

Cyto- histopathological correlation of breast lesions –A rural hospital based study

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Abstract

Introduction: Breast carcinoma is the most frequent cancer among women worldwide. Breast lesions most commonly present as lump. Fine needle aspiration cytology (FNAC) is an ideal initial diagnostic modality considering patient's comfort, lack of requirement of anesthesia, rapid analysis and reporting, and few false positive results.

Materials and Methods: In the present study cyto-histological correlation was done in 61 patients.

Observation and Result: Out of 61 patients, 43 were benign, 17 were malignant and one was inflammatory on cytological examination. On histopathological examination 41 were benign and 19 were malignant and one was found to be inflammatory. Cyto-histopathological correlation was found in 96.7% cases.

Conclusion: FNAC is a useful preliminary tool for diagnosing the breast lumps in our set up.

Keyword: Benign, Breast, Fine needle aspiration cytology, Histopathology, Malignant.

Introduction

Breast carcinoma is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed in 2012 (second most common cancer overall). This represents about 12% of all new cancer cases and 25% of all cancers in women. The rate of incidence varies from 19.3 per lac women in Eastern Africa to 89.7 per lac in Western Europe. However, the mortality rate is less and is 6-19 per lac because of availability of facilities for early diagnosis and treatment of breast cancer in developed countries.

But over last ten years, breast cancer has been rising steadily, and for the first time now, breast cancer is the most common cancer in women in India, way ahead of cervical cancer. Both, the incidence, as well as deaths, due to breast cancer are more than cervical cancer. It is estimated that during the year 2012, about 144,937 new cases of breast cancer were diagnosed and 70,218 women were died of cancer in India.⁽¹⁾

Breast lesions most commonly present as lump. Fine needle aspiration cytology (FNAC) is an important initial diagnostic modality in breast lumps as there is no need for anesthesia and rapid analysis and reporting can be done with few false positive results.⁽³⁾ FNAC is one of the important components of 'triple approach', which has been widely accepted for the preoperative diagnosis of breast lesions which includes clinical and radiological examination in conjunction with FNAC features, to diagnose the breast lesions and to determine the best management plan for the patient.⁽⁴⁾

However, a definitive diagnosis sometimes cannot be made by FNAC alone, either due to inherent limitations of any cytological examination or the inability to obtain adequate material for diagnosis.⁽⁵⁻⁸⁾

This study is undertaken to study the burden of breast diseases in a rural area. The information gathered about the prevalence and spectrum of breast lesions helps in the development of strategies for proper health

care planning. It can also be helpful in determining usefulness of FNAC in our setup.

Aims & Objectives

1. To study the morphological spectrum of various breast lesions in patients with an apparent breast lump.
2. To correlate the cytological findings with histopathological examination.
3. To determine the accuracy of aspiration cytology in the diagnosis of the breast lesions.

Materials & Methods

This hospital-based cross sectional descriptive study was carried out in Department of Pathology, C.C.M. Medical College, Durg (Chhattisgarh) for a total duration of 12 months from January 2015 to December 2015.

The present study included 61 females presenting with palpable breast lump in the outpatient department. FNAC was carried out using 10 ml plastic disposable syringe and disposable needles of 23-24 gauge. The smears were stained with Field's stain and Giemsa stain. Smears with adequate material were followed for subsequent histopathological correlation on tru-cut biopsies, lumpectomies and mastectomies. The patients with inconclusive cytology and who underwent FNAC but did not undergo subsequent histopathological investigation were excluded from the study.

Observations & Results

The age range for total 61 patients was 15-75 years. Majority of patients (57%) patients were in age group between 15-30 years (Table 1). Out of 61, 10 (16%) patients were unmarried.

Table 1: Age wise distribution of patients enrolled in study (n=61)

| S. No. | Age Group (in years) | No. of Patients (n=61) | % of patient |
|--------|----------------------|------------------------|--------------|
| 1. | 15-30 | 35 | 57 |
| 2. | 31-45 | 15 | 25 |
| 3. | 46-60 | 09 | 15 |
| 4. | 61-75 | 02 | 03 |
| Total | | 61 | 100 |

Out of 61 cases, one case was diagnosed as inflammatory lesion, 43 cases (70.5%) were benign and 17 (27.9%) were malignant on cytology. The inflammatory lesion was mastitis. The benign lesions on cytology included fibroadenoma and fibrocystic disease (Table 2).

