

Pattern of palpable breast lesions on fine needle aspiration: A retrospective analysis of 902 cases

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ABSTRACT

Background: Breast lumps constitute a significant proportion of surgical cases in women of both developed and developing countries. The aim of this study is to look the frequency distribution of various breast lesions on fine needle aspiration (FNA).

Materials and Methods: The 902 patients who presented with palpable breast lump, irrespective of age and sex were included in the study. Frequency distribution of various breast lesions with respect to age and sex was studied. Cytology grading in breast carcinoma was correlated in 69 cases with histology grading.

Results: The majority ($N = 871$) of patients were females with maximum ($N = 566$) patients between second and third decade. The 773 patients had benign breast lesions and maximum ($N = 341$) patients were in the second decade. Fibroadenoma was the commonest benign lesion followed by fibrocystic change and mastitis. Out of 119 malignant breast lesions, 31.93% [$N = 38$] were between 41-50 years of age, 28.57% [$N = 34$] in 51-60 years and 22.68% [$N = 27$] in between 31-40 years of age. Out of 119 malignant breast lumps and majority were infiltrating ductal carcinoma ($N = 108$). Cytology grading correlated maximum with histology grade in Grade I followed by Grade II and Grade III.

Conclusion: With experienced hands, FNA is safe, cost effective and a reliable technique for preoperative evaluation of palpable breast lumps. FNA features are more informative when combined with physical and radiology findings (Triple test). Fibroadenoma, fibrocystic change and mastitis form the major bulk of benign breast lesions. Epithelioid cells when seen in inflammatory breast FNA smears, tuberculosis must be ruled out. In India, breast carcinoma arises in younger patients as compared to western countries. Grading of breast carcinomas must be done on FNA smears for selecting neoadjuvant therapy. Clinical breast examination and mammography screening in females should be encouraged in developing countries from the third decade onwards for early detection of breast carcinoma.

Key Words: Breast, benign, cytology, FNA, grading, malignant

INTRODUCTION

Breast lumps constitute a significant proportion of surgical cases in both developed and developing countries. Vast majority of them are in women and are benign. It is needed to distinguish benign lumps from malignant preoperatively for definite treatment.^[1,2] The triple test includes physical breast examination, mammography and fine-needle aspiration (FNA) and has proved a reliable tool for accurate diagnosis of palpable breast masses.

The use of FNA for preoperative assessment of breast cancer has gradually declined in United States (US), Canada and United Kingdom (UK). The reasons are high error rates due to lack of experienced cytopathologists at individual laboratories and inability to provide adequate and suitable samples for assessment of prognostic markers. It is largely replaced by image-guided core-needle biopsy. Nevertheless, FNA continues to be used worldwide, especially in developing countries and is widely accepted as

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a reliable technique for preoperative evaluation of palpable breast lumps.^[3-9] Scope of FNA has now extended into identifying the subtypes of benign, malignant lesions and residual disease for the purpose of planning the therapeutic protocol and eventual follow-up.^[10,11] The present study is intended to look the frequency distribution of various lesions of palpable breast lumps.

MATERIALS AND METHODS

The present study is a retrospective cohort study of 902 patients between April 2002 and May 2013 who presented with palpable breast lump. Medical records of these patients were retrieved and reviewed. Detailed clinical history, physical examination and mammography/ultrasonography (USG) findings were noted.

All the patients underwent FNA in cytology clinic after prior written consent. FNA was done with standard technique and aseptic precautions by using 10 cc disposable syringe and 22-23 gauge needles. Material was smeared on glass slides. Slides were stained with Leishman's, Hematoxyline and Eosin [H and E] and Papanicolaou stains. Ziehl Neelsen (ZN) staining was done wherever required. In case, material obtained was not satisfactory, a repeat aspiration was done. In case of more than one swelling, aspiration was done from each swelling. USG/Mammography was done in 490 patients. Surgical specimens of 525 breast lumps were received for histopathological examination. Tissues

were 10% formalin fixed and paraffin processed. The 3-4 μ m thick sections were stained with H and E stain. ZN staining was performed wherever required.

Diagnosis of each lump was based on physical examination, FNA and/or mammography/USG features and/or histological features. Cytology grading of breast carcinomas done by using Robinson's grading system based on six cytomorphology features viz: Cell dissociation, cell size, cell uniformity, nucleoli nuclear margins, and chromatin pattern. Carcinomas were graded into Grade I, II and III. Out of 115 breast carcinomas, surgical specimens were received in 69 cases. Histology grading was done by Elston and Ellis's modification of Bloom-Richardson method based on histological features viz: Proportion of tubule formation, nuclear pleomorphism and mitotic count/10 hpf. Cytology grading was correlated with histology grading in 69 cases.

