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Fine Needle Aspiration Cytology Of Palpable Breast Lesions With Histopathologic Correlation

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Abstract

Introduction: Breast cancer is one of the commonest malignancies in women worldwide and adequate preoperative evaluation is the most essential part of management of breast lumps. Management of breast lumps is challenging in resource poor settings. Although core needle biopsy has evolved as the diagnostic tool of choice for breast lumps, fine needle aspiration cytology (FNAC) still remains an important diagnostic tool. With this background, a prospective study to highlight the role of FNAC in the diagnosis of breast lesions and correlate the cytomorphologic features with histological appearance to improve the diagnostic sensitivity & specificity of FNAC.

Material and Methods: A prospective study on breast aspirates was done from September 2019 to June 2021. All patients presenting with palpable breast lesions to the Department of Pathology, Annapoorana medical college and hospitals, Salem were subjected to an FNAC procedure after a detailed history, general physical and local examination and the results of 100 cases were categorized into 5 groups C1 through C5 as per the NHSBSP criteria.

Results:

The results showed: C1 category- 2 cases, C2 category-63 cases, C3 category-7 cases, C4 category-3 case, and C5 category-25 cases. Maximum cases were seen in C2 category. Among them fibroadenoma was most common breast lesion (46). In the C5 category of malignant cases, infiltrating ductal carcinoma was the most common lesion (24). All the cases underwent an excision and the overall sensitivity in the study was 100%, the positive predictive value in disease was 95.24%, the negative predictive value was 100% and diagnostic accuracy 96.59%.

Interpretation & Conclusion: FNAC is an effective and valid tool as the first line diagnostic modality in the preoperative diagnosis of both benign and malignant lesions

Keywords: FNAC; Breast lump; NHSBSP criteria; Fibroadenoma; Infiltrating ductal carcinoma; Sensitivity; Diagnostic accuracy

Introduction

Fine needle aspiration cytology (FNAC) is a technique which is routinely done on palpable lesions, such as superficial growths of the skin, sub cutis, soft tissues and organs like thyroid, breast, salivary glands, and superficial lymph nodes. FNAC is a very simple procedure that can be easily repeated. FNAC of the breast can be done on both palpable and nonpalpable lesions. It is a well-accepted procedure and is a valuable tool in the diagnosis and patient management of breast lesions. It has high diagnostic accuracy.[1,2] this helps the clinician in planning the correct surgical or medical treatment. Nonetheless, some variation has been reported.[3,4] The advantages are it provides rapid and

accurate diagnosis, diagnostic as well as therapeutic in cystic conditions. Its distinct advantage is that it can be done during the outpatient visit without the need of the anesthesia, thus eliminating the cost of outpatient surgery. It also allows discussion with the patient of various treatment plans for malignant mass on the same visit.

The scope of cytology also extends into identifying the subtypes of benign and malignant breast lesions. It is also used in the detection of minimal residual disease for the purpose of planning a therapeutic protocol and eventual follow-up. Thus, it plays a major role as an important preoperative assessment procedure along with clinical correlation and imaging which are referred to as the "Triple test" which in addition to the fine needle aspiration cytology includes clinical breast examination and mammography. [5] Limitation of FNAC is its inability to differentiate into in situ and invasive carcinoma.[6]

However, FNAC still is popular modality of diagnosis because of its overall accuracy in experienced hands, least invasiveness, ability for repeat testing and speed of giving results. The overall accuracy of FNAC in diagnosis of breast lesions is reported to be about 97.40%. The diagnostic sensitivity, specificity, and predictive value of a positive result of FNAC for diagnosing breast lesions are 93.80%, 98.21%, and 92.70% respectively [7]

In relation to malignancy, reports have shown a sensitivity of 94.5%, specificity of 98%, diagnostic accuracy of 97%, positive predictive value of 95.8%, and negative predictive value of 97.4% [5]. In literature, false negatives range from 7.5% to 21.9% and even in biopsies diagnosed by frozen section a 4% false negative rate is seen. [5]

The purpose of this study is to evaluate our experiences with fine needle aspiration cytology in a series of patients and compare the diagnostic accuracy of fine needle aspiration cytology with postoperative histopathology.

Materials & Method

A prospective study on breast aspirates was done over a period from September 2019 to June 2021. All patients presenting with palpable breast lesions to the Department of Pathology, Annapoorana medical college and hospitals, Salem were subjected to an FNAC procedure after a detailed history, general physical and local examination. The slides were fixed in 95% ethyl alcohol as soon as they were made for Hematoxylin & Eosin stains. A few air-dried smears were taken for the Leishman stain. ZN stain was done where it was necessary.

