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Case Report

Metastatic lobular breast carcinoma positive for syndecan-1 mimicking a plasma cell neoplasm: a case report

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ABSTRACT

The metastases of breast cancer to bone marrow can mimic plasma cell neoplasia morphologically due to presence of plasma cell-like neoplastic cells and even positive staining for a carcinoma metastasis with plasma cell marker CD138/ Syndecan-1 may cause confusion in diagnosis. This case report details a 71-year-old female initially suspected of plasma cell myeloma due to hypercalcemia and multiple lytic bone lesions. However, a bone marrow biopsy revealed syndecan-1 positive metastatic lobular breast cancer mimicking a plasma cell neoplasm. Bone marrow aspirate smears and the bone marrow biopsy showed plasmacytoid cells that were strongly positive for syndecan-1, indicating metastatic lobular breast carcinoma. The overexpression of syndecan-1 was a critical marker in identifying the breast cancer cells, emphasizing the diagnostic challenges when syndecan-1 positive metastatic lobular BC presents with plasmacytoid features.

Keywords: bone marrow, lobular breast carcinoma, metastatic breast cancer, plasmacytoid neoplasms, syndecan-1

Introduction

The most frequent cancer in women and the second largest cause of cancer-related deaths globally is BC. Long-term survivors are more likely to experience metastases, even though new treatments have greatly improved patient outcomes. Due to the incredibly complicated pathogenic mechanisms underlying the development and spread of cancer, the classic BC classification method—which evaluates conventional biomarkers and clinical-pathologic features—is unable to account for the variation in each patient's clinical course (1-3).

It is quite uncommon for breast cancer to go to the bone marrow. Invasive ductal carcinoma is the most frequent histology of bone marrow metastases from breast cancer, and it is followed by invasive lobular carcinoma. Fifty to eighty percent of cases had hormone receptors found. Most cases of bone marrow metastasis from cancer cells are asymptomatic. One rare manifestation of metastatic BC is symptomatic bone marrow metastases. To confirm the diagnosis, a bone marrow biopsy was carried out. Therefore, a research area of key relevance is the significance and urgency of identifying target molecules for effective therapy options

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and prognostic markers for bone marrow metastases from BC (4,5).

Increasing evidence suggests that syndecan-1 (CD138), a transmembrane heparan sulfate proteoglycan expressed in epithelial cells, may play a role in breast cancer progression and metastasis. Syndecan-1 is involved in several cellular processes including adhesion, proliferation, and migration. Altered immunohistochemical expression patterns of syndecan-1 in tumor and stromal cells have been associated with different clinical outcomes and may contribute to metastatic dissemination (1,2,6).

In this case report, we present a 71-year-old female patient who underwent a bone marrow biopsy with a prediagnosis of plasma cell myeloma due to the presence of multiple lytic bone lesions on imaging while being examined for hypercalcemia. She was later found to have syndecan-1 positive metastatic lobular breast cancer, which mimicked a plasma cell neoplasm.

Case Report

The diagnostic process in this patient is summarized chronologically for clarity. The patient initially presented with fatigue, back pain, and hip pain, accompanied by hypercalcemia and elevated tumor markers. Radiological imaging revealed multiple lytic bone lesions, raising a strong clinical suspicion of plasma cell myeloma. Bone marrow aspiration and biopsy were subsequently performed and demonstrated plasmacytoid cells with CD138 positivity. However, further immunohistochemical evaluation and radiological correlation revealed a breast lesion, and additional breast-specific markers confirmed the diagnosis of metastatic lobular breast carcinoma involving the bone marrow. This clinical presentation (including hypercalcemia, multiple lytic bone lesions, and plasmacytoid morphology in bone marrow) closely mimicked plasma cell myeloma and therefore represented a significant diagnostic challenge.

