Cytomorphology of breast lesions with historadiological correlation in a tertiary care centre of Puducherry

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Abstract

Introduction: Breast cancer is the leading cause of morbidity & mortality worldwide. Breast being a surface organ, is easily palpable for aspiration. Diagnosis is often done by correlating fine-needle aspiration cytology (FNAC) findings with mammography. The aim of this study was to evaluate the FNAC in the diagnosis of breast lesions and to correlate cytological findings with histopathology findings along with mammography.

Methodology: Over a period of three years, 329 aspirations were performed, 158 (48.03%) cases that had followed up by histopathological examination were included in the study.

Results: Among the 158 cases studied, 154 (97.47%) cases were females and 4 (2.53%) cases were males. The incidence of breast lesions was maximum in the range of 21 to 30 years of age (24.68%). Most commonly encountered benign breast lesion was fibroadenoma (70.53%). Most commonly encountered malignant breast lesion was IDC (30.95%).Taking histopathology as the golden standard for diagnosis, we calculated the sensitivity, specificity, diagnostic accuracy, positive predicitve value, negative predictive value of FNAC and mammography. The sensitivity, specificity, positive predicitve value, negative predictive value of a mammogram were found to be 98.68%, 78.12%, 98.17% and 83.33% respectively while that of FNAC were found to be 87.23%, 100%, 96.05%, 100% and 94.87% respectively.

Conclusion: From present study it is evident that benign breast lesions are common than malignant lesions. The simplicity, rapidity, lack of morbidity, high sensitivity, high specificity and cost effectiveness of FNAC makes it the most valuable tool in the evaluation of both neoplastic and non-neoplastic breast lesions.

Keywords: FNAC, Biopsy, Fibroadenoma.

Introduction

Five to fifty five percent approximately of all females suffer from breast diseases. A routine clinical assessment is not at times enough to determine if a suspicious lump is benign or malignant.[1] Breast diseases are showing a positive rising trend globally.[2] In our country, breast cancer incidence is crawling up to be the first type of cancer in females moving cervical cancer to the second position. FNA cytology has a very high specificity (98 to 100%) and sensitivity of 89% to 98%.[10] For several years, even as early as 1933, when Stewart's series of 2,500 specimens approximately included 500 breast tissue lesions,[4] the practice of using a needle to take tissue samples for diagnosis of lesions from different anatomical parts[3] of the body has been prevalent. For cases related to breast, this method was very appropriate as it was easily accessible.

"Triple approach" i.e. clinical examination together with mammography and FNAC identifies clearly benign and malignant cases preoperatively. This made the need for preoperative definitive diagnosis even more necessary. This technique which determines the diagnosis and identifies the need for open biopsy was also recommended by Kreuzer and Boquoi[7]. It is reported that one in 20 women per 100,000 in India is likely to suffer from breast cancer during their lifetime.[6,7] Breast lesions range from inflammatory lesions to invasive cancers.[8] However, benign breast lesions are more common than the malignant breast lesions.[6] Fine needle aspiration results from samples by Franzen and Zaijicek permanently established this technique post publication of their cytology results for 2,111 cases. The above resulted FNA becoming an important tool for breast lesions[9] study and diagnosis. My current study dwells into utilization of FNA cytology in the diagnosis of breast lesions and is done by correlating the histopathological features with cytological findings. In this study, I shall evaluate the specificity, sensitivity and diagnostic accuracy.

Aims and Objectives

Aim: Evaluate and check utility of fine-needle aspiration cytology as a diagnostic tool for breast lesions.

Objectives

1. Study the cytological spectrum of all breast lesions.
2. Study the age group, sex distribution and site predilection of various breast lesions.
3. Correlate histopathology and cytology of breast lesions.
4. Correlate between radiological and cytological findings of breast lesions.
5. Study the sensitivity and specificity of FNAC of breast lesions.
6. Classify breast tumours according to recent WHO classification.

Subjects and Methods

This was an observational study which was conducted in the Department of Pathology, Mahatma Gandhi Medical College & Research Institute, a tertiary health centre in Pondicherry. This study was scrutinised and approved by the Institutional Medical Ethics Committee. This study comprised of breast FNACs done from June 2012 to May 2015 in the department.

