Review Article

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MYOEPITHELIAL CELLS: STRUCTURE, FUNCTION AND ROLE IN TUMOR FORMATION

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ABSTRACT:

Myoepithelial cells are smooth muscle like cells having epithelial origin. They are present in salivary glands, mammary gland, sweat gland and lacrimal gland. Myoepithelial cells are stellate or spindle shaped with 4 to 8 cytoplasmic processes. They play vital role during expulsion of saliva and regulates the electrolytic exchange. They also act as tumor suppressor and are considered very important role in differentiation of various salivary gland tumors and help in diagnosis of tumors.
Key words: Myoepithelial cell, Salivary gland tumor, Pleomorphic Adenoma .

INTRODUCTION:

Myoepithelial is derived from a Latin word which means muscles with epithelial origin. It was first described by Koelliker in 1847, myoepithelial cells were claimed to be ectodermal in origin by Ranvier in 1875 .[1]They are present in glandular epithelium above the basement membrane and beneath luminal cells. Their appearance is reminiscent of a basket cradling the secretory unit, hence they are also called as “Basket cell”. The ME cells have variable appearance. They play role in salivary secretion and electrolytic exchange. Role of myoepithelial cells in tumor development in salivary gland is not well researched. This article will describe the structure, functions, different markers used for identification and their role in salivary gland tumor development.[1,2]

STRUCTURE OF MYOEPITHELIAL CELLS:

Myoepithelial cells are stellate or spindle shaped cells with flattened nucleus present above basement membrane and beneath luminal cells (figure 1). They have 4 to 8 cytoplasmic processes (Figure 2). They are attached to basement membrane by desmosomes and to adjacent cells by hemidesmosomes.[1] In case of intercalated ducts, the ME cells have a more fusiform shape and are

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elongated with a few short processes. The processes in the acini lie in the 'gutter', hence the outline of the acini appears smooth but in intercalated duct the processes runs longitudinally on the surfaces creating a bulge.[2]

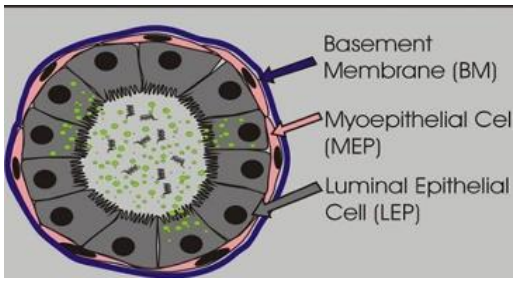

Figure1

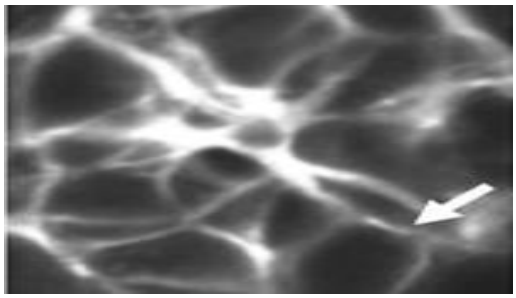

Figure 2

ULTRASTRUCUTRE OF ME CELLS:

The appearance of ME cells in electron microscope shows processes filled with longitudinally oriented fine filaments about 6nm thick. Small dense bodies which forms a cytoskeleton network in association with 10nm diameter filaments are present between thin filaments. Cytoplasmic organelles are perinuclear. The plasma membrane of the ME cells are parallel to basement membrane of parenchymal cells. Micropinocytic vesicles are present on surface facing secretory cells.[3]

DIFFERENT FORMS OF ME CELLS:[4]

ME cell can differentiate and form different morphological cell types. They are

1. **Angulate/basaloid cells:** small hyperchromatic nuclei with faint eosinophilic cytoplasm.
2. **Epitheloid cells:** polygonal with vesicular nuclei and ample cytoplasm.
3. **Clear cells:** contain clear cytoplasm due to glycogen.
4. **Spindle cells:** elongated, fusiform with pale cytoplasm.
5. **Plasmacytoid (hyaline cells):** bright eosinophilic cytoplasm with eccentric nuclei.

