



General Surgery

CYTOLOGICAL AND HISTO-PATHOLOGICAL CORRELATION OF TUMOR AND TUMOR LIKE LESIONS OF BREAST

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ABSTRACT

Introduction- The incidence of breast cancer changes significantly with age. In spite of various modalities of treatment there has been no appreciable decrease in death rate due to breast cancer. The study aims to correlate with the histological diagnosis to evaluate the accuracy the sensitivity and specificity of aspiration cytology.

Materials and methods- Cytodiagnosis of breast lesions by fine needle aspiration cytology was carried out in 406 patients having breast lump. Fine needle aspiration was performed from at least three sites in each lump.

Results- A total numbers of one hundred fifty seven cases were evaluated cytohistologically. In this study inflammatory lesions were 16 (10.08%) benign lesions 89 (66.16%) and the rest 52 (32.76%) were malignant lesions.

Conclusion- Fine Needle Aspiration Cytology (FNAC) is the best technique to differentiate benign from malignant lesions.

KEYWORDS : Cytology; breast cancer; metastasis; histo-pathology; FNAC**INTRODUCTION:**

Lesion in the breast often pose a diagnostic dilemma since decades, it has created a great interest amongst surgeon, pathologist as well as radiologist. The primary challenges in the management of breast lesions which are common in clinical practice is to differentiate benign lesions from malignant lesions. Breast carcinoma is the common malignant tumours and leading cause of carcinoma death in women. The incidence of breast cancer changes significantly with age. In spite of various modalities of treatment there has been no appreciable decrease in death rate due to breast cancer (1).

Since the advent of aspiration biopsy technique by Martin and Ellis (2) and its modification by Franzen and Co-workers the technical sphere of fine needle aspiration cytology are rolled a long way to reach up to sophisticated ultrasound, echo and mammography guided procedure to become an important diagnostic tool for various breast mass pathologies. Nevertheless the few cells that are obtained from the lesions by the use of 22/23 gauge needle are often found sufficient to make the diagnosis. Gupta et al (2000) reported a case of leiomyosarcoma by FNA (3). They used 22 gauge disposable needles with 10ml syringe and papanicolaou stain. The smears were cellular with spindle shaped and round cells with elongated, blunted or oval nuclei with pleomorphic hyperchromatic and anaplastic features. The tumor cells were present in compact sheets and with some dissociated cells. Some of the cells had prominent and sometimes multiple nucleoli. Mitoses were present with an average of 8 per 10 high power field (HPF). The cytodagnosis was correlated with cell block findings and confirmed by immunohistochemistry. Kim et al (2000) correlated the cytologic and histologic findings in 246 cases of breast lesion (4). The age ranged from 15 to 78 years. They used 23 gauge disposable needle and 10ml of syringe and papanicolaou and haematoxylin and eosin stain. The absolute and complete sensitivities for malignant lesions were 64.5% and 90.3% respectively. The specificity was 71.9%. The false negative and positive rate was 4.4% and 0.7% respectively. The predictive rate for a malignant cytologic diagnosis was 98.4%. The rate of unsatisfactory result was 9.3%.

Shet and Rege (2000) examined 40 cytologic interpretation of phyllodes tumour (PTs) with cystic degeneration. The cystic degeneration in 7 patients (5 benign, 1 low grade and 1 high grade). The aspirates from these cases yielded fluid and were usually labelled fibrocystic change on the original cytology. Smears were retrospectively analysed with special attention to the background, presence and nature of epithelial and stromal fragment, foam cells and naked nuclei in the background. Patients with cystic degeneration on cytology

showed thick fluid in the background, foamy macrophages (100%), apocrine cells (25%) and epithelial fragments which showed nuclear atypia in 2 cases. On review the smears, 5 of 7 patients had stromal fragments in small numbers. All cases showed 5.50% naked nuclei of fibroblastic type dispersed within the fluid background, even in the absence of stromal fragments. FNAC technique involves minimum trauma to the patients and can be carried out repeatedly in OPD without requiring well equipped surgical set up anaesthesia. It is a time saving procedure which combines the advantages of benign economical safe and accurate. Complications of these procedures are almost negligible. The present work has been undertaken in the cytology section of IMS & SUM Hospital. The cytological findings were correlated with the histological diagnosis to evaluate the accuracy the sensitivity and specificity of aspiration cytology.

