

Epithelial Myoepithelial Carcinoma: A Rare Salivary Gland Neoplasm

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Abstract: Objective: Epithelial-Myoepithelial Carcinoma is a rare entity with an incidence of <0.5% of all salivary gland neoplasms. Parotid gland is the commonest affected site(75%) followed by submandibular gland(12%) and minor glands in palate(7%). Women, usually in seventh decade of life, are commonly affected. These tumors can recur locally following resection. Epithelial-Myoepithelial carcinoma presents as a solitary, bulky mass which gradually enlarges over several months. This tumor is biphasic; composed of double layered ducts having an inner lining of small cuboidal or low columnar cells i.e. epithelial component and an outer mantle of clear cells i.e. myoepithelial component. Epithelial-Myoepithelial Carcinoma of salivary gland is a low-grade malignancy with distinct morphological features, and requires a wider recognition for better management. Case Report: We describe a case of male patient who presented with a swelling behind the left ear and was clinically diagnosed as Pleomorphic adenoma of the parotid gland. On FNAC, a differential of Adenoid Cystic Carcinoma or Epithelial-Myoepithelial Carcinoma of parotid gland were given. Histo-pathology revealed Epithelial-Myoepithelial Carcinoma which was corroborated with Immunohistochemistry. Conclusion: Epithelial-Myoepithelial Carcinoma is often misdiagnosed. Hence, a thorough pathological work-up is essential for establishing definite diagnosis so as to enable to execute appropriate and complete treatment.

Keywords: Salivary Glands, Epithelial-Myoepithelial Carcinoma, Immunohistochemistry

1. Introduction

Epithelial-Myoepithelial Carcinoma is a rare clinical entity accounting for less than 1% of all salivary gland tumors[1,23]. It was first described by Donath et al[4] in 1972 and WHO Classification[5] 1991 recognized it as a distinct clinical entity. This tumor predominantly occurs in females in the seventh decade of life, mainly affecting the major salivary glands especially the parotid gland (75%), submandibular gland (12%) and sometimes minor salivary glands in palate (7%)[6,7]. Epithelial-Myoepithelial Carcinoma is microscopically composed of both epithelial and myoepithelial elements, characterizing this biphasic tumor to consist of double layered ducts and acini which are lined by inner layer of ductal epithelial cells and an outer mantle of clear myoepithelial cells [6 - 11]. Epithelial-Myoepithelial tumor is a low grade malignancy, which often recurs locally after resection and rarely metastasizes[12].

2. Case Report

We describe a 45 years male patient who had presented with a gradually increasing, painless swelling in left parotid region since 6 months. It was 2.5cm in diameter, firm, non-tender and not adherent to the over-lying skin which didn't exhibit any discoloration or presence of discharge. Oral cavity was normal. There was no facial nerve involvement, post-auricular & cervical lymphadenopathy.

High resolution CT scan was performed which revealed a heterogeneously enhancing mass in superficial lobe of left parotid gland & suspected to be pleomorphic adenoma.

FNAC of the swelling provided a differential diagnosis of either Adenoid Cystic Carcinoma or Epithelial-

Myoepithelial Carcinoma due to the presence of dual population of tumor cells arranged in sheets and acini, characterized by scant cytoplasm and hyperchromatic nuclei, with areas of acellular basement membrane like material in background (Figure 1).

The patient underwent left superficial parotidectomy and the resected tissue was sent for histopathological examination.

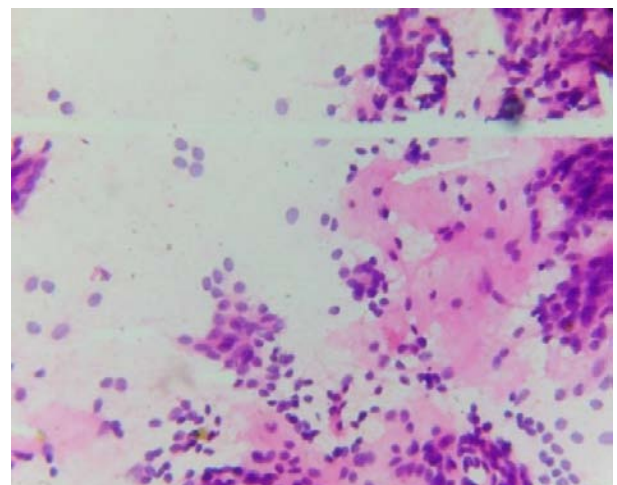


Figure 1: High Power 40x, H&E; FNAC; Cellular smear with tumor cells arranged in sheets and acini

