

# Acinic cell carcinoma of parotid gland with prominent lymphoid stroma: A diagnostic dilemma

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## ABSTRACT

“Acinic cell carcinoma (ACC) with lymphoid stroma” represents a separate subgroup of salivary gland tumors with a thin fibrous capsule, a microfollicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component. Lack of familiarity with this entity may create diagnostic problems. Recognition of this rare histologic variant is also important because it behaves far less aggressively than the conventional ACC. We describe cytological and histological findings in one such rare occurrence in the parotid gland of a 27-year-old female. Fine-needle aspiration of this mass revealed cohesive clusters of relatively uniform cells revealing mild pleomorphism, nuclear overlapping, frequent microacinar pattern, abundant granular/vacuolated/foamy/oncocytoid basophilic cytoplasm with ill-defined cytoplasmic borders. Background showed small mature lymphocytes, reactive lymphoid cells and lymphohistiocytic aggregates. Histopathological examination of resected tumor ACC with tumor cells containing periodic acid-Schiff positive diastase resistant granules arranged predominantly in microcystic pattern and surrounded by dense lymphoid stroma containing lymphoid follicle with prominent germinal centers.

**Key words:** Acinic cell carcinoma, lymphoid stroma, parotid

## INTRODUCTION

Acinic cell carcinoma (ACC) is rare salivary gland cancer comprises 1-3% of all salivary gland tumors. They are predominantly seen in the parotid gland, but many examples in the minor salivary gland have been recorded. Rare cases of ACC located within intraparotid lymph nodes have been reported.<sup>[1,2]</sup> Marked lymphocytic infiltrate is a common feature in ACC.<sup>[3]</sup> However, ACC with lymphoid stroma represents a separate subgroup with a thin fibrous capsule, a microfollicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component.<sup>[3]</sup> Lack of familiarity with this entity may create diagnostic problems on fine-needle aspiration (FNA)

cytology and are sometimes misdiagnosed as chronic sialadenitis.<sup>[4]</sup> In fact, this neoplasm can also be mistaken for other malignant, more aggressive neoplasms. Recognition of this rare histologic variant is also important because it behaves far less aggressively than the conventional ACC. We herein report one such case of a 27-year-old female, presenting with swelling in the right parotid region since 1 year. In addition, we discuss the diagnostic dilemma associated with such cases.

## CASE REPORT

A 27-year-old female patient presented with a swelling in the right parotid region since 1½ year, which was insidious in onset and progressive in nature. The swelling was not associated with pain. On local examination, there was a firm, nontender, round swelling with a smooth surface measuring 2 × 2 cm in size. Computed tomography scan revealed a well-defined, round, lobulated lesion of 1.9 × 2.3 cm in size, located in the deep lobe of right parotid gland. FNA of this mass revealed cohesive cluster of relatively uniform cells revealing mild pleomorphism, nuclear overlapping, frequent microacinar pattern, eccentrically placed round

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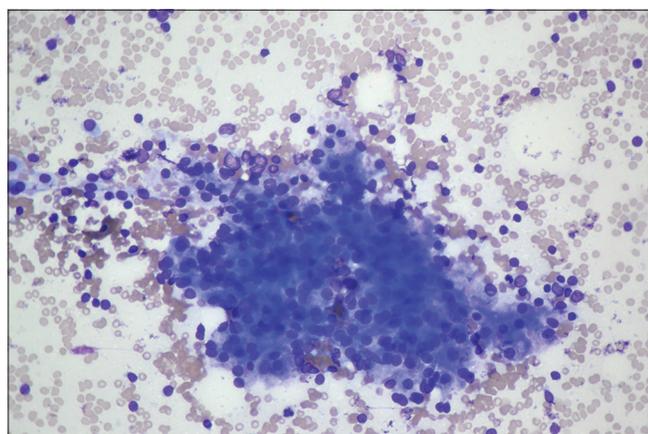
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to ovoid nuclei with bland nuclear chromatin, tiny nucleoli, abundant granular/vacuolated/foamy/oncocytoid basophilic cytoplasm with ill-defined cytoplasmic borders. Background was bloody, but clean and showed small mature lymphocytes, reactive lymphoid cells, and lymphohistiocytic aggregates [Figure 1]. Cytological diagnosis of ACC of parotid was given and right parotidectomy was done. On gross examination, deep lobe of parotid showed a well-circumscribed growth measuring 2 × 2 cm with uniformly grey white cut surface. Histopathological examination of the resected tumor revealed ACC with tumor cells containing periodic acid-Schiff (PAS) positive diastase resistant granules arranged predominantly in microcystic pattern and surrounded by dense lymphoid stroma containing lymphoid follicle with prominent germinal centers [Figure 2].

