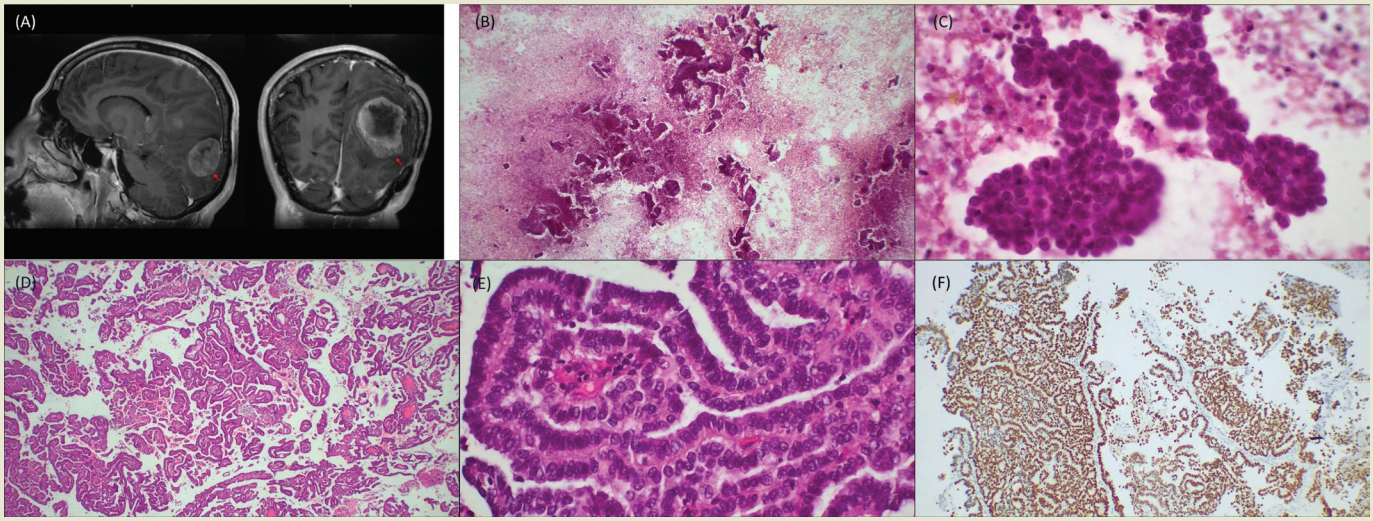
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BRIEF REPORT

Acinic cell carcinoma mimicking Warthin's tumor: A diagnostic challenge on fine-needle cytology

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Abstract

The cytologic diagnosis of acinic cell carcinoma (ACC) can be challenging due to its polymorphous appearance and sharing cytomorphologic characteristics with other benign and malignant neoplasms as well as non-neoplastic diseases, even though various histomorphological aspects of ACC have been documented. We presented a 39-year-old female patient applied with right pre-auricular parotid swelling spreading infra-auricular region which was gradually increased in size for 3 months. Ultrasonographic examination revealed hypoechoic well-circumscribed mass with 17 × 22 × 29 mm size. Magnetic resonance imaging revealed intra-parotid solid lesion with cystic areas, slightly hypointense on T1 and hyperintense on T2 weighted images. The mass was pushing the retromandibular vein medially, still lateral to it in the caudal images, but in dumbbell-shape spreading through parapharyngeal space in superiorly cranial images. Fine-needle aspiration cytology was also performed with guidance of ultrasonography. The cytological examination of the lesion was characterized by the predominance of heterogeneous lymphoid cells, clusters of epithelial cells with a variety of cytologic appearances, including granular, transparent, vacuolated, and oncocytic, and the presence of numerous naked nuclei with a protein-like foamy background. Due to intense lymphocytic inflammation, it was considered as benign primary parotid tumor such as Warthin's tumor. The excision material was examined histopathologically. Immunohistochemical analysis showed that this carcinoma was positive for DOG1, SOX10, cytokeratin 7 and negative for mammaglobin. This salivary gland tumor was reported as a rare variant of ACC with lymphoid-rich stroma. To improve the diagnostic accuracy, various morphological aspects of ACC should be considered in the pathological practice.

