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Case Report

A Case of Epithelial Myoepithelial Carcinoma - Correlation of IHC & Histopathological Findings

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ABSTRACT

Epithelial myoepithelial carcinoma is a rare biphasic low grade neoplasm of salivary glands; it most commonly occurs in the parotid gland but can also arise in minor salivary glands. Here a case of 58-year-old female presented with left cheek swelling of one-year duration. CT scan revealed a localized submandibular salivary gland tumor mass not involving surrounding tissues. Histological examination showed a mixture of ductal elements; cuboidal cells bordering small lumina surrounded by polygonal clear cells of myoepithelial component without any evidence of nuclear atypia or mitotic figures. Final diagnosis of epithelial myoepithelial carcinoma was made on the basis of characteristic morphological and immunohistochemical features.

Key words: **Epithelial- Myoepithelial Carcinoma, Salivary Gland, Case Report**

Introduction

Epithelial - myoepithelial carcinoma (EMC) is a rare malignancy of salivary gland. This unusual salivary tumor so descriptively named by Donath *et al.* in 1972 and included in the WHO classification of salivary tumors in 1991(1). It has been reported under a variety of names including adeno-myoepithelioma, clear cell adenoma, tubular solid adenoma, monomorphic clear cell tumor, glycogen-rich adenoma, glycogen-rich adenocarcinoma and clear cell carcinoma (2,3). It chiefly occurs in the parotid gland, representing about 1% of all salivary gland tumors (4). In addition, the major sites of involvement are the maxillary sinus, trachea, larynx, hypopharynx, and minor salivary glands, although

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it has also been reported in the mucous glands of the upper and lower aero-digestive tract. Patients are mostly women in their fifth to eighth decades, the reported age range being 8-103 years (5, 6).The lesion may be encapsulated, but the capsule may be incomplete and tumor nodules extend through it. Nuclear pleomorphism and metastasis are rare, although perineural and vascular invasion may occur. Because of cytological bland appearance; this tumor has been de-scribed as a type of adenoma. Prognosis is usually favorable (7).

Case Report

A 58 year-old woman reported intermittent pain and a mass in the left side of cheek. On examination, a fixed firm mass of 3×2.5 cm was seen on the left palate area. Her medical and surgical history was noncontributory. There was no palpable cervical lymphadenopathy, and facial nerve function was intact. A computed tomographic (CT) scan showed a non-homogeneously enhancing mass in the left palate extending to the midline of the oral cavity. There was no evidence of pathologic adenopathy. Surgery was performed and specimen sent for pathology examination at Green Cross Pathology and Molecular Laboratory, Ahmedabad. The cut surface showed well-circumscribed gray-white multiple nodules. Sections were prepared by the conventional routine method and stained with hematoxylin and eosin. Microscopically tumor was multinodular and infiltrated adjacent tissues (Fig. 1). Histologically, the specimen showed two cell types, an outer layer of myoepithelial cells and an inner layer of cuboidal eosinophilic duct-like cells (Fig. 2). The cuboidal eosinophilic cells were surrounded by polygonal myoepithelial cells. The peri-epithelial stroma is partially hyalinized in some areas.

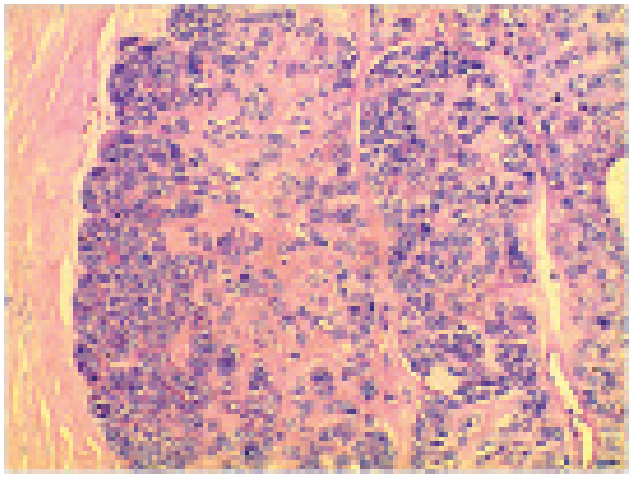

Fig. 1: Epithelial-myoepithelial carcinoma, showing multinodular growth pattern with infiltrating margins in adjacent tissues. (H & E ×200)

