Case Report

Mucoepidermoid carcinoma - A common neoplasm at an unusual site, mimicking a benign cyst on cytology: Diagnostic pitfall!

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Abstract

Mucoepidermoid carcinoma (MEC) is known to be a relatively common neoplasm of the major and minor salivary glands that can secondarily involve skin. The clinical manifestations, diagnostic cytology and histopathology of MEC presenting as a clinically benign periauricular cystic nodule have been analyzed. The challenge of accurate diagnosis can be illustrated by the fact that initially, on cytology, this tumor was misdiagnosed as a benign epidermal inclusion cyst due to the presence of mucin-filled cells which were misinterpreted as cyst macrophages. This case report emphasizes the need to include parotid tumors in the differential diagnosis of all periauricular cyst-like expansions. We also briefly discuss the reasons for false-positive cytology in this case. Delay in accurate diagnosis may result in larger surgical procedures, such as radical neck dissection, that may otherwise be avoided.

Keywords: Epidermal inclusion cyst, mucoepidermoid, periauricular

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INTRODUCTION

Mucoepidermoid carcinoma (MEC) is the most common malignant salivary gland tumor, first studied and described as a distinct pathologic entity by Stewart *et al.* in 1945.[1] The tumor was initially titled "Mixed epidermis and mucous secreting carcinoma," later replaced by "MEC."[2] The tumor comprises both epidermal and mucous cells in varying proportion, hence the name. It arises from the pluripotent reserve cells of the excretory ducts of salivary glands and accounts for 15% of primary carcinomas of the major and minor salivary glands.[3] Although the salivary gland is the more common site of occurrence for MEC, occasional cases have been reported in the palate, retromolar area, floor of the mouth, buccal mucosa, lips, tongue, lacrimal glands, bronchi, nasal mucosa, esophagus, maxilla, mandible, liver, cervix, penis and anus.[3,4] MEC may develop at any age; however, the average age at presentation is between 20 and 60 years with a female preponderance.[3]

We describe a histopathologically proven case of MEC located in the postauricular region that presented as a cystic skin nodule. It was clinically misdiagnosed as a benign cyst and mistakenly deemed as an epidermal inclusion cyst on

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fine-needle aspiration cytology (FNAC). The case was lost to follow-up following surgical excision.

CASE REPORT

A 26-year-old female presented to the outpatient department with complaints of a globular swelling located behind the right ear for the past 1 year. It was insidious in onset, gradually progressive in size and not associated with ear discharge, hearing loss, fever and/or nasal blockage.

On clinical examination, a cystic, nontender swelling measuring 3 cm × 3 cm was observed 1 cm behind the postauricular groove. Local and systemic examinations were unremarkable, and all basic investigations were within normal range. The lesion was clinically suspected to be a benign cyst, following which, fine-needle aspiration was done for cytological examination. Cellular smears showed clusters and singly scattered nucleated squamous cells along with cyst macrophages, neutrophils and lymphocytes in an amorphous and hemorrhagic background [Figure 1a and b]. A diagnosis of infected epidermal inclusion cyst was suggested, following which the cystic nodule was excised and sent for histopathological examination. The patient was then lost to follow-up.

Grossly, a single irregular gray-brown tissue bit measuring 2 cm × 1.5 cm × 1.5 cm was received, which on cut section, showed mucinous, hemorrhagic and gray–brown areas [Figure 2a and b]. Microscopy showed a tumor with predominantly cystic, focally preserved solid areas composed of clusters of well-differentiated mucinous cells (mucicarmine positive), few sheets and nests of squamous cells, intermediate cells and clusters of clear cells with occasional mitosis, surrounded by pools of mucin [Figures 3-5]. The mucinous nature of MEC was highlighted by special stains such as Alcian blue [Figure 6a], mucicarmine [Figure 6b] and AB-PAS [Figure 6c]. Ki-67 proliferation index was <2% [Figure 7]. A diagnosis of MEC low grade was given. A retrospective analysis of the cytology revealed the mucinous background.