Table 2: Cytological diagnosis of breast lesions on FNAC (n=61)

| Category | Cytological diagnosis | No of patients (n=61) | % of patient |
|---------------------|-----------------------|-----------------------|--------------|
| Inflammatory (n=01) | Mastitis | 01 | 1.6 |
| Benign (n=43) | Fibroadenoma | 38 | 70.5 |
| | Fibrocystic disease | 05 | |
| Malignant (n= 17) | | 17 | 27.9 |
| Total | | 61 | 100 |

Out of 61 cases, 41 (67.3%) cases were benign and 19(31.1%) were malignant; one was inflammatory (chronic lymphocytic mastitis) on histopathological examination. The spectrum of malignant lesions on histopathology included classic (NOS) invasive ductal carcinoma, mucinous carcinoma, medullary carcinoma, metaplastic carcinoma (carcinosarcoma) and squamous cell carcinoma (Table 3).

Table 3: Histopathological diagnosis of breast lesions (n=61)

| Category | Histopathological diagnosis | No of patients (n=61) | % of patient |
|---------------------|---|-----------------------|--------------|
| Inflammatory (n=01) | Chronic lymphocytic mastitis | 01 | 1.6 |
| Benign (n=41) | Fibroadenoma | 36 | 67.3 |
| | Fibroadenosis | 01 | |
| | Fibrocystic disease | 01 | |
| | Lactating adenoma | 01 | |
| | Benign phylloides tumor | 02 | |
| Malignant (n=19) | Classic (NOS) invasive ductal carcinoma | 14 | 31.1 |
| | Mucinous carcinoma | 01 | |
| | Medullary carcinoma | 01 | |
| | Metaplastic carcinoma (carcinosarcoma) | 01 | |
| | Squamous cell carcinoma | 02 | |
| Total (n=61) | | 61 | 100 |

Out of all patients diagnosed malignant on histopathological examination i.e. 19 cases, 8 cases (13%) were in age group of 46-60 years. Out of 41benign lesions, majority of cases (55%) were in age group of 15-30 years (Table 4).

Table 4: Age wise distribution of patients with various breast lesions on histopathology (n=61)

| S. No. | Age Group (in years) | Patients with inflammatory lesions % (n=01) | Patients with benign lesions % (n=41) | No. of Patients with malignant lesions % (n=17) |
|--------------------|----------------------|---|---------------------------------------|---|
| 1. | 15-30 | 00(00) | 55.7 (34) | 3.3 (02) |
| 2. | 31-45 | 1.6 (01) | 11.6 (07) | 11.4 (07) |
| 3. | 46-60 | 00 (00) | 00 (00) | 13.1(08) |
| 4. | 61-75 | 00 (00) | 00 (00) | 3.3(02) |
| Total 100 % (n=61) | | 1.6 (n=01) | 67.3(n=41) | 31.1 (n=19) |

Out of 61 cases, one case was diagnosed as inflammatory on cytology and as lymphocytic chronic mastitis on histopathological examination. Out of 43 cases diagnosed as benign on cytology, two were found to be malignant on histopathology and 41 were benign. Out of 17 cases diagnosed malignant on cytology, all cases were found to be malignant on histopathology (Table 5).

Table 5: Cyto-histopathological correlation of patients enrolled in the study (n=61)

| Cytology | Histopathology | | Total |
|-----------|----------------|-----------|-------|
| | Benign | Malignant | |
| Benign | 41 | 02 | 43 |
| Malignant | 00 | 17 | 17 |
| Total | 41 | 19 | 60 |

The sensitivity and specificity of FNAC was found to be 100% & 89.5% respectively. The positive predictive value was 95.3% and negative predictive value was 100% for FNAC. Out of total cases, 10.5% cases were false negative. There was no false positive case in our study.

Discussion

Clinically palpable breast mass is the most common presentation of breast lesions in females. It is also the usual presentation of carcinoma breast.⁽⁹⁾ The application of FNAC for diagnosis of palpable breast masses was first introduced by Martin and Ellis in the year 1930.⁽¹⁰⁾ It has since become an increasingly popular diagnostic procedure owing to its distinctive advantages of being easy, fast, sensitive, economical and safe with excellent patient acceptability.⁽¹¹⁾ FNAC of the breast has two main goals. One is to confirm a radiological and clinical benign lesion and avoid unnecessary surgery and the other is to confirm a malignant diagnosis and allow definite treatment planning.⁽¹²⁾

In the present study FNAC was performed on 61 patients and these were followed for histopathology.

