Papillary Pattern in Acinic Cell Carcinoma of Parotid Gland: A Potential Diagnostic Pitfall on FNAC

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Abstract
Fine needle aspiration cytology (FNAC) is often the first investigation in the work up of salivary gland lesions. However, its diagnostic accuracy is limited by the high rates of false positives and false negatives. Usually, acinic cell carcinoma is prone to be underdiagnosed because of the cytological similarity of the tumor cells to normal acinar cells, however rarely, a predominant papillary architecture on cytology may cause confusion with adenocarcinomas. We present a case of a 45-year-old male with a painful swelling of the right parotid region. FNA smears revealed a predominant papillary architecture and focal acinar pattern. A provisional diagnosis of acinic cell carcinoma was given, which was confirmed on histopathology. Familiarity with the cytomorphologic features of acinic cell carcinoma is cardinal for an accurate diagnosis and appropriate management.

Keywords: Acinic cell carcinoma, papillary pattern, salivary gland tumor

INTRODUCTION
Salivary gland tumors represent 3% of all neoplasms of the head and neck. Acinic cell carcinomas (ACC) account for

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12–17% of primary salivary gland cancers and 3.4% of all salivary gland neoplasms. It shows a female preponderance and is considered to be a low-grade malignancy with a 5-year survival rate of 80–90%.[1,2]

Fine needle aspiration cytology (FNAC) is a useful investigation in the initial preoperative evaluation of patients with salivary gland lesions, with a reasonably high sensitivity and specificity. The cytologic diagnosis of ACC is particularly challenging owing to its varied morphological spectrum.

Case Report

A 45-year-old male presented with a swelling of the right parotid region since 3 months. On palpation, the swelling was soft, well-defined, and not adhered to deep structures. Ultrasonography showed a solid tumor 4 cm in diameter. FNA smears were highly cellular and showed cells arranged predominantly as papillae, focal acini, and as singly scattered [Figure 1]. The cells had eccentrically placed nuclei and abundant slate gray cytoplasm showing vacuolations and fine red granularity [Figure 2]. Many stripped nuclei were also seen in a clean background. No mitotic figures, inflammatory cells, foamy macrophages, or epithelial ductal fragments were observed.

A diagnosis of ACC was suggested and total parotidectomy was done. Histopathologic examination showed a partially encapsulated lobulated tumor composed of cells arranged predominantly in sheets with focal acinar, microcystic, and papillary pattern [Figure 1c and d]. Tumor cells were large, round-to-polygonal, with abundant amphophilic granular cytoplasm and central round vesicular nucleus [Figure 2c]. Occasional psammoma bodies were also seen. No significant atypia or mitosis or necrosis was seen. Focal infiltration of the surrounding soft tissue by the tumor was noted. Thus, a final diagnosis of ACC was rendered.

Discussion

ACC of the salivary glands is a rare, slow growing tumor of the salivary glands, first described by Nasse in 1892.[3] Although previously considered benign by the World Health Organization, it is now considered a malignant epithelial neoplasm of salivary glands.[4,5] The most frequent site of occurrence is parotid gland (80%), others being intraoral minor salivary gland (17%), submandibular gland (4%), and rarely extra-salivary sites such as breast, pancreas, and lungs.[4,5]

FNA of the parotid gland is usually the first investigation in the preoperative assessment of parotid lesions. It offers a safe, reliable, rapid, and cost-effective means to differentiate nonneoplastic from neoplastic disease, and between benign and malignant tumors.