RESULTS

Out of 902 patients, 3.43% ($N = 31$) were male and 96.56% ($N = 871$) were female. Age of the patients ranged from 17-72 years with 62.74% ($N = 566$) were in the age group of 21-40 years. The 85.69% ($N = 773$) had benign breast lumps and 13.19% ($N = 119$) had malignant breast lumps. In 10 (1.10%) patients, FNA was inconclusive. Table 1 shows FNA diagnosis of 902 breast lumps in various age-groups. Out of 773 benign breast lesions, 44.11% ($N = 341$) were in

Table 1: Frequency of FNA diagnosis of 902 breast lesions in various age groups

Breast lesions	Age-groups							Total (%) <i>N</i> = no. of cases
	17-20	21-30	31-40	41-50	51-60	61-70	71-80	
Fibroadenoma	91	186	81	20	03	06	02	389
Fibrocystic change	07	52	56	44	14	04	00	177
Mastitis	04	42	11	07	02	04	00	70
Gynecomastia	00	11	00	14	05	00	00	30
Galactocele	00	18	04	00	00	00	00	22
Simple cyst	00	07	10	02	00	00	00	19
Benign phyllodes	00	00	03	01	00	00	00	04
Fat necrosis	00	02	01	00	00	00	00	03
Epidermal cyst	00	02	01	00	00	00	00	03
Duct ectasia	00	00	00	01	00	00	00	01
Organized hematoma	00	00	01	00	00	00	00	01
Benign breast disease	10	36	07	01	00	00	00	54
Carcinoma	00	00	27	36	32	20	00	115
Malignant phyllodes	00	00	00	02	00	00	00	02
NHL	00	00	00	00	01	00	00	01
Metastasis of SCC	00	00	00	00	01	00	00	01
Inadequate	02	07	01	00	00	00	00	10
Total	114	348	218	128	58	34	02	902

NHL: Non Hodgkin's lymphoma, SCC: Squamous Cell carcinoma

the age-group of 21-30 years and 24.57% ($N = 190$) were in the age-group of 31-40 years. Out of 119 malignant breast lesions, 31.93% ($N = 38$) were between 41-50 years of age, 28.57% ($N = 34$) in 51-60 years and 22.68% ($N = 27$) in between 31-40 years of age.

Out of 70 mastitis lesions, 75.71% ($N = 53$) were acute mastitis and tuberculous mastitis was seen in 20% ($N = 14$) cases. Table 2 shows type of mastitis in various age groups. Table 3 shows FNA diagnosis of 119 malignant lesions and cyto-histological correlation in 73 cases. Table 4 shows correlation of cytology grading with histology grading in 69 cases of breast carcinoma.

DISCUSSION

FNA is widely accepted as a reliable technique in the initial evaluation of palpable breast lumps. It is simple, safe, cost-effective, minimally invasive, rapid and as sensitive as biopsy.^[3,4,8] Primary goal of FNA is to separate benign lesions from malignant lesions for the purpose of planning the therapeutic protocol and uneventful follow-up.^[10-12]

In our study, age of the patients ranged from 17-72 years with male to female ratio of 1:28. Similar age-group was observed in studies done in Asian countries.^[13,14] Higher age-group in western countries was attributed to higher life expectancy.^[15] Out of 902 patients, maximum patients ($N = 773$) had benign lesions. Malignant lesions were found in 13.19% ($N = 118$). It has been emphasized in the past that vast majority of the lesions in breast are benign.^[1,16-20]

Fibroadenoma was the most frequently ($N = 389$) diagnosed lesion on FNA with maximum ($N = 277$) patients between 17-30 years. Multiple fibroadenomas were seen in 11.56% ($N = 45$) patients. Definitive FNA diagnosis was made in 46.27% ($N = 180$) patients based on diagnostic triad of cellular smears with bimodal pattern, numerous single bare bipolar nuclei and fragments of fibromyxoid stroma. Absence of any component of diagnostic triad and low cellularity are the common causes of pitfalls in correct diagnosis of fibroadenoma.^[21] In remaining 209 cases, fibromyxoid stroma was not seen. Correct diagnosis in these cases was achieved by correlating FNA features with clinical and radiological features.

