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CURRENT TOPICS IN BREAST PATHOLOGY

The morphological spectrum of salivary gland type tumours of the breast

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Summary

Salivary gland like tumours of the breast constitute a wide spectrum of entities each one showing peculiar features and clinical behaviour. They can be subdivided as follows: (1) tumours showing pure myoepithelial cell differentiation, such as pure benign and malignant myoepitheliomas; (2) tumours with mixed epithelial and myoepithelial cell differentiation, such as pleomorphic adenoma, adenomyoepithelioma and adenoid cystic carcinoma; and (3) tumours with pure epithelial cell differentiation, such as acinic cell carcinoma, oncocytic carcinoma, mucoepidermoid carcinoma and polymorphous adenocarcinoma.

These tumours share similar features with the salivary gland counterparts, but different clinical behaviour. Most salivary gland type tumours of the breast are negative for oestrogen and progesterone receptor and lack HER2 gene amplification, therefore they are classified as 'triple negative' tumours. Nevertheless, some of the malignant entities (such as classical adenoid cystic carcinoma) exhibit good behaviour and do not need any treatment in addition to local control.

The aim of the present paper is to review the morphological and prognostic features of salivary gland like tumours of the breast, in order to highlight the correct clinical management.

Key words: Myoepithelium; myoepithelioma; adenomyoepithelioma; pleomorphic adenoma; adenoid cystic carcinoma; acinic cell carcinoma; oncocytic carcinoma; mucoepidermoid carcinoma; polymorphous adenocarcinoma.

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INTRODUCTION

Breast and salivary glands structurally are both tubulo-acinar glands and, as expected, share some tumours due to their similar morphology. The first author who underlined the similarities between tumours of the breast and salivary glands was Azzopardi, who devoted to this subject an entire chapter of the book 'Problems in Breast Pathology'.[1] Thereafter a great amount of work was done, leading to the concept that a wide spectrum of salivary glands tumours, both benign and malignant, show the same morphological features in the breast, but different clinical behaviour. These differences, if not well known in clinical practice, can lead to incorrect treatment.

The aim of the present paper is to review most of the recently published papers that focus on similarities and differences between tumours of the salivary glands also shared by the breast. The main purpose is to highlight the correct clinical management.

Tumours of the salivary glands can affect the breast and can be classified in three main groups:[2] (1) tumours showing pure myoepithelial cell differentiation; (2) tumours with mixed epithelial and myoepithelial cell differentiation; and (3) tumours with pure epithelial cell differentiation.

TUMOURS WITH PURE MYOEPITHELIAL CELL DIFFERENTIATION

Benign myoepithelioma (BME)

BME is a tumour entirely composed of myoepithelial cells, resembling a benign smooth muscle tumour.[3] BME is a very rare lesion; it was originally described by Toth[4] and subsequently by Enghardt and Hale.[5] Since then additional single cases have been reported.[4–9] BME usually affects female patients, forming small solid to cystic nodules.[5]

Histology

BME can show an intraductal growth pattern or present nodular architecture. It is composed of spindle to polygonal cells. Absence of cytological atypia, atypical mitoses and necrosis are useful to distinguish BME from a malignant lesion (Fig. 1A).

Immunohistochemistry

BME has to be differentiated from the several benign spindle cell lesions of the breast, among which myofibroblastoma[10] and leiomyomas are the most similar lesions.[11,12] Immunohistochemistry demonstrating myoepithelial differentiation is important to drive the correct diagnosis. BMEs are typically positive for myoepithelial cell markers, such as high molecular weight keratins, p63, smooth muscle actin, calponin (Fig. 1B) and caldesmon. At a variance from leiomyoma that does not express keratins, BME is desmin negative.

Prognosis

The outlook of BME is generally favourable. Exceptions are the one case that recurred three times reported by Enghardt

