

Role of Fine Needle Aspiration Cytology in Classifying Breast Lesions with Special Reference to Borderline Cases

Naveen Kumar¹, Purva Sharma¹, Mamta Gupta², Sangeeta Sharma³, Rani Bansal⁴, Veena K. Sharma⁵

¹Assistant Professor, Department of Pathology, Mulayam Singh Yadav Medical College, Meerut, India, ²Associate Professor, ³Professor, ⁴Professor and Head, Department Of Pathology, Subharti Medical College, Svsu, Meerut, India, ⁵Professor And Head, Department Of Pathology, Muzaffarnagar Medical College, Muzaffarnagar, India.

Abstract

Introduction- FNAC is a valuable tool in the preoperative assessment of breast masses with a primary goal to separate malignant from benign masses.

Material and Methods- This study was conducted on 300 cases presenting with breast lump during the last 3 years in a tertiary care hospital of Western Uttar Pradesh. FNAC was performed in all the cases and smears were analysed and categorised according to NBSBSP classification. Cytohistologic correlation was done wherever possible.

Results- Age of patients ranged from 8 years to 74 years with mean age of 32.4 years and female to male ratio of 20.08:1. Majority of aspirates were in C2- benign category followed by C5 malignant, C4 suspicious and C3 atypical respectively. Maximum number of aspirates were reported as fibroadenoma 42.27 % followed by fibrocystic disease 33.7%. 9.12% were diagnosed as malignant lesions of which infiltrating ductal carcinoma (89.65%) was the commonest.

Conclusion- FNAC is a safe, cost effective, highly sensitive and specific outpatient procedure useful in early diagnosis and management of breast lesions and at times obviating the need of surgery. Borderline (gray zone) lesions should be followed up.

Keyword- Breast lump, FNAC, Gray zone lesions.

Introduction

Breast lump is the most common presentation in most of the breast diseases. The triple assessment of breast disease by clinical examination, mammography and Fine Needle Aspiration Cytology (FNAC) has been reported as 100% accurate in diagnosis of breast disease¹. FNAC is a valuable tool in the preoperative assessment of breast masses with a primary goal to separate malignant from benign masses as malignant

requires radical therapy and benign can be managed conservatively².

FNAC of breast lump has various benefits over open tissue biopsy. It is highly sensitive ranging from 82% to 97.5% and with specificity of >99%, easy to perform, minimally invasive and cost effective that can be performed at outpatient department with results available within shorter time and helps in planning of treatment in the breast lump^{3,4}. We can also perform molecular ancillary techniques, that is progesterone receptor (PR) and estrogen receptor (ER), proliferation antigen (Ki67) and DNA pattern analysis^{5,6}.

FNAC helps in differentiating benign from malignant but there are certain diseases in which the morphological features are overlapping such as cellular fibroadenoma, proliferative breast disease with atypical

Corresponding Author:

Dr. Purva Sharma, Assistant Professor, Department of Pathology, Mulayam Singh Yadav Medical College, Meerut, India. C-33, Moti Prayag, Garh Road, Meerut. Pin 250004.

hyperplasia, papillary lesions and low grade carcinoma making them difficult to be categorised.

However, to overcome this difficulty a standard system of reporting breast FNAC was given by National Health Service Breast Screening Program (NHSBSP)⁷ comprising of categories C1 to C5. C1-Inadequate, C2-Benign, C3-Atypical, probably benign, C4-Suspicious, C5-Malignant. C3, C4 categories consists of gray zone lesions and these are further subjected to biopsy.

The present study was conducted to evaluate the spectrum of breast lesions on aspiration cytology, to classify them according to NHSBSP and to identify the borderline cases.

Material and Methods

This study was conducted on 300 cases presenting with breast lump during the last 3 years in a tertiary care hospital of Western Uttar Pradesh. Inclusion criteria were cases presenting with palpable breast lump and breast lesion detected on radiology.

The cases with nipple discharge without palpable breast lump were excluded from the study.

FNAC of palpable breast lump was performed with a 22-24 gauze disposable needle attached to a 10 ml disposable plastic syringe fitted in syringe holder and sample was obtained by to and fro motion.

