Research Article

Cytological Profiling of Various Breast Lesions and its Correlation with ER and PR Status

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Abstract

Background: Breast lumps constitute a significant proportion of surgical cases in women of both developed and developing countries. The aim of this study is to look the frequency distribution of various breast lesions on fine needle aspiration (FNA) with special reference to breast carcinoma and its correlation with ER and PR status.

Materials and Methods: The 192 patients who presented with palpable breast lump, irrespective of age and sex were included in the study. Frequency distribution of various breast lesions with respect to age and sex was studied. Cytology grading in breast carcinoma was correlated in 20 cases with histology grading and its ER, PR status.

Results: The majority (N = 184) of patients were females with maximum (N = 101) patients between third and fourth decade. The 154 patients had benign breast lesions and maximum patients were in the second decade. Fibroadenoma was the commonest benign lesion followed by fibrocystic change and mastitis. Out of 35 malignant breast lesions, 45.4% [N = 15] were between 41 - 50 years of age, 27.2% [N = 9] in 51 - 60 years and 15.1% [N = 5] in between 31 - 40 years of age. Out of 35 malignant breast lumps and majority were infiltrating ductal carcinoma (N = 33). Cytology grading correlated maximum with histology grade in Grade I followed by Grade II and Grade III and correlation with ER and PR status was also done.

Conclusion: With experienced hands, FNA is safe, cost effective and a reliable technique for preoperative evaluation of palpable breast lumps. FNA features are more informative when combined with physical and radiology findings (Triple test). Fibroadenoma, fibrocystic change and mastitis form the major bulk of benign breast lesions. Epithelioid cells when seen in inflammatory breast FNA smears, tuberculosis must be ruled out. In India, breast carcinoma arises in younger patients as compared to western countries. Cytological Grading of breast carcinomas must be done on FNA smears for selecting neoadjuvant therapy. Prognostic factors like tumor size, expression of estrogen, progesterone receptors should be considered. Clinical breast examination and mammography screening in females should be encouraged in developing countries from the third decade onwards for early detection of breast carcinoma.

Keywords: Breast; Benign; Cytology; FNA; Grading; Malignant

Introduction

Breast lumps constitute a significant proportion of surgical cases in both developed and developing countries. Vast majority of them are in women and are benign. It is needed to distinguish benign lumps from malignant preoperatively for definite treatment [1,2]. The triple test includes physical breast examination, mam-mography and fine needle aspiration (FNA) and has proved a reliable tool for accurate diagnosis of palpable breast masses [3].

Fine needle aspiration cytology (FNAC) is an easy, quick-to-perform, outpatient, and virtually painless procedure, the use of which continues to increase worldwide, especially in developing countries

[4]. The effectiveness of the study can be maximized with the help of a radiologist. It is widely accepted as a reliable technique and has been proved to be a significant patient-friendly procedure for the preoperative evaluation of palpable breast lumps. The scope of FNA has now increased to classifying the subtypes of benign, malignant lesions, and residual disease in order to plan the treatment protocol and the subsequent follow-up [5]. Hence, this study was undertaken to see the pattern of palpable breast lesions on FNA and to assess cytological grading correlating with histological grading and ER and PR status in breast carcinomas. The prognostic markers important for deciding the treatment modality should be conveyed to the surgeon, as recognition of the aggressiveness of the disease is central to the effective medical management of breast cancer and avoid the needless morbidity [6].

Materials and Methods

A prospective study on breast aspirates was conducted on cases in the department of pathology and attending OPD or hospitalized patients in surgery department of L.L.R Hospital, Kanpur between December 2013 and November 2015.

Medical records of the patients presenting with palpable breast lesions were reviewed and detailed clinical history, physical examination, and mammography/ultrasonography (USG) findings were noted. All the patients underwent FNA in cytology clinic after prior written consent. FNA was done with standard technique and aseptic precautions by using 10 cc disposable syringe and 22 - 23 gauge needles. Material was smeared on glass slides. Slides were stained with, Hematoxylin and Eosin [H and E]. Ziehl Neelsen (ZN) staining

was done wherever required. In case, material obtained was not satisfactory, a repeat aspiration was done. In case of more than one swelling, aspiration was done from each swelling.

Diagnosis of each lump was based on physical examination, FNA and/or mammography/USG features. Cytology grading of breast carcinomas done by using Robinson's grading system based on six cytomorphology features viz: Cell dissociation, cell size, cell uniformity, nucleoli nuclear margins, and chromatin pattern. Carcinomas were graded into Grade I, II and III. Out of 35 breast carcinomas, surgical specimens were received in 20 cases. Tissues were 10% formalin fixed and paraffin processed. The 3 - 4 μm thick sections were stained with H and E stain. Histology grading was done by Elston and Ellis's modification of Bloom Richardson method based on histological features viz: Proportion of tubule formation, nuclear pleomorphism and mitotic count/10 hpf. After correlating with histological grade, paraffin blocks made out of the respective breast tissue were sent for determination of estrogen and progesterone receptor status.

