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CORRESPONDENCE

Review on current treatment options for lesions of uncertain malignant potential (B3 lesions) of the breast: do B3 papillary lesions need to be removed in any case by open surgery?

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Abstract

Background In breast tissue, pre-malignant lesions are classified as BIRADS 3. The treatment of this heterogeneous group varies with expertise and tools available.

Materials and methods With the example of two case reports, the literature is reviewed on current treatment options for BIRADS 3 breast lesions.

Results About 7% of all B-type breast biopsies fall into the B3 category. Approximately 35% of these B3 lesions are due to FEA, 20% to PLs and another 20% to ADH. Due to improvement in diagnostics, the incidence is increasing, while their value as a predictive factor for malignancy has steadily been fallen.

Conclusion Depending on the histology of the needle biopsy, a complete resection with vacuum-assisted biopsy may be a treatment alternative to open biopsy.

Introduction

B3-breast lesions comprise a heterogeneous group of lesions with unknown malignant potential. However, this is generally considered to be low [1]. These lesions include classic lobular neoplasia (LN), flat epithelial atypia (FEA), atypical ductal hyperplasia (ADH), papillary lesions (PL), benign phyllodes tumors (PT), and complex sclerosing lesions (CSL) including radial sclerosing lesions (RSL) and radial scars (RS). Each of these lesions has a specific risk of breast cancer [2]. About 7% of all B-type breast biopsies fall into the B3 category. Approximately 35% of these B3 lesions are due to FEA, 20% to PLs and another 20% to ADH [3]. Due to improvement in diagnostics, the incidence is increasing, while their value as a predictive factor for malignancy has steadily been fallen [4–6]

In the past, good evidence on how to appropriately treat these lesions was not available, and often, they were excised in open surgery, perhaps subjecting the patient to an unnecessary invasive procedure. Newer techniques like vacuum-assisted biopsy (VAB) or minimally invasive breast biopsy allow the removal of a larger tissue sample than core needle biopsy: It might be discussed that these are sufficient for curative excision of these lesions. In the recent "International C Conference on lesions of uncertain malignant potential in the breast (B3 lesions)" guideline for the treatment of B3 lesions with LN, FEA, RS, and PL type, it is recommended that these lesions should be therapeutically excised by VAB instead of open surgery [1]. With the help of two clinical cases, we present a summary of the current literature about malignancy rates in B3 lesions.

Case 1

53 year breast screening participant with mammographic 9 mm lesion right breast at 10 o'clock. Mammography,

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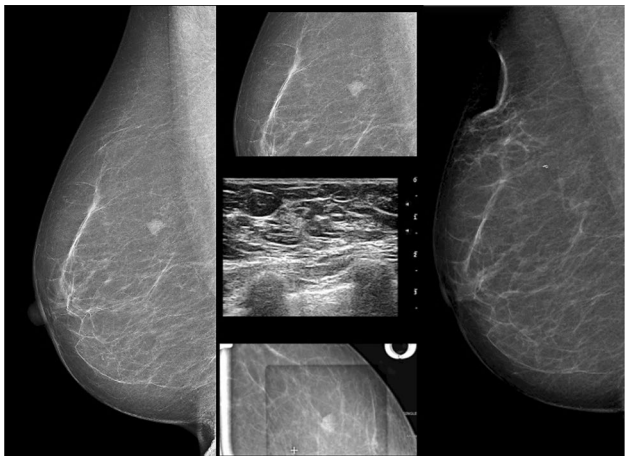

Fig. 1 Case 1 mammography, ultrasound and enlargement prior intervention and post intervention mammography control

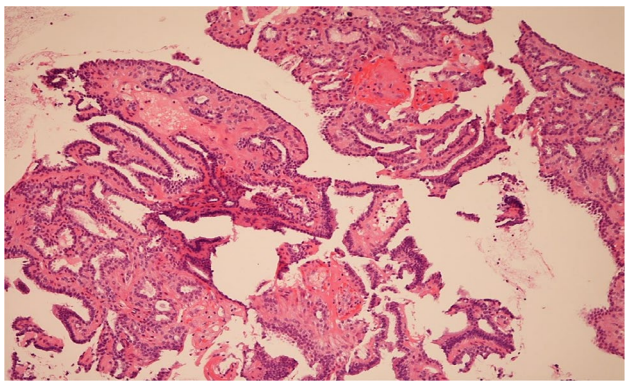

Fig. 2 Papillary lesion removed with vacuum assisted biopsy

ultrasound, and post intervention are presented in Fig. 1, the final histology papillary lesion (Fig. 2).