Smears were prepared and half slides were fixed in 95% ethyl alcohol for Haematoxylin & Eosin (H & E) and Papanicolaou(PAP) stain and remaining were air dried for Leishman-Giemsa stain.

FNAC smears were studied in detailed for findings of inflammation, benign breast disease, suspicious and malignant lesions and they were classified according to NHSBSP,2011⁷. The cytomorphological features of borderline lesions (gray zone) were analysed specifically to establish a criteria which would help in classifying these lesions.

For cytohistopathological correlation, formalin fixed paraffin embedded H &E stained sections were studied.

Results

A total of 300 cases presented with breast lump, of which bilateral disease was seen in 18 cases therefore 318 breast lumps were observed.

Table 1 : AGE AND SEX WISE DISTRIBUTION

Age Group (In Years)	Females		Males		Total (%)	
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
1-10	1	0.33	0	0	1	0.33
11-20	52	17.33	1	0.33	53	17.67
21-30	95	31.67	7	2.33	102	34
31-40	79	26.33	0	0	79	26.33
41-50	42	14	2	0.67	44	14.67
51-60	11	3.67	2	0.67	13	4.33
61-70	7	2.33	0	0	7	2.33
71-80	0	0	1	0.33	1	0.33
TOTAL	287	95.67	13	4.33	300	100

Age of patients ranged from 8 years to 74 years with mean age of 32.4 years. Majority of patients were in third decade 34% (102/300) cases, followed by 26.33% and 18% in 4th and 2nd decade respectively. There were 95.67% (287/300) female and 4.33% (13/300) males. Female : Male ratio was 22.08:1 (Table 1).

TABLE 2 : CATEGORISATION OF CYTOLOGICAL DIAGNOSIS

CYTOLOGICAL CATEGORY	TOTAL NUMBER OF ASPIRATES	PERCENTAGE (%)
C1	17	5.35
C2	246	77.35
C3	11	3.46
C4	15	4.72
C5	29	9.12
TOTAL	318	100

Majority of aspirates were in C2- benign category followed by C5 malignant, C4 suspicious and C3 atypical respectively.(Table 2).

17 out of 18 bilateral cases showed similar cytological category C2 on both sides while in one case categories were different C4 in right side and C5 in left side.

TABLE 3: SPECTRUM OF BENIGN LESIONS – C2

C2 CATEGORY		NUMBER OF ASPIRATES	PERCENTAGE (%)
Non proliferative breast disease	Fibrocystic disease	83	33.7
Proliferative breast disease without atypia	Epithelial hyperplasia	03	1.22
Benign Tumours	Fibroadenoma	104	42.27
	Benign phylloides tumour	01	0.41
	Intraductalpapiloma	01	0.41
	Lactational adenoma	04	1.63
Non-neoplastic and miscellaneous	Acute mastitis / abscess	13	5.28
	Galectocele	12	4.90
	Gynaecomastia	07	2.84
	Duct ectasia	06	2.45
	Chronic mastitis	04	1.63
	Fat necrosis	03	1.22
	Granulomatous inflammation	03	1.22
	Retention cyst	01	0.41
	Epidermal cyst	01	0.41
	TOTAL	246	100

Out of benign cases maximum number of aspirates were reported as fibroadenoma 42.27 % followed by fibrocystic disease 33.7% (Table 3).

TABLE 4 : SPECTRUM OF MALIGNANT LESIONS - C5

C5 CATEGORY	NUMBER OF CASES	(PERCENTAGE) %
Infiltrating Ductal Carcinoma	26	89.65
Infiltrating Lobular Carcinoma	01	3.45
Mucinous (Colloid) carcinoma	01	3.45
Medullary Carcinoma	01	3.45
TOTAL	29	100

29 out of 318 (9.12%) breast FNACs were diagnosed as malignant lesions. Majority of cases were infiltrating ductal carcinoma (89.65%). (Table 4).

