Original Article

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A Study of Fine Needle Aspiration Cytology of Breast Lump With The Use of National Health Service Breast Screening Program (NHSBSP) - Study Of 500 Cases

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ABSTRACT

Background: FNAC is rapid, simple, safe, cost effective and good screening procedure with high sensitivity and specificity. Clinically, the diseases of breast mainly present as palpable breast lump, pain and nipple discharge. Most of the breast lumps are benign but pose a significant anxiety to the patient, which can be allayed by giving assurance that, usually it is benign. So it is necessary to distinguish benign from malignant conditions

Methods: The present study on was carried out during June 2017 to May 2019. We categorized the patients into C1 (Inadequate), C2 (Benign), C3 (Atypia, probably benign), C4 (Suspicious of malignancy) and C5 (Malignant) category according to NHSBSP and correlated histopathologically whenever available.

Result: Total 500 cases examined. Majority of the cases were in the 3rd decade of the life. Benign category comprised of 368 cases (73.6%), followed by malignant disease 61 (12.2%). Fibroadenoma was most common comprising of 230 cases (62.3%) among benign cases. Out of 230 cases of Fibroadenoma, most (89) cases were in 21-30 years age group, followed by 11-20 years age group. Breast carcinoma was most common (31.1%) in 41-50 years age group and 61-70 (27.9%) years age group followed by 51-60 (19.7%) years age group.

Conclusion: FNAC of breast lesions is advantageous for both clinicians and patients because of its immediate results, economy, and accuracy. FNAC has got significant diagnostic value in differentiating benign from malignant lesions providing us valuable information for planning of subsequent therapeutic management and avoiding unwanted surgeries.

Keywords: *Breast lump, Fine needle aspiration cytology, National Health Service Breast Screening Program, Histopathological correlation*

Introduction

Fine needle aspiration cytology was first introduced by Martin and Ellis in 1930.[1] FNAC is rapid, simple, safe, cost effective and good screening procedure with high sensitivity and specificity.[2]

Clinically, the diseases of breast mainly present as palpable breast lump, pain and nipple discharge.[3] Spectrum of breast lesions range from benign lesions consisting of inflammatory lesion, fibrocystic disease, galactocele, fibroadenoma, benign phyllodes tumor to atypical hyperplasia, carcinoma in situ to invasive mammary carcinoma. Most of the breast lumps are benign but pose a significant anxiety to the patient, which can be allayed by giving assurance that, usually it is benign.[1] So it is necessary to distinguish benign from malignant conditions and identify the suspicious lesion so that in such cases biopsy can be done for confirmation and definitive treatment.[4]

FNAC is included as a component of triple test which was introduced by Johansen C in 1975 for the diagnostic evaluation of breast lump in elderly women. This test avoids the unnecessary open biopsy or frozen section. Triple test includes mammogram, physical examination and FNAC. When all the three tests are positive then the lump should be considered as malignant and when all the components of the triple test are negative then the lump is considered as benign.

Materials and Methods:

The present study on was carried out during June 2017 to May 2019. We reviewed cases of 500 patients with breast lump who were sent to pathology department for FNAC, categorized them into C1 (Inadequate), C2 (Benign), C3 (Atypia, probably benign), C4 (Suspicious of malignancy) and C5 (Malignant) category according to National Health Service Breast Screening Program and correlated histopathologically whenever available.

Ethical clearance from Institutional ethical committee had been obtained. Inclusion criteria: All female patients with breast lump referred by clinician for fine needle aspiration

cytology from June 2017 to May 2019 were included in the study. Exclusion criteria: a) Patients with recurrent malignancy b) Male patient with breast lump.

Patients were explained about the procedure, its benefits, side effects, risks and possible complications. Detailed clinical history and clinical examination was done. Written consent of all patients was taken. Aspirations were performed using a 22 gauze needles and smears are prepared on clean glass slides. The air dried and ethanol fixed smears were stained with May Grunwald's Giemsa, Papanicolaou and hematoxylin and eosin stain respectively.