These different forms are helpful in diagnosing salivary gland tumors. A single salivary gland tumor can have different forms of ME cells. The cell types can undergo metaplasia such as chondroid, squamous or oncocytic.

FUNCTIONS OF ME CELLS: [1,6]

1. During embryogenesis they help in branching and morphogenesis of salivary gland and promotion of epithelial cell differentiations.
2. Help in expulsion of saliva by compressing and reinforcing the parenchymal cells
3. Regulates electrolytic exchange
4. Reduces the luminal volume

5. Contribute to secretory pressure in the acini or duct.

6. Support the underlying parenchyma and reduce the back permeation of fluid.

7. Acts as tumor suppressor as they exert a paracrine anti-invasive role by promoting epithelial differentiation, synthesis of basement membrane secreting proteinase inhibitors, and inhibiting angiogenesis.

8. Involved in signalling the secretory cells and protect the salivary gland tissue.

IDENTIFICATION OF ME CELLS:

In view of the pivotal role played by these myoepithelial cells in various salivary gland neoplasms, their identification and detection is an important link in the study of salivary gland tumors. Myoepithelial cells can be identified by light microscopy through enzyme histochemistry and special stains and immunohistochemistry for their myofibrils.

A. Stains used for ME cell identification:[7,8]

1. H & E stain (only nucleus is visible) (figure 3)

2. Phosphotungstic acid hematoxylin

3. Iron hematoxylin

4. Levanol fast cyanine(Coomasie Blue)

5. Silver impregnation method

6. Immunoperoxidase stain (figure 4)

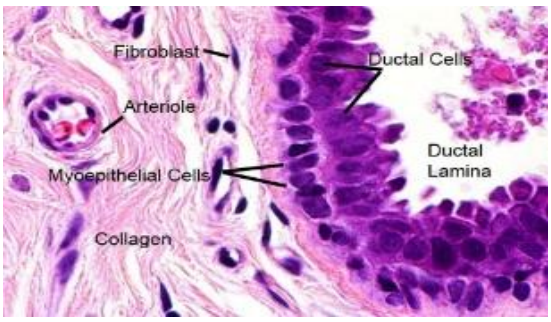

Figure 3

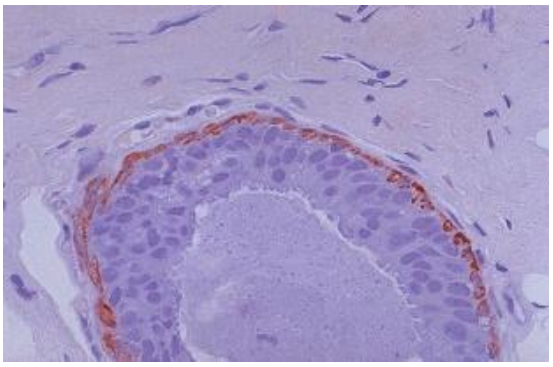

Figure 4

B. Different markers for ME cells:[9]

Smooth muscle actin is a robust myoepithelial marker and is often positive even in suboptimally fixed or infarcted tissue. Calponin shows good sensitivity for myoepithelial cells with less staining of myofibroblasts than smooth muscle actin. Smooth muscle myosin heavy chain is more specific than smooth muscle actin with less staining of myofibroblasts. p63 shows good specificity with no staining of myofibroblasts or vessels. Unlike the other myoepithelial markers which are cytoplasmic, p63 is a nuclear marker (figure 5). As a result interpretation of staining can be difficult in some sclerosing lesions, particularly if the layer is attenuated. Antibodies to basal

cytokeratins such as CK14 and CK5/6 stain (figure 6) myoepithelial cells, but are not reliable markers as they are frequently expressed at low levels. Also staining of epithelial cells can hamper interpretation. It is most effective to use a panel of antibodies. Other markers used are vimentin, Maspin, S-100.

