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Myoepithelial Cell: brief review of its role in Salivary Gland Tumours

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ABSTRACT:- Myoepithelial cells are contractile cells located between the basal lamina and the cell membrane of secretory acinar cells and intercalated duct cells. Salivary gland tumours constitute about 2-7% of all head and neck malignancies. The diversity and plasticity of the star fish shaped Myoepithelial cells (MEC) has a definite role in the histogenesis of many of these tumours. These cells normally develop at around 15th - 16th week of gestation and are situated between the basal lamina and the acinar ductal cell. Their function while ranging from contraction and reinforcement of underlying parenchymal cells also aid in expulsion of saliva and preventing damage to other cells. The neoplastic myoepithelial cell (NMEC) shows a lot of variation in its morphology, immuno profiling and pattern of extracellular matrix production. It can be categorized as benign and malignant based on MEC's complete participation Eg. Pleomorphic adenoma, Myoepithelioma and Malignant myoepithelioma, Adenoid cystic carcinoma, Epithelial- Myoepithelial carcinoma, Carcinoma ex pleomorphic adenoma or by its partial participation in tumours Eg. Basal cell adenoma, Basal cell adenocarcinoma and Polymorphous low grade carcinoma. In all these the NMEC are involved as either the cellular component or as ECM like the hyaline production in Cylindroma. The ability to invade adjacent structures is also by the NMEC in certain malignant tumours like the Basal cell adenocarcinoma. Many markers are sensitive for these myoepithelial cells but none are specific and an antibody panel would help in differentiation of a normal and a modified cell. Genetic alterations in the chromosomes have been associated with these NMEC and a combination of electron microscopy and enzyme histochemistry can help in a definitive diagnosis of any myoepithelial cell related neoplasm. The recent finding of MECs role in preventing tumour progression warrants further research on it.

Key Words: Myoepithelial cell, Neoplasm, Immuno Profile, Salivary gland tumours.

I. INTRODUCTION:

Myoepithelial cells were first described by Koellikar in 1847 and were claimed to be of ectodermal origin by Ranvier in 1875.[(1)] These cells are stellate shaped with four to eight radiating processes which cradle the acinar unit thus being also known as " Basket Cells".

They are found in the sweat glands, mammary glands, lacrimal glands as well as salivary glands. In 1898 Zimmerman first described the salivary glandular myoepithelium. These cells are ectodermal in origin and have contractile properties like muscles and are thus named as Myoepithelial cells. They envelop acinar and intercalated ductal cells and help in the expulsion of saliva by contraction.

Origin: The pluripotential intercalated duct reserve cell gives rise to other intercalated duct cells, acinar cells, striated duct cells and myoepithelial cells.[(2)] During embryogenesis myoepithelial cells are involved in branching morphogenesis of the developing salivary glands and promote epithelial cell differentiation.[(3)]

Functions: Salivary gland myoepithelial cells have a contractile function. These cells have a dual innervation by parasympathetic as well as sympathetic nerves and impulses from both types cause contraction. Contraction of the stellate-shaped acinar myoepithelial cells facilitates expulsion of secretions, reduces luminal volume and prevents distension of acini.[(2)] Contraction of elongated myoepithelial cells surrounding the intercalated ducts shortens and widens these structures, thereby overcoming peripheral resistance.[(2)] Myoepithelial cells are important in the formation and maintenance of the basement membrane. Fibronectin, laminin, and elastin are major components of basement membranes and are found to be produced by myoepithelial cells.[(2,4)]

Natural Tumor Suppressor cell- It is suggested that the myoepithelial cell naturally exhibits a tumor suppressor phenotype.[(5)] Myoepithelial cells usually do not transform but in case of transformation they generally give rise to benign neoplasms that accumulate rather than causing degradation of extracellular matrix.[(6)] Suppressor effects like inhibition of tumor invasion and tumor metastasis were observed in a study performed on myoepithelial cells.[(5)] It has been suggested that they exert a paracrine anti invasive role by promoting epithelial differentiation, inhibiting angiogenesis and synthesizing basement membrane secreting proteinase inhibitors.[(7)]

Salivary gland tumours are the most histologically heterogeneous group of tumours with diversified morphological features in their cells and the tissues. Neoplastic myoepithelium is a key participant in the glandular morphogenesis and is responsible for the variable histological appearances in many of the salivary gland tumours.[8] Myoepithelial cells form a natural barrier between proliferating acinar epithelial cells and the basement membrane and underlying stroma. They express high amounts of proteinase inhibitors that include tissue inhibitor of metalloproteinase 1, protease nexin-II, α-1 antitrypsin and maspin.[9] These cells have the potential to undergo divergent differentiation giving rise to different morphological cell types. There are three basic types of interplayed characteristics which can manifest in the complex histologic variations of neoplastic myoepithelial cells, namely; cytological differentiation, extracellular matrix production and architectural patterns. Myoepithelial cell plays a major role in the genesis of tumours because of their capability of dedifferentiation, metaplasia and transdifferentiation.[10]