TABLE 5 : CYTO-HISTOPATHOLOGICAL CORRELATION

CYTOLOGICAL CATEGORY	CYTO-HISTOPATHOLOGICAL CORRELATION		TOTAL
	YES	NO	
C2	35	1	36
C3	3	1	4
C4	6	1	7
C5	8	0	8
TOTAL	52	3	55

Out of 318 aspirates, histopathological sections were available in 55 aspirates (17.29%). FNAC findings correlated with histopathological diagnosis in 52 cases and 3 aspirates showed discrepancy. (Table 5).

One case was diagnosed as benign on cytology, on histology it turned out to be infiltrating ductal carcinoma with insitu component. Another case was diagnosed as cystic lesion with occasional atypical cells this also turned out to be infiltrating ductal carcinoma with extensive cystic changes with haemorrhage. Third case was given as suspicious for malignancy on cytology, on histology it was diagnosed as fibrocystic disease with florid epitheliosis and focal atypical changes. Considering histopathology as gold standard for diagnosis the p value for cytohistopathological correlation was significant (p value < 0.05). Overall sensitivity was 87.5%, specificity

97.4%, positive predictive value 95%, negative predictive value 94.5% and diagnostic accuracy was 98.3%.

Discussion

FNAC plays an important and essential role in the management of patients with breast lesions and also offers a great potential for prediction of patient's outcome, disease response to therapy and assessment of risk of developing breast cancer.⁸

Female sex and increasing age are the strongest risk factors for breast cancer.⁹In present study, age of the

patients ranged from 8 years – 74 years with the mean age of 32.4 years. Majority of the patients were in 3rd decade 34% (102/300 cases), followed by 26.3 % in 4th decade. Similar findings were observed by Khandaza et al.¹⁰

There was female preponderance (95.67 %, 287/300 cases) with F:M ratio of 22.08:1. This was in accordance with various studies^{2,11,12} which reported F:M ratio ranging from 14:1 to 24.5:1

Breast lump was the commonest clinical presentation, as it was the inclusion criteria, followed by pain and fever in 20.67% (62/300) and 7.67% (23/300) cases respectively. Chandanwale et al² and Shirley et al¹² also observed that lump was the most common presenting symptom in their studies observed in 100% and 67.8% respectively.

Cytological categorization from C1-C5 category for FNAC breast is a cost effective and practical procedure for early diagnosis of breast cancer.¹³ In the present study we observed that benign lesions were the most frequent accounting for 77.3% cases followed by malignant lesions in 9.1% of cases. Similar findings were observed by Bajwa et al.¹³

The most common benign lesion (C2) in our study was fibroadenoma 42.27% (104/246) followed by fibrocystic disease 33.7% (83/246). Fibroadenoma was also the most common lesion observed in the study by Chandanwale et al² 49% (49/100) and Echezoh et al¹⁴ 45% (45/100).

26 / 318 aspirates were categorized as gray zone lesions, 11/318 (3.4%) showed epithelial hyperplasia with atypia (C3) and 15/318 (4.7%) were reported as suspicious of malignancy (C4). Histological correlation in borderline lesions was available in 11/26 cases. 3/4 cases of C3 category were consistent with diagnosis of atypical epitheliosis and 6/7 cases were consistent with malignancy.

Our percentage of C3 was in between percentage reported by Challa et al,¹⁵ and Sankaya and Dongre¹⁶ who reported it to be 3.3% and 3.6% whereas percentage of C4 was comparable to Sankya and Dongre¹⁶ who reported it in 3.5% cases. According to Arul et al 2016¹⁷ diagnosis of C3 and C4 categories are difficult as they do

not have strict criteria for diagnosis.

In the present study, 9.12% (29/318) cases were diagnosed as malignant breast lesions. In a study conducted by Yalavarthi et al,¹⁸ 13.5% (45/334) cases were diagnosed as malignant.

In the present study cyto-histological correlation was available in 55 cases, showing that FNAC had 94.5% diagnostic accuracy, 87.5% sensitivity and 97.4% specificity of diagnosing various breast lesions.

