s) were restarted were retrospectively reviewed. Inactive disease (ID) was defined as a physician's visual analog score of less than 1 and an active joint count of 0. Disease activity was assessed by the JADAS (Juvenile arthritis disease activity score)−71 score.
Results: Of the 101 patients whose biologic therapy was discontinued, 34 experienced at least one exacerbation. Thirty patients who were followed up for at least 1 year after the exacerbation were included in the study. At the time of the flare, 26 (86.7%) patients were not using medication, three (10%) patients were on methotrexate, and one (3.3%) patient was on sulfasalazine. The characteristics of patients who flared after withdrawal of biological drugs are summarized in Table 1, and the treatment categories restarted in patients who flared are shown in Table 2. The rate of reaching inactive disease again for the cohort was 66.7% at 6 months, ranging from 50% (RF (-) polyarticular and systemic) to 76.9% (persistent oligoarticular). 76.7% of the patients had reached inactive disease at 12 months, and 28 (93.3%) had reached inactive disease at the last visit (median follow-up of 1.9 years after the flare).
Conclusion: Considering the discontinuation of biological therapies, it is essential to remember that approximately half of the patients may regain inactive disease within 6 months of a potential flare. Still, the rates of achieving inactive disease will vary among JIA categories. With this information kept in mind, the risk of exacerbation can be meaningfully compared with the drawbacks and risks of continuing antirheumatic therapy.
Disclosure
None declared

P277

Impact of diagnosis timing on treatment outcomes with FK-adalimumab vs Reference adalimumab in moderate-to-severe rheumatoid arthritis: results from auriel-ra study

C. Edwards[1], M. Romanova Michailidi[2], J. Monnet[2]
[1]University Hospital Southampton, Southampton, United Kingdom, [2]Fresenius Kabi SwissBioSim GmbH, Eysins, Switzerland
Correspondence: J. Monnet
Pediatric Rheumatology, **23(2):** P277

Introduction: Time of diagnosis is a critical determinant of patient outcomes in autoimmune diseases and in particular in rheumatoid arthritis (RA), with earlier intervention often leading to better results[1]. This is especially true in pediatrics, where delays can significantly impact long-term outcome[2]. Biosimilars offer similar efficacy and safety compared to their originators, thereby improving patient access to affordable treatments. FK-Adalimumab (FK-ada) is an adalimumab biosimilar approved for the treatment of autoimmune diseases, including RA and Juvenile Idiopathic Arthritis (JIA).
Objectives: The objective of this analysis is to assess the efficacy, safety, and quality of life (QoL) outcomes of adalimumab in RA patients based on time since diagnosis.
Methods: Patients with moderately to severely active RA receiving treatment with methotrexate were randomised 1:1 to FK-ada or Reference adalimumab (originator) in the double-blind, multicentre, phase III AURIEL-RA study. Safety, efficacy and immunogenicity endpoints were assessed at scheduled visits up to week 52, safety being the study primary objective. Patients were categorized by time since RA diagnosis at baseline: diagnosed early (<5 years since diagnosis) and late (≥5 years). Efficacy, safety and QoL were summarized for these subgroups.
Results: 288 patients were randomized to FK-ada (143) and originator (145) with 133 early diagnosed patients (68 and 65, respectively). Gender, race, ethnicity, age and disease characteristics were all well balanced at baseline. No clinically meaningful differences in efficacy and QoL were seen between treatment arms in both subgroups up to week 52. For patients diagnosed early, higher ACR20 response rates were observed starting from W12 in both treatment groups (early diagnosed: 88.1% and 84.4% for FK-ada and originator vs diagnosed later: 72.0% and 77.9%). This trend continued through W52. A similar pattern was observed for ACR50 and ACR70 response rates. By W52, more early-diagnosed patients achieved remission per DAS28-ESR Categorical (50.9% and 41.5% vs 31.3% and 32.3%) and showed greater QoL improvement (median change from baseline of HAQ-DI score: −0.8750 and −0.6250 vs −0.5625 and −0.5000). No notable differences in adverse event incidence were observed between treatment arms or subgroups through the follow-up period (51.5% and 75.4% vs 64.0% and 55.0%).
Conclusion: Early-diagnosed patients show greater clinical and QoL outcomes, highlighting the importance of timely treatment. Findings support FK-adalimumab's consistent performance and its role in broadening access to effective therapy in both adult and pediatric rheumatology.
Trial registration identifying number: Trial registration: NCT03052322
Disclosure
C. Edwards Consultant with: AstraZeneca, Eli Lilly, GlaxoSmithKlein(GSK), Roche, Speaker Bureau with: AbbVie/Abbott, alphasigma, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb(BMS), Eli Lilly, GlaxoSmithKlein(GSK), pfizer, Janssen, Roche, sanofi, ucb, M. Romanova Michailidi Employee with: Fresenius Kabi SwissBioSim GmbH, J. Monnet Employee with: Fresenius Kabi SwissBioSim GmbH

References

1. Nell VP, et al. Rheumatology (Oxford). 2004; 43:906–14
2. Costello A, et al. Arthritis Care Res (Hoboken). 2025 Mar;77(3):283–290

P278

Population-based analysis of treatment patterns in juvenile idiopathic arthritis using Korean national claims data

D.-C. Jeong[1], J. G. Ahn[2,3], M.-T. Lee[4], D. Lee[5], E. J. Min[6]
[1]Pediatrics, College of Medicine, The Catholic University of Korea, [2]Pediatrics, Severance Children's Hospital, Yonsei University College of Medicine, [3]Institute for Immunology and Immunological Diseases, Yonsei University of College of Medicine, [4]Real-World Evidence Generation Team, Pfizer Biopharmaceuticals Group, Pfizer Pharmaceuticals Korea Ltd, [5]Medical Affairs Team, Pfizer Biopharmaceuticals Group, Pfizer Pharmaceuticals Korea Ltd, [6]Medical Life Science, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic Of
Correspondence: D.-C. Jeong
Pediatric Rheumatology, **23(2):** P278

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis in children, with an unknown cause and prolonged disease course. Treatment typically involves a combination of medications to control inflammation, alleviate symptoms, and prevent joint damage. Commonl medications include nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), and biologic DMARDs (bDMARDs). bDMARDs have improved outcomes in severe or

refractory cases, but challenges remain due to disease heterogeneity and long-term management needs.
Objectives: This study aimed to investigate bDMARD treatment patterns in JIA patients using a real-world database.
Methods: A retrospective analysis was conducted using Health Insurance Review and Assessment (HIRA) national claims data from 2007 to 2019. JIA patients were classified into bDMARDs and non-bDMARDs groups, with treatment patterns compared.
Results: Among 1,728 JIA patients, 31.3% (n = 541) received bDMARDs, with 15.5% (n = 75) discontinuing treatment. The median time from diagnosis to first bDMARD was 36.7 (9.7–58.1) months, with a median treatment duration of 28.1 (11.5–54.4) months and follow-up of 24.3 (7.7–43.7) months post-discontinuation. In the non-bDMARDs group (68.6%, n = 1,187), 68.7% (n = 815) used conventional synthetic DMARDs (csDMARDs), with a 46.6% (n= 380) discontinuation rate. Methotrexate, sulfasalazine, and hydroxychloroquine were the most prescribed csDMARDs. Etanercept (69.7%) was the most common first bDMARD, followed by adalimumab (19.0%) and tocilizumab (7.6%), with 14.8% switching to a second biologic. Discontinuation rates of csDMARDs were higher in the non-bDMARDs group ($p < 0.001$).
Conclusion: This is the first comprehensive study profiling the treatment patterns of Korean patients with JIA using population-based claims data. The findings enhance understanding of real-world treatment trends, aiding clinical decision-making.
Disclosure
None declared

References

1. Martini A, Lovell DJ, Albani S et al. Juvenile idiopathic arthritis. Nature Reviews Disease Primers. 2022;81:5
2. Prakken B, Albani S, and Martini A. Juvenile idiopathic arthritis. Lancet. 2011;3,779,783:2138–49
3. Grazziotin LR, Currie G, Twilt M et al. Real-world data reveals the complexity of disease modifying anti-rheumatic drug treatment patterns in juvenile idiopathic arthritis: an observational study. Pediatr Rheumatol Online J. 2022;201:25
4. Horneff G, Borchert J, Diesing J et al. Treatment Patterns in Polyarticular Juvenile Idiopathic Arthritis: A Retrospective Observational Health Claims Data Study. Life (Basel). 2024;146
5. Min EJ, Lee SH, Jo J-Y et al. Population-Based Big Data Analysis on Disease Patterns in Patients Identified With Juvenile Idiopathic Arthritis Using National Claims Data. Journal of Korean Medical Science. 2024;40:e113

P279

Effects of dual-task exercises on cognitive status, disease activity and quality of life in childhood-onset systemic lupus erythematosus

E. P. Kısa Akdag[1], S. Şahin[2], G. Leblebici[3], I. Y. Tonyalı[4], G. Balcı[4], S. Dilek[4], E. Aslan[2], E. Tarakcı[4], Ö. Kasapçopur[2]
[1]Ergotherapy, Istanbul Medipol University, [2]Department of Pediatric Rheumatology, Istanbul Univesity Cerrahpasa, [3]Physiotherapy and Rehabilitation, Istanbul Medeniyet University, [4]Physiotherapy and Rehabilitation, Istanbul Univesity Cerrahpasa, Istanbul, Türkiye
Correspondence: E. P. Kısa Akdag
Pediatric Rheumatology, **23(2):** P279

Introduction: Many patients with cSLE suffer from cognitive dysfunction that seriously affects their quality of life, attention, visual and speech memory, motor function, reaction speed, and motor perception and physical activity.
Objectives: This study aims to investigate the effects of dual-task (DT) exercises on cognitive status, disease activity and physical function of children with cSLE.
Methods: The mental status of the children by the Montreal Cognitive Assessment (MoCA), pain status by the Mcgill-Melzack pain questionnaire, disease activity by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)−2K, physical activity by the Childhood Activity Assessment Index (CHAQ) and International Physical Activity Questionnaire (IPAQ) and steps number recorded.
Results: Thirty children with cSLE were included. McGill-Melzack Pain scores and MOCA scores were significantly improved after the intervention (36,53±16,55; 23,73±2,72 respectively) ($p<0.05$). Additionally, IPAQ MET scores were significantly increased after the intervention (5592,40±6228,61; p=0.01). Disease activity score (SLE-DAI-2K) decreased from 2.79 (SD: 3.20) to 2.18 (SD: 2.23) with the implementation of DT; however this was not statistically significant ($p>0.05$).
Conclusion: DT exercises have been shown to play a crucial role in improving cognitive function and reducing disease activity. Clinicians may consider incorporating DT into rehabilitation programs.
Trial registration identifying number: NCT05984316
Disclosure
None declared

References

1. Teixeira Santos FPS, Ferreira GA, de Paula JJ, de Souza KCP, Cançado Silva SL, Correa H. Cognitive dysfunction in patients with childhood-onset systemic lupus erythematosus may impact treatment. Adv Rheumatol. 2023;63(1). https://doi.org/10.1186/s42358-023-00300-8
2. Reilly DS, Woollacott MH, van Donkelaar P, Saavedra S. The Interaction Between Executive Attention and Postural Control in Dual-Task Conditions: Children With Cerebral Palsy. Arch Phys Med Rehabil. 2008;89(5). https://doi.org/10.1016/j.apmr.2007.10.023
3. Caldani S, Razuk M, Septier M, et al. The effect of dual task on attentional performance in children with ADHD. Front Integr Neurosci. 2019;12. https://doi.org/10.3389/fnint.2018.00067
4. Kachouri H, Jouira G, Laatar R, Borji R, Rebai H, Sahli S. Different types of combined training programs to improve postural balance in single and dual tasks in children with intellectual disability. J Intellect Disabil. 2024;28(1). https://doi.org/10.1177/17446295221148585
5. Bruderer-Hofstetter M, Rausch-Osthoff AK, Meichtry A, Münzer T, Niedermann K. Effective multicomponent interventions in comparison to active control and no interventions on physical capacity, cognitive function and instrumental activities of daily living in elderly people with and without mild impaired cognition – A systematic review and network meta-analysis. Ageing Res Rev. 2018;45. https://doi.org/10.1016/j.arr.2018.04.002
6. Abdallat R, Sharouf F, Button K, Al-Amri M. Dual-task effects on performance of gait and balance in people with knee pain: A systematic scoping review. J Clin Med. 2020;9(5). https://doi.org/10.3390/jcm9051554
7. Ramsey-Goldman R, Schilling EM, Dunlop D, et al. A pilot study on the effects of exercise in patients with systemic lupus erythematosus. Arthritis Care Res. 2000;13(5). https://doi.org/10.1002/1529-0131(200010)13:5<262::aid-anr4>3.0.co;2-8

P280

Palovarotene as a pathogenic therapy for fibrodysplasia ossificans progressiva: real-world data of single center

I. Nikishina[1], V. Matkava[1], S. Arsenyeva[1], A. Arefieva[1], E. Gasymov[2], L. Blank[2], G. Torosyan[3]
[1]Paediatric, [2]Radiology, V.A. Nasonova Research Institute of Rheumatology, [3]Federal Scientific and Clinical Center for Children and Adolescents of the Federal Medical and Biological Agency, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P280

Introduction: Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare monogenic disease manifested by uncontrolled heterotopic ossification (HO). Treatment management for these pts is a huge challenge for specialists over the world. Palovarotene, a selective retinoic acid receptor gamma agonist, is the first and only drug that has proven its effectiveness as a result of clinical trials. It is registered for use in patients with FOP in a number of countries. In literature were published only 2 clinical trials (II, III phase), in which only limited number of patients received palovarotene treatment. But no data about real clinical practice.
Objectives: To describe real-world data and large experience of palovarotene treatment and evaluate efficacy and safety.
Methods: 14 patients (pts) with severe course of FOP confirmed by ACVR1 gene mutation were selected for palovaroten administration. The drug provision was carried out by the Russian Government Program and the Circle of Goodness Foundation for the treatment of children with orphan diseases**.** All pts signed informed consent and met eligibility criteria (genetically verified FOP; female>8 y.o., male>10 y.o.). Palovarotene was taken according official instructions. Low-dose

whole-body computed tomography (WBCT) was done for evaluate progression of HO volume.
Results: All 14 pts have classic FOP phenotype with malformed great toes (14/100%), shortened thumbs (11/78%), abnormalities of cervical spine, peripheral osteochondromas (in humerus, tibia, fibia, femoral bones) and multiple HO in 14/100% pts. Genetic test (ACVR1) was done in 14/100% pts and revealed typical (p.Arg206His) in 13 pts and 1 ultra-rare mutation (p.Gly356Asp). The mean age was 12.5 y.o. (min – 8.1 y.o.; max – 17.9 y.o.). 9 pts were < 14 years. The mean height was 152 cm (min-129 cm; max – 180 cm). The mean weight was 47 kg (min-25 kg; max – 73 kg). By present time 13 pts received palovarotene (12 were received in combination with previously initiated tofacitinib therapy, 1 – as monotherapy), 1 pt is waiting for medicine delivery. The mean therapy duration is 15 months (from 1 to 25 mo). 9/13 pts used only chronic regimen (3-5 mg per day depends on weight) and 4/13 pts used additionally flare-up regimen (12.5-20 mg per day for 4 weeks). 5 pts received palovarotene < 1 years, 6 pts - < 2 years, 2 pts > 2 years. All pts had different intensity adverse reactions connected with skin and depended on the palovarotene dosage. 3 pts on chronic regimen had mild skin reactions such as dry skin, dry lip and short-duration pruritus. Other 4 pts had more severe skin damage such as rash, erythema and skin exfoliation with significant pruritus. When we reduce the dosage of palovarotene all skin symptoms relieved. 3 pts had transient dyspeptic syndrome. We evaluate HO volume by WBCT in all pts. WBCT was done twice in 7 pts with 1-year period and in all pts no significant HO progression was revealed.
Conclusion: The aggressive nature of the course of FOP, which inevitably leads to severe disability of patients, necessitates the widespread attention of practitioners to the early diagnosis of FOP, an in-depth study of the factors determining progression, and new opportunities for pathogenetic therapy allow us to count on improving the prognosis of this extremely serious disease.
Disclosure
None declared

P281

Head-to-head real-world retrospective analysis of obinutuzumab versus rituximab in childhood lupus nephritis

J. Cognard[1], C. Grosyeux[2], C. Dossier[3], B. Bader-Meunier[4], J. Hogan[3], Y.-T. Known[3], C. Dumaine[3], F. Uettwiller[5], A. Félix[6], H. Reumaux[7], L. Rossi-Semerano[8], I. Koné-Paut[8], B. Ranchin[9], A. Laurent[9], M. Fouillet-Desjonquères[9], M. Jouret[9], A. Belot[9], C. Pietrement[1], I. Melki[10]
[1]CHU Reims, Reims, [2]CHU Nancy, Nancy, [3]Robert-Debré, [4]Hôpital Necker Enfants Malades, Paris, [5]CHU Clocheville, Tours, [6]Martinique University Hospital, Fort-De-France, [7]Jeanne de Flandre University Hospital, Lille, [8]Bicêtre University Hospital, Paris, [9]Hôpital Femme-Mère-Enfants, Lyon, [10]Hôpital Armand Trousseau, Paris, France
Correspondence: J. Cognard
Pediatric Rheumatology, **23(2):** P281

Introduction: B-cell depletion therapy represents a cornerstone in the management of systemic lupus erythematosus (SLE). Obinutuzumab (OBZ), a glycoengineered, type II anti-CD20 monoclonal antibody, has shown promising efficacy in autoimmune conditions[1,2,3].
Objectives: This study retrospectively compared the efficacy and safety of OBZ versus rituximab (RTX) in childhood-onset SLE (cSLE) lupus nephritis patients.
Methods: We conducted a national, retrospective cohort study of childhood-onset SLE patients with biopsy-proven lupus nephritis who received OBZ between January 1, 2019, and December 31, 2024, at French pediatric rheumatology and nephrology centers. We assessed clinical, serological, and therapeutic outcomes—including changes in global disease activity (SLEDAI-2K) at baseline (M0) and at 3, 6, 12, and 24 months; renal response and flare rates; corticosteroid-sparing effects as measured by daily steroid dose at each timepoint; and adverse event incidence — and compared these findings to those in a cohort of cSLE patients with lupus nephritis treated with RTX.
Results: Thirty-seven patients were included (OBZ, n = 16; RTX, n = 21). Baseline demographics, prior background therapy, age at diagnosis, and sex distribution did not differ between groups. Five patients in the OBZ cohort had previously been treated with RTX. At baseline, the OBZ cohort exhibited significantly higher median SLEDAI-2K scores than the RTX cohort (22 [IQR 15–34] vs. 12 [IQR 10–15]; p < 0.001). In the OBZ group, mean SLEDAI-2K declined markedly versus baseline at 3, 6, 12, and 24 months (p < 0.001), with no further significant changes among post-baseline visits. Mean daily corticosteroid dose fell from 1.21 mg/kg at baseline to 0.20 mg/kg at 24 months (p = 0.005). Renal outcomes were favorable: 31.2 % of OBZ-treated patients reached complete renal remission by 3 months and 62.5 % by 6 months, and the mean proteinuria/creatininuria ratio decreased from 499 mg/mmol at baseline to 21.8 mg/mmol at 24 months (p < 0.001). OBZ and RTX produced comparable reductions in SLEDAI-2K, corticosteroid tapering, and proteinuria at 3, 6, 12, and 24 months (all p = 1), but the median Δ SLEDAI-2K at 3 months was significantly greater with OBZ (–14 points, IQR –17 to –11) than with RTX (–6 points, IQR –8 to –4; p = 0.002). Median B-cell depletion duration was 15.0 months (SD 10.0) in the OBZ group versus 10.0 months (SD 5.0) in the RTX group (p = 0.458). Adverse events occurred in 43.8 % of OBZ patients versus 14.3 % of RTX patients (p = 0.067), with a higher rate of viral and bacterial infections in the OBZ cohort; no deaths were reported.
Conclusion: OBZ demonstrated efficacy comparable to RTX in childhood-onset lupus nephritis, achieving high rates of renal remission with marked reductions in proteinuria. It also produced significant and durable decreases in global disease activity and corticosteroid requirements. Although the OBZ cohort experienced a modestly higher rate of infections, its potent and sustained B-cell depletion supports its potential as an alternative to RTX in refractory SLE. Prospective, randomized trials are warranted to confirm these results and further characterize the safety profile of OBZ.
Disclosure
None declared

References

1. Furie RA, Rovin BH, Garg JP et al. REGENCY Trial Investigators. Efficacy and Safety of Obinutuzumab in Active Lupus Nephritis. N Engl J Med. 2025 Apr 17;392(15):1471–1483
2. Furie RA, Aroca G, Cascino MD, et al. Ann Rheum Dis 2022;81:100–107
3. Onuora S. Obinutuzumab effective for lupus nephritis. Nat Rev Rheumatol. 2025 Apr;21(4):193

P282

A retrospective review, evaluating the effectiveness of a stretch and casts under general anaesthetic for children with fixed flexion deformities of the knee

L. Stone, S. Maillard
Rheumatology, Great Ormond Street Hospital, London, United Kingdom
Correspondence: L. Stone
Pediatric Rheumatology, **23(2):** P282

Introduction: A retrospective review, evaluating the effectiveness of a Stretch and Casts under General Anaesthetic for children with Fixed Flexion Deformities of the knee
Objectives: The objective of the study is to audit and analyse children with a confirmed diagnosis of active Juvenile Idiopathic Arthritis (JIA) who demonstrate a restricted range of movement in one or both knees, who have undergone a stretch and cast under General anaesthetic followed by intensive rehabilitation and then discharged with a home exercise programme.
Methods: This is a retrospective review of 18 paediatric patients who presented with a fixed flexion deformity (FFD) of the knee, measuring between – 45 to – 10 degrees off of extension. All patients required patella mobilisations and a gentle stretch into extension until end range was reached. At that point, either a serial cast or a splint (gaiter) was applied. The immobilisation was maintained for five nights before removal. A gaiter is then worn at night.
Each child participated in an intensive rehabilitation programme involving twice-daily physiotherapy sessions. Each received 16 physiotherapy sessions: 90 minutes in the morning and 60 minutes in the afternoon. Upon completion, patients were discharged with a home exercise programme, to be completed 5 days a week and scheduled for follow-up between two and six weeks.
Results: - **Initial Outcome (at Discharge):**
- All 18 patients (100%) showed clinical improvement, achieving knee extension between –5° to 0° (neutral extension).

- This indicates the intervention was effective in improving knee extension at the time of discharge.
- **Follow-Up (2–6 weeks):**
- 14 patients (78%) maintained full extension at 0°, indicating high treatment durability and likely good HEP adherence.
- 3 patients (17%) showed continued improvement:
- 2 improved from −3° and −5° to 0°
- 1 remained stable at −3° (no worsening, partial improvement sustained).
- 1 patient (5%) regressed significantly from 0° to −20° flexion contracture. Notably, this was attributed to poor compliance with the HEP, as reported by family.

Interpretation:
- The intervention appears highly effective for immediate gains in knee extension.
- Sustained benefits were observed in the majority (94%) when patients were compliant with the HEP.
- Regression was associated with non-adherence, highlighting the critical role of HEP compliance in maintaining post-discharge outcomes.

Conclusion:
These results suggest that a combination of splinting/casting, intensive physiotherapy, and a structured home exercise program is effective in restoring extension for children with active JIA, providing compliance with the home exercise programme is maintained.

Disclosure
None declared

P283

Combination therapy with biological dmards and JAK inhibitors in cases of refractory JIA

M. Sim[1], B. Almoosawi[2], O. Aragon Cuevas[3], J. L. Bennett[4], S. Cooray[5], J. Fisher[2], I. Nengroo[6], N. Pai[6], L. Paterson-Brown[7], E. Twynam-Perkins[7], M. Wood[1]
[1]Paediatric Rheumatology, Leeds Teaching Hospitals NHS Trust, Leeds, [2]Paediatric Rheumatology, [3]Pharmacy Department, Alder Hey Children's NHS Foundation Trust, Liverpool, [4]Paediatric Rheumatology, Great North Children's Hospital, Newcastle upon Tyne, [5]Paediatric Rheumatology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, [6]Paediatric Rheumatology, Nottingham Children's Hospital, Nottingham, [7]Paediatric Rheumatology, Royal Hospital for Children Glasgow, Glasgow, United Kingdom
Correspondence: M. Sim
Pediatric Rheumatology, **23(2):** P283

Introduction: Despite biological disease-modifying anti-rheumatic drugs (bDMARDs), 25% of JIA patients enter adulthood with active disease[i]. Janus kinase inhibitors (JAKis) may only achieve inactive disease in about half of JIA patients. bDMARD/JAKi combination therapy has been used predominantly in refractory inflammatory bowel disease, but also in rheumatoid arthritis, ankylosing spondylitis, and Still's disease in adults.
To our knowledge, there are no published case reports of combination bDMARD/JAKi therapy in JIA. We present a UK multicentre case series of bDMARD/JAKi combination therapy in refractory JIA.
Objectives: To describe current UK experience of bDMARD/JAKi combination therapy in refractory JIA.
Methods: Cases of refractory JIA managed by bDMARD/JAKi combination therapy were identified across 7 tertiary centres. Written consent was obtained, and data collected on patient characteristics, treatment history, adverse effects, and outcomes.
Results: 10 patients were identified (6 Systemic; 1 Psoriatic; 2 Polyarticular, 1 Extended oligoarticular), with median age of 3.5 years at diagnosis. A median 5 DMARDs (all types, range: 3-8) were used before combination therapy, over a median 6.5 years (range: 3-15). The indication in all cases was failure of disease control, with one case of HLH.
bDMARDs combined with tofacitinib included: tocilizumab (n=5), anakinra (n=2), infliximab (n=2), or adalimumab (n=1), whereas baricitinib was combined with tocilizumab (n=1), anakinra + emapalumab (n=1), or rituximab (n=1). 9/10 remain on combination therapy (median 11 months). 3 switched combinations, and 1 reverted to bDMARD monotherapy due to non-adherence.
Full data were available for 7 patients. Historical joint damage was seen in 4/7. In the 12 months before combination therapy, all received IV methylprednisolone (median cumulative dose 110mg/kg), with 5/7 also receiving oral prednisolone (median duration 108 days ≥0.3mg/kg). Steroid adverse effects were seen in 6/7 including growth concerns (n=4), adrenal suppression (n=3), cataracts (n=1), and vertebral compression (n=1). Following combination therapy, all 7 reported steroid reduction, with no systemic glucocorticoid use since initiation in the 4/7 on combination ≥12 months. At last follow-up (median 14 months), 3/7 were in clinical remission on medication and 4/7 had active disease managed by: steroid joint injection only (n=2), low-dose oral steroids (n=2), and changing JAKi (n=1).
There was an incidental case of CMV on screening, and another of mild VZV in a previously immune child. No serious side effects including bacterial infections or venous thromboembolism were reported.
Conclusion: Following individual risk-benefit assessment and multidisciplinary discussion with the family and child, bDMARD/JAKi combination therapy may enable reduction of steroid burden and improved control in refractory JIA. Clinical trials are required to investigate long-term safety and efficacy.

Disclosure
None declared

Reference

1. Glerup M et al. Long-Term Outcomes in Juvenile Idiopathic Arthritis: Eighteen Years of Follow-Up in the Population-Based Nordic Juvenile Idiopathic Arthritis Cohort. Arthritis Care Res (Hoboken). 2020 Apr;72(4):507–16.

P284

Combination of targeted therapies in juvenile idiopathic arthritis: single-center experience

M. I. Gonzalez Fernandez, B. Lopez Montesinos, M. Marti Masanet, L. Lacruz Perez, I. Calvo Penades
Pediatric Rheumatology Unit, Health Research Institute Hospital La Fe (IIS La Fe), Hospital Universitario y Politecnico La Fe, Valencia, Spain
Correspondence: I. Calvo Penades
Pediatric Rheumatology, **23(2):** P284

Introduction: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and can be particularly challenging to manage in refractory cases. While both biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted-synthetic DMARDs (tsDMARDs) have individually shown efficacy in JIA, evidence on their combined use remains scarce, especially in pediatric populations.
Objectives: To describe the experience with combination targeted therapy in patients with refractory JIA treated at the Pediatric Rheumatology Unit of a single center.
Methods: This is a retrospective study in patients diagnosed with JIA and followed in the Pediatric Rheumatology Unit of a tertiary hospital between February 2019 and May 2025. Patients who received dual targeted therapy -either two bDMARDs or a bDMARD combined with a tsDMARD- were included. Demographic, clinical and treatment data were collected through the electronic medical records.
Results: Among approximately 338 patients with JIA under follow-up, 5 received combination targeted therapy. All had previously been treated with at least three different DMARDs. Sixty percent were female, with a median age at last visit of 12,4 years (Q1-Q3: 11,5-18,2) and a median age at disease onset of 1,6 years (Q1-Q3: 1,3-3,2). Diagnoses included: systemic JIA (n=1), RF-negative polyarticular JIA (n=1; suspected autoinflammatory disease based on clinical features and evolution), enthesitis-related arthritis (n=1), RF-negative JIA with ulcerative colitis (n=1; colitis onset occurred years after arthritis), and psoriatic JIA with refractory uveitis (n=1).
Current combinations consisted in tocilizumab + baricitinib (n=2), adalimumab + baricitinib (n=1), ustekinumab + upadacitinib (n=1), and golimumab + tofacitinib (n=1). All patients were also receiving methotrexate. The median duration of current combination therapy was 12,5 months (Q1-Q3: 9,9-21,7). One patient had previously received two other targeted therapies combinations: anakinra + tofacitinib and tocilizumab + tofacitinib.

At last follow-up, two patients were in remission, one had a partial response, one was in remission from ulcerative colitis but had partial joint response, and one had recently initiated combination therapy. No significant adverse events were observed during the follow-up; only mild infections (e.g., viral syndromes, common colds) occurred, with no serious complications.

Conclusion: We report a case series of five patients with difficult-to-treat JIA who received combination therapy with a bDMARD and a tsDMARD, representing 1.5% of all JIA patients under follow-up in our unit. This proportion cannot be contextualized, as, to our knowledge, no similar JIA series have been reported. Notably, all had early-onset disease. The combination therapy was well tolerated, with no significant adverse events observed in the four patients with available follow-up.

Although evidence remains limited, this approach may be considered in refractory cases or when JIA coexists with other difficult-to-manage immune-mediated conditions. In this context, experience has already been reported in pediatric inflammatory bowel disease.

Disclosure

M. I. Gonzalez Fernandez: None declared, B. Lopez Montesinos: None declared, M. Marti Masanet: None declared, L. Lacruz Perez: None declared, I. Calvo Penades Speaker Bureau with: GSK, Pfizer, Novartis, Abbvie, Sobi.

P285

Efficacy and safety of a modified high-dose pamidronate protocol in paediatric chronic non-bacterial osteomyelitis

M. Meurs[1,2], M. H. A. Jansen[1,2], S. A. J. ter Horst[2,3], E. H. M. van Nieuwenhove[1,2], B. J. Vastert[1,2], S. de Roock[1,2], J. F. Swart[1,2]
[1]Pediatric Immunology and Rheumatology, University Medical Centre Utrecht, [2]Faculty of Medicine, Utrecht University, [3]Radiology, University Medical Centre Utrecht, Utrecht, Netherlands
Correspondence: M. Meurs
Pediatric Rheumatology, **23(2):** P285

Introduction: Chronic non-bacterial osteomyelitis (CNO), including chronic recurrent multifocal osteomyelitis (CRMO), is a rare autoinflammatory bone disease in children. Pamidronate is a common second-line treatment, typically administered over three consecutive days every three months (CARRA protocol). [1] While effective, this protocol is logistically demanding requiring frequent hospitalizations and overnight stays. To date, no studies have evaluated a simplified one-day pamidronate protocol. This study compares this alternative approach to the traditional approach in clinical practice.

Objectives: To assess the clinical efficacy and safety of a high-dose, single-day intravenous pamidronate protocol repeated once after three months, compared to the conventional three-day protocol, in paediatric CNO patients.

Methods: We conducted a single center retrospective cohort study of 36 paediatric CNO patients. Patients received either the standard protocol (1 mg/kg/day for three consecutive days, n=14) or a modified protocol (2 mg/kg as a single infusion, n=22), repeated once after three months. The primary outcome was treatment success at 6, 12, and 24 months, defined as absence of treatment escalation (i.e., no need for additional pamidronate infusions or initiation of TNF inhibitors), based on clinical and radiological response. Secondary outcomes included safety, infusion-related reactions, and adverse events. Statistical analyses included chi-square/Fisher's exact tests and Kaplan-Meier survival estimates.

Results: The modified high-dose pamidronate protocol demonstrated comparable efficacy to the standard protocol. There were higher efficacy rates for the modified protocol at 6 months (63.6% vs 30.8%, p=0.060), 12 months (50.0% vs 28.6%, p=0.211), and 24 months (37.5% vs 14.3%, p=0.227), but these differences were not statistically significant. Significantly fewer patients in the modified group required escalation to TNF inhibitors (36.4% vs 71.4%, p=0.040). No adverse events were observed after pamidronate use other than infusion reactions which were mild and similarly distributed over both groups.

Conclusion: The single-day, high-dose pamidronate protocol repeated once after three months shows similar efficacy as the standard multi-day protocol in achieving remission in paediatric CNO patients, with a similar safety profile. These findings support this new protocol as a potential treatment alternative to reduce hospitalization and healthcare costs without increasing adverse event risk.

Disclosure

None declared

Reference

1. Zhao Y, Wu EY, Oliver MS, Cooper AM, Basiaga ML, Vora SS, et al. Consensus Treatment Plans for Chronic Nonbacterial Osteomyelitis Refractory to Nonsteroidal Antiinflammatory Drugs and/or With Active Spinal Lesions. Arthritis Care Res. 2018 Jul;70(8):1228–37.

P286

2024-25 Japan college of rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for systemic juvenile idiopathic arthritis without/with macrophage activation syndrome, oligoarthritis, polyarthritis, and uveitis

N. Okamoto[1,2], H. Umebayashi[3], M. Shimizu[4], H. Takase[5], H. Keino[6], M. Mizuta[7], Y. Sugita[1], K. Maruyama[8], T. Yasumi[9], M. Mori[10,11]
[1]Department of Pediatrics, School of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, [2]Department of Pediatrics, Osaka Rosai Hospital, Japan Organization of Occupational Health and Safety, Sakai, [3]Department of Rheumatism, Infection Disease, Miyagi Children's Hospital, Sendai, [4]Department of Pediatrics, Perinatal and Maternal Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, [5]Miyata Eye Hospital Tokyo Clinic, [6]Department of Ophthalmology, Kyorin University School of Medicine, Tokyo, [7]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kobe, [8]Department of Vision Informatics, Graduate School of Medicine, The University of Osaka, Suita, [9]Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, [10]Department of Lifelong Immunotherapy, Institute of Science Tokyo, Tokyo, [11]Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan
Correspondence: N. Okamoto
Pediatric Rheumatology, **23(2):** P286

Introduction: Medical conditions and drug approvals vary depending on the country or region. Therefore, guidelines tailored to each country or region are necessary. Japan College of Rheumatology (JCR) published the first guideline for the treatment of juvenile idiopathic arthritis (JIA) in 2025.

Objectives: To establish treatment recommendations and the optimal treatment strategy for JIA patients in Japan.

Methods: This work was organized by JIA guideline development subcommittee of JCR and was supported by the Health and Labour Sciences Research Grants for Research on Intractable Diseases from the Ministry of Health, Labor and Welfare of Japan. JIA guideline development team was consisted with pediatric rheumatologists and ophthalmologists. The thirty-five clinical questions (CQs) were developed and brushed up by members of the guideline development team. A systematic review (SR) team was consisted with pediatric rheumatologists, adult rheumatologists and ophthalmologists. SR was executed using Grading of Recommendations Assessment, Development and Evaluation methodology. Five background questions and four questions on uveitis were narratively reviewed. All guideline development process was supervised by guideline development expert, and confirmed by the Medical Information Distribution Service (Minds). Based on the results of SR and opinions of Parent/Patient Panel, we created recommendations for treatment-related CQs and repeated revisions and voting until a high level of agreement was achieved.

Results: Twenty-eight recommendations were developed (11 strong and 17 conditional). For 7 CQs, recommendation was not established because of less evidence. The quality of evidence was very low or low for 75% of the recommendations. Recommendations on systemic JIA without MAS are provided for the use of glucocorticoids (GCs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic DMARDs (bDMARDs). Recommendations on systemic JIA with macrophage activating syndrome are provided for the use of GCs, cyclosporin A. Recommendations on oligoarthritis and polyarthritis are provided for the use of nonsteroidal antiinflammatory drugs, GCs, csDMARDs and bDMARDs. Recommendations on uveitis are provided

for the use of topical or systemic GCs, methotrexate and bDMARDs. We created the originated treatment algorithms based on the recommendations and the conditions for approval of drugs in Japan.
Conclusion: This guideline provides standardized direction for all clinicians concerned to JIA treatment including general pediatricians, adult rheumatologist and ophthalmologists. We expect standardization of JIA treatment in Japan may lead to improve the prognosis for JIA patients.
Disclosure
N. Okamoto Speaker Bureau with: Novartis, Eli Lilly, AbbVie, Ayumi, H. Umebayashi: None declared, M. Shimizu: None declared, H. Takase Speaker Bureau with: Mitsubishi Tan- abe Pharma and Abbvie GK, H. Keino Speaker Bureau with: Santen Pharmaceutical Co., Ltd., M. Mizuta: None declared, Y. Sugita Speaker Bureau with: Novartis, K. Maruyama: None declared, T. Yasumi: None declared, M. Mori Grant/Research Support with: AbbVie Japan, Asahi Kasei Pharma, Ayumi Pharmaceutical Co., CSL Behring, Chugai Pharmaceutical Co., Japan Blood Products Organization, Nippon Kayaku, and UCB Japan., Consultant with: Daiichi Sankyo and Taisho Pharmaceutical Holdings Co, Speaker Bureau with: MSD K.K, MSD, AstraZeneca, and Sanofi.

P287

"Methotrexate intolerance in turkish children with juvenile idiopathic arthritis: a validity and reliability study of the miss questionnaire"

N. Akay[1], H. C. Culpan[2], U. Gul[1], E. Aslan[1], E. Kilic Konte[1], E. Aslan[1], A. Gunalp[1], M. Yildiz[1], S. Sahin[1], A. Adrovic[1], K. Barut[1], O. Kasapcopur[1]
[1]Department of Pediatric Rheumatology, [2]Department of Public Health, Istanbul University-Cerrahpasa, Faculty of Medicine, Istanbul, Türkiye
Correspondence: N. Akay
Pediatric Rheumatology, **23(2):** P287

Introduction: Methotrexate (MTX), a folic acid analog, is a frequently utilized agent in the field of pediatric rheumatology, particularly in cases of juvenile idiopathic arthritis (JIA), due to its anti-inflammatory and immunomodulatory properties. Despite the high efficacy of the treatment in most patients, an intolerance rate of 10–20% limits its use.
Objectives: The objective of this study was twofold: first, to adapt the MTX Intolerance Severity Score (MISS) questionnaire into Turkish, and second, to evaluate its reliability and investigate the characteristics of JIA patients with MTX intolerance.
Methods: This is a methodological study conducted in a Pediatric Rheumatology outpatient clinic of Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, with 134 patients aged between 2-18 diagnosed with JIA and regularly using MTX for at least 3 months during follow-up. The demographic and clinical data of the patients were retrospectively reviewed and recorded. The Turkish version of the MISS questionnaire was developed following the "guidelines for the process of cross-cultural adaptation of self-reported measures".
Results: Of the 134 patients who participated in the study, MTX intolerance developed in 75 (56%) patients over a median time of 1 (1-12) months after initiation of treatment. Of the 75 patients with MTX intolerance, 43 (57.3%) were female, the median age at initiation of MTX treatment was 81 (34-146) months, the average initial MTX dose was 10 (7.5–20) mg, the total duration of MTX use was 40 (16–89) months, and the disease activity score JADAS 27 at the initiation of MTX treatment was 10 (3–13). During follow-up, the dose of methotrexate was increased in 40 of 75 patients (53.3%), and intolerance developed in 16 of these patients (40%) after the dose increase (p=0.001). The MISS presented an internal consistency of 0.86 (95%CI 0.82-0.89). The questionnaire scores for patients with MTX intolerance averaged 12 (1–25). According to the MISS questionnaire responses, the most common symptoms in patients who developed intolerance were nausea after MTX (n=72, 96%), nausea upon thinking about MTX (n=66, 88%), vomiting after MTX (n=47, 62.7%), restless when taking MTX (n=48, 64%), and refusal to take MTX (n=45, 60%), crying when taking MTX (n=36, 48%), and irritable when taking MTX (n=35, 46.6%) (p<0.001). MTX was discontinued in 42 (56%) patients who developed intolerance.
Conclusion: With this study, the MISS questionnaire has been validated in Turkish, and its reliability in correlation with clinical findings has been demonstrated. Given these results, identifying risk factors for MTX intolerance and developing treatment strategies to prevent its onset will enable long-term MTX survival in children.
Disclosure
None declared

References

1. Bulatović M, Heijstek MW, Verkaaik M, et al. High prevalence of methotrexate intolerance in juvenile idiopathic arthritis: development and validation of a methotrexate intolerance severity score. *Arthritis Rheum*. 2011;63(7):2007–2013. https://doi.org/10.1002/art.30367
2. Londe AC, de Amorim JC, Julio PR, Wulffraat NM, Marini R, Appenzeller S. Cross-Cultural Adaptation and Validation of the Methotrexate Intolerance Severity Score Questionnaire in Portuguese (Brazil) for Children and Adolescents with Juvenile Idiopathic Arthritis. *J Clin Med*. 2023;12(3):1116. Published 2023 Jan 31. https://doi.org/10.3390/jcm12031116

P288

Implementation of therapeutic drug monitoring (TDM), pharmacogenetics and medreview in pediatric rheumatology

P. Dalla Zuanna[1,2,3], G. Paternuosto[4], D. Curci[4], G. Pauli[5], A. Parzianello[2], M. Klanjscek[2,4], S. Sindici Forgiarini[2], M. Franzin[4], G. Ponis[4], M. Lucafò[6], R. Franca[2], A. Fabretto[1], R. Addobbati[4], A. Tommasini[2,4], A. Taddio[2,4], P. Rossi[7], M. P. Trojniak[4], E. Cecchin[8], A. Arbo[4], S. Pastore[4], G. Stocco[2,4]
[1]Diagnostica avanzata traslazionale, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, [2]Department of Medical, Surgical and Health Sciences, University of Trieste, [3]Clinical and Experimental Pharmacology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, [4]Institute for Maternal and Child Health, IRCCS Burlo Garofolo, [5]University of Trieste, trieste, Italy, [6]Department of Life Sciences, University of Trieste, [7]Centro Regionale di Farmacovigilanza, trieste, [8]Clinical and Experimental Pharmacology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, aviano, Italy
Correspondence: P. Dalla Zuanna
Pediatric Rheumatology, **23(2):** P288

Introduction: TDM, pharmacogenetics and MedReview are precision medicine tools within active pharmacovigilance, relevant to maximize therapy effectiveness and minimize adverse drug reactions (ADRs). It is therefore important to implement and validate these methods across healthcare settings, including pediatric rheumatology.
Objectives: Implement the use of TDM, pharmacogenetics and MedReview in pediatric rheumatology patients, increasing their application and drafting pharmacological counselings to enhance their usefulness. Assess clinical impact by evaluating the rate of out-of-range TDM, actionable genotypes, patients with at least one actionable genotype and suspected clinically significant ADRs potentially linked to active pharmacovigilance data.
Methods: This observational study involved pediatric patients with rheumatic diseases treated with adalimumab, infliximab or methotrexate (MTX). TDM of biologics and anti-drug antibodies (ADA) was performed via immunochromatography and ELISA. Four genetic variants (ITPA rs1127354, MTHFR rs1801133, ATIC rs2372536 for MTX; FCGR3A rs396991 for biologics) were analyzed using TaqMan assay. ITPA enzyme activity (for MTX) was measured by HPLC-UV. MedReview included drug interaction analysis using INTERCheck, Lexicomp® and Drug Interactions checker databases. TDM therapeutic ranges were based on literature. Genotypes differing from wild-type with clinical/pharmacokinetic impact were considered actionable. Suspected ADRs (CTCAE grade ≥2, or grade 1 which resulted in therapy change) were deemed clinically significant.
Results: We enrolled 117 pediatric rheumatic patients (median age 10.75 years, 74 females; main diagnoses: juvenile idiopathic arthritis and idiopathic uveitis), collecting 525 samples. We performed 240 TDM, 464 pharmacogenetic analysis (116 per variant), 146 ITPA activity analyses, 372 MedReviews and pharmacologic counselings. Use of active pharmacovigilance tools rose significantly: before the study, pharmacogenetics, MedReview, and ITPA activity were unused while TDM was sporadic. TDM was out of range in 29.6% of cases and 8.3% of biologic-treated patients developed ADA. Actionable genotypes were 26.8% and 92.2% of patients had at least one. ITPA activity was below therapeutic cut-off in 33.6% of patients. Fourteen types of drug

interactions were found. Finally, 54.1% (20/37) of suspected ADRs were potentially linked to at least one pharmacovigilance result.
Conclusion: This study increased the use of active pharmacovigilance tools and showed they are often needed, given the high rates of out-of-range TDM and actionable genotypes. It was also found that many suspected ADRs can be linked to at least one tool used, supporting their role in ADRs prevention. Further analysis on their impact on therapeutic efficacy are ongoing.
Disclosure
None declared

P290

Hydroxychloroquine-induced pigmentation in Japanese paediatric patients

R. Yatabe[1], K. Akamine[1], S. Akahoshi[2], N. Mikami[1], R. Harada[1], R. Hamada[1]
[1]Department of Nephrology and Rheumatology, [2]Clinical Research Support Center, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan
Correspondence: R. Yatabe
Pediatric Rheumatology, **23(2):** P290

Introduction: Hydroxychloroquine (HCQ), an antimalarial drug, is used to treat various rheumatic diseases. HCQ is particularly effective in treating a broad range of symptoms associated with systemic lupus erythematosus (SLE), mitigating organ damage and reducing the risk of flares, thrombosis, infection, and death. It is therefore commonly prescribed for SLE in both Japan and the West. While HCQ is widely known to have retinopathy as an adverse effect, it is less well known to induce pigmentation of the skin and mucous membranes. Previously reported cases of HCQ-induced pigmentation occurred in adult patients, where its incidence reportedly ranges from 7.3% to 26.3%. Its incidence in children, however, remains unclear.
Objectives: To investigate the frequency and characteristics of HCQ-induced pigmentation in Japanese, paediatric patients.
Methods: The present, retrospective, cohort study enrolled Japanese children who visited our hospital between October 2024 and January 2025 and had ≥ 3 months of HCQ use. Data were collected from medical records, caregiver or patient questionnaires on awareness about pigmentation, and physical examinations. Fitzpatrick skin types, which reflect the skin's response to ultraviolet radiation exposure, were also assessed.
Results: Twenty-six patients (median age: 15 years; interquartile range [IQR]: 12.0–16.5) were included. Pigmentation occurred in 11 patients (42.3%). The Fitzpatrick skin types in the pigmentation group (P group) vs. non-pigmentation group (NP group) were: type II (18.2% vs. 60%), type III (36.4% vs. 20%), type IV (36.4% vs. 20%), and type V (9.1% vs. 0%). The median cumulative HCQ dosage was 154.4 g (IQR: 104–241) in the P group and 145.6 g (IQR: 31.9–270) in the NP group. The median treatment duration was 916 days (IQR: 701–1573) in the P group and 744 days (IQR: 196–1661) in the NP group. The triggering events that made the patients aware of their pigmentation were the persistence of pigmentation following sun exposure in three patients (27.3%), persistent scarring from mosquito bites in two patients (18.2%), and residual bruising after trauma in one patient (9.1%). Pigmentation in the P group occurred in the following areas in the order of decreasing frequency: the lower extremities (n=6; 54.5%), lips (n=5; 45.5%), upper extremities (n=4; 36.4%), non-lip, facial areas (n=3; 27.3%), and diffusely over the entire body (n=1; 9.1%). Six of 11 patients with pigmentation discontinued HCQ, three of the six experienced a consequent improvement in their pigmentation.
Conclusion: Pigmentation occurred more frequently in paediatric patients receiving HCQ than in adults, appearing in about 40% of the patients examined. While no clear association with the cumulative dosage or treatment duration was found, higher Fitzpatrick phototypes may reflect greater susceptibility. The lower extremities were the most common site of pigmentation in both paediatric and adult patients. Our findings suggested that HCQ-induced pigmentation may not be a rare adverse effect in children. Although the pigmentation may improve after discontinuation of HCQ, the underlying disease activity should decide whether the treatment is to be continued or stopped.
Disclosure
None declared

P291

Variation in biologic and targeted synthetic dmard use in JIA subtypes: results of a national UK survey

S. Cooray[1], S. Compeyrot-Lacassagne[1], E. S. Sen[2], K. Rajani[1], A. L. Solebo[3], P. Brogan[1,4] on behalf of UK National Institute of Health Research and Versus Arthritis Paediatric Rheumatology Clinical Studies Group and JIA Topic Specific Group
[1]Department of Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, [2]Department of Paediatric Rheumatology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, [3]Department of Paediatric Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, [4]Infection, Immunity and Inflammation Department, University College London Great Ormond Street Institute of Child Health, London, United Kingdom
Correspondence: S. Cooray
Pediatric Rheumatology, **23(2):** P291

Introduction: In recent decades, the range of biologics and synthetic disease-modifying anti-rheumatic drugs (DMARDs) for treating Juvenile Idiopathic Arthritis (JIA) has expanded, offering more therapeutic options. However, access to these treatments is inconsistent across the UK, with disparities between paediatric and adolescent/adult services, as well as across the four nations. The UK Paediatric Rheumatology Clinical Studies Group and JIA Topic Specific Group developed a survey to evaluate access to biologic and targeted synthetic DMARDs (b/tsDMARDs) to identify regional, age-related, and specialty-specific variations.
Objectives: The survey aimed to assess variations in the choice, and order of use, of b/tsDMARDs for different subtypes of JIA across the UK, where practice was influenced by specialty, patient age, regional access, and cost barriers.
Methods: A 26-question survey was distributed to multidisciplinary teams (MDTs) in paediatric and adolescent/adult rheumatology centres across the UK. The survey gathered demographic information, treatment p
References, and data on b/tsDMARD availability, with qualitative feedback on challenges faced by centres in different regions.
Results: Responses were received from and 1 adolescent/adult rheumatology and 10 paediatric centres across England, Scotland and Wales. Multidisciplinary team contributions comprised of 105 individuals including 40 consultants; 18 residents/fellows; 20 clinic nurse specialists and 8 specialist pharmacists and included input from gastroenterology, dermatology and opthalmology.
Key findings were:
- Four of the eleven centres (36.4%), two in devolved nations, lacked a specialist rheumatology pharmacist.
- Scotland was able to directly access anti-IL1 and anti-IL6 therapies for the treatment of Still's, and was the only nation able to access canakinumab. In England/Wales, anakinra/tocilizumab therapy is permitted only after failure of, or intolerance/contraindication to, methotrexate treatment.
- In paedatric patients, only adalimumab is commissioned for uveitis in the absence of arthritis, infliximab is only avilable with concurrent arthritis, and tocilizumab is not commissioned for this indication. Ophthalmologists can only access adalimumab (given 2-weekly) for isolated uveitis in paediatric patients but not in adult patients.
- Adult services had access to a greater breadth of therapies particularly for rheumatoid factor positive polyarticular JIA particularly JAK inhibitors (JAKi), baricitinib and upadicitinib and newer anti-TNFs, however they had to reclassify the disease as 'rheumatoid arthritis'. For psoriatic and enteropathic JIA, a number of b/tsDMARDS are only available via dermatology (anti-IL17A and anti-IL12/23) and gastroenterology (anti-IL23/JAKi) with concurrent skin/gut disease.
Conclusion: The survey revealed significant disparities in access to b/tsDMARDs for JIA across the UK. Access to therapies like canakinumab for Still's disease and treatments for psoriatic and enteropathic JIA or uveitis varies significantly, particularly across regions and specialties. These differences emphasize the need for more consistent access to therapies, ensuring that all patients, regardless of location or age, receive timely and appropriate treatment.
Disclosure
None declared

P294

Therapeutic drug monitoring for patients with juvenile idiopathic arthritis (JIA), jia-associated uveitis (JIAU) and non-jia chronic anterior uveitis (CAU) receiving adalimumab: the gosh experience

T. Doudouliaki[1], S. Compeyrot-Lacassagne[1], A. L. Solebo[2,3]
[1]Rheumatology, [2]Ophthalmology, Great Ormond Street Hospital, [3]UCL GOS Institute of Child Health, University College London, London, United Kingdom
Correspondence: T. Doudouliaki
Pediatric Rheumatology, **23(2):** P294

Introduction: Improved understanding of biologic therapeutic drug monitoring (TDM) is needed to address the significant challenge of treatment failure in Juvenile Idiopathic Arthritis (JIA) and uveitis.
Objectives: We aimed to (i) describe the primary indications for Adalimumab TDM in patients with JIA, JIA associated uveitis (JIAU), and Chronic Anterior Uveitis (CAU); (ii) to investigate the associations between serum drug levels, antidrug antibodies (ADAbs), and disease activity; (iii), and identify factors influencing immunogenicity.
Methods: Retrospective cohort study with a standardised dataset collected for 140 patients treated with Adalimumab at Great Ormond Street Hospital (GOSH) between 2019 and 2024. Data were extracted on TDM indication (reactive vs proactive monitoring), drug levels, ADAb titres, concurrent use of Disease Modifying Antirheumatic Drugs (DMARDs), and disease activity scores. Comparative analyses were undertaken to explore associations between immunogenicity, drug pharmacokinetics, and clinical outcomes.
Results: TDM data on 140 children are presented, comprising 86 (61.4%) girls, and 47, 77 and 16 with JIA, JIAU and CAU respectively. Of the total, 117 (83.6%) had reactive TDM. Patients with active disease (arthritis, uveitis, or both) had statistically significant lower drug levels (8.25 vs 10.4 mg/L, p= 0.009). In a linear regression model, the primary factor influencing adalimumab drug levels was the presence of ADAbs. Patients with ADAbs titre above 22 AU/ml had statistically significant differences in the drug level compared to patients without ADAbs when adjusted for confounders (regression coefficient of –6.189, SE = 1.770, 95% CI [–9.696, –2.682], p <.001). In a binary logistic regression model, patients who were not on concomitant DMARD use had 60.5% more chance of developing ADAbs (p=0.031).
Conclusion: This study suggests the clinical relevance of TDM in identifying drivers of treatment failure in paediatric patients receiving Adalimumab for JIA, JIAU, and CAU. ADAbs are likely to have a central role in altering drug pharmacokinetics and reducing therapeutic efficacy. Concomitant DMARD use may mitigate immunogenicity. These results offer the foundation for future research with the ultimate goal to set therapeutic drug level targets, enhance the precision and efficacy of treatments and improve patient outcomes in Paediatric Rheumatology for patients with JIA, JIAU and CAU.
Disclosure
None declared

References

1. Doeleman MJH, de Roock S, El Amrani M, van Maarseveen EM, Wulffraat NM, Swart JF. Association of adalimumab trough concentrations and treatment response in patients with juvenile idiopathic arthritis. Rheumatology (Oxford). 2021 Dec 24;61(1):377–382
2. Skrabl-Baumgartner A, Seidel G, Langner-Wegscheider B, et al. Drug monitoring in long-term treatment with adalimumab for juvenile idiopathic arthritis-associated uveitis Archives of Disease in Childhood 2019;104:246–250.
3. Welzel T, Golhen K, Atkinson A, Gotta V, Ternant D, Kuemmerle-Deschner JB, Michler C, Koch G, van den Anker JN, Pfister M, Woerner A. Prospective study to characterize adalimumab exposure in pediatric patients with rheumatic diseases. Pediatr Rheumatol Online J. 2024 Jan 2;22(1):5

P295

Therapeutic drug monitoring for patients with juvenile idiopathic arthritis and/or chronic anterior uveitis (CAU) receiving infliximab: a single centre experience

T. Doudouliaki[1], S. Compeyrot-Lacassagne[1], A. L. Solebo[2,3]
[1]Rheumatology, [2]Ophthalmology, Great Ormond Street Hospital, [3]UCL GOS Institute of Child Health, University College London, London, United Kingdom
Correspondence: T. Doudouliaki
Pediatric Rheumatology, **23(2):** P295

Introduction: Juvenile Idiopathic Arthritis (JIA) and uveitis often require escalation to biologic therapies like Infliximab. Treatment failure due to immunogenicity and inflammation-driven drug clearance is an increasingly important challenge, with children at risk of loss of disease control/remission.
Objectives: Retrospective study aiming to: (i) characterise the primary indications for Infliximab therapeutic drug monitoring (TDM) in patients with Juvenile Idiopathic Arthritis (JIA), JIA-associated uveitis (JIAU), and Chronic Anterior Uveitis (CAU); (ii) explore the associations between serum drug concentrations, antidrug antibodies (ADAbs), and disease activity; and (iii) identify factors contributing to immunogenicity.
Methods: Retrospective cohort study with a standardised dataset collected for patients treated with Infliximab infusions at Great Ormond Street Hospital (GOSH) between 2018 and 2024. Data were extracted on TDM indication (reactive vs proactive monitoring), trough drug levels, ADAb titres, concurrent use of Disease Modifying Antirheumatic Drugs (DMARDs), and disease activity scores. Comparative analyses were undertaken to explore associations between immunogenicity, drug pharmacokinetics, and clinical outcomes.
Results: TDM data on 24 children are presented, 16 (66%) were girls and comprising 2, 19 and 3 with JIA, JIAU and CAU respectively. The majority (62%) had reactive TDM. Five reactive samples were taken due to a skin rash, and 3 out of five because of a reaction during the infusion. Notably, all three of these infusion reaction samples tested positive for ADAbs. Increasing age at TDM was significantly associated with higher drug levels (regression co-efficient:1.35, SE: 0.46, 95% CI: 0.39–2.31, p<0.01). There were no differences in the drug levels between those with active versus inactive disease (14.5 vs 19.8 mg/L, p=0.24), or those with negative, low or high ADAb levels (p=0.33). In a linear regression model including sensitivity analysis, treatment duration (regression co-efficient: 75.9, 95% CI: 37.8 to 114.0, p<0.001) and DMARD use (regression co-efficient: −221.3, 95% CI: −367.4 to −75.1, p<0.01), were both significantly associated with infliximab antibody levels, with treatment duration showing a positive association and DMARD use a negative one.
Conclusion: The use of concomitant DMARDs appeared to play a protective role against the development of ADAbs, which may be clinically relevant given that all patients who experienced infusion-related adverse reactions had detectable ADAbs. These findings may serve as a stepping stone for future research aimed at establishing therapeutic drug level targets, improving treatment precision and efficacy, and ultimately enhancing outcomes for patients with JIA and/or CAU.
Disclosure
None declared

References

1. Ruperto N, Lovell DJ, Cuttica R, et al. A randomized, placebo-controlled trial of infliximab plus methotrexate for the treatment of polyarticular-course juvenile rheumatoid arthritis. *Arthritis Rheum*. 2007;56(9):3096–3106
2. Ruperto N, Lovell DJ, Cuttica R, et al. Long-term efficacy and safety of infliximab plus methotrexate for the treatment of polyarticular-course juvenile rheumatoid arthritis: findings from an open-label treatment extension.*Ann Rheum Dis*. 2010;69(4):718–722.

P296

Methylprednisolone pulse therapy in children with autoimmune and autoinflammatory diseases: evaluation of acute glycemic response and long-term metabolic safety

V. Podzolkova, A. Vitebskaya
Department of Children's Diseases, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation
Correspondence: V. Podzolkova
Pediatric Rheumatology,
23(2): P296

Introduction: Glucocorticosteroids (GCS) are widely used in pediatric rheumatology for their potent anti-inflammatory effects. However, GCS therapy may induce carbohydrate metabolism dysfunction. Methylprednisolone pulse therapy (MP-PT) is associated with fewer side effects compared to long-term GCS oral administration, but its impact on glucose metabolism in children remains poorly studied.
Objectives: To evaluate short- and long-term effects of MP-PT on carbohydrate metabolism in children with chronic autoimmune and autoinflammatory diseases.
Methods: We analyzed glucose levels in 15 patients (13 girls, 2 boys; median age 14.9 years) before, during, and after MP-PT (3 infusions over 3 days; median of total dose 27.0 (IQR: 23.0–31.6) mg/kg). Before the MP-PT, all patients had normal fasting venous blood glucose and glycated hemoglobin (HbA1c) levels. Capillary glucose levels were measured using glucometers at 2, 4, 7, 10, 21, 24, 28, 31, 34, 45, 48, 52, 55, 58, 69, and 72 hours after the first MP-PT administration. To assess the long-term effects of MP-PT on carbohydrate metabolism, we followed the patients for 2.7 (IQR: 0.5-4.6) years. Statistical analysis was performed using the StatTech v. 4.8.1 software.
Results: During MP-PT, capillary glucose levels exceeded the normal range in all patients 4–10 hours after initiation of treatment, peaking at 7 hours post-infusion: 10.8 (IQR: 9.9–11.8) mmol/L. The hyperglycemic response attenuated with subsequent infusions: peak glucose levels at 7 hours after the second and third doses were significantly lower than on the first day — 9.1 (IQR: 8.2–10.7) mmol/L ($p<0.05$) and 8.9 (IQR: 7.4–9.2) mmol/L ($p<0.01$), respectively. Glycemia showed a tendency toward normalization within 24 hours after each GCS administration. At 72 hours, glucose levels did not correlate with age, BMI SDS, cumulative methylprednisolone dose, or peak glycemic values observed during MP-PT. No statistically significant differences in glycemic parameters were found between patients receiving MP-PT for the first time and those with prior exposure to pulse therapy. Long-term follow-up over a median of 2.7 (IQR: 0.5–4.6) years revealed no delayed metabolic complications.
Conclusion: MP-PT in children causes transient, self-limiting hyperglycemia without long-term metabolic consequences. The glycemic response decreases with repeated doses, suggesting a possible adaptation to the treatment.
The main limitations of the study include a small sample size due to strict protocol adherence, potential bias from female predominance, and the invasive nature of glycemic monitoring, which may have affected patient recruitment.
Disclosure
None declared

P297

Clinical outcomes of low-to-moderate–dose glucocorticoids in paediatric inflammatory multisystem syndrome (PIMS)

Y. Levinsky[1], N. Shirman[1], G. Amarilyo[1], K. Kaidar[1], L. Harel[1], Y. Butbul Aviel[2], M. Heshin-Bekenstein[3], M. H. Saied[4], O. Goldzweig[5], A. Miler[6]
[1]Pediatric rheumatology, Schneider children's medical center of Israel, Petah Tikva, [2]Pediatric rheumatology, Yonatanbutbul@gmail.com, Haifa, [3]Pediatric rheumatology, Dana Children's Hospital, Tel Aviv, [4]Pediatric rheumatology, MohamadHs@clalit.org.il, Haifa, [5]Pediatric rheumatology, Kaplan medical center, Rehovot, [6]Pediatric rheumatology, Technion Faculty of Medicine, Haifa, Israel
Correspondence: Y. Levinsky
Pediatric Rheumatology, **23(2):** P297

Introduction: Paediatric inflammatory multisytem syndrome (PIMS) is an autoinflammatory disease following SARS-CoV-2 exposure. Standard treatment includes intravenous immunoglobulin (IVIG) and corticosteroids. While some reports suggest pulse steroids, ACR guidelines recommend initiating low-to-moderate dose glucocorticoids (1-2 mg/kg).
Objectives: This study aimed to assess the response of patients treated with low-to-moderate dose corticosteroids and compare outcomes to a historical cohort treated with pulse steroids.
Methods: A multi-center, retrospective study collected data on patients initially treated with low-to-moderate dose corticosteroids. The primary outcome was treatment escalation after 24 hours. Clinical and laboratory data were compared to a historical cohort to assess disease severity and outcomes.
Results: Among 41 patients receiving low-to-moderate dose corticosteroids, 7 (17.1%) required escalation. Thirteen (34.2%) needed vasopressors, and 2 (5.3%) required mechanical ventilation. Compared to 26 patients treated with pulse steroids, no differences were found in age, sex, fever characteristics, Kawasaki-like symptoms, or hemodynamic instability. Inflammatory markers (CRP, ESR) were similar, though ferritin was lower in the study group. Hospitalization was longer in the pulse steroid group. Echocardiography showed 87.5% of the study group had normal findings
Conclusion: Low-to-moderate dose glucocorticoids are effective for most PIMS patients, with only 17% requiring escalation. No differences were seen in vasopressor or ventilation needs. Given shorter hospital stays and favorable cardiac outcomes, this approach is effective, although pulse steroids may be considered in severe cases.
Disclosure
None declared

P298

Real-world use of belimumab in childhood-onset SLE in spain: cross-sectional analysis from a multicenter study (jules registry)

A. Boteanu[1,2], on behalf of JULES registry, C. Udaondo Gascón [3], J. C. Hernandez [4], D. Clemente [5], J. C. Nieto [6], E. Enriquez [7], I. Calvo [8], B. Sevilla [9], E. Pardo [10], B. Magallares [11], A. Capilla [12], B. Bravo [13], G. Diez-Cordoves [14], M. Camacho [15], G. Graña [16], J. J. Bethencourt[17], P. Mesa del Castillo [18], N. Palmou[19], M. Lopez [20], J. Sanchez [21], M. I. Gonzalez [22], C. Moriano [23], D. Dios-Santos [16], L. Martin [14], D. Fernandez [24], L. Trujillo[13], A. M. Brandy[25], L. Exposito[26], C. A. Guillen [27] on behalf of JULES Registry
[1]Rheumatology, H.U. Ramón y Cajal, [2]Rheumatology, Clinica Universidad de Navarra, [3]H.U La Paz, Madrid, [4]H.U San Juan de Dios, Barcelona, [5]H.U Niño Jesus, [6]H.U Gregorio Marañon, [7]H.U 12 Octubre, Madrid, [8]H.U. La Fe, Valencia, [9]H.U San Cecilio, Granada, [10]H.U Central Asturias, Oviedo, [11]H. de la Santa Creu y Sant Pau, Barcelona, [12]H.U La Merced, Sevilla, [13]H.U Virgen de las Nieves, Granada, [14]HRU Malaga, Malaga, [15]HU Virgen del Rocio, Sevilla, [16]H.U A Coruña, A Coruña, [17]H U Canarias, Tenerife, [18]HCU Virgen de la Arrixaca, Murcia, [19]HU Marques de Valdecilla, Santander, [20]H.U Vall d´Hebron, [21]H.U Parc Tauli, Barcelona, [22]H.U La Fé, Valencia, [23]HU Leon, Leon, [24]H. do Meixoeiro, Vigo, [25]H U Cabueñes, Gijon, [26]H.U Canarias, Tenerife, [27]H.U Ramón y Cajal, Madrid, Spain
Correspondence: J. C. Hernandez
Pediatric Rheumatology, **23(2):** P298

Introduction: SLE is a multisystemic autoimmune disease with several manifestations. Childhood-onset SLE (cSLE) has a more severe disease course than adult-onset SLE, with a higher frequency and severity of major-organ involvement and damage accrual. Low disease activity is an important goal. Belimumab (BEL) is the first biological drug approved for cSLE
Objectives: The aim of this study is to identify whether low lupus disease activity status on BEL is an achievable goal in cSLE and to describe the characteristics of cSLE patients treated with BEL in real world practice included in the JULES registry, a Spanish multicenter, hospital-based, cSLE registry.
Methods: We analyzed cross-sectional data from 67 patients treated with BEL for cSLE from a total of 250 included in the JULES registry. For the description of the cohort, summary statistics of central tendency and dispersion and percentage statistics were used for numerical and categorical variables respectively.
Results: 67 patients (26.8%) of the 250 patients included in the JULES registry were treated with BEL. The mean age to diagnosis was 12.9 (3.2) years, with a mean age at inclusion in the registry of 20.4 (8.3). 86.6% were female. Lupus nephritis (LN) prevalence was 56.1%, arthritis was seen in 74.6% and the most common laboratory abnormalities were leucopenia 68.2%, lymphopenia 62.5%, anti-DNA (89.6%) and hypocomplementemia (94%). The most frequent LN class was IV (23.9%), followed by class III (10.4%) and class II (10.4%). The main reasons for BEL initiation were arthritis (44.8%), mucocutaneous manifestations (40.3%), systemic manifestations (37.3%), LN (26.9%) and hematological involvement (22.4%). 20.9% of patients initiated BEL in the first 6 months of the disease. The mean duration of BEL treatment was 27.78 months (31.65). The mean SLEDAI and SLICC scores were 3.11 (2.12) and 0.46 (1.25) points respectively. 19.4% of BEL-treated patients have inactive disease (SLEDAI 0-1), 70.1% low disease

activity (SLEDAI 2-5), and 10.4% moderate activity. In patients with LN, 32.8% achieved complete remission and 10,4% partial remission, 4.5% experienced an improvement and ESRD was observed only in 3% of patients. 74.6% had managed to completely withdraw prednisone and 77.6% were still on BEL treatment. The reasons for suspension were inefficacy (14.9%), adverse events (4.5%) and complete remission of the symptoms (3%).