The sensitivity and specificity of parotid FNA in distinguishing neoplastic from nonneoplastic disease is reported by various studies to be between 79% and 100%, and between 71% and 100%, respectively.[6] FNA of ACC shows cells arranged in an acinar pattern with dispersed, bare nuclei in the background. In some cases, a capillary meshwork or even papillary formations around a fibrovascular core can be seen, as were visible in our case. This picture could lead to an erroneous diagnosis of adenocarcinoma. Differential diagnosis to be considered when a prominent papillary pattern is found on cytology include polymorphous low grade adenocarcinoma (PLGA), papillary cystadenocarcinoma, epithelial-myoepithelial carcinoma, and rarely pleomorphic adenoma. However, at least focal serious acinar differentiation with its characteristic cytoplasmic zymogen granules is the hallmark of ACC.[7]

The cells are round, oval, or polygonal, with eccentrically placed nuclei and a strikingly granular cytoplasm, with some cases showing vacuolations and oncocytic appearance. The frequent presence of numerous bare nuclei in the background of the smear has been thought to be due to the high cytoplasmic lability of the acinar cells. The papillary cystic variant shows presence of papillae and cystic macrophages.[2,4] The cytologic diagnosis of ACC is challenging owing to the myriad of differential diagnoses, which include both benign and malignant entities. Several studies have shown FNA to have a comparatively low diagnostic accuracy for ACC, i.e., 67.5%.[8]

The differentiation of ACC from normal or hyperplastic salivary acini is exiguous owing to the similarity of monotonous tumor cells to normal acinar cells. A clue to the recognition of normal salivary acini is the presence of intermingled adipose tissue and ductal epithelial cells.[5,7] The prominence of oncocytic cells in ACC may create differential diagnostic problems with oncocytoma. Tumor cells in oncocytoma usually have a denser and more granular cytoplasm with prominent nucleoli, a finding rarely seen in ACC. In addition, bare nuclei are not so frequently found in oncocytoma.[5,7] Warthin’s tumor may also create diagnostic difficulties with ACC, in some cases due to scarce or no lymphoid component along with sheets of oncocytic cells, and in cases of ACC denominated with lymphoid stroma. Cytologic smears with predominance of large cells with abundant clear-to-vacuolated cytoplasm may be seen in epithelial-myoepithelial carcinoma and low-grade mucoepidermoid carcinoma. Intracellular mucin vacuoles seen in mucoepidermoid carcinoma are not found in ACC. Stromal hyaline globules and presence of biphasic population of atypical myoepithelial cells and epithelial cells helps in distinguishing epithelial myoepithelial carcinoma from ACC. Metastatic tumor deposit to the parotid from renal cell carcinoma must also be considered in the differential diagnosis. A clue to the diagnosis is the characteristic vascular pattern and nuclear atypia in RCC.[2,9] The definitive diagnosis of ACC is based on histopathologic examination. The cells may be acinar, intercalated, ductal, vacuolated, or clear, and arranged in various patterns including solid, solid-lobular, acinar-microcystic, papillary cystic, tubuloductal, and follicular. Although a single cell type and growth pattern often dominate, many tumors have combinations of cell types and growth patterns. The solid/lobular and microcystic patterns are most frequent, followed by papillary-cystic and follicular patterns.[4,5]
In a study by Gomez et al., the recurrence rate after surgical removal of ACC has been found to be 6% after 3 years and 19% after 5 years, 10 years, and 15 years. The authors have recommended complete surgical removal with a total parotidectomy and the consideration of postoperative radiotherapy in high-grade tumors, which have a recurrence rate of 33%.

**Conclusion**

In conclusion, ACC has a polymorphous appearance, and may overlap with a number of benign and malignant salivary gland tumors as well as metastatic cancer from other organs, thus making the cytodiagnosis of ACC on FNA extremely difficult. Close attention to the cytomorphologic characteristics may help in reducing diagnostic errors.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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**Figure 1:** (a) FNA smears from parotid swelling depicted predominantly papillary pattern (MGG stain, ×100). (b) Higher magnification (MGG stain, ×200). (c) Lobulated tumor showing microcystic and papillary pattern (H and E, ×100)

**Figure 2:** Cytological smears showed focal acinar pattern of cells, with eccentric nucleus and abundant cytoplasm (a: MGG stain, ×200). (b) Higher magnification (MGG stain, ×400). (c) Acinar pattern in the tumor with cells showing abundant granular cytoplasm (H and E, ×200)