Case Report - Oncology

Epithelial-myoepithelial carcinoma of the parotid gland: Clinicopathological aspect, diagnosis and surgical consideration

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ABSTRACT

The present paper describes the clinical and pathological features of epithelial-myoepithelial carcinoma (EMC) of the parotid gland. This rare tumor represents <1% of all salivary gland tumors and arises most commonly in the parotid gland, but it has also been described in the submandibular gland, minor salivary glands and palate. EMC is considered to be a low-grade malignant tumor that may commonly recur locally after resection in 23-50% of cases. The complex and varied morphological expression of this neoplasm has attracted numerous investigators, who have presented valuable but often contradictory data. After an in-depth analysis of the clinicopathological aspects of EMC, we speculate that adequate resection with negative soft-tissue margins is the minimum recommended and necessary therapy.

Keywords: Epithelial-myoepithelial carcinoma, neoplasms, parotid gland, salivary gland

INTRODUCTION

Epithelial-myoepithelial carcinoma (EMC) is a rare biphasic tumor of the salivary gland. It is generally composed of variable proportions of two cell types: An inner layer of duct lining cells and an outer layer of clear cells, which typically form double-layered duct-like structures. Clear cells, which are of myoepithelial origin, often predominate in number.[1] The clinical behavior and histologic findings of EMC originally prompted its previous classification as an adenoma (so-called glycogen-rich, clear cell adenoma) or adenomyoepithelioma.[2] In the year 1991, the World Health Organization recognized EMC as a distinct entity and subtype of salivary gland adenocarcinoma and it became part of the new classification system.[1] EMC represents <1% of all salivary gland tumors and arises most commonly in the parotid gland, but it has also been described in the submandibular gland, minor salivary glands and palate. There is a female predominance, with a peak occurrence in the seventh decade of life. Clinically, EMC usually appears as a bulky, slowly growing mass within the parotid gland. Computed tomography (CT) and magnetic resonance appearances are non-specific[3] and the cytological diagnosis may be challenging.[4] A more accurate definition of the disease can be achieved by histological and immunohistochemical study. EMC is considered to be a low-grade malignant tumor that may commonly recur locally after resection in 23-50% of cases. This is often because the capsule, which normally delimits this neoformation, may be incomplete. Less frequent is the finding of lymph node and hematogenous metastasis.[5] Dedifferentiation has also been reported.[6] We herein report a new case of EMC and discuss the clinicopathological aspects, differential diagnosis and surgical approach of this rare tumor.

CASE REPORT

The present case is about a 42-year-old female patient who presented to our university hospital with a 6-month history of a painless swelling in the region of the right parotid gland. Upon clinical examination, a 3-cm diameter firm mass was palpable in

the gland. The growth was well demarcated and it had a smooth external appearance [Figure 1a and b]. It had a moderately firm consistency, was fixed to neighboring tissues and was not painful on palpation. The oral cavity was normal on inspection. There was no associated facial weakness or cervical lymphadenopathy. A CT scan, performed at another center, showed a non-homogeneously enhancing mass in the right parotid gland [Figure 2]. There was no gross invasion of the parapharyngeal-space fat planes and there was a smooth interface with the remainder of the parotid gland. There was no evidence of adenopathy. Under general anesthesia, partial superficial parotidectomy was performed,[7] and a nodular, well-circumscribed mass was surgically excised with a surrounding suprafacial portion of normal parotid gland [Figure 3]. There were no signs of recurrence 24 months after the operation [Figure 4a and b].