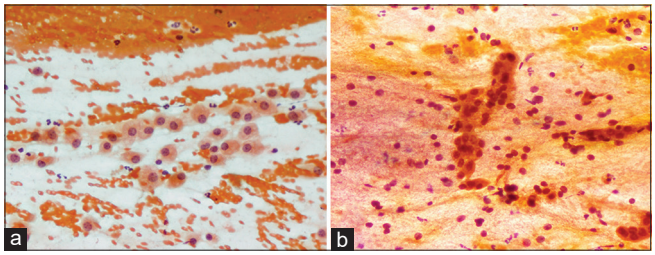

Figure 1: (a) Cytology showed singly scattered nucleated squamous cells along with cyst macrophages and inflammatory infiltrate in a hemorrhagic background (PAS, ×200). (b) Cluster of nucleated squamous cells in a background of mucin admixed with hemorrhage (PAS, ×200)

DISCUSSION

Salivary gland tumors constitute 5% of head-and-neck neoplasms, and among them, MEC is the most common malignant tumor of both major and minor salivary glands.[5] Parotid gland is the most common site of occurrence of MEC, followed by the palate, submandibular gland and other minor salivary glands. This neoplasm can also arise as a primary skin tumor and has been considered to be of a sweat gland derivation, or it may resemble a cutaneous metastasis, especially from the salivary gland or bronchus.[3] The first case of high-grade MEC of the salivary gland presenting with skin metastases at the time of diagnosis was reported by Locati *et al*.[6] and this was found to be associated with chemoresistance and aggressive behavior. Approximately <5% of this high-grade tumor present with metastatic disease at the time of diagnosis, and the most common site of metastasis is lung.[3]

The etiology of MEC is yet to be established completely. Exposure to ionizing radiations has been suggested in few cases. A gene translocation at t (11;19)(q21;p13) encoding a transcription factor CREB (cAMP response element-binding protein) has been detected in more than 80% of the MEC cases.[7,8]

Clinically, MEC presents as a solitary painless and enlarging mass, especially in the salivary glands, most commonly affecting the parotid gland. Many times, the tumor presents as an ulcerated soft-tissue lesion with granular or papillary surfaces. In rare instances, it can present as a fluctuant, smooth-surfaced cystic swelling simulating a mucocele, which can be attributed to the cystic degeneration of the central cells or due to progressive enlargement of the swelling. High-grade tumors can be painful. Various neoplastic and nonneoplastic lesions of salivary glands can present with a prominent cystic architecture, MEC being one of them.[9] In the present case, a painless cystic nodule was seen in the postauricular region, which is a rare site of occurrence of MEC.

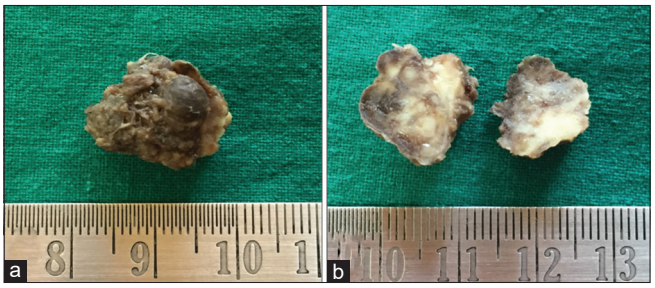

Figure 2: (a) Grossly, single gray–brown nodular tissue bit measuring 2 cm × 1.5 cm × 1.5 cm. (b) Cut section shows mucinous, hemorrhagic and gray–brown areas