The histopathological findings of respective cases whenever available were noted and classified according to WHO (2019) classification of breast neoplasm. Cytological and histological diagnosis was arrived independently at different times and correlated to obtain the accuracy of FNAC in breast lumps.

To measure the performance of FNAC we took into account true positive, true negative, false positive and false negative cases and calculated various parameters as follows: [5] Sensitivity = (True positive) / (True positive + False negative). Specificity = (True negative) / (True negative + False positive) Positive predictive value = (True positive) / (True positive + False positive). Negative predictive value = (True negative) / (True negative + False negative). Diagnostic accuracy or Efficiency = (True positive + True negative) / (True positive + False positive + True negative + False negative)

Result

The objective of this study was to determine the spectrum of breast lesions and their morphological features on aspiration cytology, correlation with histopathology as well as to study the diagnostic accuracy of FNAC.

Total 500 cases were examined. Age of the patients ranges from 12 to 82 years. Majority of the cases were in the 3rd decade of the life. 49.8% cases were left sided, 45.6% cases were right sided and 4.6% cases were bilateral.

Out of all 500 cases, disease in benign category were most common, comprising of 368 cases (73.6%), followed by malignant disease (C5) 61 (12.2%).

Out of 368 cases of benign category Fibroadenoma was the most common entity comprising of 230 cases (62.3%). And out of 230 cases of Fibroadenoma, most (89) cases were in 21-30 years age group, followed by 11-20 years age group. Fibrocystic breast disease was most common in 21-30 years age group, followed by 31-40 years age group.

In our study, Breast carcinoma was most common (31.1%) in 41-50 years age group and 61-70 (27.9%) years age group followed by 51-60 (19.7%) years age group. In our study, benign lesion were most common in early age group (21-30 followed by 11-20) as compared to malignant lesion which were most common in later age group(41-50 years).

Out of 32 cases of C1 category, 2 were available histologically, both were diagnosed as IDC NOS. Among 368 cases of benign category, 29 cases were available histologically. Of the 15 cases of Fibroadenoma, 12 were confirmed histologically, while 2 diagnosed as fibrocystic disease and 1 as a borderline phyllodes tumor. Among 12 cases of C3 category, 2 were available histologically, 1 diagnosed as benign phyllodes tumor and 1 as IDC NOS.

Among 27 cases of C4 category 18 were available histologically. Of the 18 cases, 15 were diagnosed as IDC, 1 as invasive lobular carcinoma, 1 as carcinoma with neuroendocrine features and 1 as a cystic papillary neoplasm.

Among 61 cases of C5 category, 33 were available histologically. Of the 33 cases of mammary carcinoma, 28 diagnosed histologically as IDC, 2 as Carcinoma with medullary features and 1 as Metaplastic SCC. 1 case of mammary carcinoma with mucinous differentiation was confirmed histologically. One case of mammary carcinoma with squamous differentiation was diagnosed as poorly differentiated carcinoma.

In our study, 27 cases were true negative, 51 cases were true positive and 02 cases were false negative. None of the case was reported as false positive.

In our study, sensitivity of FNAC was 96.2%, specificity was 100%, positive predictive value was 100%, negative predictive value was 93.1% and diagnostic accuracy was 97.5%.

Discussion

Breast lesions are one of the most commonly encountered lesions in women. All physicians accept the necessity of obtaining prompt pathological confirmation of the nature of any mass in the breast suspected as benign or malignant. Since the most important prognostic factor at the time of presentation is the extent of the disease, it is imperative that a reliable preoperative diagnosis is established as early as possible with a view to institute proper treatment and reduce the mortality rates. In recent years, mammary cytology has been considered as an effective means of early diagnosis of breast masses. [7]

In our study, most common age group affected was 21-30 years age group Of all the 500 cases, 148 (29.6%)

Table 1: Distribution of breast lesions according to NHSBSP (National Health Service Breast Screening program) Categories (n=500).

Diagnosis	No. of cases	Percentage
C1 (Inadequate)	32	6.4%
C2 (Benign)	368	73.6%
C3 (Atypia, probably benign)	12	2.4%
C4 (Suspicious of malignancy)	27	5.4%
C5 (Malignant)	61	12.2%
Total	**500**	**100%**

Table 2: Age wise distribution of mammary carcinoma.

