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Immunoprofile of reactive salivary myoepithelial cells in intraductal areas of carcinoma ex-pleomorphic adenoma

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Summary The myoepithelial cell (MC) is a component of various secretory glands, including salivary glands. Besides its function, a tumor suppressor and a tumor facilitating functions have been attributed to this cell. We investigated the immunoprofile of benign MC in intraductal areas of carcinoma ex-pleomorphic adenoma (CXPA), comparing them with the MC in duct-like areas of pleomorphic adenoma, origin of the malignant tumor. Antibodies against myoepithelial markers—CK14, α-SMA, calponin, P63, CD10, and D2-40—plus laminin and maspin was applied in four selected cases of intracapsular and minimal invasive CXPA with only luminal differentiation presenting areas of intraductal carcinoma. The immunohistochemical reactions of all the antibodies showed stronger staining in benign MC surrounding the malignant epithelial cells than in benign MC in duct-like areas of pleomorphic adenoma, thus revealing that in the malignization process the benign MC become differentiated and produce important proteins related to the tumor suppressor function.

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Introduction

The myoepithelial cell is a component of various secretory glands, including salivary and breast glands, and is located between the basement membrane and the basal plasma membrane of the luminal cells. These cells have pinocytic vesicles, microfilaments, and dense bodies resembling smooth muscle cells, and are recognized immunohistochemically by the positivity of myofilaments.

In salivary gland tumors, neoplastic myoepithelial cells are the main component of various benign and malignant tumors, contributing to the diversity of histological patterns and to the low-grade biologic profile of these tumors.

In the breast, tumors with myoepithelial component are rare and the studies focus on the best way to identify the normal myoepithelial cells in order to characterize the in situ condition of a tumor.

Its function as a contractile cell, facilitating the excretion of the products of both salivary and breast glands, have been well known for some time. But with recent scientific advances in molecular and biologic studies, new functions have been attributed to the myoepithelial cell.

Some studies, mainly in breast tumors, have emphasized the role of myoepithelial cells as tumor suppressor, providing an important defense against cancer invasion. This function was based on the capacity of myoepithelial cells to accumulate abundant extracellular matrix and secrete relatively low levels of matrix-degradation proteinases but relatively high levels of maspin and various other anti-invasive proteinase inhibitors.[1,2] Additional studies have demonstrated that myoepithelial cells exert an invasion-suppression effect via paracrine down-regulation of MMP expression in fibroblasts and tumoral cells.[3] It is also been demonstrated that the myoepithelial cell presents a distinct tumor suppression phenotype as an over expression in genes belonging to the classes of extracellular matrix proteins, angiogenic inhibitors and proteinase inhibitor and decreased expression in genes of angiogenic factors.[4]

On the other hand, numerous in vitro and in vivo studies using diverse experimental systems have demonstrated that the growth, survival, polarity, and invasive behavior of breast cancer cells can be modulated by myoepithelial and various stromal cells, and several genes have been implicated as playing an important role in this process.[5–7]

In order to add some knowledge to this subject, we investigated the immunoprofile of benign myoepithelial cells in in situ areas of carcinoma ex-pleomorphic adenoma (ISCXPA), comparing them with the myoepithelial cells in ductlike areas of pleomorphic adenoma (PA).

Material and methods

The present study protocol was approved by the Ethics Committee of School of Medicine of the State University of Campinas, Brazil.

Four cases were chosen from a previous study of 16 cases of CXPA,[9] retrieved from the files of the Department of Clinical Pathology at the State University of Campinas Medical School. These tumors were defined as malignant epithelial neoplasm arising in association with a primary or recurrent PA. The selected cases presented only epithelial (luminal) malignization and were classified as intracapsular and minimally invasive carcinoma in which areas of intraductal carcinoma could still be observed (areas of in situ carcinoma). These areas were characterized by the presence of benign myoepithelial cells surrounding the malignant luminal epithelial cells highlighted by myoepithelial immunohistochemical markers.

Clinical data are expressed in Table 1.

Serial sections of 3 μm thickness were obtained from the paraffin-embedded tissue. Dewaxed sections were subjected to antigen retrieval. Endogenous peroxidase was blocked by incubation with 3% hydrogen peroxide and methanol (1:1).

Table 1 Clinical data of the carcinoma ex-pleomorphic adenoma cases

Case	Sex	Age	Localization
# 1	Female	44-year-old	Submandibular gland
# 2	Female	37-year-old	Submandibular gland
# 3	Male	58-year-old	Parotid gland
# 4	Female	50-year-old	Parotid gland

Table 2 Clone, pretreatments for antigen retrieval, dilutions, and incubation time of primary antibodies

Antibody	Clone	Pretreatment	Dilution	Incubation
α-SMA[a]	1A4	No treatment	1:200	30 min
Calponin[a]	Calp	Pepsin 0.4%; pH 1.8; 37 °C; 30 min	1:150	30 min
CK14[b]	LL002	Citrate 0.01 M; pH 6.0; 95 °C; 30 min	1:50	30 min
P63[a]	A4A	Citrate 0.01 M; pH 6.0; 95 °C; 30 min	1:75	40 min
CD10[b]	56C6	Tris—EDTA, pH 8.9, 95 °C; 30 min	1:50	Over night
D2-40[a]	D2-40	Tris—EDTA, pH 8.9, 95 °C; 30 min	1:200	Over night
Laminin[c]	LAM 89	Pepsin 1%; pH 1.8; 37 °C; 60 min	1:1800	30 min
Maspin[d]	G167-70	Citrate 0.01 M; pH 6.0; 95 °C; 30 min	1:200	30 min

α-SMA, α-smooth muscle actin; CK, cytokeratin.
[a] DakoCytomation, Carpinteria, CA, USA.
[b] Lab Vision, Fremont, CA, USA.
[c] Sigma, Saint Louis, MO, USA.
[d] BD PharMingen, San Diego, CA, USA.