## DISCUSSION

Acinic cell carcinoma is a rare salivary gland tumor. The variant with lymphoid stroma is even rarer.<sup>[5]</sup> Marked lymphocytic infiltrate is a common feature in ACC.<sup>[3]</sup> However, ACC with lymphoid stroma represents a separate subgroup with a thin fibrous capsule, a microfollicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component.<sup>[3]</sup> Recognition of this rare histologic variant is also important because it behaves far less aggressively than the conventional ACC.<sup>[6]</sup>

Nagel *et al.*<sup>[7]</sup> studied cytologic findings in fine-needle aspiration biopsy obtained from 40 primary and 18 recurrent ACC. Cytomorphologically, ACC is characterized by acinar differentiated tumor cells. In addition to these diagnostic clue cells, other types of neoplastic cells including vacuolated cells, cells resembling oncocytes, and nonspecific glandular cells are encountered.



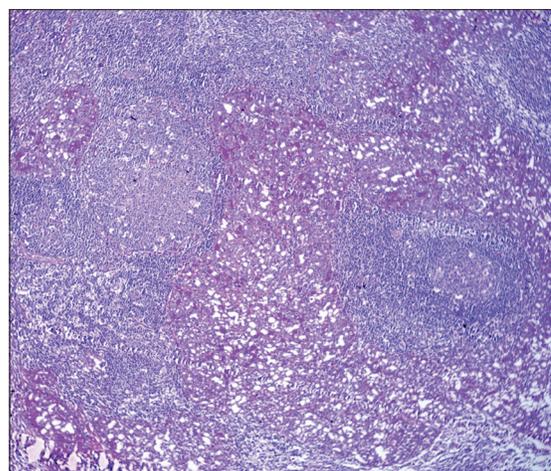
**Figure 1:** Higher magnification revealing cohesive clusters of relatively uniform cells revealing mild pleomorphism, frequent microacinar pattern, eccentrically placed round to ovoid bland nuclei abundant foamy cytoplasm and ill-defined cytoplasmic borders (Giemsa stain, ×40)

A pronounced lymphocytic reaction is a hallmark in 10% of ACC aspirates. Both the variety of tumor cell differentiation and the pronounced lymphocytic reaction observed in ACC aspirates may result in confusion with other salivary gland lesions.

A separate subgroup of ACC with a thin fibrous capsule, a microfollicular growth pattern and a prominent lymphoid infiltrate completely surrounding the epithelial component was first documented in 1997 by Michal *et al.*<sup>[6]</sup> who reported a series of 12 cases.

These tumors were enveloped by this fibrous pseudocapsule, thus mimicking an intraparotid lymph node containing a metastasis. Two additional anterior cases<sup>[1,2]</sup> published as ACC arising in intraparotid lymph nodes were thought to belong to this subgroup by the authors of this series. In this proposed entity by Michal *et al.*<sup>[6]</sup> only a microcystic growth pattern was reported in ACC with lymphoid stroma in contrast to conventional ACC, which usually display a mixture of two or more patterns including solid/lobular, microcystic, follicular and papillary-cystic. In our case too, only a microcystic pattern was encountered.