Age group	Mammary carcinoma
11-20	-
21-30	2
31-40	10
41-50	19
51-60	12
61-70	17
71-80	-
81 and above	1
Total	**61**

Table 3: Cyto histological correlation of cases C1, C2 and C3 category.

Cytological diagnosis		Fibroadenoma	Fibrocystic disease	Benign phyllodes tumor	Borderline phyllodes tumor	Malignant phyllodes tumor	Mastitis	Duct ectasia	IDC NOS	Total
C1	Inadequate	-	-	-	-	-	-	-	2	2
C2	Fibroadenoma	12	2	-	1	-	-	-	-	15
	PBD without atypia	4	1	1	-	-	-	-	-	6
	Fibrocystic disease	1	2	-	-	-	-	-	-	3
	Phyllodes tumor	-	-	-	1	2	-	-	-	3
	Duct ectasia	-	-	-	-	-	-	1	-	1
	Acute mastitis	-	-	-	-	-	1	-	-	1
C3	Atypia, probably benign	-	-	1	-	-	-	-	1	2

Table 4: Cyto histological correlation of C4 and C5 category cases.

FNAC Category		Histopathology								
		IDC	ILC	Carcinoma with medullary features	Carcinoma with neuroendocrine features	Cystic papillary neoplasm	IDC with mucinous component	Metaplastic SCC	Poorly differentiated carcinoma	Total
C4	Suspicious of malignancy	15	1	-	1	-	-	-	-	17
	Suspicious of papillary neoplasm	-	-	-		1	-	-	--	1
C5	Mammary carcinoma	28	-	2	-	-	-	1	-	31

FNAC Category		Histopathology								
		IDC	ILC	Carcinoma with medullary features	Carcinoma with neuroendocrine features	Cystic papillary neoplasm	IDC with mucinous component	Metaplastic SCC	Poorly differentiated carcinoma	Total
	Mammary carcinoma with mucinous differentiation	-	-	-	-	-	1	-	-	1
	Mammary carcinoma with squamous differentiation		-	-	-	-	-	-	1	1

Table 5: Cyto histological correlation in 80 follow up cases (n=80) [6]

Cytological diagnosis	No. of cases	HPE available	Histo pathological diagnosis			False Positive	False Negative
			Benign	Malignant	Total		
Benign	368	29	27	02	29	-	02
Suspicious of malignancy	27	18	00	18	18	-	-
Malignant	61	33	00	33	33	-	-
Total	**456**	**80**	**27**	**51**	**80**	**00**	**02**

Table 6: Statistical analysis of FNAC.

Parameter	Formula	Calculation	Percentage
Sensitivity	TP X100/TP+FN	51x100/51+2	96.2%
Specificity	TN X100/ TN+FP	27x100/27+00	100%
Positive predictive value	TP X 100/TP+FP	51x100/51+00	100%
Negative predictive value	TN X100/ TN+ FN	27x100/27+2	93.1%
Diagnostic accuracy	TP+TN X100/TP+FP+ TN+ FN	51+27x100/51+00+27+2	97.5%

Table 7: Cyto histological correlation of C1 category.

Cytological Category		Invasive ductal carcinoma NOS	Total
C1	Inadequate	2	2

Table 8: Cyto histological correlation of C2 category.

Cytological diagnosis		Fibroadenoma	Fibrocystic disease	Benign phyllodes tumor	Borderline phyllodes tumor	Malignant phyllodes tumor	Mastitis	Duct ectasia	Total
C2	Fiberoadenoma	12	2	-	1	-	-	-	15
	PBD without atypia	4	1	1	-	-	-	-	6
	Fibrocystic disease	1	2	-	-	-	-	-	3
	Phyllodes tumor	-	-	-	1	2	-	-	3
	Duct ectasia	-	-	-	-	-	-	1	1
	Acute mastitis	-	-	-	-	-	1	-	1
	Total	**17**	**5**	**1**	**2**	**2**	**1**	**1**	**29**

Table 9: Cyto histological correlation of C3 category.