KEYWORDS
acinic cell carcinoma, lymphoid-rich stroma, salivary gland cytology, Warthin's tumor

1 | INTRODUCTION

The diagnosis and treatment of salivary gland tumors can be determined with the help of fine-needle aspiration (FNA) cytology. Studies have verified the validity of FNA in a first diagnostic paradigm, particularly for the salivary gland lesions that are palpable.[1,2] It is a safe and economical diagnostic tool. 1%–6% of all parotid gland neoplasms are acinic cell carcinomas (ACC) which are known as low-grade cancers. The age of patients with ACC ranges from 14 to 79 years old, with a predominance of females. The acinar cellularity of a well-differentiated ACC without pleomorphism is remarkably similar to the cellularity of a hyperplastic or normal salivary gland, making it challenging to distinguish this tumor based on the cytology. The primary distinction is that acinar cells coexist with adipose tissue and ductal epithelial cells in a normal salivary gland.[2,3] On the histology for ACC, a number of morphologic patterns, such as solid, microcystic, follicular,

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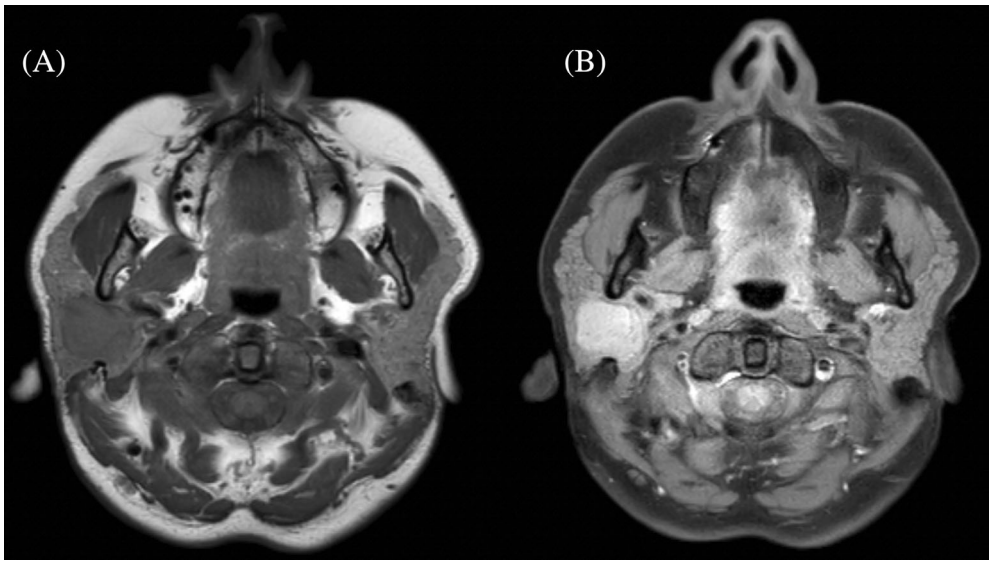


FIGURE 1 A right intra-parotid retromandibular solid mass lesion slightly hypointense on T1 (A) and hyperintense on T2 (B) weighted images.

and papillary-cystic patterns, have been described. And another uncommon but well-known type of ACC is the one with lymphoid-rich stroma.[4,5] Although the histomorphological characteristics of this type are widely understood, FNA diagnosis can be difficult due to mimicking to other benign salivary gland neoplasms including Warthin's tumor.[2] The cytologic characteristics of this type of ACC were reported rarely in the literature.[1–3] In here, we reported the most significant cytological characteristics of an uncommon ACC variant with lymphoid stroma. To our knowledge, this is the first case report from Turkey in the English literature presenting this ACC variant with both cytological and histopathological findings.

2 | CASE PRESENTATION

A 39-year-old female patient applied to our Otorhinolaryngology out-patient department with main complaint of a right pre-auricular parotid swelling spreading infra-auricular region which was gradually increased in size for 3 months. She also complained of intermittent mild pain in this region. On the physical examination, the mass was 2 × 3 cm in size, solid in consistency, mildly mobile and non-tender. The mass was relatively deep located on palpation. Neither lymphadenopathy nor facial paralysis was detected in the patient. Ultrasonographic examination revealed a 17 × 22 × 29 mm in size hypoechoic well-circumscribed mass. Magnetic resonance imaging (MRI) performed revealed an intra-parotid solid lesion 19 × 37 mm in size, slightly hypointense on T1 and hyperintense on T2 weighted images (Figure 1) which has cystic areas in lesion. The mass was pushing the retromandibular vein medially, still lateral to it in the caudal images, but the mass was dumbbell-shaped and spreading through the parapharyngeal space in superiorly cranial images (Figure 2). A FNA cytology was also performed with guidance of ultrasonography.

