

Morphologic spectrum of co-existing lesions in breast malignancy – A study of mastectomy specimens

Mohit¹, Shachi Dixit^{2*}

¹Associate Professor, Department of Pathology, Career Institute of Medical Science, Lucknow, Uttar Pradesh, India

²Assistant Professor, Department of Pathology, World College of Medical Science & Research, Jhajjar, Haryana, India

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Abstract

Breast lesions is a family of heterogeneous entities with varying forms of presentation, morphology and clinical nature. Most of these lesions are traditionally classified into benign and malignant conditions. However, some lesions show marginal features and lie in a grey-zone between benign and malignant due to unreliable predictability. Pathological categorisation of such lesions is challenging, and under-diagnosis may leads to over-treatment or under-treatment. The shortage of these lesions makes acquisition of clinical evidence problematic and restricts the advancement of a sufficient evidence base to support informed decision making by clinicians and patients. Emerging molecular evidence is providing a greater understanding of the biology of these lesions, but this may or may not be reflected in their clinical behaviour. In the present study. we discuss some breast lesions that may leads to cancer malignancy. The idea of categories of breast lesions of uncertain malignant nature and breast lesions of limited metastatic potential, are recommended.

Keywords: Cancer malignancies, Breast lesions, Morphology, Pathology.

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Introduction

Breast cancer is a heterogeneous disease, comprising numerous distinct entities that not only have different biological features.[1] There are numerous appearances of evidence to propose that breast cancer is a group of different diseases with different risk factors, pathological features, clinical presentations, response to therapy and outcomes, which affect the same anatomical organ and originate in the same anatomical structure. Histopathologists suggested the diversity of breast cancer and have endeavoured to devise approaches to classify the disease into meaningful groups.[1]

Breast cancers can be classified into biologically and clinically meaningful subgroups according to histological grade [2] and histological type. [3] Grade is an assessment of the degree of differentiation (i.e. tubule formation and nuclear pleomorphism) and proliferative activity (i.e. mitotic index) of a tumour, and mirrors its aggressiveness. 2 Interestingly, grade has been shown to correlate with the genetic and transcriptomic features of breast cancers and microarray-based genomic signatures for histological grade have been devised. [4]

Histological type, on the other hand, refers to the growth pattern of the tumours. The histological diversity of adenocarcinomas in the breast has long fascinated pathologists, who have identified specific morphological and cytological patterns that were consistently associated with distinctive clinical presentations and/or outcomes. These patterns are called 'histological types'. The commonest type of breast carcinoma is the so-called invasive ductal carcinomas not otherwise specified (IDC-NOS) or of no special type (IDC-NST).[5]

Which is a diagnosis of exclusion and comprises adenocarcinomas that fail to exhibit sufficient characteristics to warrant their classification in one of the special types. Breast cancer special types account for up to 25% of all breast cancers and the latest edition of the World Health Organisation classification recognizes the existence of at least 17 distinct histological special types.[5]

Role of Different lesions

In the young non-lactating breast, the parenchyma is mainly comprised of fibroglandular tissue, with little or no subcutaneous fat. With aging and parity, more and more fat gets deposited in both the subcutaneous and retromammary layers. [6] Histopathological measurement of accurate breast cancer size is regarded as the gold standard, whereby therapeutic decisions heavily rely on tumor size assessment by radiological imaging. With increasing use of breast-conserving surgery and neoadjuvant chemotherapy, the accuracy of radiological breast imaging is essential for an optimized and individualized therapy. The term high-risk breast lesion is given to a breast lesion that carries an increased risk for the future development of breast cancer or carries suspicion of a more sinister pathology around or in association with the lesion. The term has some overlap with borderline breast disease. Many radiologists recommend excision of these lesions when they are revealed on pathological analysis after a core biopsy. In the following sections we are briefing about the different types of lesions in breast that can be risky for the cancer malignancies.

Breast cysts

In women between 35 and 50 years of age, breast cysts are the commonest cause of breast lumps. [6] A cyst occurs when fluid accumulates due to obstruction of the extralobular terminal ducts, either due to fibrosis or because of intraductal epithelial proliferation. When internal echoes or debris are seen, the cyst is called a complex cyst.

*Correspondence

Dr. Shachi Dixit

Assistant Professor, Department of Pathology, World College of Medical Science & Research, Jhajjar, Haryana, India.