Cytologic Interpretation

All the lesions were categorized into 5 categories C1 to C5 as per NHSBSP breast reporting criteria.[8] As follows C1-Inadequate, C2- Benign, C3- Atypia probably benign, C4- Suspicious of malignancy, C5-Malignant

Lesions were graded using Robinson's criteria based on 6 parameters- cell dissociation, nuclear size, cell uniformity, nucleoli, nuclear margins, and nuclear chromatin. Each parameter was given a score of 1, 2 or 3. The scores were added up to get the total scores for grading the carcinomas.[9] Grade 1-Score of 6 to 11, Grade 2-Score of 12 to 14, Grade 3 –Score of 15 to 18. The lesions which were confirmed on histopathology were further graded using scarf bloom Richardson grading (SBR).

Statistical Analysis:

The sensitivity, specificity, positive predictive value, and overall accuracy of fine needle aspiration as a diagnostic tool was calculated wherever biopsies had been performed.

Results

The present study includes FNAC of 100 cases of breast lesions, spread over a 22- month period from September 2019 to June 2021 at the Department of Pathology, Annapoorana medical college and hospitals, Salem. Two patients had bilateral aspirates. The observations of the study were as follows: Patient's age ranged from 15 to 80 years in which females were 99 and 1 male. The most common age group of incidences was 21-40 years (n=42) followed by 41- 60 years

The commonest presenting symptom was a lump in the breast. This was observed in all cases. 30 cases in addition had associated pain, two cases presented with nipple discharge in addition to the lump, four cases showed nipple retraction, and two case showed evidence of ulceration adjacent to the lump.

In 100 cases 55 cases had right side lump, 43 cases had left side lump and 2 cases presented with bilateral lump. In our study most commonly lump

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was located in 22 cases in lower inner quadrant and 22 cases in upper outer quadrant. Least common was seen in lower outer quadrant in 15 cases.

In 100 cases 98 cases were adequate for reporting and 2 cases were inadequate comprised of proteinaceous material with scant cellularity. 100 FNAC were analysed and grouped into 5 categories from C1 – C5. Out of 100 FNAC cases 2 cases were reported as inadequate.

Table-1. Categorization in cytology of breast lesions.

Category	No of cases
C1	2
C2	63
C3	7
C4	3
C5	25

C2 Catgory Benign Lesions

Out of 100 cases 63 were reported as benign lesion under C2 category. The most common quadrant involved was lower inner quadrant and upper outer quadrant. Most common lesions were fibroadenoma, which were 46 cases. Total 3 cases of inflammatory lesions were seen, among them one was granulomatous mastitis. Almost all cases were correlated with histopathology.

Table No.2- Showing FNAC and histopathology correlation.

	FNAC	Histopathology	
Diseases	**No of cases**	**Positive**	**Negative**
Fibroadenoma	46	40	6
Fibrocystic disease	2	1	1
Benign breast disease	5	3	2
Fibroadenomatoid hyperplasia	6	1	5
Simple cyst	1	0	1
Inflammatory	3	2	1
Total	63	47	16

Out of 63 benign cases 3 were reported as inflammatory lesions. 2 cases presented with right breast lump and one case with left side lump. maximum cases i.e. 46 cases were reported as fibroadenoma. 40 cases were histopathologically also diagnosed as fibroadenoma. One case was malignant on histopathology and reported as IDC breast. The smears from all the cases showed classical features of fibroadenoma.

In 46 cases who got operated, 40 cases were confirmed as fibroadenoma on histopathology. Also 2 cases were diagnosed as fibrocystic disease. Smears showed many foamy histiocytes and few clusters of ductal epithelial cells. Apocrine cells were also seen. Background naked bipolar nuclei, stromal fragment were seen. Both cases were operated and one was confirmed on histopathology as fibrocystic disease.

C3 Category

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A C3 category diagnosis of atypia, probably benign at cytology was diagnosed on 7 cases. One case was male patient. They presented with ill-defined lump. Smears from the patients showed cohesive clusters of ductal epithelial cells and myoepithelial cells with few bare nuclei and stromal fragments in the background.

All 7 cases were operated and 5 cases including one case in male patient were diagnosed on histopathology as IDC. Sections showed atypical ductal cells arranged in predominantly tubular pattern. One case was reported as tubular adenoma on histopathology.

C4 Category Suspicious Of Malignancy

Three cases were reported as suspicious of malignancy. Smears showed few clusters of pleomorphic ductal epithelial cells with cellular and nuclear pleomorphism. All patients underwent surgery and histopathological all were diagnosed as infiltrating ductal carcinoma.

