Benign sclerosing lesions of the breast – an update

Joseph Loane

Abstract

Benign sclerosing lesions of the breast comprise primarily sclerosing adenosis and radial scar/complex sclerosing lesions (RS/CSL). Other benign lesions which may become fibrosed and malignant tumours frequently associated with a sclerotic stromal reaction, may enter their differential diagnosis either radiologically or on pathological examination. This updated review focuses on the core biopsy diagnosis and operative pathology of these lesions with particular reference to their prognosis and recent trends in their management.

Keywords core biopsy diagnosis; management; prognosis; radial scar/complex sclerosing lesion (RS/CSL); sclerosing adenosis

Introduction

Sclerosing lesions of the breast comprise primarily sclerosing adenosis and radial scar/complex sclerosing lesions (RS/CSLs). Other benign lesions, such as intraductal papilloma can be associated with fibrosis or sclerosis, and may enter the differential diagnosis of a sclerosing lesion, particularly if limited material is sampled or on breast core biopsy. Likewise it is the nature of some breast cancers to evoke a sclerosing stromal reaction in the breast and various other patterns of fibrosis and sclerosis have been associated with malignant disease, including central scarring associated with a response to Letrozole treatment. These latter benign and malignant lesions will not be covered here except where they enter the differential diagnosis of sclerosing adenosis or RS/CSL which form the main focus of this updated review.

Sclerosing adenosis

Incidence

Sclerosing adenosis is a very common finding in the adult female breast. It is frequently found incidentally in its microscopic form in otherwise normal breasts and is considered within the normal spectrum. It may also present as one of the range of benign changes that together make up fibrocystic change. Its presentation clinically as a worrying mass, or radiologically as a mass lesion or indeterminate calcification, however is less common. Thus, although pathologists will encounter sclerosing adenosis on a regular basis, its setting and diagnosis usually poses little difficulty.

Aetiology and pathogenesis

Several theories for the aetiology of sclerosing adenosis have been proposed. It is considered by some as an abnormal pattern of age-related regression or post-lactational involution within the breast.[1] Lack of an association with parity or lactation in one large study[2] would seem to count against this. Others suggest that it represents a proliferative process, a view supported by the infrequent but well-documented finding of perineural 'invasion' within the lesion.[1,3] It arises predominantly from the terminal duct lobular unit and evolves through an earlier stage of florid proliferation of epithelial cells to a later stage of stromal fibrosis and loss of lobular boundaries.

Pathology

The macroscopic appearance of cases presenting clinically is of a diffuse firm mass with indistinct but generally rounded margins within which flecks of calcification may be apparent. If presenting within fibrocystic change, then a cystic component may be evident. On histology, sclerosing adenosis, as the name indicates, comprises lobules expanded by proliferated acini (adenosis) with, in addition, a variable amount of intervening stromal sclerosis that may result in compression and distortion of the acinar structures. In general, the lesion has a well-defined outline maintaining the impression of an expanded lobule, a helpful point in its distinction from carcinoma (Figure 1). The dual layer of inner epithelial and outer myoepithelial cells lining the acini is maintained. Myoepithelial cells may be prominent on H&E staining, giving the lesion a proliferative and occasionally worrying appearance. Use of cytokeratin 14 and/or other myoepithelial marker, if necessary, can easily confirm that this is a benign process. Acinar calcification, which may be the mode of presentation on mammography, is a frequent finding.

Other changes can occur within or be superimposed upon sclerosing adenosis. Apocrine change can present particular problems when it occurs in conjunction with sclerosing adenosis as its frequently pleomorphic nuclei and prominent eosinophilic cytoplasm compressed within the lesion can present a very worrying first impression. Careful consideration of the setting of the apocrine change should prevent overcalling this lesion.

Risk of malignancy

Jensen et al[2] reported an increased risk of subsequent invasive breast cancer 2.3 times that of the normal population in a large series of patients with a prior benign breast biopsy containing sclerosing adenosis, without either other proliferative disease without atypia (PDWA) or atypical hyperplasia in the background, who were followed up for a mean of 17 years. The presence of other PDWA reduced the risk to 1.7 times the background population, while the presence of atypical hyperplasia increased it to 6.7, although the numbers of patients in this category were quite small. The authors conclude that sclerosing adenosis should be included in the broad category of histological lesions designated as proliferative disease without atypia. Two nested case control studies, again with small numbers of cases, did not find any increase in the risk of subsequent malignancy however. A more recent study from the Mayo Benign Breast Disease Cohort[4] comprising 2672 patients with sclerosing adenosis without atypia and a long follow up period reported a risk of subsequent malignancy of 1.97 (95% CI 1.76–2.21), similar to that of Jensen et al.