A 71-year-old female patient had a medical history of fatigue, back pain, and hip pain that had been present for the past five months. Increases in the calcium concentration (Ca:11.8 mg/dl; NA=8.6-10.6 mg/dL)) and tumor marker CA15-3 level (111U/mL; NA= 0-34.5), CA19.9 level (65.8 U/ml; NA: 0-39) were detected in the serum. There was no cytopenia. Immunoglobulin levels (IgA: 3,04 g/L; NA= 0.7-4, IgG: 12 g/L; NA= 7-16, IgM: 0.99 g/L; NA: 0,4-2,3), creatinine concentration (0,62 mg/dl; NA=0.5-0.9) and erythrocyte sedimentation rate (26 mm/h; NA= <25), thyroid hormone tests (TSH:1.3 ng/dl; NA:0.27-4.20, T3:3.4 ng/dl;NA=2-4.4, T4:1.07 mlU/dl; NA:0.93-1.27), were in normal reference range. In the serum immunoelectrophoresis, the kappa/lambda ratio was intact (0,794g/L) and the monoclonal gammapathy was not detected (IgG:12.3 g/L; NA:7-16g/L, IgA:3.04 g/L; NA:0.7-4, IgM:0.99 g/L; NA:0.4-2.3). On the radiological imaging, there were mottled lucencies, compression fractures and multiple lytic bone lesions, evaluated as a malignant hypercalcemia. Simultaneously, with the preliminary diagnosis of a plasma cell myeloma, the radiological imaging, bone marrow aspiration and tru-cut biopsy were performed on the patient. Aspirated smears showed a large, mature plasma cell-like population with abundant basophilic cytoplasm, round eccentric nuclei, and nucleoli.

In the histological samples of bone marrow tru-biopsy, the plasmacytoid cells with eccentrically located nuclei, which fill the intertrabecular focal area in a nodular fashion, with distinguishable nucleoli and abundant eosinophilic cytoplasm, were observed (Figure 1A, 1B).

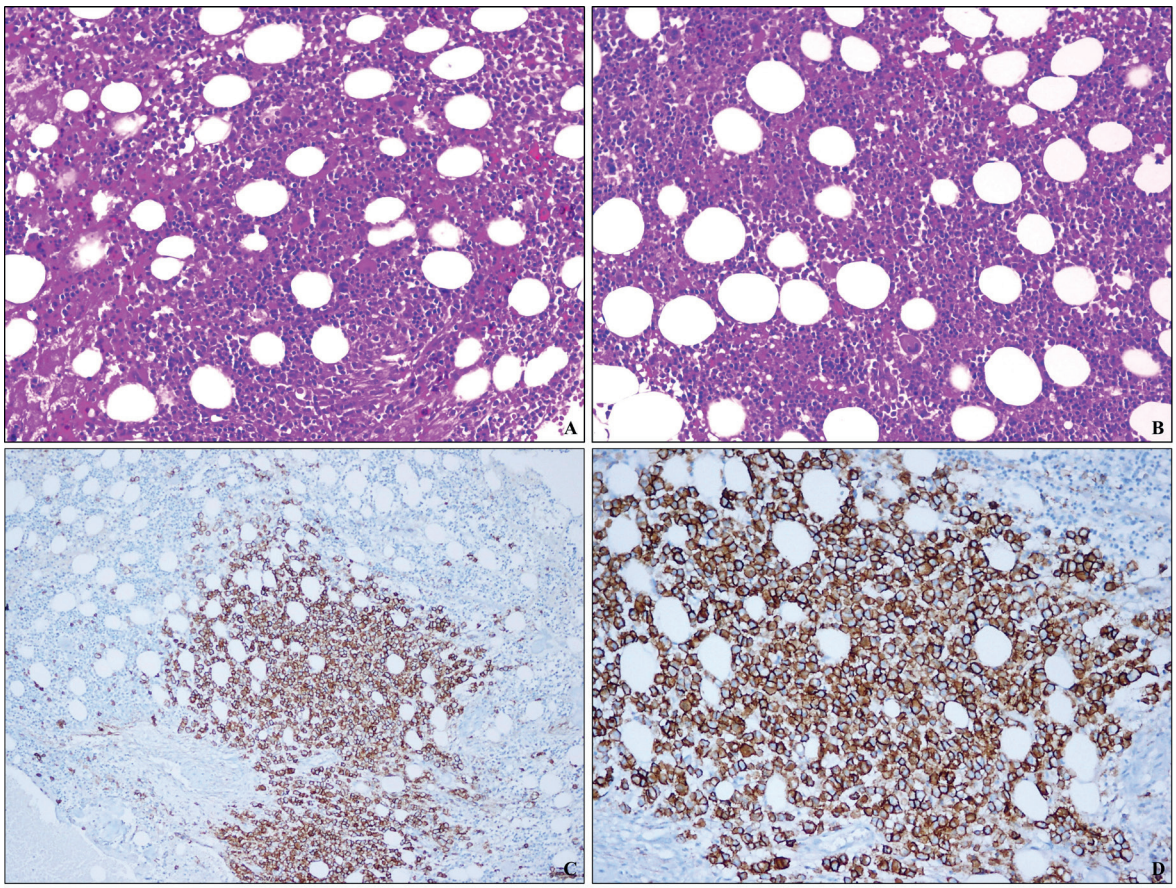


Figure 1. Representative light microscopic images (A, B) showing plasma cell-like neoplastic cells with abundant eosinophilic cytoplasm and eccentric nuclei in the bone marrow (H&E, ×200). Immunohistochemical staining demonstrates strong CD138 positivity in tumor cells (C, D; ×100, ×200).