PATHOLOGY

A nodular, well-circumscribed mass was surgically excised with a surrounding portion of normal parotid gland. The specimen comprised a 4 cm × 3.5 cm × 1 cm lobulated portion of tissue. Grossly, the lesion was apparently well circumscribed, multilobated and grey-white in appearance; the cut surface revealed many small cysts with hemorrhagic content [Figure 5]. Histological examination showed a multilobular appearance with well-circumscribed multiple nodules surrounded by a dense fibrous stroma. The tumor was not encapsulated and had an incomplete, dense fibrous pseudocapsule partially surrounding the neoplastic tissue: The tumor showed expansive edges. The tumor comprised mainly a population of large, polygonal clear cells, only focally spindled and with large nuclei that were often nucleolated. The cells had indistinct cytoplasmic borders and were of the myoepithelial type. These cells were arranged in sheets, nests and tubules surrounded by an abundant homogeneous, eosinophilic, hyalinized stroma with small inconspicuous vessels in its context [Figure 6]. In some areas, another population of cells was evident, arranged in ductal structures and surrounded by the above-described population of cells; this population comprised small cuboidal, eosinophilic cells with uniform round nuclei surrounding luminal spaces occupied by eosinophilic proteinaceous material [Figure 7]. There was no mitotic activity, atypia, or necrosis. Occasional microscopic tumor foci were present in adjacent areas; the salivary gland tissue was otherwise unremarkable. The tumor approached the surgical margins but appeared to be completely excised. Immunohistochemical evaluation revealed positivity for CKAE1/AE3 and CK7 in the small cuboidal, epithelial eosinophilic cells surrounding luminal spaces, arranged in ductal structures; the myoepithelial cells were strongly reactive for p63 [Figure 8], smooth muscle actin [Figure 9], vimentin and S-100 protein. There was scattered, weak staining for glial fibrillary acidic protein among the neoplastic myoepithelial

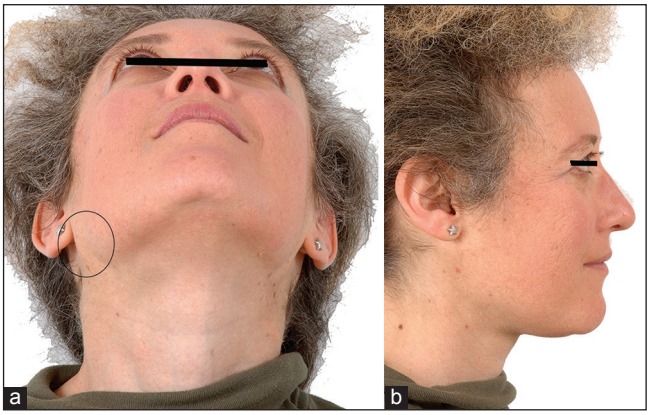

Figure 1: (a and b) Preoperative clinical evidence with a smooth external appearance in the right side

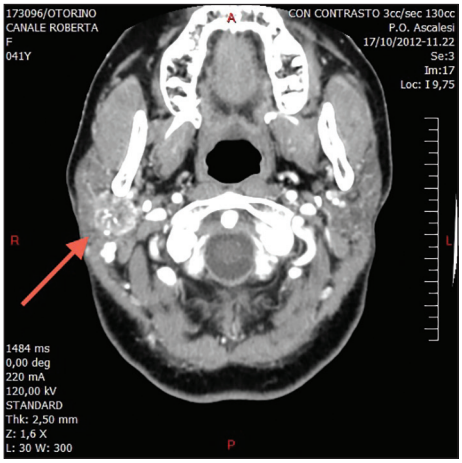

Figure 2: A computed tomography scan shows a non-homogeneously enhancing mass in the right parotid gland

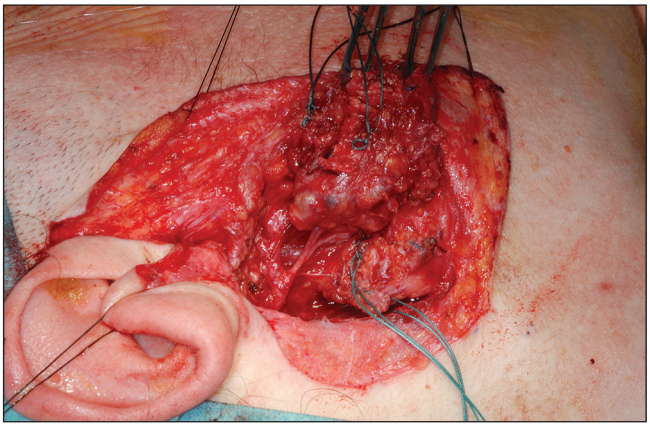

Figure 3: Partial superficial parotidectomy

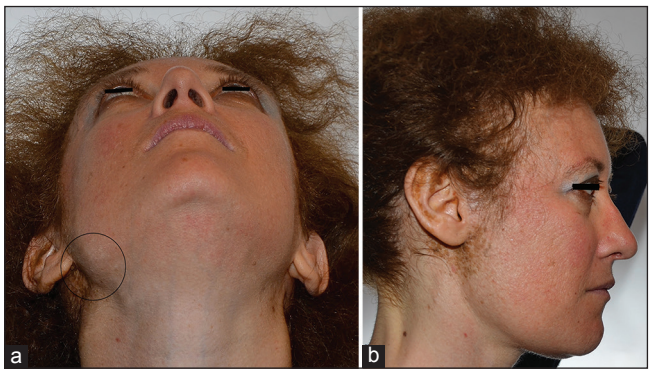

Figure 4: (a and b) Postoperative clinical control with evident minimal depressure