Cytological Category		Benign phyllodes tumor	IDC NOS	Total
C3	Atypia, probably benign	1	1	2

Table 10: Cyto histological correlation of C4 category.

Cytological category		IDC	ILC	Carcinoma with medullary features	Carcinoma with neuroendocrine features	Cystic papillary neoplasm	Total
C4	Suspicious of malignancy	15	1	-	1	-	17
	Suspicious of papillary neoplasm	-	-	-		1	1

Table 11: Cyto histological correlation of C5 category.

FNAC Category		Histopathology								
		IDC	ILC	Carcinoma with medullary features	Carcinoma with neuroendocrine features	Cystic papillary neoplasm	IDC wihmucinous component	Metaplastic SCC	Poorly differentiated carcinoma	Total
C5	Mammary carcinoma	28	-	2	-	-	-	1	-	31
	Mammary carcinoma with mucinous differentiation	-	-	-	-	-no	1	-	-	1
	Mammary carcinoma with squamous differentiation		-	-	-	-	-	-	1	1
	Total	**28**		**2**			**2**	**1**	**1**	**33**

Table12: Comparison of performance of FNAC of 80 cases confirmed by histological diagnosis.

Study name	Year	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value	Diagnostic Accuracy
Bhagat R et al[6]	2013	93.0%	98.0%	96.7%	96.0%	96.0%
I.Vijayabharathi et al [15]	2015	97.18%	98.74%	97.18%	98.74%	99.26%
Kujur et al[16]	2015	96.15%	96.29%	96%	96.29%	96.22%
Kalpana R Sulhyan et al[17]	2017	91.52%	100%	100%	94.56%	94.58%
Our study		96.2%	100%	100%	93.1%	97.5%

cases were observed in second decade of life and 122 cases (24.4%) in 3rd decade of life. The breast diseases are common during adolescence and reproductive age group as major hormonal changes produce alteration in mammary tissue.

We had correlated cytological findings with histopathological findings whenever available.

Of 32 cases of C1 category, 2 cases were available histologically. Both were diagnosed as invasive ductal carcinoma, not otherwise specified. Most carcinomas produce aspirates with moderate or abundant cellularity. On the other hand, carcinomas with a scirrhousstroma, and those in which tumour density is low, yield a more scantily cellular smear.[8] Of the 2 cases of invasive mammary carcinoma, lump was mobile and small, which may be a cause of inadequate smear. In such cases core needle biopsy is advisable.

In C2 (Benign) category, 29 cases were available histologically. Out of 15 cases of fibroadenoma, 12 cases were confirmed, 2 were diagnosed as fibrocystic disease and 1 as a borderline phyllodes tumor.

The typical clinical presentation of fibroadenoma is a firm, discrete and highly mobile lump in a young woman. In our study, in all the cases of fibroadenoma, lump was

