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Review

Lesions of uncertain malignant potential in the breast (B3): what do we know?

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Breast lesions classified as of uncertain malignant potential (B3) on biopsy form a diverse group of abnormalities, which pose a diagnostic and management challenge. In this paper, we discuss the imaging and pathology features as well as the management of the most controversial B3 lesions, consisting of papillary lesions, complex sclerosing lesions/radial scars, lobular intraepithelial neoplasia, and atypical epithelial proliferation of ductal type. As there is an association with malignancy at the time of diagnosis, as well as an increase in the risk of subsequent development of cancer, a multidisciplinary discussion is almost always required to tailor treatment.

Introduction

The European Guidelines for quality assurance in breast cancer screening and diagnosis stipulate that all breast needle core biopsies (NCB) should be classified under the following five categories: B1, normal; B2, benign; B3, lesion of uncertain malignant potential; B4, suspicious for malignancy; and B5, malignant. The B3 subgroup is of particular interest as it consists of lesions that, although benign on histology, are known to either show heterogeneity or have an increased risk of associated malignancy. This category includes papillary lesions, radial scars (RS)/complex sclerosing lesions (CSL), lobular intraepithelial neoplasia (LIN), atypical epithelial proliferation of ductal type, and phyllodes tumours.[1]

With the increasing use of digital mammography and the widespread availability of vacuum-assisted biopsy (VAB) systems, there has been an increase in the proportion of NCBs reported as B3 in some series and a drop in the positive predictive value for malignancy from 25% to 10%.[2] One of the reasons for this is believed to be the increase in the detection of RS/complex sclerosing lesions. As surgical excision is no longer the only available treatment for some of these entities, the management of B3 lesions has become complex and requires a multidisciplinary team approach in the decision-making process.

This article gives an overview of the most controversial B3 lesions, describes their imaging features, and discusses the management options.

Papillary lesions

The pathological entity of a papillary lesion covers a spectrum of disease that can develop within the breast.

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These lesions are rare and occur in less than 3% of all solid tumours.[3] Papillary lesions may be classified as solitary intraductal papillomas, multiple intraductal papillomas, atypia-ductal carcinoma *in situ* (DCIS) within a papilloma, micropapillary DCIS, and papillary carcinoma.[4]

The appearances in the breast vary clinically, radiologically, and pathologically, and familiarity with features of malignant and benign lesions is required to plan management. In particular, as with any other breast malignant lesion, the presence of an irregular mass with indistinct, microlobulate or spiculate margins, with or without the presence of microcalcification should raise the suspicion for an invasive micropapillary carcinoma.[5]

Histopathology (Fig.1)

Papillary lesions are composed of papillary fronds, which are attached to the inner mammary ductal wall by a fibrovascular core and extend into the lumen of the duct. Ductal epithelial and myoepithelial cells line the fibrovascular core, and it is these epithelial cells that can undergo degrees of apocrine metaplasia.[6]

Epidemiology and imaging features

Intraductal papillomas are generally solitary, located in the retro-areolar region, and occur more frequently in post-menopausal women. They often present with clear nipple discharge.[7] They are typically small and often mammographically occult. When visible they appear as well-circumscribed retro-areolar masses or a dilated retro-areolar duct. Sonographic appearances range between a well-defined solid mass or mass within a cyst or a dilated duct. Sometimes ductography may be required for diagnosis, which demonstrates an intraluminal filling defect or ductal dilatation.[5] Some centres use mammary ductoscopy, an endoscopic technique allowing direct visualisation of the ducts under local anaesthetic, as an alternative technique with good results.[8] Patients with a solitary papilloma without atypia have a twofold risk of developing breast cancer.[9]

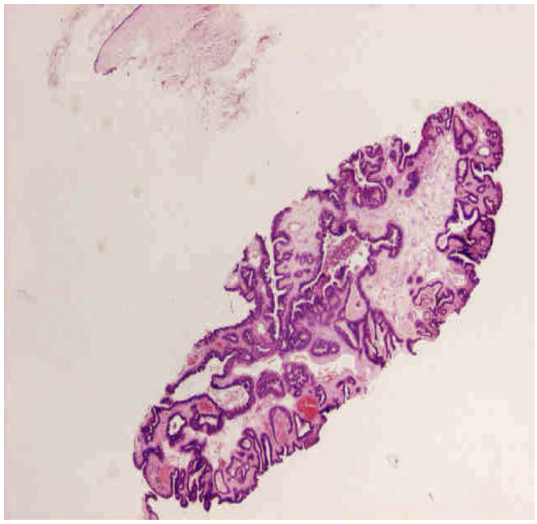

Figure 1 Core biopsy showing a benign papillary lesion composed of a fibrous core covered by two layers of benign epithelial cells.

Patients with multiple intraductal papillomas (MP) are generally younger and only occasionally present with nipple discharge or a palpable mass. The diagnosis is most often incidental.[7] Although MPs are less frequent than solitary papillomas, they are associated with an increased risk of breast cancer both in relation to the general population and to patients with solitary papillomas.[9] MPs are more often peripherally located and are more likely discovered on mammography as microcalcifications.[10]

Management

The management of papillary lesions remains uncertain and most definitely requires a multidisciplinary team approach. The main difficulty is distinguishing benign from malignant lesions as manifested by a significant upgrade rate in subsequent surgical excisions demonstrated in several studies.[11–16] The general consensus is that papillary lesions with atypia need to be surgically excised to ensure benignity.[17] Controversy exists in the management of papillary lesions without atypia. Following benign diagnosis of a papilloma at NCB, a small percentage will be upgraded to malignancy following surgical excision.[17,18] There is, however, evidence to suggest that the same does not apply to VABs. A study by Zografos *et al.*[19] suggested that the surgical excision upgrade rate following VAB was 0% in lesions without atypical features. In a further study by Chang *et al.*,[17] the upgrade rate for benign papillomas was also 0%. This suggests that, following VAB for papillary lesions without atypia, where a large amount of tissue is excised and there is no radiological–pathological discordance, conservative treatment should be strongly considered.

RS/CSL

RS are benign lesions, which were first described by Linell *et al.*, in 1980.[20] They are classified as CSL when their size on pathology exceeds 10 mm and are classically non-palpable.

Histopathology (Fig. 2)

RS are pseudo-infiltrative lesions, which are characterised by a fibro-elastic core with entrapped ducts demonstrating an intact myoepithelial layer and ductules radiating outwards to form a stellate pattern.[21–23] They are often seen in the presence of benign changes such as cysts, sclerosing adenosis, and epithelial hyperplasia.[23] Due to the pseudo-infiltrative appearance, distinction from a tubular carcinoma can be difficult. There are theories to suggest that the presence of atypia often seen in association with a RS/CSL may be due to preceding change prior to the development of invasive carcinoma,[20] although others disagree.[24]