The age range was 15-75 years with mean age being 30.8 years in our study. In study by Shagufta et al, Manju et al and Koirala et al, the age range was 16-80, 15-60 and 15-67 years respectively.^(13,14,15) The mean age was 37.26 years and 36.2 years in the study by Shagufta et al, and Koirala et al respectively.^(13,15) The mean age was slightly lower in our study as benign lesions were more common in our study.

The breast pathology was common in age group of 15-30 years (57%) followed by 31-45 years (25%), 46-60 years (15%) and 61-75 years (3%) respectively in our study.

On cytology out of 61, 43 (70.5%) cases were benign, 17 (27.9%) cases were malignant and 1.6% cases were inflammatory in our study. In the study by Shagufta et al, benign lesions were 45.83%, malignant lesions were 30.76% and inflammatory lesions were

8.65%, highly suspicious/atypical lesions were 8.33% and unsatisfactory smears were 6.41% on cytology.⁽¹³⁾ In the study by Manju et al 60% cases were benign, 28.5% cases were malignant and 8.5% cases were inflammatory and 2.8% were in the category of atypical or intermediate probably benign on cytology.⁽¹⁴⁾ In the study by Koirala et al, 66.7% cases were benign and 15.6% cases were malignant and 17.8% cases were suspicious for malignancy on cytology.⁽¹⁵⁾ Benign lesions are more common in all other studies as in our study but the percentage of benign lesion was highest in our study. The percentage of malignant lesions in our study was almost comparable with that of other studies.

Out of 61 cases, 38 cases (62.2%) were diagnosed as fibroadenoma & 5 cases (8.1%) cases were diagnosed as fibrocystic disease and one (1.6%) case was diagnosed as chronic mastitis on cytology in our study. In study by Shagufta et al, the most common benign lesion in descending order of frequency on FNAC were; benign epithelial cells 21.15%, followed by fibroadenomas 14.42%, fibrocystic changes 8.3%, acute mastitis 3.8%, granulomatous mastitis 3.5%, papillary breast lesions, Lactational changes 0.96%, and periductal mastitis and fat necrosis 0.64% each.⁽¹³⁾ In study by Manju et al, benign breast lesions on cytology included fibroadenoma (45.7%), fibrocystic disease (8.5%), epithelial hyperplasia (2.8%), simple cyst (2.8%), mastitis (5.7%), granulomatous mastitis (2.8%) and ductal hyperplasia with atypia (2.8%).⁽¹⁴⁾ In our study and the study by Manju et al the most common benign lesion on cytology was fibroadenoma.⁽¹⁴⁾

On histopathological examination out of 61 cases, 41 (67.3%) cases were benign and 19 (31.1%) cases were malignant and 1 case (1.6%) was inflammatory in our study. In the study by Shagufta et al 54.04% cases were malignant, 35.2% cases were benign and 9.7% cases were inflammatory.⁽¹³⁾ In the study by Manju et al 94.2% cases were benign and 5.7% cases were malignant.⁽¹⁴⁾ In the study by Koirala et al, 67.7% cases were benign and 33.3% cases were malignant.⁽¹⁵⁾ In our study and study by Manju et al and Koirala et al the majority of the cases fall in the category of benign lesions whereas in study by Shagufta et al malignant lesions were more common in the study population as compared to benign lesions.^(13,15)

On histopathological examination, 36 (59.1%) were fibroadenoma, 2 (3.3%) were benign phylloides tumor, one (1.6%) was fibroadenosis, one (1.6%) was fibrocystic disease, one (1.6%) was lactating adenoma and one (1.6%) was chronic lymphocytic mastitis in our study. Among 19 malignant cases, 14 (23.1%) were classic invasive duct carcinoma, 2 (3.3%) were squamous cell carcinoma, one (1.6%) was mucinous carcinoma, one (1.6%) was medullary carcinoma, one (1.6%) was metaplastic carcinoma in our study. In study by Shagufta et al, 22.44% cases were fibroadenoma, 6.12% cases were acute mastitis, 6.12% cases were fibrocystic change, 3.57% cases were

granulomatous mastitis, 1.53% were lactational change, 1.53% were intra duct papilloma, 1.02% were epithelial hyperplasia, 1.02% were lactating adenoma, 0.51% were tubular adenoma, 0.51% were blunt duct adenosis, and 0.51% were sclerosing adenosis. The most common malignant lesion was infiltrating duct carcinoma 50.5%, followed by lobular carcinoma 2.04%, mucinous carcinoma 0.5%, poorly differentiated carcinoma 0.5%, and metaplastic carcinoma 0.5%.⁽¹³⁾ In the study by Koirala et al, 44.4% cases were of fibroadenoma, 8.8% cases were of fibroadenoma with fibrocystic change, 8.8% cases were of gynaecomastia and 4.4% cases were of fibrocystic change. The most common malignant lesion was invasive ductal carcinoma 28.8% followed by mixed (ductal and lobular carcinoma) 4.4%.⁽¹⁵⁾ Fibroadenoma was found to be the most common benign tumor & infiltrating duct carcinoma was the most common malignant tumor in our study, the same result were found in studies too.^(13,15)