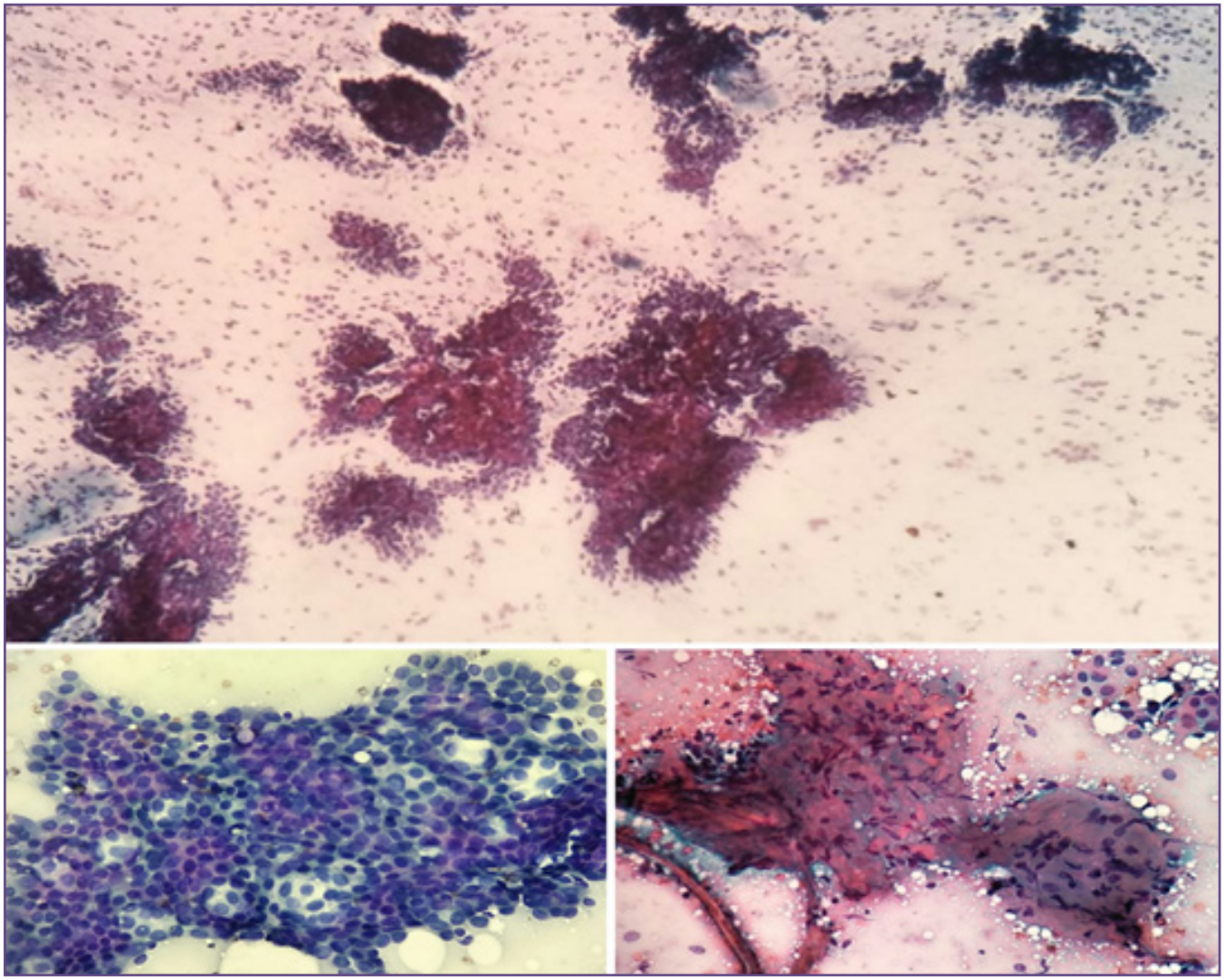

Fig. 1: Fibroadenoma.