Conclusion: In the Spanish cSLE registry (JULES), 26.8% of patients were treated with BEL. In this complex and severe population, BEL is an effective and safe treatment for cSLE, allowing to achieve low disease activity state and corticosteroid withdrawal.

Funding
The Spanish registry of juvenile SLE (JULES) is funded by GSK. The authors did not receive any grant for their participation in the registry.

Disclosure
None declared

P299

Cardiac manifestations in juvenile systemic lupus erythematosus: a case series from a tertiary care center

A. Preda[1], M. R. Amaral[2], I. Cardoso[1], F. Aguiar[3], M. Rodrigues[3], I. Brito[3]
[1]Pediatrics, ULS Gaia e Espinho, [2]Pediatrics, ULS Entre Douro E Vouga, [3]Young Adult and Pediatric Rheumatology Unit, ULS São João, Porto, Portugal
Correspondence: A. Preda
Pediatric Rheumatology, **23(2):** P299

Introduction: Juvenile systemic lupus erythematosus (jSLE) is a chronic autoimmune disease with multisystem involvement, often more severe than in adults. [1,2] Cardiac manifestations, though less common, are clinically significant and may arise at any stage. [2] They can affect the pericardium, myocardium, endocardium, or valves, with pericarditis, myocarditis, Libman-Sacks endocarditis, and conduction abnormalities being most reported. Early recognition is crucial for prognosis. [1]

Objectives: To describe cardiac involvement in jSLE patients from a Portuguese tertiary center, focusing on type, timing, diagnosis, and treatment.

Methods: A retrospective descriptive study included jSLE patients followed between January 2013 and April 2025. Cardiac involvement was identified from clinical records and confirmed by clinical and/or diagnostic evaluation, including ECG and echocardiography. SLE was classified per 2019 ACR/EULAR criteria.

Results: Among 38 jSLE patients, 9/38 (23.7%) had cardiac involvement. Median age at diagnosis was 15 years (IQR: 12–16). Females represented 6/9 (66.7%). In 2/9 (22.2%), jSLE coexisted with another autoimmune disease: one had secondary Sjögren's syndrome, one an overlap with dermatomyositis. One had pre-existing Tetralogy of Fallot. The remaining developed cardiac disease attributed to jSLE. Manifestations included pericarditis in 3/9 (33.3%), myocarditis in 1/9 (11.1%; with pericarditis), pulmonary hypertension in 3/9 (33.3%), heart failure in 1/9 (11.1%), and systemic hypertension in 4/9 (44.4%). Multiple forms occurred in 3/9 (33.3%). No Libman-Sacks endocarditis, conduction abnormalities, or valve disease were observed.Systemic involvement was also frequent: mucocutaneous in 7/9 (77.8%), musculoskeletal in 6/9 (66.7%), renal in 7/9 (77.8%), hematologic in 8/9 (88.9%), neurologic in 2/9 (22.2%). Corticosteroids were used in 7/9 (77.8%). Most frequent immunomodulatory were mycophenolate mofetil (8/9; 88.9%), hydroxychloroquine (8/9; 88.9%), and azathioprine (2/9; 22.2%). bDMARD theraphy included rituximab in 3/9 (33.3%) and belimumab in 2/9 (22.2%). Several received combined therapy. Two patients (22.2%) died from cardiac complications. Median SLEDAI at diagnosis was 8.5 (IQR: 8.0–16.5) in those with cardiac involvement and 9.5 (IQR: 6.0–12.0) in those without (p=0.60). Biologics were used in 5/9 (55.6%) with cardiac disease vs. 8/29 (27.6%) without (p=0.23).

Conclusion: Cardiac involvement occurred in nearly one-quarter of jSLE patients, with varied manifestations and notable morbidity and mortality. No significant differences in disease activity or conventional immunosuppressant use were found, but biologics were more frequent in those with cardiac disease. These findings support routine cardiovascular monitoring and tailored care in jSLE.

Disclosure
None declared

References

1. Chiewchengchol D, et al. Mucocutaneous manifestations in juvenile-onset systemic lupus erythematosus: a review of literature. Pediatr Rheumatol Online J. 2015;13:1. https://doi.org/10.1186/1546-0096-13-1.
2. Hang JC, Xiao R,et al. Child-onset systemic lupus erythematosus is associated with a higher incidence of myopericardial manifestations compared to adult-onset disease. Lupus. 2019;28(1):95–101. https://doi.org/10.1177/0961203318804889.

P300

Belimumab in juvenile systemic lupus erythematosus- safety and effectiveness data from the biker registry

A. Zimmer[1], A. Klein[1], N. Brueck[2], J. Kuemmerle-Deschner[3], F. Dressler[4], J.-P. Haas[5], C. Hillekamp[1], A. Hospach[6], J. Klotsche[7], K. Minden[8], R. Trauzeddel[9], W. Daniel[10], G. Horneff[1]
[1]Pediatric Rheumatology, Asklepios Hospital for Children, Sankt Augustin, [2]Pediatric Rheumatology, Uniklinik Dresden, Carl Gustav Carus, Dresden, [3]Pediatric Rheumatology, Uniklinik Tübingen, Tübingen, [4]Pediatric Rheumatology, Medizinische Hochschule Hannover, Hannover, [5]Pediatric Rheumatology, Deutsches Zentrum für Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Garmisch-Partenkirchen, [6]Pediatric Rheumatology, Olgahospital, Stuttgart, [7]Pediatric Rheumatology, Deutsches Rheuma Forschungszentrum, [8]Pediatric Rheumatology, Kinderklinik der Charité, Campus Virchow, [9]Pediatric Rheumatology, Helios Klinikum Berlin-Buch, Berlin, [10]Pediatric Rheumatology, Sankt Josef Stift, Sendenhorst, Germany
Correspondence: A. Zimmer
Pediatric Rheumatology, **23(2):** P300

Introduction: Belimumab, the first biologic approved for treating juvenile systemic lupus erythematosus (jSLE) from the age of 5 years, inhibits B-cell activation by blocking BLYSS, a key factor in managing jSLE.

Objectives: To investigate use, efficacy and tolerability of Belimumab therapy in jSLE patients in clinical practice.

Methods: This ongoing non-interventional study utilizes data from the BiKeR registry, including jSLE patients meeting EULAR/ACR criteria and indicated for Belimumab, with efficacy assessed via Selena-SLEDAI, lab (ds-DNA antibodies, complement-C3 and -C4) and clinical (physician/patient global assessment of disease activity (0–100)) parameters over 24 months, and safety data evaluated through adverse event reports, compared to a control group of SLE patient not treated with Belimumab.

Results: As of the data cutoff (04/16/2025), 21 SLE patients on belimumab therapy (30.6 treatment years) and 17 control patients (16.4 observation years) have been enrolled. Baseline characteristics showed high disease activity in both groups based on lab and clinical findings. Clinical data from 11 patients (after 12 months) and 7 patients (after 24 months) under belimumab therapy show improvements in Selena-SLEDAI, physician global assessment, ds-DNA antibodies, and C3 complement. In two patients, elevated ds-DNA antibodies became undetectable, with normal complement C3- and C4-levels and resolution of disease signs.

Adverse events (AEs) occurred in 10 belimumab patients (47.6%) at a rate of 0.98 AEs/patient-year (95%CI: 0.69-1.40), compared to 7 control patients (41.2%) at 0.98 AEs/patient-year (95%CI: 0.60-1.60). No serious AEs and no therapy discontinuations were reported for belimumab. Steroid dosage could be reduced ≤7.5mg/d in most patients after 12 months and in all after 24 months of belimumab treatment. Two belimumab receiving patients had three reported disease flares or new organ manifestations (one lupus nephritis and one hepatitis, one unspecified flare regarding to "severe back pain"). In the control group, two patients experienced a total of two flares.

Conclusion: - Data from clinical practice regarding jSLE patients undergoing belimumab therapy in childhood with a longer follow-up concerning efficacy and safety are yet insufficient.
- Our results indicate good efficacy so far.
- There were no new safety signals.

- Steroid dosage could be reduced ≤7.5mg/d in most patients after 12 months and all after 24 months.
- As the observation continues, the inclusion of additional patients in the BiKeR-Belimumab registry would be highly appreciated.

Disclosure

A. Zimmer Speaker Bureau with: Travel grands: Novartis, Lilly; Speakers bureau: Lilly, Glaxo-Smith-Kline, A. Klein Speaker Bureau with: Speakers fee: Novartis, Lilly, N. Brueck Consultant with: Advisory Board Fresenius, Kabi, Speaker Bureau with: honorary fee Chougai Pharma, J. Kuemmerle-Deschner: None declared, F. Dressler Consultant with: advisory Boards: Novartis and Mylan, Speaker Bureau with: speakers bureau: Abbvie, Novartis, Pfizer,, J.-P. Haas: None declared, C. Hillekamp: None declared, A. Hospach Consultant with: Consulting fees: Novartis, SOBI, Speaker Bureau with: Speakers bureau: Novartis and SOBI, J. Klotsche: None declared, K. Minden Speaker Bureau with: honoraria from Amgen, Biogen, gsk, Novartis and medac, R. Trauzeddel: None declared, W. Daniel Grant/Research Support with: Novartis, Roche, Pfizer, Abbvie, Speaker Bureau with: received honorary fees from Novartis, Pfizer, Abbvie, MEDAC, Roche, and Sobi, G. Horneff Grant/Research Support with: Grants Novartis, MSD, Roche, Grant/research support from: Pfizer, Roche,MSD, AbbVie, Chugai, Novartis, Consultant with: Advisory Speaker: Pfizer, Novartis, Sobi; Consultant MSD, Lilly, Speaker Bureau with: Speakers bureau: Pfizer, Roche, MSD, Sobi, GSK, Sanofi, AbbVie, Chugai, Bayer, Novartis

P301

Refined autoantibody profiles in juvenile systemic lupus erythematosus

A. Klaumuenzer[1], F. Engelke[2], N. Fischer[1], M. Krumrey-Langkammerer[1], S. Dollinger[1], A. Sprengel[1], B. Huegle[3], C. Kleemann[4], T. Witte[2], J. P. Haas[1]
[1]German Center of Pediatric Rheumatology, Garmisch-Partenkirchen, [2]Dep. for Rheumatology and Immunology, MH Hannover, Hannover, [3]Rheumatic Centre Rhineland-Palatinate, Bad Kreuznach, [4]Pediatric Rheumatology and Immunology, University of Leipzig, Leipzig, Germany
Correspondence: A. Klaumuenzer, F. Engelke
Pediatric Rheumatology, **23(2):** P301

Introduction: Juvenile systemic lupus erythematosus (jSLE) is one of the most frequent systemic autoimmune diseases in childhood and may involve most of the organ systems including kidney, CNS, joints and others. Activation of B-cells and the production of autoreactive Antibodies (aAB) is one of the hallmarks of jSLE. Detection of aAB, such as ds-DNA-AB, anti-Smith etc. is a relevant tool in the diagnostic process. In the past years, research for biomarkers has led to new panels of aAB tested in adult SLE patients [1].
Objectives: We tested a new aAB panel [2] in a population of jSLE patients.
Methods: Sera of jSLE patients have been sampled in a single center within a 10 year period (2013-2024). Presence of IgG autoantibodies (aAB) against 67 antigens were analyzed in 86 patients with confirmed jSLE. Analysis used the Luminex method with the cut off value determined using the ≥98 quantile of the fluorescence intensity values in healthy controls (n=123)[2].Statistics included Chi-square test and Pearson correlation.
Results: The cohort included jSLE patients (female n= 76; 92.7%) diagnosed according to the EULAR/ACR criteria [3]. At time of sampling, the patients´ age ranged from: 5.5-20.5y (14.9y mean), the duration of disease from 1 to 122 mo. and SLEDAI from 0 to 63. Three had signs of neuro-psychiatric SLE, 25 had arthritis, 9 nephritis, 8 peri-/myocarditis, 46 decreased complement and 31 leukopenia.
Autoantibodies were detected against (%): dsDNA 69.5, anti-Cardiolipin 29.3, anti-Phospholipid 64.6, Sm 20.7, U1-RNP 24.4, Histone 36.6, Ro-52 39.0, Ro-60 25.6, La 13.4. The new panel revealed aAB against (%): HNRNPA1 13.4; IL-37 11.0; NONO 13.4; SNRPB 24.4; SNRPB2 15.9; TMPO 12.2; CCL4 14.6; MVP 12.2; PPL 9.8, RPLP2 39.6; SNRNP70 12.2. The number of positive aABs was not correlated with the duration of disease (0.05), moderately correlated with the SLEDAI (0.2) and well correlated with the IgG-level (0.5).
In contrast to data from adult SLE patients [4] within the Ro-SSA positive patients, 18.3% were positive for Ro-52+ and 4.9 for Ro-60+ only, while the combination of Ro-52+ and Ro-60+ was found in 20.7% of the patients. Significant negative correlations of aAB against SNRPB and SNRPB2 were found in patients with nephritis ($p<0.01$) and/or peri-/myocarditis ($p<10^{-8}$), while aAB against NONO significantly correlated with the presence of fatigue ($p<0.05$) and the absence of vasculitis ($p<0.0001$).
Conclusion: Refined panels testing aAB profiles in patients with jSLE enable to analyze different patterns of autoreactive activity and are a promising tool in order to define biomarkers.
*These authors equally contributed to the manuscript. This study was supported by an unrestricted grant of the "Verein Hilfe für das rheumakranke Kind e.V."

Disclosure

None declared

References

1. Ling, H.Z., et al., *Discovery of new serum biomarker panels for systemic lupus erythematosus diagnosis.* Rheumatology (Oxford), 2020. **59**(6): p. 1416–1425.
2. Engelke, F., et al., *Identification of novel autoantibodies in Sjogren's disease.* Front Immunol, 2025. **16**: p. 1,524,940.
3. Rodrigues Fonseca, A., et al., *Comparison among ACR1997, SLICC and the new EULAR/ACR classification criteria in childhood-onset systemic lupus erythematosus.* Adv Rheumatol, 2019. **59**(1): p. 20.
4. Robbins, A., et al., *Diagnostic Utility of Separate Anti-Ro60 and Anti-Ro52/TRIM21 Antibody Detection in Autoimmune Diseases.* Front Immunol, 2019. **10**: p. 444.

P302

Kikuchi-fujimoto's disease in systemic lupus erythematosus: single center experience

A. Shin[1], S. Kang[2], D. Kim[1], S. Kim[1], S. Lee[2], J. Lee[2], J. Kim[1], Y.-J. Kim[1], H.-S. Cha[2], K. Ahn[1]
[1]Pediatrics, [2]Medicine, Samsung Medical Center, Seoul, Korea, Republic Of
Correspondence: A. Shin
Pediatric Rheumatology, **23(2):** P302

Introduction: Kikuchi-Fujimoto's disease (KFD) or histiocytic necrotizing lymphadenitis is a benign and self-limited disease of unknown etiology. It presents with localized lymphadenopathy, predominantly in the cervical region, accompanied by fever and leukopenia. An association has been reported between KFD and systemic lupus erythematosus (SLE), and its diagnosis has been reported to precede, postdate, or coincide with the diagnosis of SLE.
Objectives: We aimed to investigate the initial demographic characteristics and clinical presentations among SLE patients with or without KFD.
Methods: From 2005 to 2024, patients with SLE were identified from electronic medical records. Among these, patients with KFD mentioned in electronic medical records were identified. Laboratory values and the presence of lupus nephritis were further reviewed.
Results: A total of 1,040 patients with SLE were identified. Among them, 44 patients (4.2%) had KFD. The demographic and median laboratory values at the time of SLE diagnosis between patients with KFD and patients without KFD were following; median age (31 years vs. 39 years), female (91% vs 90%), white blood cell count (4,350/mm^3 vs. 4,850/mm^3), hemoglobin (12 g/dL vs 12 g/dL), platelet (217/mm^3 vs. 204/mm^3), anti-ds-DNA (12 IU/mL vs 38 IU/mL), C3 (65 mg/dL vs 81 mg/dL), and C4 (14 mg/dL vs 19 mg/dL). Among them, lupus nephritis was observed in 23% of patients with KFD and 39% of patients without KFD (P=0.027).
Conclusion: KFD may occur in SLE patients at a rate of one in about 25 patients. Further studies are needed to analyze the natural course of these patients in detail.

Disclosure

None declared

P303

Juvenile-onset systemic lupus erythematosus with anti-mi-2 positive inflammatory myositis: a case report

A. Ham[1,2], S. Cooray[1], J. M. MacMahon[1]
[1]Department of Paediatric Rheumatology, Cambridge University Hospitals NHS Foundation Trust, [2]School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom
Correspondence: A. Ham
Pediatric Rheumatology, **23(2):** P303

Introduction: Juvenile-onset systemic lupus erythematosus (jSLE) is a rare inflammatory autoimmune condition. The co-existence of myositis in SLE has not been extensively studied, but the estimated frequency in adults is between 4-16%.[1] In jSLE, a handful of case reports describe the presence of myositis and other overlapping features of juvenile idiopathic inflammatory myopathy (IIM). Myositis-specific antibodies (MSA) are useful biomarkers, which have been found to be positive in up to 60% of patients with juvenile dermatomyositis (JDM) but are not typically measured in SLE.[2]
Objectives: We present a novel case of anti-Mi-2 antibody positive myositis in the context of newly diagnosed jSLE.
Methods: Case report.
Results: A 15-year-old girl presented with a 2-month history of daily fevers, widespread erythematous macular rashes, fatigue, and progressively worsening arthralgia, myalgia and weakness. Additionally, she reported dysphonia, dysphagia to solids, and significant weight loss. More acutely, she developed pleuritic chest pain and breathlessness. Physical examination revealed diffuse arthralgia, myalgia and proximal muscle weakness. Nailfold capillaroscopy showed dilated capillaries with drop-out. Swallow assessment was normal. Laboratory testing showed elevated inflammatory markers (ESR 109 mmHg; CRP 45 mg/L), anaemia (Hb 93 g/L), lymphopaenia (lymphocytes 0.9*10^9/L), hypocomplementaemia (C3 0.66 g/L; C4 0.03 g/L), hypergammaglobulinaemia, thrombocytosis and mild transaminitis. ANA, dsDNA (>400 iu/mL), anti-Ro and anti-Scl70 autoantibodies were positive. Echocardiography and high resolution chest CT confirmed a small pericardial and pleural effusions, respectively. Musculoskeletal MRI revealed diffuse bilateral myositis in pelvic girdle and proximal thighs; CK was normal and MSA testing was positive for anti-Mi-2 alpha antibodies. The patient met ACR/EULAR criteria for SLE but not IIM/JDM, as despite significant myositis, she lacked typical skin and other features. She was commenced on pulsed IV methylprednisolone followed by weaning oral prednisolone, and maintenance of mycophenolate mofetil and hydroxychloroquine. Treatment resulted in symptomatic improvement and normalisation of inflammatory markers, dsDNA and C3/C4.
Conclusion: We report a novel case of jSLE with overlap myositis and positive anti-Mi-2 alpha antibodies at onset. In JDM, MSA aid phenotypic characterisation; anti-Mi-2 antibodies are associated with severe muscle involvement.[2] A recent multicentre cohort study of children and adults with SLE showed 6.3% had myositis and 25% of those affected had detectable MSA.[3] Together with our findings, this suggests that screening for MSA in SLE myositis may be a useful biomarker, although further studies are required to evaluate diagnostic utility. Consent to published had been obtained.
Disclosure
None declared

References
1. Tiniakou et al. *Lupus Sci Med*. 2022;9(1).
2. Papadopoulou et al. *Nat Rev Rheumatol*. 2023;19(6):343–362.
3. Bitencourt et al. *Lupus*. 2020;29(7):776–781.

P304

Monogenic lupus in children: a descriprive study of clinical findings and treatment outcomes

A. Alisan[1], Z. Orhan[2], B. Atmis[2], A. Karabay Bayazit[2], G. Parmaksiz[3], M. Hangul[4], R. M. Kisla Ekinci[1]
[1]Pediatric Rheumatology, [2]Pediatric Nephrology, Cukurova University Faculty of Medicine, [3]Pediatric Nephrology, Baskent University Faculty of Medicine, [4]Pediatric Pulmonology, Adana City Training and Research Hospital, Adana, Türkiye
Correspondence: A. Alisan
Pediatric Rheumatology, **23(2):** P304

Introduction: Monogenic lupus represents a rare subset of systemic lupus erythematosus (SLE), characterized by early-onset disease caused by single-gene mutations. Unlike classical picture of polygenic SLE, monogenic lupus shed insights into the pathogenic mechanisms underlying autoimmunity, such as complement system, nucleic acid degradation and sensing pathways. Understanding of monogenic lupus opens the door to targeted therapies and personalized care for affected children.
Objectives: In this study, we aimed to identify the main clinical and laboratory findings and responses to the treatment of monogenic lupus in a single referral center.
Methods: We included the children with monogenic lupus diagnosed in a single referral pediatric rheumatology center. We retrospectively collected the data, including demographic characteristics, laboratory, genetic and radiological data and treatment responses. Patients with irregular or insufficient follow-up (below 6 months) were excluded from the study.
Results: The study included 9 children (4 females, 5 males) from 8 unrelated families. The most common genetic cause was DNASE1L3 deficiency (n=4). The causative genes in remaining patients were as follows: TREX1 (n=2), DNASE1/DNASE1L3 (n=1), C2 (n=1), and TLR7 (n=1). In the entire cohort, the median age at symptom onset and diagnosis were 5 (range, 1.5-17) and 12.5 (range, 4-18) years, respectively. The most common clinical properties were as follows: Fever (n=5), mucocutaneous (n=9), musculoskeletal (n=5), renal (n=5) and pulmonary (n=4) involvement. Urticaria was present in all patients with DNASE1L3 variants. Chilblains were consistent in the two siblings with TREX1 variants. Pulmonary hemorrhage was present in all but one patient with DNASE1IL3 deficiency. Autoantibodies were present in 5 of 9 patients.
Treatment included systemic steroids in all patients, of which 3 necessitated at least 3 pulses of methylprednisolone. JAK inhibitors were successfully used as second choice in 2 patients with familial chilblain lupus due to TREX1 variants, who are still in remission on drug. Disease modifying antirheumatic drugs were utilized including hydroxychloroquine (n=7), cyclophosphamide (n=4), rituximab (n=3), mycophenolate mofetil (n=6), azathioprine (n=2) and plasmapheresis (n=2).
Three patients were still on low-dose systemic steroids (<0.5 mg/kg/day) at the time of study. One patient with DNASE1L3 deficiency was deceased due to massive pulmonary hemorrhage at the age of 17 years.
Conclusion: This case series highlights the phenotypic diversity among the patients with monogenic lupus. Since whole exome sequencing is costly to perform all pediatric lupus patients, characterization of the distinct phenotypes of monogenic lupus might lead to more precise genetic testing and targeted treatment.
Disclosure
None declared

References
1. Alperin JM, Ortiz-Fernández L, Sawalha AH. Monogenic Lupus: A Developing Paradigm of Disease. Front Immunol. 2018 Oct 30;9:2496.
2. Qin Y, Ma J, Vinuesa CG. Monogenic lupus: insights into disease pathogenesis and therapeutic opportunities. Curr Opin Rheumatol. 2024 May 1;36(3):191–200.

P305

Assessment of retinal and peripheral microvascular changes in juvenile systemic lupus erythematosus: a comparative study using optical coherence tomography angiography and nailfold videocapillaroscopy

B. Menentoğlu[1], D. B. Güzel[2], S. D. Arık[1], G. Kavrul Kayaalp[1], A. Gencer[2], F. Çakmak[3], F. G. Demirkan[4], O. Akgun[1], E. Pempegül Yıldız[5], N. Sayın[2], N. Aktay Ayaz[1]
[1]Pediatric Rheumatology, Istanbul University, [2]Ophthalmology, Kanuni Sultan Süleyman Training and Research Hospital, [3]Pediatric Rheumatology, Başakşehir Çam and Sakura State Hospital, [4]Pediatric Rheumatology, Kanuni Sultan Süleyman Training and Research Hospital, [5]Pediatric Neurology, Istanbul University, Istanbul, Türkiye
Correspondence: B. Menentoğlu
Pediatric Rheumatology, **23(2):** P305

Introduction: Microvascular dysfunction plays a central role in the pathogenesis of Juvenile systemic lupus erythematosus (jSLE), and its early detection may help predict disease activity and prevent long-term organ damage. Optical coherence tomography angiography (OCTA) is a noninvasive imaging technique that provides high-resolution, real-time imaging of the retinal microvasculature. Since the retina is considered a window to the systemic microcirculation, OCTA is a potential tool for assessing subclinical vascular involvement. Nailfold

videocapillaroscopy (NVC) is another noninvasive method used to assess peripheral microcirculation.
Objectives: The aim of this study was to investigate the relationship between retinal microvascular changes detected by OCTA and NVC findings in patients with jSLE. In addition, the study aimed to investigate the relationship of these imaging findings with clinical disease activity and relevant laboratory markers.
Methods: In this prospective observational study, 29 patients diagnosed with jSLE based on the SLICC criteria and without any ocular involvement, along with 11 age-and sex-matched healthy controls (HC) were enrolled and evaluated. Disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). All participants underwent a comprehensive ophthalmologic evaluation, including measurements of axial length (AL), central corneal thickness (CCT), and spherical equivalent refraction. Retinal imaging included assessment of retinal nerve fiber layer thickness (RNFL), central macular thickness (CMT), and retinal microvasculature using OCTA. All patients with JSLE underwent standardized, simultaneous NVC. Capillary density, morphology, and the presence of microvascular abnormalities including microhemorrhages and neoangiogenesis were evaluated and compared with OCTA parameters.
Results: In the 29 patients with jSLE, the median age at diagnosis was 12.2 years (IQR: 9.1–13.8), and the median age at assessment was 16.2 years (IQR: 12.5–17.7). NVC evaluation revealed a normal pattern in 11 patients and a nonspecific pattern in 18 patients. The median vessel density of the deep capillary plexus was lower in JSLE [53 (IQR 51.95–52.35)] compared to controls [53.6 (IQR 52.87–54.12)] (p = 0.041). Similarly, the median vessel density of the superficial capillary plexus was also reduced in the patient group [48.35 (IQR 47.6–49.1)] relative to controls [50.1 (IQR 49.12–50.62)] (p = 0.05). However, no significant differences were observed between JSLE patients and HC in SE, AL, CCT, or CMT with p-values of 0.10, 0.47, 0.12, and 0.54, respectively. When patients were stratified by disease activity based on SLEDAI scores (<4 vs. ≥4), both deep and superficial capillary plexus vessel densities remained comparable (p = 0.19 and p = 0.09, respectively). Comparison of OCTA parameters with NVC findings revealed that the superficial capillary plexus vessel density was significantly lower in patients who exhibited dilated capillaries on NVC (median: 48.05, IQR: 47.0–48.8) compared to those without capillary dilatation (median: 48.95, IQR: 48.58–49.26; p = 0.02).
Conclusion: This study suggests that retinal microvascular changes detected by OCTA may be present in jSLE patients without clinical ocular involvement. The observed association between increased superficial capillary plexus vessel density and dilated capillaries on NVC indicates a possible link between retinal and peripheral microvascular alterations. These findings may indicate that OCTA and NVC could be useful noninvasive tools for detecting subclinical vascular involvement in jSLE; however, larger studies are needed to confirm their clinical significance.
Disclosure
None declared

P306

Primary headaches in pediatric lupus: prevalence and clinical characteristics

B. Menentoğlu[1], G. Kavrul Kayaalp[1], S. D. Arık[1], A. Dudaklı[1], C. Baykan[2], O. Akgun[1], H. Maraş Genç[3], F. G. Demirkan[4], F. Çakmak[5], E. Pempegül Yıldız[3], N. Aktay Ayaz[1]
[1]Division of Pediatric Rheumatology, Istanbul University, Istanbul, [2]Pediatrics, Artvin Yusufeli State Hospital, Artvin, [3]Division of Pediatric Neurology, Istanbul University, [4]Division of Pediatric Rheumatology, Kanuni Sultan Süleyman Training and Research Hospital, [5]Division of Pediatric Rheumatology, Başakşehir Çam and Sakura State Hospital, Istanbul, Türkiye
Correspondence: B. Menentoğlu
Pediatric Rheumatology, **23(2):** P306

Introduction: Neuropsychiatric involvement is more common in pediatric lupus than in adult cases. Headache is one of the most common and significant neurological manifestations in SLE, yet its definition remains unclear. Distinguishing whether a headache is attributable to lupus or is a primary headache can be challenging. While primary headaches are thought to be common in lupus, the exact frequency and patterns remain unclear.
Objectives: The aim of this study was to investigate the prevalence, frequency, patterns, and related clinical features of primary headaches in pediatric lupus patients in a standardized manner.
Methods: This study included 29 pediatric lupus patients, who were regularly followed-up with a diagnosis of pediatric-onset SLE, and 40 age- and sex-matched healthy controls. Headache presence, frequency, intensity, and patterns were assessed using a standardized questionnaire. Additionally, all patients underwent a comprehensive history and physical examination by a pediatric neurologist, along with a fundoscopic examination to exclude secondary causes of headache. Based on the diagnostic criteria of the International Classification of Headache Disorders (ICHD-3), headaches were classified as migraine with aura, migraine without aura, cluster-type, or tension-type.
Results: Primary headache was significantly more common in the SLE group (n=9, 31%) compared to the control group (n=3, 7.5%) (p=0.01). Among the pediatric lupus patients with primary headache, 7 had migraine and 2 had tension-type headache. In the control group, 2 patients had migraine and 1 had tension-type headache. No significant association was found between headache presence and age at diagnosis or disease duration in the lupus group (p=0.66 and p=0.61, respectively). Aura was not observed in either the patient or the control group. There were no significant differences in the SLEDAI scores at diagnosis or at the time of evaluation between lupus patients with and without headache (p=0.68 and p=0.87, respectively). The median cumulative corticosteroid dose did not differ significantly between lupus patients with headache (median: 3.3 grams, IQR: 0.6–7.5) and those without headache (median: 4.9 grams, IQR: 0.9–8.8) (p=0.63). Additionally, no significant differences were observed between the headache and non-headache groups regarding ANA, anti-dsDNA, anti-Sm, or antiphospholipid antibody positivity.
Conclusion: Primary headaches are more prevalent in pediatric lupus patients compared to healthy controls, with migraine being the most common type. However, headache occurrence did not correlate with disease activity, age at diagnosis, corticosteroid dose, or autoantibody profiles. These findings suggest that while primary headaches are common in pediatric lupus, their relationship with disease-specific factors remains unclear, highlighting the need for further investigation into additional contributing factors.
Disclosure
None declared

References

1. de Oliveira I, de Fontes BR, de Ataíde Mariz H, Duarte ALBP, Sampaio Rocha-Filho PA. Headache in patients with systemic lupus erythematosus: A matched case–control study. Headache. 2025 Apr;65(4):568–577.
2. Feld J, Tayer-Shifman OE, Su J, Anderson M, Touma Z. Primary headache in SLE -systematic review and meta-analysis. Semin Arthritis Rheum. 2024 Dec;69:152,566.
3. Samy E, Zahran ES, Sabry M, Elshony H. Headaches in SLE patients: a cross-sectional analysis of clinical, immunological, and Radiological Correlations. BMC Rheumatol. 2024 Oct 31;8(1):57.

P307

Evaluation of disease activity and damage index in patients diagnosed with juvenile systemic lupus erythematosus

D. Aydın[1], B. Sözeri[2], G. Kavrul[3], S. Atamyıldız Uçar[2], E. Tunce[2], N. Aktay Ayaz[3], B. Öksel[1], H. Ilgaz Tüzen[4], B. Kasap Demir[4], D. Alkan[5], S. Özdel[5], G. Oğuz[6], S. Türkuçar[6], G. Otar Yener[7], H. K. Dursun[8], K. Öztürk[8], M. Çakan[9], T. Kasap[10], S. Yüksel[11], B. Bozkaya Yücel[12], N. Şahin[1], H. E. Sönmez[1]
[1]Department of Pediatric Rheumatology, Kocaeli University, Kocaeli, [2]Department of Pediatric Rheumatology, Health Sciences University, Umraniye Training and Research Hospital, [3]Department of Pediatric Rheumatology, İstanbul University, İstanbul, [4]Department of Pediatric Rheumatology and Nephrology, İzmir Katip Çelebi University, İzmir, [5]Department of Pediatric Rheumatology, Ankara Etlik City Hospital, Ankara, [6]Department of Pediatric Rheumatology, Pamukkale University, Denizli, [7]Department of Pediatric Rheumatology, Eskişehir City Hospital, Eskişehir, [8]Department of Pediatric Rheumatology, Istanbul Medeniyet University, [9]Department of Pediatric Rheumatology, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, İstanbul,

[10]Department of Pediatrics, [11]Department of Pediatric Rheumatology, Çanakkale Onsekiz Mart University, Çanakkale, [12]Department of Pediatric Rheumatology, Samsun Training and Research Hospital, Samsun, Türkiye
Correspondence: B. Öksel
Pediatric Rheumatology, **23(2):** P307

Introduction: Juvenile Systemic Lupus Erythematosus (jSLE) is a rare pediatric rheumatic disease marked by systemic inflammation that can cause organ damage. Compared to adults, it often follows a more severe course in children. Corticosteroids are widely used for their rapid anti-inflammatory effects; however, their adverse events have made steroid-sparing strategies increasingly important in disease management.
Objectives: This study aimed to evaluate the impact of corticosteroid use on disease activity and damage index in patients diagnosed with jSLE.
Methods: This was a multicenter, retrospective study including patients who were followed for at least 12 months due to jSLE. Low-dose corticosteroid therapy was defined as 0.01–0.03 mg/kg/day (maximum 7.5 mg/day) of prednisolone. The annual cumulative steroid dose (mg/day) was calculated by dividing the total amount of steroid received on treatment days by the product of 365.25 and the number of years. Data collected included SLE Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) at the initial and final visits, laboratory findings, and flare characteristics
Results: A total of 138 patients from 11 centers were enrolled. Of these, 121 (87.7%) were female and 17 (12.3%) were male. The median age at diagnosis was 14 years (range: 2–16), and the median follow-up period was 36 months (range: 12–170). At diagnosis, 21 patients had organ damage, while 19 had organ damage at their last visit. Of the 10 patients who had damage at diagnosis, damage persisted in the final visit. Observed damage included cataracts (n=5, 3.6%), nephrotic-range proteinuria (n=5, 3.6%), erosive arthritis (n=4, 2.9%), cognitive dysfunction (n=3, 2.3%), avascular necrosis (n=2, 1.4%), and one patient each (0.7%) with decreased GFR (<50%), retinal changes or optic atrophy, venous thrombosis, pancreatic insufficiency, stroke, transverse myelitis, end-stage renal disease, pulmonary hypertension, pleural fibrosis, reduced lung capacity, previous myocardial infarction, valvular involvement, muscle atrophy, vertebral height loss, and scarring alopecia. Although follow-up durations were similar between groups, patients with damage had higher SLEDAI scores at both initial and final visits and took longer to achieve low-dose steroid therapy. Additionally, the proportion of patients who achieved Lupus Low Disease Activity State (LLDAS) was significantly lower in the damage group (p=0.02).
Conclusion: Organ damage in jSLE is associated with increased morbidity and mortality. Identifying and mitigating factors that contribute to long-term damage is essential. While glucocorticoids are effective and accessible agents for disease control, they should be used at the lowest effective dose and for the shortest duration possible to minimize adverse outcomes.
Disclosure
None declared

References
1. Hanif, M., Sarker, C., Al-Abadi, E., Armon, K., Bailey, K., Bohm, M., Brennan, M., Ciurtin, C., Gardner-Medwin, J., Hawley, D. P., Kinder, A., Leahy, A., Malik, G., McLaren, Z., Moraitis, E., Mosley, E., Ramanan, A. V., Rangaraj, S., Ratcliffe, A., Riley, P., … Smith, E. M. D. (2025). Contributors to organ damage in childhood lupus: corticosteroid use and disease activity. *Rheumatology (Oxford, England)*, *64*(5), 3028–3038.
2. Davidson, J. E., Fu, Q., Rao, S., Magder, L. S., & Petri, M. (2018). Quantifying the burden of steroid-related damage in SLE in the Hopkins Lupus Cohort. *Lupus science & medicine*, *5*(1), e000237.

P308

Papilledema as a sign of severe neurological involvement in juvenile systemic lupus erythematosus

B. Öksüz Aydın[1], F. Aydın[1], S. Teber[2], S. Kaynak Şahap[3], Z. B. Özçakar[1]
[1] Pediatric Rheumatology, [2] Pediatric Neurology, [3] Pediatric Radiology, Ankara University Faculty of Medicine, Ankara, Türkiye
Correspondence: B. Öksüz Aydın *Pediatric Rheumatology,* **23(2):** P308

Introduction: Systemic lupus erythematosus (SLE) is a serious, potentially life-threatening, chronic autoimmune disease that affect multiple organs and systems. Neuropsychiatric SLE (NPSLE) occurs in 14–95% of patients with SLE and presents with a variety of non-specific symptoms. Ocular involvement, which affects any part of the eye, is a rare manifestation of NPSLE.
Objectives: The presence of neurological involvement in SLE is crucial for determining patient prognosis. However, patients may not always exhibit specific symptoms. Ocular involvement, in particular, may be overlooked.
Methods: We present two patients with jSLE who had no neurological symptoms but were diagnosed with papilledema during routine eye examinations. Subsequent investigations revealed severe neurological involvement.
Results: Patient 1
A 12-year-old girl complained of a rash on her face and joint pain in her knees and fingers for six months. Laboratory tests revealed thrombocytopenia and hypocomplementemia. ANA, anti-dsDNA and anti-ribosomal P protein were positive. Before hydroxychloroquine treatment, the patient underwent an ophthalmological examination which revealed blurred optic disc borders. Lumbar puncture revealed a cerebrospinal fluid pressure of 50 cm H20. Cranial MRI revealed widespread vasculitis. Hydroxychloroquine, corticosteroids, and aspirin were started.Acetazolamide was started for intracranial hypertension. The patient received a total of six monthly doses of intravenous cyclophosphamide (CYC). Maintenance treatment was continued with mycophenolate mofetil (MMF). At the three-month follow-up, all symptoms had resolved.
Patient 2
A 16-year-old girl presented with joint pain and swollen eyelids. Laboratory investigations revealed anaemia and hypocomplementemia. ANA, anti-dsDNA and lupus anticoagulant were positive. Prior to hydroxychloroquine treatment, an ophthalmological examination revealed oedematous optic disc margins, tortuous vessels and hyperemic discs. The cranial MRI scan was consistent with widespread vasculitic involvement. Hydroxychloroquine, corticosteroids and aspirin were started. Intravenous CYC treatment was planned for a total of six doses. The patient's symptoms resolved completely during the two-month follow-up period.
Conclusion: The neuropsychiatric involvement of SLE may be overlooked when symptoms are absent or ignored. In this regard, a baseline ophthalmological examination can provide guidance. It is essential that all SLE patients undergo an ophthalmological examination by experienced specialists at the time of diagnosis.
Disclosure
None declared

References
1. Yu HH, Lee JH, Wang LC, Yang YH, Chiang BL. Neuropsychiatric manifestations in pediatric systemic lupus erythematosus: a 20-year study. Lupus. 2006;15(10):651–7.
2. Nikolaidou A, Beis I, Dragoumi P, Zafeiriou D. Neuropsychiatric manifestations associated with Juvenile Systemic Lupus Erythematosus: An overview focusing on early diagnosis. Brain Dev. 2024;46(3):125–34.
3. Chen JJ, Kumar N, McEvoy KM, Leavitt JA. Papilloedema and autoimmune retinopathy from systemic lupus erythematosus. Neuro-Ophthalmology. 2018;42(2):117–21.

P309

Comparative evaluation of the performance of revised sapporo and 2023 ACR/EULAR classification criteria in a paediatric antiphospholipid syndrome cohort with long-term follow-up into adulthood

S. Hussain[1], T. McDonnell[2], C. Ciurtin[3]
[1]Department of Rheumatology, Barts Health NHS Trust, [2]Department of Ageing, Rheumatology and Regenerative Medicine, [3]Centre for Adolescent Rheumatology, University College London, London, United Kingdom
Correspondence: C. Ciurtin
Pediatric Rheumatology, **23(2):** P309

Introduction: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by increased risk of thrombosis and

pregnancy morbidity with persistently elevated antiphospholipid antibodies (aPL). Paediatric antiphospholipid syndrome (pAPS) is a less investigated phenotype.
Objectives: We aimed to characterise a single-centre cohort of adolescents and young adults (AYA) with pAPS, diagnosed basen on expert opinion and followed-up into adulthood. We compared the performance of the new 2023 ACR/EULAR criteria, which have not yet been tested in pAPS, with the revised Sapporo criteria.
Methods: We screened our childhood-onset connective tissue disease database comprising 215 cases to identify AYA diagnosed with pAPS based on expert opinion to characterise the disease phenotype and compare the two classification criteria.
Results: We identified 12/215 AYA aged 16-35 (F:M= 10:2, 50% Asian, 25% Black African, 16.6% White and 8.3% Middle-Eastern) diagnosed with pAPS between 9-17 years of age based on expert opinion, and followed-up for 3-20 years; 91% of which had another associated autoimmune disease, including childhood systemic lupus erythematosus (cSLE)/Sjogren and juvenile dermatomyositis (JDM); 8/12 (66.6%) of them were persistently aPL triple positive, while another two (16.6%) had high risk aPL profiles. Despite previous literature reporting a lower proportion of thrombotic vs. non-thrombotic manifestations in pAPS, in our cohort 8/12 AYA had at least one thrombotic event, while 4/8 had up to 4 episodes of arterial/venous thrombosis despite ongoing anticoagulation. There was no history of pregnancy morbidity in this cohort. Four AYA had only non-thrombotic pAPS manifestations (3/4 had high-risk aPL profile). For pAPS manifestations, 8/12 cases were treated with aspirin and warfarin, 2/12 with direct oral anticoagulants (DOACs) and 2 with aspirin alone. One young person received plasma exchange for catastrophic APS. Out of 12 pAPS cases, 8/12 fulfilled the revised Sapporo, while 9/12 fulfilled the 2023 ACR/EULAR classification criteria at diagnosis, suggesting slightly lower sensitivity, but overal no signiifcant difference between the performance of the two sets of criteria for pAPS classification. A small proportion of AYA in our cohort (5/215) had persistently elevated aPL (four AYA with cSLE and one with JDM) without clinical pAPS manifestations (fulfilling neither the Sapporo nor the 2023 ACR/EULAR criteria). Both criteria had a 100% specificity in classifying the pAPS cases.
Conclusion: The 2023 ACR/EULAR classified 75%, while the revised Sapporo criteria classified 66% of AYA with pAPS diagnosed by expert opinion in this long-term follow-up cohort, suggesting that childhood-specific criteria may be warranted. In this small cohort, macrovascular thrombosis affected 66% of AYA diagnosed with pAPS, with 33% experiencing up to 4 major thrombotic events, suggesting a more severe phenotype. Future large cohort studies are needed to define the natural course and long-term complications of pAPS.
Disclosure
None declared

P310

Implementing treat-to-target in childhood lupus: early outcomes and lessons from a UK paediatric centre

E. Nolan[1,2], O. Lloyd[2], M. W. Beresford[1,2], C. Sarker[1], C. E. Pain[1,2], L. McCann[1,2], E. M. D. Smith[1,2,3]
[1]Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, [2]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, [3]School of Infection & Immunity, University of Glasgow, Glasgow, United Kingdom
Correspondence: E. Nolan
Pediatric Rheumatology, **23(2):** P310

Introduction: International experts recommend a Treat-to-Target (T2T) approach to optimise the management of childhood-onset systemic lupus erythematosus (cSLE), with the aim of reducing flares and long-term damage[1]. T2T is an approach in which treatment is escalated or adjusted until predefined goals, such as childhood lupus low disease activity (cLLDAS), cSLE clinical remission on steroids (cCR) and cSLE clinical remission off steroids (cCR-0), are reached[2,3].
Objectives: To implement a T2T approach at a tertiary UK hospital, and assess its feasibility and initial impact on clinical outcomes and treatment, including SLEDAI score, physician global assessment (PGA), and corticosteroid dosing.
Methods: A dedicated T2T clinic was established. Appointments were standardised to collect relevant clinical and laboratory data for target calculation. A preliminary treatment plan was made in clinic and finalised post-clinic, after target review. T2T fidelity was assessed using a devised T2T implementation score based on documentation of: target specified, target calculated, corticosteroid dose recorded, treatment plan aligned with target, and appropriate follow-up (4–6 weeks if target not met; 3 months if achieved).
Results: Between July-2023 and March-2025, 15 cSLE patients attended 74 T2T appointments (median 4 per person, range: 2-9). Eleven (73%) achieved a T2T target (cLLDAS, cCR or cCR-0) during this period. The cSLE patients not achieving or maintaining targets were either non-adherent to treatment or had <6 months' follow-up. Overall, median SLEDAI-2K scores decreased from 5 (IQR 3, 8) at baseline to 4 (IQR 2.5,7) at last visit. When comparing patients based on adherence, non-adherent patients had an increase in SLEDAI-2K score from 7 (IQR 5.5, 9.5) at baseline to 9 (IQR 7.5, 11.5) at last visit. Median PGA scores reduced from 1 (IQR 0.5, 1.5) to 0.75 (IQR 0.375,1), with PGA higher in non-adherent patients, 1.25 (IQR 0.875, 1.625) at baseline to 1 (IQR 0.875, 1.375) at last visit. All patients on corticosteroids at T2T initiation had undergone subsequent dose reductions (mean 83% reduction); 11/15 discontinued corticosteroids entirely by the last visit. Assessment of the T2T implementation score indicated that 89.5% of key T2T components were documented and followed, with delayed follow-up being the most common barrier, affecting 54% of visits.
Conclusion: These findings demonstrate that T2T implementation is feasible in a single tertiary centre with establishment of a bespoke T2T clinic. This has been associated with initial improvements in disease activity and corticosteroid reduction. Non-adherence remains a barrier to target attainment. Further work should expand T2T to diverse settings and explore perspectives of patients, families, and clinicians through qualitative research.
Disclosure
None declared

References

1. Smith EMD, et al. cSLE T2T International Task Force. Towards development of treat to target (T2T) in childhood-onset systemic lupus erythematosus: PReS-endorsed overarching principles and points-to-consider from an international task force. Ann Rheum Dis. 2023.
2. Smith EMD, et al. PReS-endorsed international childhood lupus T2T task force definition of childhood lupus low disease activity state (cLLDAS). Clin Immunol. 2023. 3. Smith EMD, et al. Defining remission in childhood-onset lupus: PReS-endorsed consensus definitions by an international task force. Clin Immunol. 2024.

P311

Risk of flare upon glucocorticoid tapering in children with systemic lupus erythematosus

H. Kisaoglu[1], N. Akay[2], T. D. Kuzuca[3], V. Cam[4], S. Demir[3], S. Sahin[2], S. Ozen[4], O. Kasapcopur[2], M. Kalyoncu[5]
[1]Pediatric Rheumatology, University of Health Sciences Kayseri Medical Faculty, Kayseri, [2]Pediatric Rheumatology, Istanbul University Istanbul-Cerrahpasa Faculty of Medicine, Istanbul, [3]Pediatric Rheumatology, Eskisehir Osmangazi University Faculty of Medicine, Eskisehir, [4]Pediatric Rheumatology, Hacettepe University Faculty of Medicine, Ankara, [5]Pediatric Rheumatology, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye
Correspondence: H. Kisaoglu
Pediatric Rheumatology, **23(2):** P311

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease with an unpredictable course. Glucocorticoids are the mainstay of treatment in SLE with its rapid onset of action and efficacy. But, undesirable effects with their long-term use diminish its use in moderate to high doses in management of SLE [1]. Most guidelines recommend tapering of glucocorticoids to 5-7,5 mg/day at 6th month of treatment [2] but it is not clear if tapering contributes to subsequent flares in children with SLE.
Objectives: We aimed to investigate whether glucocorticoid tapering increases the risk of subsequent flares in children with SLE.

Methods: Longitudinal data of children, diagnosed with SLE between 2012-2024, fulfilling the SLICC criteria [3], were reviewed. Visits were included if a prednisolone equivalent glucocorticoid dose was ≤15 mg/day. Clinical activity domains, serological features, treatments and tapering information was extracted from visit data. Subsequent flare was defined as the observation of flare either in the next 3 months or at the subsequent visit of data point.Visits were compared according to the observation of a subsequent flare and analysed using the generalized linear mixed model analysis to identify features that associated with flares.
Results: A total of 1374 visits of 95 children were included, spanning a median duration of 29 months (IQR: 14 - 56). While glucocorticoid tapering was observed in 341 (24.8) visits, 112 (8.2%) visits were followed by subsequent flares. The flare rate was similar in visits with tapering compared to those without glucocorticoid tapering (7.0% vs. 8,5%, p: 0.43). Higher than 5 mg/day prednisolone equivalent doses of glucocorticoids decreased the odds of subsequent flares (OR: 0.11; p: 0.001), but neither tapering nor tapering towards a lower than 5 mg/day prednisolone dose increased the odds for flare (p> 0.05).
Conclusion: A significant number of flares does not occur upon glucocorticoid tapering, and tapering of glucocorticoid treatment might not be the main driver behind flares. Our results needs to be validated with large-scale multinational studies, including children treated with newer therapies to uncover the associations behind flares and to improve the glucocorticoid tapering practices.
Disclosure
None declared

References

1. Bertsias G, Askanase A, Doria A, Saxena A, Vital EM. A path to Glucocorticoid Stewardship: a critical review of clinical recommendations for the treatment of systemic lupus erythematosus. *Rheumatology* 2024;63: 1837–49.
2. Groot N, Graeff N de, Avcin T, Bader-Meunier B, Brogan P, Dolezalova P, et al. European evidence-based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus: the SHARE initiative. *Ann Rheum Dis* 2017; 76: 1788–96.
3. Petri M, Orbai A-M, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012; 64: 2677–86.

P312

Comparison of clinical and laboratory differences across age groups in patients with juvenile-onset systemic lupus erythematosus: data of retrospective study

M. Kaleda, I. Nikishina, A. Shapovalenko, T. Pachkoria
Pediatrics, V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** P312

Introduction: Patients with juvenile onset consists about 10-20% of all cases of systemic lupus erythematosus (SLE). The manifestations of juvenile-onset SLE (jSLE) vary significantly between individuals in different age groups, which can complicate diagnosis and affect treatment and long-term prognosis.
Objectives: to compare age-specific clinical and/or laboratory patterns in children at onset of jSLE.
Methods: In retrospective study was included all patients with jSLE, who undergoing in-patient treatment in our center from 1992 to 2024 yy. Patients were grouped based on age at onset of disease: prepubertal (≤9 years), peripubertal (10-13 years) and adolescents (14-18 years). Diagnosis of SLE was reviewed based on 2012 SLICC criteria. We analyzed demographic, clinical and laboratory data, disease activity (used SLEDAI-2K score).
Results: A total of 291 patients (14.1% boys) with jSLE were included: 19.9% prepubertal onset; 44.7% peripubertal, 35.4% adolescents. The ratio boys:girls changed from 1:6 in the prepubertal group to 1:9 in adolescents. The median of disease activity by SLEDAI-2K increased with age: 10.5 [6.0; 16.75] in prepubertal group, 12.0 [9.0; 19.0] in peripubertal group, 13.5 [9.25; 19.75] in adolescents. Prepubertal patients more often had chronic cutaneous lupus (48.3%), than peri-pubertal (32.3%), p=0.049, also than adolescents (31.1%), p=0.041. The frequency of CNS involvement increased with age (10.3%, 19.2% and 23.3%) with statistically significant between pre-pubertal pts and adolescents, p=0.049. The numbers of patients with arthritis increased with age (67.2% in, 70.8%, 77.7%) without statistically difference between groups, p>0.05. The frequency of leukopenia also increased with age (46.6%, 64.6% and 61.2%) with statistically significant between prepubertal and peripubertal groups, p=0.024. Thrombocytopenia was less frequently detected in older children (39.7% in prepubertal, 27.7% in peripubertal groups and 23.3% in adolescents) with statistically significant between pre-pubertal patients and adolescents, p=0.031. Adolescents had more frequently anti-dsDNA positive (85.4%, 78.5%, 63.8%) with statistically significance between pre-pubertal and peripubertal patients (p = 0.047), prepubertal patients and adolescents (p=0.0027). Antiphospholipid antibodies were more often detected in adolescents (20.4%, 16.9% and 6.9%, respectively), statistical significance was between prepubertal patients and adolescents (p=0.024).
Conclusion: Adolescents had a greater activity of SLE, a higher frequency of CNS involvement, anti-DNA and antiphospholipid antibodies, younger children more often had chronic cutaneous lupus, and a higher frequency of thrombocytopenia. These data confirm the hypothesis that the pathomechanisms of jSLE formation may vary depending on the age.
Disclosure
None declared

P313

Clinical presentation of children with lupus nephritis from a low and middle income country (LMIC): an initial report from Indian PSLE nephritis registry

J. N. Bathia[1], S. Poddar[2], D. Deblina[2], S. Pradhan[3], S. Perungo[4], M. Janarthanan[5], K. Vala[6], P. Pais[7], S. Uthup[8], J. Singhal[9], S. Guha[10], S. Raut[11], S. Balan[12], S. Akhtar[2], P. Pal[1], R. Sinha[2]
[1]Pediatric Rheumatology, [2]Division of Pediatric Nephrology, Institute of Child Health, Kolkata, [3]Division of Pediatric Nephrology, Sardar Vallabhbhai Patel Post Graduate Institute of Pediatrics,, Cuttack, [4]Pediatric Nephrology, [5]Department of Clinical Immunology & Rheumatology, Sri Ramachandra Institute of Higher Education and Research, Chennai, [6]Department of Pediatric Nephrology,,Smt. GR Doshi and Smt. KM Mehta Institute of Kidney Diseases and Research Center, Gujarat University of Transplantation Sciences, Ahmedabad, [7]Department of Pediatric Nephrology, St John's Medical College, St John's National Academy of Health Sciences, Bengaluru,, [8]Department of Pediatric Nephrology, Government Medical College, Thiruvananthapuram, [9]Pediatric Nephrology Service, Renal Unit, King Edward Memorial Hospital, Pune, [10]Department of Pediatrics,, Vivekananda Institute of Medical Sciences, Kolkata, [11]Department of Nephrology, North Bengal Medical College and Hospital, Siliguri, [12]Department of Rheumatology and Clinical Immunology, Amrita Institute of Medical Sciences, Cochin, India
Correspondence: J. N. Bathia
Pediatric Rheumatology, **23(2):** P313

Introduction: Systemic Lupus Erythematosus (SLE) is a systemic multisystem autoimmune disease with usual age predominance between 15-44 years.Childhood onset SLE occurs in up to 20% of cases with a prevalence of 3.3-8.8 per 100000 pediatric population.Lupus nephritis (LN), is a major determinant of morbidity and mortality in patients with SLE. Incidence of LN is more common amongst children (50-82%) as compared to adults (20-40%) and with greater disease severity and earlier accrual of disease damage than in adults.Although the 5-year survival rate of pediatric LN (pLN) has improved markedly, the mortality rate seen in pLN still higher. There is of very limited data from Low -Middle Income Countries (LMICs) on renal outcomes in these children.
Objectives: It is a collaborative effort of pediatric nephrologists and rheumatologists from centers across India with the aim to study the epidemiology, clinic-pathologic characteristics, treatment patterns, and kidney outcomes of Indian children with LN, and to assess the factors affecting kidney outcomes. The current data aims to describes the initial presentation of children with LN at the time of enrollment in the registry.
Methods: The Indian Pediatric Lupus Nephritis registry was initiated in 2020 across multiple centers in India. Children (≤ 18 years) diagnosed

with Lupus (as per 2012 SLICC criteria), presenting with nephritis, and confirmed by kidney biopsy are beingprospectively enrolled. Clinical data, laboratory investigations, kidney biopsy results, and treatment responses are being documented prospectively. The current report documents their initial presentation.
Results: 154 children (75% female) biopsy-proven LN children were enrolled by July 2024 with the median age being 12 years (IQR: 10-14 years). 9 children (6%) were <7 years. Nearly two-thirds had LN at SLE diagnosis and the rest developed within maximum of 5 years of initial presentation. Common manifestations at presentation included edema (75%), hypertension (54%), and proteinuria (98%), of which 68% presented with nephrotic-range proteinuria. Acute Kidney Injury (AKI) was observed in 43%, with 20% in stage 3. 94% of our cohort had low complements (C3, C4 or both) and 96% was ANA positive. Class IV LN was most common (45%). Muco-cutaneous manifestation was the most common extra-renal manifestation (59%) followed by hematological involvement (28%) then neuropsychiatric manifestation (10%). 3% had significant infection at the time of diagnosis of LN.
Conclusion: This initial analysis from the prospective multicentre registry from India, we have demonstrated that pLN often manifests with significant renal involvement at or near the time of SLE diagnosis, It highlighs the need for routine kidney screening in SLE patients. 10% of patients presented with subclinical nephritis hence lies the importance of thorough renal evaluation. Children enrolled in the registry are being followed up to assess the renal responses, and associated treatment toxicities, which will help optimize the management of pLN in LMICs.
Disclosure
None declared

P314

Pediatric neuropsychiatric systemic lupus erythematosus: case series from a tertiary care center in eastern India

J. N. Bathia[1], R. Singh[1], A. Nandi[1], C. R. P. Goud[1], P. Pal[1], S. Mukherjee[2], J. Chaudhuri[2]
[1]Pediatric Rheumatology, [2]Pediatric Neurology, Institute of Child Health, Kolkata, India
Correspondence: J. N. Bathia
Pediatric Rheumatology, **23(2):** P314

Introduction: Neuropsychiatric systemic lupus erythematosus (NPSLE) is a serious manifestation of childhood onset SLE.
Objectives: To evaluate the demographic profile, clinical features, serological and, radiological findings, treatment and outcome of patients diagnosed as NPSLE.
Methods: It is a retrospective observational study of data of patients diagnosed as having NPSLE, admitted between January 2015 to December 2024 at Institute of Child Health, Kolkata. NP-SLE was defined as per the ACR 1999 classification. SLE was classified as SLICC 2012 criterea. CNS manifestations due to secondary causes were ruled out.
Results: 30 patients had NPSLE, 27 were females and 3 males. The median age at onset of disease was 10 years (IQR 2.75). 22 patients had NP manifestations at diagnosis of SLE diagnosis. Neuropsychiatric manifestatons were variable. The most common manifestation was headache (16) followed by seizures (15), cognitive dysfunction (12) anxiety (10), acute confusional state (10), mood disorders (9), cerebro vascular disease (3), limb weakness (2), movement disorder (5), myelopathy (2), vertigo (1) and bulbar palsy with ptosis (1), central retinal vein thrombosis (1). Other systems involved were renal (10), mucocutaneous (10), musculoskeletol (8), hematological (6), gastrointestinal (5), cardiovascular (4), respiratory tract (1). Anti-nuclear antibody (ANA) was positive in all patients, anti-double stranded DNA was positive in 27 and 5 patients were positive for antiphospholipid antibodies.Other systems involved were renal (10) mucocutaneous (10), musculoskeletol (8), hematological (6), gastrointestinal (5), cardiovascular (4), respiratory tract (1). MRI brain was done in 28. Diffuse brain shrinkage was the most common finding seen (7), white matter signal abnormalities (4), non-hemorrhagic infarcts (2), meningeal enhancement (2), cerebral sinus venous thrombosis (1), cerebral sinus venous thrombosis with hemorrhagic infarct (1), demylination (1), normal (5). Induction was done with pulse methyl predinsolone (pMP) in 4, pMP + 6 doses cyclophosphamide (Cyc) in 7, pMP + 1 to 4 doses of Cyc + 2 doses of rituximab in 10, pMP followed by mycophenolate mofetil (MMF) induction in 8 and pMP + 2 rituximab in 4 events, manintainence was with MMF or azathiprine, hydroxychloroquine sulphate was given to all. Aspirin given in those with APLA positive. LMWH given for thrombosis. All responded to therapy median duration (15 days). One patient with prolonged infection had 2 subsequent flares as immunotherapy could be started, 3 more had one subsequent NP flare each. Varying other system flares were noted subsequently in the form of mucotaneous manifestations, musculoskeletol, however 8 had subsequent renal involvement. Infection was associated at onset in 2 and subsequently occured in 3 with one having XDR tuberculosis. There was no mortality.
Conclusion: NPSLE is a serious manifestation of childhood onset SLE. Over the years number of doses of Cyclophosphamide usage has reduced with only 1 to 3 doses of cyclophasphamide during induction with two doses of rituximab with good response and prolonged remission. Prompt diagnosis of NPSLE and aggressive immunomodulator therapy results in good response.
Disclosure
None declared

P315

Transcobalamin-2 levels in juvenile systemic lupus erythematosus: a potential biomarker of disease activity and inflammation

K. Uçak[1], Y. Gunay[1], S. Dümür[2], M. Küçür[3], E. K. Köfte[1], E. Aslan[1], A. Günalp[1], F. Haşlak[1], M. Yıldız[1], A. Adroviç[1], K. Barut[1], S. Şahin[1], Ö. Kasapçopur[1]
[1]Department of Pediatric Rheumatology,, Istanbul University-Cerrahpasa, Cerrahpaşa Faculty of Medicine,, [2]Department of Medical Biochemistry, Istanbul Atlas University, [3]Tıbbı Biyokimya Anabilimdalı, Istanbul University-Cerrahpasa, Cerrahpaşa Faculty of Medicine,, İstanbul, Türkiye
Correspondence: K. Uçak
Pediatric Rheumatology, **23(2):** P315

Introduction: Juvenile-onset systemic lupus erythematosus (jSLE) is a chronic autoimmune disease with more severe clinical manifestations than adult-onset SLE. It frequently involves vital organs such as the kidneys and central nervous system, requiring early diagnosis and close disease monitoring. Transcobalamin-2 (TC-2), a vitamin B12 transport protein, has been linked to disease activity in autoimmune disorders. However, its relevance in jSLE remains largely unexplored.
Objectives: This study investigated whether serum Transcobalamin-2 (TC-2) levels, a vitamin B12 binding protein known to fluctuate in autoimmune conditions, are associated with inflammation and disease activity in jSLE.
Methods: This cross-sectional study included 40 patients with jSLE, 20 patients with familial Mediterranean fever (FMF), and 20 healthy controls. Nutritional assessments were conducted to exclude confounding factors related to B12 or folate intake. Serum TC-2, methylmalonic acid (MMA), and homocysteine levels were measured by ELISA. Clinical data were recorded, and jSLE disease activity was assessed using ESR, complement levels, anti-dsDNA titers, and the SLEDAI-2K score. Statistical analysis was performed using SPSS.
Results: TC-2 levels were lower in jSLE (0.65 ± 0.23 ng/ml) and FMF patients (0.66 ± 0.25 ng/ml) compared to controls (0.89 ± 0.47 ng/ml), though the difference was not statistically significant ($p > 0.05$). No significant correlation was found between TC-2 levels and SLEDAI-2K or other disease activity markers in the jSLE group. Median and range values of TC-2, homocysteine, and MMA were also analyzed across groups but did not indicate a clear association with disease activity.
Conclusion: Contrary to some previous reports, our findings suggest that TC-2 levels are not significantly associated with disease activity in jSLE. Although lower TC-2 levels were observed in patients compared to controls, they did not reach statistical significance. These results contribute to the growing body of literature investigating the role of vitamin B12 metabolism in autoimmune diseases, suggesting that TC-2 may have limited utility as a standalone inflammatory biomarker in jSLE.
Trial registration identifying number: T.C. CERRAHPAŞA FACULTY OF MEDICINE DEAN'S OFFICEEthics committee approval numbered E-83045809-604.01.02-45715 was received by the Clinical Research Ethics Committee.

Disclosure
None declared

References

1. Sahin, S., Adrovic, A., Barut, K., Canpolat, N., Ozluk, Y., Kilicaslan, I., Caliskan, S., Sever, L., & Kasapcopur, O. (2018). Juvenile systemic lupus erythematosus in Turkey: demographic, clinical and laboratory features with disease activity and outcome. Lupus, 27(3), 514–519
2. Ermens, A. A., Vlasveld, L. T., & Lindemans, J. (2003). Significance of elevated cobalamin (vitamin B12) levels in blood. Clinical biochemistry, 36(8), 585–590.
3. Fràter-Schröder M, Leumann E, Grob PJ, Hitzig WH. Erhöhung des ungesättigten Trans-cobalamins II bei Autoimmunerkrankungen: Verlaufsstudien bei Lupus erythematodes und Dermatomyositis [Elevation of unsaturated transcobalamin II in autoimmune diseases: study of the process in lupus erythematosis and dermatomyositis]. *Schweiz Med Wochenschr*. 1980;110(40):1441–1443.
4. Dułak NA, Rytlewska M, Jaskólska M, Chmielewski M. A new perspective on vitamin B12 deficiency in rheumatology: a case-based review. *Rheumatol Int*. 2024;44(4):737–741. https://doi.org/10.1007/s00296-024-05539-y
5. Molad Y, Rachmilewitz B, Sidi Y, Pinkhas J, Weinberger A. Serum cobalamin and transcobalamin levels in systemic lupus erythematosus. *Am J Med*. 1990;88(2):141–144. https://doi.org/10.1016/0002-9343(90)90463-n

P316

Satisfactory clinical response to anifrolumab in a teenager with refractory cutaneous systemic lupus erythematosus

K. Chiotopoulou, K. Liontou, K. Kourtesi, A. Chira, L. Fotis
3rd Department of Pediatrics, National and Kapodistrian University of Athens, Athens, Greece
Correspondence: L. Fotis
Pediatric Rheumatology, **23(2):** P316

Introduction: Cutaneous involvement in juvenile systemic lupus erythematosus (jSLE) is common and can be severely disfiguring. While conventional treatments like corticosteroids, hydroxychloroquine, and immunosuppressants remain first-line, a subset of patients experience refractory disease, particularly in cutaneous domains. Anifrolumab, a monoclonal antibody targeting type I interferon receptor, has shown promise in adult SLE, but its application in pediatrics is still under investigation.
Objectives: To present a case of severe, refractory cutaneous jSLE that achieved remission after the introduction of Anifrolumab, and to contribute real-world evidence supporting its pediatric use.
Methods: A 14-year-old girl with jSLE presented with persistent malar rash, photosensitivity, arthralgia, myalgia, and a positive ANA. She was treated with hydroxychloroquine, corticosteroids, methotrexate, mycophenolate mofetil, belimumab, intravenous immunoglobulin, azathioprine, and rituximab, achieving only partial systemic improvement. Despite intensive immunosuppressive therapy, she continued to experience a painful, disfiguring facial rash that necessitated frequent corticosteroid use, to which she was poorly responsive. Four years after diagnosis, anifrolumab (300 mg IV monthly) was initiated in combination with methotrexate.
Results: After 12 doses of Anifrolumab, complete resolution of cutaneous manifestations was observed, with no new flares. The patient reported subjective improvement in well-being. However, a new-onset headache emerged. Although a clear causal link could not be established, the symptom raised concern. Ultimately, the headache was effectively managed with low-dose tricyclic antidepressants, allowing treatment continuation.
Conclusion: This case supports the clinical utility of Anifrolumab in adolescents with refractory cutaneous lupus, where conventional and even biologic treatments fail. Apart from a possibly related headache, which was medically controlled, the drug was well-tolerated. Further studies are needed to clarify safety and efficacy in pediatric populations. Consent to published had been obtained.
Disclosure
None declared

References

1. Mina R, Brunner HI. Pediatric SLE: state of the art. *Autoimmun Rev.*
2. Morand EF et al. Trial of Anifrolumab in Active SLE. *N Engl J Med.*2020;382:211–21.
3. Armbrust W, et al. Anifrolumab in Pediatric Refractory Cutaneous Lupus. *Pediatr Rheumatol.*
4. Li S, et al. Use of Saphnelo in adolescents with cutaneous SLE. *JAMA Netw Open.*
5. AstraZeneca Clinical Trial D3461C00030. Anifrolumab in Pediatric SLE. Accessed 2024.

