Original Research

HISTOPATHOLOGICAL SPECTRUM OF BREAST LESIONS: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Breast lesions encompass a wide spectrum of inflammatory, benign proliferative, fibroepithelial, borderline and malignant lesions and histopathology is still fundamental to definitive diagnosis.
Materials and Methods: This is a retrospective observational study of the histopathological spectrum of the breast samples received in a tertiary care path lab of three years. The age, sex, laterality, type of specimen, clinical presentation and final histopathological diagnosis were noted in the records of 286 breast specimens. The lesions were divided into non-neoplastic, benign neoplastic, borderline and malignant and the malignant ones were graded according to the modified Bloom-Richardson system.
Results: The mean age was 38.7 +/- 15.6 years, with a female predominance (98.6%). A total of 206 cases (72.0%) were benign lesions, 68 cases (23.8%) malignant lesions, 6 cases (2.1%) were borderline phyllodes tumors and 6 cases (2.1%) were inflammatory/non-neoplastic lesions. The commonest benign lesion was fibroadenoma (104/286, 36.4%) followed by fibrocystic change (42/286, 14.7%). Invasive carcinoma of no special type was the commonest malignancy (52/68, 76.5%). Age older than 40 years, skin/nipple changes and positivity of the axillary nodes were significantly associated with malignancy ($p<0.001$). The vast majority of invasive carcinomas were grade II (53.8%) and stage pT2 (48.1%).
Conclusion: The study reveals that benign breast lesions outnumber non-benign lesions, but histopathology is essential for the diagnosis of malignant and borderline lesions which need to be treated definitively.

Keywords: Breast Lesions, Histopathology, Fibroadenoma, Invasive Breast Carcinoma, Nottingham Grade, Retrospective Study.

INTRODUCTION

Breast pathology is a broad spectrum of processes including inflammatory pathologies, benign proliferation, fibroepithelial neoplasms, in situ carcinoma and invasive carcinoma [1]. Clinical signs of breast lesions can be similar, and a palpable lump could be either a harmless fibroadenoma in a young woman, or an invasive carcinoma in an older patient. Thus, the final diagnosis, risk stratification and management planning can only be made through histopathological examination [2].
Nowadays, most breast specimens are diagnosed on the basis of routine hematoxylin and eosin examination and the WHO classification emphasizes integration with morphology and immunohistochemistry and molecular characteristics. Histologic type, tumor size, Nottingham grade, lymphovascular invasion, nodal status and margin status are major factors that retain their prognostic value and influence further testing of a breast carcinoma [3-6].
In the practice of hospital-based pathology, benign breast diseases are more common than malignancy, and they include fibroadenoma, fibrocystic change, sclerosing adenosis, duct ectasia, mastitis and phyllodes tumors [7]. While the prognosis is usually good for benign lesions, some are of a proliferative nature with atypia and some are classified as borderline fibroepithelial tumors and need a careful diagnosis due to recurrence or possible risk of cancer [8]. Clinicians and pathologists can use local data on the spectrum of breast lesions because disease frequency and patterns of referral differ by region and are distributed according to age. This study was conducted to determine the histopathological spectrum of breast lesions seen in tertiary care centre and to compare the major categories with age, presentation and the grade of malignancy of the tumour.

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MATERIALS AND METHODS

The study was a retrospective, observational study conducted in Department of Pathology of a tertiary care teaching hospital. Specimens included lumpectomies, excisions, core biopsies and mastectomies and wide local excisions. The cases where less than four tissue samples were obtained, autolyzed specimens, repeat samples from the same lesion, and incomplete records were excluded.

Data pertaining to patient age, sex, clinical presentation, laterality, specimen type and radiological impression (where available) were obtained from requisition forms and patient pathology records. The gross findings included tumor size, circumscription, cystic change, necrosis and lymph node sampling. Routine processing of tissue sections was followed by hematoxylin and eosin staining and two pathologists examined the tissue. When necessary, special stains and immunohistochemistry were performed to confirm the diagnosis.

Lesions were classified as non-neoplastic/inflammatory, benign neoplastic, borderline or malignant according to standard histopathological criteria. Invasive breast carcinomas were classified based on WHO classification and graded on the basis of Nottingham (modification of Bloom Richardson) system. For resection specimens, the tumor size category and nodal status were documented. The data were analyzed statistically in SPSS version 26. Categorical variables were presented as frequency and percentages, and continuous as mean +/- SD. Association was tested by the chi-square test and $p<0.05$ was the statistically significant accepted value.