Cytological features consisting of a high percentage of cellularity were observed in the smears (Figure 3). A single population of neoplastic cells with abundant, finely granular to vacuolated cytoplasm,

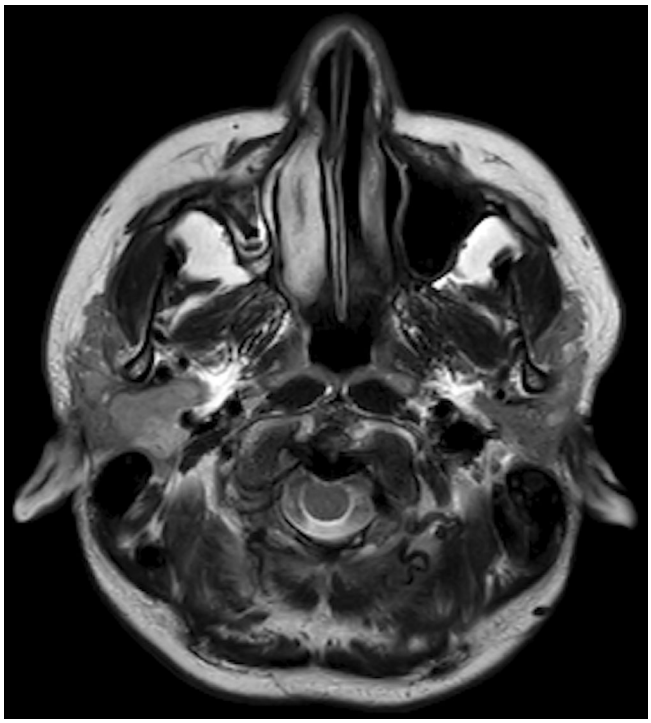


FIGURE 2 The mass was deeply located in more cranial images, and was reaching the right parapharyngeal space.

and single centrally located nucleus with prominent nucleoli were detected in the specimen. Moreover, there were also three-dimensional collections of tumor cells, some of which showed indistinct acinar differentiation. Some of these tumor cells were characterized by abundant eosinophilic granular cytoplasm in some areas had oncocytic appearance. The background showed predominantly a heterogeneous population of reactive lymphoid cells. Due to intense lymphocytic inflammation, it was thought that the case could have benign primary parotid tumor such as Warthin's tumor (Figure 3).

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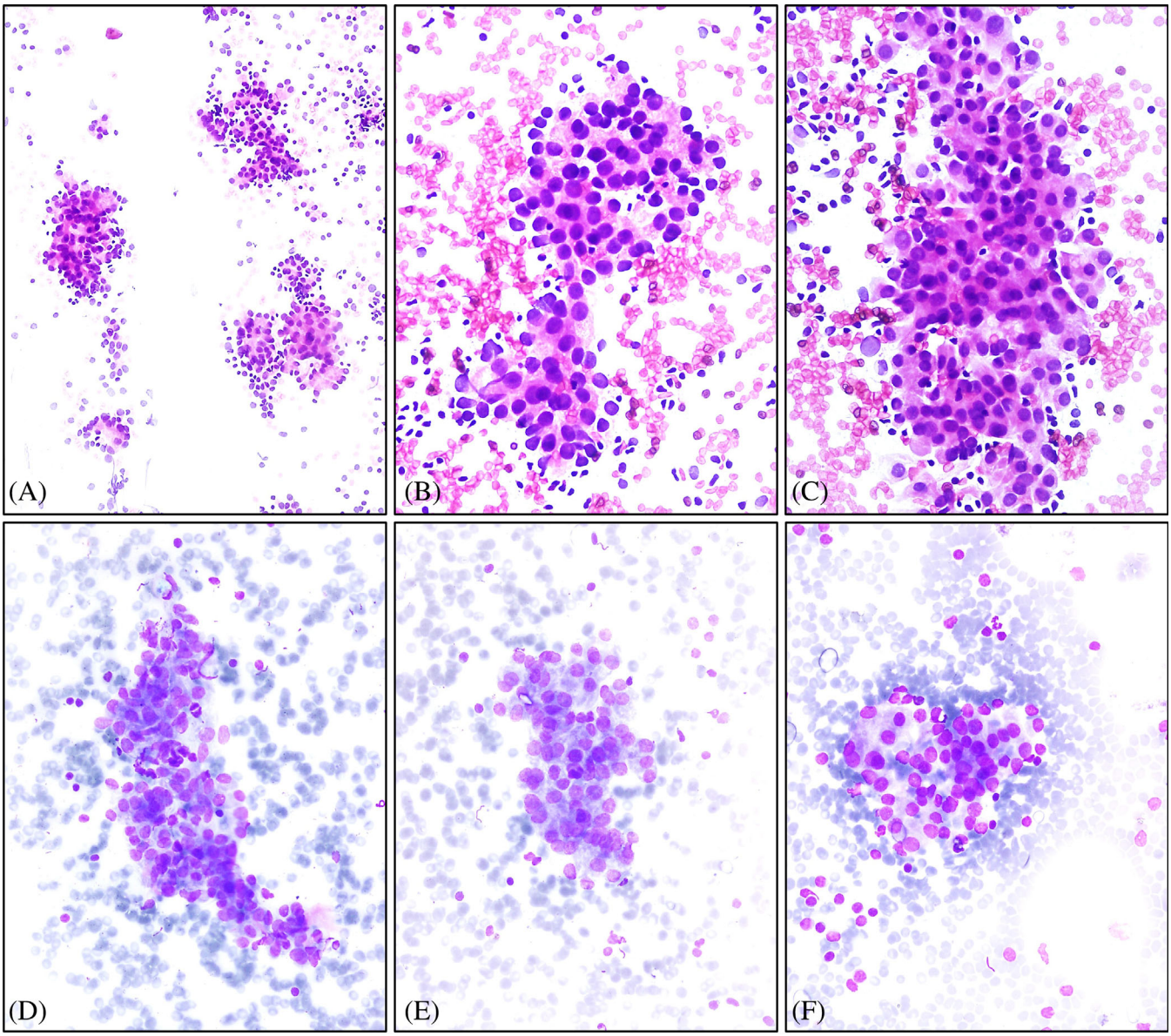