Role in salivary gland tumours- Neoplastic development in salivary glands may be regarded as an epigenetic event, imposed by an oncogenic stimulus onto morphogenesis and cell differentiation.[11]The neoplastic myoepithelial cells are considered to be a key cellular participant in the morphogenetic process responsible for different histological appearances of salivary gland tumors. Neoplastic myoepithelium modify the matrix synthesizing property by production of large amount of basement membrane (BM) and non-basement membrane elements. Dominant component of non BM matrix is chondroitin sulfate which appears bluish gray and myxochondroid material which is Alcian blue-positive.[12] The other form of matrix produced by neoplastic myoepithelium is the eosinophilic hyalinized material, which represents the basement membrane-related (type IV collagen and laminin) and interstitial matrix (fibronectin and type I and type II collagens) components.[13] It is believed that salivary gland adenomas can be viewed as neoplasms lying on a spectrum histologically separable by the dimensions of the participating cell types and type of extracellular matrix by neoplastic cells.[14] Cells with myoepithelial differentiation occur in salivary gland tumors. They are situated at the base of the tumor cell complexes. They produce a basement membrane like material, an ability they obviously share with the normal basket cells as well as with the smooth muscle cell under special conditions. This "basal secretion" of basement membrane material leads to the formation of the cylindrical masses within the tumor cell complexes which is so typical for cylindromas. Fibroblasts obviously do not participate in the formation of this material. These "active" myoepithelial cells contain not only typical myofibrils, but also large amounts of ergastoplasm indicating an intensive synthesis of proteins to be secreted into the interstitium.[15]Myoepithelial cells are responsible for the morphological complexity of tumours mainly pleomorphic adenoma where the interstitial material is produced by these cells.

Identification of myoepithelial cells- Although myoepithelial cells can be identified by light microscopy through enzyme histochemistry and special stains and immunohistochemistry for their myofibrils, these techniques can be misleading in salivary gland neoplasms. Thus, the most reliable means of identifying neoplastic myoepithelial cells is with a combination of histochemistry and electron microscopy.[16]Positive enzyme histochemical reactions for alkaline phosphatase, acid phosphatase and ATPase was regarded by many as characteristic of myoepithelium.[17] The light microscopic appearance of myoepithelial cell is primarily angulate/basaloid, epitheloid, clear, spindle shaped and plasmacytoid (fig.1) The clear cells are mucin free glycogen rich clear cells.[17]

Myoepithelial cell differentiation in salivary gland tumours at a glance[18]

Benign salivary gland tumours

No myoepithelial cell differentiation- Canalicular adenoma
Warthin's tumour
Oncocytoma
Sebaceous adenoma
Ductal papilloma

Partial myoepithelial cell differentiation- Basal cell adenoma

Predominant myoepithelial cell differentiation- Pleomorphic adenoma
Myoepithelioma

Malignant salivary gland tumours

No myoepithelial cell differentiation- Acinic cell carcinoma
Salivary duct carcinoma
Hyalinizing clear cell carcinoma
Squamous cell carcinoma
Oncocytic carcinoma

Partial myoepithelial cell differentiation- Basal cell adenocarcinoma
Polymorphous low grade carcinoma
Mucoepidermoid carcinoma

Predominant myoepithelial cell differentiation- Adenoid cystic carcinoma
Myoepithelial carcinoma
Epithelial-myoepithelial carcinoma
Myoepithelial carcinoma ex pleomorphic adenoma

Myoepithelial host defence against cancer invasion

Myoepithelial cells contribute to the synthesis of surrounding basement membrane. They may exert paracrine effects on glandular epithelium and also regulate the progression of benign tumours to invasive carcinomas. Myoepithelial tumours exhibit the rare property of accumulating rather than degrading extracellular matrix material. Myoepithelial cells secrete relatively low levels of matrix degrading proteinases but relatively high levels of other anti-invasive proteinase inhibitors. Some of these inhibitors accumulate within the myoepithelial matrix and they can induce epithelial morphogenesis and inhibit tumour cell invasion in vitro.[19]

II. CONCLUSION

The myoepithelial cell plays a vital role in the histogenesis of many salivary gland neoplasms. They show variation in morphology and extracellular matrix production. They are natural tumour suppressor cells and have anti invasive properties. Generally carcinomas with myoepithelial participation are slow growing with limited metastasizing capacity. However their participation in salivary gland neoplasms is still unclear and warrants extensive studies with definitive markers for normal and neoplastic myoepithelial cell differentiation.

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