P317

Neuropsychiatric disease in juvenile systemic lupus erythematosus

M. I. N. Marques, I. Madureira, M. Conde, C. Henriques, M. P. Ramos
Pediatric Rheumatology Unit, Hospital Dona Estefânia - ULS São José, Lisbon, Portugal
Correspondence: M. I. N. Marques
Pediatric Rheumatology, **23(2):** P317

Introduction: Neuropsychiatric disease in Juvenile Systemic Lupus Erythematosus (NP-jSLE) has a reported prevalence of 14-95% in all jSLE cases and typically occurs early in jSLE disease. NP involvement can be difficult to diagnose, as clinical presentation varies greatly with both central and peripheral nervous systems manifestations, and lacks a specific diagnostic test for its accurate diagnosis.
Objectives: Characterization of demographics, clinical and complementary findings, treatment, and outcome of children with NP-jSLE, followed in a Pediatric Rheumatology Unit.
Methods: Single center retrospective analysis from 2008 to April 2025 of children diagnosed with NP-jSLE: case definition was a score of ≥7 in the Italian Algorithm of attribution of NP events**.**
Results: Of the 61 patients with jSLE, 12 (20%) had NP-jSLE. 10 (83%) were female, median age of jSLE diagnosis of 13 yo (5-16yo). Nine (75%) had NP involvement at jSLE diagnosis and in three this occurred after the first year of diagnosis (1-5years).
In total, there were 21 NP-jSLE manifestations: 18 involving the central nervous system (CNS) and 3 the peripheral nervous system (cranial neuropathy). Eight focal CNS neurological syndromes (NS) (cerebrovascular disease [n=3/8: 2 ischemic lesions, 1 focal vasculitis]; movement disorder [n=4/8: 3 chorea, 1 facial tics]; myelopathy [n=1/8]), 7/8 with positive antiphospholipid antibodies. Four diffuse NS (1 demyelinating disorder, 1 cognitive impairment, 1 acute confusional state, 1 aseptic meningitis). Six diffuse psychiatric syndromes (2 psychosis, 3 anxiety disorder, 1 depression).
At NP-jSLE diagnosis, all had positive ANA (≥1:80), 9 had positive DsDNA antibody. Two had anti-ribosomal P antibodies and presented with diffuse psychiatric syndrome. All patients underwent MRI scan, with abnormal findings in 8 cases (2 white matter hyperintensity, 2 ischemic lesions, 1 focal vasculitis, 1 demyelinating lesion, 1 disseminated myelitis). Additionally, 9 patients underwent lumbar puncture, 1 showing pleocytosis, and 2 increased proteinorrachia, and none with oligoclonal bands.
All patients received targeted treatment: 11 high dose corticosteroids, 6 cyclophosphamide, 4 rituximab, 5 iv immunoglobulin. All patients were treated with hydroxychloroquine and those with psychiatric manifestations also had symptomatic treatment.
During follow up, the patient with disseminated myelitis died of disease progression, 1 had recurrence of an ischemic cerebrovascular event, 1 was lost to follow-up, and the others showed clinical improvement with no NP disease recurrence.
Conclusion: Our study showed a similar prevalence of NP-jSLE, with a female prevalence. Focal CNS syndromes were more frequent, followed by diffuse psychiatric syndromes, and most were diagnosed at the onset of the disease. NP is a challenge to diagnose since valid and reliable biomarkers are lacking, and there are many confounding factors for neuropsychiatric manifestations.
Disclosure
None declared

P318

Genetic insights into early-onset systemic lupus erythematosus in India: findings from a cohort of 365 pediatric patients

M. Sharma, R. Pilania, D. Suri, V. Pandiarajan, S. Sharma, M. Dhaliwal, S. Singh, A. Rawat

Advanced Pediatric Centre, Post Graduate Institute Of Medical Education And Research, Chandigarh, India
Correspondence: M. Sharma
Pediatric Rheumatology, **23(2):** P318

Introduction: Early-onset systemic lupus erythematosus (EOSLE) is a rare autoimmune disorder with significant morbidity in children. Monogenic lupus, caused by single-gene mutations, often presents with early-onset and severe phenotypes, requiring specialized diagnostic approaches. This study explores the genetic basis of EOSLE in the largest cohort of patients with pediatric SLE (pSLE) from India.
Objectives: Unraveling the Genetic Landscape of Early-Onset Systemic Lupus Erythematosus in India: Insights from a Large Cohort Study of 365 Patients
Methods: This prospective observational study investigated monogenic causes in 97 of 365 pSLE patients. Inclusion criteria for study comprised patients with EOSLE (age ≤8 years) and/or those with a clinical suspicion of monogenic lupus. Monogenic cause was suspected in 97 patients. Genetic screening was performed using targeted next-generation sequencing on the Ion S5 system in 55 of 97 patients [complement defect gene panel in 28 and type 1 interferonopathy gene Interferon (IFN) panel in 27]. Remaining 42 patients underwent whole exome sequencing (WES).
Results: Among 97 patients who underwent genetic sequencing, 22 (22.68%; 11 boys and 11 girls) were found to carry pathogenic or likely pathogenic variants. Median age of symptom onset in patients with monogenic lupus was 2 years (range: 2 months - 9 years). Consanguinity was reported in 7/22 (31.8%) patients. Variants were detected in C1QA (n=7), C1QC (n=2), C1R (n=1), C1QB (n=1), C3 (n=2), ACP5 (n=2), TMEM173 (n=1), DNASE2 (n=1), ADAR (n=1), TREX1 (n=1), DNASE1L3 (n=1), PEPD (n=1), SLC7A7 (1) genes. Functional complement deficiencies and elevated Type 1 interferon signatures were consistent with genetic findings.
Conclusion: This study highlights the genetic heterogeneity of EOSLE in India, with monogenic causes identified in 22.68% of cases, with C1q deficiency caused by genetic defects in C1QA, C1QC, and C1QB being the most common defect. Overall, C1QA was the most common single gene defect detected in 7/97 (7.2%) patients screened. Our findings support the need to evaluate underlying genetic causes in childhood lupus.
Disclosure
None declared

References
1. Belot A, Rice GI, Omarjee SO, Rouchon Q, Smith EMD, Moreews M, et al. Contribution of rare and predicted pathogenic gene variants to childhood-onset lupus: a large, genetic panel analysis of British and French cohorts. Lancet Rheumatol. 2020 Feb 1;2(2):e99–109.
2. Batu ED, Koşukcu C, Taşkıran E, Sahin S, Akman S, Sözeri B, et al. Whole Exome Sequencing in Early-onset Systemic Lupus Erythematosus. J Rheumatol. 2018 Dec;45(12):1671–9
3. Tirosh I, Spielman S, Barel O, Ram R, Stauber T, Paret G, et al. Whole exome sequencing in childhood-onset lupus frequently detects single gene etiologies. Pediatr Rheumatol Online J. 2019 Jul 30;17(1):52.

P320

Juvenile sle and bdmard therapy: clinical profiles, treatment course, and outcomes

M. R. Amaral[1], A. Preda[2], I. Cardoso[2], F. Aguiar[3], M. Rodrigues[3], I. Brito[3]
[1]Pediatrics, ULS Entre Douro e Vouga, [2]Pediatrics, ULS Gaia e Espinho, [3]Young adult and pediatric Rheumatology Unit, ULS São João, Porto, Portugal
Correspondence: M. R. Amaral
Pediatric Rheumatology, **23(2):** P320

Introduction: Juvenile systemic lupus erythematosus (jSLE) is a rare, chronic autoimmune disease with greater severity and cumulative damage than adult-onset SLE. [1] Management involves long-term immunosuppression, but some patients show refractory disease or drug toxicity. In such cases, bDMARD therapies are used as adjunctive options. While their use in adults is supported, evidence in pediatric real-world settings is limited. [2]
Objectives: To describe jSLE patients receiving biologic therapy at a tertiary center in Portugal, focusing on demographic, clinical, and laboratory features, treatment course, disease activity, and complications.
Methods: This retrospective descriptive study included patients diagnosed with jSLE per ACR/EULAR criteria, followed between January 2013 and April 2025, who received at least one bDMARD. Medical records were reviewed for demographics, clinical and immunological features, reasons for bDMARD initiation, treatment course, disease activity and adverse events. Descriptive statistics were used.
Results: A total of 38 patients with jSLE were followed, of whom 13 received bDMARD therapy. Among these, 11 were female. Median age at diagnosis was 14.0 years (IQR: 12.0–16.0), and 19.0 years (IQR: 17.0–23.0) at biologic initiation.
The most frequent features included: positive anti-dsDNA antibodies (100%), constitutional symptoms (92%), polyarthritis (85%), mucocutaneous involvement (77%), and acute cutaneous lupus (77%). Lupus nephritis occurred in 69% and hematologic abnormalities in 69%.
The main indication for bDMARD therapy was persistent clinical and immunological disease activity despite conventional treatment. Rituximab was the most frequently used agent (n=7), followed by belimumab (n=5). One patient received both belimumab and anifrolumab for better control of persistent cutaneous manifestations. While patients receiving rituximab tended to be older and had more frequent renal involvement, those on belimumab more often presented with hematologic and cutaneous manifestations. No statistically significant differences were observed between the groups.
At around 6 months following the initiation of bDMARD therapy, a reduction in disease activity as measured by the SLEDAI score was observed in most patients, with a median ΔSLEDAI of −4.
No serious adverse events attributable to bDMARD therapy were reported. One patient died during follow-up due to a cardio-pulmonary complication unrelated to bDMARD treatment.
Conclusion: In this real-world cohort, bDMARD therapy was mainly used in refractory or severe jSLE, with clinical improvement in most patients and no serious adverse events. Despite differing clinical patterns, outcomes were similar between agents. bDMARD therapy appear to be a safe and effective option in selected pediatric cases.
Disclosure
None declared

References
1. Watson L, Leone V,et al. Disease activity, severity, and damage in the UK Juvenile-Onset Systemic Lupus Erythematosus Cohort. *Arthritis Rheum*. 2012;64(7):2356–65. https://doi.org/10.1002/art.34410.
2. Smith EMD, Lythgoe H,et al. Real world treatment of juvenile-onset systemic lupus erythematosus. *Semin Arthritis Rheum*. 2022;52:151,949. https://doi.org/10.1016/j.semarthrit.2021.151949.

P321

Evaluating the standardized steroid regimen (SSR) for childhood-onset systemic lupus erythematosus: retrospective insights from real-world data

M. Kasap Cuceoglu[1,2], J. L. Huggins[1], T. Ting[1], J. Smith-Rodriguez[1], A. Merritt[1], H. I. Brunner[1]
[1]Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, United States, [2]Pediatric Rheumatology, Konya City Hospital, Konya, Türkiye
Correspondence: M. Kasap Cuceoglu
Pediatric Rheumatology, **23(2):** P321

Introduction: Corticosteroids remain a cornerstone of therapy in childhood-onset systemic lupus erythematosus (cSLE) due to their potent anti-inflammatory and immunosuppressive effects. However, long-term corticosteroid (CS) use is associated with significant side effects. Therefore, achieving a balance between efficacy and safety is crucial. The SSR is a standardized CS dosing protocol developed by international consensus[1] that considers patient weight and includes tapering strategies which are essential to minimize CS toxicity while effectively controlling cSLE activity.
Objectives: To retrospectively assess the agreement between oral CS dosing (prednisone equivalent) prescribed by clinicians and SSR-recommended doses, and identify predictors of dosing differences

Methods: For all cSLE patients treated at outpatient clinic in Division of Pediatric Rheumatology, historic CS dosing as per the electronic medical record were extracted at Cincinnati Children's Hospital and Medical Center from 6 providers. Demographic and clinical variables, including race, age, gender, disease duration, organ system involvement, CS doses, and prescribing providers, were obtained. Patients with renal involvement started visits after renal biopsy, and those with extra-renal involvement started with steroid initiation, with at least four consecutive visits between 2014 and 2024 (1-6 month intervals, some with up to 7 visits per patient).
Historic CS dosing was compared to CS dosing as per SSR Calculator[2]. Absolute and relative (%) of dosing differences of daily prednisone (DDDP = historic – SSR) were compared. In univariate analysis predictors of DDDP were explored and included (yes/no): lupus nephritis (LN), prednisone >10mg; intravenous (IV) CS treatment in the prescription as pulse methylprednisolone. Other types of corticosteroids (prednisolone, methylprednisolone, etc.) were converted to equivalent prednisone and used in the calculations.
Results: Among 263 visits of 52/24 cSLE patients (total: 76 patients; 84.2% female) without/with biopsy-proven LN were included, with a median age at diagnosis of 14.5 (5.95-21.05) years. CS treatment commenced within 9.1 days post diagnosis (range: 0-178). The range (min-max) of oral CS (prednisone) dose was 1-60 mg/day. IV CS (methylprednisolone) was prescribed to 42 patients in 78 visits. As SSR, IV CS was recommended in 42 different patients in 68 visits. Of the 263 visits, 39.16% (n=103) occurred in patients with LN and 60.84% (n=160) were for management of extra-renal disease. Irrespective of LN presence, there was a strong association of and SSR dosing (LN: r=0.86, p<0.0001; no LN: r= 0.76, p<0.0001; cSLE overall: r=0.80, p< 0.0001). In 62 visits (23.6%), historic and SSR dosing was identical. In 100/101 visits historic doses were higher/lower than the SRR dosage. Inferential tests showed significant differences in DDDP within both groups (LN:t=2.93, p=0.0041; extra-renal: t=2.23, p=0.0274) (Figure 1, Panel B). In 47/263 (17.8%) visits demonstrated absolute DDDP of >10mg (relative:46-147 % of SSR dosing). Of 38/47 (80.9%) visits DDDP was 10-20 mg (relative: 75-147% of SSR dosing) in 9/47 (19.1%) visits DDDP was 20-40 mg (relative:46-75 % of SSR dosing). Larger DDDP were often observed in visits of patients with extrarenal involvement (31/49, 65.9%) and during the first 4 weeks after CS initiation (24/49,51%).
Conclusion: This study demonstrates a strong overall agreement between historic CS dosing and the SSR protocol in cSLE management, though prednisone dosing differences of > 10 mg occurred, mostly in the setting of absent LN and around diagnosis. If confirmed, this could suggest the need for an update of the SSR to better standardize CS dosing of cSLE patients without LN.
Disclosure
None declared

Reference

1. Chalhoub NE, Wenderfer SE, Levy DM, et al. International Consensus for the Dosing of Corticosteroids in Childhood-Onset Systemic Lupus Erythematosus with Proliferative Lupus Nephritis. Arthritis Rheumatol 2022;74(2):263-73. doi: 10.1002/art.41930. https://pocs.shinyapps.io/SSR_Version2

P322

Clinical course of systemic lupus erythematosus in patients resident in frontline areas of Ukraine

N. S. Shevchenko[1,2], T. O. Holovko[1,2], L. F. Bogmat[2], I. M. Bessonova[2]
[1]Department of Pediatrics, V.N.Karazin Kharkiv National University, [2]Department of Rheumatology and comorbidities, SI "Institution for Children and Adolescents Health Care of NAMN of Ukraine", Kharkiv, Ukraine
Correspondence: N. S. Shevchenko
Pediatric Rheumatology, **23(2):** P322

Introduction: The densely populated Kharkiv region of Ukraine has been at the center of a military incident since the beginning of 2022, which led to an unprecedented process of migration and changes in the living conditions of millions of residents, including sick children. Wartime in the country is characterized by changes in the work of outpatient clinics, restrictions on access to inpatient care, disruption of monitoring of chronic diseases, and problems with nutrition. Most patients with serious diseases left their permanent place of residence, moving to safer cities in Ukraine or abroad. At the same time, children suffering from rheumatic diseases, including systemic lupus erythematosus (SLE), remained in the places.
Objectives: To investigate the course of SLE in children living in eastern Ukraine (Kharkiv region) during wartime.
Methods: The medical histories of 10 patients with SLE who continued to live in the Kharkiv region (front-line territory of eastern Ukraine) were analyzed and a comparative analysis was conducted with the status until 2022.
Results: The vast majority were girls (8 people), the average age was 14.9 ± 0.7 years, the duration of the disease at the beginning of 2025 was 48.9 ± 4.8 months. All children fell ill before the war, the age of patients with SLE was 13.92 ± 0.39 years. During 2022 - 2025, 5 out of 10 patients had disease activation, the causes of which were staying in cold rooms (2), changes in treatment (1), lack of medication (1), acute viral infection (1). The average values of SELENA-SLEDAI in the group significantly increased (5.9 ± 0.9 (from 2.0 to 10.0) versus 3.9 ± 0.8 (from 2.0 to 8.0), p<0.05). The average degree of SLE activity was observed in 4 people, high - in one. The exacerbation of the process was characterized by the presence of such severe manifestations as hemorrhagic syndrome in the form of subcutaneous hematomas, impaired consciousness (delirium), the development of pleurisy with the presence of pleural effusion, which were noted in children for the first time. Facial erythema of the "butterfly" type was somewhat more common (p < 0.05). Laboratory indicators of SLE revealed persistent leukopenia (2 out of 10), significantly higher C-reactive protein ((3.47 ± 1.86) mg among patients before 2022 and (15.03 ± 9.08) mg – after 2022, p < 0.05), lower C3 complement values (0.99 vs. 0.82 g/l; p < 0.05), higher total antinuclear antibodies (1.48 vs. 4.52 units, p < 0.001) and antibodies to double-stranded DNA (6.99 vs. 20.01 units, p < 0.001). Rheumatoid factor (RF) positivity remained in one patient.
Conclusion: The analysis showed that despite the long course and the availability of therapy, in children living in dangerous conditions, the frequency of exacerbations of SLE in the fifth year of the course significantly exceeds the general indicators of the pre-war period. Exacerbations were characterized by the manifestation of severe symptoms and a significant increase in immunological indicators.
Disclosure
None declared

P323

Evaluation of the classification performance of the acr 1997, slicc 2012, EULAR/ACR 2019 criteria in a monogenic lupus cohort

N. Akay, S. Sahin, U. Gul, E. Aslan, E. Kilic Konte, E. Aslan, A. Gunalp, M. Yildiz, A. Adrovic, K. Barut, O. Kasapcopur
Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa, Faculty of Medicine, Istanbul, Türkiye
Correspondence: N. Akay
Pediatric Rheumatology, **23(2):** P323

Introduction: Monogenic lupus is a rare and severe form of systemic lupus erythematosus (SLE) characterized by early onset, familial transmission, and clustering, and is defined by mutations in more than 50 single genes responsible for cellular immune mechanisms.
Objectives: Due to its clinical and immunological differences from multifactorial SLE, we aimed to compare the classification performance of existing classification criteria in a monogenic lupus patient cohort.
Methods: Demographic, clinical, and laboratory data of 27 patients with genetically confirmed monogenic lupus who are currently followed up at the Cerrahpaşa Pediatric Rheumatology Clinic were retrospectively reviewed, and clinical and laboratory characteristics were evaluated for compliance with the ACR 1997, SLICC 2012, and EULAR/ACR 2019 SLE classification criteria.
Results: Of the 27 patients diagnosed, 19 (70%) met the ACR 1997 criteria, 19 (70%) met the SLICC 2012 criteria, and 17 (63%) met the EULAR/ACR 2019 criteria. Among the patients who failed to meet the EULAR/ACR 2019 classification criteria due to negative antinuclear antibody (ANA) results, 3 (30%) satisfied the SLICC 2012 classification

criteria, and 4 (40%) met the ACR 1997 classification criteria. Of the 27 patients, 15 (56%) met all three classification criteria, while 6 (22%) did not meet any classification criteria. One patient didn't meet the SLICC 2012 and EULAR/ACR 2019 criteria due to insufficient immunological parameters, but met the ACR 1997 criteria with ≥ 4 clinical findings (mucocutaneous, arthritis, hematological, and neurological). One patient did not meet ACR 1997 and SLICC 2012 criteria because of at least four missing clinical or immunological parameters, but met EULAR/ACR 2019 criteria with an ANA titer ≥ 1/80 and one clinical and one immunological parameter.Three patients did not meet the EULAR/ACR 2019 criteria due to ANA negativity; however, they met the ACR 1997 and SLICC 2012 criteria.

Conclusion: Monogenic lupus is a clinical condition resulting from single-gene variations of classical lupus, presenting with early onset and distinct phenotypes. Although classic SLE findings are not always present, when evaluated in terms of compliance with the ACR 1997, SLICC 2012, and EULAR/ACR 2019 SLE classification criteria currently in use, it has been demonstrated that none of these three criteria is superior to the others. Due to the limited number of studies on this topic in the literature and the small number of patients, there is a need for more multicenter studies on this subject.

Disclosure

None declared

References

1. Al-Mayouf SM, Akbar L, Abdwani R, et al. Performance of the EULAR/ACR 2019 classification criteria for systemic lupus erythematosus in monogenic lupus. *Clin Rheumatol*. 2022;41(9):2721–2727. doi:https://doi.org/10.1007/s10067-022-06209-9
2. Babgi E, Al Marri M, Al-Mayouf SM, et al. Comparison of systemic lupus international collaborating clinics 2012 classification criteria and European league against rheumatism/American college of rheumatology 2019 classification criteria for early detection of childhood onset systemic lupus erythematosus (multi-center study). *Lupus*. 2024;33(6):629–637. doi: https://doi.org/10.1177/09612033241240830

P324

The first case of obinutuzumab use to treat a child with life threatening JSLE in the UK

O. Saad, N. Rafiq
Evelina London Children Hospital, London, United Kingdom
Correspondence: O. Saad
Pediatric Rheumatology, **23(2):** P324

Introduction: B-cell targeted therapies such as Rituximab and Belimumab work well for treating juvenile lupus (1-3), however, there is a medical dilemma when a patient either reacts to one of the commonly used agents or is refractory to their use.

Objectives: To postulate the use of obinutuzumab in juvenile lupus as a potential alternative to other B-cell targeted therapies.

Methods: Case presentation:

A 9 years old girl fulfilled 8 SLICC criteria for lupus diagnosis (acute autoimmune haemolytic anaemia, leukopenia, proteinuria, acute cutaneous rash, low complement, positive ANA, anti-Sm and antiphospholipid).

The patient was initially managed with steroids, hydroxychloroquine and rituximab. Unfortunately, patient had severe reaction to rituximab in the form of widely spread hives. MMF was decided before the patient developed rapid respiratory deterioration and was admitted to PICU with Macrophage Activation Syndrome. CT chest showed an ARDS like picture. IV anakinra was instituted and was then escalated to continuous infusion as patient was clinically unstable with recalcitrant fever, rashes and rising ferritin levels. A more aggressive treatment including IVIG, IV Ciclosporin and IV cyclophosphamide were consecutively decided. Despite initial stabilization, patient was persistently pyrexial and lung infiltrates did not change. Following extensive multidisciplinary discussions, plasmapheresis was decided. Due to inadequate response and previous rituximab reaction, obinutuzumab was administered after multidisciplinary consensus and informed parental consent.

Dosing followed the NOBILITY trial protocol with paediatric adjustments: 1000 mg/1.73m^2 IV on Days 1 and 15. No serious infections or infusion reactions occurred.

Results: Patient was stabilised clinically. Ventilatory support was gradually weaned with consequent extubation. Cardiac function and CXR returned back to normal. Anakinra was weaned and eventually stopped together with ciclosporine. Six cyclophosphamide doses were completed according to Eurolupus protocol. MMF was started as a maintenance therapy. Folowing multidisciplinary discussions, no further Obinutuzumab doses were advised.

Conclusion: Obinutuzumab may offer a promising therapeutic alternative in JSLE patients with refractory disease, particularly where conventional therapies, including rituximab, have failed or induced severe allergic reactions.

This report aligns with findings from adult trials such as NOBILITY and supports the exploration of obinutuzumab in paediatric lupus patients. Larger paediatric studies and longer follow-up are warranted. Consent to published had been obtained.

Disclosure

None declared

References

1. Brunner HI, Abud-Mendoza C, Mori M, Pilkington CA, Syed R, Takei S, et al. Efficacy and safety of belimumab in paediatric and adult patients with systemic lupus erythematosus: an across-study comparison. RMD open. 2021 Sep;7(3).
2. Watson L, Beresford MW, Maynes C, Pilkington C, Marks SD, Glackin Y, et al. The indications, efficacy and adverse events of rituximab in a large cohort of patients with juvenile-onset SLE. Lupus. 2015 Jan;24(1):10–7.
3. Peterknecht E, Keasey MP, Beresford MW. The effectiveness and safety of biological therapeutics in juvenile-onset systemic lupus erythematosus (JSLE): a systematic review. Lupus. 2018 Nov;27(13):2135–45.

P325

Developing a dual-target strategy for childhood lupus: findings from systematic review and co-creation workshops

O. Lloyd[1], E. Nolan[1,2], J. Ainsworth[2], E. Smith[1,3]
[1]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, [2]Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, [3]School of Infection & Immunity, University of Glasgow, Glasgow, United Kingdom
Correspondence: E. Nolan
Pediatric Rheumatology, **23(2):** P325

Introduction: Childhood-onset systemic lupus erythematosus (cSLE) significantly impacts health-related quality of life, affecting function, mental health, education and employment. While Treat-to-Target (T2T) approaches are gaining traction, current targets overlook these broader outcomes.

Objectives: To co-create a dual-target framework with cSLE patients and parents to better capture and address the impact of cSLE, placing equal emphasis on patient priorities and medical T2T goals.

Methods: A systematic review was conducted using Scopus, PubMed, and Web of Science to identify key factors influencing function in cSLE. A UK Patient and Public Involvement and Engagement (PPIE) group was established, including eight patients and five parents. Two patient partners played a key role in enhancing group cohesion, leading discussions and fostering collaboration, enabling children and young people (CYP) to feel supported and respected. The group participated in two virtual sessions and one in-person workshop, focusing on identifying the most important daily impacts of cSLE and exploring how to measure them. Two artists attended the in-person session to visually capture the emerging dual-target framework.

Results: The review identified no prior work on dual-target approaches, highlighting a gap in aligning patient priorities with T2T targets. The predominant factors identified from the literature affecting function included fatigue, pain and mental health. Key themes also emerged from the PPIE sessions. Despite achieving good disease control, CYP reported persistent struggles with fatigue, pain, and low mood, affecting school attendance, social engagement, and physical activity. Fatigue and mental health, were dominant themes, consistently described as disruptive to many aspects of daily life. When reviewing existing patient assessment tools, they expressed that these were overly formal, unengaging, and failed to capture progress

between clinics. Instead, they envisioned a dynamic, app-based tool incorporating widgets to track fatigue, mental health, pain, school attendance, and symptoms. To support the dual-target approach, CYP proposed integrating educational content, medication reminders, self-management tips, and a platform to connect with peers. Parents supported this vision and suggested a 'parent mode' offering practical guidance and supporting communication with the clinical team, and in particular, specialist nurses. A visual representation of the co-created dual-target framework was captured by artists during the in-person session.
Conclusion: Findings highlight the need to expand T2T strategies to include patient priorities. This co-developed dual-target framework places equal emphasis on daily function, wellbeing, and clinical goals, supporting a holistic approach. CYP are now empowered to co-create and lead as partners in ongoing development.
Disclosure
None declared

P326

A rare and challenging entity: a multicenter national study on drug-induced lupus in children

O. Koker[1], S. Sahin[2], N. Akay[2], E. Tunce[3], M. C. Polat[4], T. D. Kuzuca[5], S. Sener[6], S. Demir[5], E. H. Sonmez[7], B. C. Acar[4], B. Sozeri[3], O. Kasapcopur[2]
[1]Pediatric Rheumatology, Marmara University Faculty of Medicine, [2]Pediatric Rheumatology, İstanbul University-Cerrahpaşa, Faculty of Medicine, [3]Pediatric Rheumatology, University of Health Sciences, Ümraniye Training and Research Hospital, Istanbul, [4]Pediatric Rheumatology, University of Health Sciences, Ankara Bilkent City Hospital, Ankara, [5]Pediatric Rheumatology, Eskisehir Osmangazi University Faculty of Medicine, Eskisehir, [6]Pediatric Rheumatology, Adana City Research and Training Hospital, Adana, [7]Pediatric Rheumatology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye
Correspondence: O. Koker
Pediatric Rheumatology, **23(2):** P326

Introduction: Drug-induced lupus erythematosus (DILE) is a rare autoimmune disorder that typically emerges following chronic exposure to certain medications. This condition, which shares clinical and serological features with systemic lupus erythematosus (SLE), may present as a flare of an existing disease, the manifestation of previously subclinical lupus, or as a new-onset lupus-like syndrome. While the symptoms and clinical course are variable, the underlying pathophysiological mechanisms remain poorly understood.
Objectives: This study aims to shed light on the uncertainties surrounding the clinical presentation, management, and follow-up of pediatric patients diagnosed with DILE.
Methods: This multicenter study was conducted with contributions from seven pediatric rheumatology centers. Medical records of patients diagnosed with drug-induced SLE were retrospectively reviewed. Demographic characteristics, clinical and serological profiles, suspected drug exposures, treatment approaches, and prognostic data were collected. Categorical variables were summarized as frequencies and percentages, while continuous variables were described using median, minimum, and maximum values.
Results: Seventeen patients (14 females and 3 males) diagnosed with DILE were included in the study. The current median age was 15 years (interquartile range [IQR]: 12.5–20), while the median age at diagnosis was 11 years (IQR: 9–14). Newly diagnosed SLE was observed in 83.3% of patients, while disease flare was noted in 11.1%. The median disease duration was 30 months (IQR: 6–73.5). In five patients (27.8%), the condition was associated with anti–tumor necrosis factor (TNF) therapy. The drugs associated with the table included enalapril, etanercept, ethosuximide, ibuprofen, infliximab, isoniazid, canakinumab, methimazole, methotrexate, minoxidil, paracetamol, and trimethoprim-sulfamethoxazole. The most frequent clinical manifestations involved cutaneous (n = 13, 72.2%), musculoskeletal (n = 12, 66.7%), and hematological (n = 11, 61.1%) systems. All patients tested positive for antinuclear antibodies (ANA), and anti-histone antibody positivity was observed in 61.1% (n = 11). All but one patient required treatment, with corticosteroids being the most commonly used therapeutic agent.
Conclusion: In our study, patients diagnosed with drug-induced lupus presented with a clinical phenotype resembling idiopathic SLE; however, the course was not marked by major known complications. It was observed that recently introduced medications or those with expanding indications and increasing use such as anti-cytokine therapies may trigger this condition with diverse clinical and serological profiles. Therefore, even in the absence of specific findings, it is crucial to thoroughly investigate potential drug triggers in patients presenting with lupus-like manifestations, as early recognition and appropriate management are essential.
Disclosure
None declared

P327

Induction therapy and treatment targets for paediatric lupus nephritis: real-life clinical strategies from the JIR-clips initiative

V. Natoli[1,2], S. Seher[3], A. Belot[4,5], F. Hofer[6], L. Lamot[7,8], K. Pateras[9], P. Riley[10], S. Sahin[11], E. M. D. Smith[12,13], R. Carlomagno[14], S. Kamphuis[15] on behalf of Lupus Nephritis Working Group (JIR-CliPS Network)
[1]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili, Università degli Studi di Genova, [2]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [3]Division of Pediatric Rheumatology, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Türkiye, Ankara, Türkiye, [4]National
Reference Center for Rheumatic, Autoimmune and Systemic Diseases in Children (RAISE), Pediatric Nephrology, Rheumatology, Dermatology Unit, Hôpital Femme Mère Enfant, Hospices Civils de Lyon, [5]Centre International de Recherche en Infectiologie, University of Lyon, Institut National de la Santé et de la Recherche Médicale, U1111, Université Claude Bernard, Lyon 1, Le Centre National de la Recherche Scientifique, Lyon, France, [6]Fondation RES, Lausanne, Switzerland, [7]Department of Pediatrics, School of Medicine, University of Zagreb, Zagreb, [8]Department of Pediatrics, University Hospital Center Zagreb, Zageb, Croatia, [9]Faculty of Public and One Health, University of Thessaly, Karditsa; and Department of Statistics, Athens University of Economics and Business, Athens, Greece, [10]Department of Paediatric Rheumatology, Royal Manchester Children's Hospital, Manchester, United Kingdom, [11]Division of Pediatric Rheumatology, Department of Pediatrics, Cerrahpasa Medical Faculty, Istanbul University-Cerrahpasa, Istanbul, Türkiye, [12]Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, [13]University of Glasgow, School of Infection & Immunity, Glasgow, United Kingdom, [14]Unit of Rheumatology, Immunology and Allergology, Department of Pediatrics, Lausanne University Hospital, Lausanne, Switzerland, [15]Department of Paediatric Rheumatology, Sophia Children's Hospital, Erasmus University Medical Centre, Rotterdam, Netherlands
Correspondence: V. Natoli
Pediatric Rheumatology, **23(2):** P327

Introduction: Juvenile lupus nephritis (LN) is a severe and potentially life-threatening complication of juvenile-onset systemic lupus erythematosus (jSLE). International recommendations are often extrapolated from adult-onset SLE data and do not always reflect real-life paediatric care across diverse healthcare systems.
Objectives: To describe global real-world clinical strategies for the induction treatment and targets in paediatric LN.
Methods: A survey was conducted from June 2022 to May 2023 as part of the JIR-CliPS initiative. The questionnaire explored physician demographics, therapeutic approaches during induction, treatment targets, and local constraints. Descriptive statistics were used to summarize responses.
Results: A total of 121 physicians from 35 countries participated: 26.4% were from South America, 22.3% from Western Europe, 21.4% from the Middle East, 14.9% from Eastern Europe, 8.3% from Africa, and 4.9% from Oceania. According to World Bank Gross Domestic Product (GDP) classification, 61% were from high-income countries, 26% from middle-income, and 13% from low-income settings. Most respondents were paediatric rheumatologists (66.4%), with over 10 years of experience in LN (48.8%), and working in university hospitals (67.8%). Induction treatment strategies varied by LN class. For class I LN, 72%

of physicians prescribed prednisone (PDN), alone or with azathioprine (AZA, 26%). In class II, 100% used PDN, with 49% combining it primarily with AZA. For class III and IV LN, PDN (92% and 90%, respectively) was most frequently used with either mycophenolate mofetil (MMF) (77% and 79%) or cyclophosphamide (CYC) (53% and 79%). Rituximab (RTX) was more commonly used in class IV (40%) compared to class III (22%). In class V LN, the most common strategy included PDN (89%) and MMF (78%); less common was the use of CYC (43%) or RTX (30%). Regarding treatment targets, 77% of respondents targeted partial renal response—defined as ≥50% reduction in proteinuria to at least sub-nephrotic levels (urine protein/creatinine ratio <350 mg/mmol and preserved renal function—by 3 months. Complete renal response—defined as urine protein/creatinine ratio <50 mg/mmol and normal or near-normal renal function—was the primary target for 68% of physicians at 6 months and 93% at 12 months. Achieving low-dose PDN (0.1–0.2 mg/kg/day) by 6 months was considered a key objective by 86% of respondents. The majority of the physicians (59%) reported not following a fixed tapering protocol, instead adapting the taper based on patient response.

Conclusion: This international survey highlights the diversity of induction approaches used in paediatric LN across regions and healthcare systems. While PDN combined with MMF or CYC is commonly used for proliferative LN, substantial variability persists. These findings underscore the need for adaptable, evidence-based algorithms and greater awareness of international guidelines among paediatric rheumatologists. In light of recent advances in adult LN recommendations, efforts to align paediatric practice with evolving standards are warranted, while also taking into account local constraints that may limit their implementation.

Disclosure

None declared

P328

Treat-to-target strategies in juvenile systemic lupus erythematosus: a scoping review of current evidence and future directions

V. Natoli[1,2,3], E. Jones[4], E. M. D. Smith[1,5]

[1]Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [2]Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili, Università degli Studi di Genova, [3]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [4]School of Medicine, University of Liverpool, Liverpool, [5]University of Glasgow, School of Infection & Immunity, Glasgow, United Kingdom

Correspondence: V. Natoli

Pediatric Rheumatology, **23(2):** P328

Introduction: Treat-to-target (T2T) has emerged as a promising strategy to improve long-term outcomes in systemic lupus erythematosus (SLE). While T2T principles are well established in adult- SLE, their adaptation to juvenile-onset SLE (jSLE) is more recent.

Objectives: To systematically review the current literature on T2T in jSLE.

Methods: A systematic literature search was conducted across PubMed, Scopus, Ovid, and Web of Science. Keywords included variations of "jSLE", "treat-to-target", "Lupus Low Disease Activity (LLDAS)" and "remission". Eligible studies were peer-reviewed English-language articles including SLE patients diagnosed before age 18. Screening and selection of articles followed PRISMA guidelines. The literature search was performed in April 2025, with no date limits applied. Studies were included if they addressed any of the following: development and validation of targets, implementation strategies, impact on clinical outcomes, barriers and facilitators to target attainment, integration of biomarkers, and T2T in lupus nephritis. Reviews, editorials, case reports, conference abstracts, non-English publications, and studies not focused on paediatric T2T strategies were excluded.

Results: A total of 347 records were identified through database searches, of which 27 studies met the inclusion criteria. Of these, 7 addressed the development of T2T targets or conceptual frameworks, 4 focused on the validation of T2T targets, and 5 described implementation strategies. Nine studies evaluated the impact of target attainment on clinical outcomes, while 15 explored barriers and facilitators to achieving T2T goals. T2T approaches in lupus nephritis were examined in 4 studies, and 2 studies incorporated biomarkers to support the T2T approach. Across cohorts, the proportion of patients reaching LLDAS or Childhood LLDAS (cLLDAS) ranged from 67% to 100%, whilst 11% to 61% achieved remission on-treatment, and 2% to 31% remission off-treatment, depending on the definitions. Attainment of LLDAS or remission was consistently associated with a lower risk of disease flares and organ damage. Positive predictors of target achievement included absence of renal or subacute cutaneous involvement, normal complement and anti-dsDNA levels, treatment with biologic drugs, and good treatment adherence. Conversely, African/Caribbean ethnicity, male sex, persistent proteinuria, serological activity and poor compliance were associated with reduced likelihood of achieving treatment targets.

Conclusion: T2T strategies in jSLE are clinically relevant and feasible, with LLDAS and remission linked to better outcomes. However, varied definitions and study designs limit comparability. Recently published paediatric-specific targets mark progress, with priorities now including validation, biomarker integration, and standardised implementation.

Disclosure

None declared

P329

Post-covid rheumatic and inflammatory manifestations in children: a three-year observational study from a single pediatric rheumatology center in georgia

E. Nakhutsrishvili, T. Kutubidze

Givi Zhvania Pediatric University Clinic of Tbilisi State Medical University, Tbilisi, Georgia

Correspondence: E. Nakhutsrishvili

Pediatric Rheumatology, **23(2):** P329

Introduction: The COVID-19 pandemic has triggered widespread concern regarding its long-term consequences in the pediatric population. While children were initially believed to be less severely affected, accumulating evidence suggests that post-viral immune dysregulation may lead to a variety of rheumatologic and inflammatory complications. Pediatric patients may develop diverse post-infectious syndromes, including multisystem inflammatory syndrome in children (MIS-C), vasculitis, and autoimmune manifestations. This study aims to describe the clinical and immunologic spectrum of such manifestations following SARS-CoV-2 infection.

Objectives: To characterize the clinical, laboratory, and imaging findings of post-COVID rheumatic and inflammatory conditions in children and adolescents referred to a pediatric rheumatology clinic over a three-year period.

Methods: From 2022 to 2025, 50 pediatric patients were followed at the TSMU Givi Zhvania Pediatric University Clinic, Tbilisi, Georgia. Inclusion criteria were a history of confirmed COVID-19 infection (PCR/antigen), documented close contact with a confirmed case, or positive SARS-CoV-2 IgG antibodies. No enrolled patient had received a COVID-19 vaccine. Detailed demographic, clinical, laboratory, and imaging data were collected prospectively.

Results: The cohort comprised 62% females and 38% males. Age distribution was: 4 patients <1 year, 10 aged 1–4 years, 24 aged 5–12 years, and 12 aged 12–18 years. SARS-CoV-2 infection was confirmed in 46% of patients, 28% had close contact with an infected individual, and 26% were IgG-positive without documented symptoms. The most common clinical presentation was arthralgia or arthritis (56%), including 2 cases ultimately diagnosed with juvenile idiopathic arthritis. Cutaneous or vascular involvement (vasculopathy) was observed in 32%, often manifesting as livedo reticularis, purpura, or acrocyanosis. Fever and constitutional symptoms such as fatigue were prominent in 12%. Laboratory investigations showed elevated inflammatory markers (ESR and/or CRP) in 52% of patients. Hyperferritinemia was noted in 22%, and elevated D-dimer levels in 7 patients. Antinuclear antibodies (ANA) were positive in 8 patients, though only 3 met classification criteria for a defined rheumatic disease. Echocardiographic abnormalities included coronary artery dilation in 2 patients and coronary artery aneurysm in 1 case. Despite treatment, 18% of patients continued to experience persistent rheumatic symptoms, requiring long-term follow-up and therapy, while 82% achieved full recovery.

Conclusion: This single-center observational study highlights the diverse spectrum of post-COVID rheumatic and inflammatory manifestations in children. Arthralgia, vasculopathy, and systemic inflammation were common, even among unvaccinated patients with asymptomatic or mild COVID-19. These findings underscore the need for heightened clinical vigilance, early referral to pediatric rheumatology, and ongoing research into the immunopathogenesis of post-viral autoimmune activation in children.
Disclosure
None declared

P330

PI4KA-related disorder: genetic explanation of a complex phenotype between autoinflammation and autoimmunity?

N. Brück[1], A. Schnabel[1], M. Smitka[1], C. Wolf[1], K. Hackmann[2], M. A. Lee-Kirsch[1,3]
[1]Department of Pediatrics, [2]Institute for Clinical Genetics, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, [3]Department of Pediatrics, University Center for Rare Diseases, Dresden, Germany
Correspondence: N. Brück
Pediatric Rheumatology, **23(2):** P330

Introduction: PI4KA-related disorder is a clinically variable condition with neurological dysfunction (limb spasticity, developmental and intellectual delay, seizures), gastrointestinal manifestations (inflammatory bowel disease and intestinal atresia) and immunodeficiency. A 17-year-old male with a history of spastic paraplegia, developmental delay, and recurrent fever presented with systemic inflammation, polyarthritis, and autoimmune symptoms. Genetic testing identified biallelic variants in the PI4KA gene.
Objectives: To describe a new phenotype of PI4KA-related disorder mimicking systemic Lupus erythematosus.
Methods: We present the case of a 17 years old patient who presented with progressive spastic paraplegia, epilepsy and intellectual disability from the first year of life. At the age of 17, he was hospitalized with fever and pleuropneumonia, polyarthritis, chilblain-lesions of the fingers and systemic inflammation (CRP 120 mg/l, ferritin 500 µg/l, calprotectin 95 mg/l). Immunological investigations showed lymphopenia, complement deficiency, elevated antibody profile (ANA 1:10.240, dsDNA and anti-Sm highly positive) and a strong interferon signature.
Results: Exome sequencing and segregation of identified variants in the parents was performed.We detected two biallelic variants of uncertain significance (VUS) in **PI4KA encoding** phosphatidylinositol 4-kinase. PI4KA synthesizes phosphatidylinositol 4-phosphate, an integral lipid of Golgi membranes required for membrane trafficking and signal transduction. A dysregulation of these processes may therefore cause the patient's inflammatory condition [1,2]. Of the PI4KA VUS identified in the patient, one was found 12x heterozygously in gnomAD and predicted to be deleterious, while the other has not been described in gnomAD with unclear functional prediction. Although immunosuppressive therapy (prednisolone, methotrexate, anakinra) resulted in partial symptom improvement, the patient's inflammatory markers (CRP, Ferritin) remained elevated, and the clinical picture fluctuated, especially during steroid tapering. A therapeutic trial with JAK inhibition (baricitinib) was initiated due to clinical similarities with type I interferonopathies and systemic lupus erythematosus without success [3,4]. Tapering of steroids became possible after switch to canakinumab combined with methotrexate.
Conclusion: This case highlights the importance of genetic testing in diagnosing rare complex disorders like PI4KA-related conditions. The identification of biallelic PI4KA variants provides a potential genetic explanation for the patient's multi-systemic disease. Further functional analysis is necessary to determine the causality PI4KAVUS in disease pathogenesis and to derive improved treatment strategies. Consent to published had been obtained.
Disclosure
None declared

References

1. Saettini F, Guerra F et al. Biallelic PI4KA Mutations Disrupt B-Cell Metabolism and Cause B-Cell Lymphopenia and Hypogammaglobulinemia. J Clin Immunol. 2024;45(1):15.
2. Salter CG, Cai Y et al. Biallelic PI4KA variants cause neurological, intestinal and immunological disease. Brain. 2021;144(12):3597–3610.
3. d`Angelo D, Di Filippo P et al. Type I Interferonopathies in Children: An Overview. Front Pediatr. 2021;9:631,329.
4. Aringer M, Costenbader K et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol. 2019;71(9):1400–1412.

P331

Diagnostic challenges in childhood-onset IGG4-related disease: a case series study

O. Shpitonkova[1], V. Podzolkova[1], M. Osminina[1], E. Afonina[2], Y. Kostina[2], S. Davtian[3], N. Podchernyaeva[1]
[1]Department of Children's Diseases, I.M. Sechenov First Moscow State Medical University, [2]Department of Pediatric Rheumatology №1, Clinic of Children's Diseases Sechcenov's Center of Maternity and Childhood, [3]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation
Correspondence: V. Podzolkova
Pediatric Rheumatology, **23(2):** P331

Introduction: IgG4-related disease (IgG4-RD) in children is a rare and under-researched condition. Its clinical presentation often differs from that observed in adults, which complicates early diagnosis and management [1–3].
Objectives: The aim of our study is to summarize the clinical, laboratory, and imaging findings in a series of pediatric cases with IgG4-RD.
Methods: We conducted a retrospective analysis of clinical cases and compared our findings with data from the current literature. The study included six pediatric patients (1 male, 5 females) with a median age of 12 years. Data on clinical presentation, laboratory tests, imaging, treatment, and outcomes were collected from medical records.
Results: Four presented with orbital involvement, one had both diabetes insipidus and orbital lesions, and one exhibited systemic symptoms including fever, arthralgia, hematuria, productive cough, hepatosplenomegaly, and periorbital edema. Differential diagnoses considered included neoplastic, allergic, autoimmune disorders and vasculitis. Serum IgG4 levels were normal in four patients and not assessed in two. Orbital CT scans revealed mass-like lesions in five patients; one scan was normal. Histopathological confirmation via percutaneous biopsy and immunohistochemistry (IHC) demonstrated fibrosis, infiltration with >40% IgG4+ plasma cells, and obliterative phlebitis in all cases. Systemic involvement was evaluated as follows: chest CT showed ground-glass opacities in two patients, both of whom presented with non-orbital manifestations. Salivary gland ultrasound revealed altered echogenicity in three patients. All six patients had abdominal involvement, including mild hepatomegaly, gallbladder wall thickening, and pancreatic abnormalities. The median time to diagnosis was 9 months. Treatment strategies varied: three patients received systemic glucocorticoids combined with cytotoxic agents, while three others were treated with mycophenolate mofetil monotherapy. Four patients achieved complete remission, whereas two with systemic involvement showed only partial response. Patients in remission remain on maintenance therapy with mycophenolate mofetil, while those with partial response continue combination therapy with methylprednisolone and mycophenolate mofetil.
Conclusion: IgG4-RD in children is rare and poses significant diagnostic challenges. While orbital involvement is common, multisystem disease and normal serum IgG4 levels may complicate diagnosis. Definitive diagnosis relies on histopathology with IHC staining to IgG4. Some patients respond well to immunosuppressive therapy, although treatment regimens require further standardization.
Disclosure
None declared

References

1. Hara S, Yoshida M, Sanada H, Suzuki Y, Sato Y, Mizushima I, et al. Pediatric IgG4-related disease: a descriptive review. Expert Rev Clin Immunol. 2024 Jan 2;20(1):97–119.

2. Karim F, Loeffen J, Bramer W, Westenberg L, Verdijk R, Van Hagen M, et al. IgG4-related disease: a systematic review of this unrecognized disease in pediatrics. Pediatr Rheumatol. 2016 Dec;14(1):18.
3. Kaya Akca U, Kose H, Kurt T, Ulu K, Guliyeva V, Kılbas G, et al. A rare disease with many faces: a multicentre registry of IgG4-related disease in children. 2025 Apr 1;64(4):2185–92.

P332

Childhood-onset behçet's disease in a latin american tertiary center: distinct clinical and treatment patterns based on HLA-B*51 positivity

M. França[1], T. Souza[2], R. Machado[1], V. Matias[3], S. Farhat[1], L. Steuer[1], L. Forero[1], V. Balbi[1], N. Aikawa[1,4], K. Kozu[1], C. Silva[1], A. Elias[1], L. Campos[1]
[1]Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, [2]Faculdade de Medicina, Universidade de Brasília, Distrito Federal, [3]Faculdade de Ciências Médicas da Santa Casa de São Paulo, [4]Division of Rheumatology, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil
Correspondence: A. Elias
Pediatric Rheumatology, **23(2):** P332

Introduction: Behçet's disease (BD) is a rare pediatric vasculitis with limited epidemiological data in Latin America centers, especially in children where initial symptoms can be non-specific and disease progression may be protracted. The frequency of HLA-B51, which is associated with increased disease risk, is also lower compared with countries along the Silk-Road. It is possible that in Brazil, a country characterized by mixed population, other HLA alleles might contribute to BD susceptibility.
Objectives: To identify the HLA alleles in childhood-onset BD patients and characterize clinical manifestations and therapies associated with them.
Methods: The study included 32 childhood-onset BD patients followed at a tertiary and university Pediatric Rheumatology Center in Brazil, diagnosed ≤ 18 years-old, based on expert pediatric rheumatologists' opinion and/or according to the international criteria for BD (ICBD) or the pediatric BD classification criteria (PEDBD). Medical records were reviewed to assess HLA alleles, clinical and therapeutic characteristics of these patients. For further analyses patients were classified according to the presence or absence of HLA-B51 and the groups were compared regarding demographic data, clinical characteristics and treatment.
Results: Demographic data of 32 childhood-onset BD patients were: median age of 4.5(0.5-12) years at diagnosis, female sex in 16(50%) and white ethnicity in 25(78%) of cases. HLA-B51 allele was identified in 16 of 32 patients (50%). Other HLA alleles were found as following: HLA-B15 (n=8), HLA-B35 (n=6), HLA-B42 (n=3), HLA-B53 (n=3), HLA-B39 (n=2), HLA-B58 (n=1), HLA-B57 (n=1), HLA-B52 (n=1) and HLA-B14 (n=1). The presence of other HLA alleles was significantly higher in patients with negative HLA-B51 compared to patients with positive HLA-B51 (75% vs. 38%, p=0.04). HLA-B51 negative patients were significantly older than HLA-B51 positive patients [7.5 (0.5–12) vs. 3 (0.5–11) years; p=0.02] at diagnosis, in contrast to female sex that was less frequent in the former group (31% vs. 69%, p=0.04). The frequency of patients that fulfilled at least one confirmation criteria (PEDBD and/or ICBD) was similar between groups (57% vs. 44%, p=0.72). Likewise, no differences were observed between the groups regarding clinical manifestations, including fever, oral/genital ulcers, articular, cutaneous, ocular, neurological and gastrointestinal involvement. Further analysis of treatment showed that colchicine use was also similar in both groups (94% vs. 98%, p=0.5). However, HLA-B51 negative patients significantly required the use of additional immunosuppressants agents (60% vs. 23%, p=0.05), especially corticosteroids (56% vs. 19%, p=0.03) and azathioprine (69% vs. 19%, p=0.006).
Conclusion: Patients who were negative for HLA-B51 but positive for other HLA alleles were diagnosed at a later stage and required multiple immunosuppressive therapy. These results indicate that in patients outside the Silk Road, other HLA alleles may be associated with BD and could lead to a delayed diagnosis.
Disclosure
None declared

P333

Challenges in diagnosing and managing early-onset takayasu arteritis in children: a single-center experience from Kazakhstan

A. Otegen, I. Arshynbek, A. Kappassov, Z. Mukusheva, A. Akhmambetova, M. Asylbekova, Z. Albekova, A. Dildabayeva
Pediatric Rheumatology, CF "University Medical Center", Astana, Kazakhstan
Correspondence: A. Otegen
Pediatric Rheumatology, **23(2):** P333

Introduction: Takayasu arteritis (TA) is a rare large-vessel vasculitis that typically affects adolescents and young adults. Disease onset before the age of 10 is exceptionally uncommon and presents significant diagnostic challenges. According to the Bureau of National Statistics of Kazakhstan, the pediatric population under 18 years is 6,841,527. As our center serves approximately half of the country's pediatric population, the 28 children diagnosed with TA at our facility correspond to a catchment area of roughly 3.42 million children. Based on this, the estimated prevalence of pediatric TA in our region is approximately 0.82 cases per 100,000 children. Unfortunately, official statistics on the number of children under 10 years are not publicly available, limiting accurate early-onset TA prevalence estimates. In low-resource settings, early symptoms may be overlooked due to their nonspecific nature and limited access to pediatric rheumatology services.
Objectives: To describe the clinical features, diagnostic delays, treatment approaches, and short-term outcomes in children with early-onset TA managed at a tertiary pediatric center in Kazakhstan.
Methods: A retrospective review of 28 pediatric patients diagnosed with TA between 2015 and 2023 was conducted. Seven patients (25%) with disease onset at or before 10 years of age were selected for detailed analysis. Data included clinical presentation, laboratory and imaging findings, treatment regimens, complications, and outcomes.
Results: Among the seven children (five females, two males), the median age at onset was 7.1 years (range: 3.9–8.0), and the median diagnostic delay was 6 months (range: 2–14). Arterial hypertension was observed in 71%, headache and fatigue in 57%, and dizziness in 43%. Asymmetry or absence of peripheral pulses was found in 57%. In two cases, the disease began with incidental hypertension; three presented with systemic inflammatory symptoms, and two with limb ischemia signs. The median ESR at diagnosis was 48 mm/h. Angiographic findings showed type III involvement in five patients and type IIa in two. One child had an ischemic stroke, and another had a splenic infarction. All patients received high-dose systemic corticosteroids and the interleukin-6 inhibitor tocilizumab. Methotrexate was used in five cases (71%), and cyclophosphamide and mycophenolate mofetil in one patient each. No surgical or endovascular interventions were required. All patients improved clinically during follow-up, with no severe treatment-related adverse events.
Conclusion: Early-onset TA in children under 10 years is diagnostically challenging due to subtle and variable early symptoms. Routine blood pressure and pulse assessment should be prioritized in young children with systemic complaints. Despite delays and vascular complications, immunosuppressive therapy—especially early IL-6 inhibition—was effective. These findings support the development of pediatric-specific protocols in resource-limited settings.
Disclosure
None declared

P337

Aspirin dosing and ivig failure strategies in Kawasaki disease: insights from Israeli pediatric centers

A. T. Suchi[1,2], Y. Uziel [1,2], A. Ziv[1,2], R. Haviv[1,2]
[1]Pediatric Rheumatology, Meir Medical Center, Kfar Saba, [2]Medical School, Tel Aviv University, Tel Aviv, Israel
Correspondence: A. T. Suchi
Pediatric Rheumatology, **23(2):** P337

Introduction: Kawasaki disease (KD) is a common childhood vasculitis, with coronary artery aneurysms (CAA) as its most serious complication. Intravenous immunoglobulin (IVIG) is the standard treatment, historically given with high-dose (80-100mg/kg/day) acetylsalicylic acid (ASA). However, recent studies including in Israel, show that the low

dose ASA (3-5mg/kg), to facilitate platelet aggregation inhibitory effect, may have a better outcome, and benefit in KD CAA. About 10-15% are resistant to the first IVIG dose and need a second line therapy.
Objectives: To examine the approach regarding ASA dosing consistency and the second-line treatment after IVIG failure across pediatric centers in Israel.
Methods: In early 2025, an electronic questionnaire was sent to 24 pediatric centers across Israel, asking 2 clear questions, regarding ASA dosing and second line approaches in cases of IVIG-resistant KD. Data were statistically analyzed using Excel (Microsoft).
Results: All 24 Israeli pediatric medical centers responded, of which ten (42%) used high-dose ASA (80–100 mg/kg/day), four (16.5%) used medium-high dose (50–80 mg/kg/day), four (16.5%) used medium-low dose (30–50 mg/kg/day), while six (25%) used low-dose ASA (3–5 mg/kg). For IVIG resistant cases, pediatricians at 14 centers (58.5%) administered a second IVIG dose, four (16.5%) used high-dose IVIG combined with glucocorticoids, four (16.5%) used glucocorticoids alone, and two (8.5%) used the tumor necrosis factor-α inhibitor infliximab as a second-line treatment.
Conclusion: Although data gathered during the last 15 years show no benefit in high dosing of ASA in KD patients, there's still a significant variability in ASA dosing in Israel. Also, second-line therapies approaches vary significantly for IVIG-resistant KD patients. Standardized and evidence-based treatment protocols are needed to ensure consistent care
Disclosure
None declared

P338

The mighty giants-an experience of kawasaki disease in children from a tertiary centre in Bristol, United Kingdom

A. Batchu Prithvi[1], C. Govardhan[1], K. Darma[2], M. Roderick[2], A. Ramanan[1]
[1]Paediatric Rheumatology, [2]Paediatric Immunology, Bristol Royal Hospital for Children, Bristol, United Kingdom
Correspondence: A. Batchu Prithvi
Pediatric Rheumatology, **23(2):** P338

Introduction: Kawasaki disease (KD) is a medium vessel vasculitis affecting young children. Small coronary artery aneurysms tend to regress, medium to giant coronary artery aneurysms(CAA) accounting for nearly 2% may persist leading to complications such as myocardial infarction, vessel rupture and even sudden death(1).
Objectives: To describe clinical profile, echocardiography and coronary outcomes in children diagnosed with KD with giant CAA.
Methods: A retrospective observational study was conducted at Bristol Royal Hospital for Children to include children diagnosed with KD with giant CAA between 2011-2025. Giant CAA were defined as per AHA guidelines (Z score of $\geq$10 or absolute coronary artery dimension of $\geq$ 8 mm(2). Clinical features, echocardiography and coronary outcomes were recorded and analyzed using descriptive statistics.
Results: Among 166 children diagnosed with KD between 2011-2025, 13 (7.8%) had giant CAA. Median age at presentation was 8 months (4-57) with more boys affected (Male: Female= 1.6:1). 6(46.2%) children fulfilled criteria for complete KD; 7(53.8%) were incomplete KD. Median duration of fever was 8(3-12) days. Presenting symptoms were rash (100%), mucosal changes (69.2%), bilateral non-purulent conjunctivitis (69.2%), extremity changes (53.8%) and lymphadenopathy (30.8%). 2 children (15.4%) presented as node-first KD. Right coronary artery was most commonly involved in 10 (76.9%) followed by left anterior descending artery in 6 (46.1%). 1 child had axillary artery aneurysm and 1 child had axillary and brachial artery aneurysm in addition to CAA. Maximum Z score was +50. Other cardiac findings included pericardial effusion in 7 (53.8%), severe LV dysfunction in 2 (15.4%) and thrombus in 2 (15.4%). Median laboratory investigations-CRP 172 (62-172) mg/L, ESR 77 (38-119) mm/hour, WCC 22 (14-39) $*10^9$/L, neutrophils 17(12-21) $*10^9$/L, sodium 135 (132-137) mmol/L and platelets 977 (568-1546) $*10^9$/L. All children received intravenous immunoglobulin (IVIG) and aspirin. Additional treatment included intravenous methylprednisolone- 13 (100%), weaning oral steroids-12 (92.3%), 2nd dose IVIG-11 (84.6%), (39.29%), infliximab- 5 (38.5%) and anakinra- 2 (15.4%). Follow up at 1 year showed reduction in coronary artery Z scores in 2/9 children (22.2%) with persistence in 7/9 children. 1 child had extensive myocardial damage and underwent heart transplant with good outcome and 1 child succumbed secondary to rupture of giant aneurysm during initial presentation.
Conclusion: Giant coronary artery aneurysm is considered a dreadful complication of KD and despite aggressive immunotherapy can persist and result in short- and long-term complications.
Disclosure
None declared

References

1. Jiang S, Li M, Xu K, Xie Y, Liang P, Liu C, et al. Predictive factors of medium-giant coronary artery aneurysms in Kawasaki disease. Pediatr Res [Internet]. 2024 Jan [cited 2025 May 10];95(1):267–74. Available from: https://www.nature.com/articles/s41390-023-02798-6.
2. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association | Circulation [Internet]. [cited 2025 May 10]. Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001295

P339

Kawasaki disease – experience of bristol royal hospital for children, United Kingdom, 2011-2025

A. Batchu Prithvi[1], C. Govardhan[1], K. Darma[2], M. Roderick[2], A. Ramanan[1]
[1]Paediatric Rheumatology, [2]Paediatric Immunology, Bristol Royal Hospital for Children, Bristol, United Kingdom
Correspondence: A. Batchu Prithvi
Pediatric Rheumatology, **23(2):** P339

Introduction: Kawasaki Disease (KD) is a medium vessel vasculitis with estimated incidence of 8.1/100,000 children.[1] KD can result in coronary artery aneurysms (CAA) in around 25%[2] of untreated patients, and is the leading cause of acquired heart disease in children in developed countries.[2] Prompt recognition and treatment of KD is crucial to preventing complications. Intravenous immunoglobulin (IVIG) therapy has been shown to be effective in reducing the incidence of CAA to approximately 5%.[3] A prospective British Paediatric Surveillance Unit study showed that despite comprehensive education about KD amongst clinicians, CAA incidence in the UK still remains higher than our international counterparts at 19%[2], an incidence similar to the untreated group.
Objectives: We sought to review outcome data of KD over a 15-year period
Methods: A retrospective observational study was conducted at Bristol Royal Hospital for Children to include children <18 years with KD between 2011-2025. Clinical features, echocardiography and outcomes were recorded and analysed using descriptive statistics.
Results: A total of 182 patients were identified from electronic patient records. 16 had incomplete data and were excluded. A total of 166 patients were included. M:F=1.7:1. Median age (IQR) of patients was 36 months (15-62), 38 (22.9%) of whom were under 1 year. 69 fulfilled criteria for complete KD where as 90 were incomplete and 7 atypical. 5 children presented as a lymph node first KD, 3 had 2nd episode of KD.53 (31.9%) had coronary artery changes in first echo at our centre with 13 children (7.8%) having giant CAA (Z score $\geq$ 10 and/or absolute dimension > 8 mm). Additional echocardiographic findings included-pericardial effusion in 10, reduced ventricular function in 2. All children received IVIG and aspirin. In addition, 35 received 2nd dose IVIG, 43 oral steroids, 47 IV pulse steroids, 14 infliximab, 2 anakinra. Follow up echocardiography at 6-12 months was available in 115 children and showed persistence of CAA in 21 (18.3%). 1 child succumbed and 1 child developed severe myocardial dysfunction requiring transplant.
Conclusion: Our CAA incidence at 12 months was 18.3%. Over last 10 years, education of paediatricians of KD in the UK has significantly increased. Poor outcomes suggesting the need for improved and alternative therapies.
Disclosure
None declared

References

1. Harnden A, Alves B, Sheikh A. Rising incidence of Kawasaki disease in England: analysis of hospital admission data. BMJ 2002;324:1424–5.
2. Tulloh RMR, Mayon-White R, Harnden A, et al. Kawasaki disease: a prospective population survey in the UK and Ireland from 2013 to 2015. *Arch Dis Child*. 2018;103(12).