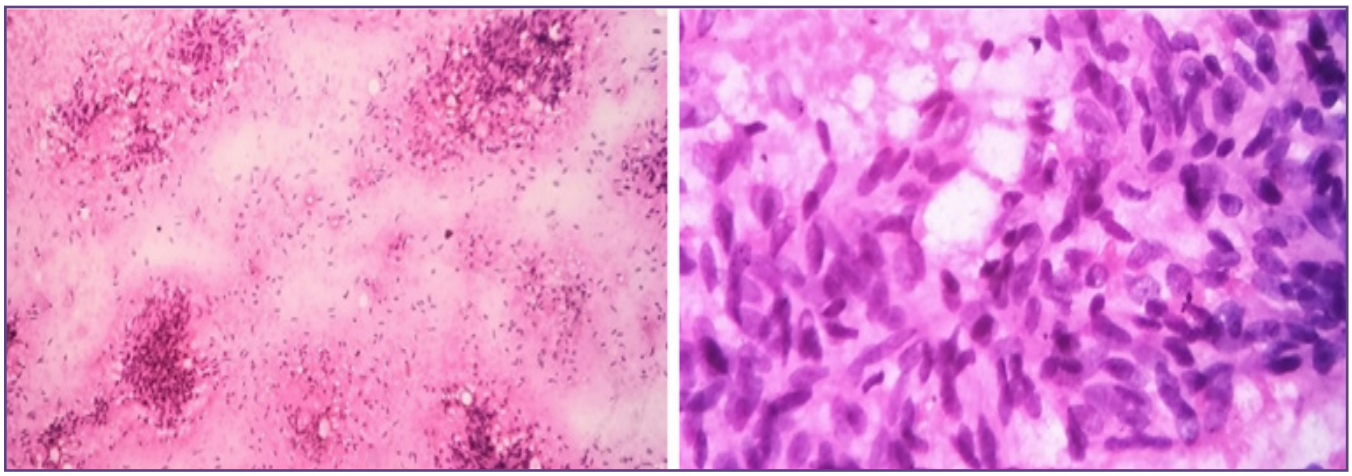

Fig. 2: Phyllodes tumor. Smear showing sheets of stromal cells and numerous spindle shaped bare nuclei in the background (H&E, 10X).

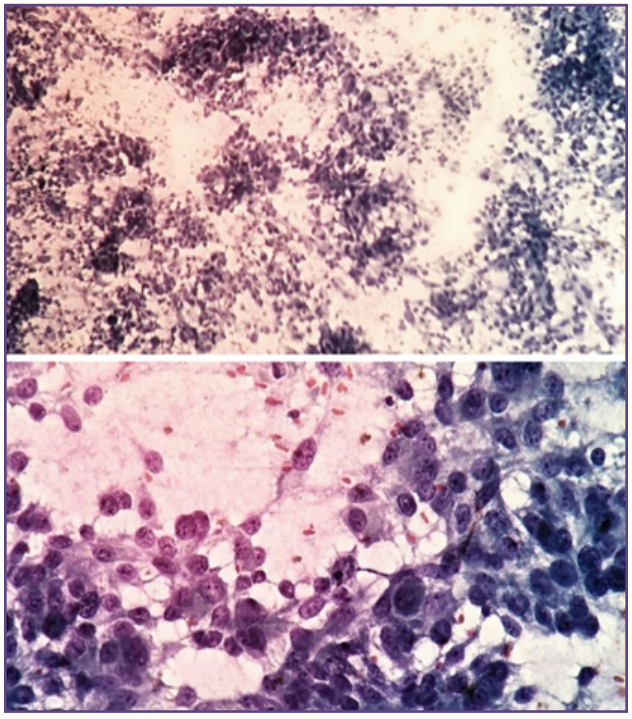

Fig. 3: Mammary carcinoma.

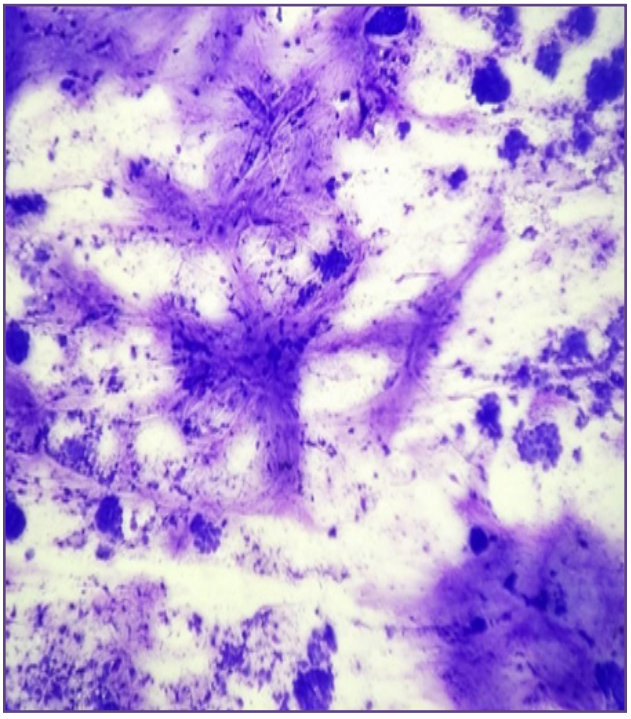

Fig. 4: Mammary carcinoma with mucinous differentiation. Smear showing clusters of ductal epithelial cells along with mucinous material (MGG, 10X).

mobile. Microscopically, the diagnosis is often obvious at low power with cellular smear having large frond-like epithelial groups with peripheral finger-like projections. These are sometimes likened to the antlers of stags.