Following the manufacturer's instructions and standard operating protocols, formalin-fixed, paraffin-embedded tumor tissue was subjected to immunohistochemical indicating using a monoclonal antibody against the CD138 (clone B-A18, 0.10 μg/ml, Cell Marque, Roche, USA), pancytokeratin (clone PCK26, 46.3 μg/ml, Ventana, Roche, USA), mammoglobulin (clone 31A5, 0.05 μg/ml, Cell Marque, Roche, USA), GCDFP-15 (clone EP1582Y, 0.32 μg/ml, Cell Marque, Roche, USA) and GATA-3 (clone L50-823, 1.49 μg/ml, Cell Marque, Roche, USA), cytokeratin 20 (clone SP33, 1.9 μg/ml, Ventana, Roche, USA), TTF-1 (clone SP141, 5,7μg/ml, Ventana, Roche, USA), Napsin A (clone MRQ-60, 1.6 μg/ml, Cell Marque, Roche, USA), PAX-8 (clone MRQ-50, 7 μg/ml, Cell Marque, Roche, USA), estrogen (clone SP1, 1 μg/ml, Ventana, Roche, USA), progesterone (clone 1E2, 1 μg/ml, Ventana, Roche, USA), HER2 (clone 4B5, 6 μg/ml, Ventana, Roche, USA), E-cadherin (clone 36, 0.314 μg/ml, Ventana, Roche, USA) and uroplakin (clone SP73, 0.013 μg/ml, Cell Marque, Roche, USA) antigen. The immunohistochemical panel and diagnostic interpretation are summarized in Table 1 for clarity.

Neoplastic cells observed in the bone marrow biopsy showed a positive reaction with CD138 (Figure 1C, 1D). No staining was observed with both kappa and lambda immunohistochemistry. Simultaneous examination of thorax computed tomography revealed an area of increased density in the subcutaneous tissue showing slightly increased FDG uptake in the retroareolar area of the left breast, and in the

Table 1. Immunohistochemical panel used in the diagnostic work-up

Marker	Clone	Result	Diagnostic implication
CD138 (Syndecan-1)	B-A18	Positive	Plasmacytoid morphology mimicking plasma cell neoplasm
Pancytokeratin	PCK26	Positive	Confirms epithelial origin
Mammoglobulin	31A5	Positive	Supports breast origin
GCDFP-15	EP1582Y	Positive	Supports breast carcinoma
GATA-3	L50-823	Positive	Strong marker of breast origin
CK20	SP33	Negative	Excludes colorectal origin
TTF-1	SP141	Negative	Excludes lung origin
Napsin A	MRQ-60	Negative	Excludes lung adenocarcinoma
PAX-8	MRQ-50	Negative	Excludes renal/gynecologic tumors
Estrogen receptor	SP1	Negative	Triple-negative phenotype
Progesterone receptor	1E2	Negative	Triple-negative phenotype
HER2	4B5	Negative	Triple-negative phenotype
E-cadherin	36	Negative	Consistent with lobular carcinoma
Uroplakin	SP73	Negative	Excludes urothelial origin

