



Dynamics of myoepithelial cells in salivary gland lesions: An update

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Keywords

Basket cells, myoepithelial cells, non-ductal cells, salivary gland tumors

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Received: 06 September 2018;

Accepted: 15 September 2018

doi: 10.15713/ins.jodm.11

Abstract

Myoepithelial cells (MECs) are one of the non-secretory components of salivary gland acini. They are specialized cells capable of contraction aiding in the expulsion of saliva. They lie on the basement membrane of salivary gland acini and intercalated ducts. Tamarin described their resemblance as “like an octopus sitting on a rock.” Despite their smooth muscle-like properties, the presence of cytokeratin filaments confirms the epithelial origin of MECs. These cells are difficult to identify in routine hematoxylin and eosin staining. Several histochemical and immunohistochemical markers have been advocated for its identification. Neoplastic MECs are vital in the morphogenesis of various salivary gland tumors and are responsible for the histologic diversity of these tumors. This review describes the dynamics of the MEC, its pathophysiology, morphologic, and cytologic changes in various salivary gland tumors.

Introduction

Myoepithelial cells (MECs) are vital components of several exocrine glands including salivary glands, lacrimal glands, and mammary gland. They are smooth muscle-like cells forming interlacing network with their long processes. They are located on the terminal secretory unit of the exocrine glands. Discovered by Krause in 1865, these cells have been described by various authors as “star-shaped cells,” “spindle-shaped cells,” or “basket cells.”^[1]

In the salivary gland, these cells lie between the basement membrane and acinar cells of the terminal acini and intercalated ducts. Despite having an epithelial origin, these cells exhibit smooth muscle-like properties, hence termed as MECs.^[2]

Recent studies have shown MEC to play a major role in salivary gland tumor histogenesis. The present review describes the dynamics of the MEC including its pathophysiology and its role in the morphogenesis of various salivary gland neoplasms.

Ultrastructure

In electron micrographs, MEC is composed of a cell body with 4–8 cytoplasmic processes with secondary branching. The outer surface of MEC has invaginations for nerve fiber abutments and the inner plasma membrane parallels the basement membrane

of parenchymal cells, joined by desmosomes. The cells and their processes are filled with parallel streams of myofilaments. The cell body has a nucleus which is elongated, dense, and irregular and the cell organelles are present in the perinuclear cytoplasm. Numerous micro pinocytotic vesicles, or caveolae, are located on the plasma membrane of MEC.^[3,4]

Functions^[1,5,6]

- Supports acinar cells
- Aids in secretory function of salivary glands
- Produces basement membrane proteins such as fibronectin, laminin, and elastin
- Helps in the transportation of metabolites between the epithelial cells and connective tissue stroma
- Prevents distension of the acini due to the accumulation of secretory products in the acinar cells
- Recent studies have shown a tumor suppressor role by inhibiting angiogenesis, invasion, and metastasis.

Identification of MECs

The ultrastructure of MECs is well described; however, its identification under light microscopy is difficult due to its varied growth patterns, especially in pathological conditions. Various

histological, histochemical, and immunohistochemical markers have been advocated to identify these cells.^[7]

Histological Methods

Hematoxylin and eosin

MECs, on staining with hematoxylin and eosin, appear fusiform with a long axis parallel to the basement membrane^[7] [Figure 1a - c].

Special stains include silver staining, tannic acid-phosphomolybdic acid-Levanol fast cyanine 5RN stain (Coomassie blue).

Enzyme histochemistry methods

Enzyme histochemistry using alkaline phosphate and adenosine triphosphate as markers can be used to demonstrate MEC.^[7]

Immunohistochemistry (IHC)

IHC markers for MEC can be useful for diagnosing benign as well as invasive lesions. Smooth muscle actin, calponin, and smooth muscle myosin are the widely used markers for identifying MEC and demonstrate its contractile activity. Cytokeratins 5 and 14 expressions of these cells are consistent with its ectodermal origin. P63, CD-10, S-100, and podoplanin are among the other markers that were positive for MEC^[8] [Figure 1d].

MECs in Salivary Gland Pathology

Salivary gland neoplasia shows more complex histopathology than any other organ systems, thus posing diagnostic difficulty. The classification system of these neoplasms is based on histogenesis or cell of origin. However, the final histopathology depends on the morphogenesis of the tumor. Hence, it becomes necessary to know the different morphologic features and cellular differentiation processes in these tumors. MEC differentiation plays an important role in morphogenesis and hence has an impact on the histopathology of various salivary gland tumors.^[9]

Neoplastic MECs display histologic diversity due to variation in the morphologic patterns of the cell in tumors such as pleomorphic adenoma and myoepithelioma. These morphologic patterns are a result of interactions between three fundamental characteristics of the neoplastic MECs:

1. Cytologic differentiation
2. Production of extracellular matrix
3. Architectural patterns.^[9]

Cytologic differentiation

The various cytologic patterns displayed by MEC differentiation^[10,11] are mentioned in Table 1.

These cells can also undergo chondroid, squamous, and oncocytic metaplasia.