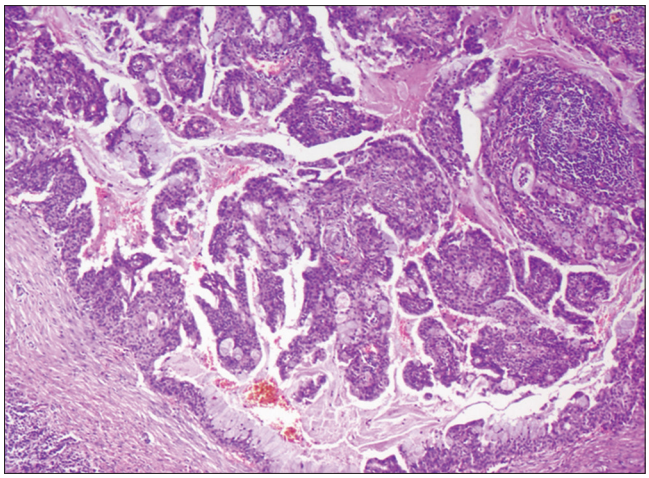

Figure 3: Microscopically, a tumor composed predominantly of cystic and focal solid areas (H&E, ×40)

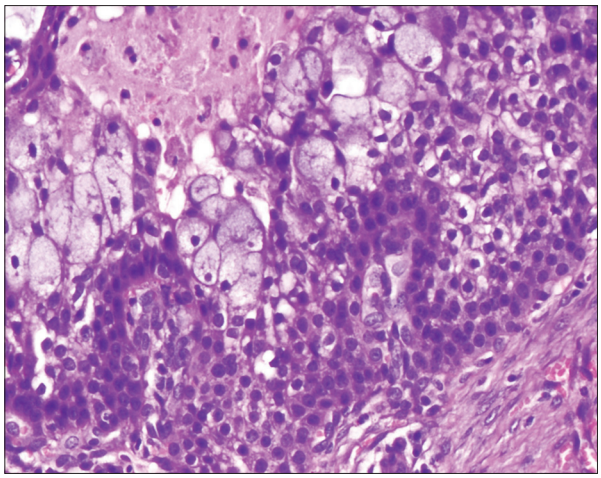

Figure 4: Higher power view of nests of intermediate cells and cyst macrophages (H&E, ×200)

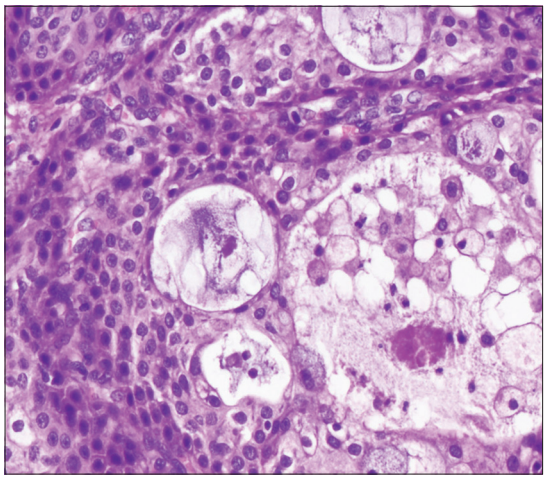

Figure 5: Higher power view of clusters of well-differentiated mucinous cells surrounded by nests of squamous cells (H&E, ×200)

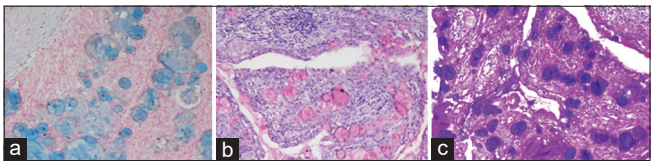

Figure 6: (a) The Alcian blue stain highlights the mucinous nature of mucoepidermoid carcinoma (Alcian blue, ×100). (b) Focal intracellular and extracellular staining for mucin (mucicarmine, ×100). (c) Focal intracellular and extracellular staining for mucin (AB-PAS, ×100)

FNAC has a prominent role in the evaluation of all salivary gland swellings, more so in diagnosing cystic lesions; however, its accuracy may be limited by low cellularity and dilution by watery or mucoid material.[9] The overall sensitivity and specificity of FNAC in accurately diagnosing salivary lesions are variable, as reported by different authors in the literature.[10-12] The possibility of false-positive or false-negative results can be attributed to the presence of cystic structures formed due to obstruction of the draining ducts in both benign and malignant tumors.[11] MEC on cytology shows cohesive sheets of tumor cells with squamous differentiation, abundant cytoplasm and intracytoplasmic mucin vacuoles. The most important diagnostic criteria are the identification of three cell types: intermediate, mucus producing and squamous cells in the smear.