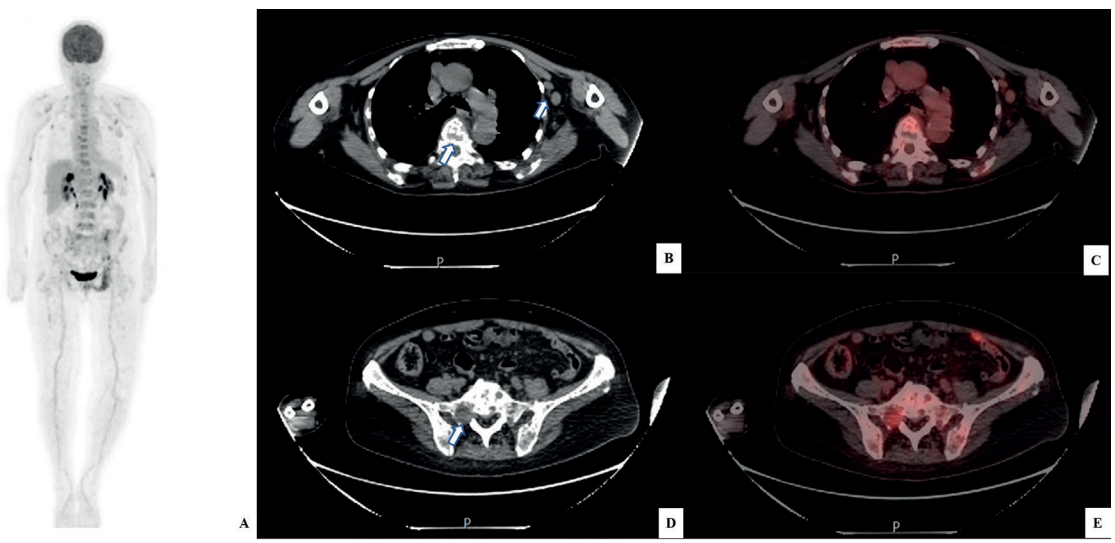


Figure 2. ^{18}F-FDG, PET/CT MIP image (A) revealed multiple FDG-avid metastatic tumor in the skeletal system (B, C); increased FDG uptake was observed in axillary lymph nodes (SUV_{max} 2.8); (D, E) increased FDG uptake was noticed in the right part of the sacrum (SUV_{max} 6.1).

skeletal system, including the sacrum, and in 4-5 lymphadenopathies (Figure 2). The largest of the lymph nodes is 2 cm in diameter and was detected in the left axilla. And while examining the bone marrow biopsy with ultrasound guidance, tru-cut biopsy was collected from the lymph nodes in the left breast and axilla. When a mass was detected in the breast, the immunohistochemistry for pancytokeratin (Figure 3A, 3B), mammoglobulin (Figure 3C), GCDFP-15 (Figure 3D) and GATA-3 were applied to the bone marrow biopsy due to the suspicion of metastasis, resulting in a positive reaction for each staining. The immunohistochemistry for cytokeratin, TTF-1, Napsin A, PAX-8, estrogen, progesterone, HER2, E-cadherin and uroplakin showed negative. Invasive lobular breast carcinoma and breast carcinoma metastasis in the axillary lymph node were detected in the tru-cut biopsy specimens of the patient's breast.