Materials and methods

Cytodiagnosis of breast lesions by fine needle aspiration cytology was carried out in 406 patients having breast lump who attended the surgery OPD or patients directly referred to the Pathology Department of the institution, during the period from September 2014 to September 2016.

The study included the female patients with varied age groups. The patients who were not available both for cytologic and histopathological examination have been excluded from the study. The cases showing unsuitable smears in cytological examination were also excluded from the study.

The histologic diagnosis of lump was considered to be final and there after the cytology smears of the individual cases were correlated with histologic diagnosis. Fine needle aspiration was performed from at least three sites in each lump. The aspirated material was spread on slides as thinly as possible and the slides were subsequently air dried and / or wet fixed with 95% ethyl alcohol.

Fine needle aspiration was performed from at least three sites in each lump. The aspirated material was spread on slides as thinly as possible and the slides were subsequently air dried and / or wet fixed with 95% ethyl alcohol.

Prior to the needle aspiration, the size, consistency and mobility of the mass were carefully assessed. After determination of the sites to be punctured, the skin was sterilized with tincture iodine and washed with rectified spirit. The mass was grasped between the fingers of the left hand. The needle attached with the syringe was inserted into the mass

the plunger was then withdrawn slowly, thus creating a negative pressure moved in different directions within the mass. Throughout the procedure, negative pressure was maintained in the syringe by keeping the plunger retracted. In case the blood was aspirated the procedure was stopped and needle was withdrawn only to repeat the same at another site. When the aspiration was complete, the plunger was released to equalize the pressure in the syringe before withdrawing the needle, thereby preventing the cells from entering into the lumen of the syringe.

The syringe was then withdrawn and the needle was removed. The sterile cotton soaked with antiseptic lotion was applied on the aspirated site to stop any leakage of blood. Keeping the tip of the needle on the surface of a clean grease free slide, the plunger of the syringe was pushed so as to force the aspirated material in the needle on to the slide. With the help of the spreading slide the aspirate was smeared in the manner as blood smears are prepared. Minimum three smears were prepared out of the material obtained from each aspiration and then it is subjected to staining procedure.

Results

The present work "Cytological and histopathological correlation of tumor and tumor like lesions of breast" was carried out. Fine needle aspiration cytology was performed on 406 patients of different age groups and sexes. Biopsies were available in 157 cases for cyto-histo correlation. One case considered unsuitable for reporting either because this revealed only blood. In two hundred forty nine cases biopsy specimen were not available for histopathological study and thus excluded from our study. Either they revealed fibrofatty tissue, or few cells or necrotic debris or the cytodagnosis was considered sufficient for further therapeutic treatment. Hence, a total number of one hundred fifty seven cases were evaluated cytohistologically (Table 1a, 1b) (Figure 1a, 1b, 2a, 2b, 3a, 3b, 4a, 4b, 5a, 5b).

TABLE. 1a

Inflammatory lesions	Benign lesions	Malignant lesions	Total no. cases
16(10.08%)	89(56.7%)	52(32.76%)	157

TABLE. 1b

Total no. of male	Total no. female	Total no. cases
14(8.81%)	143(90.99)	157

Different types of breast lesions out of which predominant one is benign constituting 89 (66.15%) followed by malignant 52 (32.76%) and inflammatory lesion 16 (16.08%) with a female predominance 143 (90.99%) (Table. 1a, 1b).

TABLE. 2 Categories of breast lesions

Lesions	No. of cases	Age range (in yrs.)
Inflammatory	16(10.18%)	(15-42)
Benign	89(56.07%)	(8-53)
Malignant	52(32.76%)	(30-85)
Total	157	(8-85)

The categories of breast lesions in the present study were total of 157 cases, out of this inflammatory lesions were 16 (10.08%) benign lesions 89 (66.16%) and the rest 52 (32.76%) were malignant lesions (Table 2).

TABLE 3 Distribution of histologically confirmed breast lesions.