Acinic cell carcinoma with lymphoid stroma has to be distinguished from ACC arising in an intraparotid lymph node. Except for the frequently occurring Warthin tumors, primary salivary gland tumors, which develop in lymph nodes of the parotid gland, are rare. These tumors arise from heterotopic intranodal salivary inclusions with acinar and ductal formations.<sup>[8]</sup> Hilus structure with salivary inclusions and marginal sinuses support origin within intraparotid lymph node. Absence of an occult carcinoma in the salivary gland tissue is mandatory for the diagnosis of primary salivary gland tumor within a lymph node.<sup>[9]</sup> ACC with lymphoid stroma may be confused with lymph node metastasis from low-grade



**Figure 2:** Periodic acid-Schiff (PAS) staining of the tissue section revealing PAS positive diastase resistant granules in the tumor cells. Note the surrounding prominent lymphoid stroma (PAS stain, ×20)

from low-grade adenocarcinoma. However, nodal metastasis is not the primary presentation in low-grade adenocarcinoma. The lack of subcapsular sinuses may be helpful in ruling out nodal metastasis.<sup>[10]</sup> We think that the main differential diagnosis here is nonsebaceous lymphadenoma, especially as ACC with lymphoid stroma does not show cellular atypia and other overt histological features of malignancy. Lymphadenoma is a rare and benign salivary gland neoplasm with 37 cases reported to date,<sup>[8]</sup> it is composed of epithelial component in a dense lymphoid background. The epithelial component displays a wide spectrum of histological differentiation, with solid/lobular, cystic, glandular growth patterns and basoloid, ductal cells and/or polygonal cells with slightly basophilic nongranular PAS negative cytoplasm. Myoepithelial cell participation, highlighted by immunohistochemistry, may be seen. A lymphoepithelial differentiation is possible. Acinar cell differentiation in ACC is the key differential criteria eliminating nonsebaceous lymphadenoma.<sup>[9,10]</sup>

The important cytologic differential diagnosis of ACC with prominent lymphoid infiltrates includes chronic sialadenitis and Warthins tumor. Chronic sialadnitis shows sparse cellularity and consists of clusters of basaloid ductal cells admixed with blood, proteinaceous debris, small mature lymphocytes and a few fragments of fibrous tissue. Acinar cells are sparse or absent. Cytological smears of Warthins tumor show granular debris and monolayered sheets of oncocytes, in addition to the prominent lymphoid background.

It is necessary to identify serous acinar differentiation for the diagnosis of ACC. However, a positive signal for  $\alpha$ -amylase, a specific marker of normal acinar cells, is not detected in many ACC cases, so it is not always useful for the diagnosis. Although  $\alpha$ 1-antichymotrypsin,  $\alpha$ 1-antitrypsin, transferrin, lactoferrin, secretory component, and lysozyme have been applied as markers of ductal and acinar cells, they are currently not generally used. A recent paper reported that DOG1 staining is a marker of salivary acinar cells, and strong staining can be applied to support the diagnosis of ACC.<sup>[11]</sup>

Acinic cell carcinoma with lymphoid stroma behaves far less aggressively than the conventional ACC1 with no evidence of disease within the follow-up period ranging from 19 months to 14 years.<sup>[6]</sup> Features associated with poor outcome including positive surgical margins, histologic extracapsular extension, frequent mitoses, atypical mitoses, vascular and perineural invasion, nuclear pleomorphism and necrosis<sup>[12]</sup> are not seen in ACC with lymphoid stroma, which explains its favorable outcome. Management of ACC consists of wide local excision with clear surgical margins and long-term follow-up.<sup>[13]</sup>

## CONCLUSION

Acinic cell carcinoma with lymphoid stroma is an unusual tumor, rarely encountered by pathologists and probably underdiagnosed as ACC arising in intraparotid lymph node. Increased familiarity with the spectrum of cytomorphologic findings and the potential diagnostic pitfalls in ACC will improve the cytodagnosis of this neoplasm. This tumor has an excellent prognosis but adequate and long-term follow-up after surgery appears to be the most appropriate management, seeing the limited number of cases. Further studies are needed to better define the diagnosis criteria of this entity.

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