3. Newburger, J. W., M. Takahashi, M. A. Gerber, M. H. Gewitz, L. Y. Tani, J. C. Burns, S. T. Shulman, A. F. Bolger, P. Ferrieri, R. S. Baltimore, W. R. Wilson, L. M. Baddour, M. E. Levison, T. J. Pallasch, D. A. Falace and K. A. Taubert (2004). "Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association." Circulation 110(17): 2747–2771

P341

Gastrointestinal involvement in childhood iga vasculitis: a retrospective study from a tertiary care center in Eastern part of India

D. Patro[1,2], H. Das[1], K. Panda [3], Y. Dayanidhigodesi[1]
[1]Pediatrics, IMS and SUM Hospital, Bhubaneswar, [2]Pediatric Rheumatology, Manipal Hospitals, Bengaluru, [3]Pediatrics Gastroenterology, IMS and SUM Hospital, Bhubaneswar, India
Correspondence: D. Patro
Pediatric Rheumatology, **23(2):** P341

Introduction: IgA Vasculitis (IgAV) is a small vessel vasculitis which is usually self- limiting. However gastrointestinal (GI) involvement is observed in 50-75% of patients. The spectrum of gastrointestinal involvement in IgA vasculitis ranges from vomiting, pain abdomen to hematemesis, hematochezia, melena, intussusception to requirement of surgery, Intensive care and blood components which overall dictates the prognosis of the child. Few literature exists on patients who experiences an atypical disease course.
Objectives: To describe the clinical and laboratory characteristics of IgAV with GI involvement.
Methods: IgAV was initially diagnosed according to EULAR/PRINTO/PRES criteria and those in whom GI manifestations were present. 22 patients treated in Institute of Medical Sciences (IMS) and SUM Hospital, Bhubaneswar, India under the care of Pediatric Rheumatology and Gastro-enterology between May 2023 till April 2025 were enrolled. Data were collected during hospital admission and during follow up visits.
Results: Out of the 22 patients enrolled; 4 did not have GI involvement. So, a total of 18 patients were analyzed. Male to female was 2:1. The age of presentation ranges between 2 years to 15 years. The day of presentation ranged between day 3 to 30. Post-prandial angina and nausea/vomiting was seen in most of the children.Ultrasonography and Contrast CT abdomen with enterography was able to pick few cases in case of a dilema. Steroids were used in 15 patients (Pulse dose in N=7). Cryoprecipitate along with Intravenous steroids was used in 2 Male patients; out of which one had a severe GI vasculitis with frank blood in stool who responded to IVIG and Inj Cyclophosphamide. Steroid Sparing agents used were Methotrexate (N=1), Mycophenolate (N=3), Cyclophosphamide (N=1); IVIG (N=1). Severe renal involvement (IgAV Nephritis) was seen in one girl child. An adolescent male child was operated for Ileo-colic intussusception who later developed skin manifestations with microscopic hematuria and was diagnosed to be IgAV.
Conclusion: Our study emphasizes that Gastrointestinal involvement is one of system which should alert the clinician when to be vigilant and when to treat aggressively just like the severe renal, pulmonary and neurological involevement in IgA vasculitis.
Disclosure
None declared

P342

Corticosteroids alone in Kawasaki disease due to constraints: a retrospective analysis of data from resource-limited settings

D. Bhattarai[1], R. Baral[2], A. Pokharel[3], A. Neupane[4]
[1]Pediatric Immunology & Rheumatology, Advanced Centre for Immunology & Rheumatology, Kathmandu, [2]Pediatrics, Western Regional Hospital, Pokhara, [3]Otorhinolaryngology, Civil Hospital, [4]Pediatrics, Advanced Centre for Immunology & Rheumatology, Kathmandu, Nepal
Correspondence: D. Bhattarai
Pediatric Rheumatology, **23(2):** P342

Introduction: Though intravenous immunoglobulin (IVIg) is regarded as a gold standard for the treatment of Kawasaki disease (KD), corticosteroid is recently discussed with an interest. Due to a lack of prospective data, its effectiveness is still debatable as the primary mode of treatment.
Objectives: To study the effectiveness of corticosteroids in the treatment of KD
Methods: Clinical records of all children diagnosed with KD (as per AHA guidelines) in the only available pediatric rheumatology center in Nepal between August 2020 and February 2025 were retrieved and analyzed. The lead author (DB) has diagnosed or followed up on all cases. Demographics, clinical details, drugs, and outcomes were analyzed.
Results: A total of 117 cases of KD were diagnosed in the study period. Detailed clinical records could be found on 112 (95.72%) children. Of them, 94 (83.92%) were primarily diagnosed at our center whereas 18 (16.07%) were already diagnosed as cases of KD elsewhere and subsequently referred to us for possible complications. 102 (91.07%) were cases with classic KD. Though IVIg was offered as the primary treatment modality, only 75 (66.96%) were treated with it, which included all of our cases with atypical/incomplete KD, too. The remaining 37 (33.03%) could not afford it for various reasons, namely, the unavailability of IVIg locally at the time of illness, financial constraints (due to high cost), and social taboos. Among 65 classic KD, 6 had IVIg resistance or persistence of fever [2 had macrophage activation syndrome (MAS)]. 8 had coronary ectasia or aneurysm.
37 cases with KD (all classic KD) could not receive IVIg as a first modality of treatment (at our center or referring center) due to various socioeconomic constraints. They were offered an oral corticosteroid dose (0.75-1.5mg/kg/day) from a clinician as a desperate measure of treatment (along with naproxen). Only 5 of them had a persistent fever (without MAS) and 5 were diagnosed with coronary ectasia/aneurysm till 6 months follow up after the afebrile period. There was no significant difference between the children under IVIg or corticosteroids alone.
Conclusion: Due to the high cost and lesser availability of IVIg, resource-limited settings compel some patients to take corticosteroids alone despite being prescribed IVIg. Corticosteroids are less studied in clinical trials in KD. However, our results show promising results of steroids on KD.
Trial registration identifying number: Not applicable
Disclosure
None declared

P344

Behçet's disease — a case series from Georgia

G. Jajanidze[1,2]
[1]M.Iashvili Children Central Hospital, [2]Tbilisi state medical university, Tbilisi, Georgia
Correspondence: G. Jajanidze
Pediatric Rheumatology, **23(2):** P344

Introduction: Behçet's Disease — A Case Series from Georgi
Behçet's Disease, Vasculitis, Pediatric Rheumatology
Objectives: Behçet's disease is a variable-vessel vasculitis characterized by recurrent oral aphthae and various systemic manifestations, including ocular disease, skin lesions, gastrointestinal involvement, neurologic symptoms, vascular disease, and arthritis. Most clinical features of Behçet's syndrome are attributed to vasculitis. Among systemic vasculitides, Behçet's disease is unique for its ability to affect blood vessels of all sizes (small, medium, and large) and types (arterial and venous).
Methods: We present a retrospective case series of six pediatric patients diagnosed with Behçet's disease at a children's hospital in Georgia. Data collected included clinical presentation, gender, laboratory and imaging findings, treatment approaches, and management outcomes. Particular attention was paid to differences in clinical manifestations and disease severity by gender.
Results: Among the six patients, three (50%) were male and three female, with a mean age of 12.5 years. All patients presented with painful oral ulcers and gastrointestinal involvement. Erythema nodosum was observed in three patients—all female. Myalgia and

arthralgia were reported in five patients. One male patient developed central nervous system involvement, specifically venous sinus thrombosis. Optical coherence tomography (OCT) revealed progression of optic nerve swelling and bilateral visual field loss. The pathergy test was positive in only one male patient. HLA-B51 was tested in four patients and was positive in three males. One female patient had a known genetic predisposition.
Conclusion: This case series highlights the clinical heterogeneity of pediatric Behçet's disease. While all patients shared common features such as oral ulcers and gastrointestinal symptoms, male patients appeared to exhibit more severe and systemic complications.
Disclosure
None declared

P345
Eggerthella lenta down regulated flavone and flaconol biosynthesis promoted Kawasaki disease
H.-C. Kuo[1,2]
[1]Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, [2]College of Medicine, Chang Gung University, Taoyuan, Taiwan, Province of China
Correspondence: H.-C. Kuo
Pediatric Rheumatology, **23(2):** P345

Introduction: Kawasaki Disease (KD) is a multisystemic vasculitis of unknown etiology in children. The incidence of KD varies by geographic area and correlates with differences in gut microbiota patterns, with the highest incidence in Asian.
Objectives: This study aimed to investigate alterations in fecal microbiota and assess their relationship with systemic inflammation in KD patients.
Methods: A total of 59 patients and 55 matched controls were included. Fecal samples were collected at the onset of KD. The V3/V4 regions of 16S rDNA were sequenced using the MiSeq platform. PICRUSt 2 was used to analyze the potential functional pathways involved in gut dysbiosis.
Results: Alpha ($p<0.042$) and beta ($p<0.001$) diversity in KD were significantly decreased when compared to the control group. After multivariate regression, among the seven critical microbes, increased Bacteroides ovtaus ($p=0.016$) and decreased Eggerthella lenta ($p=0.014$) could also predict KD risk using receiver operating characteristic curve (ROC) analysis (Eggerthella lenta: area under the ROC curve, AUC=0.841, odds ratio=23.956; Bacteroides ovatus: AUC=0.816, odds ratio=31.365). Notably, Bacteroides ovatus was positively correlated with blood segment cells ($p=0.006$), but negatively correlated with blood lymphocytes ($p=0.013$). After multivariate regression, flavone and flavonol biosynthesis decreased in children with KD ($p<0.001$).
Conclusion: Our results indicated that both Bacteroides ovatus and Eggerthella lenta may deregulate flavone and flavonol biosynthesis, consequently modulating immune cells and potentially triggering KD. This study suggests that alterations in the gut microbiota are closely associated with immune responses and provides a new perspective on the etiology, pathogenesis, and treatment of KD.
Disclosure
None declared

P347
Cardiomyopathy and pulmonary embolism as initial clues to takayasu arteritis in a child: a case of diagnostic delay and therapeutic individualization
I. Arshynbek, A. Akhmambetova, Z. Mukusheva, M. Assylbekova
Pediatric Rheumatology, CF "University Medical Center", Astana, Kazakhstan
Correspondence: I. Arshynbek
Pediatric Rheumatology, **23(2):** P347

Introduction: Takayasu arteritis is a rare large-vessel vasculitis that often begins in adolescence, may mimic other diseases, and is more common in individuals of Asian descent. Our fourth-level referral center receives patients from across Kazakhstan; currently, around 30 children with Takayasu arteritis are under follow-up, highlighting the importance of early diagnosis and a multidisciplinary approach.
Objectives: To present a rare pediatric case of Takayasu arteritis with an atypical initial manifestation as dilated cardiomyopathy and bilateral pulmonary embolism, highlighting diagnostic complexity and individualized treatment approach.
Methods: A 14-year-old girl of Asian origin initially presented with ear pain and systemic symptoms, including fatigue and weight loss, which led to an initial suspicion of malignancy. After clinical deterioration, she was referred to a cardiology center, where she was diagnosed with dilated cardiomyopathy (EF 16%), bilateral pulmonary embolism, and Takayasu arteritis.
Results: At admission, the patient reported severe fatigue, weight loss (10 kg), appetite loss, dizziness, and subfebrile episodes. Initially evaluated for suspected lymphoma, she was later transferred to a cardiology center after clinical deterioration.Laboratory tests revealed elevated CRP (87 mg/L), NT-proBNP (21,838 pg/mL), D-dimer (16.84 mg/L), and anemia (Hb 78 g/L). Imaging confirmed bilateral pulmonary embolism with infarct pneumonia, a left ventricular thrombus, and angiographic signs of type V Takayasu arteritis. Involved vessels included the brachiocephalic trunk, both subclavian and renal arteries, the celiac trunk, abdominal aorta, and bilateral carotid arteries (with complete occlusion on the right). Optimal heart failure therapy was selected: sacubitril/valsartan 25 mg/day, bisoprolol 3.75 mg/day, spironolactone 50 mg/day, furosemide 40 mg/day, dopamine 3 mcg/kg/min, and warfarin 2.5 mg/day. In the rheumatology department, treatment was initiated with methylprednisolone 30 mg/day (with gradual tapering), mycophenolic acid 1500 mg/day, and biologic therapy with the IL-6 inhibitor tocilizumab at a dose of 8 mg/kg (320 mg IV every 28 days). The patient showed progressive improvement: normothermia, stabilized blood pressure, and improved cardiac function (EF up to 25%). Inflammatory markers significantly decreased: CRP to 1.7 mg/L, NT-proBNP to 4252 pg/mL, D-dimer to 0.48 mg/L, and Hb to 128 g/L.
Conclusion: This case illustrates an uncommon presentation of Takayasu arteritis in a child, initially mimicking malignancy and heart failure. Diagnosis was achieved through a multidisciplinary approach and imaging. The patient responded well to individualized therapy and remains under follow-up for continued biologic treatment. Consent to published had been obtained.
Disclosure
None declared

P348
Development of an international collaborative study group and registry for characterizing childhood-onset takayasu arteritis
J. Bistolarides[1], on behalf of International childhood-onset Takayasu Arteritis (IcTAK) Workgroup, M. Kasap Cüceoğlu[2], S. Gagne[3], M. Sestan[4], N. McPhate[5], K. Morishita[5], V. Sivaraman[6], L. Wagner-Weiner[7], M. Jelusic[4], D. Cabral[5], S. Ozen[2]
[1]Medical College of Wisconsin, Milwaukee, United States, [2]Hacettepe University, Ankara, Türkiye, [3]University of Pittsburgh, Pittsburgh, United States, [4]University of Zagreb School of Medicine, Zagreb, Croatia, [5]University of British Columbia, Vancouver, Canada, [6]Ohio State University, Columbus, [7]University of Chicago, Chicago, United States
Correspondence: J. Bistolarides
Pediatric Rheumatology, **23(2):** P348

Introduction: The rarity of childhood-onset Takayasu arteritis (c-TAK) has resulted in small cohorts for study that has limited the potential for evaluating its course and outcomes.
Objectives: To engage Pediatric Rheumatologists internationally to contribute patient data to a research network targeted to characterizing c-TAK and improving disease outcomes. This will be achieved through the following: Aim 1: Create an international c-TAK registry, Aim 2: Evaluate the performance of existing disease activity measures, and Aim 3: Create and validate a preliminary disease activity score specifically for c-TAK.
Methods: Member sites of Childhood Arthritis Rheumatology Research Alliance (CARRA) and Pediatric Rheumatology European Society (PReS) are invited to enroll patients in this c-TAK registry. The

registry is to capture children with a physician diagnosis of c-TAK aged ≤ 18 years at disease onset. Data entry is hosted on Research Electronic Data Capture (REDCap) platform. Registry data includes demographic characteristics, clinical symptoms, organ involvement, laboratory features, vascular imaging, treatment, physician global assessment (PGA) of disease activity, and the features needed to calculate the Pediatric Vasculitis Activity Score (PVAS), Indian Takayasu Activity Score (ITAS2010 and ITAS-A), and 2018 European League Against Rheumatism (EULAR) criteria for active large vessel vasculitis. The assessment of damage using the pediatric vasculitis damage index (PVDI) is collected at follow-up. Data is collected retrospectively from patient medical records at diagnosis, 12-months, and at the final visit on file beyond 15 months (if applicable).

Results: As of abstract submission, the registry has collected data on 72 patients from 12 countries and 31 unique clinical sites. Additional enrollment has begun at 40 other sites, including from 13 additional counties. To date the cohort comprises 80% females. The average age at diagnosis is 12.14 +/- 4.81 years; the average time to diagnosis after first symptoms is 7.53 +/- 13.07 months; 66% received intravenous pulse glucocorticoids (GC) at time of diagnosis, while 85% were started on oral GC. Primary treatments (n=63) prescribed at time of diagnosis include methotrexate (62%), anti-TNF biologic (27%) cyclophosphamide (24%), ongoing intermittent pulse IV GC (11%), and tocilizumab (11%). Secondary treatments included antihypertensives (54%) and anti-coagulants (48%).

Conclusion: Creation of an international c-TAK registry is feasible owing to global collaborations between member sites of CARRA and PReS, and the capabilities for electronic communications and data transmission. Registry data will improve knowledge of presenting symptoms and treatment of c-TAK and increase understanding of the value of current disease activity measures. The successful realization of further project aims is expected.

Disclosure

J. Bistolarides: None declared, M. Kasap Cüceoğlu: None declared, S. Gagne: None declared, M. Sestan: None declared, N. McPhate: None declared, K. Morishita: None declared, V. Sivaraman: None declared, L. Wagner-Weiner: None declared, M. Jelusic: None declared, D. Cabral: None declared, S. Ozen Consultant with: Novartis, SOBI, Amgen

P349

Painful subcutaneous edema is associated with early age at diagnosis in immunoglobulin a vasculitis patients: a multicenter study

L. V. Steuer[1], C. R. Doria [1], M. S. França[1], P. S. Marra [1], S. D. Cordoba[1], L. F. Forero[1], R. N. Machado[1], S. C. Farhat[1], G. Clemente [2], V. Curi[2], C. A. Len[2], L. M. Carvalho[3], F. H. Gomes[3], V. P. Ferriani[3], R. G. Almeida[4], F. R. Stztajnbok[4], L. M. Campos[1], A. M. Sallum[1], V. A. Balbi[1], N. E. Aikawa[1], B. O. Carneiro [1], M. Carneiro-Sampaio[1], K. T. Kozu[1], C. A. Silva[1]

[1]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, **[2]**Pediatric Rheumatology Unit, Universidade Federal de Sao Paulo, Sao Paulo, **[3]**Pediatric Rheumatology Unit, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, **[4]**Rheumatology Division, Instituto de Puericultura e Pediatria Martagão Gesteira, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Correspondence: L. V. Steuer

Pediatric Rheumatology, **23(2):** P349

Introduction: Painful subcutaneous edema (PSE) in children and adolescents with immunoglobulin A (IgA) vasculitis (IgAV) occurs at disease onset, mainly in lower and upper limbs. While this feature has been described in case reports and case series,[1,2] to our knowledge, no studies have evaluated the risk factors associated with the presence of PSE in a large IgAV population.

Objectives: To evaluate initial factors of IgAV associated with PSE and its outcomes in children and adolescents in a multicenter study.

Methods: A multicenter study involving four university referral centers in Brazil evaluated 686 children and adolescents (≤ 18 years-old) with IgAV at first 3 months after diagnosis. All patients fulfilled validated EULAR/PRINTO/PRES classification criteria for IgAV. The charts were systematically and retrospectively assessed for demographic data, initial clinical manifestations, laboratory exams and treatments. IgAV patients with PSE were compared to those without PSE. The study received appropriate ethics approval by all participating centers. This study was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (#2022/13837-5 to KK & MC-S) and (#2022/12925-8 to NEA & CAS).

Results: PSE was found in 219/686 (31.9%) of IgAV patients during the first 3 months. The sites were lower limbs 192/214 (89.7%), upper limbs 85/214 (39.7%), face 29/214(13.5%), scalp 5/214 (2.3%), back 3/214 (1.4%) and chest 2/214 (0.9%). Multiple localizations of PSE occurred in 81/214 (37.8%). Persistent PSE (≥6 weeks of duration) was found in 4/215 (2%) and recurrent PSE was found in 7/217 (3%). The median age at IgAV diagnosis was significantly lower in PSE patients compared to those without this manifestation [5.0 (1.25-14.8) vs. 6.3 (0.25-17.5) years, p=0.001]. There was a higher duration of purpura and/or petechiae in the PSE group [15 (1-90) vs. 14 (1-120) days, p=0.03] and a significantly higher frequency of petechiae (52.5% vs. 41.3%, p=0.01). Increased CRP was significantly higher in IgAV with PSE compared to without PSE (52.6% vs 41.1%, p=0.03), likewise thrombocytosis (>400.000/mm3) (43.8% vs 35.1%, p=0.04). Logistic regression demonstrated that only age at IgAV diagnosis was inversely associated with PSE (OR=0.986; 95% CI 0.981-0.992; p<0.00001).

Conclusion: PSE occurred in approximately one third of IgAV patients at disease onset, mainly located on lower and upper limbs, and diagnosed predominantly at early age. Recognizing PSE as part of the clinical spectrum of IgAV may help tailor treatment strategies, especially in cases with persistent/recurrent PSE, avoiding prolonged discomfort.

Disclosure

None declared

References

1. Shimizu A, Shimabukuro M, Shimizu M, Asai S, Tomizawa S, Hatakeyama S, Yamada Y. Painful subcutaneous edema of the lumbar region in IgA vasculitis. Pediatr Int. 2019;61(6):624–625.
2. Marcia M, Parodi E. Lumbar swelling and migrating edema in 3- and 4-year-old boys. SAGE Open Med Case Rep. 2022 25;10:2050313X221102112.

P350

Prolonged skin involvement distinguishes adolescent from childhood-onset iga vasculitis: a multicenter study

L. F. Forero[1], P. S. Marra [1], R. N. Machado[1], C. R. Doria [1], S. D. Cordoba[1], L. Vineyard Steuer[1], M. S. França[1], S. C. Farhat[1], I. M. Buscatti[1], G. Clemente [2], M. T. Terreri[2], M. Dantas[2], L. M. Carvalho[3], F. H. Gomes[3], N. Maronese[3], A. R. Fonseca[4], M. F. Rodrigues[4], A. Watanabe[1], L. M. Campos[1], A. M. Sallum[1], V. A. Balbi[1], N. E. Aikawa[1], V. S. Viana[1], L. R. Melo[1], C. A. Martinez[1], M. Carneiro-Sampaio[1], K. T. Kozu[1], C. A. Silva[1]

[1]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, **[2]**Pediatric Rheumatology Unit, Universidade Federal de Sao Paulo, Sao Paulo, **[3]**Pediatric Rheumatology Unit, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, **[4]**Rheumatology Division, Instituto de Puericultura e Pediatria Martagao Gesteira - Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Correspondence: L. Vineyard Steuer

Pediatric Rheumatology, **23(2):** P350

Introduction: Recently, a single-center study from Turkey on immunoglobulin A vasculitis (IgAV), formerly known as Henoch-Schönlein Purpura (HSP), demonstrated that adolescents exhibited more severe disease manifestations compared to children.[1] However, to the best of our knowledge, there is no multicenter study with a diverse ethnic background comparing demographic data, clinical and laboratory features, and treatments in children and adolescents.

Objectives: To compare demographic data, clinical and laboratory features, and treatments in children versus adolescents with IgAV/HSP in a large multicenter study.

Methods: A multicenter study involving four university and tertiary centers in Brazil evaluated 687 children and adolescents (≤ 18 years-old) with IgAV/HSP at first 3 months after diagnosis. All patients fulfilled the validated EULAR/PRINTO/PRES classification criteria for IgAV/HSP. The charts were retrospectively assessed for demographic data, initial clinical manifestations, laboratory tests and treatments. Data were compared between children (<10 years-old) and adolescents

(≥ 10 years-old), according to WHO age range definition.The study received appropriate ethics approval by all participating centers. This study was supported by grants from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (#2022/13837-5 to KK & MC-S) and (#2022/12925-8 to NEA & CAS).

Results: IgAV/HSP was diagnosed in 599/687 (87%) children [5.33 (0.88-9.91) years-old] and 88/687 (13%) adolescents [11.33 (10-17.5) years-old]. The median duration of purpura/petechiae was significantly lower in children compared to adolescents [14 (1-120) vs. 15 (2-90) days, p=0.04]. The frequency of persistent purpura/petechiae (defined as ≥6 weeks of duration)[2] was significantly reduced in the former group (7.2% vs. 19.5%, p=0.002), as well as the frequency of gastrointestinal bleeding (17% vs. 34.1%, p=0.01) and proteinuria (49.7% vs. 84%, p=0.002). In contrast, the frequencies of arthritis/arthralgia (82.7% vs. 73%, p=0.03) and orchitis (16.6% vs. 4.8%, p=0.04) were significantly higher in children. Further analysis of laboratory tests showed that the median value of serum IgA was significantly lower in children than in adolescents [179.1 (40-1002.0) vs. 279.0 (104.0-488.0) mg/dL, p=0.01], whereas thrombocytosis was higher (40.1% vs. 23%, p=0.007). Logistic regression demonstrated that persistent purpura/petechiae after IgAV/HSP diagnosis (OR=18.337; 95% CI 1.245-270.137; p=0.034) was the only independently associated variable with dependent variable (adolescent).

Conclusion: In this large multicenter cohort, IgAV/HSP onset occurred rarely at adolescence, but notably associated with a more prominent disease course compared to childhood onset. Prolonged purpura/petechiae after IgAV/HSP diagnosis was associated with adolescent-onset IgAV/HSP, reinforcing the need for vigilant monitoring in this subgroup.

Disclosure

None declared

References

1. Coşkun S, Güngörer V, Ekici Tekin Z, Çelikel E, Kurt T, Tekgöz N, Sezer M, Karagöl C, Kaplan MM, Polat MC, Öner N, Acar BÇ. Preadolescent-versus adolescent-onset immunoglobulin A vasculitis: The impact of age on prognosis. Pediatr Int. 2023;65:e15426.
2. Roman C, Dima B, Muyshont L, Schurmans T, Gilliaux O. Indications and efficiency of dapsone in IgA vasculitis (Henoch-Schonlein purpura): case series and a review of the literature. Eur J Pediatr 2019;178:1275–1281.

P353

Unraveling relapse risk in pediatric iga vasculitis: clinical predictors from a multi-center cohort

D. Turudic[1], M. Sestan[1], N. Kifer[1], M. Held[2], S. Srsen[3], M. Batnozic Varga[4], M. Frkovic[1], A. Gagro[5], M. Jelusic[1]
[1]University Hospital Centre Zagreb, Department of Paediatrics, University of Zagreb School of Medicine, [2]University Hospital Centre Zagreb, Department of Internal Medicine, University of Zagreb School of Medicine, Zagreb, [3]University Hospital Centre Split, Department of Paediatrics, University of Split School of Medicine, Split, [4]University Hospital Centre Osijek, Department of Paediatrics, University of Osijek School of Medicine, Osijek, [5]Children's Hospital Zagreb, University of Osijek, Medical Faculty Osijek, Zagreb, Croatia
Correspondence: M. Sestan
Pediatric Rheumatology, **23(2):** P353

Introduction: IgA vasculitis (IgAV), the most prevalent form of childhood vasculitis, is generally self-limiting but may follow a relapsing course in a significant subset of patients. Relapses can lead to prolonged morbidity, increased healthcare utilization, and, in some cases, progressive organ involvement—particularly of the kidneys. Early identification of children at higher risk of relapse is crucial for guiding monitoring strategies, optimizing treatment decisions, and potentially improving long-term outcomes.

Objectives: This study aimed to identify clinical and laboratory predictors of relapse using univariate time-to-event and categorical outcome analyses.

Methods: This study combined retrospective and prospective data collection, encompassing 808 children diagnosed with IgAV according to EULAR/PRINTO/PRES criteria between 2009 and 2024 across five tertiary pediatric rheumatology centers. Of these, 184 patients were enrolled prospectively. Two univariate statistical approaches were applied for retrospective cohort: (1) Cox proportional hazards models, with time-varying coefficients where needed, assessed time to first relapse; (2) Multinomial logistic regression categorized patients by relapse frequency (no relapse, single relapse, or multiple relapses), using "no relapse" as
Reference. Univariate Andersen-Gill Cox proportional hazards models were used to evaluate associations between clinical variables and time to relapse in prospective cohort. Covariates included skin involvement, arthritis, gastrointestinal (GI) involvement, serum calprotectin levels, kidney involvement, hematuria, proteinuria, and complement components (C3, C4, CH50).

Results: A total of 144 patients experienced documented relapses (male-to-female ratio: 0.64:1), with a median age of 6.12 years (95% CI: 4.56–7.69). The median time to first relapse was 1.23 months. In Cox models, early clinical features including severe rash (HR = 27.99, 95% CI: 20.1–39.0), nephritis (HR = 27.69, 95% CI: 19.8–38.7), hematuria (HR = 25.73, 95% CI: 18.7–35.5), and long-term rash (HR = 3625.63, 95% CI: 1260–10429) were strongly associated with relapse and demonstrated time-dependent effects. Hemoglobin was associated with higher early hazard (HR = 1.03, 95% CI: 1.01–1.06, p < 0.001), while IgG (HR = 0.92, 95% CI: 0.87–0.98) and proteinuria (HR = 0.57, 95% CI: 0.37–0.88) were associated with reduced relapse risk. In multinomial regression, predictors of both single and multiple relapses included age (OR for multiple = 1.14, 95% CI: 1.05–1.24), severe rash, nephritis, hematuria, and hands rash (all p < 0.05). Long-term rash was the strongest predictor of relapse severity (OR = 9.75 for multiple relapses, 95% CI: 5.43–17.51). Face rash was associated with single relapse only (OR = 3.22, 95% CI: 1.46–7.10), and ASTO was associated with slightly lower risk in both Cox (HR = 0.999, p = 0.025) and multinomial models. In prospective cohort severe skin involvement was strongly associated with a higher hazard of relapse (HR = 11.72; 95% CI: 4.94–27.84; p < 0.001). Elevated serum calprotectin levels were also linked to increased relapse risk (HR = 1.001 per unit increase; 95% CI: 1.000–1.001; p < 0.001). In contrast, the presence of arthritis (HR = 0.11; 95% CI: 0.03–0.46; p = 0.0023) and GI involvement (HR = 0.27; 95% CI: 0.08–0.88; p = 0.0289) were associated with a significantly reduced relapse risk.

Conclusion: Severe skin involvement, long term rash, nephritis and elevated serum calprotectin levels are significant predictors of relapse in pediatric IgAV, while arthritis and GI symptoms appear protective. These findings underline the potential role of serum calprotectin as a biomarker and support individualized follow-up approaches based on clinical presentation at diagnosis. This work was supported by Croatian Science Foundation project HRZZ-IP-2024-05-6848.

Disclosure

None declared

P355

Variation in treatment approaches in iga-vasculitis among pediatricians and pediatric rheumatologists: a cross-sectional international survey

T. Elbaz[1], Y. Illous[1], B. Kandell[2], S. Ozen[3], M. Heshin-Bekenstein[1,4]
[1]School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv University, [2]Statistics, The Academic College of Tel Aviv-Yafo, Tel Aviv, Israel, [3]Pediatric Rheumatology, Hacettepe University, Ankara, Turks and Caicos Islands, [4]Pediatric Rheumatology Service, Dana Children's Hospital of Tel Aviv Medical Center, Tel Aviv, Israel
Correspondence: M. Heshin-Bekenstein
Pediatric Rheumatology, **23(2):** P355

Introduction: IgA Vasculitis (IgAV) is the most common small-vessel vasculitis in children. Although there is no evidence-based recommendations for treating IgAV, the European SHARE recommendations published in 2019 provided international expert consensus for its treatment.

Objectives: To explore the treatment and disease follow-up approaches in IgA Vasculitis among pediatricians and pediatric rheumatologists throughout the world, based on the disease presentation, including organ involvement and severity.

Methods: A 24-question electronic, cross sectional international survey was sent to pediatricians and pediatric rheumatologists through electronic platforms. Responses were anonymous and voluntary.

Responses were analyzed for variability by geographic location, gender, experience, subspecialty and practice setting (hospital vs. clinic). 196 pediatricians were included in the analysis, of which 123 were pediatric rheumatologists.
Results: Geographic variability, gender, subspecialty, practice setting and clinical experience were all found to significantly affect the choice of treatment for HSP. Geographic location showed the greatest variability, followed by subspecialty. For example, in cases of severe gastrointestinal (GI) symptoms, the administration of high-dose Methylprednisolone IV at 30 mg/kg/day for three days, followed by tapering was more common in North America compared to Asia and Europe (p=0.043). For mild GI symptoms, pediatric rheumatologists were less likely to choose NSAIDs compared to general pediatricians (p=0.024) and preferred hydration and rest (p=0.024). Practice setting influenced treatment choices, with hospital-based physicians favoring IV steroids for severe GI and renal involvement more than clinic-based physicians (p=0.032). Gender was shown to have a limited impact, with minor differences noted in specific GI treatments. Clinical experience primarily affected steroid tapering duration, with more experienced physicians favoring shorter tapering periods (p=0.03).
Conclusion: To the best of our knowledge, this is the first international study to assess real-world treatment approaches to IgA vasculitis in children. The study reveals significant variability in the treatment p
References for IgAV, affected primarily by geographic location and subspecialty, with lesser contribution of clinical setting, years of practice and gender. These findings highlight the need to develop standardized, evidence-based clinical guidelines to the treatment approach for IgAV, in order to reduce variability and improve the care of children with IgA-Vasculitis.
Disclosure
None declared

References
1. Ozen S et al. European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative. Rheumatology. 2019 Sep 1;58(9):1607–16.
2. Day C, Shute R. UK Kidney Association guideline review:'The initial management of IgA vasculitis (Henoch-Schönlein purpura) in children and young people'in conjunction with 'The management of complications-associated IgA vasculitis (Henoch-Schönlein purpura) in children and young people'. Archives of Disease in Childhood-Education and Practice. 2024 Aug 1;109(4):196–201.

P356

Cluster analysis of igav patients determines an older group associated with a more severe disease course

N. Kifer[1], D. Kifer[2], M. Sestan[1], S. Srsen[3], M. Frkovic[1], A. Gagro[4], M. Jelusic[1]
[1]University of Zagreb School of Medicine, UHC Zagreb, [2]University of Zagreb Faculty of Pharmacy and Biochemistry, Zagreb, [3]University of Split School of Medicine, UHC Split, Split, [4]Children's Hospital Zagreb, University of Osijek, Medical Faculty Osijek, Zagreb, Croatia
Correspondence: N. Kifer
Pediatric Rheumatology, **23(2):** P356

Introduction: IgA vasculitis (IgAV) is generally self-limiting with a favorable prognosis. However, a number of patients develop acute and chronic complications due to gastrointestinal and renal involvement.
Objectives: To perform a cluster analysis to determine separate subgroups depending upon clinical and laboratory parameters.
Methods: Patients included were diagnosed with IgAV and IgAVN based on EULAR/PRINTO/PRES criteria in the period from 2009 to 2024 in three largest Croatian pediatric clinics. The parameters used for cluster detemination included: joints, gastrointestinal and renal involvement, generalized rash, CRP, ESR, C3, C4, presence of blood in stool, and hematuria. Clustering was conducted in R using Ward's D linkage, with distance increasing for each discordant response. Fisher's exact test and Wilcoxon's rank-sum test were used to analyze the associations between the number of relapses and age at diagnosis across clusters.
Results: The study included 798 patients, of whom 50% were male. The median age at diagnosis was 6.4 years (IQR: 4.5-8.6 years). Cluster analysis of response patterns identified five distinct subgroups. The first cluster was the only cluster where all exhibited renal disease, most of them had arthritis and around half had gastrointestinal (GI) symptoms. This group had the highest burden of multi-organ involvement. The second and smallest cluster was comprised of patients mostly with elevated CRP, and occasionally GI disease, without arthritis and renal disease. The third and largest group consisted entirely of patients with gastrointestinal involvement and almost all had arthritis. The fourth cluster was comprised of patients with arthritis, along with elevated ESR and CRP levels. The fifth group included patients presenting primarily with arthritis, either in isolation or accompanied by elevated CRP, only seldom with generalized rash but without other systemic involvement. Generalized skin rash, elevated C3 and C4 were observed across all five groups. Notably, the first cluster had a significantly higher relapse rate compared to the other groups (32% vs. 14%, p<0.001), as well as a greater proportion of patients aged 7 years or older (59% vs. 36%, p<0.001), with a median age of 7.6 years (IQR 5.7–11.5). In contrast, the fourth cluster had the fewest relapses and included the youngest patients, with a median age of 5.3 years (IQR 4.1–6.9).
Conclusion: This cluster-based analysis highlights the clinical heterogeneity of IgAV, identifying five distinct patient subgroups with differing patterns of organ involvement. Importantly, the subgroup with renal involvement was associated with older age at diagnosis, and a significantly higher relapse rate, whereas the group with isolated arthritis and elevated inflammatory markers experienced fewer relapses. These findings may support more tailored approaches to disease monitoring and management based on early clinical presentation.
This work was supported by Croatian Science Foundation project HRZZ-IP-2024-05-6848
Disclosure
None declared

P357

Indication for skin biopsies in patients with iga vasculitis – results from the juvenile inflammatory rheumatism (JIR)-clips network

N. Kifer[1], M. Jelusic[1], T. Giani[2], A. Snipaitiene[3], M. Ganeva[4], F. Hofer[5], M. Hofer[6], T. Kallinich[7,8,9], D. Gorczyca[7], on behalf of JIR-CLiPS network
[1]Department of Pediatrics, University of Zagreb School of Medicine, UHC Zagreb, Zagreb, Croatia, [2]Department of Pediatrics, Rheumatology Unit, Meyer Children's Hospital IRCCS, Florence, Italy, [3]Department of Pediatrics, Lithuanian University of Health Sciences, Kaunas, Lithuania, [4]Department of Pediatric Rheumatology, Medical University Sofia, Sofia, Bulgaria, [5]Fondation Rhumatismes-Enfants-Suisse, Lausanne, [6]Department of Pediatrics, Hôpital Riviera-Chablais, Rennaz, Switzerland, [7]Charité Universitätsmedizin Berlin, [8]Deutsches Rheuma-Forschungszentrum, an institute of the Leibniz Association, Berlin, [9]German Center for Child and Adolescent Health, Berlin site, Germany
Correspondence: N. Kifer
Pediatric Rheumatology, **23(2):** P357

Introduction: Severity and duration of skin manifestations of IgA vasculitis (IgAV) are linked to prognosis and treatment choices. No universally accepted guidelines for performing a skin biopsy exists.
Objectives: The JIR-CliPS network collects real-life clinical practice strategies (CliPS) to highlight variations in diagnosing and managing IgA vasculitis, with a focus on atypical skin rashes, biopsy indications, and the assessment of skin severity.
Methods: An online questionnaire was used to investigate diagnostic approaches in cases with IgAV with atypical skin manifestations. Clustering was conducted in R using Ward's D linkage, with distance increasing for each discordant response. The project is supported by COST (European Cooperation in Science and Technology) action CA21168.
Results: From September 2022 to January 2025, a total of 111 responses were collected from physicians across 41 different countries, mostly pediatric rheumatologists (83%). This analysis focuses on the indication to perform skin biopsies in various clinical scenarios. 79% perform biopsies in recurrent atypical rash, 66% in atypical persisting rash, 47% in atypical rash at onset, 47% in diffuse atypical rash at onset, 29% in recurrent typical rash, 21% in typical persisting rash, 9% in diffuse typical rash at onset, and 5% in all typical rash at onset.

Cluster analysis of the response patterns revealed six distinct subgroups. Group 1: The largest subgroup, selecting 4-8 scenarios. Nearly all chose atypical rash at onset, which we considered to also include recurrent, diffuse, and prolonged (>4 weeks) atypical rashes. Most included also recurrent typical rash and 14% selected all 8 scenarios. Group 2: Selected biopsy for all four atypical rash scenarios. Group 3: The smallest group, choosing 3 scenarios: diffuse atypical rash at onset, prolonged atypical rash, and recurrent atypical rash. A few chose a fourth indication – prolonged typical rash. Group 4: Selected 2-5 indications, always including recurrent typical and atypical rash and frequently prolonged atypical rash. Group 5: Chose 1-2 scenarios, consistently including prolonged atypical rash and in nearly half recurrent atypical rash. Group 6: Chose 1-2 indications, predominately recurrent atypical rash and sometimes diffuse atypical rash. To assess participants' perceptions of skin changes, they were asked what they consider to be severe changes. Most cited rash affecting >75% BSA (90%), >50% BSA (76%), persistent rash (55%), recurrent rash (28%), and finally any atypical rash (20%). Interestingly, those who would biopsy recurrent typical rash were more likely to associate severity with recurrence (p=0,034).

Conclusion: Physicians showed diverse approaches to performing skin biopsies in suspected IgA vasculitis with isolated skin involvement as well as diverse severe skin definiton. Six distinct clusters emerged, reflecting differing indications for biopsy in diagnosing IgAV.

Disclosure

None declared

P358

Primary central nervous system vasculitis: a case series

N. Kara Çanlıoğlu, S. Atamyıldız Uçar, E. Tunce, B. Sözeri
Pediatric Rheumatology, Ümraniye Training and Research Hospital, Istanbul, Türkiye
Correspondence: S. Atamyıldız Uçar
Pediatric Rheumatology, **23(2):** P358

Introduction: Primary central nervous system vasculitis (PCNSV) is a rare, severe condition that can lead to significant neurological damage, including stroke, seizures, and headaches. It involves inflammation of the brain and spinal cord's blood vessels, resulting in various clinical symptoms.

Objectives: This study aimed to describe the clinical, laboratory, and radiological characteristics of pediatric patients diagnosed with primary CNS vasculitis, as well as to evaluate the treatment strategies and outcomes. The focus was on the importance of early diagnosis and appropriate management to prevent further neurological damage.

Methods: We performed a retrospective review of seven pediatric patients diagnosed with PCNSV at Ümraniye Training and Research Hospital between January 2016 and May 2025. Clinical features, laboratory results, and imaging studies were analyzed. Laboratory tests included C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lupus anticoagulant, anti-beta2 glycoprotein, anti-cardiolipin antibodies, and complement C3 and C4 levels. Imaging studies, such as Magnetic resonance imaging (MRI) and Magnetic resonance angiography (MRA), were conducted to assess vascular involvement.

Results: The mean age of the patients was 7.5 years (range: 1.5–14 years). Among 75 rare vasculitis cases followed in our clinic, seven (0.089%) were diagnosed with PCNSV. The most common symptoms were acute headache and focal neurological deficits, especially hemiparesis [1]. Six patients presented with hemiparesis and two with headache.

Inflammatory markers (CRP and ESR) were negative in all patients. D-dimer was elevated in four cases, and vWF antigen levels were high in two (>550 ng/ml, 160%). All patients tested negative for lupus anticoagulants, anti-beta2 glycoprotein, and anti-cardiolipin antibodies. anti-nuclear antibodies were positive at a 1/100 titer in two cases. Complement C3/C4 levels were normal, and anti-neutrophil cytoplasmic antibodies were negative in all.

7 patients had positive angiography. Stenosis was found in the right internal carotid and middle cerebral artery (1), left internal cerebral artery (1), right superior and posterior inferior cerebellar arteries (1), and left posterior cerebral artery (1). One had lenticulostriate artery dilation due to reperfusion. Another had partial thrombosis in the right transverse and sigmoid sinuses and jugular vein on venography. In the angiography-negative case, MRI revealed ischemia extending from periventricular white matter to basal ganglia.

All patients were treated with enoxaparin (200 IU/kg/day) and corticosteroids; three received pulse steroids. Azathioprine was added to three patients. Currently, five are in remission and two remain under treatment.

Induction therapy with cyclophosphamide and corticosteroids, followed by maintenance with mycophenolate mofetil or azathioprine, has been reported as effective [3]. Similarly, we achieved remission in high-risk patients with glucocorticoids and azathioprine.

Conclusion: In conclusion, PCNSV is a rare, difficult-to-diagnose condition that should always be considered in children with headaches or stroke-like symptoms.

Disclosure

None declared

References

1. Benseler, S., & Schneider, R. (2004). Central nervous system vasculitis in children. Current Opinion in Rheumatology, 16(1), 43–50.
2. Salvarani C, Hunder GG, Brown RD Jr. Primary Central Nervous System Vasculitis. N Engl J Med. 2024 Sep 19;391(11):1028–1037.

P359

Features of the modern course of anca-associated systemic vasculitis in children

O. A. Oshlianska[1,2], K. A. Yats[2]
[1]of pediatrics, pediatric infectious diseases, immunology and allergology, Shupyk National Healthcare University of Ukraine, [2] pediatric, State Institution "Ukrainian Center of Maternity and Childhood of the National Academy of Medical Sciences of Ukraine", Kyiv, Ukraine
Correspondence: O. A. Oshlianska
Pediatric Rheumatology, **23(2):** P359

Introduction: Systemic vasculitis in children is a rare pathology. According to a survey by the Association of Pediatric Rheumatologists of Ukraine, only 36 cases in 2024 were under the supervision of pediatric rheumatologists in Ukraine.

Objectives: Analysis of the diagnosis problem and pathomorphosis of pediatric ANCA-associated vasculitis (ANCA-SV) in Ukraine.

Methods: A single-center retrospective clinical study of the course of 15 ANCA-associated systemic vasculitis (ANCA-SV) were managed in 2015-24 years (activity indicators and catamnesis data). 12 cases met the diagnosis of granulomatosis with polyangiitis according to the ACR classification criteria (2022) had received 9.08 points (4-13), 1 eosinophilic granulomatosis with polyangiitis, 1 micropolyangiitis, 1 case was considered as unspecified vasculitis.

Results: The majority of patients with ANCA-SV were girls (11/4), the average age of onset was 13.1 years (6-16), the time to diagnosis was 14.42 months (1-71). Most patients had constitutional symptoms at onset (86.6% fever, 60% weight loss). Respiratory tract diseases (66.6% nasal and/or oral mucosal ulcers, 26.6% cartilage destruction, 66.6% sinusitis) was the first frequent manifestation, a subpharyngeal abscess developed later in 1 patient. Hearing impairment was noted in 6 cases. Lung lesions were often observed (73.3% interstitial lesions, 40% cavities and infiltrates), 1 case was complicated by pneumothorax. Gastrointestinal tract was affected in 40% of patients, 1/2 of them with bleeding. 1 patient suffered from cerebrovasculitis, 1 had craniofacial neuritis, 1 - orbital disease, multifocal mononeuritis was registered in 2 cases. 66.6% of patients had arthritis, ¼ complained of myalgia. In 7 patients manifestations of cutaneous vasculitis were noted, in 2 - toes gangrene, in 2 - venous thrombosis. Glomerulonephritis was observed in 12 patients (80%, only in 2 of them a kidney biopsy was performed). A biopsy of other localizations (lungs, bone) was performed in other 2 patients. cANCA was detected in 10 cases, pANCA - in 4 cases, 1 patient was not performed. BVAS at the time of diagnosis was 14.66±0.84 (7-22), PVAS 13.28±1.23 (9-19). Corticosteroids pulse therapy combined with cyclophosphamide was used as induction therapy in 8 cases (53.53%), rituximab was added in 5 cases (33.3%). Cyclophosphamide prescribed as maintenance DMARD in 12 patients (80%), in 4 (26.66) mycophenolate mofetil had used. Analysis of the subsequent course of ANCA-SV showed that remission was

achieved after 6 months. in 9 cases (60%, BVAS 0-3), 2 had relapse, 2 were fatal (pulmonary hemorrhage, stroke), data is not yet known about 2 cases.
Conclusion: Despite modern diagnostic capabilities pediatric ANCA-SV are not always detected in a timely manner. Treatment of them in children in Ukraine complies with international guidelines, requires improvement of intensive therapy in cases with complications.
Disclosure
None declared

P361

Low dose aspirin at treatment initiation in kawasaki disease : retrospective analysis of 5 years data

P. Pal, A. Mukherjee, J. Bathia, R. Pratima, A. Nandi, R. Singh
Pediatrics, Institute of Child Health Kolkata, Kolkata, India
Correspondence: P. Pal
Pediatric Rheumatology, **23(2):** P361

Introduction: The cornerstone of initial treatment for Kawasaki Disease (KD) is IVIG & aspirin. However, globally there is non uniformity in the initial aspirin dosage used. In the U.S., high-dose aspirin (80–100 mg/kg/day) is recommended, while Japan and Western Europe uses 30–50 mg/kg/day. The Royal Children's Hospital, Melbourne uses a much lower dose of 5 mg/kg/day from the start.Once the fever resolves for 48 hours, aspirin is reduced to a low dose (3–5 mg/kg/day) for its anti-platelet effect, continued until coronary artery (CA) abnormalities are no longer seen on echocardiography.At our centre, the practice is to start treatment with IVIG (2g/kg) and low-dose aspirin (5 mg/kg/day) from the beginning, rational being that IVIG is the principal anti-inflammatory agent in KD and higher doses of aspirin causes more side effects.
Objectives: To study treatment response in KD patients receiving low dose of aspirin(3-5mg/kg) with 2gm/kg IVIg at treatment initiation in terms of fever defervescence and normalisation of inflammatory markers.
Methods: Observational cross-sectional study on KD cases diagnosed according to AHA 2017 guidelines between 2019-2025. Persistence of fever and CRP values after 36 hours of completion of IVIg infusion were noted.
Exclusion criteria is 1)Patients receiving high dose aspirin @>30mg/kg 2)Patients receiving Infliximab or steroids as part of initial intensification therapy.
Results:
166 KD patients were admitted during the study period. Since 14 patients data were incomplete and 72 were excluded on the basis of exclusion criteria, 80 patients formed the study population who received only IVIG and low dose aspirin. Of these IVIG resistance were noted in 10 patients ie. 12.5%.
All patients irrespective of IVIg resistance status showed significant decrease in CRP values although the percentage varied.
Conclusion: The reported incidence of IVIg resistance globally is 10-20%, from centers using a higher initial dose of aspirin. The incidence of IVIg resistance in our cohort with low dose aspirin was similar. This observational study shows that the dose of initial aspirin usage has minimal effect in lowering the inflammation in KD. The incidence of fever defervescence and lowering of CRP in our low aspirin group corresponded to data available globally in which higher doses of aspirin are conventionally used.
Drawbacks:
Small sample size from a single center without any control group. We didnot compare the incidence in coronary artery aneurysm formation in our cohort with data from the moderate or high dose aspirin groups.
Trial registration identifying number: CTRI/2024/06/06827
Disclosure
None declared

P362

Patterns of vascular involvement in childhood takayasu arteritis

G. Clemente[1,2,3], A. Cheng[1,2], E. Go[4], K. Morishita[5], D. Cabral[5], D. Noone[6], S. Benseler[7], R. Yeung[1,2] on behalf of On behalf of the PedVas Initiative
[1]Division of Rheumatology, [2]Cell and Systems Biology Research Program, The Hospital for Sick Children (SickKids), Toronto, Canada, [3]Department of Pediatrics, Federal University of Sao Paulo, Sao Paulo, Brazil, [4]Children's Healthcare of Atlanta, Scottish Rite Hospital, Atlanta, United States, [5]Department of Pediatrics, University of British Columbia, Vancouver, [6]Department of Pediatrics, Stollery Children's Hospital, Edmonton, [7]Department of Pediatrics, Alberta Children Hospital, Calgary, Canada
Correspondence: S. Benseler
Pediatric Rheumatology, **23(2):** P362

Introduction: Patients with childhood-onset Takayasu arteritis (c-TAK) exhibit heterogeneous phenotypes, and therefore, identifying patient subsets is crucial for improving diagnosis and enabling personalized treatment.
Objectives: The aim of this study is to determine patterns of blood vessel involvement in c-TAK using data-driven, unsupervised machine learning approach.
Methods: An inception cohort study with c-TAK patients from 22 International centers was conducted using imaging data at time of diagnosis. Multi-layer non-negative matrix factorization (NMF), a dimensionality reduction technique that identifies summary indicators, was applied to detect signatures of co-involved vessels. Following the first-level NMF, a second-level NMF was conducted using the first-level scores. Patients were then assigned to groups based on their highest-scoring signature, and clinical associations were evaluated. Stability was assessed iteratively by rerunning the analysis, excluding one patient at a time. Additionally, comparisons with a previous TAK angiographic classification [1] were analyzed using χ^2 test.
Results: Seventy-seven c-TAK patients were included. The median age at diagnosis was 13 years, and 68% were female. Three subgroups of vessel involvement were found using NMF-based pattern recognition framework: Arch - represented mostly by the involvement of aortic arch (which included ascending aorta), aortic branches, and with less contributions from the descending aorta (thoracic and abdominal segments); Mid-aorta - included mainly descending aorta, renal arteries, and splanchnic vessels; and Diffuse - the entire aorta and all its branches plus the pulmonary arteries. Clustering solutions remained consistent across perturbed datasets, indicating accurate and stable patient groupings.
These subgroups differed significantly in the prevalence of meaningful clinical features and management approaches. Stroke (p=0.041), decreased blood pressure in the upper limbs (p=0.010), aneurysms (p=0.045), and use of antiplatelets (p=0.038) were more prevalent in patients with the Aortic arch pattern. Systemic hypertension (p=0.001) and use of antihypertensives (p=0.049) were more common in the Mid-aorta group. Constitutional symptoms (p=0.030) and limb claudication (p=0.013) were more frequently observed in patients with the Diffuse pattern.
Lastly, there was an overlap between our Aortic arch pattern and Mid-aorta patterns with previous classification (Goel et al), but the Diffuse subgroup was unique.
Conclusion: The new c-TAK patterns, identified through a data-driven approach, defined clinically relevant and recognizable subgroups that may improve diagnosis, guide management, and ultimately impact disease outcomes.
Disclosure
None declared

Reference

1. Goel R, Gribbons KB, Carette S, et al. Derivation of an angiographically based classification system in Takayasu's arteritis: an observational study from India and North America. Rheumatology (Oxford). 2020;59(5):1118-27.

P363

An observational study of children with severe gastrointestinal manifestations in henoch schonlein purpura treated with single dose cyclophosphamide

R. Singh, A. Nandi, R. P. Goud, J. N. Bathia, P. Pal
Pediatric rheumatology, Institute of Child Health, kolkata, India
Correspondence: P. Pal
Pediatric Rheumatology, **23(2):** P363

Introduction: Henoch-Schonönlein Purpura (HSP), also known as IgA vasculitis is a small vessel vasculitis. Patient generally presents with the classic tetrad of rashes, poly-arthralgia, abdominal pain, and renal disease. Gastrointestinal involvement colicky abdominal pain, vomiting, intussusception, hemorrhage, ileal perforation. Intravenous corticosteroids are initial treatment for GI manifestation, since enteral absorption altered due to submucosal edema. Cyclophosphamide is a cytotoxic immunosuppressant that can be used in treatment of HSP with cerebral vasculitis, pulmonary hemorrhage and severe GI involvement. Single dose of i.v cyclophosphamide may be beneficial in HSP with severe GI involvement non responsive to high dose steroids.
Objectives: TO STUDY EFFECT OF SINGLE DOSE CYCLOPHOSPHAMIDE IN CHILDREN WITH SEVERE GASTROINTESTINAL MANIFESTATIONS IN HENOCH SCHONLEIN PURPURA
Methods: Retrospective observational study on patients with gastrointestinal bleeding in HSP despite on pulse dose methyl prednisolone, further treated with single dose (500mg/m2) intravenous cyclophosphamide.
Results: In this case series, 12 children (2 girl and 10 boys) aged 6-15 years with HSP who developed gastrointestinal bleeding resistant to both 2mg/kg or pulse (10-30mg/kg) intravenous methyl prednisolone responded to single dose (500mg/m2) i.v cyclophosphamide.
Single dose cyclophosphamide was given at a median duration of 12 day of illness.
1 patient developed alopecia 3 weeks post cyclophosphamide infusion and 1 patient developed secondary hospital acquired infection during hospital stay. All patients responded to single dose i.v cyclophosphamide with no further episodes of gastrointestinal bleed. None of them neither required surgical intervention nor developed any further GI bleeding following treatment with cyclophosphamide.
Conclusion: Single dose of i.v cyclophosphamide may be beneficial in HSP with severe GI involvement non responsive to high dose steroids.
Disclosure
None declared

P364

Coronary thrombosis in Kawasaki disease: comparative data pre & post covid period

R. Singh, A. Nandi, R. P. Goud, J. N. Bathia, P. Pal
Pediatric Rheumatology, Institute of child health, Kolkata, India
Correspondence: P. Pal
Pediatric Rheumatology, **23(2):** P364

Introduction: Coronary thrombosis is a well described complication in Kawasaki disease (KD), usually in giant coronary aneurysms (CAA) after 2 weeks. Following the Covid pandemic, there has been a shift in clinical presentations of different diseases. This case series of 6 patients over 17 years with multiple CAA & thrombus aims to compare the pattern of coronary thrombosis before and following the pandemic.
Objectives: A comparative analysis of Kawasaki disease cases from the pre- and post-COVID-19 eras was conducted to evaluate potential differences in clinical presentation, duration of illness, incidence of thrombus formation, and associated prognosis
Methods: PRE COVID PERIOD (2007- 2019) :
CASE 1: 10 months girl presented on day 18 of fever. Diagnosed as complete KD, echo showed giant aneurysm in LMCA, distal RCA, LAD with clot. Treated with IVIG, oral steroid, heparin, alteplase. However during alteplase infusion baby succumbed to death due to myocardial infarction.
CASE 2: 6 weeks old male with KD shock. On day 14 had proximal LAD giant aneurysm(+14.9Z), LMCA and RCA ectasias. IVIG, infliximab. Echo 7 days later showed a thrombus in LAD. LMWH 2mg/kg was initiated. Follow up showed dissolution of clot and regression of aneurysms by 2 years.
CASE 3: 2-year 3-month male with KD shock presented on day 5 of fever. Child treated with IVIG and Aspirin, and later Infliximab due to increasing size of LMCA and LAD aneurysm. But 20 days later child develop LAD thrombus. Child treated with LMWH and aspirin. F/U Echo after 2 months later showed resolution of thrombus and regression of aneurysms.
POST COVID PERIOD (2020- present day):
CASE 4: A 3-month-old boy, with fever for 26 days, giant aneurysm in LAD with thrombus, small aneurysm in LMCA & RCA, diagnosed as complete KD. Treated with Infliximab, IVIG, oral steroids, aspirin, LMWH, oral cyclosporine, clopidogrel. 6 weeks echo showed persistent CAA, with resolution of thrombus.
CASE 5: A 2-month-old boy with high grade fever for 10 days with multiple giant aneurysms involving all major coronaries with thrombus in LAD. IVIG, aspirin, LMWH, infliximab, streptokinase. At 5 years follow-up, persistent giant aneurysm of LAD with complete dissolution of clot.
CASE 6: A 9 month old boy presented with 11 days of fever, irritability, thrombocytosis, diagnosed as incomplete KD with RCA & LCX, giant CAA in LAD, LMCA with thrombus. Treated with IVIG, infliximab, cyclosporine, LMWH, steroids. Follow up echo after 5 days show persistent thrombus in LMCA with new developing LAD thrombus.
CASE 7: A 6 year old girl, presented with KD shock on day 6 of fever, initial echo showing LMCA, LAD small CAA. Treated with IVIG, steroids, aspirin. Day 9 echo revealed giant CAA in LAD, received Infliximab, pulse methyl prednisolone, LMWH. Repeat echo on day 11 showed persistent giant CAA in LAD with thrombus. LMWH dose was increased, 2nd dose of Infliximab, cyclosporine was given. Echo after a month shows diminution of thrombus with multiple CAA.
CASE 8: 9 months infant diagnosed as KD on D11 of fever with multiple CAA, giant aneurysms of LMCA and LAD, with a 4 x 5 mm large thrombus in LMCA and went on to develop a 6 x 5 mm thrombus in LAD within 4 days of initiation of therapy with IVIG+ Infliximab. Baby was managed further with Cyclosporine, dual antiplatelets, sc LMWH 2mg/kg. Echo after 10 days showed resolution of both thrombi.
CASE 9: A 1-year infant, with Incomplete KD presented on day 4 of fever, initial echo showing small CAA in LAD with large thrombus (6mm x 2.4mm). Treated with IVIG, steroids, aspirin, Infliximab, LMWH, clopidogrel and cyclosporin. Repeat echo on day 10 showed persistent CAA in LAD but resolution of thrombus.
Results: Post-pandemic observations revealed an increased incidence of thrombus formation in patients with Kawasaki disease, with onset occurring approximately two weeks earlier compared to the pre-pandemic cohort. In some cases, thrombus progression was noted despite appropriate therapeutic intervention.
Conclusion: Following the pandemic we have observed an increased incidence of thrombosis, earlier onset by 2 weeks that sometimes progressed in spite of therapy.
Disclosure
None declared

P366

Clinical spectrum and outcomes in pediatric and adult iga vasculitis

S. Demir[1], B. C. Uludoğan[2], E. Pala[3], A. Aliyeva[2], R. Yildirim[4], A. Kavaz Tufan[5], N. Cetin[5], N. S. Yaşar Bilge[2], T. Kasifoglu[2]
[1]Pediatric Rheumatology, [2]Rheumatology, [3]Pediatrics, Eskisehir Osmangazi University, Eskisehir, Türkiye, [4]Rheumatology, The royal Wolverhampton NHs Trust, Wolverhampton, United Kingdom, [5]Pediatric Nephrology, Eskisehir Osmangazi University, Eskisehir, Türkiye
Correspondence: S. Demir
Pediatric Rheumatology, **23(2):** P366

Introduction: IgA vasculitis (IgAV), formerly known as Henoch-Schönlein purpura (HSP), is a type of small vessel vasculitis characterized by purpura, abdominal pain, arthritis, and renal involvement, predominantly seen in childhood. In contrast, it can rarely manifest in adults and demonstrate a more severe form especially in terms of renal involvement.
Objectives: The aim of this study is to analyze the differences in clinical and pathological manifestations, treatment patterns and response between pediatric and adult patients with IgAV, aiming to determine whether pediatric patients present differently from adult patients.
Methods: This retrospective study analyzed patients diagnosed with IgA vasculitis (IgAV) who presented to the pediatric and adult rheumatology clinics at Eskişehir Osmangazi University Hospital. Patients fulfilling the 1990 ACR and the Ankara 2008 EULAR/PRINTO/PRES classification criteria for Henoch-Schönlein purpura were included in this study. The cohort was divided into two groups based on the age of

disease onset: childhood-onset (<18 years) and adult-onset (>18 years). Comparative analyses were conducted to evaluate demographic, clinical, laboratory, and histopathological features among the two groups.
Results: A total of 142 patients with childhood-onset IgAV (cIgAV) and 69 with adult-onset IgAV (aIgAV) were included in the study. The female-to-male ratio was 0.56 in the cIgAV group and 0.63 in the aIgAV group. The mean follow-up duration was significantly longer in adults compared to children (51 ± 68 vs. 11 ± 13 months; $p < 0.001$). While seasonal distribution was similar between groups, predisposing factors—particularly drug exposure and surgical history—were more frequently observed in adults (63.8% vs. 43.7%; $p = 0.006$). The prevalence of skin involvement, arthritis/arthralgia, and gastrointestinal symptoms (e.g., abdominal pain, hematochezia) was comparable between the two cohorts. However, renal involvement was significantly more common and severe in the adult group (39.1% vs. 21.1%; $p = 0.006$), with markedly higher rates of hematuria ($p < 0.001$), proteinuria ($p = 0.006$), acute kidney injury ($p < 0.001$), and acute nephritic syndrome ($p = 0.003$). Although renal and skin biopsies were more frequently performed in adults ($p = 0.002$ and $p < 0.001$, respectively), no statistically significant differences were observed in histopathological grading according to the ISKDC classification ($p = 0.097$). Laboratory findings also revealed a more unfavorable inflammatory and renal profile in the adult group, with significantly higher ESR ($p = 0.043$), serum creatinine ($p < 0.001$), and lower albumin levels ($p < 0.001$). CRP levels were elevated in adults but did not reach statistical significance ($p = 0.454$). Treatment patterns differed significantly between age groups. NSAID use was more common in pediatric patients ($p < 0.001$), whereas the need for corticosteroids and other immunosuppressive agents—such as colchicine, azathioprine, cyclophosphamide, and ACE inhibitors—was significantly greater in adults. Despite similar relapse rates, chronic kidney disease (13.2% vs. 0%) and mortality (7.4% vs. 0%) were observed exclusively in the adult cohort, both reaching statistical significance.
Conclusion: Our findings demonstrate that adult-onset IgA vasculitis presents with a more severe clinical course compared to childhood-onset cases, particularly in terms of renal involvement and treatment burden.
Disclosure
None declared

P367

A child with sensorineural hearing loss, uveitis, and unexpected death

S. Pastore[1], F. Burlo[2], A. Taddio[1,2], G. Gortani[1], M. De Gaspari[3]
[1]Institute for Maternal and Child Health "IRCCS Burlo Garofolo", [2]Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, [3]Department of Cardiac, Thoracic, Vascular Sciences and Public Health, Cardiovascular Pathology Unit, University of Padua, Azienda Ospedaliera, Padua, Italy
Correspondence: S. Pastore
Pediatric Rheumatology, **23(2):** P367

Introduction: Cogan syndrome is a rare vasculitis typically involving the ocular and cochleovestibular systems, with only about fifty pediatric cases reported. Clinical presentation varies depending on the vessels affected. In children, the most common features are sudden hearing loss and ocular involvement.First-line treatment includes corticosteroids, often combined with NSAIDs. Immunosuppressants such as methotrexate, mycophenolate mofetil, azathioprine, or cyclophosphamide are added when prolonged steroid therapy is required. In refractory cases, biologics like infliximab or tocilizumab may be considered.
Objectives: This abstract describes an atypical case of Cogan syndrome in a young boy.
Methods: We detail the diagnostic process of Cogan syndrome in a child, with clinical, laboratory, and ultimately autopsy findings.
Results: A four-year-old boy presented with fatigue, weight loss, myalgias, and recent hearing loss. Blood tests showed microcytic anemia, leukocytosis, thrombocytosis, hypergammaglobulinemia, and elevated ESR. Oncologic, hematologic, gastrointestinal, rheumatologic, immunologic, infectious, cardiac, nephrologic, ocular, audiologic, and musculoskeletal diseases were excluded.
Steroids were started for suspected autoinflammatory disease, without improvement. Suspecting IL-1-mediated inflammation, anakinra was initiated with rapid response. However, episcleritis and rising inflammation soon developed, suggesting Cogan syndrome. Infliximab was started but was ineffective; tocilizumab was then introduced, with benefit.After a year of remission, the boy had brief episodes of palpitations, but evaluations were unremarkable. A month later, he was found dead at home at age six.Autopsy revealed thickened aortic valve cusps and near occlusion of the left coronary ostium. Histology showed transmural inflammation and severe intimal proliferation, causing coronary stenosis. Death was attributed to ischemic ventricular arrhythmia due to coronary vasculitis.
Conclusion: Cardiovascular involvement in Cogan syndrome is rare in children. Coronary artery vasculitis is even less common and typically presents alongside aortitis, and sudden death has only been reported in two pediatric cases to date.
Despite clinical remission under tocilizumab, silent coronary vasculitis led to fatal arrhythmia in our patient.
This case illustrates a rare manifestation of Cogan syndrome in a child and highlights the urgent need for evidence-based guidelines on the evaluation, follow-up, and management. Consent to published had been obtained.
Disclosure
None declared

References

1. Rücklová K, von Kalle T, Koitschev A, et al. Paediatric Cogan´s syndrome—review of literature, case report and practical approach to diagnosis and management. Pediatr Rheumatol Online J. 2023 Jun 8;21(1):54.
2. Arnaud L, Audemard-Verger A, Belot A, et al. French protocol for diagnosis and management of Cogan's syndrome. Rev Med Interne. 2025 Feb;46(2):74–88.
3. Pagnini I, Zannin ME, Vittadello F, et al. Clinical features and outcome of Cogan syndrome. J Pediatr. 2012 Feb;160(2):303–307.e1.

P369

When the rash doesn't fit: psoriasiform dermatitis revealing persistent inflammation in kawasaki disease

S. Delli Noci[1], M. Seyler[2], F. Anselmi[3], S. Ayadi[4], M. Boucheddad[5], T. A. Duong[6], F. Bajolle[7], B. Bader-Meunier[2], C. Durand[3], A. Frassati-Biaggi[8], S. Fraitag[9], F. Pitet[2], L. Rossi-Semerano[10], I. Kone Paut[10], P. Dusser[10,11]
[1]Division of Rheumatology, Bambino Gesù Children's Hospital, Rome, Italy, [2]Department for Immunology, Hematology and Pediatric Rheumatology, Necker Hospital, AP-HP, Paris, [3]Pediatric Rheumatology Department, AP-HP, Paris-Sud University Hospitals – Bicêtre Hospital, Le Kremlin-Bicêtre, Paris, [4]Dermatology Department, AP-HP, Paris-Sud University Hospitals – Bicêtre Hospital, Le Kremlin-Bicêtre, Paris, [5]Department of General Pediatrics and Continuous Care, Southern Oise Public Hospital Group (GHPSO), Creil, [6]Department of General and Oncologic Dermatology, Ambroise-Paré Hospital, AP-HP, Université Paris-Saclay – UVSQ, [7]Department of Pediatric Cardiology, Necker Hospital, AP-HP, Université de Paris, [8]Pathology Department, [9]Dermatology Department, Necker Hospital, AP-HP, Paris, [10]Pediatric Rheumatology Department, AP-HP, Paris-Sud University Hospitals – Bicêtre Hospital, Le Kremlin-Bicêtre, Paris, [11]"Exposome and Heredity" Team, CESP, INSERM U1018, Université Paris-Saclay, Gustave Roussy, Villejuif, France
Correspondence: S. Delli Noci
Pediatric Rheumatology, **23(2):** P369

Introduction: Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology that primarily affects children under five years of age. Exanthema is reported in 50%–90% of cases, typically within the first five days of illness, presenting as a diffuse, nonspecific erythematous maculopapular rash, often described as morbilliform, scarlatiniform, or urticarial. Less commonly, pustular or erythema multiforme-like eruptions have been described, usually during the convalescent phase. The occurrence of psoriasiform dermatitis during the active phase of KD is exceptional and may pose diagnostic challenges.
Objectives: To describe a rare case of psoriasiform dermatitis during the active phase of KD, and to highlight the importance of differential diagnosis and multidisciplinary management in the setting of persistent systemic inflammation.