Inflammatory lesions	No. of cases	Age group in yrs
Acute mastitis.	02(1.26%)	24-40
Chronic non specific mastitis	02(1.26%)	15-22
Plasma cell mastitis	01(0.63%)	35
Granulomatous mastitis	06(3.78%)	16-50
Galactoceles	02(1.26%)	25-26
Filariasis	01(0.63%)	42
Hydatid cyst	01 (0.63%)	42
Molluscum contagiosum	01(0.63%)	35
Total	16(10.08%)	15-50
Benign		
Fibroadenoma	43(27.09%)	12-53
Fibrocystic disease	15(9.45%)	23-43

Benign phyllodes tumors	07(4.41%)	35-50
Epithelial Hyperplasia	4(2.52%)	32-50
Intraductal papilloma	01(0.63%)	40
Florid papillomatosis	2(1.26%)	12-41
Duct Ectasia	1(0.63%)	45
Radial scar	1(0.63%)	42
Gynecomastia	8 (5.04%)	50
Hamartoma	1(0.63%)	8
Infected squamous papilloma	1(0.63%)	41
Fibrolipoma	1(0.63%)	38
Benign cystic lesions	3(1.89%)	22-51
Fat necrosis	1(0.63%)	39
Malignant		
IDC(NOS)	38(23.94%)	30-85
ILC	02(1.26%)	60-68
Medullary carcinoma	02(1.26%)	35-55
Tubular carcinoma	1(0.63%)	42
Papillary carcinoma	1(0.63%)	50
Mucinous carcinoma	3(1.89%)	35-68
Metaplastic carcinoma	1(0.63%)	60
MFH	1(0.63%)	55
Paget's disease	1(0.63%)	60
Squamous cell carcinoma	1(0.63%)	60
Stromal sarcoma	1(0.63%)	60
Total	52(32.76%)	30-85

The Chronic Granulomatous mastitis was the most common inflammatory lesion, 06 (3.78%). Commonest benign lesion was the fibroadenoma 43 (27.09%) and commonest malignant lesion was the infiltrating duct carcinoma (NOS) 38 (23.94%) cases (Table 3).

TABLE. 4 Clinical findings in relation to breast lesions

Inflammatory lesions.	No. of lesions	Nipple retraction	Ulceration	LN involvement
Ac. mastitis	2	0	0	0
Chr. mastitis	3	0	0	0
Gr. mastitis	6	1	0	0
Galactoceles	2	0	0	0
Benign lesions				
Fibroadenoma	43	0	0	0
Fibrocystic disease	15	0	0	0
Benign phyllodes	7	0	0	0
Epithelial hyperplasia	4	0	0	0
Intra ductal papilloma	1	0	0	0
Florid papillomatosis	2	0	0	0
Malignant lesions				
Carinoma	50	4	5	11
Sarcoma	2	1	1	2
Total				

Nipple retraction in 0.63% of benign lesion (granulomatous mastitis), 3.15% of malignant lesions, ulceration in 3.78% of malignant conditions and lymphadenopathy associated with 8.19% of malignant lesions (Table 4).

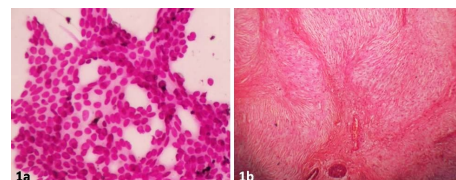


Figure 1a Cytosmear showing increased stromal cellularity of benign phyllodes tumor. Diffquick (400x). **1b.** Micro section showing stromal hypercellularity with intervening of ductal epithelium of Benign phyllodes tumor. H&E (100x)

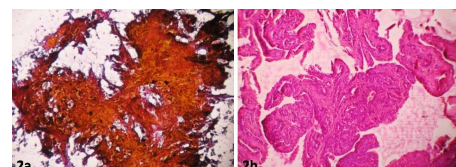


Figure 2a Cytosmear showing fibrovascular core. **2b** corresponding micro section showing fibrovascular core surrounded by benign looking duct epithelial cells. H&E (100x)