E-mail: dixit.shachi@gmail.com

Chronic abscess of the breast

Patients may present with fever, pain, tenderness to touch and increased white cell count. Abscesses are most commonly located in the central or subareolar area. [7]

Fibrocystic breast condition

This condition is also referred as fibrocystic change, fibrocystic disease, chronic cystic mastitis, cystic disease, or mammary dysplasia. It appears differently based on the stage and extent of morphological changes. As stage extends, there may be focal areas of thickening of the parenchyma, with or without patchy increase in echogenicity. Focal fibrocystic changes may appear as solid masses or thin-walled cysts. [8]

Duct ectasia

This lesion appear variably. Typically, duct ectasia may appear as a single tubular structure filled with fluid or sometimes may show multiple such structures as well. Old cellular debris may appear as echogenic content. If the debris fills the lumen, it can be sometimes mistaken for a solid mass, unless the tubular shape is picked up.[9]

Fibroadenoma

Fibroadenoma is the 3 rd most common breast lesion after fibrocystic disease and carcinoma. This is an estrogen-induced tumor that forms in adolescence. It usually presents as a firm, smooth, oval-shaped, freely movable mass, rarely tender or painful, size usually under 5 cm. Calcifications may occur. In some patients, the mass may appear complex, hyperechoic or isoechoic.[10]

Cystosarcoma phyllodes

This is mostly diagnosed in the older woman and are a large lesion and hence can also be a giant fibroadenoma. The mass may involve

the whole of the breast. It usually reveals well- defined margins and an inhomogeneous echo structure, sometimes with variable cystic areas. The incidence of malignant change is low.[6]

Lipoma

Lipoma is a well-defined and slow-growing tumor. It may be a chance finding or the patient may present with complaints of increase in the size of the involved breast, though no discretely palpable mass can be made out. The tumor is soft and can be deformed by compression with the transducer. A thin capsule can usually be identified and the tumor often reveals an echogenic structure, with a stippled or lamellar appearance. [11] Frequent association with atypical ductal hyperplasia, atypical lobular hyperplasia, malignant lesions and bilaterality imply that MP may represent a step in the progression of a precursor lesions to papillary carcinoma.

In addition, other type of lesions is also observed that leads to breast malignancy. Breast cancer risk was more strongly associated with atypical hyperplasia among premenopausal women than postmenopausal women. [12] Hartmann LC et al. [13] showed non proliferative lesions in 66% cases, proliferative lesions without atypia in 29% cases and atypical hyperplasia in 3.6 % cases and concluded that RR associated with atypia was 4.24 . Their study showed that in women with biopsies who were confirmed of Benign Breast Disease (BBD), the risk of developing breast cancer was 1.7 times that for women with no history of surgery for BBD. The women at highest risk for breast cancer were those with hyperplasia with moderate or marked atypia. For these women, the risk for breast cancer was 2.6 times that for women without BBD.

Table 1: Epithelial breast lesions and the risk of developing invasive carcinoma[14]

Pathologic lesion	Relativerisk	Absolutelife timerisk
Nonproliferative Breast Changes (Fibrocysticchanges)		
Ductectasia	1	3%
Cysts		
Apocrine change		
Mild hyperplasia		
Adenosis Fibroadenoma without complex features		
Proliferative Disease Without Atypia		
Moderate or florid hyperplasia	1.5to2.0	5-7 %
Sclerosingadenosis		
Papilloma		
Complex Sclerosing lesion (radialscar)		
Fibroadenoma with complex features		
Proliferative Disease With Atypia		
Atypical ductal hyperplasia (ADH)	4.0to5.0	13-17%
Atypical lobular hyperplasia (ALH)		
Carcinoma insitu		
Lobular carcinoma insitu (LCIS)	8.0to10.0	25-30%
Ductal carcinoma insitu (DCIS)		

Conclusion

There is existence of the of rare borderline breast lesions of yet undefined nature and uncertain clinical behaviour. These include breast lesions of uncertain malignant nature and those with uncertain/negligible metastatic potential. This may leads to cancer malignancies in future when benign lesions left neglected. Characterizing the benign lesions can help improve consistency of management and reduce the chance of under-treatment or over-treatment resulting from definite categorization as benign or malignant. Clinicians and patients can make informed decisions about management of these breast lesions in view of the information regarding the uncertainty of their nature. Further studies of these lesions are warranted.

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