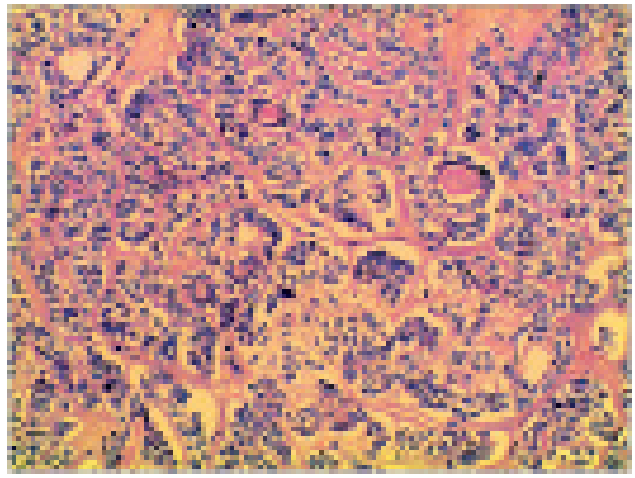

Fig. 2: The tumour is composed of ductal epithelial cells and clear myoepithelial cells. (H & E ×200)

Immunohistochemistry(IHC)- A panel of antibodies: cytokeratin (CK), epithelial membrane antigen (EMA),S100 protein, p63,α-smooth muscle actin (SMA) was applied to further sections and appropriate positive and negative controls were employed. The immunohistochemistry was scored semi quantitatively, based on the proportion of immunoreactive cells and the intensity of reactivity: + positive for a limited number of cells; ++ intensely positive for numerous cells. Results shows epithelial component is selectively well highlighted by Pancytokeratin (CK) (Fig. 3) and epithelial membrane antigen (EMA). Myoepithelial component is demonstrated by S100 , SMA (Fig. 4) and p63 (Fig. 5).