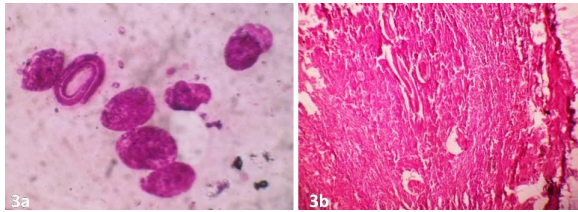


Figure 3a Cytosmear showing adult filarial worm & eggs. Diffquick (400x) **3b** corresponding micro section showing fibrovascular core surrounded by benign looking duct epithelial cells. H&E (100x)

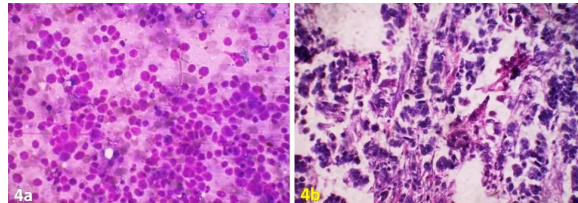


Figure 4a Cytosmear of lobular carcinoma showing epithelial cells in clusters & in single files, many with nuclear moulding. Diffquick (100x) **4b** Microsection of infiltrating lobular carcinoma showing epithelial cells in clusters, Indian file pattern invading into stroma. H&E(100x).

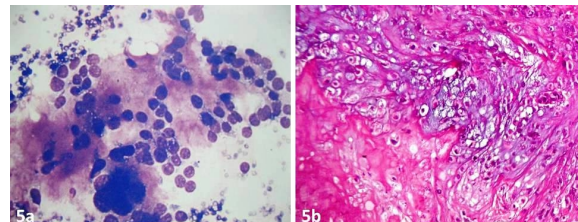
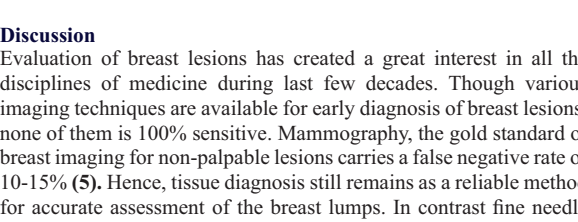


Figure 5a Cytosmear of metaplastic carcinoma showing chondromatous areas. Diffquick (100x) **5b** Corresponding microsection of metaplastic carcinoma showing cartilaginous differentiation H&E (100x)



Discussion

Evaluation of breast lesions has created a great interest in all the disciplines of medicine during last few decades. Though various imaging techniques are available for early diagnosis of breast lesions, none of them is 100% sensitive. Mammography, the gold standard of breast imaging for non-palpable lesions carries a false negative rate of 10-15% (5). Hence, tissue diagnosis still remains as a reliable method for accurate assessment of the breast lumps. In contrast fine needle aspiration cytology as an ideal technique, is safe, aspiration cytology as an ideal technique, is safe, simple procedure for an early diagnosis and also accurate (6, 7). Hence this is gradually gaining wide spread acceptance it reserves.

Fine Needle Aspiration Cytology has been successfully used and recommended by many authors (8, 9) as a diagnostic tool for assessment of various breast lesions. Many reports are available regarding its safety, rapidity, cost effectiveness and sensitivity of this technique in the above mentioned advantages of F.N.A.C., the study was undertaken to access the accuracy of cytodiagnosis in breast lesions.

A total number of 406 cases of breast lesions were subjected to F.N.A.C. during the study of these 249 cases had to be excluded due to lack of non availability of biopsy specimen specially in inflammatory benign lesions. Thus a total number of 157 cases were available for cytohistopathological correlation.

In all the cases aspiration was carried out with 22 gauge needle which proved to be satisfactory for obtaining material and follow up, no complication was noted. The material was sufficient for cytological study in 157 cases.

The smears were subjected mostly to M.G.G. H & E and Papanicolaou stain. M.G.G. Stain was preferred to Papanicolaou stain. M.G.G. Stain was preferred because it stained the cytoplasm and cytoplasmic granules better than wet fixed cells, in which nuclear staining was better. Besides, M.G.G. staining procedure was simpler as compared to Papanicolaou staining, which was elaborate and time consuming. Out of 157 breast lesions aspirated, 105(66.15%) were benign and 52 (32.76%) were found to be malignant on histological examination. The mean age at presentation of both benign and malignant lesions was 43.5 years.