Another common benign breast lesion we encountered was fibrocystic change ($N = 177$) with maximum patients ($N = 108$) between 21-40 year. Though hormones play a role in its development exact pathogenesis remains obscure.^[21] Fibrocystic change is not a specific cytological diagnosis. Cytology samples must be evaluated in the context of clinical and mammography findings. Some of these lesions simulate carcinoma clinically, radiologically, and microscopically.^[22] More than 90% of the fibrocystic change were non-proliferative and FNA smears showed many macrophages, apocrine cells with or without scanty chronic inflammatory cells. Small clusters of ductal epithelial cells without atypia were seen. Few cases showed predominant ductal cells without atypia and were diagnosed as proliferative type. Compared to the general population, proliferative fibrocystic change with or without atypia has relative risk of developing carcinoma.^[23]

Mastitis was seen in 7.76% ($N = 70$) patients with maximum ($N = 42$) patients between 21-30 years. Acute mastitis/abscesses, which is also known as puerperal or lactational mastitis, was seen in 78.57% ($N = 55$) with maximum ($N = 40$) between 21-30 years. Early diagnosis and management is of value.^[23-25] Tuberculous mastitis is relatively rare with reported incidence varying from 3-4.5% in developing countries like India.^[26] Few reports, including our dealing with cytomorphologic features have been published in the past.^[27] Clinical and radiological features are not diagnostic and easily can be confused with breast cancer or pyogenic abscess. Out of 14 patients, majority ($N = 12$) presented with painless, firm mass and remaining two patients had hard lump. The 13 were females and one was male. FNA diagnosis was based on presence of epithelioid cells, caseous necrosis with or without acid-fast bacilli (AFB) or positive AFB culture. Out of 14 cases, 11 cases were confirmed on histology. Diagnosis of fat necrosis ($N = 3$) and duct ectasia was made based on FNA, clinical and radiological features.

Gynaecomastia accounted in 3.32% ($N = 30$) patients with maximum ($N = 19$) patients between 41-60 years and 11 patients in between 20-30 years. Gynaecomastia in young age is related to hormonal pubertal changes where as in later years, it may be caused by hormonally active tumors, cirrhosis or medications.^[28] Similar observations were made in our study.

Table 2: Type and frequency of mastitis on FNA in various age groups

Type of mastitis	17-20	21-30	31-40	41-50	51-60	61-70	71-80	<i>N</i> = number of cases
Acute/Abscesses	4	40	05	03	02	01	00	55
Tuberculous	0	04	05	02	00	03	00	14
Granulomatous	0	00	01	00	00	00	00	01
Total	4	44	11	05	02	04	00	70

Table 3: Frequency of 119 malignant lesions on FNA and correlation of FNA and histology diagnosis of 73 lesions

Type of malignant lesion	FNA diagnosis	Histology diagnosis
<i>N</i> = Number of cases	<i>N</i> = Number of cases	<i>N</i> = Number of cases
Infiltrating ductal Ca (108)	65	62
Mucinous Ca (1)	1	1
Medullary Ca (2)	2	2
Infiltrating lobular Ca (1)	0	1
Sarcomatoid Ca (1)	0	1
Invasive papillary Ca (1)	0	1
Secretory Ca (1)	1	1
Malignant phyllodes (2)	2	2
NHL (1)	1	1
Metastasis of Sq. cell Ca (1)	1	1
Total (119)	73	73

Table 4: Correlation of cytology and histology grading of 69 breast carcinomas

Cytology grade (number of cases)	Histology grade			Correlation (%)
	I	II	III	
Grade I (8)	8	00	00	100
Grade II (44)	0	39	05	88.63
Grade III (17)	0	04	13	76.47

Galactocele accounted for 2.43% ($N = 22$) patients and all the patients were lactating. We came across 19 cases of simple cyst in our study, which are easily diagnosed by ultrasonography. Confident benign diagnosis can be rendered with FNA and surgical excision can be avoided. They can be managed with follow-up imaging studies.^[29,30]

Common sites for epidermal inclusion cyst (EIC) are head, neck, trunk and extremities. Published cytology literature on EIC in breast is scanty and to date less than 46 cases have been reported. They remain underreported because of their insignificant clinical presentation.^[31-33] FNA smears showed numerous anucleate and nucleated benign squamous cells. Imaging can follow asymptomatic lesions. Potential complications such as infections and malignant changes shall be ruled out on FNA.

Cytological appearance of benign phyllodes many times overlaps with fibroadenoma. Clinical, mammography and ultrasound examination have little diagnostic value except larger size (>3 cm) and increase in size are suggestive of phyllodes.^[34] We came across, four cases of benign phyllodes in our study. In three cases definitive diagnosis was given based on predominance of stromal components over epithelial, fragments of highly cellular myxoid stroma and numerous single spindle shaped bare nuclei. Nuclear atypia and mitotic figures were absent. In one case,

cytomorphologic features were similar to fibroadenoma except smears were more cellular. Based on strong clinical suspicion including larger size, FNA diagnosis was suggested. Subsequently histopathology confirmed the diagnosis.