FIGURE 3 (A) Cell clusters in the background of lymphoid cells in aspiration smears (×200, Papanicolaou stain). (B) Round to oval eccentric nucleus with opened-up chromatin, oval to polygon-shaped cells in clusters with moderately granular cytoplasm (×400, Papanicolaou stain). (C). Oval to polygonal cells with minor nuclear atypia, and a few cells with a nucleolus and, an eccentric nucleus with fine granular chromatin (×400, Papanicolaou stain). (D–F). Representation of the described cell clusters with the May Grunwald Giemsa stain (×400, May Grunwald Giemsa stain). [Color figure can be viewed at wileyonlinelibrary.com]

Subsequently, the patient underwent a right partial parotidectomy which was containing cervical lymph nodes at level 1 and 2 superficial parts and most of level 4. The mass located just over the facial truncus was solid, spreading medially and reaching the deep lobe of the parotid gland to the parapharyngeal space. Identification of the main truncus of facial nerve and dissecting its branches was challenging because of the position of mass, but a nerve protecting excision could be done, and all of the branches were intact checked by facial nerve stimulation during surgery and monitoring at the end of the surgery. The mass was totally excised with large amount of surrounding parotid tissue. The facial nerve functions were normal after the surgery, and no other complications were noted.

The sections from formalin fixed and paraffin-embedded tissues in 2.5 μm thickness were stained with hematoxylin and eosin (H&E). Microscopically, the histologic sections revealed a well-defined lesion encircled by a delicate fibrous capsule. The lesion was made up of microcystic and solid-patterned clusters of neoplastic acinar cells within a dense lymphoid infiltrate (Figure 4A). The neoplastic cells had numerous foamy cytoplasmic bodies with fine granularity, prominent nucleoli, and central nuclei (Figure 4B). The microcysts included a foamy substance with a protein-like composition. Serous acinar differentiation and cytoplasmic granules became more prominent with periodic acid-Schiff (PAS) stain (Figure 4C). Immunohistochemical analysis showed that this carcinoma was positive for DOG1