The mean age incidence in an Indian series of Reddy et al, 1970 was 42.3 years. They opined that cancer of breast in India women occurred a decade earlier than western women. This seems justified when compared to the mean age at presentation in the series of Watson et al (1987) which was 56.77 years (8).

In the present work, the age incidence of breast malignancy showed a rising trend from 3rd decade onwards and the percentage of malignant lesions increased in 5th decade i.e. 13 (15.9%). Similar observations were reported by Watson et al 1987 (8). But in the 6th decade onwards there was a sudden fall in the percentage of malignancy. This might be due to very small number (2 cases) correlated in the age of 51-75 years.

The clinical findings like size, margin, skin involvement and ulceration were of no much significance in differentiating malignant from benign lesions. Only fixity and nipple retraction were associated with malignant lesions.

Carcinoma of breast is reported to be more common In the present study, 19.53% of the malignant lesions were present in the left breast and 11.97% were present in the right breast. This is identical to the observation of several authors. In present study benign lesions were common in left breast i.e. 50 (31.50%), in right breast 39 (24.57%) and upper outer quadrant was the commonest site in both sides.

Also it was suggested by Rocha et al, 1997 accuracy improve if the aspiration was done by the pathologist (11). Similar view was expressed by Barroes et al 1986 percentage of the positive result with breast cancer aspiration significantly increased when a physician specialising in fine needle aspiration of breast performed the procedure (12). When the cytopathologist performs the aspirates, he gets the advantage of direct confrontation with the lesion and can form his opinion about the case. He collects additional information while needling and preparing the smear Zajicek et al 1970 (6). In the present series all the cases were aspirated personally leading to good results (Table 5).

Table 5 Accuracy of the cytological diagnosis:

Authors	Sensitivity %	Specificity %	False +ve rate %	False -ve rate %	Overall accuracy %
Zajicek (1974)	90.22	96.42	3.58	9.78	93.12
Zajdela (1975)	91.99	95.80	4.20	8.01	93.36
Frable (1984)	90.14	97.48	2.52	9.86	94.67
Palombini (1988)	95.72	89.66	10.34	4.28	94.00
Srinivas (1989)	91.66	100	0	8.34	97.70
Rocha et al, 1997	93.80	98.21	1.79	6.20	97.40
Present study (2016)	91.7	100	0	8.9	86.96

False positive and false negative are within satisfactory range. Kline (1988) has stated the false negative diagnosis range from 2-18 % in experienced hand and is attributed to schirrous, size and location of the lump, non-recognition of malignant cells and the technique (13). A false negative rate of less than 10% is usually considered acceptable. The overall accuracy in the present study is 79.4%. The results of the study confirm the accuracy of fine needle aspiration cytology.

However, the total number of cases in the study is in comparison to workers conducting thousand of aspiration over the years.

It was stated by Helvie (2010) that neither sensitivity nor specificity of both clinical examination and mammography were improving and upto 40% carcinomas in patients less than 50 years of age are considered benign by these methods (14). Cytologic findings of breast therefore are a useful adjunct in the diagnosis of breast malignancy with a positive predictive value of 100%.

No complication due to aspiration biopsy was encountered in this study. Workers like Wilson and Ehrmann (1978) and Frable (1984) have opined that this procedure is free of complication (1, 15). The only complication encountered occasionally is formation of haematoma which can be avoided by application of pressure at the aspirate site Zajicek (1970) (6). There is no evidence of FNAC dissemination of malignancy Robbins et al (1954) and Zajdela et al (1976)(10, 16).

Conclusion

Fine Needle Aspiration Cytology (FNAC) has become popular as a valuable tool in preoperative assessment of breast masses and it shows high accuracy sensitivity and specificity. It has gained popularity due to its fast and easy approach, being inexpensive and can be performed with little complications. To differentiate benign from malignant lesions is one of the major goals of FNAC. In the evaluation of breast masses, the time honored triple assessment combines clinical, radiological and pathological information and FNAC together with core needle biopsy is the initial pathological investigative methods of choice.

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