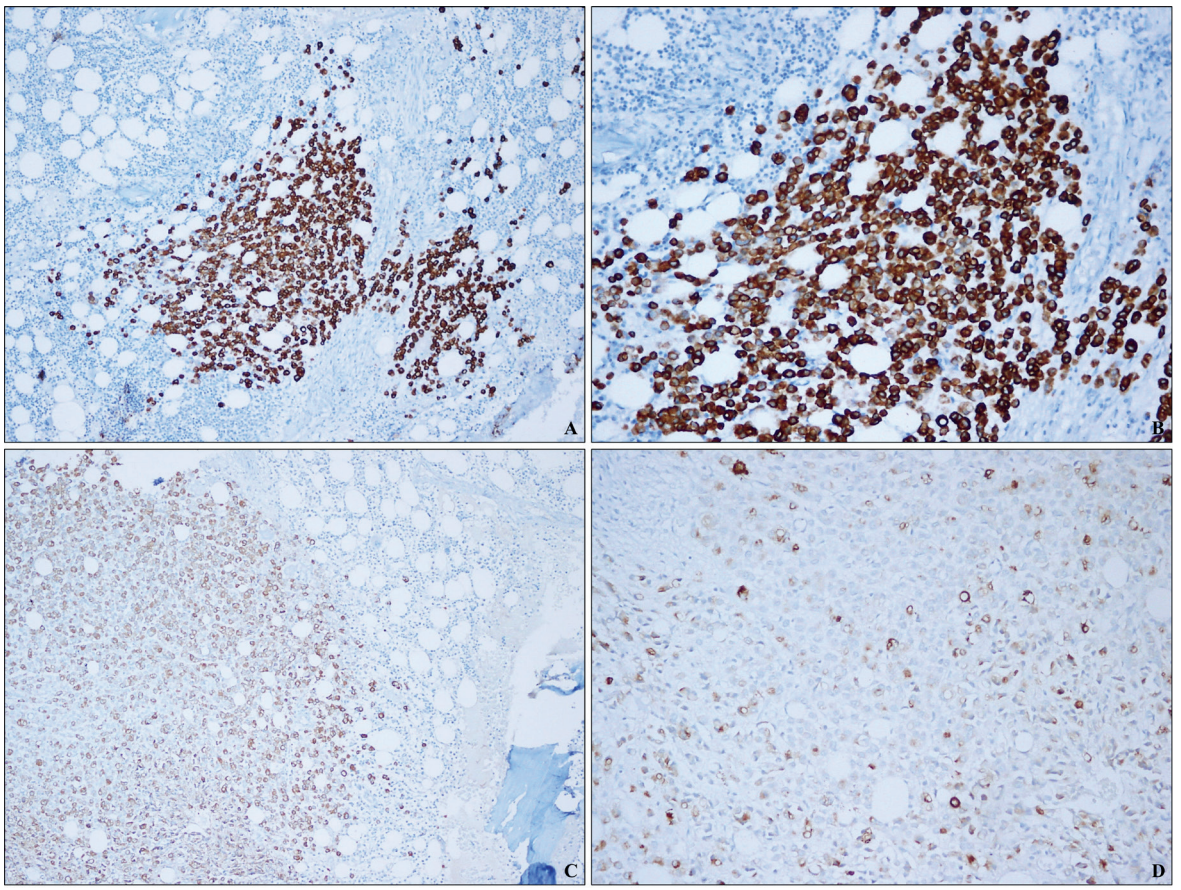


Figure 3. Representative light microscopic images of immunohistochemical staining (A, B) for pancytokeratin detected in tumor cells (x100, x200); (C) for mammoglobulin detected in tumor cells (x100); (D) for GCDFP-15 detected in tumor cells (x200).

In the light of these findings, plasmacytoid-like cells detected in the bone marrow biopsy were evaluated in favor of metastatic breast lobular carcinoma, which stained positively with CD138 and mimicked the plasma cell neoplasia.

Discussion

This case report highlights a unique diagnostic challenge involving a 71-year-old female patient who presented with symptoms of fatigue, back pain, and hip pain over the past five months, accompanied by hypercalcemia and multiple lytic bone lesions. Initially, plasma cell myeloma was suspected due to the radiological findings and the presence of CD138 (syndecan-1) positive cells in the bone marrow biopsy. However, further immunohistochemical analysis revealed that the lesion was a syndecan-1-positive metastatic lobular breast carcinoma mimicking plasma cell neoplasm. This rare presentation underscores the importance of considering metastatic breast cancer (BC), particularly lobular carcinoma, in the differential diagnosis when syndecan-1 is expressed, even when myeloma is strongly suspected.

BC-related deaths are predominantly driven by metastatic dissemination, which closely correlates with the molecular subtype of the originating tumor. Among the various forms of distant spread, bone marrow involvement carries a particularly grave prognosis and markedly restricted survival expectations. This underscores the critical need for reliable biomarkers capable of stratifying patients according to their metastatic

risk, thereby enabling earlier intervention and the development of more targeted therapeutic approaches. Emerging evidence has implicated syndecan-1 as a promising indicator of biologically aggressive BC behavior and unfavorable clinical trajectories (1-3,5). Nevertheless, the available literature predominantly addresses syndecan-1 expression in primary tumor settings, and findings remain inconsistent—likely attributable to heterogeneity in patient cohort selection and variability in methodological approaches. Within the framework of the cancer stem cell model, a distinct cellular population termed cancer-initiating cells is thought to drive both metastatic progression and disease relapse following systemic chemotherapy. Notably, marked upregulation of syndecan-1 has been identified in inflammatory breast cancer, an exceptionally aggressive BC variant (1,2,6). Herein, we report a bone marrow biopsy case initially evaluated under the presumptive diagnosis of myeloma, which was subsequently confirmed as lobular BC metastasis through positive syndecan-1 staining, and contribute this case to the existing literature along with its comprehensive histopathological and clinico-radiological characteristics. Based on our observations, syndecan-1 holds potential as a meaningful prognostic indicator, particularly in triple-negative breast tumors exhibiting an aggressive clinical course.