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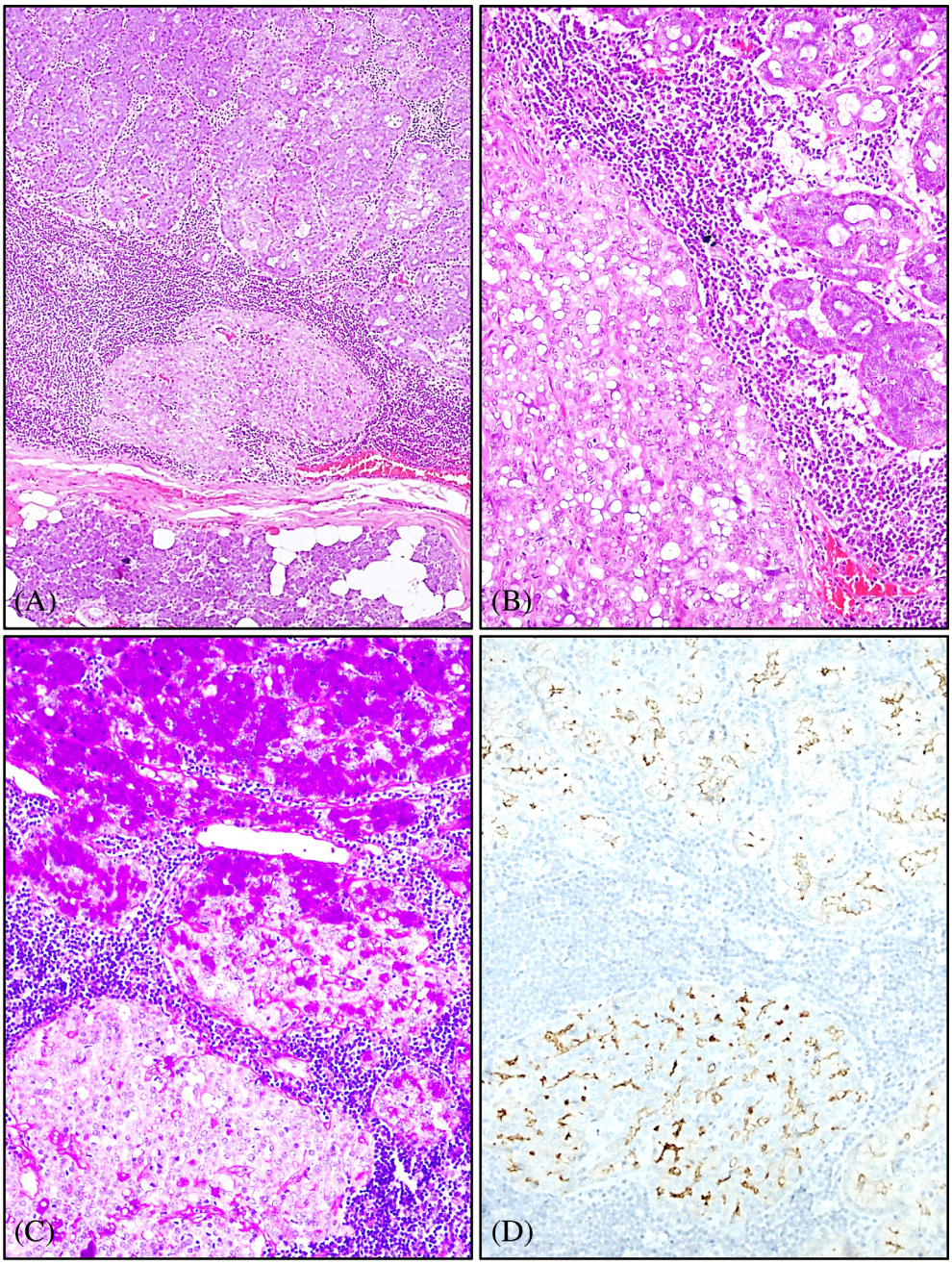


FIGURE 4 (A) Light microscopic images of dense lymphoid stroma with solid and microcystic growth pattern, surrounding malignant epithelial component, well-developed germinal centers (H&E, ×100; note that it has a thin capsule and normal salivary gland at the bottom). (B) Higher magnification of Figure 4A (H&E, ×200). (C) Positive staining of cytoplasmic granules for periodic acid-Schiff (×200). (D) Immunohistochemical staining for DOG1, strong and diffuse positivity as well as intercanalicular positivity (×200). [Color figure can be viewed at wileyonlinelibrary.com]

(Figure 4D), SOX10, cytokeratin 7 (CK7) and negative staining for mammaglobin. With these findings, the case was reported as ACC with lymphoid-rich stroma.