Results

Out of 192 patients, 4.16% (N = 8) were male and 95.83% (N = 184) were female. Age of the patients ranged from 15 - 72 years with 53.12% (N = 102) were in the age group of 21 - 40 years. The 81.77% (N = 157) had benign breast lumps and 18.22% (N = 35) had malignant breast lumps. In 3 (1.50%) patients, FNA was inconclusive. Table 1 show FNA diagnosis of 192 breast lumps in various age groups.

Breast lesion	15 - 20 yrs	21 - 30 yrs	31 - 40 yrs	41 - 50 yrs	51 - 60 yrs	61 - 70 yrs	Total (%)
Fibroadenoma	44	32	6	1	-	-	83 (43.2)
Fibrocystic changes	-	02	14	10	-	-	26 (13.5)
Fibroadenosis	10	08	03	-	-	-	21 (10.9)
Gynaecomastia	3	5	2	-	-	2	12 (6.2)
Galactocele	1	3	-	-	-	-	4 (2.08)
Simple cyst	-	1	1	-	-	-	2 (1.04)
Granulomatous lesion	-	2	-	-	-	-	2 (1.04)
Breast Abscess	-	1	1	-	-	-	2 (1.04)
Fat necrosis	-	-	-	2	-	-	2 (1.04)
Carcinoma	-	1	5	15	9	3	35 (18.4)
Inadequate							3 (1.5)
Total							192 (100)

Table 1: Frequency of FNA diagnosis of 192 breast lesions in various age groups.

Table 2 shows cytomorphological distribution of malignant breast lesions (n = 35). The most common type found in the study was Ductal carcinoma (not otherwise specified) seen in 94.4% cases. Mucinous carcinoma and lobular carcinoma seen in 5.6% of cases.

Table 3 shows distribution of cases according to cytological grading. On cytological nuclear grading by Robinson's method - This method has exclusively been used for cytology; six features are assessed, i.e. cell dissociation, cell size, cell uniformity, nucleoli, nuclear margin, and chromatin. The maximum numbers of cases were in grade-II i.e. 20 (62.8%), Grade-I accounted for 09 cases (27.2%) and Grade-III was seen in only 04 cases (12.2%).

Table 4 shows correlation of cytology grading with histology grading in 20 cases of breast carcinoma and their ER and PR status.

Type	No. of Cases	Percentage (%)
Ductal carcinoma NOS	33	94.4
Mucinous carcinoma	1	2.8
Lobular carcinoma	1	2.8
Total	35	100

Table 2: Cytomorphological distribution of malignant breast lesions (n = 35).

Grade	No. of cases	Percentage (%)
I	09	27.2
II	20	60.6
III	04	12.2
Total	33	100

Table 3: Distribution of cases according to cytological grading (n = 33).

Case no.	Cytological grade	Histological grade	ER status	PR status
1	Grade II	Grade II	Positive	Positive
2	Grade-II	Grade II	Positive	Negative
3	Grade II	Grade II	Positive	Positive
4	Grade I	Grade I	Negative	Negative
5	Grade II	Grade I	Positive	Positive
6	Grade II	Grade II	Positive	Negative
7	Grade III	Grade II	Positive	Negative
8	Grade II	Grade II	Negative	Negative
9	Grade I	Grade I	Positive	Positive
10	Grade II	Grade II	Positive	Positive
11	Grade I	Grade II	Positive	Negative
12	Grade II	Grade I	Negative	Negative
13	Grade III	Grade III	Negative	Negative
14	Grade I	Grade I	Positive	Positive
15	Grade II	Grade II	Positive	Negative
16	Grade II	Grade II	Negative	Negative
17	Grade III	Grade III	Negative	Negative
18	Grade I	Grade I	Positive	Positive
19	Grade I	Grade I	Positive	Positive
20	Grade II	Grade II	Negative	Negative

Table 4: Correlation of cytology grading with histology grading in 20 cases of breast carcinoma and their ER and PR status.

Discussion

FNA is widely accepted as a reliable technique in the initial evaluation of palpable breast lumps. It is simple, safe, cost effective, minimally invasive, rapid and as sensitive as biopsy [7]. Primary goal of FNA is to separate benign lesions from malignant lesions for the purpose of planning the therapeutic protocol and uneventful follow-up [8].

Breast cancer is a malignant disease with heterogenous prognosis. Various studies have established many prognostic markers which include staging the tumor, grading the tumor histologically, lymph node status, ER/PR status. But the quest for new prognostic markers is never ending. Earlier the tumor is diagnosed, better will be the outcome of treatment. Cytological grading may especially assume prime importance for patients who may receive chemotherapy prior to resection of the tumor and in those who present with metastasis [9].