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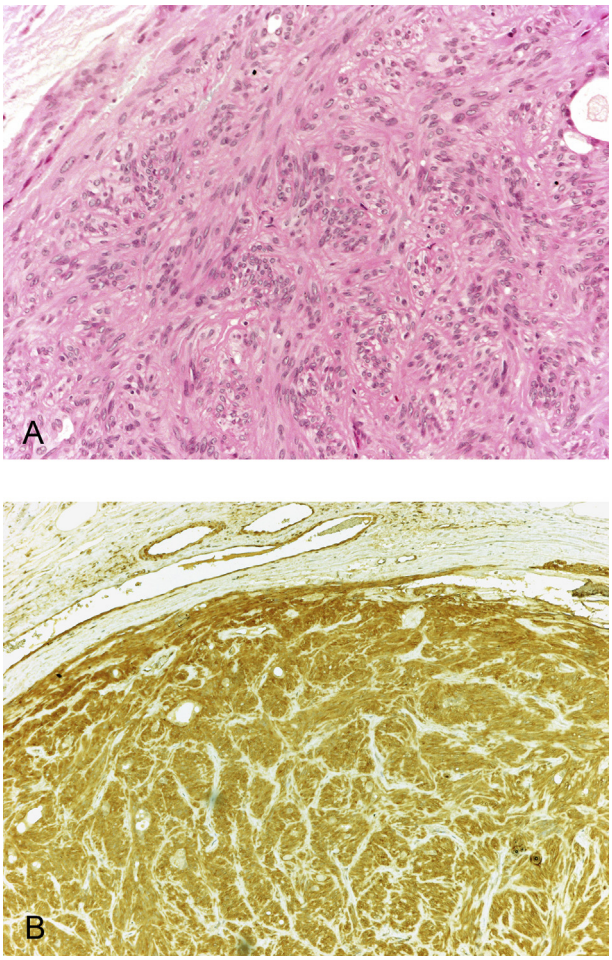

Fig. 1 (A) Benign myoepithelioma. This lesion is a nodule with well defined margins, composed of spindle eosinophilic cells devoid of any atypia. (B) The neoplastic cells are strongly positive for calponin.

and Hale[5] and the case reported by Jennens *et al.*[6] which presented one metastasis in spite of its benign appearance.

Malignant myoepithelioma (MME)

MME (synonym myoepithelial cell carcinoma) is a tumour composed of infiltrating malignant myoepithelial cells, occasionally with hyalinised stroma. In typical cases the malignant myoepithelial cells emanate from the myoepithelial cell layer of the ductules. Some cases can be associated with adenomyoepitheliomas (AME).

Pre-operative diagnosis

Pre-operative diagnosis can be difficult, especially if based on fine needle aspiration cytology (FNAC) only. Saguna *et al.*[13] described a highly cellular smear composed of large papillary-like clusters of monomorphic cells associated with naked nuclei in the background, simulating a benign breast lesion. MME FNAC findings can be misleading and, as suggested by Abd el-All,[14] whenever there are cytological features of a spindle cell lesion the nodule has to be surgically removed for an accurate histological diagnosis.

Histology

MME is a solid tumour composed of cells that vary greatly from polygonal to globoid with clear cytoplasm to spindle, eosinophilic elements. Oncocytic features and squamous cell differentiations have been described.[15–17] On rare occasions MME has been associated with *in situ* ductal carcinoma.[18] On molecular analysis the myoepithelial and the ductal components share alterations on 17q, suggesting a common origin.[19]

Immunohistochemistry

MME is positive for myoepithelial cell markers. Oestrogen (ER) and progesterone receptors (PR) are typically negative and HER2 is not amplified.

Differential diagnosis

MME should be differentiated from a wide spectrum of malignant spindle cells tumours of the breast, such as sarcomatoid carcinomas, including fibromatosis-like carcinoma. Most probably a relationship exists between MME and sarcomatoid carcinomas; both tumours can be morphologically so similar as to be assigned to a specific group only on differing immunohistochemistry. Both neoplasms share the same clinical behaviour and at present they should be treated similarly.

Prognosis

The prognosis for MME is generally poor, with a high frequency of local recurrences and distant metastases. Tsuda *et al.*[20] described a special variant of MME characterised by a central acellular zone. This latter variant tends to give lung and brain metastases.[20,21]

TUMOURS WITH MIXED EPITHELIAL AND MYOEPITHELIAL CELL DIFFERENTIATION

Pleomorphic adenoma (PA)

PA is the most common tumour in salivary glands, while it is rare in the breast. Our knowledge on PA of the breast is mainly based on single case reports.

Clinical presentation

Breast PA usually affects the retro-areolar region of female patients, with a wide age range. Occasional cases have been described in male patients.[22]

Pre-operative diagnosis

On radiological imaging it can present as a roundish lesion simulating fibroadenoma.[23,24] Sometimes it contains calcifications which usually are large. Cytological features can be difficult to interpret.[23]

Macroscopy

PA presents as a firm, well circumscribed nodule. Most of the reported cases are of about 2 cm in greatest axis.

Histology

PA of the breast shows the same morphological spectrum observed in the salivary gland counterpart (Fig. 2A,B). Specifically it is characterised by strands and glands of epithelial and myoepithelial cells, immersed in a myxo-chondroid stroma. Furthermore the myxo-chondroid stroma can contain single myoepithelial cells having stellate features.