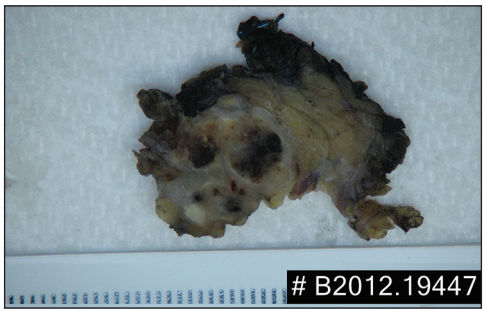

Figure 5: Macroscopic appearance of the resected tumor. Grossly, the lesion was apparently well circumscribed, multilobated and gray-white in appearance; the cut surface revealed many small cysts with hemorrhagic content

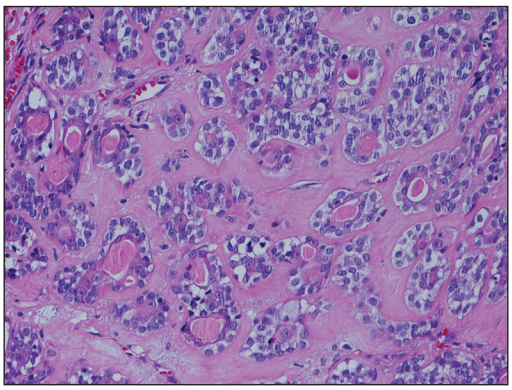

Figure 7: In some areas another population of cells was evident, arranged in ductal structures, surrounded by the clear myoepithelial cells; this population consisted in cuboidal eosinophilic small cells, with uniform, round nuclei, surrounding luminal spaces occupied by eosinophilic proteinaceous material (H and E, original magnification ×20)

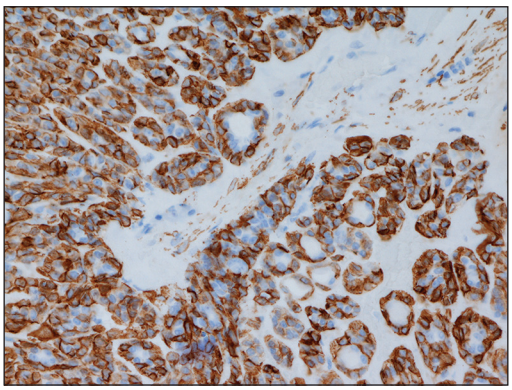

Figure 9: The myoepithelial cells were strongly reactive for smooth muscle actin (smooth muscle actin immunostain, original magnification ×20)

cells. CD117 was negative. Ki67 was positive about in 5% of the neoplastic cells.

DISCUSSION

EMC is a rare, low-grade malignant neoplasm characterized by a dual cell population of luminal ductal cells surrounded by large, polygonal clear myoepithelial cells. In the data collected by the Armed Forces Institute of Pathology, this entity constitutes barely 1% of all salivary epithelial neoplasms and nearly 2% of malignant

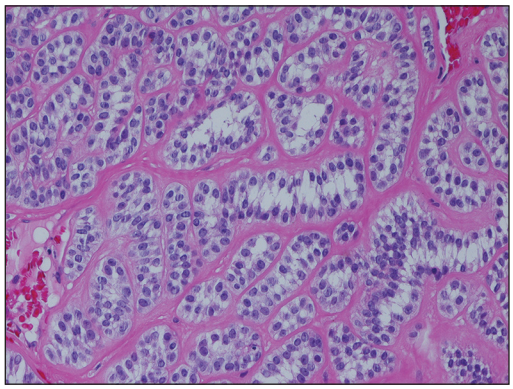

Figure 6: The tumor was mainly composed of a population of large, polygonal clear cells of myoepithelial type arranged in sheets, nests and tubules surrounded by abundant homogeneous, eosinophilic, hyalinized stroma with small inconspicuous vessels in its context (H and E, original magnification ×20)