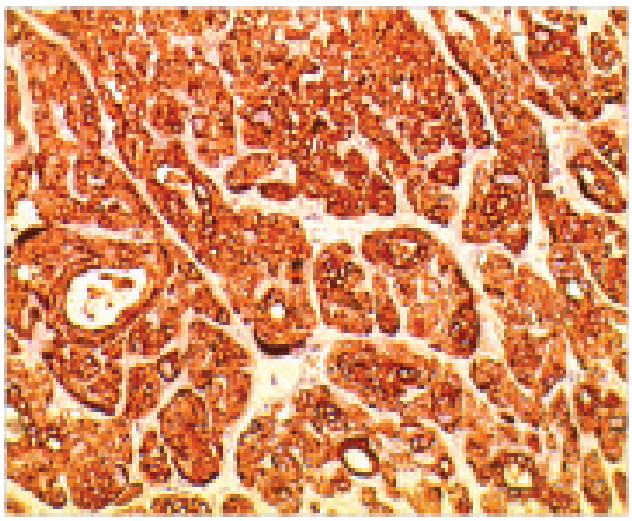

Fig. 3: Immunohistochemical staining of Pancytokeratin

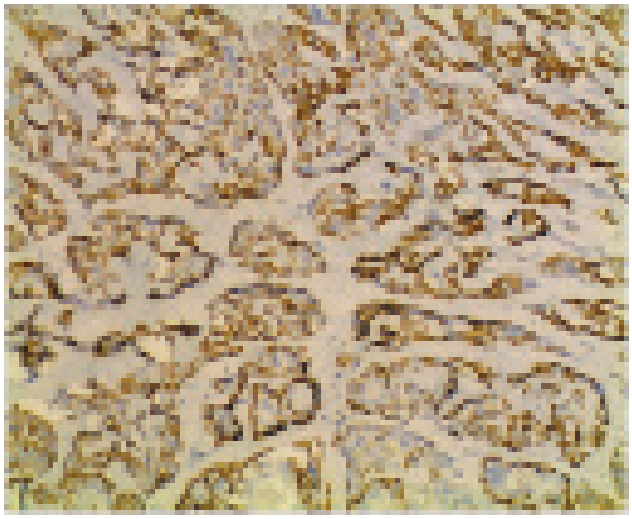

Fig. 4: Immunohistochemical staining of SMA

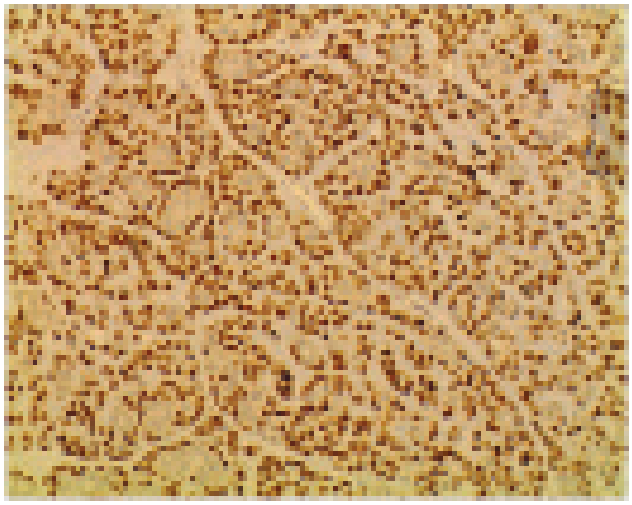

Fig. 5: Immunohistochemical staining of p63

Discussion

EMC is a low-grade malignancy, only rarely high-grade or dedifferentiated EMC cases have been reported. It also observed that some morphologically low-grade myoepithelial carcinomas behave aggressively (7). Thus, in the absence of frankly malignant cytomorphology, an invasive growth pattern is the single most useful criterion for establishing malignancy in salivary EMC.

Most tumors infiltrate adjacent normal salivary gland, adipose, muscular and bony tissues. EMCs seem to arise in two different clinical settings: either de novo or in a recurrent pleomorphic adenoma. De novo EMCs arise in normal salivary gland, tend to be more aggressive and have a short clinical history. Recurrences may not develop or may occur as a single event within a short time interval, and generally, metastases develop in the lungs. Common clinical features are sudden and rapid tumor growth, superficial ulceration, bony destruction and nerve infiltration (8).

In our case, patient presented with de novo right parotid swelling since 6 months without any evidence of metastasis. Clinically the patient was diagnosed of having pleomorphic adenoma. The cytoaspirates revealed only epithelial cells in clusters and singly in a scanty myxoid stromal background. Few spindled shaped cells were present. Thus, it was interpretated as Pleomorphic adenoma (PA).The aspirates of epithelial-myoepithelial carcinomas have been frequently misread as pleomorphic adenoma (9).

Most EMCs show a characteristic nodular or multinodular growth pattern and classic biphasic tubular histology of inner ductal cells with cuboidal epithelium and outer clear myoepithelial cell layers which are enveloped by basement membrane as seen in our case. These tumors tend to grow in a bulky lobulated fashion, with necrosis and hyalinization of large tumor nodules. The tumor has a distinctive histopathologic pattern with a proliferation of ductular structures. The ducts may be seen in cross section or longitudi-