Methods: We present the case of a 3-month-old male infant who developed a classical form of KD, including persistent fever, maculopapular rash, cheilitis, conjunctival injection, swelling of the hands and feet, and elevated inflammatory markers. Initial treatment with intravenous immunoglobulin (IVIG) and corticosteroids led to temporary resolution of symptoms.
Results: On day 8 of illness, fever recurred, and by day 10 a new cutaneous eruption emerged, prompting a second IVIG infusion and escalation to anakinra due to persistent inflammation. The new rash consisted of crusted erythematous papules predominantly on the limbs, with perioral and perineal involvement. Additional features included erosive cheilitis and crusted blepharitis. These findings were atypical for classical KD and raised suspicion of viral or bacterial co-infection, alternative vasculitis, or a drug-related eruption. Herpes simplex virus co-infection was clinically suspected, leading to empirical initiation of intravenous acyclovir and temporary discontinuation of anakinra. Concurrently, coronary artery aneurysms developed, indicating ongoing systemic inflammation. Virologic testing (PCR on blood and skin) was negative. A skin biopsy revealed a psoriasiform dermatitis without cytopathic changes, ruling out viral etiology. After multidisciplinary review, the eruption was interpreted as KD-related psoriasiform dermatitis. Anakinra and corticosteroids were then reintroduced, with progressive improvement in systemic, cardiac, and cutaneous manifestations.
Conclusion: This case highlights a rare cutaneous manifestation of KD, with a psoriasiform eruption arising during the active phase of the disease. The timing, distribution, and morphology of the lesions, alongside systemic progression, support an inflammatory rather than infectious or drug-related cause. Microbiological and histopathological investigations were essential to exclude differential diagnoses. To date, 38 cases of psoriasiform dermatitis following Kawasaki disease have been reported in the literature, mostly during the convalescent phase and with self-limiting course[1]. Although rare, psoriasiform dermatitis should be considered as part of the cutaneous spectrum of KD.
Consent to published had been obtained.
Disclosure of Interes
None declared

Reference

1. Nakayama S, Shimomura Y, Tani K, Ishikawa K, Suga Y, Fujino H, et al. Psoriasiform dermatitis following Kawasaki disease: A case report and literature review. Pediatr Dermatol. 2024 Dec 27. doi: https://doi.org/10.1111/pde.15859

P370

First-line intensification therapy with anakinra in high-risk Kawasaki disease patients

S. Romano[1], M. V. Mastrolia[2,3], T. Giani[2], I. Pagnini[2], I. Maccora[2,3], E. Marrani[2], G. Simonini[2,3]
[1]Pediatric Department, School of Sciences of Human Health, University of Florence, [2]Rheumatology Unit, ERN ReCONNET Centers, Meyer Children's Hospital IRCCS, [3]NeuroFARBA Department, University of Florence, Florence, Italy
Correspondence: S. Romano
Pediatric Rheumatology, **23(2):** P370

Introduction: Kawasaki Disease (KD) patients with a high-risk profile, defined by age (under 6 months) and/or the presence of coronary artery involvement (Z score ≥ 2.5 at diagnosis), may benefit from a more aggressive first-line anti-inflammatory approach[1].
Objectives: Given the central role of interleukin (IL)−1 in the pathogenesis of KD[2,3], this study aims to contribute to the evidence supporting the safety and effectiveness of IL-1 blockade with intravenous Anakinra, administered as first-line treatment alongside intravenous immunoglobulins (IVIg), in high-risk KD infants.
Methods: We retrospectively selected 2 cases of KD treated at Meyer Children's Hospital, who satisfied the following criteria: (a) diagnosis of KD according to the American Heart Association guidelines[1]; (b) age under 6 months and/or presence of coronary artery aneurysms (CAA) at diagnosis; (c) first-line treatment with Anakinra along with the first infusion of IVIg.
Results: Patient 1, a 3-month-old male, was diagnosed with a complete form of KD, complicated by CAA: common arterial trunk measuring 3 mm (Z score 4.6), right coronary artery (RCA) measuring 2 mm (Z score 2.19) and left anterior descending artery (LAD) measuring 2 mm (Z score 2.79). Patient 2, a 4-month-old male, was diagnosed with an incomplete form of KD, complicated by CAA: common arterial trunk measuring 2.5 mm (Z score 2.91), RCA measuring 2.2 mm (Z score 2.66) and LAD measuring 2 mm (Z score 2.66). Both patients were treated simultaneously with one infusion of IVIg and intravenous administration of Anakinra at 10 mg/kg/day, achieving fever resolution the day after. Anakinra was progressively tapered down and then shifted to daily subcutaneous administration. Periodic echocardiogram controls showed normalization of the previous coronary artery lesions, respectively, on day 18 and day 19 since fever onset. Anakinra was discontinued after about 8 weeks of therapy. In both patients, the last echocardiogram control at 12 weeks confirmed the complete resolution of the coronary complications.
Conclusion: Intravenous administration of Anakinra in KD represents an off-label use both for route of administration and for patient population. However, in refractory KD patients, it has already been shown to be effective as second-line therapy on fever, systemic inflammation and coronary artery dilatations in the open-label phase IIA clinical trial KAWAKINRA[2]. These 2 cases represent high-risk patients, both for age (≤ 6 months) and for coronary artery involvement; to the best of our knowledge, they represent the first infants with KD and CAA successfully treated with intravenous Anakinra as first-line intensification therapy. Therefore, combined first-line treatment with IVIg and anti-IL1 blockade may be considered in high-risk KD patients.
Disclosure
None declared

References

1. Jone PN, et al. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2024.
2. Koné-Paut I, et al. Phase II Open Label Study of Anakinra in Intravenous Immunoglobulin–Resistant Kawasaki Disease. *Arthritis and Rheumatology*. 2021;73(1):151–161.
3. Koné-Paut I, et al. The use of interleukin 1 receptor antagonist (anakinra) in Kawasaki disease: A retrospective cases series. *Autoimmun Rev*. 2018;17(8):768–774.

P372

A child with takayasu arteritis: missed diagnostic opprtunities and delayed presentation with lower motor neuron facial nerve palsy

W. A. K. Wanasinghe, V. Arunath, E. Ganewatte, J. Jagoda, V. Gunasekara, K. Weerasekara[1] on behalf of Select
Lady Ridgeway Hospital for Children, Colombo 08, Sri Lanka
Correspondence: V. Arunath
Pediatric Rheumatology, **23(2):** P372

Introduction: Childhood-onset Takayasu Arteritis (cTAK) is a rare large-vessel vasculitis seen in children, mainly affecting the aorta and its major branches. The clinical manifestations in paediatric patients are less specific than in adults and often severe as a result of systemic and local inflammation. Although hypertension remains the most common presenting feature in cTAK, episcleritis described as one of the rare clinical features of cTAK in the literature.
Objectives: Objective of the case report was to report a patient with cTAK who presented with lower motor neuron facial nerve palsy secondary to maligant hypertension and to discuss the missed diagnostic opportunity of a vasculitis when presented with the episcleritis.
Methods: A 4-year-old was admitted with left-sided lower motor type facial nerve palsy with the epistaxis to the local hospital. On admission, he was found to have stage 2 hypertension with the blood pressure of 220/180 mmHg. He was transferred to tertiary paediatric services for further management. Further examination revealed weak peripheral pulses in the lower limbs and bilateral renal artery bruit. Rest of the examination was unremarkable. On background review, the child had frequent hospital visits for recurrent episodes of episcleritis of unclear etiology, which were managed by ophthalmology services and he also had constitutional symptoms over a 6-month duration.He had not undergone

formal medical assessments or rheumatological workup for the episcleritis or associated constitutional symptoms until this admission.
Results: His renal flunctions were slightly raised but inflammatory markers and autoimmune panel were negative. Renal doppler study revealed renal artery stenosis in the right kidney and upper pole of the left kidney, confirmed by a computer tomography renal angiogram. Other vessel involvement was excluded in MRA, MRV and angiogram of thoracic vessels. The diagnosis of cTAK was made based on clinical and radiological findings. He was managed with the input of multidisciplinary services and treated initially with methotrexate and intravenous methylprednisolone pulses, followed by infliximab therapy. Blood pressure control was achieved with four types of antihypertensives.
Conclusion: A lack of awareness about cTAK and its uncommon clinical manifestations, such as episcleritis, among medical professionals contributed to the delayed diagnosis. This case also highlights the diagnostic challenge in a young child presenting with facial nerve palsy secondary to malignant hypertension. Rheumatological workup and close follow-up are essential in children presenting with inflammatory eye signs without a clear etiology. Additionally, measuring blood pressure is imperative in all children presenting with facial nerve palsy, as early detection may prevent catastrophic sequelae. Consent to published had been obtained.
Disclosure
None declared

P373

Factors associated with the need for surgical intervention in pediatric patients with takayasu arteritis

V. Podzolkova[1], Y. Kostina[2], O. Shpitonkova[1], V. Seraya[2], G. Lyskina[1]
[1]Department of Children's Diseases, I.M. Sechenov First Moscow State Medical University, [2]Department of Pediatric Rheumatology №1, Clinic of Children's Diseases Sechenov's Center of Maternity and Childhood, Moscow, Russian Federation
Correspondence: V. Podzolkova
Pediatric Rheumatology, **23(2):** P373

Introduction: Takayasu arteritis (TA) is a rare large-vessel vasculitis that may require surgical intervention in cases of critical vascular stenosis or aneurysm formation. However, surgery carries a high risk of complications, particularly during active inflammation. Identifying factors associated with the need for surgical intervention in pediatric TA may enhance understanding of the mechanisms underlying critical arterial changes and early clinical presentations.
Objectives: To identify clinical, laboratory, and imaging characteristics associated with the need for surgical intervention in pediatric patients with TA.
Methods: A retrospective case-control study included 47 children diagnosed with TA according to EULAR/PRINTO/PRES 2010 criteria. Twelve patients who underwent surgical treatment (group 1) were compared to 35 controls without surgery (group2). Demographic, clinical, laboratory, and imaging data were analyzed. Groups were matched by gender, age at onset, disease activity (ITAS.A score), and follow-up duration. Statistical analysis was performed using StatTech v.4.8.3.
Results: Patients requiring surgical intervention had a significantly longer disease duration before diagnosis (median: 22.5 months [IQR: 12.75–27], p = 0.004), a higher number of affected vessels at diagnosis (median: 6 [IQR: 4.75–7.25], p = 0.048), as well as elevated systolic blood pressure (mean: 161.42 mmHg [SD ±25.41], p < 0.001) and diastolic blood pressure (mean: 104.67 mmHg [SD ±16.37], p < 0.001). Fever was less frequently reported in Group 1 compared to Group 2 (33.3% vs. 80.0%, p = 0.009). In contrast, headache (83.3% vs. 45.7%, p = 0.042) and arterial hypertension (91.7% vs. 11.4%, p < 0.001) were significantly more common in patients undergoing surgical intervention. Involvement of the descending thoracic aorta (66.7% vs. 22.9%, p = 0.012), abdominal aorta (83.3% vs. 42.9%, p = 0.020), and renal arteries (66.0% vs. 2.9%, p < 0.001) was also significantly more frequent in Group 1. A total of 17 surgical procedures were performed in 12 patients, including balloon angioplasty (n = 2), bypass grafting (n = 4), prosthetic vessel replacement (n = 7), autologous vessel reconstruction (n = 3), and renal artery stenting (n = 1). Early postoperative complications occurred in 4 patients: occlusion of the operated segment in 3 cases and neck phlegmon in 1 case. One late complication — rupture of an anastomotic aneurysm — resulted in a fatal outcome.
Conclusion: In our cohort, elevated blood pressure, headache, delayed diagnosis, and a greater number of affected vessels, including renal arteries, descending and abdominal aorta were significantly more common in pediatric TA with the need for surgical intervention. The lack of typical symptoms may contribute to diagnostic delay and progression to severe vascular damage. Further research is needed to identify early diagnostic markers and optimal management strategies in pediatric TA patients.
Disclosure
None declared

P374

Predictors of renal involvement and persistent nephritis in pediatric iga vasculitis: a multicenter cohort

M. Dantas[1], V. Curi[1], N. O. Batista[1], V. A. Santos[1], J. Dib[1], J. P. Lima[1], D. Piotto[1], M. Fraga[1], A. P. Sakamoto[1], R. do Prado[1], C. A. Silva[2], L. M. Campos[2], S. C. Farhat[2], A. Watanabe[3], L. M. Carvalho[4], F. H. Gomes[4], L. L. Magalhães[4], A. R. Fonseca[5], M. F. Rodrigues[5], F. R. Stazjnbok[5], C. A. Len[1], M. T. Terreri[1], G. Clemente[1]
[1]Pediatric Rheumatology Unit, Universidade Federal de São Paulo, [2]Pediatric Rheumatology Unit, [3]Pediatric Nephrology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, [4]Pediatric Rheumatology Unit, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, [5]Rheumatology Division, Instituto de Puericultura e Pediatria Martagao Gesteira, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
Correspondence: V. Curi
Pediatric Rheumatology, **23(2):** P374

Introduction: Renal involvement occurs in about one-third of pediatric patients with IgA vasculitis (IgAV), even so, factors associated to the development and persistence of nephritis (IgAVN) remain unclear, especially in ethnically diverse populations.
Objectives: To determine associated factors with IgAVN and persistent IgAVN in a large multicenter cohort study in a mixed-ethnic country in Latin-America.
Methods: A multicenter study in four academic referral centers of Pediatric Rheumatology in Brazil assessed 687 pediatric patients who met the EULAR/PRINTO/PRES classification criteria for pediatric IgAV[1]. Demographic, clinical, laboratory and treatment data were retrospectively collected from medical records. Clinical and laboratory data at presentation as well as recurrent and persistent symptoms were compared between IgAVN and non-IgAVN patients. Those with IgAVN were further categorized into self-limited (≤3 months) or persistent (>3 months) nephritis. Ethics approval was obtained from all centers.
Results: Of the 687 patients, 253 (36.8%) developed nephritis. Among them, 17 (6.7%) had nephrotic syndrome, 109 (43%) had persistent nephritis and 46 (18.0%) underwent renal biopsy. Regarding therapy, 177 patients (70%) received steroids, 27% antiproteinurics, 11% azathioprine, 2% mycophenolate, 1% cyclosporine, and 0.4% IV cyclophosphamide. Only one patient underwent renal replacement therapy. Patients with IgAVN were older (median 76 vs 68 months; p=0.004) and more frequently presented with persistent purpura (14% vs 6%; p=0.001), recurrent purpura (28% vs 20%; p=0.02), hypertension (12% vs 4%; p=0.001), and abdominal pain (69% vs 56%; p=0.001). Persistent (6% vs 1%; p=0.01), recurrent (68% vs 12%; p=0.001), and moderate/severe abdominal pain (57% vs 42%; p=0.004) were also more common in these patients. Orchitis (22% vs 11%; p=0.01) and painful subcutaneous edema (36% vs 30%; p=0.05) were more frequent in IgAVN patients, whereas arthritis was more common in non IgAVN patients (78% vs 84%; p=0.03). Laboratory findings were mostly similar, except for elevated CRP, more frequent in IgAVN patients (61% vs 40%; p=0.001).
Patients with persistent nephritis were older at diagnosis (median 78 vs 71 months; p=0.02), and more frequently presented proteinuria and nephrotic syndrome compared to those with self-limiting nephritis (77% vs 45%, p=0.01 and 19% vs 2%, p=0.01, respectively). Interestingly, previous tonsillitis at IgAV diagnosis was more commonly detected in patients with self-limited nephritis (63% vs 33%, p=0.02). No laboratory markers were discriminative between the two groups.

Conclusion: In this large multicenter cohort in a mixed-ethnic country in Latin American, older age as well other clinical features were associated with nephritis and persistence of nephritis in pediatric IgAV. These findings may aid in the earlier identification of patients at high risk for renal involvement and enable more personalized management strategies.
Disclosure
None declared

Reference
1. Ozen S, Pistorio A, Iusan SM et al. EULAR/PRINTO/PRES criteria for Henoch–Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu's arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis 2010;69: 798–806.

P375

Fatigue in children with rheumatic diseases: a journey towards mental health

M. D. L. Aldana Galván, A. Villarreal Garza , A. V. Villarreal Treviño, F. García Rodríguez, N. E. Rubio Pérez
Pediatrics, Hospital Universitario Dr. José Eleuterio González,, Monterrey, Mexico
Correspondence: A. V. Villarreal Treviño
Pediatric Rheumatology, **23(2):** P375

Introduction: Fatigue is the tiredness experienced after engaging in both physical and mental activities. It is a common symptom in rheumatic diseases and can be related to mental health issues.
Objectives: To determine the association between fatigue and mental health problems in pediatric patients with rheumatic diseases.
Methods: Observational, cross-sectional, and analytical study. Fifty patients aged 6 to 18 years with a diagnosis of rheumatic disease, who attended the pediatric rheumatology clinic between August and November 2024, were included. Age, sex, type, and duration of the rheumatic disease were considered as confounding variables. Descriptive and inferential statistics were performed, and odds ratios with their 95% confidence intervals were calculated. Additionally, a logistic regression model was conducted with significant variables. Statistical significance was established with a pvalue < 0.05.
Results: Of the 50 patients, 18 (36%) presented fatigue and 32 (64%) did not, with a higher predominance of women in the fatigue group (100% vs 56%, p=0.001). Mental health problems were more frequent in patients with fatigue compared to patients without fatigue (72% vs 19%, OR 11.2, 95% CI: 1.48–2.44, p<0.001). A significant association was found between depression (OR: 12, p=0.018) and somatic complaints (OR: 7.5, p=0.019) with the presence of fatigue. The logistic regression analysis showed that mental health problems significantly increased the probability of fatigue (OR: 9.1, p=0.004).
Conclusion: Fatigue is a symptom that increases the risk of mental health problems in patients with rheumatic diseases and is significantly associated with depression and somatic complaints.
Disclosure
None declared

Reference
1. Medical Subject Headings. U.S. National Library of Medicine. [Internet]. Bethesda, MD: U.S. National Library of Medicine; [updated February 1, 2024; cited May 12, 2024]. Available at:https://meshb.nlm.nih.gov/.

P376

Cardiorespiratory performance assessment tools to evaluate the success of a restorative rehabilitation programme for children with juvenile idiopathic arthritis

A. Ošlak[1], R. Vauhnik [1], N. Toplak[2,3]
[1]Department of Physiotherapy, Faculty of Health Sciences, University of Ljubljana, [2]Faculty of Medicine, University of Ljubljana, [3]Dpt. of allergology, rheum, clin immunol, UCH, UMC Ljubljana, Ljubljana, Slovenia
Correspondence: A. Ošlak
Pediatric Rheumatology, **23(2):** P376

Introduction: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children and can affect the quality of life. Treatment includes pharmacological therapy, physiotherapy, and psychosocial support. Physical activity is essential for managing symptoms, maintaining functional physical capacity and improving cardiorespiratory fitness, which tends to be lower in children with JIA than in their healthy peers.
Objectives: The objective of this study was to identify the most appropriate tool for assessing cardiorespiratory fitness in children with JIA that can be used in a clinical setting to evaluate the effects of a short-term rehabilitation program.
Methods: We included children with JIA who were enrolled in a 12-day rehabilitation program. Before and after the rehabilitation program, the participants performed the 6-minute walk test (6MWT), Queens College (QC) step test, and incremental shuttle walk test (ISWT). In addition to group exercises and water-based exercises, participants could also receive individual physiotherapy sessions or occupational therapy.
Results: A total of 46 children with JIA, aged 6 to 18 years, were included in the study (30% boys, 70% girls). The most common subtype was oligoarthritis (41%), followed by RF-negative polyarthritis (26%), RF-unspecified polyarthritis (15%), psoriatic arthritis (11%), and RF-positive polyarthritis (7%). At the time of the study, 63% of patients were receiving biological therapy, 46% methotrexate, and 76% other treatments (e.g., NSAIDs, corticosteroids). There was no statistically significant difference in pre- and post-intervention results for the 6MWT or the QC step test (p=0.39; p=0.34). A significant difference was observed in the ISWT (p<0.05). There were no changes in disease activity due to the study interventions (p=0.88). The pre-rehabilitation test results were significantly lower in the 6MWT and the QC step test, while values in the ISWT were significantly higher than normative values of healthy children (1–3). Linear analysis explained only a small portion of the variability in test result differences (12%–44%).
Conclusion: Based on the study findings, no definitive conclusion could be drawn on which assessment tools are best suited for measuring short-term rehabilitation outcomes in children with JIA included in the study. However, their usefulness could be inferred through observation in the clinical setting. These findings emphasize the importance of regular physical activity for children with JIA, both in clinical and home settings.
Disclosure
None declared

References
1. McKay MJ, Baldwin JN, Ferreira P, Simic M, Vanicek N, Burns J, et al. Reference values for developing responsive functional outcome measures across the lifespan. Neurology. 2017;88(16):1512–9. doi: https://doi.org/10.1212/WNL.0000000000003847
2. van der Steeg GE, Takken T. Reference values for maximum oxygen uptake relative to body mass in Dutch/Flemish subjects aged 6–65 years: the LowLands Fitness Registry. Eur J Appl Physiol. 2021;121(4):1189–96. doi: 1007/s00421-021-04596-6
3. Vardhan V, Palekar TJ, Dhuke P, Baxi G. Normative values of incremental shuttle walk test in children and adolescents: an observational study. Int J Pharma Bio Sci. 2017;8(4):478–83. doi: https://doi.org/10.22376/ijpbs.2017.8.4.b478-483

P377

Comparison of kinesthetic and visual imagery perception in juvenile idiopathic arthritis and healthy peers: a pilot study

A. Yekdaneh[1,2], M. Yogurtcu[3], A. Duran[3], S. Kalayci[3], C. Taylan[3], N. Arman[3], A. Albayrak[1,4], N. Aktay Ayaz[5]
[1]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, [2]Physiotherapy English Program, Fenerbahçe University, Vocational School of Health Services, [3]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [4]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [5]Department of Pediatric Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Department of Pediatrics, Istanbul, Türkiye
Correspondence: A. Yekdaneh
Pediatric Rheumatology, **23(2):** P377

Introduction: Juvenile Idiopathic Arthritis (JIA) is a chronic condition that can impair physical activity, functional ability, and motor skill development, ultimately affecting quality of life (1). Kinesthetic and visual imagery are cognitive strategies known to support motor learning and performance, especially in children. However, limited evidence exists comparing these abilities between children with JIA and their healthy counterparts (2).
Objectives: The aim of the study was to compare kinesthetic and visual imagery abilities in children and adolescents with JIA versus healthy peers, and to examine the relationship between physical activity and imagery performance.
Methods: A total of 75 participants aged 7–18 years were included: 22 with JIA and 53 healthy peers. Physical activity was assessed using the Physical Activity Questionnaire for Children and Adolescents (PAQ-C/A), and exercise behavior was evaluated through the Exercise Stages of Change – Short Form (ESCSF) and the Exercise Stages of Change Questionnaire (ESCQ). Kinesthetic and visual imagery skills were measured using the Kinesthetic and Visual Imagery Questionnaire-20 (KVIQ-20).
Results: The mean age of the JIA group was 13.90 ± 3.25 years, and 15.19 ± 2.42 years for the healthy group. JIA participants exhibited significantly higher kinesthetic imagery scores compared to healthy peers ($t = -2.35$, $p = 0.027$), which may be attributed to increased bodily awareness, engagement in physiotherapy, or adaptive perceptual responses. PAQ-C/A scores did not significantly differ between groups ($t = -0.24$, $p = 0.808$). ESCQ analysis showed that 76% of the JIA group were in pre-contemplation or contemplation stages, while the healthy group was more frequently in action and maintenance stages. Exercise stage demonstrated a weak correlation with PAQ scores ($r = -0.295$) and kinesthetic imagery ($r = 0.028$).
Conclusion: Children and adolescents with JIA may demonstrate enhanced kinesthetic imagery abilities compared to their healthy peers, independent of physical activity levels. These findings suggest that cognitive and behavioral adaptations may contribute to motor imagery performance and underscore the need for comprehensive assessment strategies in pediatric rheumatology and educational settings. This enhancement in kinesthetic perception may stem from increased body awareness, regular physiotherapy, or adaptive sensorimotor mechanisms. Clinically, motor imagery techniques may offer a promising, low-risk strategy in rehabilitation settings. Further longitudinal studies are warranted to examine how disease duration, treatment exposure, and imagery training influence these cognitive-motor skills.
Disclosure
None declared

References
1. Hulsegge GH, et al. Fundamental movement skills, physical fitness and physical activity among Australian children with juvenile idiopathic arthritis. *J Paediatr Child Health.* 2015.
2. Paltiel O, Uziel Y. Juvenile idiopathic arthritis: Pathogenesis and rehabilitation perspectives. *Pediatr Rheumatol.* 2014;12(1):1–10.

P378

Is it poor activity or poor capacity? a comparative analysis of physical activity and functional capacity in children and adolescents with juvenile idiopathic arthritis and familial mediterranean fever

A. Namli Seker[1,2], N. Arman[3], A. Yeknadeh[1,4], A. Albayrak[1,5], N. Aktay Ayaz[6]
[1]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa, Institute of Graduate Studies, Istanbul, [2]Program of Podology, Aydin Adnan Menderes University, Nazilli Vocational School of Health Services, Aydin, [3]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [4]Physiotherapy English Program, Fenerbahçe University Vocational School of Health Services, [5]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [6]Department of Pediatrics Department of Pediatric Rheumatology, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye
Correspondence: A. Namli Seker
Pediatric Rheumatology, **23(2):** P378

Introduction: In children and adolescents with Juvenile Idiopathic Arthritis (JIA) and Familial Mediterranean Fever (FMF) commonly show limited physical activity levels and impaired functional performance. However, it continues uncertain whether limited physical activity leads to a decline in functional capacity, or conversely, whether reduced functional capacity two directional relationship that poses a potential paradox (1).
Objectives: This study aimed to compare physical activity levels, exercise behavior, and functional capacity between children and adolescents with FMF or JIA and their healthy peers, and to investigate the determinants of physical activity by analyzing the relationships between these parameters.
Methods: One hundred fifteen (24 JIA, 30 FMF, 61 healthy) children and adolescents aged between 10 to 18 years old were included in the study. The physical activity level of children and adolescents was assessed with the Physical Activity Questionnaire for Adolescents and Children (PAQ (A and C)), and exercise behavior was assessed with the Short Form of Exercise Change Stages (ECS-SF). Functional capacity was assessed with the Six Minute Walk Test (6MWT), Sit-to-Stand Test (SST), and Stair Climb Test (SCT). SPSS Version 27.0 program was used for statistical analysis.
Results: The mean age of the children and adolescents diagnosed with JIA and FMF and healthy controls included in the study was 14.39±2.10, 13.60±1.97 and 14.77±0.93 years, respectively. Levels of PAQ (A and C), scores of 6MWT, SST and SCT of children and adolescents with JIA and FMF were significantly lower compared to their healthy peers ($p<0.001$). Significant correlation was found between levels of PAQ and scores of ECS-SF, SST and 6MWT. Multiple regression analysis revealed a significant model (R^2:0.16), with PAQ negatively predicted by ECS-SF scores (β:−0.15) and marginally positively by 6MWT performance (β:0.01). Regression analysis conducted within the FMF and JIA identified age as the sole significant predictor of FAA (β:0.23). In contrast, within the healthy peers, the result of SCT emerged as a significant positive predictor level of PAQ (β:0.19), while age remained a significant negative predictor (β:−0.32).
Conclusion: This study provides evidence that children and adolescents with FMF and JIA demonstrate significantly reduced physical activity levels and impaired functional capacity compared to healthy peers. However, the determinants of physical activity exhibit variation between groups. In the healthy group, physical activity is closely related to functional performance, especially lower extremity strength and endurance, as demonstrated by the SCT. In contrast, in JIA and FMF group, physical activity levels are related to age, suggesting the influence of psychosocial or disease-related factors.
Disclosure
None declared

Reference
1. Gualano et al (2017). Physical activity for paediatric rheumatic diseases: standing up against old paradigms.*Nature Reviews Rheumatology*, *13*(6), 368-379.

P380

Awareness of pediatric rheumatic diseases among the mexican population

F. García-Rodríguez, S. P. Arroyo Sanchez, A. V. Escobedo Garza, V. L. Monjaraz Bustos, L. D. C. Reynoso Medina, A. V. Villarreal Treviño, N. E. Rubio Perez, on behalf of Colaborativa de Investigación en Beneficio de la Reumatología Infantil (COLIBRI)
Universidad Autonoma de Nuevo Leon, Monterrey, Mexico
Correspondence: F. García-Rodríguez
Pediatric Rheumatology, **23(2):** P380

Introduction: Pediatric rheumatic diseases (PRDs) are a group of musculoskeletal and autoimmune pathologies affecting 6–7 million children worldwide. In Mexico, the true prevalence of PRDs is probably underestimated due to the lack of epidemiological data and recognition of the disease. There is limited research focused on describing the general population's awareness about PRDs.
Objectives: To describe the general population's awareness of PRDs and their knowledge of associated symptoms and complications of these conditions.

Methods: This is a cross-sectional, descriptive study conducted between September and December 2024. It included adults aged between 18 and 80, with no gender restriction.
A multidisciplinary working group created the survey, which was evaluated in a pilot study before its implementation.
Methods included face-to-face surveys conducted by a trained interviewer and online surveys distributed through social media platforms.
Responses were grouped into 1) those answered in person within the University Hospital campus (including patients, companions, and medical or non-medical staff), 2) responses from the online surveys, and 3) those who were surveyed in person in a non-medical environment.
A descriptive analysis of the results was conducted using frequencies and measures of central tendency. Responses were compared among groups, and associations of the participants' demographic data were explored using parametric and non-parametric analysis.
Results: A total of 1,054 individuals participated in this study. The median age was 31 years (IQR 24–50), 643 (61%) were female, 806 had completed more than 9 years of formal education (76.5%), and 503 reported having paid employment (47.7%). There were 350 (33.2%) online responses, 354 in the Hospital campus (33.6%), and 350 in the non-medical environment (33.2%).
More than half of the respondents (686, 65.1%) reported having heard of rheumatic diseases, more frequently in the online group (257, 73.4% vs 222, 62.7% and 207, 59.1%). Of all the participants, 327 (48%) know someone with a rheumatic condition.
427 (63.3%) said that they were aware of PRDs; however, 370 (60%) of them were unable to name any specific condition. Only 23 (3.7%) reported knowing a child with a PRDs; juvenile idiopathic arthritis (JIA) was the most frequently mentioned (10, 40%). These responses were equally distributed among groups.
Growing pains were the most common answer when asked about the most frequent cause of musculoskeletal pain in children (302, 28.7%).
Most participants (494, 46.9%) responded that they would take their child to the hospital immediately in case of musculoskeletal pain. Fever was the most frequent answer (326, 30.9%) when asked which accompanying symptoms of joint pain, with no difference between the groups.
Conclusion: Awareness of PRDs is low, especially compared with the recognition of rheumatic diseases in adults. Even though most of the participants considered looking for quick medical attention when a child presents with musculoskeletal pain.
Disclosure
None declared

References

1. Migowa, A. N., Hadef, D., Hamdi, W., Mwizerwa, O., Ngandeu, M., Taha, Y., Ayodele, F., Webb, K., & Scott, C. (2021). Pediatric rheumatology in Africa: thriving amidst challenges. Pediatric rheumatology online journal, 19(1), 69. https://doi.org/10.1186/s12969-021-00557-7
2. McColl, J., Mwizerwa, O., Scott, C., Tse, S. M., & Foster, H. E. (2024). Pediatric rheumatology education: the virtual frontier a review. Pediatric rheumatology online journal, 22(1), 60. https://doi.org/10.1186/s12969-024-00978-0
3. Al-Eid, W. M., Madi, S. M., Bahabri, S. A., & Al-Mayouf, S. M. (2001). Evaluation of parental knowledge of Pediatric Rheumatic Diseases. Saudi medical journal, 22(6), 531–536.

P381

Architectural concept design for patient-centered therapeutic spaces in pediatric rheumatology outpatient clinics

J. Wojtowicz[1], A. Maciejko[2]
[1]Centre of Pediatric Rheumatology, REUMAPEDIC, Warsaw, [2]Department of Architecture and Urban Planning, University of Zielona Gora, Zielona Gora, Poland
Correspondence: J. Wojtowicz
Pediatric Rheumatology, **23(2):** P381

Introduction: Optimizing therapeutic environments in pediatric rheumatology outpatient clinics is an emerging field that can improve the effectiveness and quality of care, especially when based on patient-centered principles. Children with chronic and rare rheumatologic conditions require frequent visits, procedures, and ongoing medical supervision. The physical environment in which this care takes place plays a vital role in supporting both treatment outcomes and emotional well-being.
Objectives: To formulate a patient-centered architectural concept for pediatric rheumatology outpatient clinics by identifying essential design features through the Delphi method and translating them into a prototype model facility.
Methods: To define the key features of an optimal therapeutic space for this patient group, we used the Delphi method—an established research technique for building expert consensus in underexplored areas. Our expert panel included specialists from architecture and medicine, as well as Polish parents and young adult patients (aged 18–22). The panel consisted of professionals such as an architect, interior designer, building physicist, furniture designer, ergonomics expert, pediatrician, rheumatologist, pediatric rheumatologist, and a nurse. Through structured rounds of voting and discussion, the panel developed a detailed set of design recommendations.
Results: The experts identified several essential components of therapeutic space design: physical comfort (layout, furniture, assistive equipment), emotional comfort (safety, child-friendly elements, relaxation areas), sensory considerations (stimulus reduction, gait-assessment flooring, green areas), privacy (spatial zoning and individual treatment rooms), accessibility (efficiency and clarity of services), integration of technology (including virtual care), and modular spatial solutions. These elements were used to create an architectural concept design—a model outpatient facility tailored to the specific needs of pediatric rheumatology patients.
Conclusion: The resulting design concept provides a practical and flexible framework for creating therapeutic environments that are clinically effective, emotionally supportive, and tailored to patient needs. While the framework is applicable in various international contexts, its implementation should consider local cultural and systemic factors. In the next phase of the study, the model will be evaluated by pediatric patients, adolescents, and caregivers in Poland to ensure its practical value and relevance.
Disclosure
None declared

P382

Quality of life in children with juvenile idiopathic arthritis in the eastern regions of Ukraine

N. S. Shevchenko[1,2], T. O. Holovko[1,2], L. F. Bogmat[2], T. M. Matkovska[3]
[1]Department of Pediatrics, V.N.Karazin Kharkiv National University, [2]Department of Rheumatology and comorbidities, [3]SI "Institution for Children and Adolescents Health Care of NAMN of Ukraine", Kharkiv, Ukraine
Correspondence: N. S. Shevchenko
Pediatric Rheumatology, **23(2):** P382

Introduction: Health-related quality of life (HRQL) is one of the indicators of the effectiveness of juvenile idiopathic arthritis (JIA) treatment, its determination is an additional criterion of the condition of a sick child. It is known that the components of HRQL are influenced not only by medical, but also by social factors. Accordingly, patients who are in the eastern regions of Ukraine during martial law have additional risks to worse HRQL.
Objectives: To determine the health-related quality of life in children with JIA located in the eastern regions of Ukraine, and compare the obtained indicators with data until February 24, 2022.
Methods: The analysis included 71 patients: 33 girls (46.48%), 38 boys (53.52%), mean age 13.85 ± 0.34 years, oligoarthritis 23 (32.39%), polyarthritis 48 (67.61%), disease duration 5.5 ± 0.4 months. During the war, 9 children fell ill, 6 of them in the second year of the war.
Data compared with the results of 118 studies at the end of 2021: 77 girls (65.2%), 41 boys (37.7%), mean age 11.12 ± 0.34 years, polyarthritis (49.8%), oligoarthritis (46.4%), disease duration 4.23 ± 0.34 months.
The patient questionnaire was conducted using the Pediatric Quality of Life Inventory Generic Core Scale 4.0. Additionally, a psychological examination to determine psychological status was conducted for children with JIA.

Results: Before 2022, JIA activity according to JADAS-27 was 3.52 ± 0.50 points for oligovariant, 6.44 ± 0.61 for polyarthritis. Today, these indicators are 6.44 ± 0.44 and 6.81 ± 0.79 points, respectively.
Before 2022, the JIA of children with JIA according to the PedsQLTM 4.0 Generic Core Scale questionnaire for the patient during the month before the survey was 78.0 ± 2.2 points for oligovariant, 65.8 ± 6.3 points for polyarthritis. Despite the difficult circumstances of wartime, three years later, higher JIA activity indicators HRQL were noted for oligovariant (85.16 ± 4.77 points) and maintained at the same level for polyarthritis (67.19 ± 3.67).
According to the psychological examination, 42 children (59.15%) have psychological disorders (psychoemotional lability, anxiety, depressive syndrome, etc.), 9 children (12.68%) have borderline conditions. The level of HRQL for the previous month according to the patient's questionnaire did not reveal any significant differences taking into account the psychological state: without disorders 73.88 ± 5.12; with borderline changes 73.11 ± 5.78, with mental disorders 71.50 ± 6.45 points. At the same time, in children with mental disorders, a negative correlation was established between the level of activity according to JADAS and the level of HRQL ($r = -0.71$, $p < 0.05$).
Conclusion: The study confirmed that the level of HRQL is an informative criterion for monitoring disease activity. HRQL indicators did not deteriorate in children with JIA who continue to live in the eastern regions of Ukraine, under effective basic therapy. However, the definition of HRQL is insufficient to clarify the psychological state of the patient. Children need additional consultation with psychologists.
Disclosure
None declared

P383

Investigation of the effectiveness of the cognitive exercise therapy approach in patients diagnosed with juvenile idiopathic arthritis: a pilot study

S. Buran[1], O. Tüfekçi[2], N. B. Karaca[2], A. Barlak[2], E. Aliyev[3], M. O. Erkan[3], Y. Bilginer[3], E. Ünal[1], S. Özen[3]
[1]Department of Heart and Respiratory Physiotherapy and Rehabilitation, Hacettepe University Faculty of Physical Therapy and Rehabilitation, [2]Department of Basic Physiotherapy and Rehabilitation, Hacettepe University Institute of Health Sciences, [3]Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Türkiye
Correspondence: S. Buran
Pediatric Rheumatology, **23(2):** P383

Introduction: As emphasized in the guidelines of the Paediatric Rheumatology European Society (PReS), the multidimensional challenges caused by factors such as disease activity and chronic pain in juvenile rheumatic diseases require a holistic approach to disease management (1). It is emphasized that optimal disease management should combine pharmacological treatment with non-pharmacological approaches. In the pediatric rheumatology literature, non-pharmacological interventions with high levels of evidence are primarily active exercise and physical activity strategies, known for their anti-inflammatory effects (2). Cognitive Exercise Therapy Approach (BETY) is an innovative and original exercise method developed based on the biopsychosocial model. It has proven effectiveness in various adult rheumatic diseases (3).
Objectives: This pilot study aimed to investigate the effectiveness of the BETY on disease activity, pain, functionality, biopsychosocial status, and quality of life (QoL) in patients with Juvenile Idiopathic Arthritis (JIA).
Methods: Six individuals (four girls, two boys) diagnosed with JIA were included in the study. Demographic data were collected, and the following assessments were performed: disease activity using the Juvenile Arthritis Disease Activity Score-27 (JADAS-27); pain using the Visual Analogue Scale (VAS) and the Pain Catastrophizing Scale – child version (PCS-C); functionality using the Childhood Health Assessment Questionnaire (CHAQ); biopsychosocial status using the Juvenile Arthritis Biopsychosocial Questionnaire – Modified Version (JAB-Qm); and QoL using the Juvenile Arthritis Quality of Life Questionnaire (JAQQ). After the initial assessments, individuals with JIA participated in BETY group exercise sessions twice weekly for twelve weeks. The session content included a combination of BETY Nociplastic Pain Neuroscience Education, Function-Oriented Core Stabilization Exercises, and Dance Therapy Authentic Movement. At the end of the twelve weeks, all assessments were repeated. In addition, qualitative interviews were conducted with the patients and their families to explore their recovery experiences following the BETY sessions.
Results: Following the 12-week BETY intervention, statistically significant improvements were observed in general well-being (CHAQ; $p = 0.043$), psychosocial status (JAB-Qm psychosocial; $p = 0.027$), fatigue (JAB-Qm fatigue; $p = 0.027$), total biopsychosocial status (JAB-Qm total; $p = 0.046$), and QoL (JAQQ; $p = 0.046$). Qualitative feedback from both patients and families supported these findings, highlighting enhanced pain coping skills, increased physical capacity, improved social participation, and greater self-confidence.
Conclusion: This pilot study's findings can be interpreted as BETY positively affects fatigue, biopsychosocial status, and QoL in patients with JIA. Positive qualitative feedback from patients and their parents further supported the quantitative outcomes. Future randomized controlled trials with larger cohorts are planned to enhance the efficacy and clinical value of BETY as a biopsychosocial model-based exercise approach for patients with JIA.
Disclosure
None declared

References

1. Foster HE, Minden K, Clemente D, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases [published correction appears in Ann Rheum Dis. 2018 Jun;77(6):960. https://doi.org/10.1136/annrheumdis-2016-210112corr1]. Ann Rheum Dis. 2017;76(4):639–646.
2. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Rheumatol. 2019;71(6):846–863.
3. Unal E, Karaca NB, Saldirdak GA, et al. Investigation of the Effectiveness of a Biopsychosocial-Based Exercise Approach in Rheumatic Diseases: A Mixed Methods Research With Patients' Perspectives. *J Eval Clin Pract*. 2025;31(1):e70033.

P384

Clinical interpretation of fatigue in pediatric rheumatology: preliminary results on the feasibility of the fatigue severity scale

A. Yilmaz[1], N. Arman[2], A. Namli Seker[3,4], A. Albayrak[3,5], A. Yekdaneh[3,6], I. Donmez[1], N. Aktay Ayaz[7]
[1]Physiotherapy and Rehabilitation Master of Science Program, Istanbul University-Cerrahpasa,Institute of Graduate Studies, [2]Department of Physiotherapy and Rehabilitation, Istanbul University-Cerrahpasa, Faculty of Health Sciences, [3]Physiotherapy and Rehabilitation Doctorate Program, Istanbul University-Cerrahpasa,Institute of Graduate Studies, Istanbul, [4]Program of Podology, Aydin Adnan Menderes University, Nazilli Vocational of Health Services, Aydin, [5]Department of Physiotherapy and Rehabilitation, Istanbul Kent University, Faculty of Health Sciences, [6]Physiotherapy English Program, Fenerbahçe University Vocational School of Health Services, [7]Department of Pediatrics, Department of Pediatric Rheumatology, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye
Correspondence: A. Yilmaz
Pediatric Rheumatology, **23(2):** P384

Introduction: Fatigue is a common and disabling symptom in pediatric rheumatology, significantly affecting daily functioning but often overlooked in clinical assessments (1). Although the Fatigue Severity Scale (FSS) is a widely used tool in adults, its application in pediatric populations remains limited, and its psychometric properties have not been sufficiently validated in children and adolescents with rheumatic diseases.
Objectives: This study aimed to evaluate the internal consistency of the FSS in pediatric rheumatic conditions and to investigate its correlation with the Visual Analog Scale (VAS) for fatigue, providing preliminary data on its clinical applicability.
Methods: Fifty-two pediatric patients diagnosed with rheumatic diseases completed the 9-item FSS, which assesses the functional impact

of fatigue, and a 0–100 mm VAS to rate their current perceived fatigue. FSS scores ≥36 were considered clinically significant (2). VAS scores were classified as low (0–19), clinically relevant (20–49), and severe (≥50) (3). Internal consistency was assessed using Cronbach's alpha. Pearson correlation and cross-tabulation analyses were conducted to examine the relationship between the FSS and VAS scores.
Results: The FSS demonstrated strong internal consistency (Cronbach's α = 0.87). According to the FSS, 30.76% of the participants experienced clinically significant fatigue, while 46.15% reported severe fatigue on the VAS. A moderate positive correlation was observed between FSS and VAS scores (r = 0.38, p = 0.004), and between VAS scores and age (r = 0.33, p = 0.016). Interestingly, several participants who scored below the FSS fatigue threshold still reported severe fatigue on the VAS, indicating a potential discrepancy in capturing acute fatigue experiences.
Conclusion: Preliminary findings suggest that the FSS is a reliable and feasible tool for assessing fatigue in pediatric rheumatology, with good internal consistency. However, its sensitivity to acute or fluctuating fatigue may be limited. Combining the FSS with real-time subjective measures like the VAS can enhance the comprehensiveness of fatigue assessment, capturing both functional and immediate fatigue experiences. Children generally understood the FSS items with minimal need for adaptation, supporting its potential utility in pediatric settings. The observed increase in fatigue perception with age may reflect behavioral factors, cumulative disease burden, or both. Further studies with larger cohorts are needed to validate these findings and explore the mechanisms underlying fatigue in pediatric rheumatologic conditions.
Disclosure
None declared

References
1. Vlist, et al.Fatigue in childhood chronic disease. *Archives of disease in childhood*. 2019.
2. Huether, et al.Screening cut-off scores for clinically significant fatigue in early Parkinson's disease. *Clinical parkinsonism & related disorders*.2023.
3. Pollard, et al.Fatigue in rheumatoid arthritis reflects pain, not disease activity. Rheumatology.2006.

P385

Virtual reality and technology-assisted pain management in juvenile rheumatic diseases: a systematic review

E. Turak
Sağlık Bilimleri Fakültesi, Istanbul Aydın Üniversitesi, Istanbul, Türkiye
Correspondence: E. Turak
Pediatric Rheumatology, **23(2):** P385

Introduction: Juvenile rheumatic diseases, including Juvenile Idiopathic Arthritis (JIA), Juvenile Dermatomyositis (JDM), and Amplified Musculoskeletal Pain Syndrome (AMPS), represent a group of chronic inflammatory conditions that significantly impact pediatric patients' quality of life. Conventional physiotherapy faces limitations in long-term adherence, especially among children experiencing chronic pain. Recent advances in virtual reality (VR) and technology-assisted interventions offer promising complementary approaches in pediatric pain management and rehabilitation.
Objectives: This study aims to systematically evaluate the effectiveness of virtual reality and technology-assisted interventions in the physiotherapy and pain management of children diagnosed with juvenile rheumatic diseases.
Methods: A literature search was conducted using PubMed, Scopus, and Google Scholar databases between 2000 and 2025. The search focused on studies assessing virtual reality, exergaming, and telerehabilitation in pediatric populations with rheumatic conditions. A total of 13 eligible studies were included based on inclusion criteria emphasizing pain reduction, functional improvement, and treatment adherence.
Results: Most studies focused on children with JIA, with age ranges between 5 and 17 years. VR-based interventions led to reductions in pain and anxiety in 12 out of 13 studies, with 9 studies also reporting improvements in physical function. Studies involving JDM and AMPS patients also demonstrated positive outcomes, although research in these populations remains limited. Technology-assisted therapy was well-tolerated, and participant motivation and adherence to rehabilitation protocols increased.
Conclusion: Virtual reality and technology-supported physiotherapy demonstrate strong potential for managing pain and enhancing engagement in juvenile rheumatic diseases. Future clinical trials with larger samples and standardized intervention protocols are needed to confirm their long-term efficacy and expand their use beyond JIA.
Disclosure
None declared

P386

What can functional mri tell us about persistent pain in inflammatory arthritis across the life course? a systematic literature review

J. L. Bennett[1,2], L. Gatti[3], E. M. D. Smith[4], N. Basu[4], F. Sunzini[4], C. E. Pain[5]
[1]Paediatric Rheumatology, Great North Children's Hospital, [2]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom, [3]Rheumatology Unit, ERN ReCONNET Center, Meyer Children's Hospital IRCCS, Firenze, Italy, [4]School of Infection & Immunity, University of Glasgow, Glasgow, [5]Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom
Correspondence: J. L. Bennett
Pediatric Rheumatology, **23(2):** P386

Introduction: Early recognition and intervention for children and young people (CYP) with persistent pain is a priority for the Paediatric Rheumatology community and patients. Functional MRI (fMRI) offers the opportunity to expand our understanding of neurobiological mechanisms of chronic pain in inflammatory arthritis (IA).
Objectives: To summarise and compare studies that utilised fMRI to investigate pain in IA across the life course, to identify shared mechanisms for chronic pain that could inform future research specifically for CYP with IA.
Methods: In this systematic literature review, Medline, Embase, Scopus and Web of Science were searched for fMRI studies reporting pain outcomes in people with IA. Where possible, controlled vocabulary searching was used; in addition, titles, abstracts and keywords were searched for relevant terms. Inclusion criteria included full-text studies, randomised control trials, observational studies and case series; grey literature was excluded. De-duplication was performed prior to two reviewers independently screening the abstracts and full texts. Disagreements were resolved by a third reviewer.
Results: 277 studies were extracted after removing 172 duplicates. 49 studies passed abstract screening and, after full text screening, 30 met eligibility criteria. Several studies analysed the same patient cohort, such that 21 cohorts were represented with a median (IQR) IA sample size of 38 (20-54). Apart from one RCT, all studies were observational and 14 included a healthy control group. Neuroimaging methods comprised resting-state fMRI (n=13), pain stimulus fMRI (n=10), task-based fMRI (n=6), arterial spin labelling (n=2) and magnetoencephalography (n=1). 5 studies did not provide data on DMARD use.
The IA types studied were JIA (n=2), rheumatoid arthritis (RA, n=18), ankylosing spondylitis (AS, n=9), psoriatic arthritis (PsA, n=2), and spondyloarthropathies (n=2). In studies focusing on one IA type, the average age ranges (years) were 45-57 (RA), 26-39 (AS) and 9-12 (JIA).
Both JIA studies deployed resting state (rs)-fMRI. Weng et al. focused on the hippocampus in 21 drug-naïve CYP, reporting associations between altered functional connectivity (FC) of this region and disability, ESR and anxiety(1). In a cohort of 16 CYP on a range of JIA treatments, Upadhyay et al. observed that decreased FC between the default mode network (DMN) and insula was associated with greater pain intensity(2). In contrast, rs-fMRI in PsA and task-based fMRI in RA identified increased DMN-insula FC in adults with higher fibromyalgia scores. In JIA, compared with controls, there was decreased FC of sensorimotor regions as well as regions regulating emotional aspects of pain(2). In two case series of RA patients treated with TNF inhibitors, high insula activation at baseline reduced within days of therapy commencing.
Conclusion: Most fMRI studies of pain in IA have focused on adults, particularly those with RA. Comparing CYP with adults, there may be divergent associations between DMN-insula FC and pain in IA. Further

studies are required to test the extent that adult neurobiological signatures of pain in IA also apply to CYP.

Disclosure

None declared

References

1. Weng Y, et al. The Brain Structural–Functional Vulnerability in Drug-Naive Children With Juvenile Idiopathic Arthritis: Insights From the Hippocampus. Front Hum Neurosci. 2022;16:833,602.
2. Upadhyay J, et al. A multidisciplinary assessment of pain in juvenile idiopathic arthritis. Semin Arthritis Rheum. 2021;51(4):700–11.

P387

Chronic pain in patients with chronic non-bacterial osteomyelitis (CNO), incidence and potential risk factors

K. Warciak, O. Killeen
National Centre for Rheumatology, CHI-Crumlin, Dublin, Ireland
Correspondence: K. Warciak
Pediatric Rheumatology, **23(2):** P387

Introduction: CNO is a rare inflammatory bone disease predominantly affecting long bones[1-6]. Pain and bone swelling are typical presenting features[1-6]. In many, lesions are asymptomatic[1-6]. Whole-body MRI is now recognised as the gold standard for diagnosis[1-7]. Early reports suggested a self-limiting disease for the majority but more recent reports suggest many will still have radiological and clinically active disease into adulthood[7]. Chronic pain is reported but the incidence and risk factors remain poorly described to date.
Objectives: To evaluate chronic pain and identify potential risk factors in our cohort of patients with CNO.
Methods: Clinical,laboratory and radiological data was obtained retrospectively from patients health records,of patients diagnosed from 2019-2024. Patient's demographics and any reports of chronic pain defined as daily pain over three months in duration were noted, with current treatments and most recent whole body MRI imaging at their last clinical assessment.
Results: 33 patients were identified, 58%(N=19) females, 42%(N=14) males. Median age at diagnosis was 11-years (6-15 years). Average disease duration was of 4-years (1-6 years). At last follow up, 50%(N=17) reported pain. In total 15%(N=5) of patients met the criteria of chronic pain. 4 were female. Age at diagnosis was 9 to 12-years. Disease duration ranged from 1-4 years. Most recent WBMRI was, inactive disease =3, partial resolution =1, and worse =1. 4 patients required 1-2 second line agents: Methotrexate and/or anti-TNF therapy. In addition 60%(N=3) required one-year of Bisphosphonates treatment. 60%(N=3) of patients had raised inflammatory markers at time of diagnosis, measured with Erythrocytes Sedimentation Rate and/or C-Reactive-Protein. All five patients stopped regular physical activities, with reduced physiotherapy attendance. All had significant school absenteeism reported.
Conclusion: Female sex,12-years-of-age and above and raised inflammatory markers at diagnosis were identified as risk factors for chronic pain.Poor school attendance and inactivity was significant in those with chronic pain.Our study shows that chronic pain can develop in patients with CNO leading to a significant impact on quality of life and education.

Disclosure

None declared

P388

Patient-related outcomes in children with rheumatic diseases in Mexico

L. D. C. Reynoso Medina, M. M. Rodríguez Reyes, C. E. López Cardona, Z. I. García Murillo, F. A. Vásquez Triminio, A. V. Villarreal Treviño, F. García Rodríguez, N. E. Rubio Pérez, on behalf of Colaborativa de Investigación en Beneficio de la Reumatología Infantil (COLIBRI)
Reumatología Pediátrica, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Mexico
Correspondence: L. D. C. Reynoso Medina
Pediatric Rheumatology, **23(2):** P388

Introduction: Rheumatic diseases pose a risk to patients' functional capacity and are associated with functional disability, pain, and difficulty performing daily life activities. These factors significantly deteriorate the quality of life, including physical, emotional, academic, and personal development aspects. These outcomes cannot be measured directly, which is why Patient-Reported Outcomes (PROs) have been established as ideal tools for their assessment.
Objectives: To analyze the impact of disease, through PROs, in pediatric patients with rheumatic diseases.
Methods: A cross-sectional descriptive study was conducted using non-random, consecutive sampling. Pediatric patients diagnosed with chronic rheumatologic diseases who attended the Pediatric Rheumatology Service at Hospital Universitario "Dr. José Eleuterio González" during April and May 2025 were included. The Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) and the Morisky-Green test for treatment adherence were applied. Seven PROMIS-29 domains were analyzed: physical function, anxiety, depression, fatigue, sleep disturbance, social functioning, and pain interference. Each domain score ranges from 4 to 20, with scores below 10 considered adverse outcomes.
Results: A total of 30 patients were included, with a median age of 12 years (range 5–18, IQR 10–15). Twenty (66.7%) of them were female. Diagnoses included Juvenile Idiopathic Arthritis (17; 56.7%), Systemic Lupus Erythematosus (5; 16.7%), Juvenile Dermatomyositis (4; 13.3%), Scleroderma (3; 10%), and Systemic Sclerosis (1; 3.3%). Treatment adherence, assessed by the Morisky-Green test, was observed in 66.7% of patients.The PROMIS-29 domain results were: physical function (median 19; IQR 17–20), anxiety (median 17; IQR 14–19), depression (median 19; IQR 15–20), fatigue (median 16; IQR 13–20), sleep disturbance (median 16; IQR 13–18), social functioning (median 15; IQR 10–16), and pain interference (median 18; IQR 14–20). Ten patients (33.3%) showed impairment in at least one domain, of whom 70% had clinically active disease. The affected domains were: social function in 8 patients, fatigue in 3, sleep in 2, pain in 2, and depression in 1.
Conclusion: One-third of the patients showed impairment in PROMIS-29 measurements, out of these, the majority (70%) had clinically active disease. Interventions aimed at improving health-related quality of life in pediatric patients with rheumatologic diseases are crucial, as these conditions can significantly impact children's physical, emotional, and social well-being.

Disclosure

None declared

References

1. García-Galicia A, Hernández-Sánchez V, Santaella-Avalos A, Martínez-Hernández AJ, Montiel-Jarquín ÁJ, Barranco-Cuevas IA, et al. [Quality of life and disease activity assessment in juvenile idiopathic arthritis]. Rev Med Inst Mex Seguro Soc. 14 de junio de 2021;59(2):133–40.
2. Frye WS, Milojevic D. The Role of Psychology in Pediatric Rheumatic Diseases. Pediatr Clin North Am. octubre de 2022;69(5):965–74.

P389

Attitudes and barriers to vaccination in pediatric rheumatic disease

R. L. Hetrick[1], A. Chow[2], S. Chandrasena[3], G. Brock[3], M. Kohlheim[4], V. Del Gaizo[4], P. Chiraseveenuprapund[5], C. J. van Rensburg[6], M. G. El Sayed[7], B. Rutstein[8], V. Sivaraman[9,10], M. Heshin-Bekenstein[11,12], on behalf of Childhood Arthritis and Rheumatology Research Alliance (CARRA) Vaccination Workgroup.
[1]School of Medicine, Indiana University, Indianapolis, IN, [2]Pediatrics, Loma Linda University Children's Hospital, Loma Linda, CA, [3]Center for Biostatistics,, The Ohio State University Wexner Medical Center, Columbus, OH, [4]Childhood Arthritis and Rheumatology Research Alliance, Washington DC, [5]University of Utah, Salt Lake City, UT, United States, [6]Children's Hospital Research Institute of Manitoba, Winnipeg, MB, Canada, [7]Riverside School of Medicine, University of California, Riverside, CA, United States, [8]Rheumatology, Children Hospital of Philadelfia, Philadelphia, PA, Israel, [9]Pediatrics, The Ohio State University College of Medicine, [10]Rheumatology, Nationwide Children's Hospital, Columbus, OH, United States, [11]Pediatric Rheumatology, Dana Dwek Children's Hospital of Tel Aviv Medical Center, [12]School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel
Correspondence: M. Heshin-Bekenstein
Pediatric Rheumatology, **23(2):** P389

Introduction: Vaccine-preventable diseases pose greater risk to pediatric rheumatic disease (PRD) patients treated with immunosuppressive therapies and to those with underlying immune dysregulation. Despite the importance of vaccine protection, PRD patients often have lower vaccination rates compared to healthy populations. The drivers of decreased vaccine uptake in PRD patients are poorly understood.
Objectives: This study examines the caregiver attitudes and barriers surrounding immunization in PRD patients.
Methods: This study included a voluntary online survey of caregivers of PRD patients recruited through online parent support groups for PRD patients from June – July 2024. General vaccine hesitancy was assessed via a modified Parental Attitudes about Childhood Vaccines – Short Form (PACV-SF), a 4-question scale designed to screen for vaccine hesitant caregivers.[1] Additional questions on vaccination barriers were developed by the CARRA Vaccination Work Group. The primary outcome was caregiver report of immunization status. Associations with explanatory variables were assessed using chi-squared tests and Fisher's exact test for categorical variables and Wilcoxon rank-sum tests for continuous variables. Univariable and multivariable logistic regression analyses were used to examine the association between vaccination status and explanatory variables. Multivariable Model 1 includes all explanatory variables while multivariable Model 2 includes only those found to be significant in the univariable analysis.
Results: Of the 163 respondents, 104 (64%) reported that their child had received all recommended immunizations and 59 (36%) reported partial immunization, no immunization, or uncertain immunization status. General vaccine hesitancy, indicated by a score $\geq$2 on the PACV-SF, was strongly associated with a lower odds of immunization uptake (OR 0.16, 95% CI 0.08-0.32, p<0.001) in all models. Age was associated with increased odds of immunization uptake in the univariable model and multivariable Model 1. Vaccine hesitancy related to rheumatic disease was associated with decreased odds of immunization uptake in the univariable model but this association became non-significant in the multivariable models.
Conclusion: General vaccine hesitancy in caregivers strongly predicted decreased odds of fully immunized status in children. While unsurprising, this was the only factor undiminished in all multivariable models, suggesting a strong independent relationship. In contrast, vaccine hesitancy related to the child's rheumatic disease diagnosis was not significant in the multivariable models. The study's limitations include unknown generalizability due to convenience sampling and relatively small sample size. Nevertheless, this study suggests that general vaccine hesitancy may play a stronger role in caregiver immunization decisions than other barrier types.
Disclosure
None declared

Reference
1. Opel DJ, Henrikson N, Lepere K, et al. Previsit Screening for Parental Vaccine Hesitancy: A Cluster Randomized Trial. *Pediatrics*. 2019;144(5):e20190802. doi:https://doi.org/10.1542/peds.2019-0802

P390

Impact of methotrexate-associated adverse events on one-year outcomes in children with juvenile idiopathic arthritis

R. Mckenna[1], K. Hyrich[1,2,3], L. Kearsley-Fleet[1], E. A. Baildam[4], M. W. Beresford[5,6], S. Douglas[7], T. Southwood[8], J. Humphreys[1,2,3], S. A. Shoop-Worrall[1]
[1]Centre for Musculoskeletal Research, The University of Manchester, [2]Manchester University NHS Foundation Trust, [3]Kellgren Centre for Rheumatology, [4]The Alexandra Hospital, Manchester, [5]Alder Hey Children's NHS Foundation Trust, [6]University of Liverpool, Liverpool, [7]Scottish Network for Arthritis in Children (SNAC), Glasgow, [8]University of Birmingham, Birmingham, United Kingdom
Correspondence: R. Mckenna
Pediatric Rheumatology, **23(2):** P390

Introduction: Methotrexate (MTX) is a first-line treatment for juvenile idiopathic arthritis (JIA), aimed at reducing disease activity and improving function. However, MTX-associated adverse events (AEs), particularly gastrointestinal symptoms, may affect treatment experiences and patient-reported outcomes. The potential longer-term impact of AEs on wellbeing and disease activity remains unclear.
Objectives: To explore the impact of MTX-associated AEs experienced during the first year of treatment on six core JIA outcomes at one year in children and young people (CYP) with JIA.
Methods: This analysis used data from the UK JIA Biologics Register, a national prospective observational treatment cohort. CYP starting MTX between January 2003 and December 2018 with at least 12 months of follow-up were included. MTX-associated AEs were recorded by the treating physician and reported to the register at 6 and 12 months. Six JIA core outcomes were assessed at one year: patient/parent global assessment of wellbeing, physician global assessment of disease activity, active joint count, limited joint count, Childhood Health Assessment Questionnaire (CHAQ) for functional ability, and erythrocyte sedimentation rate (ESR).
Linear regression models were used to compare core outcome variables between those with and those without AEs at baseline, one year, as well as change in outcomes from baseline to one year. Multivariable linear regression models adjusted for age, gender and baseline outcome values were used to assess associations between experiencing an AE and one-year outcomes. Baseline and 1 year core outcomes were imputed to account for missing data.
Results: A total of 774 CYP starting MTX were included, of whom 234 (30%) reported at least one AE during the first year. At one year, those who experienced AEs had significantly worse global wellbeing scores (median 1.7 cm vs 0.8 cm, p = 0.014) and worse physician global assessment scores (median 0.7 cm vs 0.1 cm, p = 0.045). In the adjusted multivariable regression model, AE exposure remained significantly associated with poorer wellbeing (β = 0.45, 95% CI: 0.05–0.86). No significant differences were observed in joint counts or ESR
Conclusion: CYP who experienced MTX-associated AEs during the first year of treatment reported poorer wellbeing at one year. These findings highlight the longer-term impact of MTX-associated AEs on patient-reported outcomes.
Disclosure
None declared

P393

Patient journey in paediatric rheumatology: the example of juvenile idiopathic arthritis (JIA)

C. Normand[1,2,3], on behalf of ERN-RITA Patient Journey working group on behalf of ERN-RITA Patient Journey working group
[1]ERN-RITA, Utrecht, Netherlands, [2]KOURIR, Paris, France, [3]ENCA, Wateringen, Netherlands
Correspondence: C. Normand
Pediatric Rheumatology, **23(2):** P393

Introduction: Most of the European
Reference Networks (ERNs) have started developing various tools aimed at empowering patients and families, as well as disseminating knowledge in an accessible and understandable format. In this context, the patient journey represents an important realisation—a communication tool created by patients for patients. Due to the rarity of these conditions, it is more coherent to develop such resources at the European level, highlighting shared experiences across countries. In ERN-RITA for paediatric rheumatology, the first patient journey made available focuses on children and adolescents living with Juvenile Idiopathic Arthritis (JIA).
Objectives: Each patient journey offers the perspective of patients and their families on the condition, sharing their experiences across different phases such as symptom onset, diagnosis, treatment, follow-up, and ageing. In the case of the JIA patient journey, it was essential to capture both the patient's and family's experiences, their various interactions with the healthcare system, and the challenges and needs they expressed.
While this tool is important for patients and families, it can also serve to raise awareness among different stakeholders about the condition and open up new possibilities for more holistic and patient-centred care.
Methods: A common methodology developed by the Patient Journey Working Group has been defined for the different ERN RITA streams and is available on our website*. It includes a review of existing

literature**, the definition of elements common to our diseases, the identification of potential challenges, and the development of a shared framework applicable to all conditions.
After selecting one condition for each stream, JIA in our case, focus groups were conducted across various European countries and in different languages. The data collected was then analysed and compiled by patient partners. The resulting patient journey was subsequently validated by both patients and associated physicians.
The final step involves the design phase, ensuring effective dissemination throughout the ERN RITA network.
Results: A JIA Patient Journey is available in English to provide patients and families with a different perspective on living with the disease in daily life. While it touches on interactions with care pathways, it differs significantly in its approach.
It offers an international foundation for the future implementation of best practices across Europe and serves as a valuable resource for physicians and healthcare professionals. It helps them better understand their patients' needs and provides insights for developing training courses and practical tools to address the various aspects and impacts of the condition.
Conclusion: This JIA patient journey, developed in the frame of the ERN RITA Working Group, represents a first step toward providing patients and families with reliable, relevant, and verified information—especially in contrast to the overwhelming and often unfiltered content found online.
It should be further enriched by covering additional conditions and regularly updated to reflect evolving perspectives on care within society.
Disclosure
None declared

References

1. Patient Journey Handbook, ERN Rita, ERN-Rita-Patient-Journey-Handbook.pdf
2. Bolz-Johnson, M., Meek, J. & Hoogerbrugge, N. "Patient Journeys": improving care by patient involvement. Eur J Hum Genet **28**, 141–143 (2020). https://doi.org/10.1038/s41431-019-0555-6

P394

Co-designing the future of transitional care: a patient-centered approach from ERN reconnet

E. Marrani[1], on behalf of ERN ReCONNET Transitional Care Task Force, M. Z. Avramovic[2], D. Marinello[3], R. Talarico[4], C. Baldini[4], E. Collado-Gonzalez[5], L. Schraven[6], F. Oliveira Ramos[7], P. Triggianese[8], A. Vissink[9], A. M. Zacarias[10], M. mosca[4], T. Avcin[2], G. Simonini[1]
[1]Rheumatology Unit, IRCCS Meyer Children's Hospital, Firenze, Italy, [2]Department of Allergology, Rheumatology and Clinical Immunology, Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia, [3]ERN ReCONNET Center, [4]Rheumatology Unit, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy, [5]Asociacion Nacional del Sındrome de Ehlers-Danlos e Hiperlaxitud,, Murcia, Spain, [6]Federation of European Scleroderma Associations, Saint Maur, Belgium, [7]Unidade de Reumatologia Pediatric, Hospital Universitario Santa Maria, Lisbon, Portugal, [8]Department of Systems Medicine, University of Rome Tor Vergata, Roma, Italy, [9]Department of Oral and Maxillofacial Surgery, University of Groningen, Groningen, Netherlands, [10]Rheumatology Unit, Hospital Sant Joan de Dèu, Barcelona, Spain
Correspondence: E. Marrani
Pediatric Rheumatology, **23(2):** P394

Introduction: Transition from pediatric to adult care remains a key challenge for patients with rare and low-prevalence connective tissue disorders (rCTDs). European
Reference Networks (ERNs), including ERN ReCONNET, aim to improve patient care across Member States. However, significant differences persist in transition protocols and their implementation. The ERN ReCONNET Transition of care Task Force, composed of clinicians, patient representatives, and ERN ReCONNET coordination team members—in collaboration with ERN RITA—has undertaken a comprehensive assessment to develop a scientifically grounded, co-designed transition pathway that integrates perspectives of both patients and caregivers.
Objectives: The main objective of this initiative is to map existing transition pathways within ERN ReCONNET healthcare providers (HCPs) and identify the different unmet needs. A secondary goal is to co-design a harmonized transition model—incorporating direct input from young patients (YP) and caregivers—to be shared within and outside ERN ReCONNET centers and promote standardized, high-quality patient-centered care.
Methods: A two-phase survey approach was implemented. Phase I (December 2023–March 2024) targeted HCPs and collected 56 responses from 47 full members or affiliated partners of ERN ReCONNET (73% response rate). Phase II is currently ongoing, with the patient/caregiver survey being translated into 21 European languages. Distribution is scheduled for summer 2025, targeting at least 1,000 respondents overall.Once both datasets are available, their comparison will guide the development of a co-designed best-practice transition pathway for rCTDs, to be disseminated across the whole rCTD scientific and patient community.
Results: The HCP-directed survey revealed a marked heterogeneity in transition practices across centers, with critical gaps in patient identification, readiness assessment, and inter-center coordination. Notably, limited engagement from adult healthcare professionals and absence of formalized guidelines were reported. A lack of patient and caregiver input in current models further impedes effective transition.These findings underscore the need for a structured, co-designed approach that reflects the real needs and expectations of patients. Comparing the expectations and unmet needs of HCPs with those of YP and their caregivers will enable truly shared decision-making in the care transition process.
Conclusion: The HCP survey results demonstrate an urgent need for standardized, co-designed transition pathways for patients with rCTDs. A harmonised model, combining clinical expertise with lived experience, is being developed to enhance care continuity and patient satisfaction. The upcoming patient and caregiver survey will complete this process, resulting in a replicable framework to be adopted by ERN ReCONNET centers as well as by other centres taking care of rCTDs patients. As a next step, a dedicated meeting will be organized to share best practices and consolidate knowledge, fostering widespread implementation and collaboration.
Disclosure
None declared

Reference

1. Marrani E, Zajc Avramovic M, Marinello D, Talarico R, Baldini C, Collado-González E, Fonseca JE, Schraven L, Oliveira Ramos F, Triggianese P, Vissink A, Mosca M, Avcin T, Simonini G. Challenges in the transition of care for rare connective tissue diseases: results from the 2023 ERN ReCONNET Transition of Care Task Force survey. Rheumatol Adv Pract. 2025 Jan 11;9(1):rkae149. https://doi.org/10.1093/rap/rkae149. PMID: 39886538; PMCID: PMC11780841

P395

The educational role of the team of middle-standing pediatric rheumatologists alliance (tempra) for the continuous professional development of pediatric rheumatologists in Japan

H. Wakiguchi[1], K. Hashimoto[2], M. Yashiro[3], K. Nishimura[4], T. Ebato[5], K. Akamine[6], Y. Uejima[7], T. Sato[8], K. Ouchi[9], M. Mizuta[10], Y. Sugita[11], N. Inoue[12], Y. Kitagawa[13], N. Okamoto[11,14], Y. Nakagishi[10], M. Shimizu[15]
[1]Division of General Pediatrics and Emergency Medicine, Department of Pediatrics, Oita University Faculty of Medicine, Yufu, [2]Department of Pediatrics, Nagasaki University School of Biomedical Sciences, Nagasaki, [3]Department of Pediatrics, Okayama University Hospital, Okayama, [4]Department of Pediatrics, Yokohama City University Graduate School of Medicine, Yokohama, [5]Department of Pediatrics, Kitasato University, Sagamihara, [6]Department of Nephrology and Rheumatology, Tokyo Metropolitan Children's Medical Center, Fuchu, [7]Division of Infectious Diseases and Immunology, Saitama Children's Medical Center, Saitama, [8]Clinical Education Center for Physicians, Shiga University of Medical Science, Shiga, [9]Department of Pediatrics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, [10]Department of Pediatric Rheumatology, Hyogo Prefectural Kobe Children's Hospital, Kobe, [11]Department of Pediatrics, School of Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, [12]Department of Pediatrics, Kanazawa University, Kanazawa, [13]Nagakute Children's Clinic, Nagakute,

[14]Department of Pediatrics, Osaka Rosai Hospital, Sakai, [15]Department of Pediatrics, Perinatal and Maternal Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan
Correspondence: H. Wakiguchi
Pediatric Rheumatology, **23(2):** P395

Introduction: In Japan, a country with a long north-south axis, there are few pediatric rheumatologists practicing in each region; therefore, the Team of Middle-standing Pediatric Rheumatologists Alliance (TeMPRA) was formed in 2014 to support the continuing professional development (CPD) of pediatric rheumatologists, especially those in mid-career, to easily ask clinical questions and receive training across regions.
Objectives: To assess the current status and future prospects of TeMPRA.
Methods: We conducted a cross-sectional survey of TeMPRA members in 2024. We created a questionnaire to assess career, clinical practice, education, and perspectives. We invited a total of 37 TeMPRA members to participate in this study.
Results: Thirty-five TeMPRA members responded to the survey with a 95% response rate. Most respondents were affiliated with university hospitals, followed by community hospitals, children's hospitals, and clinics. These hospitals were geographically diverse and evenly distributed across Japan. Three-quarters were in their 40s. Half of the respondents had more than 10 years of experience as pediatric rheumatologists. Most respondents had additional subspecialties in allergy, immunology, nephrology, gastroenterology, infectious diseases, emergency medicine, hematology, or neonatology. Half of the respondents were involved in the training of young pediatric rheumatologists. All respondents expressed their hope to contribute to pediatric rheumatology regionally, and almost all in Japan, and three-quarters in the world.
Conclusion: This study showed that TeMPRA members with multiple specialties were interested in being actively involved in educational and international activities in pediatric rheumatology. Thus, TeMPRA has contributed to supporting CPD among pediatric rheumatologists in Japan. Such efforts are expected to contribute to the CPD of pediatric rheumatologists internationally, especially in the field of pediatric rheumatology where there are few specialists.
Disclosure
None declared

P397

Practical multidisciplinary implementation of developmentally appropriate healthcare in a young adult rheumatology service: the sheffield model

M. Sabkar[1], L. Deugo[2], J. Edgerton[2], M. Forsythe[1], R. Nirmal[1], R. Tattersall[1]
[1]Rheumatology, Sheffield Teaching Hospitals, [2]Rheumatology, Sheffield Children's NHS Foundation Trust, Sheffield, United Kingdom
Correspondence: M. Sabkar
Pediatric Rheumatology, **23(2):** P397

Introduction: Developmentally appropriate healthcare (DAH) recognizes adolescence and young adulthood (AYA) as distinct developmental stages requiring tailored care and system adaptation(1). UK evidence confirms significant gaps in transition/AYA care(2). Evaluation of Sheffield Teaching Hospitals' Young Adult Clinic (YAC) demonstrated compliance with key DAH principles and positive patient experiences(3).
Objectives: To present Sheffield's practical approach to implementing a developmentally appropriate rheumatology service highlighting generalisable, low resource, applicable features with particular focus on nurse-led innovations.
Methods: We undertook a service evaluation of the young adult clinic(3) benchmarking the service against a DAH toolkit, surveying 11% of YAC attendees. Using these findings we undertook a nurse-led review of the service across children's and adult rheumatology services to understand barriers and enablers to DAH.
Results: Our service looks after 250 people over 11 in children's services, 360 young people in adult services, an average of 60 patients transferred annually.