The sensitivity ranging from 80-99.4% and specificity upto 100% have been reported the past.¹⁹⁻²²

Though FNAC is a reliable tool for diagnosis of breast lesions false negatives and false positives may occur. In the present study False negative was observed in (2/55, 3.6%) and false positive in one case i.e. 1.8%. The false negative and false positive have been reported ranging from 1.7% to 13.3% and 0.6% to 6.5% respectively in the past.²³⁻²⁹

Inadequate aspirates reported in the past ranged from 8-13.3%.³⁰⁻³³ Inadequate smears in the present study were 5.35%. Our observations were lower as compared to other studies this could be due to less number of cases in the present study. As histological correlation was not available in these cases, the possibility of malignancy cannot be excluded. NHSBSP⁷ surveys highlights that further clinical correlation and diagnostic modalities should be used in all cases with inadequate aspirates before considering them benign.

Conclusion

FNAC is a safe, cost effective outpatient procedure useful in early diagnosis and management of breast lesions and at times obviating the need of surgery. In the present study most of the non neoplastic inflammatory and benign lesions were managed conservatively.

We observed a high sensitivity and specificity for diagnosis of malignant lesions with minimal false negatives and false positives. In cases with discrepancy further clinical, laboratory and radiological correlation should be sought. Borderline (gray zone) lesions should be followed up.

Ethical Clearance- Taken from institutional ethical committee.

Conflict of Interest- None

Source of Funding- Nil

References

- Cangiarella J, Simsir A. Breast. In: Orell SR, Sterrett GF editors. Fine needle aspiration cytology. 5th ed. India: Elsevier; 2012. p.156-209.
- Chandanwale S, Rajpal M, Jadhav P, Sood S, Gupta K, Gupta N. Pattern of benign breast lesions on FNAC in consecutive 100 cases: A study at tertiary care hospital in India. IJPBS 2013;129-138.
- Harigopal M, Chhieng DC. Breast cytology: current issues and future directions. The open breast cancer journal 2010;2:81-89.
- Yu YH, Wei W, Liu J. Diagnostic value of fine-needle aspiration biopsy for breast mass: a systematic review and meta-analysis. BMC Cancer 2012; 12:41.
- Dong J, Ly A, Arpin R, Ahmed Q, Brachtel E. Breast fine aspiration continues to be relevant in a large academic medical centre: experience from Massachusetts General Hospital. Breast cancer Res Treat. 2016 Jul; 158 (2): 297-305.
- Vohra P, Buelow B, Chen YY, Serrano M, Vohra MS, Berry A, et al. Estrogen receptor, Progesterone receptor, and human epidermal growth factor receptor 2 expression in breast cancer FNA cell blocks and paired histologic specimens: A large retrospective study. Cancer Cytopathol. 2016 Nov;124(11):828-35.
- guidelines for non operative diagnostic procedures and reporting in breast cancer screening Non operative diagnosis subgroup of the national group for breast screening pathology. NHSBSP publication no. 50, 2011 p 18-22.
- Zagorianakou P, Fiaccavento S, Zagorianakou N, Makrydimas G, Stefanou D, Agnantis NJ. FNAC: its role, limitations and perspective in the preoperative diagnosis of breast cancer. European Journal of Gynaecological Oncology 2005; 26(2):143-149.
- Breast cancer risk factors a review of the evidence, National Breast and Ovarian Cancer Centre; Australia. 2009.
- Khanzada TW, Samad A, Sushel C. Spectrum of benign breast diseases. Pak J Med Sci. 2009;25(2): 265-268.
- Singh A, Haritwal A, Murali BM. Pattern of breast lumps and diagnostic accuracy of fine needle aspiration cytology; A hospital based study from pondicherry, india. The internet journal of pathology 2011; doi:10.5580/11
- Shirley SE, Mitchell DIG, Soares DP, James MJ, Escoffery CT, Rhoden AM, Wolff C, Choy L, Wilks RJ. Clinicopathologic Features of Breast Disease in Jamaica: Findings of The Jamaican. West Indian Med J 2008; 57 (2): 90-95.
- Bajwa R, Zulfiqar T. Association of fine needle aspiration cytology with tumour size in palpable breast lesions. Biomedica 2010;26: 124 – 129
- Echejoh G, David D, Akeem J. Histopathologic analysis of benign breast diseases in Makurdi, North Central Nigeria. Int J M MSci 2011;3(5):125-128.
- Challa VR, Yale Guru BG, Rangappa P, Deshmana V, Gayathri DM. Cytological and pathological correlation of FNAC in assessing breast lumps and axillary lymph node swellings in a public sector hospital in India. Pathol Res Int 2013;2013: 695024.
- Sankaye SB, Dongre SD. Cytological study of palpable breast lumps presenting in an Indian rural set up. Indian J Med PaediatrOncol 2014;35:159-64.
- Arul P, Masilamani S, Akshatha C. Fine needle aspiration cytology of atypical (C3) and suspicious (C4) categories in the breast and its histopathological correlation. J cytol 2016; 33:76-9.
- Yalavarthi S, Tanikella R, Prabhala S, Tallam US. Histopathological and cytological correlation of tumors of breast. Medical Journal of Dr. D.Y. Patil University . 2014;7(3):326-331.
- Arisio R, Cuccorese C, Accinelli G, M. P. Mano MP, Bordon R, and Fessia L, "Role of fine-needle aspiration biopsy in breast lesions: analysis of a series of 4110 cases," Diagnostic Cytopathology 1998 ; 18:(6): 462–467.
- Feichter GE, Haberthur F, Gobat S, and Dalquen P, "Breast cytology: statistical analysis and cytohistologic correlations," Acta Cytologica 1997 ; 41: (2): 327–332.