Cytological differential diagnoses for MEC are both nonneoplastic conditions such as mucus retention cysts, chronic sialadenitis, lymphoepithelial cysts and neoplastic conditions such as Warthin's tumor, pleomorphic adenoma, cystadenoma and cystadenocarcinoma. In a case report by Sridharan and Hallikeri a solitary swelling of the parotid gland was initially misdiagnosed as a benign cystic swelling on FNAC, which finally turned out to be low-grade MEC on histopathology. Similarly, in a case series, Mahesh *et al*.[13] observed that three-fourth of MEC were misdiagnosed as pleomorphic adenoma.

MEC has a distinctive histopathology comprising lobules of polygonal squamous cells with little tendency to keratinize, large goblet cells with bland nuclei and intermediate cells which represent transitions between the two cell populations along with frequent mucin-filled cystic spaces.[3] Histologically, this tumor has been divided on the basis of the presence of cystic structures, cellular atypia and cell type into low-grade, intermediate-grade and high-grade tumors. Low-grade tumors are well circumscribed, cystic and mucus cell rich; intermediate-grade tumors are comparatively more solid and less circumscribed. High-grade MECs are characterized by one or more of the following features: nuclear anaplasia, increased mitotic figures, perineural, lymphovascular or bony invasion and/or necrosis.[14] Low-grade tumors arise more commonly in minor salivary glands, while high-grade tumors are seen in major salivary

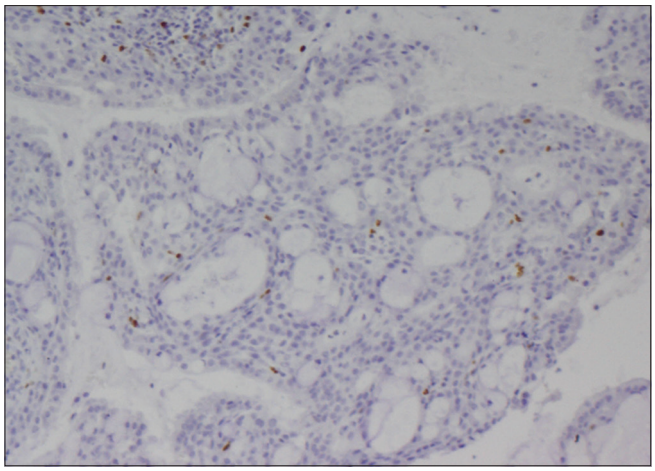

Figure 7: Low Ki-67 proliferation index (Ki-67, ×100)

glands.[15] Low-grade MEC has been characterized by prominent cystic structures, sometimes occupying more than 50% of histological sections.

Surgical excision is the treatment of choice for MEC.[16] MEC is often misdiagnosed on clinical and cytological examination as a benign cystic swelling, resulting in incomplete surgical removal with residual tumor. This results in a close or positive margin which is associated with recurrence. They have a local recurrence rate varying from 15% to 75%, usually appearing without change in histopathology, mostly during the 1st postoperative year.[3]

CONCLUSION

Among all the salivary gland neoplasms, MEC has been reported to show the highest false negativity with FNAC, most likely due to the presence of cystic architecture and cellular dilution causing failure to detect the epithelial cells. We hence emphasize that while working upon any odd periauricular cyst-like mucinous expansions, parotid malignancy should always be considered in the differential diagnosis to ensure an early diagnosis, complete removal and a better outcome.

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 initial s 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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