Pathology

Gross: A well-defined nodular mass was surgically removed with a surrounding portion of normal parotid gland. The tissue sent measured 5.5 x 4 x 2.5cm. The cut-surface revealed a well circumscribed lesion measuring 2cm in diameter with grey-white to grey-brown areas,

corresponding to the nodule on the external surface. It was firm in consistency (Figure 2).



Figure 2: Gross appearance of surgically excised tissue sent for HPE: External Surface

Microscopy: The tumor cells were arranged in cords and acini, separated by basement membrane. The acini were double layered. The inner layer was composed of cuboidal to low columnar epithelial cells with round central nuclei. The outer layer, on the other hand, comprised of cuboidal to polygonal myoepithelial clear cells (Figure 3, 4). Additionally, clusters of cells were seen within the vascular channels also.

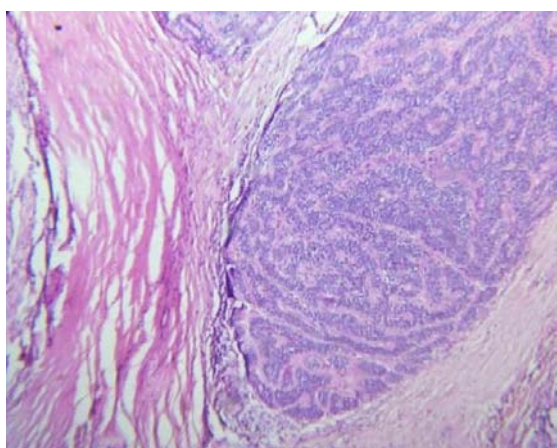


Figure 3: Low Power 10x, H&E: Tumour with capsule and acellularstroma

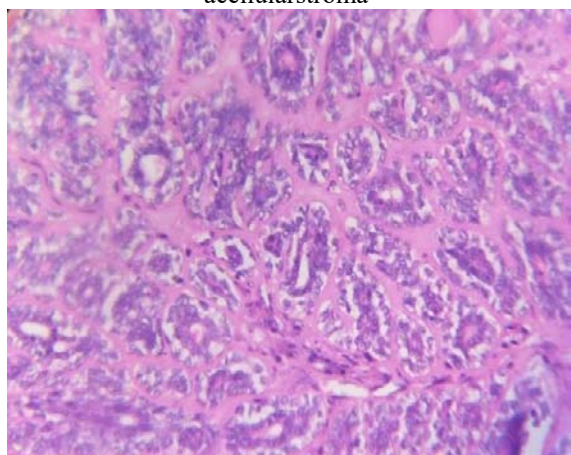


Figure 4: High power 40x, H&E: Double layer ducts separated by almost acellular basement membrane like material

Immunohistochemistry

This was done by using three markers i.e. Pancytokeratin, Epithelial Membrane Antigen (EMA) and Smooth Muscle Actin (SMA). Both, the inner epithelial and outer myoepithelial cells were positive for pan-cytokeratin (figure 5). The inner layer cells were positive for EMA but negative for SMA (figure 6) whereas the outer mantle of cells were positive for SMA but not for EMA (Figure 7). This confirmed the presence of double layered ducts with both, epithelial and myoepithelial components.

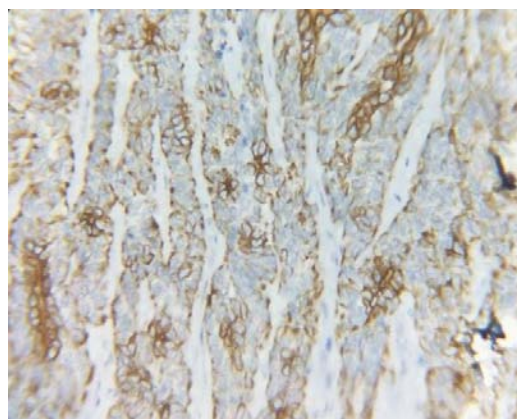


Figure 5: Immunohistochemistry: Pan-cytokeratin positive in both epithelial and myoepithelial cells.