Pre-transition Phase
- Age-bracketed (11-16) general/specialty (uveitis/CTD) joint adult-paediatric clinics
- Clipboards showing clinic information/staff photos prior to clinic and bubble diagrams (co-designed by nurses/patients) for agenda setting
- Patients seen alone by nurses
- Whatsapp group - peer support
- Weekly team meeting for therapy transition
- Nurse designed welcome patient pack

Transfer phase
- By agreement with patient/family
- Dedicated information pack
- QR code for virtual tour of YAC
- Personalised welcome letter
- Nurse led telephone calls (extra support)
- Nurse led completion of standardized transfer documents
- Enhanced reminder system to reduce non-attendance

Post transfer phase
- Clinics held in sports center
- Children's nurse attends for continuity
- Second telephone appointment 4-6 weeks after first attendance to check medicines transition/maintain contact
- dedicated administrative support

Conclusion: Our YAC model evaluation(3) prompted this project showing positive DAH compliance and satisfaction, areas for improvement/barriers to DAH (peer support/evening clinics). High quality care can be delivered by joint working and features that are largely nurse-led and innovated, low resource and widely applicable; 'doing core business better' A key feature of DAH is organizational buy in to develop and sustain services – for which this evaluation proves.
Disclosure
None declared

References

1. National Institute for Health and Care Excellence.Transition from children's to adults' services for young people using health or social care services.NICE guideline.2016.Available from:www.nice.org.uk/guidance/ng43
2. The National Confidential Enquiry into Patient Outcome and Death.Joint Care?A review of the quality of care provided to children and young adults with juvenile idiopathic arthritis.London.2025.Available from:https://www.ncepod.org.uk/2025jia/Summary%20report_JIA_Joint%20Care.pdf
3. Nirmal R,Tattersall R.Evaluating the developmentally appropriate approach of a young adult rheumatology service:using young peoples' perspectives to improve services.Sheffield, Sheffield Teaching Hospitals NHS Foundation Trust;2025.Presented at EULAR 2025

P398

Title: when the right drug is out of reach: ethical and clinical challenges in managing rare pediatric rheumatologic disorders in low- and middle-income countries

C. S. Bhat, N. Nayak
Paediatric Rheumatology, Rainbow Children's Hospital, Bengaluru, India
Correspondence: N. Nayak
Pediatric Rheumatology, **23(2):** P398

Introduction: Rare rheumatologic conditions such as Complement Hyperactivation, Angiopathic Thrombosis and Protein-Losing Enteropathy (CHAPLE syndrome), and Hyperimmunoglobulin D Syndrome (HIDS) pose significant diagnostic and therapeutic challenges. These diseases demand early and precise initiation of targeted biologic therapies. However, in low- and middle-income countries (LMICs), access to these life-saving treatments is severely limited. Drugs such as pozelimab (anti-C5 monoclonal antibody) and canakinumab (IL-1β inhibitor) offer disease-specific efficacy, yet are often inaccessible. More commonly available alternatives like etanercept and anakinra provide only partial or non-specific immunomodulation, often resulting in suboptimal outcomes. In India, acquiring the appropriate targeted biologic remains a formidable challenge.
Objectives: To highlight the clinical and ethical challenges of managing rare autoinflammatory diseases in India when ideal biologics are unavailable or unaffordable, and to examine the consequences of using less effective substitutes.

Methods: A retrospective analysis was conducted on four pediatric patients—one with genetically confirmed CHAPLE syndrome and three with genetically confirmed HIDS. We evaluated clinical presentation, treatment strategies, drug procurement pathways, cost implications, and outcomes.
Results: The CHAPLE patient initially received steroids and etanercept with minimal clinical benefit. Upon genetic diagnosis, pozelimab was identified as the appropriate therapy and was acquired through a compassionate-use program enabled by international collaboration. Following treatment, the patient exhibited marked clinical improvement within two months.
Of the three HIDS patients, one child was from India and two were from the Maldives. The Indian patient was managed with etanercept due to unavailability of canakinumab. The disease remained refractory, and the patient succumbed within a year. In contrast, the two Maldivian children received canakinumab after genetic confirmation—one transitioned from anakinra, and the other was started promptly post-diagnosis. Both showed significant clinical improvement and achieved remission, with costs covered under the Maldivian national health insurance program
Conclusion: For rare pediatric rheumatologic disorders, access to the correct biologic is essential—not optional. Delayed or inappropriate therapy exacerbates morbidity, increases long-term costs, and undermines trust. LMICs like India require expedited drug approval processes, equitable access schemes, and enhanced international partnerships to address the stark disparities in rare disease care.
Disclosure
None declared

P399

The evolving role of the paediatric rheumatology pharmacist in the united kingdom

O. Aragon Cuevas
Pharmacy, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom
Correspondence: O. Aragon Cuevas
Pediatric Rheumatology, **23(2):** P399

Introduction: The British Society of Rheumatology recommended in 2021 and 2023 that rheumatology departments in the UK ensure access to specialist pharmacists, capitalising on their clinical knowledge and skills and offer them opportunities to extend their scope of practice to meet increasing service demands [1,2]
Objectives: To showcase the variety of roles Paediatric Rheumatology Pharmacists (PRPh) can fulfil within the paediatric rheumatology MDT
Methods: A survey was distributed to UK PRPh to detemine their roles and responsibilities, including differences between adult and paediatric practice
Results: 11/15 (73%) PRPh answered the survey. Reported working schedules varied but the majority worked less then full time, and this was dependent on individual funding agreements as opposed to population catchement area. Responses highlighted that PRPh are less likely to run clinics compared to their adult counterparts. PRPh were found to alleviate their MDT colleagues' workload by taking on drug education and safety blood monitoring roles, or use their prescribing skills to manage and adjust drugs (issuing and reviewing repeat hospital-only prescriptions and day-case infusions for complex medicines). PRPh who undergo further physical assessment and clinical decision making training were found to review patients in clinic settings. They were also be part of 'one-stop' MDT or holistic/lifestyle clinics, transition to adult services or annual review clinics. A number of roles highly suited to PRPh include navigating complex commissioning pathways for high-cost drugs, leading on cost-improvement programmes (biosimilar switches, drug contract negotiating, pill swallowing schools), drug guideline development and safe prescribing education. In particular, PRPh were found to play a key role in managing drug shortages and recommending appropriate alternatives. For new formulary additions, they can ensure that formulations are age appropriate and contain safe levels of excipients. They can use their pharmacology and drug development knowledge to advice on the safest way to use medicines for children in an off-label or unlicensed manner
Conclusion: This survery demonstrates PRPh with appropriate training can become a key member of the MDT, allowing specialist nurses and clinicians to fulfil roles currently restricted due to capacity pressures. Allowing PRPh to expand their roles could lead to improved patient outcomes, reduction of prescribing errors and better job satifaction and retention within the profession[3]
Disclosure
None declared

References

1. British Society of Rheumatology, Rheumatology workforce: a crisis in numbers, 2021. Available from: BSR-workforce-report-crisis-numbers.pdf Accessed May 2025
2. British Society of Rheumatology, The People We Need: Our plan to grow the rheumatology workforce and enable excellent care, April 2023. Available from:Manifesto final c.pdf. Accessed May 2025
3. Hazen, A., Pouls, B., Nazar, H. et al.European Society of Clinical Pharmacy: 'the prescribing pharmacist: a prescription for better patient care'. *Int J Clin Pharm46*, 1245–1246 (2024)

P400

Czech national care pathway proposal for paediatric rheumatology patients

P. Šeferna, P. Doležalová, Š. Fingerhutová
General University Hospital in Prague, Prague, Czech Republic
Correspondence: P. Šeferna
Pediatric Rheumatology, **23(2):** P400

Introduction: Paediatric Rheumatic Diseases (PRD) represent a unique group of rare diseases that require coordination of care between many specialists across the care continuum, from primary care, community and social services to secondary care and specialists in regional and national centres. "Care pathway" (CP) is understood as a methodology for mutual decision making and organisation of care that resembles a detailed care plan, charting each step for a specific patient population to reach efficiently the best outcomes and quality of life. In Czechia the healthcare strategy has not been officially defined for majority of rare diseases including PRD.
Objectives: To propose the paediatric rheumatology care pathway
Methods: As a part of the national project SYPOVO the CP followed the detailed analysis of the current situation of the PR healthcare provision and formulation of general structure of the CP to include following sections: Structure of specialised healthcare (centre and network characteristics) and Patient-centred care (suspicion, diagnosis confirmation, treatment principles, long-term management).
Results: The estimated number of patients with chronic inflammatory PRD in Czechia is around 2500. Currently, majority are followed in one of the 10 units served by 16 board-certified paediatric rheumatologists (9 part-time). Only one unit has an official status of the highly-specialised centre for PRD, the other operate within larger, mostly general paediatric departments of university (7) or regional (3) hospitals. All units are overloaded with clinical duties and lack staff. The CP defines criteria for highly specialised and specialised centres including staff, space and equipment as well as access to other specialised services. Definition of competencies covers mainly clinical care (e.g. confirmation of diagnosis, Orphacoding, registry entry, regular disease outcome assessment, coordination of complex care and long-term management including transition) and pharmacotherapy (access to biologics and experimental therapies). All centres form a PR National Reference Network with the link to the European Reference Network (ERN) RITA. Referral pattern includes guidance for primary care physicians and non-specialised paediatricians on symptoms requiring specialist assessment as well as the type of referral (urgent, non-urgent).
Conclusion: The proposed care pathway provides a structured framework to improve the organisation, equity, and quality of care for children with PRD in Czechia. Its implementation can enhance early diagnosis, optimise treatment access, support care continuity, and ultimately improve patient outcomes and quality of life.
Acknowledgement
Supported by ESF+ project CZ.03.02.02/00/22_046/0002450

Disclosure
None declared

PU01

Investigating disease activity and related biopsychosocial characteristics by sex in children with JIA - a pilot study

A. Barlak[1], O. Tüfekçi[1], S. Buran[1], E. Aliyev[2], M. O. Erkan[2], Y. Bilginer[2], E. Ünal[1], S. Özen[2]
[1]Faculty of Physical Therapy and Rehabilitation, [2]Faculty of Medicine, Department of Pediatrics, Division of Rheumatology, Hacettepe University, Ankara, Türkiye
Correspondence: S. Buran
Pediatric Rheumatology, **23(2):** PU01

Introduction: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease characterized by disease activity and remission phases with unknown etiology and onset before age 16 (1). JIA is reported to be slightly more common in females (2, 3). Besides the pain and functional losses experienced by these subjects, they are also affected psychosocially. (4).
Objectives: This pilot study aimed to investigate the disease activity related to biopsychosocial characteristics of children diagnosed with JIA by sex.
Methods: Forty subjects (25 female, 15 male) with JIA were included in the study. The subjects were divided into 2 groups: male and female. Biopsychosocial status was evaluated with the Juvenile Arthritis Biopsychosocial Questionnaire-Child (JAB-Q-C) and disease activity with the Juvenile Arthritis Disease Activity Score in 27 joints (JADAS-27). The Mann-Whitney U test was used to compare the characteristics of the groups, and Spearman correlation analysis was used to analyze the relationships.
Results: The mean age was 13.10±3.19 years, and the mean body mass index was 19.16±3.97 kg/m^2. There was no significant difference between the groups in terms of scores ($p>0.05$). In males, the JAB-Q Total Score was moderately to highly correlated with all JAB-Q subscales, except the JAB-Q Joint Perception subscale. JADAS-27 score was moderately correlated with JAB-Q Total Score, JAB-Q Pain and Disease Activity subscales, and highly correlated with JAB-Q Stiffness subscale ($p<0.05$). In females, the JAB-Q Total Score was moderately to highly correlated with all JAB-Q subscales, except JAB-Q Stiffness and Sleep subscales. A poor correlation was found between the JADAS-27 score and the JAB-Q Pain subscale, and a moderate correlation was found between the JAB-Q Stiffness and Function subscales ($p<0.05$).
Conclusion: The results of this pilot study, although not statistically reflected, showed that males with JIA had higher disease activity and worse biopsychosocial status than females. While the clinical severity of the disease did not differ between males and females, it was concluded that males may experience worse biopsychosocial status due to the complex interaction of sex role expectations, impaired coping strategies, and psychosocial problems by caregivers and clinicians. It was decided to continue the study by including more cases to examine the reasons for these differences due to sex.
Disclosure
None declared

References

1. Chen, K., Zeng, H., Togizbayev, G., Martini, A., & Zeng, H. (2023). New classification criteria for juvenile idiopathic arthritis. *International journal of rheumatic diseases*, *26*(10), 1889–1892.
2. Thierry, S., Fautrel, B., Lemelle, I., & Guillemin, F. (2014). Prevalence and incidence of juvenile idiopathic arthritis: a systematic review. *Joint bone spine*, *81*(2), 112–117.
3. Sjakste, T., Paramonova, N., Rumba-Rozenfelde, I., Trapina, I., Sugoka, O., & Sjakste, N. (2014). Juvenile idiopathic arthritis subtype- and sex-specific associations with genetic variants in the PSMA6/PSMC6/PSMA3 gene cluster. *Pediatrics and neonatology*, *55*(5), 393–403. https://doi.org/10.1016/j.pedneo.2014.01.007
4. Şener, S., Karaca, N. B., Kaşlı, K., Özçadırcı, A., Batu, E. D., Başaran, Ö., Bilginer, Y., Özen, S., & Ünal, E. (2023). Comparison of Biopsychosocial Characteristics of Children with Juvenile Idiopathic Arthritis According to Common Disease Subtypes. Turkish archives of pediatrics, 58(6), 625–630.

PU03

Missing tolerance: exploring the impact of treatment duration and administration conditions on methotrexate intolerance in children

Ç. Yıldız, S. A. Bakkaloğlu
[1]Pediatric Rheumatology, Gazi University Faculty of Medicine, Ankara, Türkiye
Correspondence: Ç. Yıldız
Pediatric Rheumatology, **23(2):** PU03

Introduction: Methotrexate is a widely used conventional disease-modifying antirheumatic drug (cDMARD) in childhood rheumatic diseases, especially juvenile idiopathic arthritis (1, 2). Despite its efficacy, gastrointestinal and behavioural side effects may lead to intolerance and reduced adherence, affecting outcomes (3). To assess methotrexate intolerance, the "Methotrexate Intolerance Severity Score" (MISS) was developed, and studies have reported the prevalence of intolerance to range between 25% and 75% (3, 4).
Objectives: In this study, we aimed to investigate the development of methotrexate intolerance among patients receiving this treatment and to examine the relationship between intolerance and patients' demographic characteristics.
Methods: This cross-sectional study included patients on methotrexate for at least six months at the Pediatric Rheumatology Department of Gazi University. Data from clinical records and parent interviews were analyzed using the MISS.
Results: A total of 48 patients were evaluated; 60.4% were female, and 83.3% were diagnosed with JIA. The mean age at diagnosis was 88.5 ± 51.0 months, and the mean follow-up duration was 59.0 ± 40.1 months. Regular folic acid use was reported by 91.7% of patients. ANA positivity was observed in 45.8%. The mean MISS was 8.92 ± 8.72, and 47.9% met the criteria for methotrexate intolerance (MISS ≥6) (Table 1). Notably, a positive correlation was found between longer follow-up duration and higher MISS scores ($r = 0.409$, $p = 0.004$), suggesting cumulative exposure increases intolerance risk. While nausea was more commonly reported when methotrexate was taken with food, administration timing (before or after meals) did not significantly affect total MISS or its subcomponents—nausea, vomiting, abdominal pain, or behavioral symptoms (Table 2). Interestingly, intolerance was significantly more frequent in ANA-positive patients ($p = 0.043$), though this did not remain significant within diagnostic subgroups (Table 3).
Conclusion: Our findings underscore the high prevalence of methotrexate intolerance in children, particularly in those receiving prolonged treatment. Importantly, the association between intolerance and ANA positivity may indicate an immunological predisposition worth exploring further. Although food intake did not significantly alter intolerance scores, the trend toward increased nausea when taken with food suggests that recommending administration on an empty stomach could be beneficial. Integrating early psychosocial support into treatment plans may enhance tolerance and adherence, ultimately improving clinical outcomes. Larger, prospective studies are warranted to validate these observations and inform optimized methotrexate management strategies in pediatric patients.
Disclosure
None declared

PU06

Urinary MRP 8/14 (S100) calprotectin levels in children with juvenile idiopathic arthritis

S. Murias Loza[1], C. Udaondo Gascón[2], R. M. Alcobendas Rueda[2], A. Remesal Camba[2], V. Courel del Río[1], E. Pardo Campo[1], J. Rodríguez Suárez[1]
[1]Pediatric Rheumatology Unit, University Hospital Central of Asturias, Oviedo, [2]Pediatric Rheumatology Unit, University Hospital La Paz, Madrid, Spain
Correspondence: S. Murias Loza
Pediatric Rheumatology, **23(2):** PU06

Introduction: Serum levels of MRP8/14 calprotectin have shown a good correlation with disease activity in Juvenile Idiopathic Arthritis (JIA). Although S100 proteins are primarily expressed in granulocytes and mononuclear blood cells, their presence in renal endothelial cells

has recently been reported. Several authors have investigated the correlation of different S100 protein types in both serum and urine from pediatric lupus patients and healthy controls, with promising results. However, the behavior of urinary MRP8/14 in patients with JIA has not yet been explored
Objectives: To evaluate both urinary and serum MRP8/14 calprotectin levels in patients with non-systemic JIA across different levels of disease activity, and to analyze whether there is a correlation between urinary and serum concentrations, as well as between urinary levels and disease activity
Methods: Combined urinary and serum samples from non-systemic JIA patients followed at the Pediatric Rheumatology Unit of a tertiary hospital were collected at two time points: baseline and follow-up (at a visit 3 to 9 months after baseline). Serum MRP8/14 levels were determined by ELISA. Clinical and laboratory data were collected at both time points, including number of active joints, parent/patient Visual Analogue Scale (pVAS), medical Visual Analogue Scale (mVAS), serum/urinary creatinine, erythrocyte sedimentation rate (ESR) C-reactive protein (CRP), and neutrophil/leukocyte count, among others. Disease activity was assessed using the Juvenile Arthritis Disease Activity Score (JADAS). Statistical analysis was performed using R (version 4.4.1). Pearson's coefficient and linear regression were used to assess the correlation between urinary and serum calprotectin levels, as well as their association with disease activity. Mean urinary calprotectin levels across disease activity groups were compared using Student's t-test. Results were reported as regression coefficients, 95% confidence intervals, and p-values
Results: At the first sample collection time point, a statistically significant association was observed between serum S100 concentrations and pVAS, mVAS, ESR, JADAS, leukocyte count, and neutrophil count. At the second time point, serum S100 concentrations were significantly associated with CRP and neutrophil count. No statistically significant association was found between urinary S100 (normalized to urine creatinine) and serum S100 at either of the two collection time points. Likewise, no significant association was observed between normalized urinary S100 concentrations and any of the disease activity variables at either time point
Conclusion: The data from this study suggest that serum S100 MRP 8/14 proteins are suitable biomarkers for non-systemic JIA, as previously demonstrated in other studies. In contrast with previously reported findings in patients with pediatric lupus, no statistically significant association was found between urinary S100 levels (normalized to urinary creatinine) and serum S100 levels, nor between normalized urinary S100 concentrations and any disease activity variables in the sample. To our knowledge, no previous studies have investigated urinary S100 levels in these conditions
Disclosure
None declared

References

1. Keskitalo PL, Kangas SM, Sard S, Pokka T, Glumoff V, Kulmala P, Vähäsalo P. Myeloid-related protein 8/14 in plasma and serum in patients with new-onset juvenile idiopathic arthritis in real-world setting in a single center. Pediatr Rheumatol Online J. 2022 Jun 16;20(1):42
2. Donohue SJ, Midgley A, Davies JC, Wright RD, Bruce I, Beresford MW, Hedrich CM; MRC MASTERPLANS Consortium; UK jSLE Cohort Study and Repository. Differential analysis of serum and urine S100 proteins in juvenile-onset systemic lupus erythematosus (jSLE). Clin Immunol. 2020 May;214:108,375. Doi: https://doi.org/10.1016/j.clim.2020.108375
3. Davies JC, Midgley A, Carlsson E, Donohue S, Bruce IN, Beresford MW, Hedrich CM. Urine and serum S100A8/A9 and S100A12 associate with active lupus nephritis and may predict response to rituximab treatment. RMD Open. 2020 Jul;6(2):e001257

PU07

Registry for a prospective multi-center cohort comparing post-intraarticular-steroid injection treatment protocols in JIA-associated gonarthritis

S. Meister[1], M. Georgi[1], B. Hügle[2,3], F. Gohar[4], A. Urban[5], R. Berendes[6], R. Trauzeddel[7], J.-P. Haas[2] on behalf of participating centers of the Society for Pediatric and Adolescent Rheumatology

[1]Physiotherapy, [2]Rheumatology, German Center for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, [3]Rheumatology, Hospital for Pediatric Rheumatology, Rheumazentrum Rheinland-Pfalz, Bad Kreuznach, [4]Rheumatology, St.Josef-Stift Sendenhorst, Sendenhorst, [5]Rheumatology, St. Marien Hospital, Amberg, [6]Rheumatology, St. Marien Children Hospital, Landshut, [7]Rheumatology, Helios Hospital Berlin-Buch, Berlin, Germany
Correspondence: S. Meister
Pediatric Rheumatology, **23(2):** PU07

Introduction: There are various non-evidence-based recommendations for joint-loading in post-treatment protocols following an intraarticular corticosteroid injection (IACI) in gonarthritis associated with juvenile idiopathic arthritis (JIA) in German pediatric rheumatology centers [1]. Limited evidence exists if weight unloading maximizes the therapeutic effect of IACI.
Objectives: The aim is to collect data of weight-bearing versus reduced-weight-bearing protocols for the knee after IACI in a prospective registry to evaluate the impact on the occurrence and timepoint of flares and clinical and/or laboratory-based markers of inflammation.
Methods: Based on survey data from German centers of pediatric and adolescent rheumatology [1] and expert consensus, post-IACSI joint loading protocols were defined, used to establish the basis for comparative study groups.
Results: Prospective data collection across multiple centers began in April 2025, with the goal of including at least 50 patients aged 6-18 with JIA oligo- or polyarthritis post-IACI, to compare outcomes between those receiving complete weight-unloading and those with partial weight-bearing. The parameters include duration of bed rest, complete weight-unloading and partial weight-bearing. One group will have reduced weight-bearing (1-3 days bedrest, ≥ 1 day complete unloading) and the other non-restricted weight-bearing (no bedrest and no complete unloading, ≤ 7days partial weight-bearing). Primary Outcome will be the time to flare, defined as clinical, sonographic or laboratory-based detection of inflammation occurring more than 2 weeks after the IACI following an initial reduction of inflammatory signs. At three timepoints, routine assessments will be conducted, including measurements of CRP, ESR and JADAS, as well as evaluation of joint pain, range of motion, swelling, joint stiffness and joint status via musculoskeletal ultrasound. Gait speed over a distance of 50 ft (15m) and current pharmacological treatment will also be documented. Additionally, a questionnaire will be used to capture further parameters like physiotherapy and sports. Descriptive statistics will be used to assess correlations and differences.
Conclusion: Based on the results recommendations regarding the need and dosage of weight-bearing after an IACSI should be developed.
Trial registration identifying number: DRKS00036083
Disclosure
None declared

Reference

1. Meister et al. (2023). Treatment of JIA subsequent to intraarticular steroid injection – a survey of german pediatric rheumatologists. In Proceedings of the 29th European Paediatric Rheumatology Congress. *Pediatr Rheumatol* **21** (Suppl 2), 122 (2023).

PU08

Therapy-resistant still's disease with macrophage activation syndrome and developmental delay in a 13-month-old child

C. Suchrow[1], E. Rosswog[1], F. Röwekamp[1], S. von Hardenberg[2], K. Mönkemöller[1]
[1]Department of Pediatrics, Pediatric Rheumatology, Kinderkrankenhaus Amsterdamerstraße Köln, Cologne, [2]Institute of human genetics, Medizinische Hochschule Hannover, Hannover, Germany
Correspondence: C. Suchrow
Pediatric Rheumatology, **23(2):** PU**08**

Introduction: Still's disease is a rare systemic inflammatory disorder with a broad clinical spectrum and considerable risk to develop a life-threatening macrophage activation syndrome (MAS). A treat to target approach (T2T) aiming at early control of disease activity and clinical

inactive disease without glucocorticoids within six months (1) is a challenge for the pediatric rheumatology team.
Objectives: We present a T2T approach in a small child with complex Still's disease in clinical practice.
Methods: Retrospective analysis of clinical records.
Results: A 13-month-old girl of Tunisian consanguineous parents with duplex kidney and vertebral malformation presented with antibiotic-resistant fever >14 days, non-transient maculopapular rash, and polyarthritis. Laboratory results showed neutrophilic leukocytosis, elevated inflammation parameters (ESR, CRP), Ferritin (2345 ng/ml) and S100A8/A9 (94460 ng/ml), supporting the diagnosis of Still's disease despite absence of hepatosplenomegaly and serositis.
Methylprednisolone pulses and IL-1 blockade (Anakinra) led to prompt defervescence, >70% CRP reduction by day 7 and improvement of polyarthritis. Over three months, glucocorticoids couldn't be tapered despite IL-1 blockade (up to 8 mg/kg). IL-6 inhibition (Tocilizumab) caused severe anaphylaxis after the second dose. Anakinra was continued, Methotrexate added (off-label), allowing for glucocorticoid reduction below 0.2 mg/kg after six months. A switch to Canakinumab at age two achieved disease control. Notably, high interferon signature and sIL2 receptor >1000 U/ml with a significantly reduced S100A8/A9 (4580 ng/ml) were observed at the same time.
At 28 months, the child's developmental delay progressed (intermittent extremity ataxia, strabismus convergens, bilateral equinus contracture). MRI revealed a midline cyst (34 x 44 mm) in the third ventricle. After drainage there was subsequent improvement in speech and motor skills. The phenotype-based analysis of genomic data was inconclusive.
At 29 months the patient developed MAS with fever, pancytopenia, hyperferritinemia, hypertriglyceridemia, hypofibrinogenemia, splenomegaly and hepatopathy triggered by arespiratory syncytial virus. Steroid pulse therapy, Methotrexate discontinuation and switch to Baricitinib led to good response alongside continued Canakinumab therapy.
Conclusion: A T2T strategy in a child under two years of age with complex Still's disease and MAS led to remission under IL-1 blockade and JAK inhibition. A midline cyst complicating the course illustrates the importance of a broad pediatric perspective for rheumatology teams.**Disclosure of Interest**
None declared

Reference

1. Fautrel B, Mitrovic S, De Matteis A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis*. 2024;83(12):1614-1627. Published 2024 Nov 14. doi:https://doi.org/10.1136/ard-2024-225851

PU11

Axial spondyloarthritis in pediatric and adolescent and young adult inflammatory bowel disease: a retrospective study

K. Yamazaki[1], M. Mouri[1], E. Toyofuku[1], S. Mori[1], S. Suzuki[1], T. Nishijima[1], K. Tonozono[1], M. Kato[2], S. Ooka[1], K. Kawahata[1]
[1]Department of Rheumatology and Allergology, [2]Department of Gastroenterology and Hepatology, St. Marianna University School of Medicine, Kawasaki, Japan
Correspondence: K. Yamazaki
Pediatric Rheumatology, **23(2):** PU11

Introduction: Few reports exist on axial spondyloarthritis (ax-SpA) complications associated with pediatric inflammatory bowel disease (IBD).
Objectives: To investigate the clinical features and management of ax-SpA associated with IBD in children, adolescents, and young adults.
Methods: We selected cases diagnosed with ax-SpA associated with IBD between January 2020 and May 2024, whose onset was less than 20 years of age, and who continued treatment for more than 6 months. The cases were retrospectively reviewed for the clinical characteristics, treatment, and course of IBD and ax-SpA. All cases showed persistent inflammatory back pain, tenderness at the sacroiliac joint, positive diagnostic tests at the sacroiliac joint, and fulfilled the pediatric-specific definition of MRI-positive sacroiliitis.
Results: Four patients, three males and one female, three with Crohn's disease (CD) and one with ulcerative colitis (UC), were included. Their median age of onset was 16 years, and they had no HLA-B27 positivity. All patients were treated with a TNF inhibitor. Among three patients with CD, two were treated with adalimumab, and one, complicated by Takayasu arteritis, was started on PSL, infliximab, and azathioprine but was switched to upadacitinib due to TA flares. The UC case was started on vedolizumab, but was switched to ADA due to the onset of back pain. In all cases, IBD remained in remission or near remission, and back pain and joint pain were markedly improved. Bone marrow edema improved, but bone erosions remained in MRI.
Conclusion: TNF inhibitors have been effective in ax-SpA associated with pediatric, adolescent and young adult IBD. Early diagnosis of ax-SpA, especially when complicated by IBD, is crucial for selecting appropriate treatment. However, diagnosing pediatric ax-SpA using MRI can be challenging. This difficulty arises because the typical findings that meet the adult Assessment of SpondyloArthritis International Society (ASAS) criteria may not be present. Additionally, factors such as sacral ossification and fusion, and changes in bone marrow signal intensity during growth, must be carefully evaluated. Therefore, paying attention to signs of ax-SpA and conducting a thorough physical examination of the sacroiliac joints and spine are more helpful for diagnosing pediatric ax-SpA associated with IBD.
Disclosure
None declared

References

1. Chauvin NA, Xiao R, Brandon TG, et al. MRI of the Sacroiliac Joint in Healthy Children. *AJR* 2019; 212:1303–1309
2. Herregods N, Maksymowych WP, Jans LBO, et al. Atlas of MRI findings of sacroiliitis in pediatric sacroiliac joints to accompany the updated preliminary OMERACT pediatric JAMRIS (Juvenile Idiopathic Arthritis MRI Score) scoring system: Part I: Active lesions. Seminars in Arthritis and Rheumatism 2021;51:1089–1098

PU12

MAFB Gene mutation presenting with bone destruction and nephropathy: a case report from Kazakhstan

A. Otegen, Z. Mukusheva, M. Assylbekova
Pediatric Rheumatology, CF "University Medical Center", Astana, Kazakhstan
Correspondence: A. Otegen
Pediatric Rheumatology, **23(2):** PU12

Introduction: MAFB gene mutations are rare and may lead to complex multisystem presentations involving skeletal dysplasia and renal impairment, with very limited data from Central Asia.
Objectives: To describe the clinical presentation, diagnostic pathway, and genetic confirmation of a rare case of bone and renal pathology associated with a MAFB gene mutation in a Kazakhstani pediatric patient.
Methods: A 2-year-old boy presented with joint contractures, pain, and restricted movement in multiple joints, alongside failure to thrive and persistent proteinuria. The evaluation included clinical examination, biochemical and immunological tests, imaging (X-ray, MRI), and genetic testing via whole exome sequencing. Written informed consent was obtained from the parents for publication.
Results: Initial clinical signs appeared at 4 months, including joint pain during dressing and unexplained swelling in the right hand. The child underwent multiple hospitalizations and specialist consultations over the course of a year. Preliminary diagnoses included lymphangioma, congenital lymphedema, juvenile idiopathic arthritis (polyarticular, RF-negative), and suspected Hunter syndrome based on dysmorphic features and joint stiffness. However, no definitive unifying diagnosis could be made despite extensive workup. Signs of osteolysis, such as carpal bone demineralization and wrist joint narrowing, were not radiologically evident until after 1 year of age, highlighting the delayed skeletal manifestation of the disease. Radiographs eventually revealed significant osteoporosis and indistinct carpal bones. Persistent proteinuria (up to 0.66 g/L) was detected, with preserved renal function (GFR ~90 ml/min). Whole exome sequencing revealed

a heterozygous pathogenic variant in the MAFB gene (c.341G>A, p.Gly114Asp), confirming multicentric carpotarsal osteolysis syndrome with nephropathy. Immunosuppressive therapy, including methotrexate and etanercept, was discontinued following the genetic diagnosis. Supportive nephrological care with ACE inhibitors was initiated, and the patient is under multidisciplinary monitoring.
Conclusion: This is the first genetically confirmed case of a MAFB mutation with bone and renal involvement reported in Kazakhstan. It highlights the importance of considering rare genetic syndromes in children with unexplained skeletal and renal symptoms. Early genetic testing can lead to precise diagnosis, avoiding unnecessary therapies and guiding long-term care.
Disclosure
None declared

References
1. Zankl A, Duncan EL, Leo PJ, et al. Multicentric carpotarsal osteolysis is caused by mutations in MAFB. Hum Mutat. 2012;33(3):521–526.
2. Aggarwal A, Misra R. Juvenile idiopathic arthritis: diagnosis and treatment. Indian J Pediatr. 2011;78(4):449–455.
3. Morimoto M, Takagi M, Nakashima E, et al. Nephropathy associated with MAFB mutation: a case report. Pediatr Nephrol. 2021;36(3):697–701.

PU13

Sapho syndrome in children: our experience in the diagnosis and management of this disease

A. Kappassov, A. Dildabayeva, M. Assylbekova, Z. Mukusheva
Pediatric rheumatology, Corporate Fund "University Medical Center", Astana, Kazakhstan
Correspondence: Z. Mukusheva
Pediatric Rheumatology, **23(2):** PU13

Introduction: SAPHO syndrome is rare but likely underestimated due to the complexity of its diagnosis, caused by the variability of its musculoskeletal and skin manifestations. This is especially true when atypical areas are involved and specific skin lesions are absent. Diagnosis is often based on clinical presentation, supported by additional methods such as radiography or MRI. Standardized treatment protocols are lacking, and current therapeutic methods are empirical, focusing on pain relief and improving patients' quality of life [1].
Objectives: To study methods of diagnosing and managing SAPHO syndrome in children.
Methods: Patient M, a 16-year-old Asian boy, turned to a rheumatologist after the addition of pain in the lumbar region. The disease will make its debut in September 2022. He had been under dermatological observation for acne and had received intravenous glucocorticosteroids and oral systemic retinoids.
Results: In October 2024, the patient was examined by a rheumatologist due to confluent acne on the face, back, and torso; lumbar spine pain; tenderness of the sternoclavicular joints; pain during hip abduction; and a positive Kushelevsky sign. Pain was rated 5/10 on the VAS. Laboratory tests revealed elevated inflammatory markers (ESR 73 mm/hr, CRP 76 mg/L), HLA-B27 and ANA were negative, and stool calprotectin was normal. MRI showed bilateral sacroiliitis with active inflammation and erosions. CT revealed destructive changes in the clavicles and involvement of the sternum and first ribs. The patient was diagnosed with enthesitis-related juvenile idiopathic arthritis (HLA-B27 negative, high activity) and SAPHO syndrome (moderate activity). Treatment included pulse methylprednisolone (750 mg x3 days), subcutaneous methotrexate (15 mg/week), and adalimumab. Bisphosphonates were postponed due to low vitamin D (26.67 ng/mL). On follow-up, inflammatory markers normalized (ESR 9 mm/hr, CRP 1.8 mg/L), vitamin D improved to 67.1 ng/mL, and bisphosphonate therapy was initiated (45 mg x2). At discharge, the patient was stable with no active joint or skin symptoms and no inflammatory activity.
Conclusion: SAPHO syndrome in children is a challenging disease to diagnose and treat, requiring a multidisciplinary and individualized approach for each case. This clinical case describes the successful diagnosis and management of the disease in an adolescent with atypical manifestations. It emphasizes the importance of timely diagnosis based on clinical and instrumental data, as well as the use of modern therapeutic approaches, including biologics. The case also highlights the need for long-term follow-up of patients with SAPHO syndrome to prevent relapses and minimize complications. This experience may be useful for developing more standardized approaches to diagnosing and treating this disease in children. Consent to published had been obtained.
Disclosure
None declared

Reference
1. Semin Arthritis Rheum. (2012). Title of the article. https://doi.org/10.1016/j.semarthrit.2012.05.006

PU14

Sustained disease control in cinca/nomid syndrome: long-term efficacy of il-1 inhibition,a case report

A. Kappassov, Z. Mukusheva, Z. Albekova
Pediatric rheumatology, Corporate Fund "University Medical Center", Astana, Kazakhstan
Correspondence: Z. Mukusheva
Pediatric Rheumatology, **23(2):** PU14

Introduction: CINCA/NOMID syndrome (Chronic Infantile Neurological Cutaneous and Articular Syndrome/Neonatal-Onset Multisystem Inflammatory Disease) is the most severe phenotype within the Cryopyrin-Associated Periodic Syndromes (CAPS), representing a rare, autosomal-dominant autoinflammatory condition associated with NLRP3 mutations. Early diagnosis and treatment are critical to preventing irreversible organ damage.
Objectives: To present a case of a pediatric patient with CINCA/NOMID syndrome, focusing on clinical features, diagnostic challenges, and long-term management outcomes under IL-1 inhibition therapy.
Methods: A 13-year-old boy residing in a children's home presented with a history of recurrent fever, maculopapular rash, and polyarthritis since 2016. Based on clinical criteria, persistently elevated inflammatory markers, and disease progression, a diagnosis of Chronic Infantile Neurological Cutaneous and Articular Syndrome/Neonatal-Onset Multisystem Inflammatory Disease (CINCA/NOMID) was established. The diagnosis was further supported by expert consultation with Dr. De Benedetti. At the time of diagnosis, the patient exhibited typical features of the disease, including hypertrophy of the knee joints, sensorineural hearing loss, chronic systemic inflammation (Hb 95 g/L, ESR 45 mm/h, CRP 95 g/L), uveitis, and marked growth delay (at age 5: weight 11 kg, height 98 cm). A trial of interleukin-6 inhibitor therapy (tocilizumab) was attempted but proved ineffective after a single administration. In 2018, treatment with canakinumab (an IL-1β inhibitor) was initiated at a dose of 4 mg/kg every 8 weeks. After three months, the dosing interval was shortened to 4 weeks due to persistent disease activity. Regular subcutaneous injections have been maintained since. After seven years of continuous IL-1β blockade, the patient demonstrated significant clinical and laboratory improvement. At the time of reporting, his weight and height had 32 kg and 132 cm, respectively. Hemoglobin levels normalized (136 g/L), with substantial reductions in inflammatory markers (ESR 16 mm/h, CRP 1.10 g/L). Nevertheless, moderate functional limitations and residual joint deformities persist, requiring ongoing multidisciplinary care.
Results: Regular treatment with canakinumab (4 mg/kg every 4 weeks) led to disease stabilization, absence of fever and skin manifestations, and reduced disease activity scores (AIDAI, DAS-MWS). Despite favorable systemic control, the patient requires continued multidisciplinary follow-up due to conductive hearing loss, and endocrine growth delay.
Conclusion: This case underlines the importance of early recognition of CAPS/CINCA syndrome, particularly in children with complex inflammatory presentations. Long-term IL-1β blockade with canakinumab proves to be effective in achieving disease control and improving quality of life. Continued audiological, and endocrinological monitoring is essential. Consent to published had been obtained.
Disclosure
None declared

PU15

Familial Mediterranean fever: data from azerbaijan

A. Aliyeva[1], S. Mustafayeva[2]
[1]Rheumotology, Medical Plaza, [2]Rheumotology, Central Clinic, Baku, Azerbaijan
Correspondence: A. Aliyeva
Pediatric Rheumatology, **23(2):** PU15

Introduction: Familial Mediterranean Fever is an autosomal recessive autoinflammatory disease characterized by recurrent episodes of fever and serosal inflammation, most commonly affecting populations around the Mediterranean. Mutations in the MEFV gene, which encodes the pyrin protein, underlie the disease pathogenesis. Although FMF is well-studied in countries like Turkey and Israel, data from Azerbaijan remain limited. Given its geographic and ethnic proximity to endemic regions, the actual prevalence and genetic patterns in Azerbaijan may be underrecognized.
Objectives: FMF is an autosomal recessive, ethnically influenced autoinflammatory disorder characterized by recurrent serositis episodes—manifesting as fever along with inflammation of the peritoneum, synovium, pleura, and rarely the pericardium-lasting from 12 to 96 hours and resolving spontaneously. In this study, we aimed to present the demographic, clinical, and laboratory characteristics of our patients diagnosed with FMF,the treatments administered, and the distribution of MEFV gene variants. Additionally, we aimed to assess the geographic origin of the patients within Azerbaijan and the genotype distribution according to regions.
Methods: This study included patients under the age of 18 who were followed in three centers, met the pediatric FMF diagnostic criteria, and had available retrospective medical data. Demographic data such as age and sex, presenting symptoms, laboratory and clinical findings, colchicine response, and genetic mutation distribution were evaluated.
Results: A total of 264 patients (56% male) were included. The mean age at diagnosis was 7 years (range: 2–18). The most common symptom was fever (91%), followed by abdominal pain (44.5%), arthritis/arthralgia (19.7%), and vomiting (3.8%). Coexisting diagnoses included hypermobility (17%), JIA (11.3%), HSP (6.8%), PFAPA (3.7%), and urticaria (1.8%).
Colchicine was initiated in all patients; 97% responded positively, while 3% were colchicine-resistant. Among resistant cases, 1.9% responded to anakinra, and 1.1% were switched to canakinumab due to inefficacy or side effects.MEFV gene testing was performed in all patients. Of the 264, 201 had FMF-related variants; 53 results were pending, and 10 tested negative. The most frequent mutations were M694V (40.2%), V726A (21.3%), R202Q (12.9%), M680I (9.9%), E148Q (9.9%), and A744S (5.4%).Regionally, 24.8% of patients were from Nakhchivan, with 48% carrying homozygous M694V mutations. Others had M694V, V726A, E148Q, or M680I in heterozygous or compound heterozygous forms. From Lankaran-Astara (15%), 43% had homozygous variants (mostly E148Q, M694V, V726A, R202Q), and 57% had heterozygous/compound forms. In the Ganja-Gazakh region (15.4%), 64.5% carried homozygous mutations (mainly M694V, V726A, M680I), and 35.3% had heterozygous/compound types.
Conclusion: FMF is a severe inherited disease, and delayed diagnosis may lead to complications. This study aimed to present the phenotypic features of FMF and the distribution of MEFV gene mutations in the Azerbaijani population. Although Azerbaijan has not been widely reported as a high-prevalence region for FMF, this may be attributed to a lack of comprehensive patient data. Our findings suggest that FMF is more widespread in our country than previously assumed.
Disclosure
None declared

PU16

Late-onset savi with severe sequelae in adulthood – the first Slovak case

B. Balažiová[1], G. Hrčková[1], A. Tuchyňová[2], T. Dallos[1]
[1]Department of Paediatrics, Comenius University Medical School in Bratislava, National Institute for Children's Diseases (NÚDCH), Bratislava, [2]National Institute of Rheumatic Diseases, Piešťany, Slovakia
Correspondence: B. Balažiová
Pediatric Rheumatology, **23(2):** PU16

Introduction: STING-associated vasculopathy with onset in infancy (SAVI) is a rare monogenic autoinflammatory disorder caused by gain-of-function variants in the STING1 gene, resulting in constitutive type I interferon activation. The original cases of SAVI were characterised by early onset and a severe course of necrotizing vasculopathy with tissue loss and progressive interstitial lung disease (ILD).
Objectives: To describe the first known case of SAVI in Slovakia that was diagnosed in adulthood.
Methods: Clinical and laboratory data were analysed in retrospect by review of medical records.
Results: At age 12, the female adolescent presented with polyarticular chronic arthritis with a positive rheumatoid factor (RF) and started treatment with methotrexate. At age 21, she experienced recurrent respiratory problems initially considered to be bronchial asthma. One year later, advanced interstitial lung disease with fibrosis on HRCT and reduced diffusing capacity for carbon monoxide (DLCO 46%) were confirmed. At the same time, she developed multiple skin lesions histologically assessed as leukocytoclastic vasculitis and pustulous dermatosis, which later evolved into necrotizing ulcerative lesions distributed all over her trunk and extremities. The arthritis was treated with glucocorticoids, methotrexate, azathioprine and hydroxychloroquine, later she received cyclophosphamide for her lung disease, all with limited effect. Since the age of 34, she required non-invasive ventilatory support. At our first encounter, at age 36, she had suffered from severe joint and lung damage from both arthritis and ILD: she was wheelchair-bound with severe respiratory insufficiency (DLCO 22%) requiring continuous oxygen therapy. Inflammatory markers (ESR and CRP) were constantly elevated and serological testing was positive for RF, aCCP and ANAs with low titres of anti-dsDNA, SSA, SSB and Sm antibodies. Molecular-genetic testing revealed the heterozygous pathogenic p.R281Q STING1 variant previously described in 10 other individuals with SAVI (1). Baricitinib treatment is scheduled to be initiated.
Conclusion: Despite late insidious onset in adolescence, SAVI can take a severe course leading to extensive lung damage. A high degree of suspicion is warranted in all paediatric patients with seropositive arthritis, especially those with accompanying chronic lung disease. Consent to published had been obtained.
Disclosure
None declared

Reference

1. Weidler S, Koss S, Wolf C et al. A rare manifestation of STING-associated vasculopathy with onset in infancy: a case report. Pediatr Rheumatol Online J. 2024 Jan 4;22:9.

PU17

Management of familial Mediterranean fever in a german pediatric rheumatology center

C. Hillekamp, J. Wahl, A. Zimmer, A. Klein, G. Horneff
Pediatric Rheumatology, Asklepios Hospital for Children, St. Augustin, Germany
Correspondence: C. Hillekamp
Pediatric Rheumatology, **23(2):** PU17

Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease. Due to variable phenotypes, clinical diagnosis can be challenging. Genetic testing for MEFV mutations is crucial, but the impact on treatment decisions remains unclear. Colchicine is the first-line therapy; IL-1 inhibitors are used in colchicine-resistant cases.
Objectives: This study explores genotype-phenotype correlations in FMF patients and analyzes their impact on therapy, particularly the use of IL-1 inhibitors.
Methods: In this monocentric retrospective study, 59 pediatric FMF patients (26 males, 33 females) with at least one MEFV variant were included and classified into four cohorts. Genetic analysis was performed via sequencing, and variants were classified using the INFEVERS database. Patients were grouped into four cohorts based on variant combinations. Clinical features, colchicine dosage (mg/kg/day), and biologic therapy were analyzed.

Results: Cohort 1 (n=13), carrying two pathogenic or likely pathogenic variants, showed the longest diagnostic delay (mean 4.4 ± 3.3 years) despite high genetic burden and had the lowest frequency of fever (38%) and abdominal pain (23%). This group also had the highest rate of IL-1 inhibitor use: 31% received anakinra, 15% canakinumab, and 8% both. Cohort 2 (n=4), consisting of patients with a pathogenic or likely pathogenic variant combined with another variant of unclear or likely benign significance, had the earliest symptom onset (2.8 ± 0.6 years) and diagnosis (4.4 ± 0.2 years). No patients in this group received biologics. Due to the small sample size, further conclusions are limited. In Cohort 3 (n=27), patients had one pathogenic variant and the highest frequency of fever (56%). Two patients (7%) received anakinra and sequentially canakinumab. Cohort 4 (n=12), with only variants of unclear or likely benign significance, showed mild disease course and required no escalation beyond colchicine. Across all cohorts, 88% of patients were treated with colchicine, with an average maximum dose of 0.03 ± 0.02 mg/kg/day. Slightly higher mean dosages were observed in Cohorts 1 and 2. All patients treated with IL-1 inhibitors carried at least one pathogenic MEFV variant.
Conclusion: Pathogenic MEFV variants, particularly in homozygous or compound-heterozygous form, were associated with earlier onset, longer diagnostic delay, and increased biologic use. Early genetic testing may support timely escalation in high-risk patients. Larger studies are needed to validate genotype-based treatment strategies.
Disclosure
C. Hillekamp: None declared, J. Wahl: None declared, A. Zimmer Grant/Research Support with: Novartis, Lilly, Speaker Bureau with: Lilly, Glaxo-Smith-Kline, A. Klein Speaker Bureau with: Novartis, Lilly, G. Horneff Grant/Research Support with: Abbvie, Boehringer, Celgene, Chugai, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Sobi

References

1. Lainka E, Bielak M, Lohse P, et al. Familial Mediterranean fever in Germany: epidemiological, clinical, and genetic characteristics of a pediatric population. Eur J Pediatr. 2012;171:1775–85.
2. Ehlers L, Rolfes E, Lieber M, Müller D, Lainka E, Gohar F, Klaus G, Girschick H, Hörstermann J, Kümmerle-Deschner J, Brunner J, Palm-Beden K, Tenbrock K, von Wrangel L, Faßhauer M, Blank N, Trauzeddel R, von Stuckrad ASL, Higgins S, Welzel T, Lutz T, Hentgen V, Foell D, Wittkowski H, Kallinich T. Treat-to-target strategies for the management of familial Mediterranean Fever in children. Pediatr Rheumatol Online J. 2023 Sep 26;21(1):108.

PU18

Unmasking behçet's in a child with complex autoinflammatory background: challenges in diagnosis and treatment

G. M. Kyrykbay, Z. S. Mukusheva, M. K. Asylbekova, Z. O. Albekova, A. Z. Dildabayeva, A. N. Akhmambetova
Department of Pediatrics, Corporate Fund "University Medical Center", Astana, Kazakhstan
Correspondence: Z. S. Mukusheva
Pediatric Rheumatology, **23(2):** PU18

Introduction: Behçet's disease (BD) is a rare and severe autoinflammatory disorder, characterised by recurrent mucosal ulcerations and systemic involvement, posing significant diagnostic and management challenges.
Objectives: To describe a complex paediatric case of refractory BD with overlapping genetic variants, highlighting diagnostic uncertainties, therapeutic challenges, and the role of international expert collaboration.
Methods: A 13-year-old boy with recurrent painful oral, genital, and perianal ulcers since early childhood, persistent fevers, and joint pain was evaluated. The disease began at the age of 2–3 years, with initial symptoms including recurrent tonsillitis and mucosal ulcerations. Behçet's disease was first diagnosed in 2018 in Kazakhstan in collaboration with international experts from Slovenia. The patient was recommended to continue treatment with adalimumab, colchicine, and methylprednisolone, which initially resulted in sustained clinical improvement. However, over time, the therapeutic effect of adalimumab diminished, likely due to the development of anti-drug antibodies. From early 2023, disease relapse was observed. Subsequent treatments with canakinumab (no effect), infliximab (6 doses, no improvement), and anakinra (inconsistently administered) failed to induce remission. In 2024, the combination of apremilast and anakinra, alongside methylprednisolone, was initiated. However, according to the mother, anakinra was discontinued due to a perceived lack of effect, and the patient was maintained on apremilast and methylprednisolone only, which led to significant clinical improvement. In summer 2024, the family sought a second opinion in Turkey. Alternative diagnoses, including HA20 and pemphigus vulgaris, were excluded through whole genome sequencing and biopsy. The diagnosis of BD was confirmed, and combination therapy with apremilast, anakinra, methylprednisolone and azathioprine was recommended. Despite this, the mother continued administering only apremilast and methylprednisolone. Family history of psoriasis was noted in multiple maternal relatives. Diagnostic workup included immunological assessment, histopathology, and extended genetic testing (whole exome sequencing and whole genome sequencing).
Results: Despite immunosuppressive and biological therapies, the patient experienced persistent severe mucosal lesions requiring continuous corticosteroid support. Genetic testing confirmed heterozygous pathogenic variants in the MVK gene (c.1129G>A, p.Val377Ile) and the SLCO2A1 gene (c.763G>T, p.Gly255*). Maternal testing was negative, and paternal segregation and extended analysis (including assessment for A20 haploinsufficiency) are pending. Histopathological examination of oral mucosa confirmed neutrophil-rich chronic inflammation without features of pemphigus. HLA typing was negative. Corticosteroid-induced complications, including Cushingoid features, vertebral compression fractures, delayed growth, and delayed puberty, developed over time. A multidisciplinary international evaluation, including specialists from Kazakhstan, Turkey, Slovenia, and Lithuania, supported the diagnosis of BD with possible contribution of MKD to disease severity.
Conclusion: This case illustrates the complexity of diagnosing and managing refractory paediatric BD, especially in the presence of overlapping autoinflammatory genetic variants. It highlights the challenges associated with biologic immunogenicity and the importance of treatment individualisation. Combined therapy with apremilast and methylprednisolone resulted in marked clinical improvement and sustained disease remission. Ongoing follow-up and extended genomic analysis aim to further clarify the disease mechanisms and optimise long-term management. Consent to published had been obtained.
Disclosure
None declared

PU19

Differential diagnosis of urticarial vasculitis in sjogren's disease and autoinflammatory disease

A. Torgashina[1], I. Nikishina[2], S. Salugina[2], E. Fedorov[2], M. Beketova[2]
[1]Rare rheumatic diseases, [2]Paediatric, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** PU19

Introduction: We wanted to share a difficult case of urticarial rash (UR).
Objectives: We aimed to share our experience diagnosing and treating a patient with UR.
Methods: The patient's clinical features, laboratory findings, and treatment course were reviewed.
Results: The patient, a 35-year-old, was admitted for observation at the V.A. Nasonova Rheumatology Research Institute. According to the medical history, urticarial rashes began within the first weeks of life. These rashes recurred, lasted for more than 24 hours, and did not respond to antihistamines. At age 28, the condition worsened, with episodes of widespread urticarial rashes and fever up to 38.5°C. During this period, the patient also developed dry eyes and mouth, and needed to drink fluids to eat. At age 32, the patient first visited a rheumatologist. Lab tests showed rheumatoid factor (RF) >200 ME/ml and CRP 73 mg/l, with positive ANA, ENA screen, SSA, and SSB markers. A skin biopsy indicated small vessel vasculitis. The patient was diagnosed with urticarial vasculitis as part of Sjogren's disease, though no standard imaging of the glands was performed to confirm the diagnosis. Low-dose steroid therapy and hydroxychloroquine were followed by methotrexate, but these were ineffective. Rituximab therapy

was then started, the patient received 2000 mg and showed some improvement. However, within three months, the patient suffered a relapse with widespread rash, fever, and a CRP of 56 mg/l, despite marked depletion of B cells. At this time, the patient came under our care. Lab studies showed RF 82 ME/ml, ANF Hep2 1/1280 sp, anti-Ro >200, anti-La 2 N, IgG 19.6 g/l, CRP 69 mg/l, ESR 80 mm/h, with B cells (CD19+, CD3-) at 0.3%. C3, C4, and anti-C1q levels were normal. Tear film breakup time was 3 seconds. Schirmer tear test result was 13 mm, with no staining defects of the conjunctiva or cornea. Sialography showed uneven filling of the ducts with a cloud-like appearance, but without definite cavity formation. A minor salivary gland biopsy revealed mild sialadenitis, focus score 1.1. Saliva flow rate was 2.9 ml/min. Salivary gland ultrasound showed diffuse heterogeneity, with single, round, smooth, hypoechoic avascular formations up to 1.4 mm in size. Because of the weak glandular changes and the early onset of skin symptoms, an autoinflammatory disease was suspected. Genetic testing identified a heterozygous p.Thr350Met mutation in exon 4 of the NLRP3 gene, confirming a diagnosis of cryopyrin-associated periodic syndrome (CAPS). The patient was diagnosed with both Sjogren's disease and CAPS. The main clinical features were urticarial rashes and inflammatory activity. Given the risk of hearing loss and amyloidosis, interleukin-1 inhibitor therapy (anakinra) was started, resulting in rapid and complete improvement.
Conclusion: We are reporting the first documented case of a patient having both cryopyrin-associated autoinflammatory syndrome and autoimmune Sjogren's disease. Consent to published had been obtained.
Disclosure
None declared

PU20

Clinical, demographic and laboratory characteristics, therapeutic approaches in patients with FMF: according to the cohort of the Russian federal rheumatology center

S. Salugina, E. Fedorov, A. Torgashina, M. Kaleda, I. Nikishina, A. Sukhanina, M. Beketova
V.A.Nasonova National Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** PU20

Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease (mAID) and is prevalent among populations surrounding the Mediterranean Sea. Due to migration processes, such pts can be found in other regions, including Russia, but with a lower frequency.
Objectives: to study a cohort of pts diagnosed with FMF according to the Russian Federal Rheumatology Center
Methods: The observational study included 137 pts diagnosed with FMF (79 males) who applied as an outpatient or inpatient during the period from 2019 to 2025. The age of the pts ranged from 2 to 53 years. The diagnosis in all pts met the criteria of 2019. It was confirmed by a mutation in the MEFV gene.
Results: Among 244 pts with main mAID (FMF, CAPS, TRAPS, HIDS) pts with FMF accounted for 56.1%. The age of the onset is from 0 to 35 yo, before the age of 1y - 30 (21,9%), 1- 5 y - 73 (53,3%), >5- 10 - 18 (13.1%), >10-18–9 (6.6%), > 18 y - 6 (4.4%). Duration of the disease: 6 months.–48 years, under 5 y – 65 (47.4%), over 15 y-18 (13.1%). Our cohort was dominated by Armenians (62%). Clinical manifestations most often included fever (96.4%), abdominal pain (89.8%), chest pain (42.3%), musculoskeletal manifestations (58.4%). There were also skin rashes - 52 (37.9%) and rarer symptoms – stomatitis-20 (14.6%), febrile myalgia –9 (6.6%), uveitis in 2. All pts had elevated acute-phase markers (ESR, CRP, and/or SAA) during the attack. AA-amyloidosis was detected in 6 (4.4%), among them one adult (43 yo), the remaining 5 children (from 11.5 to 17 yo). 55.5% had a M694V mutation in the gene MEFV. 86 (62.8%) had family cases of the disease. FMF was associated with other diseases in 24 (17.5%) pts.: sJIA, rheumatoid arthritis, ankylosing spondylitis (AS), sacroiliitis - 15(10.9%), chronic non-bacterial osteomyelitis (CNO)–2, acute rheumatic fever –1, AS/hemorrhagic vasculitis-1, Behcet's disease-2, CAPS-2, hemophilia-1. 10 pts (7.3%) had PFAPA- like course of the disease. 96.4% received colchicine, glucocorticoids (GC) - 21.9%, DMARD –13.4%. Colchicine resistance and poor colchicine tolerance were noted in 16.7% and 5.6%, respectively. Biological drugs (BD) were prescribed to 29 (21.2%), among them IL-1 inhibitors (iIL-1) were received 26 (19%), canakinumab 21 (15,3%), anakinra-5 (3.7%), other BD-11(8%), among them mainly TNF inhibitors (etanercept-5, adalimumab-4), tocilizumab-1, secukinumab-1.
Conclusion: Pts with FMF are found in rheumatologist's practice in an atypical region for this disease, mainly among Armenians. They are often combined with other rheumatic and non-rheumatic diseases. FMF in our pts is characterized by typical signs of the disease and an increase in the level of acute-phase markers. Most of the pts receive colchicine, however, 16% have colchicine resistance or poor tolerance (5.6%). 21.2% require the appointment of BD, among which IL-1 inhibitors predominate.
Disclosure
None declared

PU21

Urticarial vasculitis and schnitzler syndrome: the complexity of differential diagnosis

A. Torgashina[1], I. Nikishina[2], S. Salugina[2], E. Fedorov[2], A. Suhanina[2]
[1]Rare rheumatic diseases, [2]Paediatric, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** PU21

Introduction: Chronic urticarial rash is the most common clinical manifestation of chronic spontaneous urticaria. However, it may indicate a rare disease, especially when systemic symptoms such as fever (F), joint damage, and elevated inflammatory markers are present.
Objectives: We aimed to describe our experience in diagnosing and treating a patient with urticarial rash (UR).
Methods: The patient's clinical manifestations, laboratory test results, and treatment course were described.
Results: The patient's first symptoms appeared at age 41 (pain in the small joints of the hands and morning stiffness lasting more than an hour). Three years later, the patient's condition worsened, with generalized UR (lasting more than 24 hours and unresponsive to antihistamines), recurrent F (up to 38.5°C), periodic swelling of the lips, paraorbital and occipital regions, hoarseness, and a sensation of breathing difficulty. A year later, recurrent panuveitis (U) developed. The patient was monitored by ophthalmologists and received steroid therapy with temporary and incomplete benefit. A skin biopsy showed sparse perivascular and periadnexal infiltration of neutrophilic granulocytes with some small lymphoid cells and plasma cells. There was no evidence of vasculitis. Signs of neutrophilic dermatitis. Laboratory data revealed a CRP level of 35 mg/L; RF, ANA, ENA, ANCA, ferritin, leukocytes, and eosinophils were normal. ESR 40 mm/h, C3 0.57 g/L, C4 0.05 g/L, anti-C1q >200, and IgM 2N. Monoclonal secretion of IgMκ 5.6 g/L. The p.L625P mutation in the MYD88 gene was not detected. Therefore, the patient with persistent UR had highly specific laboratory markers suggestive of both hypocomplementemic urticarial vasculitis (HUV) and Schnitzler syndrome. Histological examination of the skin biopsy favored Schnitzler syndrome, while angioedema and U were more suggestive of urticarial vasculitis. Considering this, and previous reports of successful use of IL-1 inhibitors in urticarial vasculitis, and more so in Schnitzler syndrome, the patient was prescribed anakinra. However, it was ineffective. Cyclosporine and azathioprine were also prescribed sequentially, but were poorly tolerated and had only temporary effects. Steroids provided the best relief but led to steroid dependence. Thus, the diagnosis was formulated as HUV with recurrent bilateral U, F, polyarthritis, angioedema, increased ESR and CRP, decreased C3, C4, positive anti-C1q antibodies, and MGUS IgMκ. Therapy with azathioprine and rituximab allowed for a reduction in the metilprednisone dose from 12 mg to 4 mg, relieving pain, rash, and edema, and reducing the frequency of U relapses.
Conclusion: Diagnosing a patient with persistent UR requires thorough examination and exclusion of autoinflammatory diseases. In complex cases of differential diagnosis between urticarial vasculitis and autoinflammatory diseases, evaluating the effectiveness of IL-1 inhibitors may help establish the correct diagnosis.