The nuclei are approximately the size of one or two erythrocytes and are round or slightly ovoid, having one or two small nucleoli and finely granular chromatin. Myoepithelial cells are seen scattered over the surface of the sheets of ductal epithelial cells as shown in figure 1.

The other essential feature is the presence of a generous population of bare nuclei, which include stripped epithelial and myoepithelial nuclei and some stromal cells as shown in figure 1.

Stroma is fibromyxoid. In clinical practice, the amount of stroma is variable, reflecting the histological spectrum of fibroadenomas. More fibrotic fibroadenomas may yield no stroma at all and have a rather non-specific benign pattern on FNA.[9] Such fibroadenoma are tends to fall into proliferative breast disease without atypia as seen in our 4 cases.[10] At the other end of the spectrum fibroadenomas with abundant cellular stroma merge with phyllodestumours both histologically and cytologically as seen in our 1 case.

Fibroadenoma can undergo cystic degeneration, or the ductal structures can become dilated and filled with fluid. Smears from such lesions may contain numerous 'cyst macrophages' and apocrine metaplastic cells and may be interpreted as fibrocystic change.[11] Out of 3 cases of phyllodes tumor, 1 case was diagnosed as borderline phyllodes tumor and 2 cases were as malignant phyllodes tumor.

Phyllodes tumor (PT) is a biphasic epithelial/stromal neoplasm of the breast. It is a rare tumor comprising less than 0.3% of all breast tumors. It is classified as benign, low grade (borderline) and high grade (malignant) based on histologic features. Stromal cellularity and overgrowth, atypia, mitotic activity, and invasive growth pattern at tumor periphery define whether a PT is benign, low grade or high grade.

Classic cytological features in PT are similar to fibroadenoma. However, as opposed to fibroadenoma, stromal fragments are larger, increased in number (stromal overgrowth) and are hypercellular (phyllodes fragments).

The single stromal cells in the background are plumper than the typical oval bare nuclei seen in fibroadenoma. These single cells are intact spindled cells with retained cytoplasm (not naked nuclei), and variable degrees of nuclear atypia with nucleoli and pleomorphism as shown in figure 2. However, some of these features may be entirely lacking in benign and low-grade PTs

even after retrospective review of smears, making their differentiation from fibroadenoma virtually impossible. It is not surprising that a portion of benign and low-grade PTs are initially diagnosed as fibroadenoma on cytology. This in part reflects sampling problems as hypo- and hypercellular areas tend to alternate within PTs.[11]

Another important diagnostic pitfall in PTs is the presence of significant epithelial proliferation including atypical ductal epithelial hyperplasia. If these areas are sampled, this may lead to a false diagnosis of epithelial neoplasm. It is especially difficult to differentiate cellular fibroadenoma from benign/low-grade PT.

Cytological smears of borderline phyllodes tumour usually show a mixture of stromal cells and epithelial sheets. The stromal cells may predominate. Mitoses are rare. It may be difficult or sometimes impossible to make a specific cytological diagnosis of borderline phyllodestumour. The most important thing is to recognise it as a phyllodestumour and not as a Fibroadenoma.

Predominance of stromal cells with a moderate pleomorphism ucompared with epithelial sheets may favour a diagnosis of borderline tumour. Malignant lesions tend to be larger than benign/borderline cases. In frankly malignant cases, pleomorphic, high-grade spindle cells are seen, with a fibrosarcoma-type pattern.

The C3 category defined as a smear with benign features but also showing features which may be seen with malignancy or a lesion in which the cellularity is low with subtle cytological atypia. Management of C3 reports require further investigation such as a repeat FNA, core biopsy or open surgical biopsy. The histological outcomes, most frequently encountered in the follow up of C3 lesions, largely fall into 2 general subgroups, namely benign proliferative lesions and low grade cancers.