RESULTS

A total of 286 breast specimens were included. The age ranged from 13 to 82 years, with a mean age of 38.7 +/- 15.6 years. The commonest age group was 21-30 years for benign lesions and 41-60 years for malignant lesions. Most patients were female, and the left breast was slightly more commonly involved. Lump in breast was the predominant clinical presentation.

Benign lesions accounted for 206 cases (72.0%), malignant lesions for 68 cases (23.8%), borderline phyllodes tumors for 6 cases (2.1%) and inflammatory/non-neoplastic lesions for 6 cases (2.1%). Fibroadenoma was the most common diagnosis overall, followed by fibrocystic change. Among malignant tumors, invasive carcinoma of no special type was the predominant histological subtype. Three cases of ductal carcinoma in situ and two cases of mucinous carcinoma were identified.

Malignancy showed significant association with age >40 years, hard/fixed lump, skin or nipple changes and axillary lymphadenopathy. Among invasive carcinomas in resection specimens, grade II was the most frequent grade, followed by grade III. Nodal metastasis was identified in 28 of 54 cases with lymph node sampling.

Table 1. Age Distribution and Broad Diagnostic Categories

Age group (years)	Benign/non-neoplastic	Borderline	Malignant	Total
<=20	29	0	1	30
21-30	82	1	3	86
31-40	57	2	9	68
41-50	28	2	22	52
51-60	12	1	20	33
>60	4	0	13	17
Total	212	6	68	286

Benign/non-neoplastic includes inflammatory lesions and benign neoplasms.

Table 2. Histopathological Spectrum of Breast Lesions

Diagnosis	Number	Percentage
Fibroadenoma	104	36.4
Fibrocystic change	42	14.7
Benign phyllodes tumor	18	6.3
Duct ectasia/chronic mastitis	16	5.6
Papilloma/adenosis/other benign	26	9.1
Borderline phyllodes tumor	6	2.1
Invasive carcinoma, no special type	52	18.2
Ductal carcinoma in situ	3	1.0
Special type invasive carcinomas	13	4.5
Other inflammatory lesions	6	2.1

Percentages are calculated using total cases (n=286).

Table 3. Histopathological Features of Malignant Breast Lesions

Feature	Category	Number (%)
Histological type	Invasive carcinoma NST	52 (76.5)
Histological type	Mucinous carcinoma	2 (2.9)
Histological type	Lobular carcinoma	4 (5.9)
Histological type	Other/special type	7 (10.3)
Nottingham grade	Grade I	8 (15.4)
Nottingham grade	Grade II	28 (53.8)
Nottingham grade	Grade III	16 (30.8)
Pathologic tumor size	pT1	13 (25.0)
Pathologic tumor size	pT2	25 (48.1)
Pathologic tumor size	pT3/pT4	14 (26.9)
Nodal metastasis	Present	28/54 (51.9)

Grading and pT category were assessed in invasive carcinomas with adequate resection data.

DISCUSSION

The present study showed that the majority of the breast specimens diagnosed histopathologically were benign breast lesions, and fibroadenoma was the most common diagnosis. This distribution corresponds with the distribution of breast disease observed in its epidemiology, in which benign disease is more common in younger women, and carcinoma is more common in older women [9].

Fibroadenoma predominated in the second and third decade, and this is consistent with the young female population having a tendency to hormone responsive stromal and epithelial proliferation clinically manifesting as a mobile lump. The second most common benign lesion was fibrocystic change, which occurred over a broader age range. While many fibrocystic changes are not proliferative, there is a higher risk for cancer following atypical epithelial proliferation, and accurate histological categorization is important [10].

The most common malignancy was invasive carcinoma of no special type, similar to the description of breast carcinoma morphology based upon the WHO classification [11]. The majority of cases were grade II, and a significant number had nodal metastases, indicating that the patients present at a relatively advanced stage. The Nottingham grade, which is one of the most reproducible and clinically useful morphological prognostic factors, can be done systematically [12].

The strong linkage of age >40 years, changes in skin/nipple, and axillary lymphadenopathy with malignancy further indicate the importance of quick tissue diagnosis of clinically suspicious cases. But clinical evaluation is not enough as some early cancers can be mistaken for benign ones and some benign ones can be clinically worrisome. Triple Assessment (clinical examination, imaging and tissue diagnosis) is still the most preferred method [13].

Study limitations include the retrospective design and the fact that radiological and immunohistochemical data were not available for all patients in this study and that it was conducted at a single institution. Not all malignant cases had molecular subtype analysis. However, the results offer a real world snapshot of the burden of routine breast pathology cases and highlight the ongoing critical role of histopathology in the distinction between benign, borderline and malignant breast diseases [14,15].