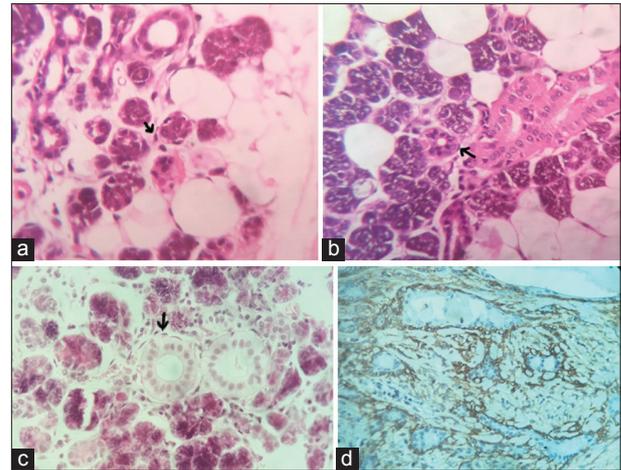


Figure 1: (a) Hematoxylin and eosin stained section of the parotid gland. Black arrow: Myoepithelial cells surrounding the acini. (b) Hematoxylin and eosin stained section of the parotid gland. Black arrow: Myoepithelial cells surrounding the intercalated duct. (c) Hematoxylin and eosin stained section of the parotid gland. Black arrow: Myoepithelial cells surrounding the striated duct. (d) Immunohistochemistry (IHC) staining demonstrating myoepithelial cells using podoplanin as IHC marker

Production of extracellular matrix

The MEC synthesizes basement membrane proteins; however, the neoplastic cells modify this ability and produce more basement membrane and non-basement membrane elements such as chondroid, myxoid, myxochondroid, fibrous, and osteoid matrix.^[2,11]

Architectural patterns

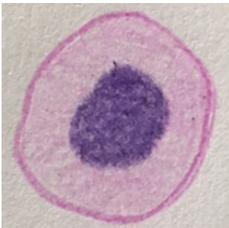
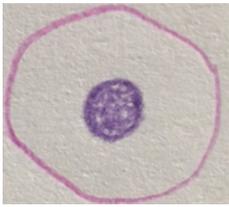
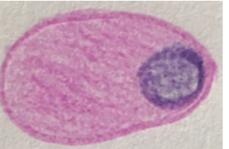
- The architectural pattern that can be seen in an epitheliomatous zone of a tumor depends on the cytologic differentiation as well as the type of extracellular matrix produced.
- Myxoid: Tumor cells are loosely and haphazardly arranged between a chondromyxoid matrix.
- Solid: Tumor cells are arranged in nests or sheets surrounded by a hyalinized matrix.
- Reticular: The epithelioid MECs are arranged in an anastomosing network.
- Microcystic/pseudocystic: It consists of loose cystic spaces formed by accumulation myxoid matrix within the nests of tumor cells.
- Cribriform/pseudoglandular: Epithelioid cells in clusters with their myxoid matrix form pseudolumen and cribriform structures.^[11,12]

Salivary Gland Tumors with MEC Differentiation

Pleomorphic adenoma and myoepithelioma

MECs are the principal type of cells in these neoplasms and usually surround the ductal cells or may form clusters or sheets

Table 1: Cytological patterns displayed by myoepithelial cell differentiation

| | | |
|----------------------------|---|---|
| Angulate/basaloid cells | Hyperchromatic nuclei with faint eosinophilic cytoplasm |  |
| Epithelioid cells | Polygonal cells with vesicular nuclei and abundant cytoplasm |  |
| Clear cells | Due to the accumulation of glycogen, the cytoplasm of these cells appears clear |  |
| Spindle-shaped cells | Elongated and fusiform cells with eosinophilic cytoplasm |  |
| Plasmacytoid/hyaline cells | Abundant eosinophilic cytoplasm and an eccentric nucleus |  |

of cells. MECs can be spindle, polygonal, or plasmacytoid interspread within a chondromyxoid matrix. In cellular pleomorphic adenomas, there is an abundance of the epithelial or MECs with minimal stroma.^[13,14]

Basal cell adenoma

MEC differentiation in the pathogenesis of basal cell adenoma is debatable; however, a few IHC studies have demonstrated that monoclonal antibodies recognized a smooth muscle phenotype sensitive for MEC differentiation in these tumors.^[15]

Adenoid cystic carcinoma

Adenoid cystic carcinoma shows both epithelial and MEC differentiation in three patterns: Cribriform, solid, and tubular. Cribriform variant displays MEC as small basaloid/angulate cells surrounding the ducts. The solid pattern displays cells in nests and sheets.^[2]

Epithelial-myoepithelial carcinoma

A tumor has a distinctive histopathologic pattern with a ductal proliferation. A constant feature is the double layer ductal lining of inner small epithelial cells and outer clear MECs.^[16]

Polymorphous low-grade adenocarcinoma

It is a malignant epithelial tumor which has an infiltrative growth pattern. It displays morphologic diversity with various histologic patterns such as myxoid and hyalinized matrix denoting MEC differentiation.^[3]

Conclusion

MEC differentiation is now considered to have a key role in the pathogenesis of salivary gland neoplasm. They are responsible for the histologic diversity seen in salivary gland neoplasms causing diagnostic difficulties. Identification of these cells will aid in decoding the cellular composition of the neoplasm which, in turn, can be used to predict its biologic behavior.

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How to cite this article: Adwani A, Kheur S, Gupta AA, Bhagat P. Dynamics of myoepithelial cells in salivary gland lesions: An update. *J Oral Dis Markers* 2018;13-16.