Case 2

53 year breast screening participant with mammographic 11 mm lesion left breast at 11 o' clock. Primary mammography, ultrasound, and ultrasound guided core needle biopsy are present in Fig. 3, the final histology papillary lesion (Fig. 4).

Histology and morphology

The histomorphology of ADH is essentially identical with a low-grade ductal carcinoma in situ (DCIS). The differentiation between the two is due to an arbitrary definition designating an ADH as a lesion of less than 2 mm in size and a lesion of ≥2 mm as DCIS [7, 8]. This makes the diagnosis—based on a core needle biopsy (CNB)—difficult as

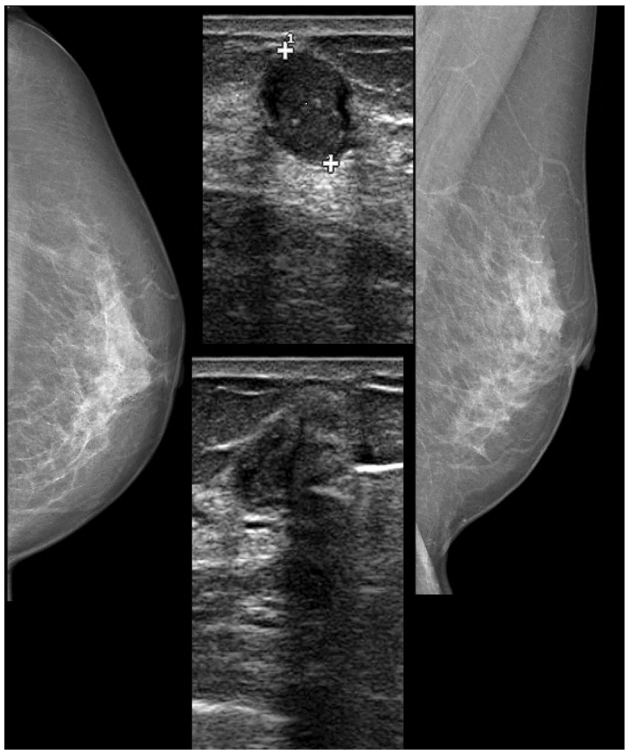

Fig. 3 Case 2 with mammography (ml and cc plane), ultrasound and core needle biopsy

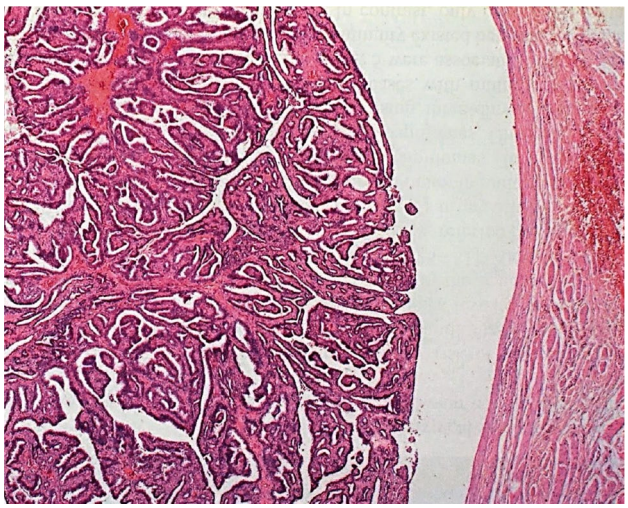

Fig. 4 Case 2: histology of ductal papilloma

the CNB often contains only a part of the lesion [1]. Thus, the guidelines of the "German Workgroup Gynecologic oncology" (Arbeitsgemeinschaft Gynäkologische Onkologie—AGO) and others have published guidelines recommending the excision of ADH based on CNB diagnostics in all cases [9]. The "First International Consensus Conference" and the AGO recommend patient monitoring as a

viable option after a completed removal of a unifocal ADH by VAB. In contrast, ADH of sufficient size to be detectable by imaging methods should be excised surgically [1]. This recommendation is based on the fear that VAB might leave undetectably small residual disease that will develop into a an invasive tumor if monitoring without surgery is implemented [10].