nally, and they may be densely packed together or separated by abundant dense hyaline material. The inner cells of these ductules constitute the epithelial component of EMCs. These mildly to moderately pleomorphic cells have irregular ovoid shapes, may overlap and have prominent nucleoli and fine chromatin. Mitotic figures are not common. The outer cell layer that surrounds the ductules is the clear cell myoepithelial component of EMCs. The nuclei are smaller than those of the epithelial cells, with a definitely condensed and triangular appearance. The cells vary from being "naked nuclei" to having abundant clear cytoplasm. In our case intracellular mucin and basement membrane were positive for PAS stain. The other histological variants are verocay like change, sebaceous differentiation, dedifferentiated EMC, oncocytic EMC, EMC ex pleomorphic adenoma, double-clear EMC and EMC with myoepithelial anaplasia (8). In routine histological sections, the morphologic variants of myoepithelial cells are clear, spindle, stellate, polygonal, angular, epithelioid and plasmacytoid.

In our case, patient presented with de novo left sided palate swelling since 1 year without any metastasis. Most EMCs show a characteristic nodular or multinodular growth pattern and classic biphasic tubular histology. By immunohistochemistry, epithelial component is highlighted by Pancytokeratin (CK) and epithelial membrane antigen (EMA) and Myoepithelial component is demonstrated by S100, smooth muscle actin (SMA), p63 and Vimentin (10). The newer markers like calponin (CALP), caldesmon (CALD), and smooth muscle myosin heavy chain may be useful tools for identifying myoepithelial cells when myoepithelial cell differentiation is not easily identified on routinely stained sections (11). In our case, immunohistochemistry was done to highlight the biphasic nature of the tumor. The myoepithelial cells were positive for p63, smooth muscle actin (SMA) and S-100.

The clear cell predominant pattern of epithelial-myoepithelial carcinoma, however, Can be confused with other clear cell tumours. Monomorphic clear cell carcinoma is found in minor salivary glands and lacks S100 positive myoepithelial differentiation. The clear cells of mucoepidermoid carcinoma contain neutral epithelial mucin (PAS positive), and squamous differentiation is also, by definition, a feature of these tumours. Sebaceous carcinoma is composed of "foamy," lipid-rich clear cells, and sometimes intracytoplasmic mucin (12). A salivary gland oncocytoma may be composed largely of clear cells, although scattered typical oncocytes are usually present to betray its true nature. The clear cells in some acinic cell carcinomas are generally considered to represent a fixation artifact, and it is not thought that a true clear cell variant exists; a careful search will show foci with the characteristic secretory granules of normal acinar cells. A parotid mass may be the first manifestation of metastatic carcinoma, particularly from the kidney, and this can also occur up to nine years after nephrectomy. The immunohistochemical reactions of renal carcinoma are variable, but they will not show the biphasic pattern of epithelial-myoepithelial carcinoma. Nevertheless, exclusion of this possibility in some instances may still require the use of imaging techniques such as abdominal ultrasound examination and computed tomography scanning (13).

Low-grade tumors are curable with surgery alone. The usual treatment is wide surgical resection, including adjacent lymph nodes. Radiation therapy may be used for tumors in which resection involves a significant cosmetic or functional deficit or as an adjuvant to surgery when positive margins are present. Patients with EMC showing marked cellular pleomorphism, tumor necrosis; angiolymphatic invasion and perineural invasion have a poor prognosis. The biologic behavior also varies, depending on the site of involvement (14).

In conclusion, EMC is a rare low-grade malignancy with distinct histological appearance. It carries a low potential for lymph node or distant

metastasis but has relatively high tendency for local recurrences. Early identification of a recurrence of EMC appears to be important because repeated resections have yielded an excellent prognosis. Because the imaging and clinical findings of this rare tumor appear to be nonspecific, the initial role of the radiologist is the preoperative identification and localization of the mass. In the present case immunohistochemical profile, morphology of the lesion and the local infiltrative as well as invasive nature were all features that enabled us to better define these tumors and made it possible to reach a diagnosis of EMC.

Acknowledgements

The authors declare that there is no conflict of interests.

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