3 | DISCUSSION

A useful method with good diagnostic accuracy for distinguishing the neoplastic diseases from non-neoplastics is FNA cytology from the parotid gland lesions. ACC is a low-grade malignant tumor that mainly affects the parotid gland. The cytologic diagnosis of ACC can be challenging due to its polymorphous appearance and this neoplasm shares the cytomorphologic characteristics with other benign and malignant neoplasms as well as non-neoplastic diseases, even though various histomorphologic aspects of ACC have been documented in the literature.[4–6] The presence of neoplastic acinar cells is the primary cytologic finding that suggests ACC. Although various variations, such as clear or vacuolated cells and oncocytic cells, may also be detected in the smears, these neoplastic cells have round to polygonal shape with a granular cytoplasm.[2,7] Considering the variants when making a cytological diagnosis of AciCC, sialadenitis can be considered in normal non-neoplastic lesions and reported as "Milan category II." Or, as in our case, it may be considered as a Warthin tumor due to the dense lymphoid stroma and diagnosed as "Milan category III." Or it may be compared to a benign salivary gland tumor (such as cellular pleomorphic adenoma) and reported to the clinician as "Milan category IVa."[8]

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However, as in our case, it is difficult to define the cytology of rare variants according to the common variants of ACC.

Although serous acinar cell differentiation is what defines ACC, it is known that several cell types and cyto-histomorphologic development patterns exist. These growth patterns include acinar, intercalated ductal, vacuolated, clear, and non-specific glandular and solid/lobular, microcystic, and papillary-cystic ones. The uncommon variant known as "ACC with lymphoid-rich stroma" accounts for 10%–29% of all ACC cases. There are often two subcategories within this variation. The first subcategory has a microcystic development pattern and dense lymphoid stroma with well-established germinal centers surrounding a sparse epithelial component. A substantial lymphoid stroma with germinal centers is present in the second subcategory as well, but its distribution is less uniform than in the first and its epithelial architecture is not microcystic.[1–3] The level of proliferation activity for "the well-differentiated ACC with lymphoid stroma" ranges from 0.5% to 3.7%, indicating low levels of proliferative activity. On the other hand, "the conventional ACC" indicated increased proliferative activity ranging from 3.4% to 45%.[1] Similarly, in our case, the neoplasm consisted of single, well-circumscribed nodules surrounded by a thin fibrous capsule. The stroma contained a diffuse infiltrate of mature lymphocytes with numerous well-formed germinal centers, especially dense at the margins. Tumor cells were arranged in solid sheets and microcystic patterns. Cellular morphology was uniform as there was no significant pleomorphism and mitotic figures were extremely scant.

In this case report, we emphasize that AciCC with lymphoid-rich stroma is less common than other variants, therefore, it is difficult to differentiate cytologically, and there is no published report from Turkey so far with its cytology. Recognizing this variant is important from a clinical standpoint since it can result in severe therapeutic mistakes. A lymphoid-rich stroma in ACC may give the tumor a heterogeneous appearance.[2,3,7,9] Furthermore, a lymphoid-rich background may cause a challenge in diagnosis of ACC as compared to other cancers. It may be considered mistakenly as a neoplasia with regional lymph node involvement, causing unnecessary treatment of lesion which is related to the morbidity. ACC can be confused with primary salivary gland tumors such as Warthin's tumor, oncocytoma, mucoepidermoid carcinoma, epithelial-myoepithelial carcinoma, and metastatic tumors of salivary glands such as renal cell carcinoma metastasis to the lymph node.[1,2,9–11] In the present case, we mistakenly diagnosed the patient as Warthin tumor cytologically.

Characteristic cytologic features of Warthin tumor include the combined presence of oncocytes with or without squamous/mucinous metaplastic cells and lymphocytes in a proteinaceous background. In AciCC cases, true oncocytes are rare, as found in most cytological Warthin tumor samples.[8,12] Clinicopathological features are helpful in differentiating between the two types of tumors because, unlike AciCC, which has lymphoid-rich stroma, Warthin's tumor primarily affects males aged 50–60 who have smoked cigarettes. It also usually develops in the contralateral parotid glands. Present case was a young and female patient. Additionally, we observed the epithelial cell clusters in the background of lymphoid cells in the cytological smears. These cells had oval to polygonal shape in clusters with moderate amount of granular cytoplasm, and round to oval eccentric nuclei containing unfolded chromatin. Cytologically, Warthin's tumor was mistakenly considered to be in the background because of the extensive lymphocytic inflammation and occasional oncocytoid cell groups. Excisional biopsy of parotid lesion was performed for the definitive diagnosis.