Disclosure
None declared

PU22

Dissecting the heterogeneity of pediatric chronic nonbacterial osteomyelitis (CNO): A Monocentric experience

I. Taietti[1,2], M. S. Prevedoni Gorone[3], I. M. Vella[1,2], G. Vanzu[1,2], S. Mazza[1], A. Licari[1,2], G. L. Marseglia[1,2], R. Castagnoli[1,2], G. Bossi[2]
[1]Pediatric Unit, Department of Clinical, Surgical, Diagnostic, and Pediatric Sciences, University of Pavia, [2]Department of Pediatrics, [3]Department of Diagnostic and Interventional Radiology and Neuroradiology, IRCCS Policlinico San Matteo Foundation, Pavia, Italy
Correspondence: I. Taietti
Pediatric Rheumatology, **23(2):** PU22

Introduction: Chronic Nonbacterial Osteomyelitis (CNO) is a rare autoinflammatory bone disorder with mainly pediatric onset. CNO is often insidious and whole-body magnetic resonance (WBMR) better defines distribution pattern of lesions identifying "silent" lesions. No specific histopathological features exist, therefore understanding its heterogeneity is crucial for early recognition and management.
Objectives: We aim to analyze the spectrum of clinical, laboratory, radiological, and histopathological features in a pediatric cohort diagnosed with CNO, to identify the different CNO clinical patterns in order to achieve timely and more accurate diagnosis.
Methods: We retrospectively analysed a CNO cohort between 2017 and 2025 at Department of Pediatrics of IRCSS Policlinico San Matteo Pavia. Demographic, clinical, laboratory, imaging, and histopathological data were collected.
Results: Seven patients were included and all of them were female. Median age of onset resulted 10 years (IQR:7.5-10.1). All patients complained bone pain, while one (12.5%) patient presented with additional limp. No patient presented with fever. WBMR revealed unifocal (n=1,14.3%; clavicle) and multifocal involvement(n=6, 85.7%), with preferential long-bones meta/epiphyseal (n=5, 71.4%), clavicle (n=4, 57%), scapular (n=3, 42.9%), and vertebral (n=2, 28.6%) localization. The median number of bone location was 4 [IQR:3-10]. The most common WBMR pattern was spongious edema (n=7, 100%) with one patient presented with vertebral collapse. The median diagnostic delay (time between symptom onset and WBMR execution) was 71 days (IQR:12.5-64.5). Histopathological findings were represented by nonspecific inflammation (n=5,71.4%) and bone remodelling with fibrosis (n=6, 85.7%). No patients presented anemia and/or thrombocytopenia. Four (57.1%) patients showed ANA positivity, one (14.3%) concomitant autoimmune disease (celiac disease) and 2 (28.6%) transient hematuria and/or proteinuria at disease-onset. ESR and RCP were negative in all cases, with one patient (14.3%) showing serum amyloid-A rise up to 473 mg/l. One (14.3%) patient presented with persistently elevated IgG4 serum levels. Notably, the higher number of bones (46) involved were detected in the patient with concomitant celiac disease. Moreover, one patient presented CNO in the context of Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis (SAPHO) syndrome and no patients were found with pathogenetic gene mutations.
Conclusion: CNO exhibits significant heterogeneity, especially in lesion distribution and clinical presentation, ranging from asymptomatic bone lesions discovered incidentally to severe unifocal/multifocal bone pain. Female and sex and early teenage onset were predominant. WBMR proves essential for early diagnosis and treatment, supporting non-invasive diagnosis aligned with the new EULAR/ACR criteria. Unfortunately, genetics is still not conclusive, and CNO pathogenesis remains to clarify.
Disclosure
None declared

PU23

Clinical variability and treatment challenges in 2 children with blau syndrome

K. Warciak[1], D. Henderson[1], K. Gallagher[1], E. MacDermott[1], M. McAleer[2], S. Chamney[3], O. Killeen[1]
[1]National Centre for Rheumatology, [2]Department of Dermatology, [3]Department of Ophthalmology, Children's Health Ireland, Dublin, Ireland
Correspondence: K. Warciak
Pediatric Rheumatology, **23(2):** PU23

Introduction: Blau syndrome (BS) is a very rare familial autoinflammatory disorder with autosomal dominant inheritance pattern[1-6]. It can be caused by a gain-of-function mutation in nucleotide-binding oligomerization domain 2 (NOD2) gene[1-6]. The syndrome is characterized by polyarthritis, uveitis and granulomatous dermatitis[1-6]. Symptoms typically present before the age of five. Diagnosis is often delayed due to overlap with other autoimmune and autoinflammatory conditions.
Objectives: To describe the first two genetically confirmed case of Blau Syndrome identified in Ireland and highlight the variability in clinical severity and management strategies.
Methods: Clinical, radiological, histological and laboratory data were retrospectively collected from the patient's medical records.
Results: Patient 1 Caucasian female presented at the age of 2.5 years with severe polyarthritis, tenosynovitis, and hypercalcaemia. Genetic testing identified a novel NOD2 mutation. Her disease course is complicated by refractory arthritis and progressive ocular disease. She developed severe panuveitis and band keratopathy, requiring several intraocular anti-VEGF injections and resulting in severe visual impairment in her right eye. Skin biopsies confirmed granulomatous dermatitis during intermittent rash episodes. She experienced two episodes of hypercalcaemia, one of which led to an acute kidney injury and renal micro-calcification. A liver granuloma was also identified. Her current treatment includes: weekly intravenous Tocilizumab, Mycophenolate Mofetil, Tofacitinib and low dose of Prednisolone. She is also on prophylactic septrin, aciclovir and bone protection. Previous treatments included: multiple intra-articular corticosteroid injections, pulsed intravenous methylprednisolone, Methotrexate, Adalimumab, and Infliximab. Her quality of life is severely impacted with reduced physical activities and school absenteeism. Patient 2 Caucasian female, the only child of a father treated for suspected sarcoidosis, presented at 11-months-of-age with a widespread, non-pruritic, papular rash following a viral illness. A skin biopsy showed granulomatous dermatitis. Genetic testing confirmed NOD2 mutation. At the age-of-one she developed polyarthritis. Her current treatment includes: Methotrexate, Folic Acid and Adalimumab. Prednisolone was slowly weaned over 14 months from diagnosis.
Conclusion: Blau syndrome should be considered in young children presenting with granulomatous dermatitis, arthritis and uveitis. These 2 cases of Blau syndrome illustrate the wide spectrum of disease severity – from mild well-controlled symptoms to severe, the multisystem involvement especially visual impairment. Early recognition and prompt, aggressive treatment are paramount to improving long-term outcomes and improving quality of life. Consent to published had been obtained.
Disclosure
None declared

PU24

The case of sapho syndrome and abdominal pain – what is the connection?

M. Vidovic[1], A. Gagro[1], A. Tripalo Batos[2], M. Masic[3], Z. Misak[3]
[1]Department of Pulmonology, Allergology, Clinical Immunology and Rheumatology, Department of Paediatrics, [2]Department of Pediatric Radiology, [3]Referral Centre for Paediatric Gastroenterology and Nutrition, Children's Hospital Zagreb, Zagreb, Croatia
Correspondence: M. Vidovic
Pediatric Rheumatology, **23(2):** PU24

Introduction: Musculoskeletal pain is one of the most common complaints in children and adolescents. It is usually benign, in some cases a symptom of rheumatic condition, and rarely of autoinflammatory bone disease like Synovitis Acne Pustulosis Hyperostosis Osteitis syndrome (SAPHO). The association between SAPHO and inflammatory bowel disease (IBD) exists and evaluation of gastrointestinal symptoms in SAPHO patients is required, but careful interpretation of results is needed.

Objectives: We present a case of 13-year old girl with SAPHO, abdominal pain and diarrhea treated in Children's Hospital Zagreb, Croatia.
Methods: A 13-year old girl with severe acne and multiple bone pain (shoulders, lower back, knees and ankles) was referred to pediatric rheumatologist. She had elevated inflammatory laboratory markers, negative antinuclear antibody and rheuma factor, positive HLA-B27 locus and negative screening for coeliac disease. She was treated with isotretion for acne previously and nonsteroidal anti-inflammatory drugs (NSAID) for bone pain. Whole body magnetic resonance imaging (MRI) showed multiple lesions typical for SAPHO syndrome. Pamidronate infusions treatment was introduced with good clinical and laboratory response and NSAID continued with gastroprotection. Four months after initial diagnosis she developed abdominal pain, diarrhea and mild fever. Inflammatory blood markers were elevated, stool sample was negative for bacteria and viruses but positive for occult bleeding and fecal calprotectin came over 2000 µg/g. Ultrasound showed thickening of cecum and ascending colon with lymphadenopathy. Both endoscopic and video capsule investigations were performed.
Results: Video capsule investigations showed mild jejunal ulcers and aphthous lesions and only few mononuclears and eosinophils with absence of neutrophils, granulomas and abscesses on pathohistological biopsy evaluation. There were not enough elements for Crohn disease diagnosis, changes are more likely to be due to chronic NSAID consumption despite gastroprotection but continued reevaluation is planned. NSAID were discontinued. Pamidronate treatment was planned for 2 more months followed by second whole-body MRI.
Conclusion: The link between SAPHO and IBD exists but is understudied, up to 4.8% of patients with SAPHO syndrome also have IBD. Nevertheless, our patient symptoms are for time being associated with NSAID treatment but close monitoring is mandatory. Consent to published had been obtained.
Disclosure
None declared

PU25

Assessment of clinical and genetic characteristics and the management and follow-up of patients with sapho syndrome

M. O. Erkan[1], E. Sag[1], M. Sezer[2], Y. Bayindir[1], V. Cam[1], D. Unal[1], H. Ercan emreol[1], O. Necipoglu banak[1], H. D. Kar[1], Y. Bilginer[1], H. O. Basaran[1], S. Ozen[1]
[1]Department of Rheumatology, Hacettepe University, [2]Department of Rheumatology, Ankara Education and Research Hospital, Ankara, Türkiye
Correspondence: M. O. Erkan
Pediatric Rheumatology, **23(2):** PU25

Introduction: SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis) is a rare inflammatory disorder characterized by musculoskeletal involvement in conjunction with dermatological manifestations.
Objectives: This study aims to investigate the clinical and genetic characteristics of patients diagnosed with SAPHO syndrome, evaluate the treatment approaches applied, and present long-term follow-up outcomes.
Methods: A total of 7 patients diagnosed with SAPHO syndrome between 2024 and 2025 were retrospectively included in the study. Demographic data, age at symptom onset, disease duration, clinical findings, imaging and laboratory results, as well as genetic analysis findings were evaluated. Parameters such as treatment response, changes in disease activity, and development of complications were analyzed during the follow-up period.
Results: Acne was the most common initial symptom, followed by axial skeleton involvement and papulopustular lesions. All of the patients were male. The mean age at diagnosis was 14.5 years. The average duration until diagnosis was 11± 15,2 months. The mean follow-up duration was 32 ± 20.1 months. The mean treatment duration was 25.0 ± 14.48 months. Notably, five patients had a history of retinoic acid use prior to being diagnosed with SAPHO, and the onset of back pain following retinoic acid use was particularly prominent. Genetic analyses investigated variants associated with autoinflammatory diseases, and only one patient was found to carry a heterozygous PSTPIP1 c.683G>A (p.Arg228His) mutation. Nonsteroidal anti-inflammatory drugs (NSAIDs) and biological agents, particularly TNF-α inhibitors, were the most commonly used treatments. Six out of seven patients achieved remission with etanercept, while one patient was switched to infliximab due to persistent cutaneous symptoms.
Conclusion: SAPHO syndrome is a rare and clinically heterogeneous disorder that can pose diagnostic and therapeutic challenges. The potential association between genetic predisposition and autoinflammatory pathways warrants further investigation.
Disclosure
None declared

PU26

A rare case of c-anca-associated vasculitis in a child with familial Mediterranean fever

Y. Tulun, C. Ozbakir, O. Altug Gucenmez
University of Health Sciences, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, Izmir, Türkiye
Correspondence: O. Altug Gucenmez
Pediatric Rheumatology, **23(2):** PU26

Introduction: Familial Mediterranean Fever (FMF) and c-ANCA–associated vasculitis are rarely seen together.
Objectives: To report a case with FMF who also presented fatigue, musculoskeletal pain, weight loss and purpuric rash.
Methods: A 10-year-old girl who were diagnosed with FMF at age 3 consulted to the emergency department with a two-week history of persistent cough, fatigue, widespread musculoskeletal pain, and weight loss. She had been on colchicine therapy with poor adherence. Initial physical examination revealed a palpable purpuric rash on the dorsum of both feet and a systolic blood pressure discrepancy between the upper and lower extremities. She was afebrile at admission. Laboratory results demonstrated mild anemia (Hgb: 11.5 g/dL), leukocytosis (WBC: 9780/µL), thrombocytosis (platelets: 582,000/µL), elevated ESR (70 mm/h), CRP (133 mg/L), ALT (116 IU/L), AST (80 IU/L), and CK (156 IU/L).
Results: The patient was hospitalized for further investigation. Imaging and laboratory tests excluded infectious and malignant causes. Serological screening for autoimmune hepatitis was negative. During hospitalization, liver enzyme levels progressively increased (ALT up to 1200 IU/L), although bilirubin, albumin, and coagulation profiles remained within normal limits. Urinalysis showed proteinuria at nephritic levels. Autoimmune workup revealed positive ANA, c-ANCA, and PR3-ANCA antibodies. Liver biopsy revealed steatohepatitis, and kidney biopsy confirmed pauci-immune glomerulonephritis. Although chest radiography and thoracic CT scans suggested pulmonary involvement, clinical findings did not fulfill the diagnostic criteria for granulomatosis with polyangiitis (GPA). Pulse steroid therapy and cyclophosphamide were initiated. Due to elevated transaminase levels, colchicine was withdrawn. Subsequently IL-1 receptor antagonist (Anakinra) was administered which led to a decrease in liver enzymes and inflammatory markers. Her musculoskeletal pain resolved completely. She remains asymptomatic and is currently under IL-1β (Canakinumab) therapy, with all laboratory values within normal range.
Conclusion: This rare case highlights the potential coexistence of FMF and c-ANCA–associated vasculitis in children. Clinicians should consider IL-1 inhibitors for vasculitis in FMF patients with atypical symptoms when standard therapies present limited effects. Consent to published had been obtained.
Disclosure
None declared

PU27

ADA2 deficiency masquerading as early-onset behçet's disease: a pediatric case underscoring genetic diagnosis

O. Necipoglu Banak, E. Sag, Y. Bayindir, E. Aliyev, V. Cam, D. Unal, H. Ercan Emreol, M. O. Erkan, H. D. Dara Kar, O. Basaran, Y. Bilginer, S. Ozen
Pediatric Rheumatology, Hacettepe University, Ankara, Türkiye
Correspondence: O. Necipoglu Banak
Pediatric Rheumatology, **23(2):** PU27

Introduction: Early-onset Behçet's disease (BD) mimics, such as monogenic autoinflammatory disorders, pose diagnostic challenges. Genetic testing has a pivotal role in distinguishing ADA2 deficiency (DADA2) from BD in children with refractory mucocutaneous and vasculitic features.
Objectives: To illustrate the diagnostic complexity of early-onset BD-like disease and emphasize the role of genetic testing in identifying ADA2 deficiency as an alternative diagnosis. This case aims to highlight clinical red flags that suggest monogenic vasculitis and the therapeutic implications of a precise molecular diagnosis.
Methods: We present the clinical course of a female pediatric patient, followed from ages 5 to 13, exhibiting evolving mucocutaneous, articular, and vasculitic symptoms that were initially suggestive of BD.
Results: A 5-year-old female presented with bilateral hand swelling, restricted joint mobility, and elevated acute-phase reactants. Symptoms began with isolated swelling of the right second digit and progressed to painful rashes resembling erythema nodosum. The initial workup excluded rheumatologic etiologies. Autoantibodies (ANA, anti-dsDNA, ANCA) were negative. Complement levels were normal, and bone marrow aspiration was unremarkable. MEFV testing was negative, but HLA B5 positivity raised suspicion for BD. At age 10, a genital ulcer led to a provisional BD diagnosis. Colchicine was started. Recurrent genital and oral ulcers were treated with short courses of prednisone. At age 13, she developed bilateral ankle arthritis and livedoid rashes. Skin biopsy revealed small-to-medium vessel vasculitis and lobular panniculitis. Further genetic analysis was sought because of the new symptoms and consanguinity. A homozygous ADA2 mutation (c.349G>A, p.Gly117Arg) was found, confirming DADA2. Etanercept led to sustained remission of ulcers, arthritis, and vasculitis within three weeks.
Conclusion: DADA2 should be considered in early-onset BD-like cases with atypical features as well. Genetic testing is crucial for timely diagnosis, enabling targeted therapy with tumor necrosis factor-alpha inhibitors and preventing prolonged immunosuppression. HLA positivity does not exclude a monogenic disorder. Consent to published had been obtained.
Disclosure
None declared

PU28

Unmasking diagnostic challenges: H syndrome mistaken for caps

S. Palmeri[1,2], A. Agrusti[1,2], V. Natoli[1,2], E. Drago[1,2], F. Penco[2], F. Schena[2], P. Bocca[2], I. Prigione[2], R. Bertelli[3], R. Papa[2], S. Volpi[1,2], R. Caorsi[1,2], M. Gattorno[2]
[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, [2]Rheumatology and Autoinflammatory Diseases Unit, [3]Laboratory of Human Genetics, IRCCS Istituto Giannina Gaslini, Genoa, Italy
Correspondence: S. Palmeri
Pediatric Rheumatology, **23(2):** PU28

Introduction: H syndrome is a rare autosomal recessive disorder caused by mutations in the SLC29A3 gene, encoding the human equilibrative nucleoside transporter 3 (hENT3). This nucleoside transporter is critical for lysosomal and mitochondrial metabolism. The syndrome manifests with a broad spectrum of systemic symptoms, including cutaneous hyperpigmentation, skin sclerosis, hepatosplenomegaly, hypertrichosis, hypogonadism, cardiac anomalies, short stature, sensorineural hearing loss, and systemic inflammation.(1, 2)
Objectives: To report a patient with H syndrome misdiagnosed as having CAPS (Cryopyrin-Associated Periodic Syndromes).
Methods: Patient records were reviewed. Plasma cytokines were measured by Ella. IL-1β secretion was assessed in supernatants of patient PBMCs and healthy donors (HD). Type I interferon signature was analyzed in the patient's blood. ASC speck was detected by flow cytometry.
Results: The patient was first evaluated at age 24 with the following clinical history: in infancy, he had recurrent non-itchy urticarial-like rashes, conjunctivitis, episcleritis, and febrile episodes with fluctuating hearing loss. Oral steroids offered temporary hearing improvement, but progressive damage led to permanent loss. He also had episodes of extremity swelling and paresthesia, especially after cold exposure, and two episodes of hemolytic anemia with fever. Abdominal pain led to two colonoscopies—one in childhood and one in adulthood—both diagnosing undifferentiated colitis. Type 1 diabetes mellitus was diagnosed in adolescence. Colchicine was ineffective. Due to suspected cryopyrinopathy, anakinra was started with initial benefit, later replaced by canakinumab. A recurrent fever gene panel (IL1RN, LPIN2, MEFV, MVK, NLRP12, NLRP3, NOD2, PSMB8, PSTPIP1, TNFRSF1A) was negative. IL-1β secretion was elevated with faster kinetics compared to HD. NLRP3 inflammasome activation peaked at 6 hours post-LPS stimulation in the patient, versus 3 hours in HD, as measured by ASC speck formation. Interferon signature was positive; plasma cytokines (IL-18, IL-1RA, IL-6, TNFRI) were normal. Reactive oxygen species (ROS) were elevated at baseline and post-stimulation in monocytes and granulocytes. Whole-exome sequencing with an extended autoinflammatory panel revealed a biallelic deletion in SLC29A3.
Conclusion: This case highlights the diagnostic challenges of H syndrome due to overlapping autoinflammatory features that may cause misdiagnosis. The patient lacked typical skin signs (hyperpigmentation, induration, hypertrichosis), seen in most cases, leading to years of misclassification despite syndrome recognition. Hearing loss initially suggested CAPS, but alternative diagnoses should be considered with atypical signs (e.g., diabetes, hemolytic anemia) and partial response to IL-1 blockade.
Disclosure
S. Palmeri: None declared, A. Agrusti: None declared, V. Natoli: None declared, E. Drago: None declared, F. Penco: None declared, F. Schena: None declared, P. Bocca: None declared, I. Prigione: None declared, R. Bertelli: None declared, R. Papa: None declared, S. Volpi Consultant with: Boehringer, Speaker Bureau with: Speaker fee from SOBI, R. Caorsi Consultant with: SOBI, M. Gattorno Consultant with: Novartis, Sobi, Fresenius Kabi, Kiniksa, Speaker Bureau with: Novartis, Sobi, Fresenius Kabi, Kiniksa

References

1. Hamad, Alaa et al. "H syndrome: A histiocytosis-lymphadenopathy plus syndrome. A comprehensive review of the literature." Hematology/oncology and stem cell therapy vol. 17,3 (2024): 159–167.
2. Ma, Hongying et al. "Equilibrative nucleotide transporter ENT3 (SLC29A3): A unique transporter for inherited disorders and cancers." Experimental cell research vol. 434,2 (2024): 113,892.

PU29

Neonatal-onset cytopenia, autoinflammation, rash, and episodes of hemophagocytic lymphohistiocytosis (NOCARH) treated with il-1 blockade, JAK inhibition and HSCT– a case report

S. Johansson[1], M. Ekelund[1], C. Langenskiold[2], S. Berg[2]
[1]Department of Pediatrics, Ryhov County Hospital, Jönköping, [2]Department of Pediatrics, University of Gothenburg, Gothenburg, Sweden
Correspondence: S. Johansson
Pediatric Rheumatology, **23(2):** PU29

Introduction: Neonatal-onset cytopenia, autoinflammation, rash, and episodes of hemophagocytic lymphohistiocytosis (NOCARH) is an ultra-rare disease described in about 20 patients. NOCARH is caused by heterozygeous variants in *CDC42*. The case-fatality is high so far in the literature (40%, 7/18). Treatment with JAK inhibition and IL-1 inhibition might be partially effective but the bonemarrow failure do respond poorly and the addition of hematological stem cell transplantation (HSCT) is an option.
Objectives: -
Methods: -
Results: Case Presentation
A full-term neonate presented with widespread rash, thrombocytopenia, hepatosplenomegaly, and cholestasis. Initially suspected to have gestational alloimmune liver disease (GALD), treatment was initiated with IVIG and exchange transfusion. Liver biopsy revealed giant cell hepatitis consistent with hyperinflammation. Diagnostic criteria for HLH-2004 were met, including elevated ferritin, triglycerides, and sIL-2 receptor levels. Genetic testing revealed a heterozygous pathogenic CDC42 variant (c.556C>T, p.Arg186Cys), previously reported in about a dozen of patients worldwide.

In spite of intensive treatment the patient remained refractory. During the first months of treatment, the child received anakinra, baricitinib, prednisone, filgrastim, and erytropoetin. Despite this she needed numerous erythrocyte and thrombocyte transfusions. At 4 months of age, baricitinib was replaced by emapalumab (anti–IFN-γ, compassionate use), which was later switched back to bariticinib due to flares. Disease control was only partially achieved, and at 6 months, the child underwent haploidentical allogeneic hematological stem cell transplantation (HSCT) from the mother.
The post-transplant course was complicated by inflammatory flares and evolving of mixed chimerism. Baricitinib, anakinra, and monthly IVIG were added. Inflammatory markers and skin involvement worsened over time, leading to intensified JAK inhibition. One-year post-HSCT, rising levels of recipient DNA in all cell lines indicated graft rejection. A second HSCT is planned for spring 2025. Despite this complex course, the child is currently demonstrating normal neurodevelopment and acceptable growth.
Conclusion: This case adds information of the clinical presentation and the treatment of this ultra-rare disease. We present a neonatal-onset disease with bone-marrow failure, autoinflammation, rash and intermittent HLH (NOCARH) driven by a CDC42 variant with a protracted, treatment-refractory course despite HSCT and aggressive immunomodulation. It highlights the critical importance of genetic diagnosis in neonatal inflammatory disorders and the need for tailored, sustained immunotherapy strategies in monogenic autoinflammatory syndromes. Graft rejection following HSCT might be a challenge in these patients. Consent to published had been obtained.
Disclosure
None declared

PU30

Diagnostic challenges of a rare genetic autoinflammatory disorder: severe early-onset mevalonate kinase deficiency with minimal mevalonic aciduria in a Sri Lankan child

V. Arunath, C. Naotunna, A. Aththanayake, E. Jasinge, K. Weerasekara
Lady Ridgeway Hospital for Children, Colombo 08, Sri Lanka
Correspondence: V. Arunath
Pediatric Rheumatology, **23(2):** PU30

Introduction: Mevalonate kinase (MK) deficiency, a rare genetic autoinflammatory disorder is caused by the mutations in MVK gene, represents the two ends of a clinical spectrum of disease, varied from severe early-onset MK deficiency and hyperimmunoglobulinemia D syndrome. Severe early-onset MK deficiency is an autosomal recessive disorder, results in recurrent febrile crises and hepatosplenomegaly and is usually associated with highly elevated urine mevalonic acid levels.
Objectives: Objective of the study was to report a patient with severe early-onset mevalonate kinase deficiency, who presented with minimal mevalonic aciduria and to describe the challanges to make the diagnosis of this rare genetic autoinflammatory disorder in low resource settings.
Methods: Index case was second-born baby girl to second-degree consanguineous parents, born by spontaneous vaginal delivery at term with a birth weight of 1706grams following an uncomplicated antenatal and perinatal period. Baby managed at neonatal unit for 5-days for asymptomatic hypoglycemia, coombs negative hemolytic anemia and thrombocytopenia with negative TORCH screening. At the age of 6-weeks, child admitted with prolonged febrile illness, poorly resolving bronchopneumonia, hepatosplenomegaly, cholestatic jaundice and bicytopenia with elevated inflammatory markers. Bone marrow biopsy showed reactive marrow and liver histology revealed giant cell hepatitis. Immunoglobulin A, G & M levels were normal however, IgD levels were not done due to unavailability. Urine organic acid levels were normal with minimal mevalonic acid levels in urine.
Results: Genetic mutational analysis was performed at a reputed overseas laboratory free of charge and it revealed homozygous pathogenic variant (NM_000431.3:c.1129G>A,p.(Val377Ile) in the MVK gene which confirmed the diagnosis of MK deficiency. Since the initial presentation, she developed recurrent febrile episodes with elevated inflammatory markers, which were managed with antibiotics and extensive diagnostic investigations. Once the genetic diagnosis was made, corticosteroids and non-steroidal anti-inflammatory drugs were used to mange her hyperinflammatory episodes. Unfortunately, child succumbed due to severe bronchopneumonia with acute crisis at the age of 2.5 years.
Conclusion: Children with MK deficiency can be presented with recurrent febrile episodes and hepatosplenomegaly with minimal mevalonic aciduria. Genetic studies are necessary to confirm the diagnosis and accurate counselling of the family. Lack of resources in developing world delays the diagnosis. Stakeholders should consider to provide the facilities to confirm the treatable conditions in children and developed world can consider to help these resource poor countries. Consent to published had been obtained.
Disclosure
None declared

References

1. Haas, D. and Hoffmann, G.F. (2006) "Mevalonate kinase deficiencies: From mevalonic aciduria to hyperimmunoglobulinemia D syndrome," Orphanet Journal of Rare Diseases, 1(1).
2. Prasad, C., Salvadori, M.I. and Rupar, C.A. (2012) "Severe phenotypic spectrum of mevalonate kinase deficiency with minimal mevalonic aciduria," Molecular Genetics and Metabolism, 107(4), pp. 756–759.

PU31

A20 Haploinsufficiency (HA20): the case report of a boy with lupus-like and inflammatory bowel disease manifestations

Z. Pytelova[1], M. Janega[1], M. Geryk[1], E. Karaskova[1], V. Curtisova[2], K. Bouchalova[1]
[1]Department of Paediatrics and Faculty of Medicine and Dentistry, Palacký University Olomouc and Olomouc University Hospital, [2]Institute of Medical Genetics, Olomouc University Hospital, Olomouc, Czech Republic
Correspondence: Z. Pytelova
Pediatric Rheumatology, **23(2):** PU31

Introduction: A20 haploinsufficiency is an autoinflammatory disease caused by a mutation in the TNFAIP3 gene [1,2].
Objectives: Our aim is to present a case report of a boy with A20 haploinsufficiency.
Methods: A case report.
Results: The patient`s difficulties started in 2019 at the age of 4 years as a HLA-B27 positive arthritis. Initial treatment with non-steroidal anti-inflammatory drugs (NSAIDs) had no effect. Methotrexate therapy was initiated in June 2022, along with physiotherapy.
In September 2022, the boy was admitted for worsening arthritis. During the hospitalization, he developed macrophage activation syndrome (MAS), which was complicated by convulsions with a necessity of a mechanical ventilation for 47 hours and total parenteral nutrition. Treatment with anakinra was initiated at 2 mg/kg/day, later increased to 3.5 mg/kg/day. Concurrently, intravenous methylprednisolone pulses (30 mg/kg/day for three days) were administered, followed by oral prednisone, which was discontinued in November 2022.
The subsequent clinical course was complicated by recurrent infections and arthritis flares. The patient also developed diarrhoea with elevated fecal calprotectin levels. In August 2023, magnetic resonance enterography showed no pathological findings. However, persistent intermittent abdominal pain and signs of terminal ileitis on ultrasound and repeated MR imaging led to colonoscopy in March 2024, which revealed mild hyperaemia of the terminal ileum.
In June 2024, due to recurrent arthritis, therapy was changed to tocilizumab 162 mg subcutaneously every 2 weeks. However gastrointestinal symptoms progressed. A follow-up colonoscopy in August 2024 demonstrated histologically active chronic inflammation resembling ulcerative colitis.
A psychiatric evaluation concluded an adjustment disorder with symptoms consistent with oppositional defiant disorder.
Due to the accumulation of infections, urgent genetic testing for primary immunodeficiencies was requested in 2024. This identified a pathogenic variant in the TNFAIP3 gene and confirmed haploinsufficiency A20 (HA20). The mutation in TNFAIP3 gene was also confirmed in the boy's mother and the boy's 2 brothers.

In October 2024, given the clinical phenotype and genetic findings, biologic therapy was switched to infliximab. At the time of abstract submission, the patient was asymptomatic.
Conclusion: The boy developed lupus-like manifestations of A20 haploinsuficiency, monogenic autoinflammatory disease with variable clinical manifestation with effect of infliximab. The case points to the importance of genetic testing in children with lupus symptomatology. Consent to published had been obtained.
Disclosure
None declared

References
1. Yu, Mei-Pinget al.. Haploinsufficiency of A20 (HA20): updates on the genetics, phenotype, pathogenesis and treatment. World Journal of Pediatrics. 2020. 16 (6): 575–584.
2. Zhang, Dan et al. Clinical characteristics and genetic analysis of A20 haploinsufficiency. Pediatric Rheumatology. 2021. 19 (1)

PU32

Off-label use of high-dose infliximab in a pediatric patient with complicated panuveitis: clinical response following adalimumab failure

A. Mauro[1], E. Naddeo[2], A. Maggi[2], C. Di Mari[3], E. L. De Rose[4], V. Ansuini[1], L. Giordano[4], L. Bernardo[4]
[1]Pediatric Rheumatology Service, "Casa Pediatrica" Unit, ASST Fatebenefratelli-Sacco, [2]Department of Pediatrics, "Vittore Buzzi" Children's Hospital, ASST Fatebenefratelli-Sacco, University of Milan, [3]"Casa Pediatrica" Unit, Department of Child and Adolescent Medicine, ASST Fatebenefratelli-Sacco, [4]"Casa Pediatrica" Unit, Department of Child and Adolescent Medicine, ASST Fatebenefratelli-Sacco, Milan, Italy
Correspondence: A. Mauro
Pediatric Rheumatology, **23(2):** PU32

Introduction: Panuveitis is one of the most severe forms of uveitis, characterized by diffuse inflammation of all ocular structures and a significant risk of irreversible visual impairment, particularly in pediatric patients. Complications such as retinal vasculitis and optic disc neovascularization require prompt and aggressive therapeutic interventions. Although the use of biologic agents has expanded treatment options for refractory cases, the use of drugs such as infliximab in pediatric age remains limited and mostly off-label.
Objectives: To report the clinical outcome of a pediatric patient with complicated panuveitis refractory to adalimumab and methotrexate, successfully treated with high-dose infliximab.
Methods: We describe the case of a 16-year-old female with a previous diagnosis of panuveitis in the right eye, complicated by ischemic venous and arterial retinal vasculitis and neovascularization of the optic disc. In 2022, the patient underwent vitrectomy, surgical ablation of epipapillary neovessels, intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF), and pan-retinal laser photocoagulation. Due to the severity of the clinical picture, systemic therapy was initiated with methotrexate (15 mg/m^2/week) and adalimumab (40 mg every 15 days), in combination with oral prednisone (25 mg/day). Methotrexate was discontinued after one month due to intolerance. Following clinical worsening, the adalimumab dosage was increased to 40 mg per week. As inflammation persisted, adalimumab was discontinued, and high-dose infliximab (10 mg/kg) was initiated, following an induction schedule (weeks 0, 2, and 6) and subsequent maintenance every 6–8 weeks. Each infusion was preceded by intravenous corticosteroid boluses.
Results: Treatment with infliximab resulted in a marked clinical improvement and ophthalmologic stabilization. The inflammatory lesions resolved completely, with no new complications observed during follow-up. The treatment was well tolerated and no significant adverse effects were reported.
Conclusion: This case suggests that infliximab infusion therapy led to a significant improvement in retinal vasculitis, representing an effective therapeutic option in pediatric patients with complicated panuveitis refractory to other biologic agents such as adalimumab. Based on the observed clinical response, high-dose infliximab may be considered a valid off-label therapeutic alternative in complex pediatric cases, underlining the importance of an early and personalized treatment approach. Consent to published had been obtained.
Disclosure
None declared

PU34

Early-onset chronic colitis and recurrent arthritis in an infant with suspected monogenic IBD: diagnostic and therapeutic challenges

E. Nakhutsrishvili, T. Kutubidze
Givi Zhvania Pediatric University Clinic of Tbilisi State Medical University, Tbilisi, Georgia
Correspondence: E. Nakhutsrishvili
Pediatric Rheumatology, **23(2):** PU34

Introduction: Early-onset inflammatory bowel disease (EO-IBD), particularly when manifesting before the age of 6 months, raises suspicion for monogenic forms of IBD. These rare conditions often present with gastrointestinal symptoms and extraintestinal manifestations, including arthritis. The complexity of diagnosis and treatment is heightened by overlapping allergic, infectious, and autoimmune processes.
Objectives: To present a challenging case of chronic blood-streaked diarrhea and recurrent monoarthritis in an infant with early-onset symptoms, ultimately raising suspicion for monogenic IBD and guiding immunological and genetic investigation.
Methods: We reviewed the clinical course of a male infant born to a mother with COVID-19 during pregnancy. The patient presented with hematochezia starting at 4 months of age and later developed recurrent swelling of the left ankle. Extensive diagnostic evaluation included stool studies, immunoglobulin profiling, endoscopy with biopsy, serologic markers (TTG, ANA), genetic testing (ongoing), and imaging. Dietary management, laboratory monitoring, and pharmacologic therapy were closely tracked.
Results: Initial symptoms were consistent with food protein-induced allergic proctocolitis. However, persistent hematochezia despite dietary exclusion and the emergence of arthritis prompted further evaluation. Colonoscopy revealed multiple colonic ulcers. Elevated IgG anti-TTG, iron deficiency anemia, low fecal elastase, and joint inflammation suggested immune dysregulation. The patient responded to systemic corticosteroids with improvement in joint symptoms and gastrointestinal bleeding. Ongoing treatment with sulfasalazine and consideration of azathioprine were guided by TPMT activity. Genetic testing for monogenic IBD was initiated in collaboration with international experts.
Conclusion: This case highlights the diagnostic challenge in differentiating food allergy from monogenic IBD in infants. Refractory hematochezia and arthritis should prompt early referral, endoscopic evaluation, and consideration of underlying genetic immune dysregulation. Early immunomodulatory treatment may significantly improve clinical outcomes. Consent to published had been obtained.
Disclosure
None declared

PU36

A rare synovial vascular malformation mimicking chronic knee arthritis-JIA: a diagnostic challenge and its implications

I. Awan, A. Sridhar
Paediatric Rheumatology, Leicester's Children Hospital, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom
Correspondence: I. Awan
Pediatric Rheumatology, **23(2):** PU36

Introduction:
Chronic knee pain and swelling in children are often attributed to juvenile idiopathic arthritis (JIA) but these diagnoses may overlook rare conditions that require specialized management. This case report presents a unique diagnosis of synovial vascular malformation (synovial haemangioma) in a paediatric patient, highlighting the challenges in diagnosing such rare conditions when symptoms mimic more common disorders like JIA.
Objectives: This report aims to add new insights into the diagnostic approach for persistent, unexplained joint swelling and underscores

the importance of multidisciplinary collaboration in paediatric rheumatology.
Methods: An 8 year old boy was initially diagnosed with oligoarticular JIA after presenting with one year history of left knee pain, swelling, and stiffness. Despite conventional treatment with NSAIDs, symptoms persisted in form of fluctuant intermittent painful knee swelling with functional limitation during walking. Examination showed swelling of the left knee joint with mild limitation of the left knee. There was no other joint, eye or spinal involvement.
As the history suggested fluctuating size of the swelling, a decision was taken to investigate further before considering Joint steroid injection to the left knee joint
Further evaluation, including ultrasound and MRI, revealed a rare synovial and intramuscular vascular malformation of the left knee joint. The diagnosis was confirmed through a multidisciplinary team (MDT) approach, involving paediatric rheumatology, oncology, orthopaedics, and interventional radiology teams
Results: Initial blood tests including FBC, CRP, Plasma viscosity were normal. The autoimmune screen was negative. The MRI revealed a lobulated mass within the suprapatellar fat pad, with low T1 signal, atypical for JIA, but suggestive of a synovial vascular malformation. After the diagnosis, the patient is followed up regularly at tertiary rheumatology centre and planned for sclerotherapy by interventional radiologist. This is recommended to help with possible complete resolution of the knee swelling and hence enabling patient to return to normal activities & quality of life.
Conclusion:
This case emphasizes the importance of considering rare diagnoses, such as synovial vascular malformations, in paediatric patients with chronic, unexplained knee swelling. The diagnostic challenge in this case was significant, as the condition mimicked more common inflammatory conditions like Oligo-JIA. This case highlights the role of advanced imaging techniques such as MRI and the need for a multidisciplinary approach in managing rare paediatric musculoskeletal conditions. Sclerotherapy is considered as successful, minimally invasive treatment, providing an optimal outcome. This report adds to the growing body of literature on rare paediatric musculoskeletal conditions and proposes a more robust diagnostic approach to ensure timely identification and intervention. Consent to published had been obtained.
Keywords:
Synovial vascular malformation, JIA, Chronic knee swelling, Sclerotherapy
Disclosure
None declared

References
1. Singh R, et al. (2019). Synovial vascular malformations in Paediatric patients: A case report of misdiagnosis and successful sclerotherapy. Journal of Paediatric Rheumatology, 37(2): 123–130.
2. Thakur A, et al. (2015). A rare case of synovial Haemangioma in a child: MRI features and differential diagnosis. Paediatric Radiology, 45(4): 678–684.
3. Baker P, et al. (2017). Synovial Haemangioma in adults: Diagnostic challenges and treatment outcomes. Clinical Rheumatology, 35(5): 1189–1194.

PU37

JAK-inhibition as treatment option for alopecia areata: a case series

C. K. Braun[1,2], I.-M. Linder[1], A. Janda[1]
[1]Department of Pediatrics and Adolescent Medicine,, [2]German Center for Child and Adolescent Health (DZKJ), Partner Site Ulm, University Ulm, Ulm, Germany
Correspondence: A. Janda
Pediatric Rheumatology, **23(2):** PU37

Introduction: Alopecia areata (AA) is an immune-mediated, non-scarring hair loss disorder that can progress to alopecia totalis (AT) or alopecia universalis (AU). The pathogenesis involves autoreactive $CD8^+$ $NKG2D^+$ T cells and an inflammatory microenvironment driven by IL-15 and IFN-γ signaling via the JAK-STAT pathway. Janus kinase inhibitors (JAKi) have emerged as a promising targeted therapy by interrupting this cytokine signaling cascade and restoring immune privilege in hair follicles.
Objectives: Reporting on use of JAKi in patients with AT/AU.
Methods: We present clinical data on five pediatric patients (2 males, 3 females; age range at therapy initiation: 6–14 years) treated off-label with various JAKi (tofacitinib, ruxolitinib, baricitinib) for AA/AU. Clinical outcomes, photo-documentation, laboratory/immunological parameters, and side effects were tracked. Additionally, autoimmune thyroiditis data are reported in 3/5 patients.
Results: All patients responded to JAKi therapy with significant hair regrowth. Two patients achieved complete remission, while one patient experienced two relapses requiring intravenous high-dose and oral corticosteroid maintenance. Mild pan-lymphopenia was observed in one patient, but no significant adverse effects were noted with any of the JAKi therapies. Notably, autoimmune thyroiditis was present in three patients and improved under JAKi treatment.
Conclusion: In this pediatric cohort, JAKi therapy demonstrated both efficacy and safety in the treatment of AA/AU. These results support the potential of JAKi as a therapeutic option for pediatric AA/AU, with favorable outcomes and manageable side effects.
Disclosure
None declared

PU39

anakinra in neonate : refractory dengue associated hemophagocytic lymphohistiocytosis

D. B. Pandya, on behalf of Dr Maulik Korvadiya, Dr Nirav Patel, Dr Pritesh Rathod, Dr Divyang Bhimani, Dr Tushar Zalawadiya, Dr Dharmesh Oza, Dr Ashish Khambhayata, Dr Nishant Dharsandiya & Dr Nihar Pathak.
Pediatric Rheumatology, Dev Pediatric Rheumatology & Immunology Center, Ahmedabad, India
Correspondence: D. B. Pandya
Pediatric Rheumatology, **23(2):** PU39

Introduction: Anakinra is found to be effective in Primary and Secondary Pediatric Hemophagocytic Lymphohistiocytosis (HLH). Anakinra is not readily available in India.
Objectives: We are presenting the case where we have used SC Anakinra (imported) in Neonatal multi-system refractory secondary HLH due to dengue virus infection.
Methods: A female neonate delivered by caesarean section to a mother with an active dengue infection, admitted in our NICU for an observation. First 48 hours, Baby was hemodynamically stable with no oxygen requirement, tolerating spoon feeding and laboratory parameters were within normal limits. Day 3 onwards, baby developed high fever, tachypnea, rashes, petechiae, altered sensorium and shock. Baby was immediately put on mechanical ventilation, inotropic support, intravenous (IV) antibiotics and supportive treatment. Laboratory results revealed rapidly deceasing trend in all three blood cells lines : hemoglobin 7gm%, WBC count 3580/cumm & platelet count 3000/ul, raised inflammatory markers : CRP 65mg/L, ferritin 1,42,000 ng/ml, LDH : 3240 iu/l, D- dimer 7050, deranged liver functions : SGOT 5477 u/ml, SGPT 770 u/ml, low albumin 1.8gm%, deranged coagulation profile, elevated serum creatinine 1.39 with PCR dengue positive (760000 copies/ml). Cranial USG showed grade 1 germial matrix haemorrhage. Abdomen ultrasound showed hepatomegaly, gall bladder wall edema and ascites. Chest X ray and Echocardiography was normal. Considering post-dengue multisystem secondary HLH, we started IV immunoglobulin (2gm/kg), IV methylprednisolone pulse (30mg/kg/day) doses and blood products (packed red cells, platelets, FFP, albumin) under cover of broad spectrum antibacterial and anti-fungal medications. There is some improvement in baby's clinical condition, but his HLH parameters were not responding. Baby was put on oral cyclosporin as a bridge agent until subcutaneous (SC) Anakinra becomes available.
Results: Baby was given SC Anakinra 5mg/kg/day for the next 10 days. On Day 4 of Anakinra, baby started improving clinically and her HLH parameters started coming back towards normal. On day 25 of life, baby was discharged home on full oral feeds, tapering oral steroids and supportive medications with normal vital parameters, normal sensorium, no oxygen requirement and improving laboratory parameters. Baby is doing well presently off medications. Genetic and Functional tests to look for possible Primary HLH are pending.
Conclusion: Subcutaneous Anakinra has proven to be life-saving and very safe in a Neonatal Refractory Secondary HLH. Consent to published had been obtained.

Disclosure
None declared

PU40

Adverse events related to methotrexate dosage error in a pediatric patient with psoriasis

B. M. Da Silva Toro[1], B. Morais[2], M. Vieira[1], I. Carvalho[2], H. Sousa[2]
[1]ULS Santa Maria, [2]ULS Estuário do Tejo, Lisbon, Portugal
Correspondence: H. Sousa
Pediatric Rheumatology, **23(2):** PU40

Introduction: Methotrexate (MTX) is a systemic immunosuppressive agent often used in rheumatology and dermatology. It's administration follows strict guidelines. Despite good tolerability, even low-dose regimens can result in severe outcomes. The authors describe a case of toxicity associated with MTX dosage error.
Objectives
Methods
Results: Case Report: An eight-year-old boy (BSA 1.2m2) with psoriasis was initiated on oral MTX (5 mg/week) and folic acid on the dermatology consultation. He had normal baseline evaluations (infectious serologies and tuberculous screening). Within one week of treatment, he developed painful rapidly progressive erythematous, erosive, and ulcerative skin lesions on the trunk, scalp and limbs and oral and genital mucositis. It was identified daily MTX administration for 5 days (cumulative dose 25 mg) due to a misunderstanding. Laboratory: mild lymphopenia (1160/uL) and hypoalbuminemia (3.3mg/dl). MTX was discontinued, daily folinic acid and prophylactic antibiotics initiated. He was admitted, with progressive recovery on conservative management and was discharged in 1 week. Maintained follow up on the Dermatology and Pediatric Rheumatology consultations.
Conclusion: MTX-related toxicity in children is sparse, particularly isolated mucocutaneous manifestations. Underlying psoriasis may contribute to exaggerated cutaneous response - psoriatic plaques have rapid keratinocyte turnover, altered epidermal barrier function and local immune activation, which may enhance MTX uptake. Pediatric patients (Vs adults) have differing folate metabolism, and potentially greater MTX sensitivity, which may predispose to atypical toxicity patterns. Absence of marked laboratory abnormalities underscores importance of early clinical signs. Research on the physiopathology behind MTX toxicity in pediatrics is needed. This case raises broader questions about MTX's interaction with inflamed tissues, relevant in rheumatology. Consent to published had been obtained.
Trial registration identifying number
Disclosure
None declared

References

1. El Masri AER, Tobler C, Willemijn B, Von Bueren AO, Ansari M, Samer CF. Case report: Hepatotoxicity and nephrotoxicity induced by methotrexate in a paediatric patient, what is the role of precision medicine in 2023? Front Pharmacol. 2023 May 2;14:1,130,548. doi: https://doi.org/10.3389/fphar.2023.1130548. PMID: 37,201,023; PMCID: PMC10185764.
2. Badurdeen S, Kang SL, Saravanan M. Accidental methotrexate ingestion in a 19-month-old child. BMJ Case Rep. 2011 Apr 26;2011:bcr1120103477. doi: https://doi.org/10.1136/bcr.11.2010.3477. PMID: 22,696,676; PMCID: PMC3083011.
3. Hensley MD, Bebarta VS, Borys DJ. A Large Case Series of Acute Pediatric Methotrexate Ingestions: Significant Clinical Effects Are Rare. Pediatr Emerg Care. 2016 Oct;32(10):682–684. doi: https://doi.org/10.1097/PEC.0000000000000785. PMID: 27,383,404.
4. Pathiraja, H., de Abrew, G., de Silva, L. et al. Methotrexate-induced leukoencephalopathy presenting as acute-onset limb weakness in a child: a case report. *J Med Case Reports* **18**, 475 (2024). https://doi.org/10.1186/s13256-024-04824-5

PU41

Experience with the use of therapeutic plasma exchange in pediatric patients with rheumatic diseases in two regional hospitals in Mexico

S. Mendieta[1], K. Alba[2]
[1]Pediatric Rheumatology, Issemym, [2]Pediatric Rheumatology, Private Practice, Mexico, Mexico
Correspondence: S. Mendieta
Pediatric Rheumatology, **23(2):** PU41

Introduction: Therapeutic plasma exchange (TPE) is a procedure capable of eliminating autoantibodies, immune complexes and other inflammatory molecules[1], replacing plasma with fluids such as albumin or blood components[1]. In autoimmune diseases, its usefulness lies in acute phases, combined with immunosuppressive drugs until these reach therapeutic concentrations necessary to control the disease. Evidence for pediatric indications is limited, and children require protocols tailored to their metabolic conditions and variations in weight and height [2] that impact circulating blood volume, posing specific challenges.
Objectives: Describe the experience in the use of RPT in pediatric patients with rheumatic diseases in two regional hospitals in Mexico, between 2017 and 2022
Methods: A retrospective analysis of pediatric patients undergoing TPE was performed. Variables such as diagnosis, indication for TPE, pharmacological treatment received in conjunction with RPT, and complications were evaluated.
Results: Nine patients from two hospitals were included: 6 from the ISSEMyM Maternal and Child Hospital (67%) and 3 from the Toluca Children's Hospital (33%). Three were male (33%) and six were female (67%), with a mean age of 12 years. The diagnoses were systemic lupus erythematosus (SLE).with kidney disease in 7 patients (77%),of which 2 (22%) had pulmonary hemorrhage, IgA vasculitis (16.5%) and autoimmune hepatitis (16.5%). The main indications were nephritis and hepatic encephalopathy, two patients received steroid monotherapy and seven patients received steroid combined with immunosuppressant. In 85% of patients (6) urea, creatinine, BUN and uric acid were elevated prior to the first session; biochemical controls after the third or fifth session reported a decrease in these levels until the resolution of the renal condition that motivated the use of TPE, patients with lung involvement were extubated early. One death was reported after the first session. Complications included renal injury secondary to hypovolemia, hypotension, fluid and electrolyte imbalance, and coagulopathy. The remaining patients improved their clinical condition after the TPE.
Conclusion: TPE represents an effective tool for rheumatic diseases, especially those with target organ damage or diseases refractory to initial treatment. Despite the observed complications, most patients showed significant improvement after the procedure, which allows us to infer that it is a safe and effective procedure, especially when complemented with immunosuppressive therapy. It is essential to share the experience with its use in pediatrics, establish criteria, and regulate its use in order to minimize risks and improve outcomes in children with autoimmune diseases.
Disclosure
None declared

References

1. Padmanabhan A, Nicole LC, Rasheed A, Klingel R, Meyer E, Pham HP, et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis. 2019;171–354.
2. Andrés A, Gustavo B-D, Carmona G. PLASMAFERESIS (Aféresis). Revista Colombiana de Terapia Intensiva pediátrica. 2016;1–28

PU42

Recurrent unifocal chronic non-bacterial osteomyelitis in a child: diagnostic and therapeutic pathway

A. Mauro[1], E. Naddeo[2], A. Maggi[2], M. Stracuzzi[3], C. Coppola[3], R. Caiazzo[3], M. S. Valentino[3], V. Ansuini[1], V. Giacomet[3], L. Bernardo[4]
[1] Pediatric Rheumatology Service, "Casa Pediatrica" Unit, Department of Child and Adolescent Medicine, ASST Fatebenefratelli-Sacco, Milan, Italy, [2]Department of Pediatrics, "Vittore Buzzi" Children's Hospital, ASST Fatebenefratelli-Sacco, University of Milan, [3]Department of Infectious Diseases Paediatrics, Ospedale Luigi Sacco, Milan, Italy, [4]Department of Pediatrics, ASST Fatebenefratelli-Sacco, Milan, Italy, Milan, Italy
Correspondence: A. Mauro
Pediatric Rheumatology, **23(2):** PU42

Introduction: Chronic non-bacterial osteomyelitis (CNO) is a rare autoinflammatory bone disease, characterized by chronic, painful, and sterile bone inflammation. Infectious origin is excluded, and non-steroidal anti-inflammatory drugs (NSAIDs) are considered first-line therapy.
Objectives: To describe the diagnostic and therapeutic course of a pediatric patient with recurrent unifocal CNO in an atypical location.
Methods: We report the case of a 10-year-old girl who presented with recurrent painful swelling of the distal phalanx of the left thumb, first appearing in July 2021. There was no history of trauma or local infection. Initial treatment with amoxicillin-clavulanate resulted in partial improvement. Imaging studies (X-ray, MRI, CT) revealed cortical irregularity and a radiolucent lesion with mild hyperdensity, suggesting osteomyelitis. Laboratory tests were normal, with negative inflammatory markers and autoimmune panel (ANA, anti-dsDNA, ENA, RF, anti-CCP). Antibiotic treatment with clindamycin (30 mg/kg/day for 6 weeks) led to temporary clinical improvement. In February 2024, due to a new flare, the patient underwent curettage of the lesion, histological examination, and microbiological culture (negative). In April 2024, she was re-hospitalized due to a further flare.
Results: During hospitalization, the patient experienced localized bone pain without systemic symptoms, associated with edema, erythema, night pain disturbing sleep, and functional limitation. Histology was consistent with chronic osteomyelitis, and the culture remained negative. Despite the atypical site, the recurrent nature, clinical features, imaging, and biopsy supported the diagnosis of unifocal recurrent CNO. NSAID therapy with naproxen (15 mg/kg/dose) was started, resulting in complete resolution of symptoms. At one- and three-month follow-up, the patient showed no pain or erythema and a marked reduction in swelling.
Conclusion: This case highlights the importance of considering CNO in children with recurrent bone inflammation, even in atypical locations. In the absence of systemic signs and positive cultures, clinical-radiological correlation and histology are key to diagnosis. NSAIDs remain the mainstay of therapy and were effective in achieving full clinical remission in this case. Consent to published had been obtained.
Disclosure
None declared

PU43

On the trail of missing vertebrae – a case of gorham-stout disease in 8-year-old boy

A. Maeser[1], J. Trelińska[2], E. Smolewska[1]
[1]Department of Pediatric Cardiology and Rheumatology, [2]Department of Pediatrics, Oncology and Hematology, Medical University of Lodz, Poland, Lodz, Poland
Correspondence: A. Maeser
Pediatric Rheumatology, **23(2):** PU43

Introduction: Gorham-Stout Disease (GSD) is a rare bone disease characterized by progressive destruction and reabsorption of bones. It predominantly affects children and young adults, with approximately 400 cases reported in the literature. The underlying etiopathogenesis is associated with dysregulated osteoblast and osteoclast activity, as well as aberrant angiogenesis and lymphangiogenesis. The clinical presentation primarily depends on the skeletal structures involved, with common manifestations including pain, swelling, and functional impairment. In some cases, systemic complications such as chylothorax may also occur. Currently, there is no standardized therapeutic approach for GSD. Management typically involves bisphosphonates and surgical intervention (mainly to treat complications), while sirolimus has also been used in some cases.
Objectives: We present a case of 8-year-old boy diagnosed with Gorham-Stout Disease.
Methods: The boy was admitted to our clinic with a suspicion of osteoporosis. A month earlier, he fell and sustained a back injury, after which he began reporting lumbar pain. At first, he was hospitalized on Pediatric Department, where an MRI of his spine was performed. A pathological fracture of the L4 vertebra was described, and the boy was referred for further rheumatological evaluation. During stay at our clinic, laboratory tests revealed only mild anemia of chronic diseases and elevated ESR. Due to the unclear etiology of osteoporosis, a whole-body MRI was performed, which described almost complete resorption of the L4 vertebral body. Densitometry indicated osteopenia. The boy was qualified for bisphosphonate therapy. During his next stay we performed a control MRI, which showed a progression of the disease. Following consultation with radiologists, a diagnosis of histiocytosis was suspected. The boy was then evaluated by a hematologist and a neurosurgeon for qualification for a vertebral biopsy, but due to high risk of spine fracture procedure was not performed. We expanded the diagnostics to include a pelvic CT, which revealed a large osteolytic lesion in the right iliac and pubic bone. Additionally, we performed a bone marrow biopsy, a trephine biopsy, and a histopathological examination of the iliac bone. All results were consulted with hematologists and later with other clinics, including those in Gdansk (Poland) and Boston (USA).
Results: Considering expert opinions and the literature, we diagnosed the boy with Gorham-Stout Disease. Currently, our patient is undergoing therapy with sirolimus. A follow-up MRI is scheduled for June 2025.
Conclusion: Gorham-Stout Disease is very rare; however, it must be considered in the differential diagnosis, for example, of CRMO, especially in cases where patients do not respond to treatment. Consent to published had been obtained.
Disclosure
None declared

References

1. Angelini A, Mosele N, Pagliarini E, Ruggieri P. Current concepts from diagnosis to management in Gorham-Stout disease: a systematic narrative review of about 350 cases. EFORT Open Rev. 2022 Jan 11;7(1):35–48. doi: https://doi.org/10.1530/EOR-21-0083. PMID: 35,076,412; PMCID: PMC8788153.
2. Ferjani HL, Makhlouf Y, Ben Nessib D, Maatallah K, Kaffel D, Hamdi W. An Atypical Cause of a Child Limp: A Gorham-Stout Disease with a Vanishing Hip. Rev Bras Ortop (Sao Paulo). 2023 Jul 31;59(Suppl 1):e101-e103. doi: https://doi.org/10.1055/s-0042-1757962. PMID: 39,027,165; PMCID: PMC11254440.
3. Zhou Z, Qiu T, Zhou J, Zhang Z, Gong X, Zhang X, Lan Y, Yang C, Zhang Y, Xiang S, Ji Y. Clinical features and current management experience in Gorham-Stout disease: a systematic review. Orphanet J Rare Dis. 2025 Mar 19;20(1):134. doi: https://doi.org/10.1186/s13023-025-03649-9. PMID: 40,102,890; PMCID: PMC11921740.

PU44

Multifocal osteonecrosis in anca associated vasculitis – a complication of long-term low-dose glucocorticoid treatment

D. Bartkus[1,2], P. Stočkūnaitė[1], A. Šnipaitienė[1,2]
[1]Department of Paediatrics, Lithuanian University of Health Sciences, Academy of Medicine, [2]Department of Paediatrics, Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Kaunas, Lithuania
Correspondence: D. Bartkus
Pediatric Rheumatology, **23(2):** PU44

Introduction: Remission induction and maintenance in ANCA associated vasculitis (AAV) involves glucocorticoid (GC) therapy with combination of various immunosuppressants. However, prolonged exposure to GCs can cause osteonecrosis (ON). Musculoskeletal system of children is in a constant state of development, making them particularly susceptible to ON. We present an AAV with multifocal ON as a result of prolonged low-dose prednisone treatment.
Objectives: To present a clinical case of ON caused by long-term low-dose GC use
Methods: Case description
Results: A 12 y/o girl initially presented with macular rash, polyarthritis and rapidly deteriorating kidney function eventually was diagnosed with PR3-AAV. Induction therapy was started with high-dose GC and cyclophosphamide. However, the patient condition continued to decline with emerging of hemoptysis with respiratory failure, focal tonic seizure episodes, and end-stage renal disease by 3 months from the first symptoms (BVAS score of 43). Additional treatment with intravenous immunoglobulin (IG) and plasmapheresis was introduced to halt disease progression. Inactive disease was reached 7 months after initial therapy. Remission maintenance was started with azathioprine (AZA) 50 mg/day and continuing GC tapering to 10 mg/daily (<2.5mg/kg/day). Almost 2 years after AAV diagnosis, while still using AZA and low-dose GC, a relapse occurred, with

generalized seizure episodes, hemoptysis and respiratory distress (BVAS 28). It required to renew high-dose GC regiment, increasing AZA dose (100 mg/daily) and re-establishment of IG therapy. During follow-up period erythrocyte sedimentation rate (ESR) levels began to rise (up to 91mm/h) with normal levels of C-reactive protein and no signs of AAV flare. Without medication adjustment (AZA, GC taper to 5 mg/daily and subcutaneous IG) ESR levels declined, but did not normalize (ranging 20–40 mm/h). 3 years after her diagnosis, the patient began complaining of arthralgia in the right foot. Changes consistent with active arthritis and tenosynovitis were observed in ultrasound and MRI was performed revealing ON of the talus. Further imaging uncovered involvement of bilateral femoral heads and proximal parts of both tibias. By this point the patient received a cumulative dose of ~ 20.5 g of prednisone over a period of 44 months for AAV treatment.
Conclusion: GC toxicity can be underestimated in patients with autoimmune disorders. This case highlights a need for a standardized assessment tool, such as pediatric GC toxicity index, use in routine clinical practice to improve patient outcomes. Consent to published had been obtained.
Disclosure
None declared

PU46

Diagnostic difficulties in child with primary hypertrophic osteoarthropathy (PHO)

D. Lazarevic[1,2], J. Vojinovic[1,2], H. Stamenkovic[1,2], T. Stankovic[1,2], M. Zecevic[2,3]
[1]University Clinical Center Nis, Clinic of Pediatrics, [2]University of Nis, Faculty of Medicine, Nis, [3]University Clinical Center Nis, Clinic for Pediatric Surgery and Ortopedics, Nis3, Serbia
Correspondence: D. Lazarevic
Pediatric Rheumatology, **23(2):** PU46

Introduction
Primary hypertrophic osteoarthropathy (PHO) is a very rare disease in children. In the most cases, the clinical picture of the disease is incomplete. When establishing the diagnosis we have to be very careful as it requires the analysis of lot of underlying secondary causes of the disease.
Objectives: Case report of a child with PHO with a positive family history of autoimmune diseases.
Methods: Differential diagnostic difficulties and summary of work in establishing the diagnosis of PHO in a child.
Results: A 9 old male child was refered to our pediatric rheumatology clinic due to digital clubbing of the fingers and toes, bone cracking and enlarged knees and ankles. He has not joint swelling, pain and morning stiffnes. Family history was positive for autoimmune diseases: mother had colitis ulcerosa while father had psoriatic arthritis. Diferential diagnostic sum up work was done. General laboratory findings were in the
Reference range. Antinuclear, ANCA, ASCA antibodies, RF and antiCCP antibodies were negative. Echocardiogram, spirometry and capilaroscopy findings were normal. Additional diagnostics methods ruled out the possibility of rheumatological, hematological, inflammatory bowel disease (fecal calprotectin negative), coeliac disease (TTG and fecal elastase negative) and cystic fybrosis (sweat test was normal). Thyroid gland function, growth and parathyroid hormone excluded endocrinopathy. An abdominal and musculosceletal ultrasound were normal. X ray of the wrist and feets have showed acroosteolysis. Due to absence of the clinical signs suggesting a secondary cause, we suspected PHO and asked for the geneticist consultation for genetic study. We are still waiting for the genetic confirmation of disease.
Conclusion: In children, there are many difficulties when diagnosing PHO, as incomplete form could lead to misdiagnosis with juvenile idiopathic arthritis and unnecessary treatment. The final confirmation of the diagnosis requires differential diagnostic sum up work to exclude all possible secondary causes of the disease. Consent to published had been obtained.
Disclosure
None declared

PU47

Clinical features of dermatomyositis associated with myositis-specific antibodies in two libyan children patients

A. A. Abushhaiwia[1], Y. Elfawires[2], N. B. Abushhiwa[3]
[1]Pediatric Rheumatology, Tripoli Children's Hospital, faculty of medicine, university of Tripoli, [2]Pediatric Rheumatology, Faculty of medicine, university of Tripoli, [3]Pathology, Faculty of Medicine, university of Tripoli, Tripoli, Libya
Correspondence: A. A. Abushhaiwia
Pediatric Rheumatology, **23(2):** PU47

Introduction: Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy characterized by muscle weakness and typical cutaneous rash. Dermatomyositis-specific antibodies,such as anti-TIF1γ, anti-SAE, anti-Mi2, anti-MDA5, and anti-NXP2, have been associated with specific clinical phenotypes.
Objectives: To describe the clinical profile of two Libyan patients with JDM and explore the potential links between MSAs and clinical manifestations.
Methods: We report two cases of juvenile dermatomyositis (JDM) associated with anti-NXP2 antibodies in Libyan children.
Results:
Case#1: A 6-year-old girl. She was born to non-consanguineous parents. Her family history was unremarkable. She was presented with a 2-month history of progressive proximal more than distal weakness of all limbs weakness associated with dysphagia and muscle tenderness, associated with edema essentially in the face and upper limbs, skin ulcers over her face, both axillary areas, Heliotrope rashaccompanied periorbital edema. Gottron's papules. Her power was grade 2 in upper limbs and grade 1 in lower limbs; tendon reflexes were sluggish. Her CMAS scoring was 2\52. Lab tests revealed elevated liver enzymes: (GOT)408/(GPT) 129. CPK was increased to 2549 (normal < 170 U/L). Her (ANA) profile was positive at 1:400 and (ANCA) were negative. Muscle magnetic resonance imaging (MRI), thigh,and leg muscles suggestive of active myositis, EMG&NCS:myopathic changes. A muscle biopsy finding revealed severe and active dermatomyositis. Myositis profile was positive only for the anti-nuclear matrix protein-2 (anti-NXP2) antibody.
Case#2 A 5-year-old girl born to nonconsanguineous parents. presented with proximal followed by distal upper and lower limb weakness and myalgias for 1 month. She developed dysphagia. Preceded by a history of periorbital edema, skin rash over hereyelides for 2 monthS. On examination, her vital parameters and systemic examination were normal, except Heliotrope rash accompanied by periorbital edema. Gottron's papules. The muscle strength was grade two in proximal and grade 3 in distal groups; tendon reflexes were sluggish except for the preserved ankle reflex. Her CMAS scoring was 4\52. Lab tests revealed elevated liver enzymes: (GOT) 324/(GPT) 82. CPK was increased to 5761 U\L. Her (ANA) profile and (ANCA) were negative.EMG&NCS : myopathic changes.A muscle biopsy finding revealed active myositis. Myositis profile was positive only for the anti-nuclear matrix protein-2 (anti-NXP2) antibody.
Both patients showed significant improvement with IVIG, steroids, and methotrexate. On follow-up, both patients continue to receive IVIG infusions every4-6 weeks and are being monitored for disease activity and treatment response.
Conclusion: These cases represent the first reported instances of JDM associated with NXP2 positivity in Libyan children. Early recognition and aggressive treatment may lead to improved outcomes. Our findings highlight the importance of testing for specific autoantibodies in JDM patients. Consent to published had been obtained.
Disclosure
None declared

PU48

Seronegative versus seropositive juvenile dermatomyositis: a center's experience

C. Pinto Oliveira[1], I. Genrinho[2], M. Diz Lopes[3], F. Aguiar[4], M. Rodrigues[4], I. Brito[4]
[1]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, [2]Rheumatology Department, Unidade Local de Saúde de Viseu Dão-Lafões, Viseu, [3]Rheumatology Department, [4]Pediatric Rheumatology Department, Unidade Local de Saúde de São João, Porto, Portugal
Correspondence: F. Aguiar
Pediatric Rheumatology, **23(2):** PU48

Introduction: Juvenile dermatomyositis (JDM) is classically characterized by progressive proximal muscle weakness and pathognomonic cutaneous manifestations [1]. The identification of myositis-specific and myositis-associated autoantibodies holds clinical relevance, particularly concerning disease phenotype and prognosis. Nevertheless, these autoantibodies remain undetectable in a substantial subset of patients [2], increasing diagnostic complexity.
Objectives: Primary: To characterize the main sociodemographic, clinical, and laboratory features of pediatric patients with JDM followed at our Pediatric Rheumatology Unit.
Secondary: To compare sociodemographic, clinical, and laboratory characteristics between patients with and without detectable myositis autoantibodies (MAs).
Methods: We designed a cross-sectional, single-center study, including patients with a clinical diagnosis of JDM. Sociodemographic, clinical, and laboratory variables were retrospectively collected from patient records. Participants were divided into two groups, based on the presence or absence of detectable MAs. A statistical analysis was performed with SPSS® software version 28.0.1.0, with a p-value ≤ 0.05 considered statistically significant. Continuous variables were analyzed using the Mann–Whitney U test, while categorical variables were compared using the Chi-square test.
Results: A total of 11 patients were included, eight of them female. Four patients had no identifiable MAs. The median age at diagnosis was 8 years (interquartile range [IQR]: 6.5) in the seronegative group and 10 years (IQR: 5) among seropositive patients.
In the seronegative group, all patients exhibited cutaneous manifestations, including heliotrope rash (n=4), facial edema (n=3), cutaneous calcinosis (n=2), Gottron's papules (n=2), and livedo reticularis (n=2). Other frequent initial symptoms included muscle weakness (n=4), myalgia (n=4), and arthralgia (n=3). Two patients developed esophageal involvement with associated dysphagia. Serum muscle enzymes were elevated in all patients, with a mean creatine kinase level of 4651.3 ± 4421.5 U/L. Electromyography revealed myopathic patterns in three patients, while two showed evidence of muscle inflammation on magnetic resonance imaging (MRI) and corresponding findings on muscle biopsy. All patients received glucocorticoids and methotrexate; three required intravenous immunoglobulin. Hydroxychloroquine and rituximab were administered to one patient each.
No statistically significant differences were observed between seronegative and seropositive patients concerning gender, age at diagnosis, clinical manifestations, muscle enzyme levels, or findings on electromyography, MRI, or muscle biopsy.
Conclusion: In our cohort, patients with seronegative juvenile dermatomyositis demonstrated clinical, sociodemographic, and laboratory profiles similar to those of seropositive patients. Muscle weakness and hallmark cutaneous features were consistent across both groups, along with elevated muscle enzyme levels. Further studies with larger sample sizes are warranted to deepen the understanding of the clinical implications of seronegative JDM.
Disclosure
None declared

References

1. Balogh, L.C., et al., *Two case reports of MDA5-type seronegative dermatomyositis.* SAGE Open Medical Case Reports, 2024. **12**: p. 2050313X241309094.
2. Pachman, L.M. and A.M. Khojah, *Advances in Juvenile Dermatomyositis: Myositis Specific Antibodies Aid in Understanding Disease Heterogeneity.* J Pediatr, 2018. **195**: p. 16–27.