Brief Explanation of the Procedure: All cases were cytologically traced and reviewed. Wherever was necessary, the smears were restained by Hematoxylin & Eosin (H&E) stain, May Grunwald Giemsa (MGG) stain and Papanicolaou (Pap) stain and reviewed again for evaluation. Available breast samples and specimens in the archives of the Department of Pathology during this period was re analysed by reviewing blocks and slides. Radiological correlation of the breast lesions during that period was also done from the archives of Department of Radiology and evaluated. 329 fine needle aspirate of breast was studied. Out of them, 158 (48.03%) cases were followed by histopathological examination. The cytological diagnosis was correlated with the histopathological diagnosis and the diagnostic accuracy was calculated. Statistical analysis was done to evaluate the results.

Statistical Methods

Statistical methods such as bar charts and pie diagram were used for descriptive purpose. Taking histopathology as the golden standard for diagnosis, the following measures were used to evaluate FNAC as a diagnostic tool: False positive, false negative, Sensitivity, Specificity, Positive Predictive value, Negative Predictive value, Diagnostic Accuracy

Results

Studies of the cytological study of breast lesions were done in the Department of Pathology, Mahatma Gandhi Medical College & Research Institute, Pondicherry over a period of June 2012 to May 2015. Out of the 329 aspirations performed during that period, 158 (48.03%) cases that had followed up by histopathological examination were included in the study.

Age Incidence of Breast Lesions:

Table 1: Age Distribution of patients with breast lesions

Age	No of Cases	Percentage
11 – 20	32	20.25%
21 – 30	39	24.68%
31 – 40	26	16.45%
41 – 50	33	20.89%
51 – 60	15	09.50%
61 – 70	11	06.96%
71 – 80	2	01.27%

During this study, the incidence was maximum in the 3rd decade of age which were 24.68% followed by 5nd decade which was 20.89% as shown in Table 1.

Benign cases were most common in the 3rd decade of age followed by 5th decade. Malignant cases were seen most in the 7th decade of age, followed by 6th decade of life. One case was seen in age less than 20 years. Suspicious cases were most common in 5th decade of age. Unsatisfactory cases were seen in 4th decade of age.

Cytological findings in breast lesions:
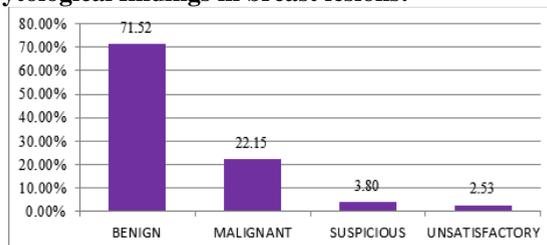
Fig. 1: Percentage of cytological diagnosis of breast lesions

There were total 158 cases, out of which there were 113 (71.52%) benign cases, 35 (22.15%) cases, 6 (3.80%) suspicious cases and 4 (2.53%) unsatisfactory cases as described in Fig 1.

Diagnosis of Breast Lesions:

Table 2: Frequency of benign breast lesions cytologically

Cytological Diagnosis	No of Cases	Percentage
Inflammatory Lesions		
Acute Suppurative Lesion	1	0.90%
Breast Abcess	1	0.90%
Chronic Mastitis	3	2.70%
Chronic Nonspecific Reaction	1	0.90%
Acute Abscess with Granulomatous Mastitis	1	0.90%
Granulomatous Mastitis	2	1.80%
Benign Proliferative Disorders		
Benign Proliferative Disease	3	2.70%
Fibrocystic Disease	15	13.51%
Benign Neoplasm		
Fibroadenoma	79	70.53%

Phyllodes Tumor	2	1.80%
Miscellaneous		
Gynaecomastia	5	4.50%
Total	113	100%

Fibroadenoma (70.53%) was the most number of benign cases diagnosed followed by fibrocystic disease (13.51%). There was no problem in diagnosing these cases. Table 2 shows the frequency of all benign breast lesions.

Table 3: Frequency of malignant breast lesions cytologically

Malignant	No of cases	Percentage
Positive for malignancy	20	46.52%
Infiltrating ductal carcinoma	13	30.95%
Intracystic papillary neoplasm	1	2.33%

Suspicious for malignancy	6	13.95%
Ductal carcinoma in situ	1	2.33%
Total	41	100%

Cytologically, 41 cases were diagnosed as malignant lesions (including suspicious cases). The frequency of malignant breast lesions has been shown in Table 3. Out of these, 20 (46.52%) cases were diagnosed as positive for malignancy. Invasive ductal carcinoma was diagnosed in 13 (30.95%) cases. Intracystic papillary neoplasm was diagnosed for one (2.33%) case. The smear showed high cellularity with papillary clusters of pleomorphic cells in a haemorrhagic background. Ductal carcinoma in situ was diagnosed in one (2.33%) case.

