Original Article

Fine Needle Aspiration Cytology of Palpable Breast Lumps - Their Cytological Spectrum and Histopathological Correlation

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Abstract

Background: *With the advent of fine needle aspiration cytology (FNAC), the approach to diagnosis and management of breast lumps has been revolutionized and it has high sensitivity and specificity.* ***Aim:*** *In this study we analyze the spectrum of FNAC diagnoses in breast lumps and compare the diagnostic accuracy of fine FNAC in differentiating the benign and malignant lesions of breast lumps with histopathological correlation.* ***Materials & Methods:*** *Two years prospective study was conducted in our institution and in that 490 aspirations, including 6 bilateral were performed. Suppurative and inflammatory lesions were excluded from the total aspirates. The cytological diagnosis was classified into 3 groups benign, suspicious and malignant. After this reporting all the available 94 cases were later subjected to mastectomy or open/excision biopsy and followed-up by histopathological confirmation. Later diagnostic accuracy of cytology reporting was compared with that of histopathology.* ***Results:*** *A total of 490 FNAC cases were reported including 373 as benign, 4 as suspicious for carcinoma and 113 as carcinoma. Majorities were premenopausal females and commonest age group was 31-40 years. Among them only 94 cases were followed-up by histopathologic confirmation. In histopathological correlation study, we had accuracy rate of 100% for benign lesion and 92.10% for malignant lesion with false negative rate of 7.90% and false positive rate of zero with fine needle aspiration cytology in the diagnosis of palpable breast lump. The overall sensitivity of fine needle aspiration in diagnosing the palpable breast lump is 92.10%, specificity is 100%, positive predictive value is 100% and negative predictive value is 94.91%.* ***Conclusion:*** *FNAC in experienced hands is a very useful tool with very high specificity and rare false positive result. Sensitivity can be further improved with clinical and imaging correlation.*

Key wards: *FNAC*

Introduction

Breast lumps are common in women. About 10% women visiting health organization clinics present with breast lumps as the chief complaint. 80-85% of breast lumps are benign and rests are malignant[1,2,3]. Breast carcinoma is the leading cause of cancer incidence and death in women. It is now the most common cancer both in developed and developing regions[4]. Early detection is the mainstay in management of breast carcinoma. FNAC is a routine procedure in clinical evaluation and initial diagnosis in breast lump worldwide[5]. Fine needle aspiration cytology has become an increasingly popular technique utilized in the diagnosis of palpable breast masses owing to its distinct advantages of being sensitive and specific, expedient, economical and safe. It is commonly used as a part of diagnostic triad, which in addition to the fine needle aspiration cytology includes clinical breast examination and imaging. In recent time the fine needle aspiration cytology has largely replaced excisional/incisional breast biopsy. Its distinct advantage is that it can be done during the outpatient visit without the need of the anesthesia, thus eliminating the cost of outpatient surgery. It also allows discussion with the patient of various treatment plans

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for malignant mass on the same visit. This has been confirmed by earlier several studies that aspiration cytology is superior to true-cut needle biopsy in establishing the diagnosis of clinically suspicious breast masses; however the sensitivity can be improved by increasing the number of core taken[6]. The purpose of this study is to evaluate our experiences with fine needle aspiration cytology in a series of patient and compare the diagnostic accuracy of fine needle aspiration cytology with postoperative histopathology. Accuracy of the needle tip in localizing the tumor in fine needle aspiration cytology was also studied by comparing the normal glandular cell aspirate with tumor cell aspirate.

Aims and Objectives

1. To find out the spectrum of benign and malignant lesions in all the FNAC performed and reported in cases presented with breast lump.
2. To compare the diagnostic accuracy of fine needle aspiration cytology in differentiating the benign and malignant lesions of palpable breast lump with histopathological correlation in all those cases where tissue biopsies were available.

