Fibroepithelial neoplasms of the breast

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Abstract

Fibroepithelial neoplasms include a large number of common lesions encountered in both symptomatic and breast screening practice. Nearly all are fibroadenomas and are harmless, but they can present a range of differing histologies. The area of most concern is the separation of fibroadenomas from phyllodes tumours, arguably an arbitrary exercise at the benign end of the spectrum. What is most important to achieve is the recognition of those lesions in the fibroadenoma-phyllodes spectrum with the potential to do harm, either in the form of recurrence or metastases. These are few in number and the key features to identify, with the rare exception of carcinoma arising in these lesions, are those that signify a progression to stromal autonomy. Such features include stromal overgrowth, stromal invasion, stromal cell atypia and stromal mitotic activity. These need to be analysed together, not in isolation. Necrosis and heterotypic elements in particular are suggestive of frank malignancy.

Keywords fibroadenoma; hamartoma; lactating adenoma; phyllodes tumour; tubular adenoma

Introduction

This review is concerned with neoplasms characterized by a co-proliferation of epithelium and stroma. Under this heading come a number of benign lesions such as lactating adenoma, tubular adenoma, fibroadenoma and the low grade end of the phyllodes tumour spectrum. At the other end of the spectrum are borderline and malignant phyllodes tumours. For some malignant phyllodes tumours only a sparse residual epithelial component may remain. The classifications of these lesions are morphology based and in many cases the comfort zone provided by pigeonholing entities into specified nomenclature hides the fact that there a number of unclear areas. For some categories these considerations may not be important; for example, whether lactating adenoma is an entity in its own right or a fibroadenoma with superimposed lactational change. For others these considerations are more significant; phyllodes tumours include some lesions that recur and some lesions that are malignant.

Fibroadenoma – conventional type

These are harmless lesions and if tissue diagnosis is made, typically by core biopsy, there is an increasing tendency for them to be left and not excised, although continued growth and/or late presentation may prompt surgery.

Fibroadenomas are well-defined lesions which may be multiple in up to 20% of cases. They are clearly delineated from the surrounding breast and, as a consequence, can be quite mobile within the breast, hence the term 'breast mice' is sometimes used. There is a great variation in size. Typically they are firm and rubbery, but can be hard on the rare occasion when there is internal calcification. Often they have a bosselated gross appearance and have a white cut surface, with clefting sometimes discernible on macroscopic examination.

As indicated above these tumours represent co-proliferations of epithelium and stroma with both elements growing in concert. Traditionally, intracanalicular variants, with the epithelium arranged in clefts, and pericanalicular variants, where the epithelium is arranged in rounded acini-like configurations, are identified, although elements of both can commonly be seen in the same lesion (Figure 1). Stroma is of uniform cellular density which varies from almost acellular in long-standing, hyaline variants, to highly cellular in so – called 'cellular fibroadenoma'. Neither the intracanalicular nor the pericanalicular pattern has any particular clinical connotation, although since the former is also seen in phyllodes tumours, intracanalicular fibroadenomas are those most likely to cause diagnostic difficulty.

Fibroadenoma – epithelial proliferations

Fibroadenomas may show a number of epithelial phenomena superimposed on their basic architecture; for example, usual ductal hyperplasia, sclerosing adenosis, squamous metaplasia and lactational change. 'Complex fibroadenoma' is recognised where there is one or more of the following features: papillary apocrine hyperplasia, cysts over 3 mm in size and epithelial calcifications (Figure 2).[1] Up to 16% of fibroadenomas fall into this category.[2] Recent large population studies have indicated that the long held belief of a modest increase in malignancy following a diagnosis of complex fibroadenoma,[2] is actually due its frequent associated with other, well established risk factors such as proliferative breast disease and not the complex fibroadenoma itself.[3] Fibroepithelial neoplasms and particularly phyllodes tumours are more prone to containing co-existing carcinoma, of which in-situ malignancy is most common; in situ ductal and lobular carcinoma have both been described at relatively equal frequency.[4] Invasive carcinoma is less common and, where this is detected, it is important to ascertain whether it is wholly confined to the dominant lesion or has extended into it from the rest of the breast.

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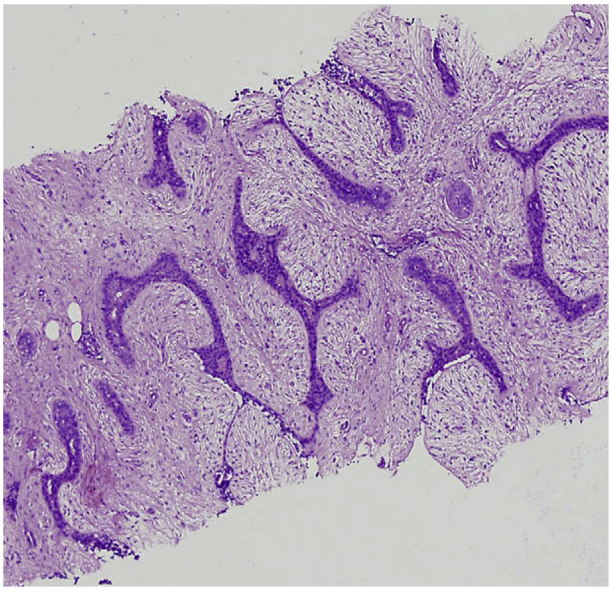

Figure 1 Fibroadenoma. Example of a typical, mostly intracanalicular pattern, fibroadenoma in core biopsies. The cores show no fragmentation and are mostly comprised of a co-proliferation of epithelium and stroma, the latter forming a sharp interface with adjacent fat. The stromal cellularity is low and there is no obvious condensation of stromal nuclei.