C5 Category Malignant

In our study 25 cases were reported as malignant on FNAC. Maximum cases were seen in upper quadrant. Most common age group was 41-60 yrs. Smears were highly cellular composed of ductal epithelial cells arranged in loose cohesive clusters and in singles. These cells had high N:C ratio, hyperchromatic nuclei and scant cytoplasm. Also seen were bizarre tumor cells. No evidence of myoepithelial cells. They were reported as infiltrating ductal carcinoma. Lesions were graded using SBR grading.

All cases underwent modified radical mastectomy and were diagnosed as malignant on histopathology. 24 cases were reported as infiltrating ductal carcinoma and one case was reported as lobular carcinoma breast. On FNAC all malignant cases were graded using Robinson's criteria. All cases were operated. On histopathology they were graded using Scarff bloom Richardson grading (SBR). 14 cases showed correlation in grading and 11 cases showed discrepancy. Maximum cases were seen in grade 2 both in cytology and histopathology.

Cytological diagnosis was correlated with histopathology in all cases. 100 FNA cases material had a corresponding histological diagnosis. With this confirmation an overall sensitivity, predictive value of a positive result and percentage of false negative indices were calculated. Out of 63 benign lesions on FNA, the discrepancies at cytology were as follows: In 46 cases of fibroadenoma on cytology. On histopathology, 40 were reported as fibroadenoma, 5 cases were reported as benign lesions & 1 case turned to be malignant. The sensitivity was 100% and positive predictive value was 86.96%.

Table 3: Benign lesion correlation

Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	100%	(91.24, 100)	Wilson Score
Specificity	0.00%	(0.0, 39.03)	Wilson Score
Positive Predictive Value	86.96%	(74.33, 93.88)	Wilson Score
Diagnostic Accuracy	86.96%	(74.33, 93.88)	

Out of 5 cases reported as benign breast disease on cytology. On histopathology 2 cases were diagnosed as fibroadenoma, 1 case as fibrocystic disease and 2 cases were diagnosed as malignant. Here PPV was less with 20%. Out of 2 cases, fibrocystic disease one case was concordant, one was discordant and were reported as normal breast tissue on histology with PPV of 50%. Out of 3 inflammatory lesion cases, only one case was concordant & other two cases were discordant wih PPV pf 33.33%

Coming to malignant lesions, out of 25 cases as malignant in cytology, all 25 cases were diagnosed as malignant on histopathology. Therefore, the FNAC proved to be 100 % sensitive and specific in the diagnosis of malignant lesions in our study.

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Table 4: Malignant lesion correlation

Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	100%	(93.98, 100)	Wilson Score
Specificity	89.29%	(72.8, 96.29)	Wilson Score
Positive Predictive Value	95.24%	(86.91, 98.37)	Wilson Score
Negative Predictive Value	100%	(86.68, 100)	Wilson Score
Diagnostic Accuracy	96.59%	(90.45, 98.83)	

Discussion

Our study included the FNAC of 100 breast lesions, in which the cytomorphological features were studied in detail. The most common age group 21-40yrs which was concordance with study done by *Gupta R et al.*, Chandanwale et al and Haque et al reported 30-40 years as most common age group.[10,11]

In our study benign lesions were more common compared to malignant lesions. This is similar to study done by Shanmugasamy K et al.. Pandit et al also commented that benign breast lesions are more than malignant cases.[12]

Majority of breast lumps were seen in right breast (55) compared to left (43) and bilateral involvement was seen in (2). This was similar to study done by Gardas V et al.[13] Maximum cases were distributed in upper outer quadrant and lower inner quadrant (22%) coincided with the work of Swapan (46.66%) and Yalavarthi S.[14,15] FNAC results were divided into 5 categories- C1 through to C5 based on NHSBSP[8] reporting criteria.

C1 Category

The C1 category caters to inadequate cases. There were 2 cases. The patients presented with small ill-defined swellings. The smears were poorly cellular in a hemorrhagic and proteinaceous background. The success of FNAC is directly related to the skill and experience of the personnel involved in taking the specimen and examining the smears.[16]

C2 Category

In the C2 category of benign lesions, there were 3 inflammatory lesions, 46 cases of fibroadenoma, 5 cases of benign breast disease, 2 cases of fibrocystic disease, 6 cases of fibroadenomatoid hyperplasia and 1 case of simple cyst. In our study among benign lesions fibroadenoma was most common which was concurrent with the findings of *Gupta R et al.and* Debra (1995) et al[17] **and** 40 cases correlated with histopathology. 1 case was diagnosed as malignant (IDC).