The terminal ducto-lobular unit (TDLU) can show a variety of different epithelial proliferations with atypia. Those with non-cohesive epithelial cells are categorized as classical LN. The participants of the consensus workshop agreed on the need for excision of LN grade 3 non-classical type after it was diagnosed by CNB, while monitoring was considered sufficient after VAB diagnosis [2]. This recommendation is due to relatively high upgrade rate to carcinoma in studies with CNB, e.g., a recent study that found a rate of 13% [11]

Neoplasia of the TDLU with a shallow layered atypia is the defining morphology of the FEA. The atypia is low grade with uniform cells of regular round shape [2]. FEA may present with calcifications and usually does not contain secondary architecture. Immunologically, low-molecular weight cytokeratin is typically not expressed and estrogen receptors are well-regulated [2]. The majority of experts agrees on the recommendation of surgical excision—with VAB as a possible tool after an FEA diagnosis based on CNB (if mammographically completely removed), while only a small minority recommends open surgical excision after a VAB discovered FEA [2]. However, there is still significant controversy about which is the best treatment for this type of lesion [11]

PT of the B3 type is either benign which accounts for the majority of PT cases or borderline in 11–30% of cases [1, 2]. PT in general are rare with less than 1% of all breast neoplasias and malignant PT which are not categorized, as B3 is the rarest form of PT. The morphology of PT has some overlap to that of benign fibroadenomas—except the hypercellularity of the stromal component ("stromal overgrowth")—and differential diagnosis, though important, may be difficult [2]. Complete resection of B3-PT should be achieved.

RS and complex sclerosing lesions (CSL) are the same entities, but differ in size. RS have foci of less than 1 cm, while lesions with larger foci are classified as CSL. Histologically, ductal hyperplasia, microcalcifications, and adenosis are present together with the characteristic stellate-like fibrotic lesion [1, 2].

PLs represent up to 5% of all biopsied breast lesions. The term PL comprises a heterogeneous group of epithelial lesions [12–14]. If there is no atypia present, the risk of malignancy is low. In contrast, a PL lesion with atypia should consequently be considered as a high-grade lesion [13].

Upgrade rates after surgical excision of benign papillomata diagnosed with CNB or vacuum-assisted biopsy (VAB) vary from 0 to 28% with atypical cells and from 0 to 20% for invasive cancer. In general, underestimating the stage (understaging) of invasive malignancy is reduced if multiple biopsy cores are taken or if larger biopsy needles are used such as in VAB. Most studies following up VAB excision of PL without atypia did not observe any upgrade to malignancy with at least 2 years of surveillance [2]. Underestimation of 1.4%–3.2% is reported. The reported upgrade rate to malignancy following VAB during the first consensus conference on lesions of uncertain malignant potential in the breast was 7.7% for PL without atypia which was higher than in the documented literature [2]. When surgical excision was performed after VAB, the upgrade rate was 7.8% with 5.2% being upgraded to DCIS (stage B5a) and 2.6% to invasive malignancy (stage B5b) [2]. It is now generally accepted that PL have been completely removed by biopsy (e.g., in VAB) do not require further diagnostic nor therapeutic treatment.

In incompletely removed PLs, the participants of the conference agreed that PL should be excised after diagnosis based on CNB. 84% of the expert considered VAB as an acceptable method for excision. If the diagnosis was based on VAB, 91% of the conference participants felt that careful patient monitoring was sufficient, while 9% thought that it is necessary to remove the lesion in open surgery [2]. This agreement was reached for PL without atypia, while the participants had the opinion that PL with atypia should, depending on the type of atypia, be treated like FEA or ADH and thereby treated according to the recommendations for those lesions (excision with open surgery rather than by VAB) [2].

A retrospective study of Liberman and coworkers published in 2006 with 3864 percutaneous imaging-guided breast biopsies yielded 50 diagnoses of benign PL. For 35 of these, patient follow-up data were available for at least 24 months. Surgery found cancer in 14% of these lesions and another 17% showed high-risk lesions upon surgery. Liberman and coworkers concluded that surgical excision might be necessary in all cases of a diagnosis of benign PL based on percutaneous breast biopsies [15].

Conclusions

B3 lesions encompass a variety of different lesions each with their own risk for malignancy. Treatment options depend on the specific risk profile of the individual lesion which is why exact diagnosis is important, though it can be challenging due to morphological overlap between different types of lesions.

PL without atypia is generally considered benign or borderline and represents the majority of PLs. Nevertheless, underestimation of the stage of the lesion based on CNB

or VAB is not uncommon. PL with atypia should not be treated as PL, but rather as FEA or ADH depending on the present type of atypia. The expert consensus is that excision of benign PL is necessary or warranted, but it does not require open surgery. Instead, VAB might be acceptable for these types of B3 lesions. Higher risk B3 lesions, however, might require excision by open surgery.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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