Apart from cytologic grade of the tumor, determination of the ER and PR status is also an important prognostic marker. This is so because the outcome of the neoadjuvant therapies (Herceptin and tamoxifen) which are instituted preoperatively, depends mostly on the presence or absence of these receptors.

In our study, table 1, shows age and sex distribution of various breast lesions. Age of the patients ranged from 15 to 72 years with 53.12% cases were in the age group of 21 - 40 years and male to female ratio of 1:23. Similar age group was observed in studies done in Asian countries [10,11]. Higher age group in western countries was attributed to higher life expectancy [12]. Out of 192 patients, 81.77% (N = 157) had benign breast lumps and 18.22% (N = 35) had malignant breast lumps. It has been emphasized in the past that vast majority of the lesions in breast are benign [13,14].

Fibroadenoma was the most frequently (N = 83) diagnosed lesion on FNA with maximum (N = 76) patients between 17 - 30 years. Definitive FNA diagnosis was based on diagnostic triad of cellular smears with bimodal pattern, numerous single bare bipolar nuclei and fragments of fibromyxoid stroma. Absence of any component of diagnostic triad and low cellularity are the common causes of pitfalls in correct diagnosis of fibroadenoma [15]. In 28 cases, fibromyxoid stroma was not seen. Correct diagnosis in these cases was achieved by correlating FNA features with clinical and radiological features.

Another common benign breast lesion we encountered was fibrocystic change (N = 26) with maximum patients (N = 16) between 21 - 40 year. Though hormones play a role in its development exact pathogenesis remains obscure [15]. Fibrocystic change is not a specific cytological diagnosis. Cytology samples must be evaluated in the context of clinical and mammography findings. Some of these lesions simulate carcinoma clinically, radiologically and microscopically. More than 90% of the fibrocystic change were non proliferative and FNA smears showed many macrophages, apocrine cells with or without scanty chronic inflammatory cells. Small clusters of ductal epithelial cells without atypia were seen. Few cases showed predominant ductal cells without atypia and were diagnosed as proliferative type. Compared to the general population, proliferative fibrocystic change with or without atypia has relative risk of developing carcinoma [16].

Gynaecomastia accounted in 6.20% (N = 12) patients with maximum (N = 7) patients between 21 - 40 years. Gynaecomastia in young age is related to hormonal pubertal changes whereas in later years, it may be caused by hormonally active tumors, cirrhosis or medications [17].

Galactocele accounted for 2.08% (N = 04) patients and all the patients were lactating. We came across 2 cases of simple cyst in our study, which are easily diagnosed by ultrasonography. Confident benign diagnosis can be rendered with FNA and surgical excision can be avoided. 3 cases were inadequate for evaluation.

Breast cancer is the second most common cancer among Indian females next only to cervical cancer. With advancement in the field of mammography, neoadjuvant therapy and breast conservation surgery in breast carcinoma, cytology grading can be used for selection of neoadjuvant therapy.

Out of 35 malignant lesions, table 2 most common diagnosis was infiltrating duct carcinoma (N = 33) followed by mucinous carcinoma, infiltrating lobular carcinoma (5.6%). Similarly, Rosen., *et al*. [18] stated that invasive duct carcinomas NOS, forms the largest group of malignant mammary tumors constituting 65 - 80% of mammary carcinomas.

According to the results of Robinson's method in table 3, the maximum number of cases belonged to grade II 60.60%, followed by 27.2% of grade I tumors and 12.2% of grade III tumors. In a similar study done by Khan., *et al*. [19] on the role of cytological grad-

ing in prognostication of breast carcinoma, found out that cytologic grades correlated well with the histologic grades. They also stated that of the six parameters studied, cell dissociation, nucleoli and chromatin pattern were the most influential features. Similarly, Chhabra., *et al.* [20] also performed a study with similar results.

Table 4 On correlating the tumor grade with ER and PR status, we found that 83.3% of grade I tumors, 63.6% of grade II were ER positive while 66.6% of grade I and 36.3% of grade II were PR positive. None of the grade III tumors were ER or PR positive. These findings are in accordance with Bhargava., *et al.* [5] who obtained similar results.

Conclusion

Benign breast lesions constitute a majority of breast lumps in surgical cases and mainly occur in second and third decades. Fibroadenoma form the major bulk of benign breast lesions, followed by duct carcinoma. Malignant lesions, although are more common in fourth and fifth decades. Clinical breast examination and mammography screening should be encouraged in female subjects from the third decade onward for the early detection of breast carcinoma. Nuclear cytomorphological features are important prognostic markers and have been considered by all the studies for breast carcinoma grading.

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