The Mayo group followed this with a description of a gene signature model for breast cancer risk prediction for women with

Joseph Loane *MB BCh BAO FRCPath Consultant Pathologist, Department of Pathology, Queen Elizabeth University Hospital, Glasgow, UK. Conflicts of interest: none declared.*

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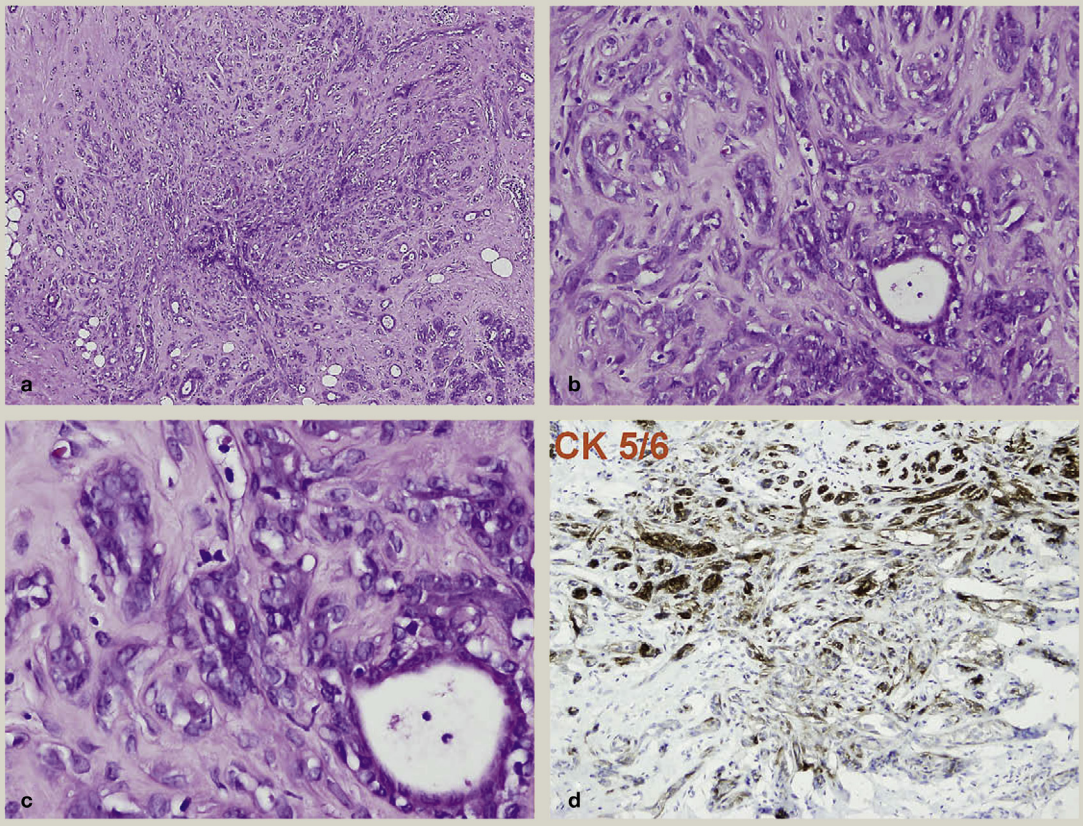

Sclerosing adenosis. **a** Low, **b** medium and **c** high power views of a focus of sclerosing adenosis showing preservation of overall lobular architecture around a central terminal duct. **c** Shows the preservation of a myoepithelial layer (peripheral cells with clear cytoplasm) and this is further illustrated in **d** by CK 5/6 immunostaining.

Figure 1

sclerosing adenosis.[5] This is the first paper to describe such a model in patients with sclerosing adenosis and represents an interesting approach. Based on the data presented in this paper however, the utility of this gene signature in practice is debatable. Although the overall accuracy of their gene signature of 80% in their test development set (dropping to 58% in their validation set), given the large proportion of false positive results reported the positive predictive value of this test is likely to be low. A high negative predictive value, which it is likely to have, though reassuring is of less utility as in practice these women will return to routine screening, that is, the test will have little impact on their future management.

Non-operative diagnosis

Clinical features

Sclerosing adenosis is most common in perimenopausal women, but has a wide age range. An increased incidence is reported in women with a family history of breast carcinoma.[2] When evident clinically, it usually presents as an ill defined solitary mass that may range in size from 0.5 to 5 cm, which may better be referred to as nodular sclerosing adenosis or adenosis tumour. Rare cases of multiple lesions and bilateral lesions have been reported. It is usually relatively fixed within the breast, but skin dimpling or fixation to deep fascia is very uncommon. In contrast to carcinoma it may present with pain and tenderness.

Radiological features

On mammogram it presents most commonly with microcalcifications that are usually clustered but may be diffuse. Calcifications may be dense, punctuate or irregular, but generally are not branching or cast-like, as seen in ductal carcinoma in situ (DCIS). The remainder present as mass lesions, asymmetrical densities or focal distortions of architecture. Ultrasound may detect cases not evident on mammogram. These present as mass lesions that are usually well circumscribed and may show marked posterior acoustic shadowing.

Core biopsy

Only one paper has addressed the question of the adequacy of pre-operative diagnosis of sclerosing adenosis by core biopsy.[6] Although the study population was (1) selected from those core biopsies without atypia or malignancy in which sclerosing adenosis comprised the majority of the lesion sampled; and (2) small (only 27 cases which met the criteria had follow-up of at least 20 months), the authors concluded that sclerosing adenosis is an acceptable result at core biopsy of circumscribed masses, of non-palpable indistinctly marginated masses and of clustered

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