Fibroepithelial neoplasms of the breast

Andrew M Hanby

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. 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 outgrowth, stromal invasion and both stromal atypia and pleomorphism. 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 phyllodes tumour spectrum. For some malignant phyllodes tumours only a sparse residual epithelial component may remain. The classifications of many 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 important; 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.

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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, or even 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 pericanilicular 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). Neither pattern has any particular clinical connotation, although since the intracanilicular pattern is also seen in phyllodes tumours, fibroadenomas with this pattern are those most likely to cause diagnostic difficulty.

Fibroadenoma – epithelial proliferations

Fibroadenomas may show a number of epithelial phenomena imposed upon their basic architecture; for example, usual type ductal hyperplasia, sclerosing adenosis, squamous metaplasia and around pregnancy and after lactational change. Additionally there is the 'complex fibroadenoma' in which 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] Although some population studies have indicated that there is a modest increase in malignancy following a diagnosis of complex fibroadenoma (3.1 × general population) versus a diagnosis of fibroadenoma (1.89 × general population),[1] the magnitude is

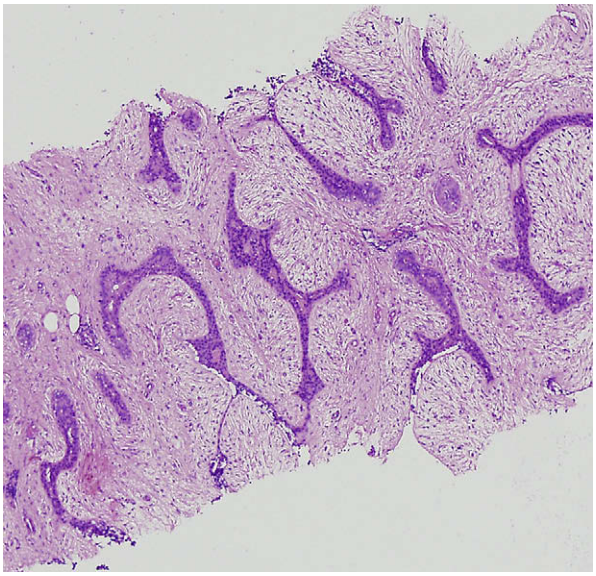

Figure 1 Fibroadenoma. Example of a typical, mostly intracanalicular pattern, fibroadenoma in core biopsies. The cores show no fragmentation and are mostly comprised of a co-proliferation of epithelium and stroma, the latter forming a sharp interface with adjacent fat. The stromal cellularity is low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

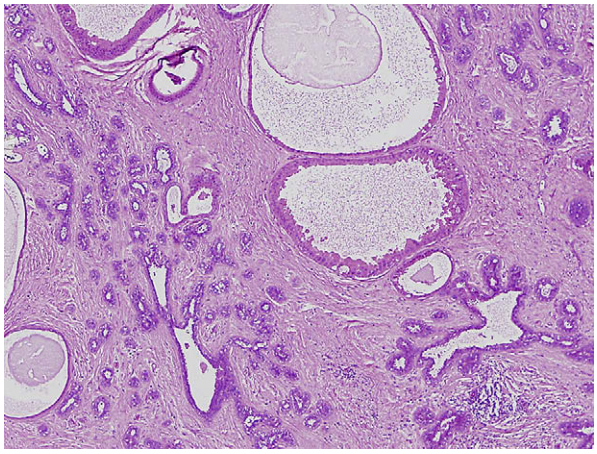

Figure 2 Complex fibroadenoma. Core biopsy showing early sclerosing adenosis and apocrine metaplasia with cyst formation and occasional calcifications.

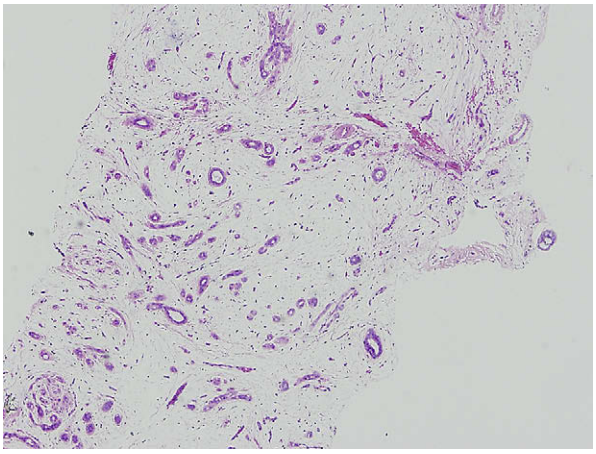

Figure 3 Myxoid fibroadenoma. A fibroepithelial neoplasm with a sharp interface with adjacent fat. The stroma is distinctly loose, mucoid and relatively acellular, and grossly the cut surface of the lesion is glistening with an almost translucent look.

such as to have no clinical implications for the individual case and treatment should be as for straightforward fibroadenomas.[2] Fibroepithelial neoplasms and particularly phyllodes tumours are more prone to containing co-existing carcinoma, of which in-situ malignancy is most common; both ductal and lobular have been described although lobular carcinoma in situ (LCIS) is most common. 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.

Practice points

- Fibroadenomas may show diverse benign epithelial changes.
- Complex fibroadenomas are associated with in breast cancer risk in large populations but is not enough to have implications for the individual patient.
- 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, more recently encompassed under the title primary pigmented adreonocortical disease (PPNAD) and associated with abnormalities in the *PRKAR1A* gene.[3] This complex also can include cardiac myxomas, cutaneous myxomas and spotty pigmentation,[4] as well as other soft tissue tumours and endocrine hyperactivity. In one case known to this author, 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 myxyoid change can be seen within the breast stroma divorced from any defined lesion with characteristics of a fibroadenoma[4] (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 PPNAD and do not have any harmful associated conditions.

Practice point

- Mxyoid fibroadenomas may, rarely, be associated with other systemic abnormalities as part of PPNAD.

Fibroadenomas with multinucleated stromal giant cells

On occasion an otherwise typical fibroadenoma may contain bizarre fibroblasts[5,6] (Figure 5). These may be plentiful and unnerving to the unwary. Crucially these rarely have associated stomal mitoses and may also be seen in phyllodes tumours[5]; such fibroblasts are not associated with any behavioural significance in either fibroadenomas or phyllodes tumours.

Practice point

- Giant cells in fibroepithelial neoplasms are generally of no significance

Lactational/lactating adenoma

As might be expected, these lesions occur during pregnancy and during lactation. They may be quite large and biopsies reveal a mass of closely packed lactating acini/glands (Figure 6). On occasion these may show infarction and this can be extensive. Whilst in some lesions the vestige of a fibroadenoma of conventional type can suggest a derivation from it, in other cases it is less clear that this lesion is a tumour or merely a dominant lactating lobe.[7] These lesions are important in so much as they