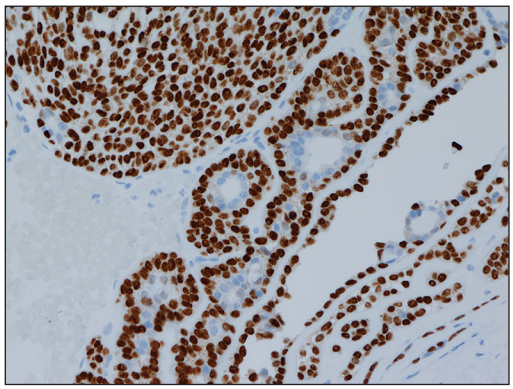

Figure 8: The myoepithelial cells were strongly reactive for p63 (p63 immunostain, original magnification ×20)

salivary epithelial neoplasms.[8] EMC is primarily a tumor of older adults, with a peak incidence in the sixth and seventh decades of life; our case is one of the rarest described, arising in a younger patient (41 years old).[9] The first description of this tumor with the terminology of EMC was introduced by Donath in 1972,[10] but tumors of the same appearance were reported previous to this under other terminology, such as adenomyoepithelioma,[11] clear cell adenoma,[12] monomorphic clear cell tumor,[13] glycogen-rich adenoma and adenocarcinoma,[14,15] clear cell carcinoma,[16] and salivary duct carcinoma.[17] Analogous to its breast and skin counterparts, this neoplasm comprises two populations of cells: myoepithelial and epithelial, as adenomyoepithelioma[18] and clear cell hydradenoma,[19] respectively. In the current classifications,[9] the terms clear cell carcinoma and salivary duct carcinoma are currently used to designate other distinct types of neoplasia. There was some confusion between the terms EMC and adenomyoepithelioma because the neoplasm in the salivary glands has the same morphology as its breast counterpart; therefore, some authors in the past have suggested renaming both of these entities as adenomyoepithelioma independent of their location.[20] Anyway, because EMCs are known to have a high rate of recurrence and a metastatic potential,[21-24] it may be better to define some significant predictive factors of behavior[25] as suggested by Seethala *et al*. and Tralongo and Daniele,[25,26] found to be predictors of disease free survival. The criteria proposed to identify more aggressive lesions are a solid growth pattern,

nuclear atypia, DNA aneuploidy, necrosis, positive surgical margins and high proliferative activity; such cases generally have a more aggressive behavior and a higher frequency of local recurrences and metastases. The same distinction was adopted in the classification of myoepithelial breast lesions by Tavassoli,[27] who divided the benign form of adenomyoepithelioma from the malignant form with more aggressive clinical behavior and histologic elements of malignancy (cytologic atypia, mitotic activity and infiltrative margins). However, the bulk of the literature since 1972 has confirmed that the salivary gland counterpart is indeed a low-grade malignancy with documented local recurrence rates ranging from 23% to 80%,[25] an incidence of metastasis reported to be about 14%[21-24] and a death rate reported to be as high as 40%.[22] Regardless, these salivary gland lesions are too rare to make any conclusions regarding their biological behavior and prognosis compared with their breast counterpart. The differential diagnosis of EMCs include primarily adenoid cystic carcinoma, canalicular and basal cell adenoma, myoepithelioma and myoepithelial carcinoma. Adenoid cystic carcinoma, as EMC, is a tumor comprising a dual cell population of epithelial and myoepithelial cells and it can have a morphology similar to that of EMC in terms of its trabecular pattern, where the prominent hyalinised stroma surrounds and squeezes the tumor cells into thin strands. In contrast to EMC, these cells are smaller and usually have more hyperchromatic, irregular and angulated nuclei. The feature that distinguishes myoepithelioma and myoepithelial carcinoma from EMC is the lack of a ductal cell component; thus, even if the morphology results in misdiagnosis, the immunohistochemistry results help to differentiate these entities. Canalicular and basal cell adenoma are benign neoplasms composed of basaloid, relatively monomorphous cells arranged in canaliculi, trabeculae and cords, with a morphology that may be confused with EMC; however, the stroma of the neoplasia is typically very loose and hypocellular, mainly in canalicular adenoma and the neoplasm is composed exclusively of epithelial cells without a myoepithelial component as confirmed by immunohistochemistry. Because EMC is considered to be a low-grade malignant tumor, adequate resection with negative soft-tissue margins is the minimum recommended and necessary therapy. Neck node dissection should be considered in cases of lymph node positivity along with chemotherapy and radiotherapy in patients with highly advanced disease, positive surgical margins, or surgically unresectable disease, although there have been almost no studies of these therapies.[28]

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