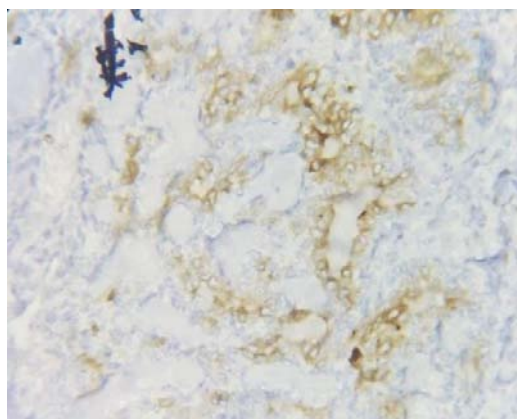


Figure 6: Immunohistochemistry, High power, 40x: EMA positive only in the inner epithelial cells and not in outer myoepithelial cells

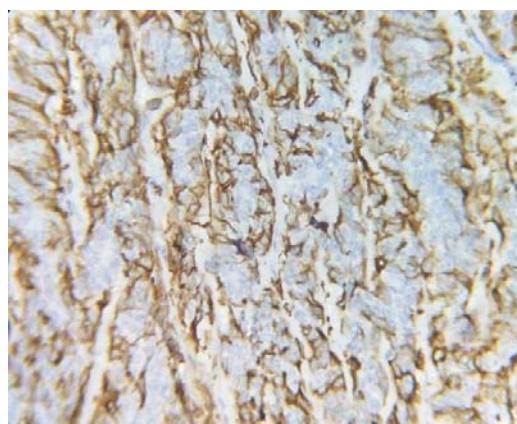


Figure 7: Immunohistochemistry, High Power, 40x: SMA positive in outer myoepithelial cells and not in inner epithelial cells.

Diagnosis: A final diagnosis of Epithelial-Myoepithelial Carcinoma of the left parotid gland was established.

3. Discussion

Epithelial-Myoepithelial Carcinoma is a rare tumor which was first described in 1972 by Donath et al[4] and incorporated in book (chapter on Salivary Glands authored by Luna[5]. It is twice more common in females than in males. Most tumors arise in the major salivary glands especially the parotid gland, but cases involving minor salivary glands have also been described [5,6]. Our case however, was a middle aged male patient with a lesion in the left parotid gland.

Clinically, this tumor is indistinguishable from the other tumors of the parotid gland. They present as a solitary, painless, slow-growing masses - as seen in our case. Painful lesions and involvement of the facial nerve are rare associated findings [6,13,14].

On CT scan, a heterogeneous mass is seen in the parotid - which is a non-specific finding [15]. Bakshi et al[8] reported Epithelial-Myoepithelial Carcinoma on fine needle aspiration cytology based on the presence of occasional clusters of round to oval malignant cells with eccentric nuclei and prominent nucleoli, moderate to abundant amount of cytoplasm and a few giant cells. FNAC forms a baseline investigative tool for screening salivary gland swellings and can accurately distinguish benign from malignant lesions. However, it is not always possible to predict the specific tumor due to overlapping features. This is the plausible reason to give a differential diagnosis in the cytology report [16,17]. In the present case also, a differential of Adenoid Cystic Carcinoma and Epithelial-Myoepithelial Carcinoma were given (figure 1). It is difficult to differentiate both on FNAC. Former shows large hyaline spheres surrounded by basaloid tumour cells and a greater proportion of myoepithelial cells. The latter has a dual population, an abundance of large clear myoepithelial cells and acellular basement membrane material [18].