Of the inflammatory lesions, 1 case was reported as granulomatous mastitis. Smears showed many histiocytes were seen. Few ductal epithelial cells were seen in clusters. Occasional multinucleated giant cells and epitheloid cell granulomas. ZN stain for AFB was negative. The patient underwent surgery and it was diagnosed on histopathology as suppurative granulomatous. Granulomatous inflammation of the breast is not a rare finding and is similar to the granulomatous inflammation in the prostate. This occurs in response to breast secretions. The lesion can mimic carcinoma both radiologically and clinically and epithelial atypia can be worrying in some cases[18].

In the C2 category series, 2 cases were diagnosed as fibrocystic disease. The age ranged from 25 to 45 years. Smears showed apocrine cell clusters and cyst macrophages were seen in plenty with few ductal epithelial cells. Both underwent surgery and 1 case was diagnosed as FCD confirmed at histology.

In our study 5 cases were diagnosed as benign breast disease. On histopathology 2 were diagnosed as malignant cases. 6 cases were diagnosed as fibroadenomatoid hyperplasia. Smears showed few monolayered sheets of ductal and myoepithelial cells. Of these, 2 cases showed antler horn pattern and 4 cases showed bare nuclei which were not numerous. Few cyst macrophages were seen in 4 cases. Thus, some of these had few features of fibroadenoma and some showed features of fibrocystic disease. Fibroadenomatous hyperplasia [19] characterizes these

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lesions and it is difficult to differentiate these from fibroadenoma both in our experience as well as in literature unless clinical correlates are available.

All patients underwent surgery. Histopathologically 1 case was diagnosed as fibroadenomatoid hyperplasia. The remaining 5 cases, on histology 1 was diagnosed as fibrocystic disease 2 were diagnosed as fibroadenoma, 1 case as benign breast disease and 1 case was diagnosed as benign phyllodes tumor

In the C3 category, there were 7 cases. 6 patients were female and 1 patient was male. The aspirates were cellular with bimodal population of ductal epithelial cells and myoepithelial cells in background of few bare nuclei. Some clusters showed atypia in the form of mild to moderate nuclear pleomorphism, nuclear overlapping and crowding with prominent nucleoli. All cases underwent surgery and 6 cases on histopathology were diagnosed to be malignant. One case on histopathology was diagnosed as tubular adenoma. At times nuclear changes may look exaggerated at cytology and this has to be kept in mind. Atypia at cytology is characterized by crowding of nuclei, overlapping of nuclei and nuclear enlargement[6]. This may also be an accompaniment of reactive changes due to inflammation[6]. The recommendation for C3 category by NHSBSP[20] is excision and therefore all the case had an excision biopsy.

In C4 category 3 cases were reported as suspicious of malignancy. Smears showed few clusters of pleomorphic ductal epithelial cells with cellular and nuclear pleomorphism. All patients underwent surgery and histopathological all were diagnosed as infiltrating ductal carcinoma.

In C5 category 25cases were reported as malignant. Upper quadrant was commonly involved in our study. IDC was most common which is similar to studies done by yalavarthi et al and Gardas V et al.[15]

All cases underwent surgery and diagnosed on histopathology as malignant. Cytohistological agreement was 100% in malignant cases similar to a study by Waghmare RS et.al.[21]

Thus in the malignant category, the diagnostic sensitivity was 100% with no false positive or false negative cases. Experienced cytologists have no difficulty in picking up the malignant breast aspirates as a result of their cytologic characteristics-cell discohesion, increased NC ratio, cell disassociation, monomorphic pattern as well as nuclear pleomorphic features. To differentiate between ductal carcinoma in situ and invasive carcinoma may be difficult at FNAC. Discohesiveness is a feature of malignancy. However, in our cases, majority of them also showed cohesive clusters of malignant cells with or without single cells. The diagnosis was made based on morphology.

Conclusion

FNA is a valuable diagnostic tool in conjunction with radiological and clinical data of palpable breast lesions. The fine needle aspiration cytology of breast lesions is valuable, easy, cost effective, time saving and diagnostic for initial investigations and screening of breast lump. It helps the surgeon in deciding further management of lump as it is sensitive and specific. FNAC results should be correlated with clinical findings and radiological investigations. The high specificity and a high negative predictive value for malignancy illustrated the high accuracy of FNAC in the diagnosis of malignancy in the breast. Thus this study concludes that FNAC is an effective and valid tool as the first line diagnostic modality in the preoperative diagnosis of both benign and malignant lesions.

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