Consisting mainly of large polygonal cells with abundant clear cytoplasm, a marked variation in nuclear size with smooth nuclear contours and prominent nucleoli, the clear cell oncocytoma is very difficult to distinguish from ACC. Cells in the ACC may have granular, vacuolar, and clear cytoplasm; in clear cell oncocytoma, an interspersed population of classical oncocytes can be observed.[1,2,7] Even these clear cells in the ACC may also be misinterpreted as mucosecretory cells of low-grade mucoepidermoid carcinoma (MEC). It is important to examine the epidermoid cells, intermediate cells, and mucus-producing cells in smears for the cytological diagnosis of MEC and to distinguish from ACC.[10] If the clear cell component of an epithelial myoepithelial carcinoma is predominant, it may cause confusion in distinguishing cytologically small basaloid epithelial cells from ACC. The epithelial cells in the ACC are round cells with small central nuclei and vacuolated cytoplasm. Small basoloid cells are not found in ACC.[2] Highly cellular cytological smears were found in our patient's cytological characteristics. The polymorphic reactive lymphoid cells made up the majority of the specimen. There was a single population of neoplastic cells in the background, each with a single central nucleus with conspicuous nucleoli, and an abundance of fine-grained to vacuolated cytoplasm. Cells with an abundance of eosinophilic granular cytoplasm were present locally. After resection, the cytological smears were re-examined and scarce cells with naked nuclei were observed.

Another tumor cytomorphologically similar to AciCC with lymphoid-rich stroma is Warthin-like MEC. This rare variant is characterized histopathologically by the presence of marked lymphocytic infiltration and cystic changes resembling Warthin's tumor. Similar to conventional MEC, Warthin-like MEC is composed of intermediate-sized neoplastic cells with a variable number of mucinous cells present. The presence of cystic contents, including a backdrop of mucus and proteinaceous material, and the number of lymphocytes is the defining cytological features. There are visible squamous, intermediate, and mucinous cells. Nuclear atypia in MEC that resembles Warthin is modest. In the Warthin-like MEC cases reported in the literature, no oncocytic cells are found.[13] Several cytologic features of our case report that can be helpful in the differential diagnosis are summarized in Table 1 which is adapted from the study of Klijanienko and Vielh.[12]

Since the cytology of mammary analogue secretory carcinoma (MASC) shares many characteristics with ACC, it is particularly challenging to distinguish between zymogen granule-poor ACC and MASC without molecular analysis or immunohistochemical analysis.[8] The presence of papillary structure, extracellular and intracellular mucinous material, vacuolated cytoplasm, tumor cells with low-grade nuclear atypia, and extensive vascularity, however, seem to be some cytological characteristics indicative of MASC. The cytoplasmic vacuoles' larger size variability, abundant extracellular and intracellular

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TABLE 1 Key cytological features of selected salivary gland tumors.

		ACC	WT	Cellular PA	MEC, clear cell	MEC, WT-like	Oncocytoma	EMEC	MASC
Tumor background	Lymphocytic	Rare	Common	Absent	Rare	Common	Absent	Rare	Rare
	Mucoid	Absent	Absent	Rare/absent	Common	Rare/absent	Absent	Absent	Mild/common
	Chondromyxoid	Absent	Absent	Rare	Absent	Absent	Absent	Absent	Absent
Tumor cell types	Myoepithelialc	Absent	Absent	Common	Absent	Absent	Absent	Rare/absent	Absent
	Vacuolated/clear	Common	Rare/absent	Absent	Rare/absent	Absent	Rare/absent	Rare	Common
	Acinic	Common	Absent	Absent	Absent	Absent	Absent	Absent	Absent
	Ductlike	Common	Absent	Absent	Rare/absent	Rare/absent	Rare/absent	Rare	Rare/absent
	Squamous	Absent	Rare/absent	Rare/absent	Common	Rare/absent	Absent	Absent	Absent
	Naked nuclei	Rare/absent	Absent	Absent	Rare/absent	Rare/absent	Rare/absent	Rare/absent	Rare/absent
	Atypia	Rare/absent	Absent	Rare/absent	Common	Rare/absent	Rare/absent	Rare/absent	Rare/absent

Abbreviations: ACC, acinic cell carcinoma; EMEC, epithelial-myoepithelial carcinoma; MASC, mammary analogue secretory carcinoma; MEC, mucoepidermoid carcinoma; WT, Warthin's tumor.

mucin, and clinical information like the patient's gender and the tumor's anatomic location are the subtle signs for differentiating MASC from ACC. Another crucial factor is the lack of basophilic cytoplasmic granules in MASC. DOG1 expression in salivary gland tissue was discovered to be mostly concentrated in salivary acini. All ACCs showed positive DOG1 staining by immunohistochemistry as well. ACC can be distinguished from MASC by the presence of strong, diffuse, and intercanalicular positivity for DOG1.[8] Molecular studies could not be performed for the differential diagnosis of ACC in our institute. Since the cell block was not obtained from cytological materials, an immunocytochemical study could not be performed, but a diffuse, strong, intercanalicular reaction was observed in DOG1 immunohistochemical staining applied to the resection material.