Practical Implications for diagnostic triage are suggested from the age-wise distribution in the present study. In patients younger than 30 years, circumscribed benign lesions were predominant, but rare malignancy and occasional phyllodes tumor were found in histopathology. This helps to select for sampling breast lumps that are enlarging, recurrent, radiologically discordant or clinically atypical, rather than just age-based assumptions [2,7].

Fibroepithelial lesions have a special importance due to the possibility of overlapping between fibroadenoma and phyllodes tumour on limited core biopsy. In this series, a small, but important, portion of cases were benign phyllodes tumours and borderline phyllodes tumours. They are recognized in order to guide the planning of the final resection margins and follow-up since local recurrence may still occur in spite of limited cytological atypia [1,4].

Inflammatory lesions were less numerous than neoplastic lesions, but are important mimics for diagnosis. Clinical and radiographic findings can mimic carcinoma in chronic mastitis, duct ectasia and granulomatous inflammation, particularly if there is skin thickening or when the gland is firm and irregular. Histology is useful for avoiding overtreatment, as well as preventing the exclusion of malignancy when it is hidden by inflammation [9].

The malignant tumour profile highlights the importance of full pathologisation. Tumor type is not enough to manage the patient, tumor size, Nottingham grade, lymphovascular invasion, margin status, and metastasis to the nodes are all documented and reproducible. These parameters are used to stage, and to determine adjuvant chemotherapy, radiotherapy and endocrine therapy [5,6].

While molecular classification has revolutionized breast oncology, morphology remains the entry

point for selection of biomarkers. For instance, high grade invasive carcinoma, no special type, mucinous carcinoma and invasive lobular carcinoma could express different receptors and have different spreading patterns. Hence, meticulous histological typing is still important even in laboratories where there is immunohistochemical backup [11-14].

The grading of a large percentage of the cases as grade II confirmed that the morphology of the majority of carcinoma samples is intermediate, as is seen in the routine practice of most pathologists. When scoring tubule formation or nuclear pleomorphism and mitotic activity, it is important to do this carefully in order to minimize interobserver variation in grade II tumors. Frequent review of the grading rules within the departments can lead to more consistency, particularly in institutions of learning [5,12].

Nodal metastasis in over half of the cases sampled where malignancy was present suggests many cases presented for definitive surgery with clinically significant disease. This note is to emphasize the need for community awareness, timely imaging, diagnosis by core biopsy, and multidisciplinary referral pathways. This would be expected to improve the percentage of small, node-negative carcinomas earlier in the course of the disease [13].

The study also shows from a laboratory point of view the extent of breast pathology workload. Core biopsy, margin evaluation, and mastectomies are required in a single breast specimen stream for rapid diagnosis, margin evaluation and structured reporting, respectively. Therefore, the grossing of the specimen and its sampling and correlation with imaging are important quality indicators in breast pathology practice, which should be standardized [14,15].

A second noteworthy point is that core biopsy was used as the initial tissue diagnosis in clinically suspicious lesions. Core biopsy allows for pre-treatment planning, receptor testing (carcinoma) and sparing of unnecessary removal (in obvious benign lesions). However, in cases where imaging and histology do not agree, or where the extent of biopsy is limited and a fibroepithelial lesion cannot be reliably differentiated from other types, excision is still indicated [13].

In the borderline lesions, the pathologist should voice doubt and uncertainty in a precise manner. Features such as stromal cellularity, stromal overgrowth, mitotic activity, infiltrative margins and necrosis determine phyllodes tumor grade. For large lesions, lesions that grow or recur, generous tissue specimen submission from excisions is essential as sample may affect grading [1].

The present results also indicate the need for breast pathology audit. The benign-to-malignant ratio, inadequate sample rate, core biopsy-excision concordance and turnaround time can be used to identify service gaps. This type of audit is particularly helpful in tertiary centres where cases can involve screening detected lesions as well as advanced symptomatic malignancies.

Last but not least, the surgical and oncologic findings must be reported in a manner that is unambiguous to the surgeon and oncologist. Diagnosis and margin comments might be adequate for benign lesions. Reports should contain tumor focality, size, histologic type, grade, lymphovascular invasion, ductal carcinoma in situ component, margins, lymph nodes and biomarker recommendations for carcinoma [14,15].

CONCLUSION

The most common benign breast diseases included fibroadenoma and fibrocystic change, and the most common malignant breast disease was invasive carcinoma of no special type. Older age and clinically suspicious features were significant factors with regard to malignancy. Histopathology continues to be essential in the diagnosis, grading and treatment of breast lesions.

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