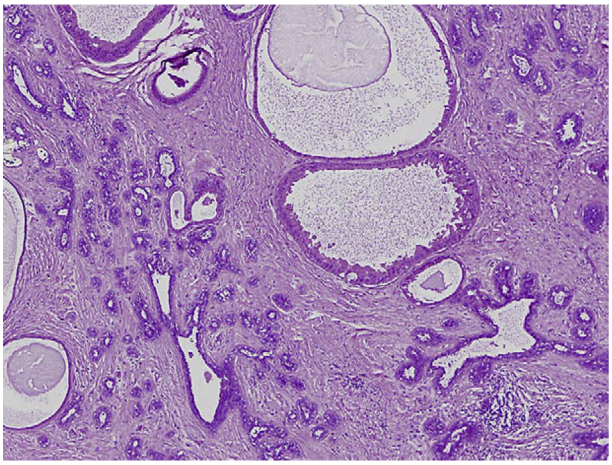

Figure 2 Complex fibroadenoma. Core biopsy showing early sclerosing adenosis and apocrine metaplasia with cyst formation and occasional calcifications.

Practice points

- Fibroadenomas exhibit varied, sometimes worrying appearances, due to diverse benign stromal and epithelial changes
- Carcinoma may rarely occur in fibroadenomas

Fibroadenoma – myxoid

Some fibroadenomas have a very loose myxoid matrix with a glistening cut surface (Figure 3). Lesions of this type have been associated with the rare Carney complex, which includes cardiac myxomas, cutaneous myxomas, spotty pigmentation and endocrine hyperactivity and is associated with abnormalities in the PRKAR1A gene.[5] In one case known to the authors, the diagnosis of the breast lesion pre-dated identification of a left atrial myxoma. In lesions associated with this syndrome, the stroma is extremely loose. Indeed, such loose myxoid change can be seen within the breast stroma divorced from any defined lesion with characteristics of a fibroadenoma[6] (Figure 4) and this change may be more obvious in the inter- rather than intra-lobular stroma. It should be noted that most myxoid fibroadenomas are not associated with Carney complex and do not have any harmful associated conditions.

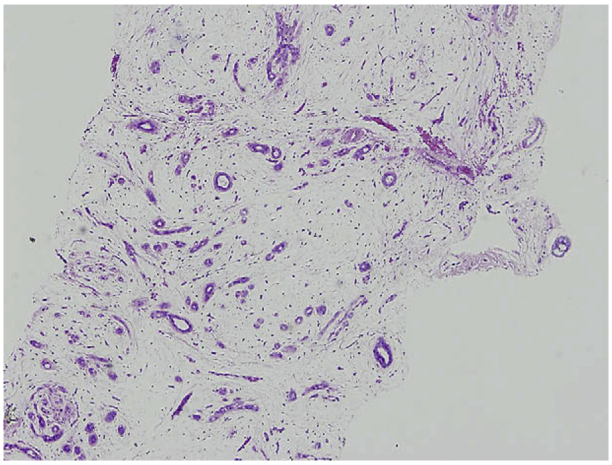

Figure 3 Myxoid fibroadenoma. A fibroepithelial neoplasm with a sharp interface with adjacent fat. The stroma is distinctly loose, mucoid and relatively acellular, and grossly the cut surface of the lesion is glistening with an almost translucent look.

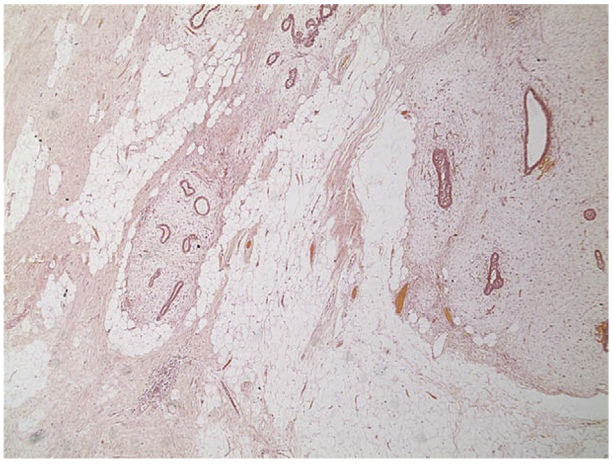

Figure 4 Pattern of mucoid change sometimes seen in primary pigmented adrenocortical disease (Carney complex). Here scattered mucoid change is seen in the breast, not specifically forming a distinct 'adenoma'. It is not known if this example was a proven Carney complex case.

Practice point

- Myxoid fibroadenomas may, rarely, be associated with other systemic abnormalities as part of Carney complex

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