Cytological & Histopathological Correlation

Table 4: Cyto–Histological correlation of breast lesions

Cytological diagnosis	No. of cases	Hp diagnosis		False positive	False negative
		Benign	Malignant		
Benign	113	107	6	-	6
Malignant	35	-	35	-	-
Suspicious	6	0	6	-	-
Unsatisfactory	4	4	0	-	-
Grand total	158	111	47	-	6

There were 47 cases (29.74%) diagnosed as malignant lesions histopathologically, out of which 41 cases showed malignant features cytologically. Remaining six cases were showing benign features cytologically. The 6 cases (3.80%) which were diagnosed as suspicious for malignancy cytologically were all confirmed malignant histopathologically. There were 111 cases (70.25%) diagnosed as benign lesions histopathologically. All cases were diagnosed as benign even cytologically.

From the above observations, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of fine needle aspiration cytology in the diagnosis of breast lesions were assessed. The sensitivity, specificity and diagnostic accuracy, positive predictive value and negative predictive value of FNAC were 87.23%, 100%, 96.05%, 100% and 94.87% respectively.

Radiological Correlation of Breast Lesions:
Radio - Cytological Correlation of Breast Lesions

Table 5: Radio-cytologicalcorrelation

Mammographic findings		Cytological diagnosis			
Findings	Total cases	Benign	Suspicious	Malignant	Unsatisfactory
Benign	30	24	1	3	2
Malignant	44	11	5	28	0
Total	74	35	6	31	2

Out of 158 cases, 74(46.43%) patients with palpable breast lump underwent mammography followed by pathological examination. Comparison of mammographic diagnosis and cytological diagnosis was done as shown in Table 5.

Mammography showed more number of malignant lesions than benign lesions. This was because the

mammography was done mostly on those patients whose age was more than 35 years. The youngest patient diagnosed with breast carcinoma both radiologically as well as cytologically was 32 years old. Maximum number of malignant cases diagnosed radiologically was aged between 4th to 5th decades of life.

Radio – histopathogical correlation of breast lesions:

Table 6: Radio histopathological correlation

| Mammographic Findings		Histopath	
Findings	Total cases	Malignant	Benign
Malignant	44	37	7
Benign	30	5	25
Total	74	42	32

From the above table 6, we can calculate the sensitivity, specificity, positive predicitve value, negative predictive value of a mammogram as a diagnostic tool in assessing a breast lump. The values are 98.68%, 78.12%, 98.17% and 83.33% respectively. So, it shows the efficacy of sreening mammography in early quick diagnosis and treatment, hence reducing specific mortality in cancer patients.
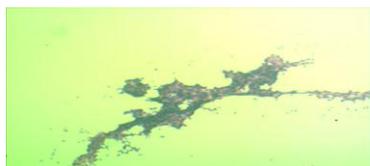

Fig. 2: Microscopy of fibroadenoma showing typical staghorn pattern of epithelial cells in cytology (H&E, 10x)
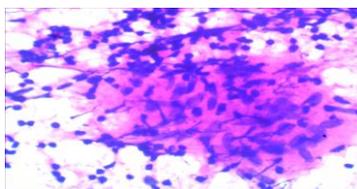
Fig. 3: Microscopy of granulomatous mastitis showing epithelioid cells arranged in clusters with lymphoid cells in the background in cytology
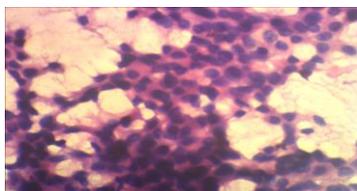
Fig. 4: Microscopy of breast carcinoma showing clusters of pleomorphic cells with hyperchromatic nucleus anisonucleosis in cytology (H&E, 40x)
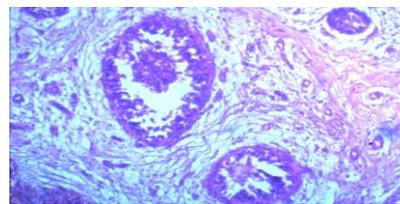
Fig. 5: Microscopy of DCIS showing round cells with increased n:c ratio with comedonecrosis in histopathology (H&E, 10x)