In our study, benign lesions were more common in age group of 15-30 years and malignancy was more common in age group of 46-60 years. In the study by Shagufta et al the mean age for benign lesions was 32.8 years and for malignant lesions 42.5 years.⁽¹³⁾ In the study by Manju et al the highest frequency of benign breast lump was seen in age group of 15-30 years and the highest frequency of malignant lesions were found in age group of 40-60 years.⁽¹⁴⁾ The results found in our study were comparable to those found in other studies.

Out of 43 benign cases on cytological examination, only 2 cases were found to be malignant on histopathological examination and all the malignant cases on cytological examination were confirmed as malignant on histopathological examination. Thus in majority of cases, i.e. 96.7%, the cytological diagnosis was consistent with that of histopathological diagnosis. The sensitivity and specificity was found to be 100% & 89.5% in our study which was comparable as found in other studies [Table 6].^(13,14,15,16,17,18,19)

Table 6: Statistical evaluation of breast lesions in various studies

| Studies | Sensitivity (%) | Specificity (%) | Positive Predictive value (%) | Negative predictive value (%) |
|----------------------|-----------------|-----------------|-------------------------------|-------------------------------|
| Shagufta et al | 90.65 | 96.84 | 97 | 90.19 |
| Manju et al | 83.3 | 100 | - | - |
| Koirala et al | 100 | 100 | | |
| Tiwari M | 83.3 | 100 | - | - |
| O Neil S et al | 97 | 78 | - | - |
| Zhang Qin et al | 97.1 | 97.3 | - | - |
| A.Z. Moham med et al | 90.6 | 100 | - | - |
| Present study | 100 | 89.5 | 95.3 | 100 |

The high sensitivity and specificity obtained in this study indicate that FNAC is a reliable diagnostic method when correctly performed and interpreted by an experienced cytopathologist and can be used as a preliminary tool for breast lesions.

However, the two cases were false negative in our study which were diagnosed benign on cytology and turned out to be malignant (invasive ductal carcinoma) on histopathology. Hypocellularity, despite of repeated aspiration was a contributing factor in one of the cases. Presence of mixed benign and malignant cells was found in another case. The case showed dissociated cells against background of benign clusters of epithelial cells along with nuclear overlapping. The nuclear crowding hindered the proper assessment of nuclear morphology. Ariga et al. in their study of patients for FNAC breast with subsequent histological correlation reported similar reasons for cytohistological discrepancy in the false negative category.⁽²⁰⁾

False negative diagnosis may be due to technical failure, misdiagnosis or the presence of mixed benign and malignant features.⁽²¹⁾ Examples of technical failure include acellular or insufficient cellular material, heavily blood stained smears, partial air drying and smearing artifacts resulting in cell disruption.⁽²⁰⁾

These discrepancies can be overcome and sensitivity of FNAC further enhanced by using techniques, such as ultra-sound guided FNA biopsy.^(4,22,23) Unavoidable limitations of FNAC can be further reduced by wider use of 'triple test' which in addition to FNAC includes physical examination and mammography as other components. There are many studies that have shown that the triple test was 100% accurate in the diagnosis of palpable breast lesions when all three elements were concordant.^(23,24) Salmal et al.⁽²⁴⁾ and Lau et al.⁽²⁵⁾ suggest the use of triple test with negative predictive value reaching 100%. Vetto et al.⁽³⁰⁾ suggested that 'modified triple test' (physical examination, ultra-sonography instead of mammography and FNAC) is more accurate and cost effective in the diagnosis of palpable breast lesions in younger women.

Conclusion

FNAC is a simpler, cost effective and reliable method and can be used as routine preliminary tool for assessment of breast lesions in our set up. It helps to take preoperative decision and further management of patient and can avoid unnecessary surgical intervention. False negative results are inevitable and be decreased by proper FNAC techniques assisted by ultra-sound.

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