Methods

The two years prospective study was conducted in the Department of Pathology, North Bengal Medical College, Sirajganj, Bangladesh from 1st January 2013 to 31st December 2014. During this period, 490 fine needle aspiration (FNA) were performed from various breast lumps. These 490 aspirations were obtained from breast masses of 484 patients. 6 patients had bilateral breast masses. Specimens were received from only 94 patients who underwent surgery in this and nearby hospitals, which formes the material for histopathological correlation.

Inclusion criteria: Among these FNAC cases, all available histopathology have been included to correlate with corresponding cytology diagnosis. In histopathology, all types of tissue biopsy viz. incisional biopsy, excisional biopsy, lumpectomy and mastectomy were included.

Exclusion criteria: Those cases which were reported as inflamatory and supurrative lesion have been excluded from this study.

Methods of collection of the data: In outpatient department a detailed history and thorough physical examination of the patient having palpable breast lump was carried out and entered in the proforma. The patient was informed about the procedure and informed consent was obtained from the patient before subjecting to fine needle aspiration cytology of the breast lump.

Clinical Methods: FNAC were performed with 21 gz needle and 10 cc syringes. Aspiration slides were routinely stained with PAP stain. In histopathology, tissues were fixed in 10% formalin. The gross and cut section findings were noted. Several bits were taken from appropriate sites for processing and paraffin embedding. From each block, sections were cut at 4-5 microns thickness and stained by H and E. All the FNAC cases have been analyzed according to the age of the patient, size of the lump, frequency and percentage of different types of cytology diagnosis as well as were correlated with available tissue diagnoses.

Ethical Clearance: Ethical committee approval was taken before the study.

Results

490 palpable breast lumps underwent fine needle aspiration cytology (FNAC) between January 2013 to December 2014 in our hospital. Among these, only 94 cases also had histopathology diagnosis to compare with the FNAC diagnosis. All FNAC patients were female. The age incidence of the patient shown in Table -I.

Table I: Distribution Of All FNAC Cases (N=490) According To Age Groups

Age in years	Benign	Suspicious Ca	Carcinoma	Total
11 -20	50	0	0	50
21 -30	128	0	5	133
31 -40	179	1	16	196
41 -50	14	1	5 2	67
51 -60	2	1	2 0	23
61 -70	0	1	17	18
71 onwards	0	0	3	3
Total	373	4	113	490

The age incidence was ranged from 16 to 84 years (mean age 41.68 years). The age incidence for the benign lesions ranged from 16 years to 51 years (means age 30.89 years). The incidence for the malignant lesions ranged from 25 to 84 years (mean age 47.25 years). The most common age group for benign lesions was between 31 to 40 years and for the malignant lesion

was 41 to 50 years. All the patients complained of lump in the breast. The other symptoms were pain in the lump, discharge per nipple and lump in the axilla. The duration of symptoms varied from few weeks to few years. One patient was having lump in her right breast, which was diagnosed as carcinoma, who had previously underwent modified radical mastectomy for her other breast carcinoma 5 years back. In twelve (12) of the 490 patients of palpable breast lump the fine needle aspiration cytology was reported as 'inadequate sampling' (showing normal glandular cells only). Following repeat fine needle aspiration cytology under ultrasound guidance all reported as fibroadenoma, later confirmed by histopathology.

All the different FNAC diagnoses, their respective frequencies and available corresponding histopathology have been shown in Table II.

Table II: FNAC Diagnoses In All Cases (N=490) With Cytologic Spectrum And Available Histopathology

Diagnosis on FNAC		Number of FNAC cases	Number of Histopathology cases
Benign N= 373	Fibroadenoma	208	30
	Fibrocystic change	42	23
	Proliferative breast disease	123	3
Malignant N= 117	Suspicious for carcinoma	4	38
	Carcinoma , Ductal	113	
Total		490	94