The 5.98% ($N = 54$) benign breast lesions could not be subcategorized into specific lesions. FNA smears in these cases had low cellular yield and showed few small cohesive sheets of ductal epithelial cells with occasional myoepithelial cell in clusters and few bare nuclei. None of these cells showed features of nuclear atypia. Inflammatory cells were not seen on the background. Repeat aspiration could be done in 32 cases and smears showed similar features. Low cellular yield can be attributed to small size, deep-seated or fibrotic/hyalinized lesions. Majority of these patients were in the younger age Hgroup. Considering the age, clinical and radiological features, these lesions were labeled as benign breast disease [Table 1]. These patients were advised follow-up. In such cases, image-guided FNA or core needle biopsy will yield more specific diagnosis.

Breast cancer is the second most common cancer among Indian females next only to cervical cancer. One of the arguments for replacement of FNA by core-needle biopsy in some western countries is the high error rate due to lack of experienced cytopathologists. But in experienced hands, FNA is highly accurate diagnostic procedure with sensitivity and specificity over 95% for palpable breast lesions.^[35,36] It may be more sensitive [97% vs. 90%] for core needle biopsy in the diagnosis of palpable breast cancers.^[37] With advancement in the field of mammography, neo-adjuvant therapy and breast conservation surgery in breast carcinoma, cytology grading can be used for selection of neoadjuvant therapy. It allows the assessment of tumors without any surgical intervention so that morbidity associated with overtreatment of low-grade tumors can be avoided.^[10,38]

Though reduction in the risk of breast carcinoma among lactated premenopausal women has been documented,^[39] 27 patients were between 31-40 year; lactated and multiparous. Reports from western world state that breast cancer in women occur predominantly in fifth and sixth decades patients.^[40]

Out of 119 malignant lesions, most common diagnosis was infiltrating duct carcinoma ($N = 108$) followed by medullary carcinoma ($N = 2$) and mucinous carcinoma, infiltrating lobular carcinoma, sarcomatoid carcinoma, invasive papillary carcinoma and secretory carcinoma in one case each. Remaining four lesions were malignant phyllodes ($N = 2$) and one case each of non-Hodgkin's

lymphoma and metastasis of squamous cell carcinoma. Histopathology diagnosis was available in 73 cases.

The 66 cases in which FNA diagnosis of infiltrating duct carcinoma was given 62 cases were confirmed on histology [Table 3]. Remaining four cases turned out to be infiltrating lobular carcinoma, sarcomatoid carcinoma, invasive papillary carcinoma and secretory carcinoma one each. It is known that in few variants of breast carcinoma, histological subtype is often missed.^[41] Lobular carcinoma is an important source of false negative diagnosis in breast FNA and could not be sub typed due to absence of specific features such as nuclear molding, absence of intra cytoplasmic lumina/vacuoles. Diagnosis of metaplastic carcinoma could not be done because FNA smears predominantly contain malignant ductal epithelial cells with few spindle cells. Third case which turned out to be invasive papillary carcinoma on histopathological examination showed occasional small necrotic papillary formations in FNA smears. Infected papilla may closely mimic carcinoma. In general, a definitive cytological diagnosis of malignancy should not be made in papillary lesions and should be left on histopathological examination.^[42] Secretory carcinoma is a rare form of breast carcinoma and primarily affect children. It can occur in adults.^[43] Due to overlapping of cytomorphologic features between some benign and malignant lesions, rarely reports can be found in English literature.^[44] In remaining malignant lesions, we did not face any difficulty in subtyping the lesion on FNA.

In 1.10% ($N = 10$) of the patients, FNA smears were inadequate for definite diagnosis. The rate of inadequate aspiration ranges from 0.7-25.3% and is influenced by nature of the lesion, available technology and the experience of operator. Repeat aspiration and image guidance definitely reduce the rate of inadequate aspiration.

In our study, cytology grading of malignant lesions correlated well with histology grading, which helped in selecting neo adjuvant therapy.

CONCLUSION

Benign breast lesions constitute a majority of breast lumps in surgical cases and mainly occur in second and third decade. Fibroadenoma, fibrocystic change and mastitis forms the major bulk of benign breast lesions. Epithelioid cells when seen in FNA breast smears, tuberculosis must be ruled out. FNA is safe, cost effective and a reliable technique for preoperative evaluation of palpable breast lumps. FNA features are more informative when combined with physical and radiology features. Grading of malignant lesions on cytology smears must be done for selecting neoadjuvant therapy. Malignant lesions though are more

common in fourth and fifth decade, substantial number of cases occurs in third decade. Clinical breast examination and mammography screening should be encouraged in females from the third decade onwards for early detection of breast carcinoma.

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