Primary and metastatic lesions exhibit distinct patterns of immunostaining intensity and location for Syndecan-1. In actuality, the majority of primary BCs exhibit broad cytoplasmic expression; in contrast, all metastatic lesions showed a particular expression pattern in their membrane staining. These results point to a shift in syndecan-1's cellular location during the metastatic phase. This could clarify how this biomarker helps neoplastic cells engraft onto the metastatic site and escape from the original site. Observations in the literature suggest that syndecan-1 plays a part in the intricate interactions between multiple myeloma cells and their bone marrow microenvironment (1,2,4,5). Similarly, in our case, diffuse strong membranous staining was detected in the metastatic lesion. As far as we researched in the English literature, our case was the second case in which this staining was detected in bone marrow localization and the first case reported in our country.

A few studies showed that Syndecan-1 expression in breast carcinoma (6-9) but only one of them (a meeting abstract) reported Syndecan-1 positivity in the bone marrow metastasis of lobular type of breast carcinoma6, which raised the controversy over the morphological similarities with myeloma. In their case report, they showed that the cells were Syndecan-1, cytokeratin 7 and 8/18, mammoglobulin, GATA-3, p120, estrogen receptor and positive (strong, 90%+) positive but cytokeratin 20, TTF-1/ Napsin, PAX-8, uroplakin, E-cadherin, progesterone and HER2 negative (6). Syndecan-1 positivity was observed in our case; however, our patient was triple-negative for estrogen, progesterone, HER2, suggesting a more aggressive type of breast carcinoma.

An additional noteworthy finding in this case is the triple-negative immunophenotype (ER-/PR-/HER2-). Triple-negative breast cancers are generally associated with more aggressive biological behavior, higher metastatic potential, and poorer prognosis compared with hormone receptor–positive tumors. Previous studies have suggested that syndecan-1 overexpression may be more frequently observed in aggressive breast cancer subtypes, including triple-negative tumors (6-9). Therefore, the strong membranous syndecan-1 expression observed in this case may reflect the aggressive metastatic potential of the tumor and may partly explain the unusual bone marrow involvement.

Syndecan-1 expression is downregulated in metastatic lesions, and it localizes selectively to the membrane. These findings corroborate earlier findings in different epithelial cancers and suggest a potential function for syndecan-1 reduction in the metastatic process. Additionally,

there is a correlation between the BC intrinsic subtype of metastatic lesions and the pattern of syndecan-1 expression, with a more diffuse immunostaining pattern in triple negative lesions (with or without hormone receptor positive). Consistent with the strong surface expression, overexpression of syndecan-1 shows promise as a dependable marker for the detection of BC cells. And also, this case report emphasizes that Syndecan-1 positivity in metastatic lobular breast carcinoma with plasmacytoid morphology may be confused with myeloma and definitive diagnosis may be difficult.

Finally, from a practical diagnostic perspective, this case highlights the limitations of relying on CD138 expression alone in the evaluation of plasmacytoid cells within bone marrow biopsies. Although CD138 is widely used as a plasma cell marker, it can also be expressed in epithelial malignancies, including breast carcinoma. Therefore, when plasmacytoid cells are identified in bone marrow specimens, especially in patients presenting with hypercalcemia and lytic bone lesions, a broader immunohistochemical panel should be considered. The inclusion of epithelial markers (such as pancytokeratin) and breast-specific markers (GATA-3, mammaglobin, GCDFP-15) can be crucial for distinguishing metastatic carcinoma from plasma cell neoplasms and preventing potential diagnostic pitfalls.

In conclusion, this case illustrates an important diagnostic pitfall in the evaluation of plasmacytoid cells in bone marrow biopsies. The presence of hypercalcemia, multiple lytic bone lesions, and CD138 positivity may strongly suggest plasma cell myeloma; however, metastatic carcinomas—particularly lobular breast carcinoma—should also be considered in the differential diagnosis. Recognition of this possibility and the use of a comprehensive immunohistochemical panel including epithelial and breast-specific markers are essential to avoid misdiagnosis and ensure appropriate clinical management.

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Ethical approval

This study was conducted according to the Helsinki principles, the patient signed the consent for the participation and nothing offensive was done against the patient's privacy. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

Author contribution

The authors confirm contribution to the paper as follows: Study conception and design: BYB; data collection: BYB, EBT, SI; analysis and interpretation of results: BYB, NZC draft manuscript preparation: BYB. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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