Benign proliferative lesions form a subgroup of actively growing benign lesions and include papillomas, fibroadenomas, radial scars/complex sclerosing lesions, sclerosingadenosis, proliferative fibrocystic change, usual epithelial hyperplasia and a small number of specific lesions such as adenomas, hamartomas and benign phyllodes tumors.

The presence of malignant lesions in the C3 category undermines the intent of the C3 category. However, without this category, the negative predictive value of the benign (C2) category would suffer due to the possibility of including false negative cases in this category.

Low grade IDC often displays minimal cytological changes but lacks overlying myoepithelial cells, diminished numbers of bare bipolar nuclei and subtle epithelial dissociation. ILC also featured in the C3 group, mainly because of paucicellularity of the sample and the coexistence of benign epithelium.[12]

In C4 category, 18 cases were available Histologically. Of the 18 cases 15 cases were diagnosed as invasive ductal carcinoma, 1 case as invasive lobular carcinoma, 1 case as carcinoma with neuroendocrine feature and 1 case as cystic papillary neoplasm.

Neuroendocrine differentiation in breast carcinomas is often overlooked in routine practice. Tang et al reported that neuroendocrine differentiation was missed in up to 69% of breast carcinomas. The misdiagnosis of NET as IDC-NOS is likely of little consequence at this time, as no consensus has been reached as to the clinical and prognostic significance of neuroendocrine differentiation.[13]

Lobular carcinomas are more fibrotic ductal carcinomas. They are responsible for many false negative cytological diagnoses. Because of this lobular carcinoma tend to yield poorly cellular aspirates composed of small uniform cells with small and relatively bland nuclei. This would lead to suspicious diagnosis.[11]

Out of 31 cases of cases of mammary carcinoma 28 were diagnosed as invasive mammary carcinoma, 2 as invasive mammary carcinoma with medullary feature and 1 as Metaplastic SCC. Cytologically, mammary carcinoma shows loosely cohesive irregular clusters of malignant duct epithelial cells with hyperchromatic and enlarged nuclei and absence of bipolar nuclei as shown in figure 3.

Cytologically, Mammary carcinoma with mucinous differentiation shows clusters of malignantductal epithelial cells along with pools of mucinouss material as shown in figure 4.

Cytologically, carcinoma with medullary features consist of highly cellular smears containing large atypical cells arranged in syncytial sheets and intimately admixed with lymphocytes, plasma cells, and neutrophils. The nuclear to cytoplasmic ratio is high in tumor cells. Tumor cells have predominantly abundant finely granular, eosinophilic cytoplasm and moderate to marked nuclear pleomorphism with prominent nucleoli.

Metaplastic carcinoma consists of carcinomatous and sarcomatous component. Carcinomatous component is indistinguishable from ductal carcinoma. In our case, Metaplastic SCC diagnosed as mammary carcinoma which may be due to aspiration of only carcinomatous component.

Squamous differentiation is sometimes seen in poorly differentiated duct carcinoma as seen in our

1 case.[11] Performance was best for the diagnosis of adenocarcinoma, ductaltype, with 65% of laboratories accurately sub classifying these lesions on cytology. Rates of exact diagnosis of lobular, medullary and mucinous carcinomas was 20%, 12%, and 27%, respectively.[14]

The variability in reported sensitivities and specificities depends on the expertise and skill of the aspirator and of the interpreter. The aim should be a sensitivity of no less than 95% and this can be achieved with increasing experience. The positive predictive value of a malignant diagnosis is approximately 99%.

Conclusion

From our study, it has been concluded that FNAC results had given us overall accuracy rate of 97.5%, sensitivity was 96.2% and specificity was 100% as no case was false positive. FNAC of breast lesions is advantageous for both clinicians and patients because of its immediate results, economy and accuracy. FNAC has got significant diagnostic value in differentiating benign from malignant lesions providing us valuable information for planning of subsequent therapeutic management and avoiding unwanted surgeries. The FNAC is safe, non-hazardous, minimally invasive, rapid, simple, repeatable, fairly reliable, out-patient based procedure, carried out without advance preparation or anesthesia and provide diagnosis within hours.

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Competing Interests

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Reference

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