21. Ibikunle DE, Omotayo JA, Ariyibi OO. Fine Needle Aspiration Cytology of breast lumps with histopathologic correlation in Owo, Ondo state, Nigeria: a five year review. *Ghana Med J* 2017; 51(1):1-5.
22. Ishikawa T, Hamaguchi Y, Tanabe M et al. "False-positive and false-negative cases of fine-needle aspiration cytology for palpable breast lesions," *Breast cancer* 2007; 14(4) : 388–392.
23. Al-Kaisi N. The spectrum of the 'gray zone' in breast cytology. A review of 186 cases of atypical and suspicious cytology. *Acta Cytol* 1994;38:898-908.
24. Koss LG, Melamed MR. *The Breast In: Koss LG, Melamed MR. Koss Diagnostic cytology and its histopathological bases. 5th ed. Philadelphia: Lippincott Williams & Wilkins. 2006 p. 1081-1147.*
25. Singh A, Haritwal A, Murali BM. Pattern of breast lumps and diagnostic accuracy of fine needle aspiration cytology; A hospital based study from pondicherry, india. *The internet journal of pathology* 2011; doi:10.5580/11.
26. Mendoza P, Lacambra M, Tan P, Tse G. Fine Needle Aspiration Cytology of the Breast: The Nonmalignant Categories. *Pathology Research International* 2011; doi:10.406/2011/547580.
27. Jarwani PB, Patel DC, Patel SM, Dayal A. Fine Needle Aspiration Cytology in A Palpable Breast Lump *GCSMC J Med Sci* 2013;2(2):12-16.
28. PriyaShetty. World Report. India faces growing breast cancer epidemic. *The Lancet* 2009; 379:992-993.
29. Arul P, Masilamani S, Akshatha C. Fine Needle Aspiration Cytology of atypical (C3) and suspicious (C4) categories in the breast and its histopathologic correlation. *J Cytol* 2016;33:76-79.
30. Feoli F, Paesmans M, Eeckhout PV. Fine needle aspiration cytology of the breast, Impact of experience on accuracy using standardized cytologic criteria. *Ata cytologica* 2008; 52(2):145-151.
31. Westenend PJ, Sever AR, Volder HJCB, Liem SJ, A Comparison of Aspiration Cytology and Core Needle Biopsy in the Evaluation of Breast Lesions. *Cancer Cytopathol* 2001;93:146–150.
32. Rosa M, Mohammadi A, and Masood S. "The value of fine needle aspiration biopsy in the diagnosis and prognostic assessment of palpable breast lesions," *DiagCytopathol*, 2011;39(6) PubMed – indexed for MEDLINE.
33. Day C, Moatamed N, Fimbres AM, Salami N, Lim S, and Apple SK, "A retrospective study of the diagnostic accuracy of fine-needle aspiration for breast lesions and implications for future use," *Diagnostic Cytopathology* 2008;36:(12): 855–860.