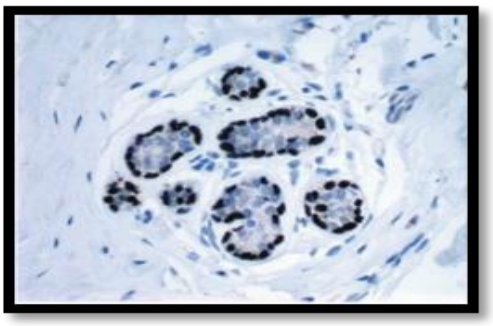

Figure5

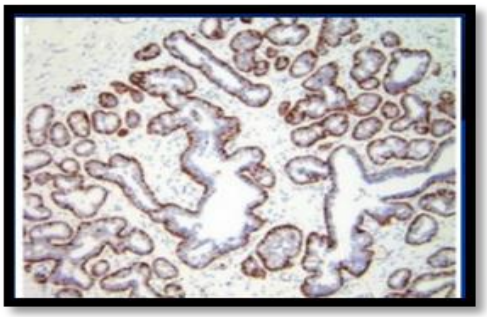

Figure 6

ROLE OF ME CELLS IN SALIVARY GLAND TUMORS:

NONNEOPLASTIC ME CELL PROLIFERATION:[10]

The bulk of research on salivary gland myoepithelial proliferations is focused on neoplasms and very little is subsequently known of myoepithelial participation in non-neoplastic conditions. Emmelin et al. found architectural changes affecting myoepithelial cells of the parotid and submandibular glands of cats after ductal ligation. Processes of myoepithelial cells protruded into the interstitial spaces, giving rise to bizarre appearances. In addition, folds of basal lamina tended to be aggregated, especially around protruberant parts of myoepithelial cells thereby increasing the space between their cell membranes and nerve endings.

NEOPLASTIC ME CELL PROLIFERATION:

1. **Basal cell adenoma:** basal cell adenoma was first described by Kleisasser and Klein in 1967. This tumor is considered as monomorphic due to lack of myxochondroid component. It can be differentiated from pleomorphic adenoma by lack of myoepithelial differentiation. Presence of hyalinised matrix in basal cell adenoma gives an evidence of myoepithelial cell participation.[10,11]

2. **Pleomorphic adenoma:** myoepithelial cells are primary proliferating cells in Pleomorphic adenoma. myoepithelial differentiation is predominant in these tumors and responsible for various "mesenchymal" components and their morphological diversity.[11]

3. **Adenoid cystic carcinoma:** Epithelial and myoepithelial differentiation in adenoid cystic carcinoma is evident in three patterns: solid, cribriform and tubular. Myoepithelial cells are present as small basaloid/

angulate cells in periductal location or in cribriform structures. Solid variant displays scattered or peripheral basaloid myoepithelial cells in small nests/sheets. Myoepithelial component can display clear cell change here similar to that seen in epithelial Myoepithelial carcinoma.[12]

4. **Epithelial myoepithelial carcinoma:** clear myoepithelial cells cuffed the epithelial tubules. Bimorphic epithelial myoepithelial carcinomas are similar to ACC in their staining of outer clear cells with myoepithelial markers in conjunction with vimentin/cytokeratins.[13]

5. **Mucoepidermoid carcinoma:** Dardick and colleagues reported that MEC have an organized pattern involving luminal epithelial cells surrounded by intermediate cells, which are considered to be modified myoepithelial cells. The histogenesis of MEC regarding the role of myoepithelial cell is controversial. Some researchers believe that this neoplasm originates from reserve duct cell either excretory or intercalated duct. Others believe that myoepithelial cells have a role in the histogenesis. Histogenesis is linked to the nature of the so called intermediate cells.[13,14]

6. **Polymorphous low-grade adenocarcinoma:** Immunohistochemical and ultrastructural studies in favour or against myoepithelial participation have been reported for this lesion. Focal staining with smooth muscle markers has been detected in this lesion. There is said to be significant if not predominant myoepithelial differentiation denoted by presence of analogous histological pattern (myxoid hyalinized matrix) as in myoepitheliomatous zone of pleomorphic adenoma and adenoid cystic carcinoma.[13,15]

CONCLUSION:

The neoplastic myoepithelial cell represents a major component of the neoplastic cellular population of the pleomorphic adenomas. It has a key role in the genesis of these tumors, being capable of dedifferentiation, metaplasia and transdifferentiation. Controversies still persist over the role of ME cells in salivary gland neoplasms. Hence for proper diagnosis and for improving the classification of salivary gland tumors, a clear and detailed understanding of myoepithelial cells is needed.

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