4 | CONCLUSION

In this case report, the ACC variant is characterized by the predominance of heterogeneous lymphoid cells, clusters of epithelial cells with a variety of cytologic appearances, including granular, transparent, vacuolated, and oncocytic, and the presence of numerous naked nuclei with a protein-like foamy background. The cytologic diagnosis of ACC can be challenging due to its polymorphous appearance and this neoplasm shares the cytomorphologic characteristics with other benign and malignant neoplasms as well as non-neoplastic diseases. To improve the diagnostic accuracy, various morphological aspects of ACC should be considered in the pathological practice.

AUTHOR CONTRIBUTIONS

Busra Yaprak Bayraka, Murat Ozturk collected the data and drafted the manuscript. Busra Yaprak Bayraka, Murat Ozturk edited the manuscript, participated in the study design and coordination. All authors read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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REFERENCES

1. Sharma A, Ahuja S, Diwaker P, Wadhwa N, Arora VK. Acinic cell carcinoma of the parotid gland: a diagnostic dilemma on cytology. *Malays J Pathol*. 2019;41(2):191-194.
2. Mir F, Rohra P, Aakash N, et al. Acinic cell carcinoma of the salivary gland associated with lymphoid-rich stroma. A diagnostic dilemma on cytology: study of two cases. *Diagn Cytopathol*. 2021;49(2):E55-E59.

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3. Nagel H, Laskawi R, Büter JJ, Schröder M, Chilla R, Droese M. Cytologic diagnosis of acinic-cell carcinoma of salivary glands. *Diagn Cytopathol*. 1997;16(5):402-412.
4. Cole GG, Salgado CM, Vargas de Stefano D, et al. Morphologic and ancillary studies of pediatric Acinic cell carcinoma: a single institute experience. *Head Neck Pathol*. 2023;17(1):204-209.
5. Michal M, Skalova A, Simpson RHW, Leivo I, Ryška A, Starek I. Well-differentiated acinic cell carcinoma of salivary glands associated with lymphoid stroma. *Hum Pathol*. 1997;28(5):595-600.
6. Liu Z, Pan C, Yin P, Liao H. Well-differentiated acinic cell carcinoma with lymphoid stroma associated with osteoclast-like giant cells of the parotid gland in children: a case report and literature review. *Int J Clin Exp Pathol*. 2018;11(3):1770-1776.
7. Orell SR. Diagnostic difficulties in the interpretation of fine needle aspirates of salivary gland lesions: the problem revisited. *Cytopathology*. 1995;6(5):285-300.
8. Singh G, Jahan A, Yadav SK, Gupta R, Sarin N, Singh S. The Milan system for reporting salivary gland cytopathology: an outcome of retrospective application to three years' cytology data of a tertiary care hospital. *Cytojournal*. 2021;6(18):12.
9. Inaba T, Fukumura Y, Saito T, et al. Cytological features of mammary analogue secretory carcinoma of the parotid gland in a 15-year-old girl: a case report with review of the literature. *Case Rep Pathol*. 2015;2015:656107.
10. Kumar N, Kapila K, Verma K. Fine needle aspiration cytology of mucoepidermoid carcinoma. A diagnostic problem. *Acta Cytol*. 1991;35(3):357-359.
11. Palma O, Torri AM, de Cristofaro JA, Fiaccavento S. Fine needle aspiration cytology in two cases of well-differentiated acinic-cell carcinoma of the parotid gland. Discussion of diagnostic criteria. *Acta Cytol*. 1985;29(4):516-521.
12. Klijanienko J, Vielh P. Fine-needle sample of salivary gland lesions. V: Cytology of 22 cases of acinic cell carcinoma with histologic correlation. *Diagn Cytopathol*. 1997;17(5):347-352.
13. Noda Y, Ishida M, Okano K, et al. Fine-needle aspiration cytology of Warthin-like mucoepidermoid carcinoma: a case report with cytological review. *Mol Clin Oncol*. 2022;16(1):5.

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