PU50

Insights on atypical juvenile dermatomyositis cases: a call for vigilance in diagnosis

I. Awan, A. Sridhar
Paediatric Rheumatology, Leicester's Children Hospital, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom
Correspondence: I. Awan
Pediatric Rheumatology, **23(2):** PU50

Introduction: Juvenile Dermatomyositis (JDM) is a rare autoimmune disease characterized by muscle weakness and distinctive skin rashes. Atypical presentations challenge clinicians, often leading to delayed diagnosis and treatment.
Objectives: This abstract presents two cases of atypical JDM, emphasizing the varied clinical manifestations and the need for heightened awareness in pediatric practice.
Methods: The cases were documented through direct patient observation, caregiver interviews, and a review of the patient's medical records, including imaging and laboratory results; clinical progression,multidisciplinary consultations, and treatment outcomes.
Results: The first case relates to a young girl presented with a classical vasculitic skin rash and muscle weakness for half a year, complicated by sensory issues due to coexisting autistic spectrum disorder (ASD). Notably, she exhibited normal muscle enzyme & Myositis specific antibodies but MRI revealed bilateral symmetrical myositis. This case underscores the diagnostic utility of advanced imaging when serum markers are unremarkable. The second case is about a young female who presented with typical helicotropic rash and Raynaud's phenomenon despite normal muscle enzymes. Unlike the first case, her MRI of the muscles was normal however her Myositis specific antibodies were weak positive for Anti-PM-Scl75, leading to a diagnosis of Amyopathic JDM.These cases illustrate the diagnostic challenge of JDM and intersection of neurodevelopmental disorders, particularly ASD in the first case and Raynaud's phenomenon in the second case, which underscores the necessity for comprehensive evaluations in atypical presentations. These cases fill a crucial gap in understanding the heterogeneity of JDM presentations, particularly in the context of normal MRI findings and coexisting conditions. The juxtaposition of the two cases provides insights into how atypical clinical features may lead to misdiagnosis or delayed treatment, underscoring the necessity for clinicians to consider a broader spectrum of symptoms. This abstract contributes to the current literature by advocating for a multidisciplinary approach incorporating pediatric rheumatology, dermatology, and psychology, promoting earlier recognition and intervention. It emphasizes the importance of personalized care strategies to address both autoimmune and developmental aspects of the disease.
Conclusion: This comparative analysis of atypical JDM presentations highlights the complexities of diagnosis and management, advocating for improved awareness among healthcare providers. By addressing these knowledge gaps, we aim to enhance patient outcomes through timely and tailored interventions. Consent to published had been obtained.
Disclosure
None declared

References

1. Miller FW, et al. (2017). Clinical and Laboratory Features of Juvenile Dermatomyositis According to Autoantibody Subgroups. Arthritis Rheumatol. 69(12):2043–2052
2. Rider LG, et al. (2013).International Consensus on MRI Use in Juvenile Idiopathic Inflammatory Myopathies.J Rheumatol. 40(7):1195–1205
3. Martinez M, et al. (2019).Juvenile Dermatomyositis: New Aspects of Pathogenesis and Clinical Management.Pediatr Drugs. 21(5):367–376

PU51

Two faces of latin anti mda-5 juvenile dermatomyositis

J. V. Ramírez Miramontes[1], R. E. Vela Davila[1], C. Y. Gonzalez Miranda[2], M. Mata[1]
[1]Pediatrics, IMSS, [2]Pediatrics, Prívate Practice, Monterrey, Nuevo León, Mexico
Correspondence: J. V. Ramírez Miramontes
Pediatric Rheumatology, **23(2):** PU51

Introduction: Anti-MDA5 autoantibodies observed in North American and European JDM populations and found to be associated with cutaneous ulceration, mucus membrane ulcers, arthritis, milder muscle disease, and RP-ILD (1).
Objectives: Patient 1:
A 4-year-old female product of twin pregnancy vía in vitro fertilization by egg donation, referred by multisystemic manifestations of 2 months evolution with recurrent fever, asthenia, adynamia, hypersomnia, rashes on the face, papules on the elbows and hands, an ulcer on the left elbow and limitation in daily activities.

Physical examination revealed hoarsness, facial edema, Gottron's papules on the elbows and metacarpophalangeal joints, an ulcer on the left elbow, arthritis of the elbows and wrists, no signs of respiratory distress, Lungs without pathological data, tachycardia, no muscle weakness. Laboratory tests with borderline hemoglobin, a normal differential count, mild elevated transaminases, a maximum CK of 243, an ESR of 39, a LDH greater than 400, and a finely speckled ANA of 1:320. She was evaluated by pulmonology and cardiology, and her myositis panel was positive for anti-MDA 5. HRCT showed patchy mixed infiltrates, bilateral subpleural infiltrates,Treatment with cyclophosphamide and rituximab was initiated. One year after the first dose of anti-CD20, the patient presented with recurrent vomiting.An endoscopy revealed Helicobacter pylori infection, gastroparesis, and subsequent follow-up with plasma cell infiltrates, with a second dose of anti-CD20 administered.
Methods: Patient 2:
A 2-year-old male presented with a 2-month evolution of nigthly recurrent fever, rashes with heliotrope erythema, Gottron's papules, no apparent muscle weakness. Negative protocol for infections, neoplastic diseases and inborn errors of immunity. The diagnosis was established 6 months later. The myositis panel with positive Anti MDA5, CT scan with interstitial lung disease, with treatment with cyclophosphamide, with improvement and maintenance treatment with mycophenolate mofetil with an asymptomatic patient.
Results: Discusión : The paediatric cohort of anti-MDA5- positive JDM reported by Tansley et al. Found a over-representation of ulcerations and milder muscle involvement in anti-MDA5-positive children, in the absence of severe lung disease but anti-MDA5 autoantibodies are frequently associated with rapidly progressive ILD, especially in patients of East Asian ancestry, including juvenile populations, Latinamerican patients used to have different behavior to Caucasian and Asian populations in several rheumatic diseases (2).
Conclusion: Conclusion We present two Latin American patients with juvenile dermatomyositis due to anti-MDA5 with interstitial lung disease and different evolution and response to treatment, with the only risk factor being skin ulcers
Disclosure
None declared

References

1. Gulnara Mamyrova et al. Anti-MDA5 autoantibodies associated with juvenile dermatomyositis constitute a distinct phenotype in North America. Rheumatology 2021;60:1839–1849
2. Isabelle Melki et al. Anti-MDA5 juvenile idiopathic inflammatory myopathy: a specific subgroup defined by differentially enhanced interferon-a signalling. Rheumatology 2019;0:1–11

PU52

A severe case of juvenile dermatomyositis with anasarca and dysphagia; sucessfully managed with therapeutic plasma exchange as a rescue therapy

V. Arunath[1], W. Botheju, M. Madarasinghe, J. Jagoda, P. Ratnayake, A. Jayawardena
Lady Ridgeway Hospital for Children, Colombo 08, [2]Teaching Hospital Karapitiya, Karapitiya, Sri Lanka
Correspondence: V. Arunath
Pediatric Rheumatology, **23(2):** PU52

Introduction: Anasarca is rare in juvenile dermatomyositis (JDM). Such patients usually have highly active disease, which requires aggressive treatment and the management is difficult due to poor response to conventional treatment. Therapeutic plasma exchange (TPE) is an underutilized modality in JDM due to lack of evidence, which can be used as a rescue therapy in high risk patients and in resource poor settings where biologic DMARDS are not freely available.
Objectives: Objective of the case report was to report a patient with severe JDM who responded to TPE in Sri Lanka.
Methods: A 7-years-old boy presented with intermittent fever and gradually worsening generalized oedema over one month duration. Progressively, he developed difficulty in walking and difficulty in getting up from seated position with severe arthralgia and myalgia. Examination revealed heliotrope rash of the eyelids, gottron's papules, nail fold capillary infarcts and generalized muscle weakness with neck weakness. Childhood myositis assessment scale (CMAS-14) was 3 on admission, which indicated significant disability. Investigations revealed hypoalbuminemia with normal urine protein excretion and creatinine phosphokinase of 16,619 U/L. Anti-nuclear antibody, myositis-specific and myositis-associated-antibodies were negative. Electromyography revealed the evidence of inflammatory myositis. High-resolution computer tomography of the chest showed the multiple soft tissue calcifications in para spinal muscles and shoulder girdle.
Results: Child was diagnosed to have severe JDM with significantly high disease activity. He was managed initially with intravenous immunoglobulin, steroids and weekly oral methotrexate. He progressively developed palatal palsy and dysphagia without any improvement in CMAS score. At this point, 6 cycles of TPE were done every other day with marked improvement in muscle weakness, reflected by CMAS score of 25. Therapy was consolidated with intravenous rituximab. Child was discharged with oral steroids and methotrexate. 2 years down the lane, he is being under the multidisciplinary care without any relapses.
Conclusion: Immunomodulatory effects of TPE are probably linked to the removal of circulating autoantibodies and other mediators involved in the disease's pathogenesis. Our patient highlights the rapid efficacy of TPE in the treatment of severe JDM. Alternative treatment options and prompt initiation of those therapies should be considered in high risk patients with severe JDM, especially in the resource poor settings. Consent to published had been obtained.
Disclosure
None declared

PU53

Lupus nephritis a veiled threat in juvenile systemic lupus erythematosus

A. A. Abushhaiwia[1], Y. Elfawires[2]
[1]Pediatric Rheumatology, Tripoli Children's Hospital, faculty of medicine, university of Tripoli, [2]Pediatric Rheumatology, Faculty of medicine, university of Tripoli, Tripoli, Libya
Correspondence: A. A. Abushhaiwia
Pediatric Rheumatology, **23(2):** PU53

Introduction: Juvenile Systemic Lupus Erythematosus (JSLE) is a multisystemic autoimmune inflammatory condition. And the kidneys being the most severely affected. Lupus Nephritis (LN) occurs in 50-82% of children diagnosed with JSLE.Having a high index of suspicion to request for renal biopsy. Early diagnosis and management are crucial to come up with an appropriate management plan.
Objectives: To highlight the importance of performing renal biopsy in children with JSLE and showing evidence of LN.
Methods: we report two cases with JSLE diagnosed with LN.
Results: Case #1: a 13-year- old Libyan girl diagnosed with JSLE presenting mainly with MSK symptoms. Only ANA was high early in her illness with normal renal function and urine analysis. She did well on oral steroids and hydroxychloroquine (HCQ).After three years, she had a relapse with arthritis, raised inflammatory markers,increase urine protein: creatinine ratio (Pr:Cr), evidence of microscopic haematuria (with RBC cast) and proteinuria. ANA titre was 1:5120 and anti dsDNA > 800 IU/ml.Renal ultrasound showed increased echogenicity of both kidneys.Putting all that together a renal biopsy was requested and showed appearance of severe lupus focal segmental proliferative glomerulonephritis, active class III S. Despite her kidney involvement, her renal function and blood pressures were always normal.Mycophenolate mofetil (MMF) and enalapril were added to her treatment plan showing good response with close monitoring of her BP, urine Pr:Cr ratio and R/E.
Case #2: a 15 -year- old Libyan girl diagnosed and managed initially as ITP for which she received steroids and four doses of Rituximab.Shortly after that she developed arthritis, ANA and anti dsDNA titres were high and C4 was low. JSLE was considered and she was treated with oral steroids, HCQ, and Azathioprine. After five years she presented in a relapse with arthralgia, alopecia, fever,raised inflammatorymarkers, ANA & anti dsDNA raised, urine Pr:Cr ratio raised, evidence of RBC cast,haematuria and proteinuria. As well as increased echogenicity of both kidneys via ultrasound. Her renal function, liver function and

BP were normal. Renal biopsy was requested and showed diffused lupus proliferative glomerulonephritis associated with lesions of extramembranous glomerulonephritis class Ⅳ Sa + class Ⅴ. Four doses of Rituximab were given accordingly and MMF and enalapril added to her plan.
Conclusion: having a low threshold for renal biopsy to diagnose LN in JSLE and not relying on severity of symptoms is important as the problem is quite common and more severe in this age group. Early intervention can protect the patients from deteriorating to ESRD and minimize the burden on them and their families. Consent to published had been obtained.
Disclosure
None declared

PU54

Chorea, deep vein thrombosis and an ovarian mass: a rare case of probable catastrophic antiphospholipid syndrome in an adolescent female

D. Henderson[1], K. Warciak[1], O. G. Killeen[1], E. McDermott[1], S. Ahmed[2], B. Nolan[2], K. Gallagher[1]
[1]Rheumatology, [2]Haematology, Children's Health Ireland at Crumlin, Dublin, Ireland
Correspondence: D. Henderson
Pediatric Rheumatology, **23(2):** PU54

Introduction:
Introduction: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder in children, defined by the presence of antiphospholipid antibodies and an elevated risk of thrombosis. Of those children affected, 16% present with neurological symptoms (1). Catastrophic APS (cAPS) is an extremely rare, potentially life-threatening complication with multiorgan involvement, which rapidly progresses within one week (2). cAPS may present as the initial clinical manifestation of APS, highlighting the need for a high level of clinician awareness of the condition.
Objectives: To describe the clinical presentation and management of a rare case of paediatric cAPS with neurological involvement.
Methods: Detailed clinical and laboratory data was obtained from the patient's health record.
Results: A thirteen-year-old girl presented with a sided deep vein thrombosis (DVT) in her right superficial femoral vein. She had recently commenced the progesterone only contraceptive pill for heavy menstrual bleeding and had an 18-month history of migraine headaches with aura. Therapeutic low molecular weight heparin was commenced. Within days, she developed acute onset neurological symptoms, including abnormal speech and choreiform movements of the head, upper limb and tongue. Laboratory investigations revealed a mild anaemia (Hb 109 g/l), positive lupus anticoagulant, anticardiolipin antibodies and beta 2 glycoprotein, while double-stranded DNA was negative and C3 and C4 levels were normal. Neuroimaging revealed no abnormality. Further imaging including an abdominal ultrasound and MRI revealed a large 17 cm cystic ovarian mass with foci of calcification. Given her DVT, new neurological symptoms, rapid progression of symptoms in less than one week and triple positive antiphospholipid antibodies, she was diagnosed with probable cAPS. She was treated with high dose intravenous steroids, anticoagulation (LMWH initially and subsequent warfarin therapy) and plasma exchange. Due to ongoing neurological symptoms, Rituximab was commenced. Following treatment there was complete resolution of neurological symptoms.
Conclusion: Neurological symptoms may follow thrombosis in APS. Chorea is a rare, but recognised neurological manifestation of APS. A high level of suspicion for cAPS is warranted to allow for prompt recognition and early appropriate treatment with immunosuppressive and anticoagulant agents. Consent to published had been obtained.
Disclosure
None declared

References

1. Madison JA, Zuo Y, Knight JS. Pediatric antiphospholipid syndrome. Eur J Rheumatol. 2020;7(Suppl1):S3-s12.
2. Zajc Avramovic M, Avcin T. Antiphospholipid syndrome in children. Best Practice & Research Clinical Rheumatology. 2024;38(3):101,986.

PU55

Severe presentation of systemic lupus erythematous in an adolescent female with alveolar haemorrhage with nephritis class IV + V

D. Patro[1], M. Dash[2], S. Satapathy[3], D. Rath[4], S. Parida[4]
[1]Pediatric Rheumatology, [2]Pediatric Infectious Disease, [3]Pediatric Pulmonology, [4]Pediatric Intensivist, IMS and SUM Hospital, Bhubaneswar, India
Correspondence: D. Patro
Pediatric Rheumatology, **23(2):** PU55

Introduction: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease with potential multi-organ involvement. In children with SLE, it has been reported that pulmonary involvement occurred in 7.6–75%. Renal involvement in such a case carries a poor prognosis.
Objectives: Severe anaemia in an adolescent girl with an episode of haemoptysis requiring multiple blood transfusion intermittently with episodic tachypnoea and tachycardia going on for months with renal involevement should prompt the clinician to think of non- infectious etiology.
Methods: A case report from a tertiary center in eastern part of India.
Results: As, she had episodic course of illness initially, the cause of anaemia was thought to be viral triggered or hemoglobinopathy. Echo was normal. Tuberculosis work up sent was negative. On admission to our unit, she had severe pallor with fatigue and lethargy. Her blood counts showed low hemoglobulin with thrombocytosis with leukopenia with high ESR and negative CRP. Chest X ray showed diffuse hazziness. HRCT thorax done was suggestive of diffuse ground glass opacity in bilateral apex with mosaic pattern of attenuation. Pulmonary function test was suggestive of restrictive lung pattern. Urine protein/creatinine ratio was high with sterile Pyuria, hematuria with granular cast. Based on the above Pulmonary- renal finding, ANA by IIF was 4+ Speckled with low complements and high dsDNA. ANCA by ELISA was negative. DAT was positive with elevated LDH. Connecting the dots, she had alveolar haemorrhage (Pulmonary vasculitis) in a background of lupus flare (SLEDAI of 29). We pulsed the child with Methylprednisolone for 3 days with monthly Inj cyclophosphamide followed by gradual tapering of steroids and bone/sun protective measures. Therapeutic Plasma Exchange (TPE) and treament intensification was discussed but it was kept on hold as the girl improved in the due course. Renal biopsy showed full house pattern in IF with LM suggestive of Classs IV+ V with AI of 5/CI of 4. At the time of discharge from our unit, her hemoglobin and blood pressure has been stabilized and her exercise tolerance had improved.
Conclusion: The occurrence of SLE with AH with nephritis in paediatric patients is exceedingly rare, with few reported cases in the literature. This case emphasises the significance of considering SLE/Granulomatous polyangitis as a differential diagnosis in such a presentation and the need of multi-disiplinary team. This case also reflects the management protocol in Low Middle Income Countries (LMIC) where assess to biologicals are difficult which hampers the treat to target (T2T) goal.
Disclosure
None declared

PU57

Splenic infarction in juvenile systemic lupus erythematosus: a rare clinical entity

B. Pedreira[1], E. Freitas[2], M. I. N. Marques[3], C. Henriques[3], M. Conde[3], M. P. Ramos[3], I. Madureira[3]
[1]Pediatrics Department, Hospital Dr. Nélio Mendonça, Funchal, [2]Pediatrics Department, [3]Pediatric Rheumatology Unit, Hospital Dona Estefânia - ULS São José, Lisbon, Portugal
Correspondence: M. I. N. Marques
Pediatric Rheumatology, **23(2):** PU57

Introduction: Juvenile systemic lupus erythematosus (jSLE) is a chronic autoimmune disease that can affect any organ system. Splenic infarction (SI) is caused by occlusion of the spleen vascular supply,

leading to ischemia and tissue necrosis. It's a rare condition, associated with predisposing factors such as oncological, hematological or infectious diseases. There are only 9 cases reported in jSLE, in the vast majority associated to anti-phospholipid syndrome(APS).
Objectives: To describe a rare presentation of a 12-year-old (yo) girl with newly diagnosed jSLE, who developed SI and a large perisplenic collection.
Methods: Case report.
Results: A 12yo girl was referred to a tertiary hospital with a 5-month history of fatigue, labile mood and depressive symptoms and a 2-month history of low-grade fever, dry cough and pleuritic chest pain. In the 2 days before admission, she developed eyelid edema, left upper quadrant abdominal pain and vomiting.
Analytically, anemia (hemoglobin of 8.2 g/dL), elevated ESR (120 mm/h), ferritin (539 ng/mL), LDH (648 U/L) and D-dimers (93836µg/L). Urinalysis showed significant non-nephrotic proteinuria. Immune studies indicated complement consumption (C3, C4 and CH50), and positive Coombs test, ANA (1:160), anti-dsDNA(5935UI/ml), and anti-Sm antibodies. Thrombophilia screening, including anti-phospholipid antibodies were negative.
Diagnosis of jSLE was made with multisystemic involvement, including pulmonar (pneumonitis and hemorrhage), renal (class IV lupus nephritis), gastrointestinal (acute pancreatitis and mesenteric vasculitis), and neuropsychiatric (anxiety and depression) manifestations. Abdominal ultrasound at diagnosis showed a spleen at the upper limit of normal size with an extensive area of SI, without evidence of thrombii in large or medium abdominal vessels. Follow-up imaging at 15 and 30 days showed hypoperfusion of the superior and inferior poles and a globally heterogeneous parenchyma. A large subcapsular splenic collection was noted, compatible with liquefied splenic parenchyma or hematoma (maximum dimensions of 11.6×7x 8.7cm). During hospitalization, she was treated with hydroxychloroquine, high dose of corticosteroids, cyclophosphamide, rituximab, IV immunoglobulin, enalapril and antibiotic prophylaxis.
Two months after diagnosis, abdominal ultrasound revealed a spleen of normal size with no visible collection and peripheral heterogeneous parenchyma. She is currently clinically stable.
Conclusion: This case is notable as it represents the first patient reported with jSLE without APS. SI in jSLE should be considered, especially in school-aged girls presenting with abdominal pain, fever, and hematologic abnormalities. In our patient, SI occurred without evidence of splenic vessel obstruction, suggesting a possible role of small-vessel vasculitis. Early recognition through clinical suspicion and appropriate imaging is crucial to prevent complications and improve outcomes. Consent to published had been obtained.
Disclosure
None declared

PU58

Multiple venous thrombosis as a manifestation of antiphospholipid syndrome in systemic lupus erythematosus in an adolescent boy

M. Janega, Z. Pytelová, K. Bouchalová, D. Pospíšilová
Department of Paediatrics, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital, Olomouc, Czech Republic
Correspondence: M. Janega
Pediatric Rheumatology, **23(2):** PU58

Introduction: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by arterial, venous, or microvascular thrombosis, pregnancy morbidity or non-thrombotic manifestation in patients with persistent antiphospholipid antibodies (aPL). In comparison with APS in adults, paediatric APS has a more severe presentation with frequent recurrences of thrombotic events and a higher probability of life-threatening catastrophic APS.
Objectives: To present a case report of a boy with secondary APS as the first manifestation of a systemic disease.
Methods: A case report.
Results: A 17-year-old boy was examined by a haematologist for pathological coagulation and positivity of lupus anticoagulant antibodies (LA) after having been admitted for infectious mononucleosis a month before. He complained of left thigh pain, but an ultrasound showed no thrombosis. A week later, due to the persistent pain of the same thigh, the ultrasound yet confirmed femoro-popliteal thrombosis. The boy was admitted to the intensive care unit. Clinically, fever was present. Laboratory examination showed elevation of inflammatory parameters with anaemia and thrombocytopaenia and systemic lupus erythematosus (SLE) related antibodies – antinuclear antibodies and antibodies against double-stranded DNA. After consulting a paediatric rheumatologist, a diagnosis of secondary APS associated with SLE was made. Intravenous pulse corticosteroid therapy (1g per day), anticoagulant therapy (low molecular-weight heparine 0,8ml subcutaneously per day and warfarine at a dose that matched INR range 2-3) and hydroxychloroquine (400mg per day) were initiated. During the insertion of the central catheter, the doctor accidentally detected another thrombosis of the left arm, which was verified by the ultrasound in the axillary, brachial vein and both subclavian veins. Immunosuppressive therapy using azathioprine was initiated. By the time, the obstructed vessels gradually recanalized. He was subsequently transferred to antiplatelet therapy using acetylsalicylic acid (50mg per day). Repeated examination for LA after 12 weeks was positive whilst other antiphospholipid antibodies were yet negative. At the last follow-up in April 2025, the boy reported no problems and was in stable condition.
Conclusion: Symptomatic deep vein thrombosis, repeated positivity of LA and SLE-related antibodies revealed that it was secondary APS as a manifestation of SLE trigerred by infectious mononucleosis. Treatment consists of therapy of the underlying disease with a therapeutic dose of anticoagulants. aPL should be tested in every child with thrombosis. Consent to published had been obtained.
Trial registration identifying number: This research was supported by the Czech Ministry of Health (DRO FNOI, 00098892) and IGA_LF_2025_030.
Disclosure
None declared

Reference

1. Mojca Zajc Avramovic, Tadej Avcin. Antiphospholipid syndrome in children. Best Practice & Research Clinical Rheumatology. 2024 Aug 1;101986–6.

PU59

Complex clinical course in a female adolescent with sle: diagnostic and therapeutic challenges and experience with anifrolumab

M. Carvalho[1], C. Nunes[1], F. Costa[2], M. Moniz[2], C. Escobar[2], C. Conceição[3], M. Conde[3], M. Cabral[4]
[1]Pediatric Service, [2]Intensive Care Unit, Pediatric Service, Hospital Professor Doutor Fernando Fonseca, [3]Hospital de Dona Estefânia, ULS São José, [4]Pediatric Rheumatology Consultation, Hospital Professor Doutor Fernando Fonseca, Lisbon, Portugal
Correspondence: M. Cabral
Pediatric Rheumatology, **23(2):** PU59

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that can affect any organ system. SLE management is individualized based on disease activity, organ involvement, and patient comorbidities.
Objectives: Describe a clinical case
Methods: Describe a clinical case
Results: Case report
A 15-year-old female adolescent, diagnosed 6 months earlier with systemic SLE (with discoid lupus lesions, bicytopenia and positive lupus anticoagulant) was admitted for prolonged fever and diarrhea. The patient had been treated with hydroxychloroquine, acetylsalicylic acid and prednisolone 15 mg/day. Initial etiological investigation revealed a positive Interferon-Gamma Release Assay (IGRA) and necrotizing lymphadenopathy on abdomen computed tomography scan. A diagnosis of tuberculous lymphadenitis was established, and anti-tuberculosis treatment regimen was initiated. The patient remained with fever and ten days after starting anti-tuberculosis treatment, there was an analytical deterioration with pancytopenia (hemoglobin 5,6 g/dL, leukocytes 1200/µL, platelets 79 000/µL), elevated triglycerides (359 mg/dL), and increased ferritin (1160 mg/dL). Macrophage activation syndrome (MAS) was considered, and was treated with 5 pulses of methylprednisolone (followed by oral prednisolone 60mg/day) and a single dose of immunoglobulin, leading to resolution of

fever within 24 hours of treatment. During hospitalization, emotional lability was observed, and a new-onset seizure occurred following the initiation of corticosteroid therapy. Brain angio-MRI revealed multiple nonspecific changes, with no evidence of posterior reversible encephalopathy syndrome, thrombosis or other abnormalities related with tuberculosis. A lumbar puncture was performed, revealing 1 cell/mm^3, protein level of 30 mg/dL and positive antinuclear antibodies. A diagnosis of neuropsychiatric lupus was established, and treatment with cyclophosphamide was initiated. Subsequently, the result of the soluble CD25 test showed no significant elevation, making MAS unlikely. The final diagnosis was a flare-up of LES, with hematological and neurological involvement. The patient's clinical condition improved, and the patient was discharged 40 days after admission. Twenty days after discharge, the patient was readmitted to the hospital due to a flare-up of LES, which manifested again with severe cutaneous, hematological and neurological involvement. Following this, treatment with anifrolumab was associated, resulting in good disease activity control.
Conclusion: Organ involvement in SLE, particularly neurological involvement, can be challenging to diagnose and significantly impacts treatment decisions. Anifrolumab is a targeted biologic that offers a novel approach to SLE treatment, particularly for patients with moderate to severe SLE who are inadequately controlled by standard therapy, with an extraordinary improvement in our patient. Consent to published had been obtained.
Disclosure
None declared

PU60

Systemic lupus erythematosus preceded by epstein barr virus

S. Jiménez[1], N. V. Vargas[2]
[1]Pediatric rheumatology, [2]Pediatrics, Instituto Mexicano Del Seguro Social, Monterrey, Mexico
Correspondence: S. Jiménez
Pediatric Rheumatology, **23(2):** PU60

Introduction: The Epstein Barr virus (EBV), which belongs to subfamily Gamma herpesvirinae, has a strong tissue tropism for B lymphocytes. The virus is associated with a wide variety of neoplasms and common autoimmune diseases, like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and multiple sclerosis (MS). Most lupus patients show evidence of EBV infection, some antibodies cross-react with autoantigenic proteins suggesting that the virus may contribute to autoimmunity through molecular mimicry. Among the wide spectrum of complications of SLE, one of the most common and severe is lupus nephritis (50%–70% of SLE patients in the first five years of diagnosis).
Objectives: The aim of this case is to review the clinical presentation, diagnostic approach, and therapeutic interventions for a 6-year-old patient who developed SLE after EBV infection.
Methods: We present the case of a previously healthy 6-year-old female presented with a six-month history of upper respiratory symptoms and infiltrative syndrome (fever predominantly in the evening, cervical, axillary and inguinal adenomegaly). The Initial laboratories showed bicytopenia, hemoglobin of 9.5 mg/dL, direct coombs test 2+, EBV viral load of 65 copy/ml, ANA negative, antiDNA negative, low C3 and C4 of complement, diagnostic approach was performed to rule out malignancy, infection and autoimmunity. Excisional biopsy of the left cervical lymph node (08/10/24) reported reactive follicular hyperplasia pathology. She did not meet the criteria for systemic lupus erythematosus and was kept under close surveillance.
After 8 weeks she developed nephrotic syndrome, requiring further rheumatologic evaluation, with follow up laboratories showing normocytic normochromic anemia, ANA 1:160 homogeneous, antiDNA +600, antiSmith +600, and antiRo 181, serology now positive and the diagnosis of SLE was confirmed. Prompting remission induction with cyclophosphamide was started.
Results: Currently with cyclophosphamide, antimalarial, tapering prednisone, dual antihypertensive, and calcium and vitamin D supplementation with good response, a kidney biopsy was taken and the results are pending.
Conclusion: In summary, this case highlights the need for multiple differential diagnoses, including SLE and monitoring for an infectious disease such as Epstein-Barr virus, which is associated with multiple diseases, both rheumatic and malignant. Furthermore, close monitoring is essential for patients with a high suspicion of developing autoimmune disease. Keeping in mind that the criteria for SLE may not all present simultaneously, as in our patient, evaluations should be performed periodically, as they could be merely the beginning of an autoimmune disease. Consent to published had been obtained.
Disclosure
None declared

References

1. Han, L., Zhang, Y., Wang, Q., Xin, M., Yang, K., Lei, K., & Sun, M. (2018). Epstein-Barr virus infection and type I interferon signature in patients with systemic lupus erythematosus. *Lupus*, 961,203,317,753,069. Advance online publication. https://doi.org/10.1177/0961203317753069
2. Chen, X., Li, H., Wu, C., & Zhang, Y. (2023). Epstein–Barr virus and human herpesvirus 6 infection in patients with systemic lupus erythematosus. *Virology journal*, *20*(1), 29. https://doi.org/10.1186/s12985-023-01987-3
3. Wang, L., & Law, H. K. (2015). The Role of Autophagy in Lupus Nephritis. *International journal of molecular sciences*, *16*(10), 25,154–25,167. https://doi.org/10.3390/ijms161025154

PU62

Self-healing juvenile cutaneous mucinosis: a case report

I. Rukavina[1], A. Balic[2], M. Bradamante[2], M. Jelušić[1]
[1]Pediatric Department, [2]Dermatology Department, University Hospital Centre Zagreb, Zagreb, Croatia
Correspondence: I. Rukavina
Pediatric Rheumatology, **23(2):** PU62

Introduction: Self-healing juvenile cutaneous mucinosis (SHJCM) is an extremely rare skin disorder characterized by the abnormal accumulation of mucin in the skin and in some cases, deeper tissues as well. It is self-limiting condition that typically affects children and adolescents with fewer than 20 reported cases in the literature. The skin manifestations may include papules, plaques, edema or nodules, often located on the face, neck, hands, or trunk. Generally, it presents a benign course.
Objectives: Here we describe a 13-year old boy with histologically confirmed SHJCM.
Methods: The boy, aged 13, exhibited the condition with painless swelling in three fingers of his right hand, two years ago. This was followed by swelling on the left cheek one year ago and bilateral uveitis six months ago. Uveits was treated with local corticosteroid therapy and had been resolved in a several weeks. There was no other clinical symtpoms.
Results: Blood tests conducted at the time of diagnosis revealed normal inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Head MRI showed T1 and T2 hypointense reticulation of subcutaneous fat on the buccal left side with thickening of the skin. Deeper, there was infiltration and thickening of the zygomaticus major muscle. Histopathological examination of the skin biopsy and subcutaneous tissue revealed proliferation of fibroblasts with larger accumulations of mucin present within the papillary and reticular dermis and even more abundant at the border with subcutaneous fat tissue. His total IgE was elevated (810 kIU/L). Additional investigations, including complete blood count, thyroid hormones, serum biochemistry, antinuclear antibodies, rheumatoid factor, anticitrullinated antibodies, angiotenzin converting enzym, antineutrophil cytoplasmic antibodies, antistreptolysin titer, immunoglobulin and protein electrophoresis, urinalysis, and hand MRI, were all normal. Based on clinical picture and these findings, the diagnosis of self-healing juvenile cutaneous mucinosis was established.
Conclusion: SHJCM is a rare disease whereby awareness of its features and presentation may help in diagnosing it and preventing unnecessary testing and aggressive treatment for a rather benign disease. Consent to published had been obtained.
Disclosure
None declared

PU63

En coup de sabre syndrome with alopecia in a 5-year-old boy: a rare case report

A. A. Abushhaiwia[1], Y. Elfawires[2]
[1]Pediatric Rheumatology, Tripoli Children Hospital,Faculty of Medicine, university of Tripoli, [2]Pediatric, Faculty of medicine, university of Tripoli, Tripoli, Libya, Tripoli, Libya
Correspondence: A. A. Abushhaiwia
Pediatric Rheumatology, **23(2):** PU63

Introduction: En coup de sabre is a rare subtype of linear morphea that typically appears on theparamedian forehead or frontoparietal scalp. We present the case of a 5-year-old boy child with linear brownish prominent asymptomatic lesions on the forehead and hair-loss patches on the scalp. Following a thorough clinical examination, brain imaging,and skin biopsy, the patient was diagnosed with en coup de sabre morphea and treatedwith oral steroids and weekly methotrexate.
Objectives: To highlight the importance of thorough diagnostic evaluation, including the skin biopsy in establishing an accurate diagnosis and avoiding misdiagnosis.
Methods: A 5-year-old Libyan boy came to our paediatric rheumatology clinic with a history of prominent painless swelling on his forehead and multiple painless lumps or nodules on the body parts, as well as a hyperpigmentation rash (size 0.5-0.25 cm) that hadbeen present since he was three. Months later, signs of alopecia developed on his scalp,leading his family to seek medical consultations with a dermatologist and apaediatrician, where he was first diagnosed with a typical presentation of neurofibromatosis type1, as well as arthralgia and arthritis of his big toes.The diagnosis of linear Morphea was confirmed by a skin biopsy.His CBC, ESR, CRP,and immunogloubin assay were all normal, with the exception of ANA, which demonstrated a titer of 1:160 and mild iron deficiency anemia (low blood iron, low serumferritin, and normal TIBC).
Results: These findings are consistent with linear Morphea en coup de sabre. No neurological,developmental, or ophthalmological changes were identified. Cerebral magnetic resonance imaging revealed no intracranial abnormalities.Alopecia progressed despite topical treatment, requiring the use of systemic immunosuppressive therapy.Oral treatment with prednisolone, methotrexate, and iron supplements was successful.A two-month treatment course of methotraxte (10 mg/week) and oral steroids (prednisolone 1 mg/kg/day) showed significant improvement in symptoms, including decrease in hair loss patches and hair growth. However, after discontinuing steroids,the patient experienced a relapse in March, with symptoms returning.
Conclusion: This case report demonstrates the challenges of diagnosis and managing rare conditions like Encoup de Sabre Syndrome with alopecia. Especially when presenting with unusual symptoms. Despite initial improvement with methotrexate and steroids,the patient had a relapse after discontinuing steroids.This case emphasizes the significance of close monitoring and maybe modifying treatment strategies to obtain optimal illness control. Consent to published had been obtained.
Disclosure
None declared

PU64

Emerging autoimmune features in a pediatric patient with congenital hydronephrosis: a case report

E. Nakhutsrishvili, T. Kutubidze
Givi Zhvania Pediatric University Clinic of Tbilisi State Medical University, Tbilisi, Georgia
Correspondence: E. Nakhutsrishvili
Pediatric Rheumatology, **23(2):** PU64

Introduction: Autoimmune diseases in early childhood can present with non-specific symptoms and subtle clinical findings. Cutaneous involvement may be an early sign, preceding the development of systemic features. We report a case of a 4-year-old child with congenital hydronephrosis who presented with progressive skin changes and systemic symptoms, raising suspicion for an evolving autoimmune condition.
Objectives: To describe the clinical presentation, laboratory findings, and diagnostic approach in a young child with suspected early autoimmune disease and to highlight the importance of early recognition and multidisciplinary evaluation.
Methods: We reviewed the clinical records of a 4-year-old child with a history of congenital hydronephrosis under nephrologic follow-up. The child presented with recurrent fever, abdominal pain, and progressively worsening skin lesions over a three-month period. A comprehensive clinical examination and laboratory evaluation, including autoimmune serology, were conducted.
Results: The child appeared pale, hypotonic, and underweight (13 kg, 5th percentile). Skin examination revealed hard, shiny, thickened plaques. Laboratory results showed normocytic, normochromic anemia. Autoimmune workup demonstrated a high-titer ANA (1:1280, homogeneous pattern), positive anti-nucleosome antibodies (++), and mildly elevated anti-PM-Scl antibodies. ANA quantitative level was 5.9. EBV IgM positivity was noted but not accompanied by lymphoproliferative symptoms. No definitive diagnosis was established at this stage, but features were suggestive of early systemic autoimmune involvement, potentially within the scleroderma spectrum or an overlap syndrome.
Conclusion: This case underscores the importance of considering autoimmune diseases in pediatric patients presenting with persistent systemic symptoms and cutaneous changes, even in the absence of a family history. Early serological markers may guide further evaluation and follow-up. A multidisciplinary approach is essential for timely diagnosis and intervention to prevent progression and organ involvement. Consent to published had been obtained.
Disclosure
None declared

PU66

Behçet's disease in a 15 years old girl : a case report

A. A. Abushhaiwia
Pediatric Rheumatology, Tripoli Children's Hospital,faculty of medicine, university of Tripoli, Tripoli, Libya
Pediatric Rheumatology, **23(2):** PU66

Introduction: BD is distinguished by a combination of recurrent aphthous stomatitis, genital ulcers, and skin and ocular diseases. The cause is uncertain. Behçet's illness remains challenging due to atypical manifestations and the disease's heterogeneity.
Objectives: highlights the significance of early recognition and prompt therapy of BD in child patients as well as the particular presentation of Behçet's syndrome in children and the challenges associated with its diagnosis.
Methods: Assessment of medical history, laboratory results, and therapeutic response
Results: A 15-year-old girl who was previously healthy presented to the pediatric rheumatology clinic with a history of recurrent episodes of painful mouth ulcers that spontaneously resolved after ten days for the past year (more than six episodes per year) and painful swelling in her left knee for six weeks.Additionally, during the previous months, her mother experienced frequent episodes of folliculitis in her extremities that were followed by pustule formation.Her parents are not consanguineous, and she has five healthy siblings. There were no neurological, cardiopulmonary, renal, or gastrointestinal, ophthalmology symptoms, or signs.Her Physical examination was normal, except for 4 oral aphthae and some acneiform lesions, arthritis left knee.Prompting more accurate investigate of SLE, IBD, and Behçet's syndrome.Laboratory study Including complete blood count with renal and hepatic function, C-reactive protein, ESR, B and C and HIV viral markers,, and calprotectin levels, which were all negative. Serology (including rheumatoid factor, antinuclear antibodies, anti-cardiolipin and beta 2 glycoprotein antibodies, lupus anticoagulant, anti-dsDNAabs, ENA and celiac disease markers were negative.) urine routine examination, chest radiograph, and abdominal ultrasound, echocardiography, eyes examination revealed normal findings. Pathergy test was positive. Our patient presented with recurrent oral ulcers, papulopustular skin lesions, and a positive pathergy test, meeting the diagnostic criteria for Behçet's disease as per both the ISG and ICBD criteria.the patient

scored 4 (recurrent oral aphthosis, cutaneous lesions, and positive patheragy test) and was diagnosed with Behçet´s syndrome. HLA- B51 test, which was later requested, was positive.after diagnosis, she was received 1.5 mg of oral colchicine daily, which led to a decrease in the size and number of oral aphthous lesions There were no further occurrences reported, along with the patient's response to colchicine therapy, provides supportive evidence for Behçet's diagnosis in the current child.
Conclusion: Early recognition and treatment of Behçet's syndrome in children can significantly improve outcomes. This case highlights the importance of considering Behçet's in pediatric patients with recurrent oral ulcers and skin lesions. Consent to published had been obtained.
Disclosure
None declared

PU67

Successful management of kawasaki disease with coronary artery involvement in a 5 year-old libyan girl : complete resolution within 5 months

A. A. Abushhaiwia[1], S. S. Jdour[2]
[1]Pediatrics Rheumatology,, [2] Pediatric Cardiology, Tripoli Children's Hospital, Faculty of Medicine, university of Tripoli, Tripoli, Libya
Correspondence: A. A. Abushhaiwia
Pediatric Rheumatology, **23(2):** PU67

Introduction: Kawasaki disease (KD) is an acute systemic vasculitis, that results in consequences such as coronary artery abnormalities as a complication.Approximately 25% of untreated CKD patients develop coronary artery dilatation or aneurysms (CAAs).However, the majority of the lesions resolve over time.Treatment with high doses of IVIG and aspirin can reduce the risk of developing coronary artery aneurysms by 2%–3%.
Objectives: We describe a five-year-old girl who was diagnosed with KDnand coronary artery involvement.
Methods: a case report
Results: A 5 years old female child presented to the emergency pediatric department, with thehistory of remittent fever for the past 10 days along with congestion of eyes and cervical lymphadenopathy for the same duration Her parents gave history of appearance of rash over upper chest and abdomen on the second day of her illness, which resolved spontaneously, and excoriation in the genital area She had visited a general physician as per whose advice she had taken antibiotics without any remission of her symptoms. She was then referred to our hospital. Clinical examination revealed cracked lips, strawberry tongue, and multiple cervical lymphadenopathies on the left side involving. There were four mobile and non-tender lymph nodes each measuring about 2 cm in diameter. Her conjunctiva, oropharynx and nasal mucosa, were found congested with high fever 39c. She had a periungual desquamation in fingers of both extremities from about 4th day of admission. Other systemic examinations were within normal limits. On admission significant laboratory findings were of leucocytosis of $12X10^3$ predominantly neutrophilia of 85%, anemia with haemoglobin of 9 g/dl, thrombocytosis of $853\ X10^3$, CRP was 76 mg\dl, ESR 130 mm\hr, AST 18.6 U\L, ALT 9.7 U\L, s.albumin 2.8 g\dl. A screening echocardiography was done and was found mild dilatation of right coronary artery 3.9 mm = Z-score 4.7.Treatment for KD was started immediately with high dose intravenous immunoglobulin (IVIG) as a single dose 2gm\kg and high dose aspirin 50mg\kg\day four divided dosed for 5 days with remarkable improvement as the fever subsided with in 24 hours of treatment and was stepped down to 3 mg/kg. Serial follow up echocardiograms showed resolution of the dilated coronary arteries over time and currently we are pleased to report that the coronary arteries of this child, five months after her diagnosis of the condition, reveal normal z-scores of less than 2.5 relative to her body surface area.
Conclusion: The administration of intravenous immunoglobulin (IVIG) and aspirin were pivotal in reducing inflammation, preventing coronary artery damage, and promoting recovery. This case underscores the importance of timely and appropriate treatment, as well as regular follow-up, to prevent long-term complications. Consent to published had been obtained.
Disclosure
None declared

PU68

Multiple thrombus formation in Kawasaki disease: a rare and intriguing case

R. Singh, A. Nandi, R. P. Goud, J. N. Bathia, P. Pal
Pediatric Rheumatology, Institute of Child Health, Kolkata, India
Correspondence: P. Pal
Pediatric Rheumatology, **23(2):** PU68

Introduction: Kawasaki disease (KD) is an acute systemic vasculitis that involves coronary arteries in young children. Even though giant aneurysms are rare, they can be complicated by thrombus formation, leading to myocardial ischemia, myocardial infarction, and even death.
Objectives: We report a 9 months infant diagnosed as KD on D11 of fever with multiple CAA, giant aneurysms of LMCA and LAD, with a 4 x 5 mm large thrombus in LMCA and went on to develop a 6 x 5 mm thrombus in LAD within 4 days of initiation of therapy with IVIG+ Infliximab.
Methods: 9 month male child with primary diagnosis of COMPLETE KAWASAKI DISEASE WITH MULTIPLE CAA was treated with IVIG 2gm/kg + Infliximab 10mg/kg + oral Cyclosporin 5mg/kg/day + LMWH 2mg/kg + aspirin+ Clopidogrel.He showed response with Resolution of thrombi within 19 days of initiation of therapy. Both the thrombi resolved and the giant aneurysms in LMCA and LAD reduced to moderate sized aneurysms within 20 days. This was subsequently corroborated by CTCA after 6 weeks.
Results: Baby was managed with IVIG+ Infliximab+ Cyclosporine + dual antiplatelets+ sc LMWH 2mg/kg. Echocardiography was initially done daily for first 10 days till stabilization of thrombus size and subsequently on alternate days till resolution of thrombus after another 10 days.
Conclusion: Frequent echocardiographic monitoring during the acute phase of KD helps in early detection of complications like progression in size of aneurysms and formation of thrombi. Timely aggressive management can lead to dissolution of thrombi and also regression in size of aneurysms. Consent to published had been obtained.
Disclosure
None declared

PU70

Contribution of the initial inflammatory assessment (IIA) in rheumatic diseases of children in bouaké

A. Traore[1,2], K. J. Koffi[1,2], J. J. Goua[2], J. C. Yao[1,2], E. S. C. Kouakou[1,2], F. J. C. Daboiko[1,2,3]
[1]Rhumatologie, Université Alassane Ouattara, [2]Rhumatologie, Centre Hospitalier Universitaire de Bouaké, [3]Departement de medecine et spécialités, Université Alassane Ouattara, Bouaké, Côte d'Ivoire
Correspondence: A. Traore
Pediatric Rheumatology, **23(2):** PU70

Introduction: Rheumatic diseases (RDs) include conditions that have different causes, evolve differently and may have variable consequences. Rheumatic diseases are classified into inflammatory and non-inflammatory rheumatic diseases. This distinction is guided by the clinical signs of local inflammation (pain, heat, redness and joint swelling) and by the biological inflammatory syndrome. The initial inflammatory work-up (IIW) therefore plays an important role in the diagnosis and follow-up of RDs. The diagnosis of RDs sometimes requires inaccessible investigations due to the poverty of our populations.
Objectives: To evaluate the initial biological inflammatory assessment (sedimentation rate and CRP, CBC) in the diagnosis of rheumatic diseases in children in Bouaké.
Methods: This was a prospective cohort study over a 1-year period (January-December 2023). Children under 18 years of age with an established diagnosis admitted to the rheumatology department of the Bouaké University Hospital were included.
Results: During this period we admitted 35 children, 23 of whom were girls (65.7%) and 12 boys (34.3%), giving a sex ratio (M/F) of 0.52. The average age was 13.51+/−3.7 years [2-17 years]. 94.3% of the children

attended school. Clinically, pain was the main reason for admission, evolving in a chronic mode (68.6%). The average duration was 16.7 months. The pain was inflammatory (77.1%), with peripheral and polyarticular involvement (42.8%). The BII showed the following variations: normal, hyperleukocytosis, isolated accelerated VS (1H), isolated elevated CRP and inflammatory syndrome in 22.9%, 20.0%, 20.0%, 5.7% and 51.4% respectively. Inflammatory/autoimmune rheumatism (RAII) accounted for 54.30% of the aetiological classes and was dominated by JIA in 63.1%. The BII was positive in 18 children with RAII and in all cases of osteoarticular infections (OAI). There was a link between RAII and positive SV with a p-value of 0.03.
Conclusion: Initial Inflammatory Assessment (IIA) is a highly valuable first-line diagnostic work-up in rheumatology. A positive BII with or without an inflammatory syndrome should prompt a search for RAII, OAI in children.
Disclosure
None declared

PU72

A young boy with necrotizing lymphnode, brain and bone marrow

D. B. Pandya[1], on behalf of Dr Rajiv Doshi, Dr Ankur Kothari, Dr Kosha Sheth, Dr Parag Dagli & Dr Abhishek Bansal
[1]Pediatric Rheumatology, Dev Pediatric Rheumatology & Immunology Center, Ahmedabad, India
Correspondence: D. B. Pandya
Pediatric Rheumatology, **23(2):** PU72

Introduction: Kikuchi-Fujimoto disease (KFD) is a benign and self-limiting disease characterized by low-grade fever and regional lymphadenitis. Hemophagocytic Lymphohistiocytosis (HLH) and encephalopathy are extremely rare presentations.
Objectives: We are presenting a case of KFD with multi-system refractory HLH and rapidly progressive life-threatening necrotizing encephalopathy.
Methods: 7 years old Indian boy presented to us in an out-patient department with 2 weeks complaints of intermittent fever, bilateral tender cervical lymphadenopathy and some non-specific evanescent rash just for a day with normal general condition. His previous CBC charts showed slowly decreasing trend in all three blood cell lines with no actual cytopenias, negative CRP, elevated ESR (102mm/1st hour) with negative screen for endemic infections. We suspected KFD as our differential, but advised further work to look for SLE & Systemic JIA with impending MAS or malignancy and stared him on oral naproxen until fresh reports become available. His initial lab result showed normal blood film, mild elevation in LDH, liver enzymes and ferritin (450ng/ml) with negative direct coombs test, negative ANA and normal complements levels.
Results: Unfortunately the next night, he presented to ER with hyperpyrexia(temp 107f), persistent rash, altered sensorium with very poor GCS, convulsions and circulatory collapse. He was immediately put on ventilator and inotropic support. Laboratory tests showed severe pancytopenia, markedly elevated ferritin (~70,000), raised LDH, raised liver enzymes & deranged coagulation profile. He was given high dose intravenous (IV) pulse methylprednisolone (30mg/kg/day) under cover of prophylactic anti-fungal, anti-viral and antibiotics with support of blood products like packed red cells, FFP and cryoprecipitate. 2D echo revealed severe cardiac dysfunction with EF of 10%. Bone marrow examination showed hemophagocytosis with no evidence of malignancy. Lymph node biopsy revealed necrotizing lymphadenitis favouring KFD. IV Immunoglobulin 2gm/kg and oral cyclosporine was added. His HLH parameters responded partially to above treatment but GCS was persistently low. MRI Brain revealed severe bilateral diffuse necrotizing encephalopathy. We planned for either IV Tocilizumab (TCZ) or subcutaneous (SC) Anakinra followed by plasma exchange, but unfortunately the child did not give us more time and he died.
Conclusion: KFD is not always a benign disease, it can present with fatal complications. Children with suspected KFD must be kept under close observation and the trend in CBC parameters is very much important rather than an actual cytopenia/s. We should keep a low threshold for starting early glucocorticoids in such cases irrespective of pending work up for other potential mimics. Early introduction of biologics, intravenous tocilizumab or subcutaneous anakinra may help in such case for better CNS outcomes. Consent to published had been obtained.
Disclosure
None declared

PU74

JAK-STAT pathway targeting in pediatric refractory pyoderma gangrenosum: a case report on the role of baricitinib

F. Di Stasio[1], M. Rossano[1], F. Vianello[1], L. Baselli[1], S. Lanni[1], G. Beretta[1], N. Monzani[2], E. Conti[1], R. Cavalli[2], F. Minoia[1], G. Filocamo[1]
[1]Pediatric Immunorheumatology Unit, [2]Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy
Correspondence: F. Di Stasio
Pediatric Rheumatology, **23(2):** PU74

Introduction: Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis that may be idiopathic or associated with systemic conditions such as inflammatory bowel disease, malignancies, and autoinflammatory syndromes. Its pathogenesis involves immune dysregulation and genetic predisposition, including mutations in inflammasome-related genes. Standard treatment typically includes glucocorticoids and DMARDs, with biologics such as TNF-α and IL-1 inhibitors reserved for severe or refractory cases. Recent findings highlight the involvement of the IL-23–IL-17 axis, where IL-23 promotes Th17 differentiation via pathways like STAT3 and JAK2, leading to IL-17A production and subsequent neutrophil recruitment. The use of Janus kinase (JAK) inhibitors, targeting this axis, may offer a therapeutic approach for refractory PG.
Objectives: We present a case of severe paediatric PG, refractory to multiple therapies, successfully treated with JAK-inhibitors.
Methods: Patient data were retrospectively collected from medical records.
Results: A 15-year-old girl presented with severe PG involving the face, genital, and perianal areas. Laboratory tests revealed neutrophilic leukocytosis and elevated ESR and CRP. Extensive investigations ruled out systemic diseases typically associated with PG. Skin biopsy confirmed marked neutrophilic infiltration with necrosis, reactive neoangiogenesis, and fibrosis. Interferon signature was negative, and whole-exome sequencing did not identify mutations linked to known autoinflammatory disorders.
Despite therapy with TNF-α inhibitors (adalimumab, infliximab) and anakinra, her ulcers worsened, requiring repeated sedation for wound care and hyperbaric oxygen therapy.
Due to refractory course, steroidal toxicity, and risk of disabling sequelae, JAK-inhibition with baricitinib was started alongside ciclosporin A, leading to gradual healing of skin lesions, normalization of inflammatory markers and significant steroidal-sparing effect. Over the following 23 months, no disease activity was observed in previously affected areas, though progressive exophthalmos developed at a previously involved site.
Following an episode of preseptal cellulitis, she experienced a periocular flare with worsening exophthalmos. A biopsy of a retrobulbar lesion revealed fibrosis and granulation tissue consistent with sequelae of previous acute inflammation. Disease reactivation was managed by adding Ustekinumab, an inhibitor of IL-12 and IL-23, to ongoing baricitinib therapy.
Conclusion: This is the first reported case of JAK-I treatment in pediatric PG. Targeting the IL-23/IL-17 axis may represent a promising therapeutic option for refractory PG. Consent to published had been obtained.
Disclosure
None declared

PU75

A rare case of primary sjögren's syndrome in childhood: features of diagnosis and therapy

I. Arshynbek, Z. Albekova, Z. Mukusheva, M. Assylbekova
Pediatric Rheumatology, CF "University Medical Center", Astana, Kazakhstan
Correspondence: I. Arshynbek
Pediatric Rheumatology, **23(2):** PU75

Introduction: Primary Sjögren's syndrome (pSS) is a rare autoimmune disorder in pediatric populations, characterized by immune-mediated injury to exocrine glands, particularly the salivary and lacrimal glands, leading to chronic dryness of mucosal surfaces (sicca symptoms). In children, the disease can present atypically with multisystem involvement, including cutaneous vasculitis, pulmonary nodules, and arthritis, potentially resulting in significant morbidity.
Objectives: To present a rare case of childhood primary Sjögren's syndrome with multisystem involvement, emphasizing diagnostic difficulties and the importance of timely, individualized immunosuppressive therapy for improved outcomes.
Methods: A 13-year-old female patient, A., was hospitalized twice at the National Research Center for Maternal and Child Health of Kazakhstan for the evaluation and management of suspected autoimmune disease.
Results: The patient was admitted with complaints of skin rash on the lower legs and feet, enlargement of the parotid glands, ocular discomfort in cold weather, and swelling of the ankles and knees. These symptoms were associated with the consumption of large amounts of sweets and citrus fruits. Laboratory findings revealed seropositivity for rheumatoid factor (330.00 IU/mL), antinuclear antibodies (ANA) at a titer of 1:640 with a granular pattern, strongly positive anti-Ro-52 (+++), anti-SSA (+++), and anti-SSB (+++). Instrumental investigations demonstrated multiple pulmonary nodules (granulomas) on chest CT. Ultrasound of the parotid glands indicated bilateral sialadenitis. Histopathological examination of the skin biopsy confirmed a diagnosis of panvasculitis. Due to high disease activity involving the lungs, salivary glands, joints, and vasculature, immunosuppressive therapy was initiated, including B-cell therapy Rituximab 500 mg IV administered at Day 0 and Day 14, followed by 500 mg IV every 6 months thereafter, based on clinical evaluation, mycophenolic acid 1750 mg/day, hydroxychloroquine 200 mg/day, and pulse therapy with methylprednisolone 750 mg IV for 3 days, followed by oral tapering of methylprednisolone at 24 mg/day. Given active joint involvement, intra-articular administration of glucocorticosteroids was performed in the right knee and both ankle joints. The patient was discharged with clinical improvement. The joint syndrome partially resolved, with improved range of motion. Skin lesions regressed, and parotid gland involvement decreased.
Conclusion: Primary Sjögren's syndrome in pediatric patients is a rare but complex autoimmune disorder requiring early recognition and a multidisciplinary approach to prevent severe complications. This case underscores the importance of timely diagnosis, thorough immunological evaluation, and advanced therapeutic interventions in improving clinical outcomes for pediatric patients. Consent to published had been obtained.
Disclosure
None declared

PU76

Misdiagnosis of malignancy under the mask of rare genetic condition progressive ossificans heteroplasia

I. Nikishina[1], S. Arsenyeva[2], V. Matkava[1], A. Firsa[1]
[1]Paediatric, V.A. Nasonova Research Institute of Rheumatology, [2]Paediatric, V.A. Nasonova Scientific Research Institute of Rheumatology, Moscow, Russian Federation
Correspondence: I. Nikishina
Pediatric Rheumatology, **23(2):** PU76

Introduction: Diseases associated with GNAS mutation have variety clinical manifestations. One of them is ultra-rare hereditary progressive ossificans heteroplasia (POH) which presented as formation of heterotrophic ossification (HO) in soft tissues. Sometimes POH may be misdiagnosis of other diseases such as trauma, paralysis, cancer.
Objectives: To describe a clinical case of misdiagnosed malignant peripheral nerve sheath tumor (MPNST).
Methods: Case report. Boy 13 y.o. has been suffering from the tingling and pain in the left foot and tibia for a year. Painful formation up to 1 cm appeared later on the plantar of the left foot and caused gait disturbance. MRI/ultrasound detected the neoplasm lasted from plantar to tibia. Diagnosis of neurofibromatosis/calcifying aponeurotic fibroma was proposed after first biopsy. But X-Ray and CT of left foot found multiple calcinosis and ossificates. Repeated biopsy was performed. Histological examination revealed only bone tissue formation. Presence of left extremity asymmetrical reticular HO reminded hereditary condition and POH was suggested. Molecular genetic testing of histological sample verified somatic mutation of the GNAS gene and patient was directed to geneticist. Full set of genetic analyses in a patient and his parents didn`t confirm the GNAS mutation. Because of these manipulations patient lost about two years.
Results: Finally, patient was consulted by rheumatologists. We identified huge neoplasm (8x5 cm) on the left foot with local reaction and vascularization. At first sight we realized that these clinical features didn't correspond to POH despite the verified somatic GNAS mutation. Patient was consulted by oncologist again, lung CT detected multiple metastatic lesions. Morphological examination verified MPNST G3. Lower-leg amputation was done due to aggressive growth of tumor. I3VE №6 and CEV №7 chemotherapy protocols were performed without positive results. Inspite of all efforts the child died unfortunately.
Conclusion: HO is a new challenge for oncologists, geneticists, rheumatologists. It is important to establish the type of HO in order to choose the correct management strategy. Delay of correct diagnosis and treatment lead to dramatic final in this case. Paradoxically, it can be assumed that it would have been better for this patient if, at the beginning of the path to diagnosis, he had not met a doctor who was informed about such a rare disease as POH. Consent to published had been obtained.
Disclosure
None declared

PU77

Neonatal inflammatory skin and bowel disease type 1: a case report from the UAE

S. Lootah[1], A. Galadari[2], B. Krishnamurthy[3]
[1]Pediatric Rheumatology, Al Jalila Children Hospital, Dubai Health, [2]Dermatology, Dermatology Center, Dubai Health, [3]Pediatric Gastroenterology, Al Jalila Children Hospital, Dubai Health, Dubai, United Arab Emirates
Correspondence: S. Lootah
Pediatric Rheumatology, **23(2):** PU77

Introduction: Neonatal inflammatory skin and bowel disease type 1 is a rare genetic disorder due to mutations in the *ADAM17* gene. ADAM17 (also known cas TACE) is critical for epidermal and gut development via EGFR signaling and for resolving inflammation via cytokine shedding.
Objectives: To describe the clinical manifestations and treatment of a case with NIBDS1.
Methods: This is a retrospective review of a 23-month-old Arab girl with a genetically confirmed diagnosis of NISBD1.
Results: The patient was referred to us at 18 months of age. She had whole-exome sequencing at another institution, which revealed pathogenic *ADAM17* mutation: c.611del p.(Pro204Hisfs*9) on chromosome 2 (chr2:9,667,922), confirming the diagnosis of NISBD1. She is born at 34 weeks of gestation to consanguineous parents (first cousins). ECHO showed atrial septal defect secundum. On day two of life, she developed an erythematous macular rash and treated for MRSA skin infection. In the next months, she had intermittent erythematous flare ups in the neck, arm and knee folds and in the perioral and perianal areas. She also exhibited dry brittle hair and wiry disorganized eyebrows, and preserved nails. She was gaining weight poorly and had episodic diarrhea, sometimes with fresh blood in stools, often correlating with skin flare-ups. Laboratory investigations revealed hypochromic microcytic anemia, elevated CRP and ESR, and normal renal and liver function tests. Immunoglobulin levels and T and B cell counts were within normal ranges for age. Gastrointestinal evaluation revealed lymphonodular hyperplasia and small aphthous ulcers in the colon. An anal fissure and a small skin tag at the 6 o'clock position were also noted. Histological analysis showed focal active colitis/proctitis. She was managed with topical corticosteroids, emollients, barrier creams (e.g. ceramides) and infection control measures. Gastrointestinal management involved cow's milk-free diet, high-calorie nutritional support and sulfasalazine. At her most recent follow-up, she demonstrated improvement in skin condition with residual xerosis. However,

there was no regrowth of hair or improvement in eyebrow appearance. Growth velocity remained suboptimal, prompting an increase in caloric intake. Notably, diarrhea ceased, inflammatory markers normalized, and her hemoglobin level improved.
Conclusion: Our patient presented with clinical features similar to other cases reported in the literature. She seems to be responding fairly well to sulfasalazine and topical skin targeted treatment. Consent to published had been obtained.
Disclosure
None declared.

PU78

Knowledge of contraceptive methods among adolescents with rheumatologic diseases

N. E. Rubio Perez, F. García Rodriguez, A. V. Villareal Treviño, F. A. Vasquez Triminio, M. M. Rodríguez Reyes , L. D. C. Reynoso Medina, Z. I. García Murillo, on behalf of Colaborativa de Investigación en Beneficio de la Reumatología Infan- til (COLIBRI)
Pediatria, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico
Correspondence: D. C. Reynoso Medina
Pediatric Rheumatology, **23(2):** PU78

Introduction: Adolescents with rheumatologic diseases should be approached holistically, addressing not only their physical health but also psychosocial and educational aspects during clinical visits—including sexual and reproductive health. Pregnancy in adolescents with rheumatologic conditions can have significant negative consequences, potentially worsening disease activity and leading to adverse pregnancy outcomes such as pregnancy loss, severe prematurity, growth restriction, and teratogenesis. Therefore, it is essential to discuss contraception to help prevent unplanned pregnancies and associated risks.
Objectives: To describe the level of knowledge regarding contraceptive methods among adolescents with rheumatologic diseases.
Methods: This was a cross-sectional, observational study in which questionnaires were administered to adolescent patients with chronic rheumatic diseases—including juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), scleroderma, and antiphospholipid syndrome (APS)—who were seen at the pediatric rheumatology clinic of Hospital Universitario Dr. José E. González in Monterrey, Mexico.
Results: Ten patients aged 12 to 17 years were included; 90% were female, and 60% had a diagnosis of JIA. Regarding knowledge of contraception, 60% were aware of contraceptive methods. Among these, 83.3% had received information from parents and school (mainly high school). The most commonly known methods were the intrauterine device (IUD), condom, combined oral contraceptive pills, abstinence, and emergency contraception. Participants recognized the importance of using contraceptive methods to prevent unwanted pregnancies and sexually transmitted infections.
Conclusion: Adolescents with rheumatologic diseases possess some knowledge about contraceptive methods; however, greater emphasis should be placed on discussing these topics during medical consultations.
Disclosure
None declared.

References

1. R. Lisa. Sammaritano Therapy Insight: guidelines for selection of contraception in women with rheumatic diseases. Nat Clin Pract Rheumatol, 3 (2007), pp. 273–281 https://doi.org/10.1038/ncprheum0484
2. K.W. Drossaers-Bakker, A.H. Zwinderman, D. van Zeben, F.C. Breedveld, J.M.W. Hazes. Pregnancy and oral contraceptive use do not significantly influence outcome in long term rheumatoid arthritis. Ann Rheum Dis, 61 (2002), pp. 405–408

PU79

The respectare concept as a component of pain therapy

J. Mattei, on behalf of Jana Mattei, Martina Kadoke, Lea Höfel, Tanja Bauer, Johannes-Peter Haas
Nursing Directorate, Kinderklinik Garmisch-Partenkirchen gemeinnützige GmbH, Garmisch-Partenkirchen, Germany
Correspondence: J. Mattei
Pediatric Rheumatology, **23(2):** PU79

Introduction: Numerous studies show the positive effects of physical touch in a therapeutic setting. It can reduce anxiety, stress, agitation and pain and it promotes well-being, relaxation and blood circulation. One possibility of therapeutic touch is the Respectare® concept developed by Annette Berggötz. The ritual touch method, which involves resting the hands on the body and limiting touches, is intended to convey a feeling of security and presence.[i].
Objectives: This study analyzes the effects of Respectare® in pain therapy in children and adolescents.
Methods: Patients undergoing inpatient treatment at the Center for the treatment of pain in young people, Garmisch-Partenkirchen were given the voluntary offer to try the Respectare® concept. They were asked to fill out a questionnaire before and after the treatment. The questionnaire included general multiple-choice questions about demographics and previous experiences as well as Likert scale questions, for example about well-being and pain situation before and after touching according to Respectare®.
Results: Since 2023, 45 patients have tried the Respectare® concept. 45 questionnaires have been collected, of which 2 had to be excluded because of contradictory answers.
The patients overall liked the intervention (average score of 9 on a scale from 0 (did not like it at all) to 10 (liked it very much) and were able to engage with it well (average score of 9 on a scale from 0 (not at all) to 10 (completely). Clearly, Respectare® had a positive effect on well-being. Before the intervention, most patients rated their comfort on a scale from 0 (very uncomfortable) to 10 (very well) with a modal value of 4; after the intervention, this value increased to 8. Additionally, the lowest value on the well-being scale improved from 2 to 4 after the Respectare® touch.
Respectare® also improved the current pain situation in 16 patients, although 2 reported a worsening afterwards. In 27 the pain remained unchanged.
For the majority of patients, predominantly positive effects were furthermore measured in terms of relaxation, perception of stress and emotional state/mood.
Conclusion: Annette Berggötz's goal was actually achieved in practice. Other positive effects can be demonstrated, including influences on the perception of pain. Accordingly, Respectare® can be a useful therapeutic component in pain therapy for children and adolescents.
Disclosure
J. Mattei Employee with: low.

Reference

1. Berggötz, A. (2013) Kinder respektvoll berühren

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.