Papillary lesions of the breast

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Papillary lesions of the breast comprises a spectrum of disease entities, with a common morphologic pattern of consisting of many fibrovascular stromal cores arising from the walls of the duct, and these cores are lined by epithelial cells, with a variable layer of intervening myoepithelium. The spectrum of papillary lesions ranged form benign to malignant, and classification of papillary lesions into these categories may be difficult, especially in the setting of needle core biopsies. This is especially so in the differentiation of the followings:

1. benign papilloma and papillary ductal carcinoma in situ (DCIS),
2. papillomas that are involved by florid epithelial hyperplasia (FH), atypical duct hyperplasia (ADH) and DCIS (low grade),
3. papillomas with FH and solid papillary carcinoma
4. benign entrapped epithelium and invasion

The correct differentiation of these entities is important, as the management and prognostic implication is different between benign and malignant diagnoses.

Benign papilloma and papillary DCIS

In both lesions, there is prominent papillary pattern with well formed fibrovascular cores. Well established histologic features that are considered helpful [1] are in papilloma, there is mixed epithelial and myoepithelial cells, with haphazard cellular architecture, and the epithelial nuclei is normochromatic. The papillae are prominent and fibrotic, and apocrine metaplasia may be seen. In papillary DCIS, the epithelial cells are arranged in a more rigid architecture, with hyperchromatic nuclei, and the papillary fronds are more delicate and elaborate. Within the lesions, the myoepithelial cells may be present in diminished number [2.3] or absent altogether [4]. However, a complete layer of myoepithelial cells can be identified around the papillary DCIS, attesting to the in situ nature of the disease. Immunostaining for myoepithelial cells can play an important role in the correct diagnosis of these lesions. Different myoepithelial markers have been evaluated, and p63, calponin and CK14 were considered by some authors as good markers [3,5,6].

Papillomas involved by different epithelial proliferations

Lesions considered under this category have the basic structure of a papilloma, only being superimposed by different types of epithelial proliferation. FH is frequently seen within papillomas, and foci of FH may appear as solid epithelial proliferation, but the characteristic architectural arrangement can still be discerned. Papillomas may also be involved by atypical ductal hyperplasia (ADH), and the characteristic histologic features of ADH can still be discerned within the papilloma. In most situations, the ADH involves part of the papilloma, hence the involved area will show solid epithelial proliferation,

whereas the other area retains the features of a benign papilloma. Another diagnostic problem is to decide when a papilloma with ADH becomes a papilloma with DCIS. To date, different criterion have been used, some authors would diagnose DCIS when the atypical focus is more than 0.3 cm within the papilloma [7,8], whereas others will use involvement of more than one third (up to 90%) within a papilloma irrespective of size [9], and still others would make a diagnosis of DCIS within papilloma when the atypical proliferation shows all the combined architectural and cytological features of DCIS, irrespective of the size and extent [4,10]. It should be noted that these criterion only apply to low grade DCIS. When high grade lesions are present within a papilloma, a diagnosis of carcinoma should be made irrespective of the size or extent. Immunohistochemistry has also a role to play in the differentiation of this group of lesion, particularly in the setting of core biopsy, in which the architectural characteristics of the epithelial proliferation may not be clearly displayed. Cytokeratins 5/6 and cytokeratin 14 have both been reported to be reliable to differentiate between florid epithelial hyperplasia (positive for both) and papillomas with ADH or DCIS (negative for both markers) [3,11,12].

Papillomas with FH and solid papillary carcinoma

Solid papillary carcinoma is usually considered a DCIS, characteristically occurring in elderly patients. Histologically, the cellular proliferation is solid and rounded, with an underlying network of widely spaced broad fibrovascular cores, separated by solid proliferation of the tumor cells. The tumor cells possess typically oval to spindled nuclei with eosinophilic granular cytoplasm, and there is prominent nuclear streaming, similar to florid epithelial hyperplasia [13]. Morphological differentiation of solid papillary

carcinoma from papilloma with extensive FH can be based on the presence of uniform cell population, and polarization of the cells around the fibrovascular cores in the former. Immunohistochemistry to highlight the absence of myoepithelial cells within solid papillary carcinoma [13], the absence of staining of for cytokeratins 5/6 [11] and the presence of neuroendocrine differentiation in many cases will help to establish the diagnosis.

Benign entrapped epithelium and invasion

In papillomas, fibrosis, hyalinization and entrapment of benign epithelial element may give an impression of invasion. To avoid over-diagnosing this as carcinoma, one should not base the diagnosis of malignancy on the presence of epithelial nests that look like invasion. Instead, the diagnosis of carcinoma has to be based on the cytologic and architectural characteristics of the papillary lesion instead. Several histologic features can be useful in this differentiation (14), including the benignity of the entrapped epithelium, which tends to follow the direction of the collagen in the background. In addition, these clusters are typically present in the altered stroma, and they do not penetrate into the normal stroma. Myoepithelial are present, but may be attenuated. The adjacent superimposed epithelial cell changes are also of a benign nature.

Many papillary lesions are histologically confusing, yet it is important to diagnose these lesions correctly. Careful assessment of any superimposed epithelial changes, the presence of myoepithelial cells, coupled with judicious use of immunohistochemistry will allow a correct diagnosis to be made in most cases.

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