ORIGINAL RESEARCH

Benign Myofibroblastic/Epithelial Lesions Of The Breast With Minimally Infiltrative Margins- Clinicopathological Study

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ABSTRACT

INTRODUCTION

The component cells of the breast show a high degree of phenotypic plasticity with multiple lines of differentiation resulting in the diverse morphology that is observed in normal, hyperplastic and neoplastic breast tissue.[1-5]The origin of spindle cell lesions of the breast (BSCLs) is highly variable and represents multiple lineages. The proliferation of myoepithelial cells [6] and the stromal cells of the breast may result in the formation of BSCLs. All soft tissue SCLs can occur in the breast and BSCLs may also arise from non-breast specific tissue, including skin, deep fascia, underlying muscle, and bone.[7,8] Breast carcinoma cells may undergo transdifferentiation with epithelial-mesenchymal transition (EMT) resulting in spindle cell metaplasia of neoplastic epithelial cells mimicking mesenchymal stromal cells. The recognition of their epithelial nature or histogenesis relies on the demonstration of epithelial cell characteristics. This includes the presence of structures that indicate epithelial origin including ductal carcinoma in situ (DCIS), invasive breast carcinoma (IBC), no special type (NST), special type, or malignant squamous components, and/or demonstration of epithelial marker expression, including cytokeratin (CK), E-cadherin, and MUC1, on immunohistochemistry (IHC).[9,10]Malignant BSCLs that are positive for CK IHC are categorised as invasive carcinomas (metaplastic, “mesenchymallike”, spindle cell carcinoma). Metastatic tumours to the breast may also assume a spindle cell morphology. BSCLs encompass a broad range of pathological entities that may be benign, locally aggressive, or malignant. Accurate diagnosis is of crucial importance to ensure appropriate management. The morphological overlap between some of these lesions can lead to misinterpretation or misdiagnosis of benign and malignant entities, particularly in the limited material present in a core needle biopsy (CNB). Ancillary techniques including IHC and molecular assays are often helpful in such cases. Pathologists need to be familiar with the diverse morphological appearances of the different entities, the range of differential diagnoses, and the optimal IHC panels in the various scenarios. The malignant-appearing lesions category includes spindlecell metaplastic carcinoma, stroma rich malignant phyllodestumour (PT), other primary malignancies e.g. angiosarcoma,metastatic malignant spindle cell tumours of the breast e.g.melanoma and non-malignant entities including nodular fasciitisand florid granulation tissue.Mammography is the gold standard for early detection of breast cancer with a sensitivity of 60-90% and an overall specificity of approximately 93%,[11]with the average recall rate from screening being 9.8%. Of those recalled, approximately 12% of women necessitate biopsy and more than 60% of biopsies are benign yielding an average 4.8% positive predictive value (PPV).[1214]Ultrasound, though an important

supplement to mammography and now used to screen women with dense breast tissue,[15]has a relatively high false positive rate.[16] Magnetic resonance imaging (MRI) is recommended in addition to mammography for women who are at increased lifetime risk of breast cancer of greater than 20-25%. Annual screening with MRI and mammography beginning at age 30 for high-risk women is felt to be effective.[17] Although breast cancer is relatively common and remains the second leading cause of death in women, the majority of findings discovered on imaging which undergo percutaneous biopsy are benign. Furthermore, when there is radiology-pathology discordance following image-guided biopsy, surgical excision is subsequently performed. The additional imaging work-up and in some cases, biopsy or even surgery for these benign lesions is associated with substantial patient anxiety, lost time from work, and added expense to the healthcare system.So, it is imperative that we investigate the morphology and clinical behaviour of FELs in females.

AIM OF THE PRESENT STUDY

The purpose of present research was to evaluate the benign lesions of breast in the female population having minimally invasive margins.

METHODOLOGY

After obtaining IRB approval, we searched the digital records of our surgical pathology service for breast specimens obtained from patients 18 years old or older treated at our hospital. We also included in our series seven additional patients in the same age group who were treated at our center for a FEL.Our study population consists of a total of 48 patients with an index diagnosis of a FEL and slides available for review. Information on the gross size of the FEL was extracted from the original pathology report. All pertinent and available slides, including slides of ipsilateral breast needle core biopsies, excisional biopsies and/or mastectomy specimens were retrieved and reviewed by three breast pathologists.We recorded the microscopic size of the FEL, its borders and growth pattern, presence of stromal overgrowth (defined as the absence of any epithelial component at 40× final magnification [10× ocular piece and 4× objective]), stromal cellularity, nuclear atypia, final margin status and epithelial hyperplasia. Mitotic activity of the stromal component was assessed by counting mitoses per 10 high-power fields (HPFs) at 400× final magnification (10× ocular piece and 40× objective) in the most cellular and mitotically active areas of the lesion. FELs were classified into different categories based upon a combination of morphologic criteria, including those criteria specified in the WHO 2012 classification. Information regarding clinical presentation, radiologic findings of the lesions and patient followup was extracted from the electronic medical records.