Discussion

Breast cancer incidents are very commonly found and one among many clinical problems faced by Indians. Even though there has been a little success in preventing this, we can significantly reduce mortality and morbidity by in-time detection of the incidence of cancer. FNAC for breast lesion diagnosis is a very accurate and established procedure. Mostly patients are in a state of anxiety. It has been reported that only 0.0045% of chances are there for tumor to be transferred along the needle track by FNA procedure.[10] The present study showed that majority of breast lesions were in the 3rd decade of life, followed by 5th decade. Study by Shirish S Chandanwale et al[11] in Maharashtra and Vijayabharathi et al[12] in Visakhapatnam showed similar findings as present study. Malignant breast lesions show frequency different in the present study when compared to other studies.[11-14] This can be due to decreased health awareness in a rural population which does not enforce them to seek medical attention but ignore it when they present with any vague symptoms.

In comparative analysis of FNAC and histopathology diagnosis, we observed six cases of cytologically interpreted errors which were all false negative cases. Among the false negative cases, two were fibrocystic disease cases which turned out to be malignant (IDC); one was benign proliferative breast disease which was recurrent phyllodes tumor borderline type histopathologically, one fibroadenoma case which turned out malignant (IDC); one was a granulomatous fibrocystic disease case which was marked epithelial proliferative lesion with low grade DCIS in histopathology; one was fibrocystic disease cytologically which turned out to be malignant (mucinous carcinoma).

Hypocellularity of aspirates was a contributory factor in two cases. Traumatic aspirate were found contributory in two cases. Presence of mixed benign as well as a malignant lesion in the same breast was found to be a contributory factor in two cases. Choi et al suggested many causes of false negative diagnosis, the most common being interpretive error followed by cystic change, needle out of focus, bloody aspiration and scanty cellularity.[15] So, the present study is comparable to studies conducted by Choi et al.[15]

Cytohistological discrepancies frequently encountered are inherent to FNAC of breast masses[16]. There is some inconclusive evidence in literature indicating that such discrepancies could be due to histological staging and type of carcinoma.[17] These discrepancies can be overcome and sensitivity of FNAC further enhanced by using techniques, such as ultra sound guided FNA biopsy.[17-19] This would ensure that the aspirator hits the target area. All clinically or cytologically highly suspicious lesions need to be resolved ultimately with excisional biopsy or frozen section.[20]

Table 7: Analytic comparison of senstivity, specificity, positive predictive value and negative predicitve value with other studies

Authors	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Present Study	87.23%	100%	100%	94.87	96.05%
Vijayabharathi et al[12]	97.18%	98.74%	97.18%	98.74%	98.26%
Kulashekhar Bhattacharya et al[24]	99.3%	97.4%	96.79%	99.5%	98.27%
Rubin et al[26]	87%	100%	100%	89%	-
Shanmugasamy et al[27]	92.86%	100%	100%	97.92%	98.3%
Bhagat et al[22]	93.7%	98.1%	96.7%	96.2%	96.4%
Sahil I. Panjvani et al[21]	97.82%	100%	100%	97.82%	98.90%
Pandey A et al[23]	98.3%	98.8%	98.3%	98.9%	98.7%

The overall accuracy of cytology in the diagnosis of breast lesions was reported to be 85 to 100%. Comparative analysis of present study with other studies[12, 21-27] as shown in Table 7, showed almost similar results. Since the sensitivity and specificity rates of FNAC are not always 100%.the technique should be used with its limitations in mind.[28-30] These 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 the triple test was 100% accurate in the diagnosis of palpable breast lesions when all three elements were concordant.[18,31] Salmai et al[31] and Lau et al[32] suggested the use of triple test with negative predictive test reaching 100%. Vetto et al[33] suggested that modified triple test (physical examination, ultrasonography instead of mammography and FNAC) was more accurate and cost effective in the diagnosis of palpable lesions in younger women.

Conclusion

FNAC is a patient friendly, easy, reliable, repeatable and simple diagnostic test. It is a quick and safe OPD procedure to diagnose breast lesions and can be employed at the bed side. When performed by an expert pathologist, the diagnostic accuracy of FNAC is very high. A high sensitivity and a high positive predictive value proved that a positive FNAC in the breast means a definite diagnosis of the concerned pathology when compared with the final histology report.

Aspiration cytology differentiates between benign and malignant condition preoperatively, so reduces patient's anxiety and also helps the surgeon to plan the surgery. FNAC also gives cytological grade of malignant lesion which correlates well with histopathological grade, and is also one of the prognostic criteria. FNAC has reduced the rate of open biopsies and hence the surgical workload.

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