Epithelial-Myoepithelial Carcinoma is a low potential malignancy. Spread to local lymph nodes can occur, but is rare [12]. The usual treatment is wide surgical excision including removal of adjacent lymph nodes. Adjuvant radiotherapy can be added but its role is still controversial [6]. Post-operative recurrence rate is high; therefore, adequate resection with negative margins is the minimal requirement of the surgery [2,6,12]. Although extremely rare, cases of distant metastasis to kidney and lung have also been reported [9,12].

Histopathology is the definite tool for the diagnosis of Epithelial-Myoepithelial Carcinoma. On macroscopic examination, these tumours range in size from 2-8cms and are usually solitary with bulky and bosselated appearance. The cut-surface of the tumour shows a single lobule or multiple lobules with grey-white areas (figure 2). The tumours are well circumscribed and may be partly encapsulated and may show local invasion into surrounding tissues, like blood vessels [10]. Invasion into blood vessels was seen in present case also.

Microscopically, Epithelial-Myoepithelial Carcinoma has a distinctive pattern. A constant feature is double layer ductal lining consisting of inner epithelial cells and outer myoepithelial cells [6 - 8,10,11,13]. Similar microscopic picture was obtained in the present case (Figure 3, 4). The tumour shows proliferation of ductal structures which may be either densely packed or separated by stroma. The inner layer consists of cuboid to low columnar ductal epithelial cells with round central nuclei and granular eosinophilic cytoplasm. On the other hand, the outer mantle is composed of ovoid to polygonal large myoepithelial cells with eccentric nuclei smaller than that of epithelial cells. The cytoplasm is abundant and pale or clear. These myoepithelial cells are predominant and overlie the external well developed basement membrane. The intervening stroma is composed of almost acellular collagen. Rarely, tumors may invade the surrounding structures like blood vessels. Mitotic figures and nuclear pleomorphism are seldom present [5,6,9,10,13].

Simpson et al[10] described three morphological patterns. First, the classical pattern with distinct two layers of ducts with basement membrane. Secondly, the clear cell or myoepithelial cell predominant pattern where sheets of clear cells are divided into alveolar arrangement by thin intervening stroma[10]. Identifying the inner epithelial cells is difficult. Third is the sclerotic pattern in which scant double layered ducts are separated by thick hyalinised stroma[10].

The bimodal differentiation of Epithelial-Myoepithelial Carcinoma is corroborated with Immunohistochemistry [5,6,10]. Ductal epithelial cells in the inner layer are positive for Pan-cytokeratin as well as Epithelial Membrane Antigen (EMA) in apical portion. The myoepithelial cells in the outer layer show positivity for Smooth Muscle Actin (SMA), S-100, Vimentin and Calponin[6,10,19,20]. In the present case the diagnosis was backed up with immunohistochemistry where similar findings had been obtained (Figure 5).

Pancyto-keratin is an epithelial marker but is positive for both epithelial and myoepithelial cells (figure 5). EMA is an epithelial marker which is negative in myoepithelial cells (figure 6) and SMA is a specific marker for myoepithelial cells which is negative in epithelial cells (figure 7).

The pathological differential diagnosis includes other clear cell carcinomas of salivary glands like Adenoid Cystic Carcinoma, Myoepithelioma and Myoepithelial Carcinoma, Canalicular or Basal cell Adenoma, Mucoepidermoid Carcinoma and Clear cell Oncocytoma[10,11,20].

The histogenesis of Epithelial-Myoepithelial Carcinoma is uncertain. It has been suggested that there is a bidirectional differentiation from a stem cell to form myoepithelial and intercalated ductal epithelial cells [6]. Dardick et al[21] postulated that basal reserve cells of excretory duct- and intercalated duct- myoepithelial units are stem cells from which all tumors arise.

Epithelial-Myoepithelial Carcinoma is often misdiagnosed. Hence, a thorough pathological work-up is essential for establishing definite diagnosis so as to enable to execute appropriate and complete treatment.

4. Conclusion

Although rare, Epithelial-Myoepithelial Carcinoma is a low grade malignancy with distinct morphological features. It requires a wider recognition for encertaining correct diagnosis. FNAC is not specific but only aids in suspecting Epithelial-Myoepithelial Carcinoma. Histopathological examination along with Immunohistochemistry enhances the confidence for accurate diagnosis.

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