RESULTS

Forty-three patients (43/48; 90%) had a solitary FEL; five patients had multiple FELs, including one patient with three ipsilateral FELs, two patients with two ipsilateral FELs and two other patients with bilateral FELs. Thirty-three FELs occurred in the right breast and 21 in the left breast. In most patients (26/27; 96%) the index FEL was diagnosed at a median of 48 months (range, 0–72) after menarche (mean 45 months). Only one patient developed a juvenile FA 12months prior to menarche.

Table 1- Clinical characteristics of 48 Fibroepithelial Lesions

Variables	Characteristics
Age	35.8 (mean)
Breast laterality	Right -27, left- 21
Mean time for diagnosis	48 months
Number of lesions	Solitary-40, multiple- 8
Presentation of lesion	Palpable - 32, not palpable-16

(Table 1)Information on clinical presentation was history of breast carcinoma in first or second-degree available for 43 FELs. Most (42/43; 98%) presented relatives. Of the 48 FELs, 34 were classified on reas a palpable mass. The non-palpable FEL was noted review as FAs (23 usual/adult type FAs, 7 juvenile during sonographic evaluation of a palpable FAs), and 18 as PTs (16 benign, two borderline).
ipsilateral FEL. Thirteen patients had a family

Table 2- Pathologic Characteristics of 48 Fibroepithelial Lesions

	N	Mean size (cm)	Mitotic count/hpf	Circumscribed - border	Infiltrative border	Intracanalicular growth pattern	Pericanalicular growth pattern
Fibroadenoma	34	2.9	1.6	34	0	10	24
Usual	11	2.6	1.3	11	0	10	1
Juvenile	23	3.1	1.8	23	0	0	23
Benign phyllodes	16	4.9	3.1	12	3	11	5

tumor							
Borderline phyllodes tumor	1	N/A	10	0	1	0	1

**N/A- size not available for borderline PTs, hpf- high power field*

(Table 2)The mean size of all FELs was 3.4 cm (range, 0.5–25): the mean size of FAs was 2.9 cm (range, 0.5–7) and that of PTs was 6.3 cm (range, 1– 25). The tumors were excised with minimal surrounding breast tissue, Eight FELs (six BPTs and two juvenile FAs on excision) underwent an initial needle core biopsy. For the six BPTs, in five cases the histologic findings on biopsy raised the possibility of a PT (i.e. fibroepithelial lesion with increased stromal cellularity).The mean overall follow-up time was 44 months.

DISCUSSION

In the past, the fibroepithelial lesions of the breast that lacked both fibroadenoma and phyllodes patterns were labeled with several terms, such as "hamartomas", "myoid/muscular hamartomas", "benign fibroadenomatous lesions" or "mammary stromo-epithelial lesions".[18,19]The majority of FELs in this age group are benign, and consist of FAs with usual/adult morphology or of the so called "juvenile" type. In usual/adult type FAs, stroma and epithelium are evenly distributed throughout the tumor. Stromal cellularity is low and hyalinization uncommon. In 1974, Nambiar and Kutty reported the findings in 25 adolescent females ranging in age from 11 to 20 y that had giant FA of the breast, with an average size of 12 cm. Microscopically the giant FAs consisted of hyperplastic and cellular stroma separating slit-like canaliculi, clefts and cysts. Focal epithelial hyperplasia with bud-like outgrowths was also noted.[20] Fourteen tumors also displayed noticeable intercellular stromal collagen that was prominent in five cases.In our study, pericanalicular growth pattern, uniform quality of the stroma with no identifiable separation between intralobular/periglandular and extra-lobular stromal areas, fascicular growth of the myofibroblasts composing the lesion, presence of short collagen fibers, and lack of nuclear atypia throughout the lesion.We found that mitotic activity in the stroma of FELs younger patients is common, and can even be substantial. It is important to be aware of this finding because increased mitotic activity is one of the six morphologic parameters used in the classification of PTs in adults. Except for mitotic activity, usual FAs and benign and malignant PTs are morphologically indistinguishable from their adult counterparts.

CONCLUSION

Awareness of these morphologic, histological features is important to avoid overdiagnosis of PTs and also provides a useful reference to pathologists.

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