Majority of the cases, 373 cases (76.12%) were found to be benign in contrast to 117 cases (23.87%) reported either as suspicious of carcinoma or as carcinoma. Among benign conditions, commonest cytology diagnosis was fibroadenoma (208 cases) followed by "proliferative breast disease" (123 cases). Among 490 total FNAC cases, 94 cases had undergone subsequent biopsy and follow up histopathology were available. Among 373 benign cases, 59 cases had histopathology correlation. In contrast, biopsy was available in 35 cases from 113 FNAC cases which were reported as "carcinoma" and in all 4 cases which were reported as "suspicious of malignancy" on FNAC (Figure-I). In the present study, 490 aspirations were performed over a period of 2 years. 396 cases were lost to followup. Out of 490 patients, 94 cases were followed-up by histopathologic confirmation. These 94 cases were considered as the study group for the cytological and histopathological correlation of tumors of the breast. Among 94 cases underwent for follow-up biopsy (Table-III) the 59 cases of benign report by fine needle aspiration cytology, 56 were confirmed by histopathology. False negative were 3 cases. The results of the benign lesions were - accuracy rate for benign lesions was 100%, false positive was 0%.(Figure-I)

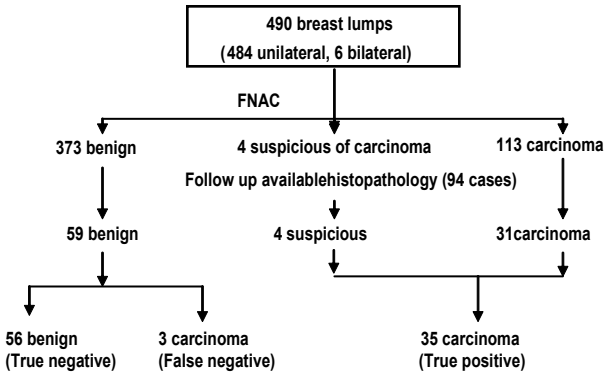

Figure I: Flow chart of result of the study

Of the total 38 cases of histologically confirmed breast carcinoma lesions (Figure-I), fine needle aspiration cytology reported 31 as carcinoma, 4 as suspicious for carcinoma and 3 as benign lesions. False negative was 3 and false positive was zero. (Table III) of the four FNAC suspicious carcinoma lesions, wide local excision biopsy done, the histopathology confirmed as infiltrating ductal carcinoma. Later all four cases underwent modified radical mastectomy on the same hospital admission, as we had no facility of intraoperative frozen section biopsy. There was no unsatisfactory (inadequate) sampling for malignant lesions. The results of the malignant lesions were as follows. Accuracy rate for malignant lesion was 92.10%, false negative rate was 7.90%.

Table III: Statistic Table

Test result (FNAC)	Disease Carcinoma	Not diseased (Benign)	Total
Positive	35 (True positive)	0 (False positive)	35
Negative	3 (False negative)	56 (True negative)	59
Total	38	56	94

Among 3 cases of false negative, two cases of right breast lump was diagnosed as fibrodinoma in a 48 and 50 years old females depending on the presence of uniform cells in sheets with myoepithelial cells and minimal nuclear atypia on fine needle aspiration cytology.

On local excision biopsy, the histopathology confirmed as infiltrating ductal carcinoma. In another one cases of left breast lump in 40 years female, diagnosed as fibrocystic disease with mild atypia by fine needle aspiration cytology. On local excision biopsy of that breast lump, histopathology confirmed as infiltrating ductal carcinoma. Later all this three cases underwent modified radical mastectomy on the same hospital admission. In our research of FNAC with histopathological correlation (94 cases) revealed benign in 56 patients, and malignant in 35 patients with false negative results of 3 and false positive zero. The diagnostic accuracy of fine needle aspiration for benign lesions was 100% and malignant lesions were 92.10% with false negative rate of 7.90% and false positive rate of 0%. The overall sensitivity of fine needle aspiration cytology in diagnosing the palpable breast lump in our study was 92.10%, specificity was 100%, positive predictive value of 100% and negative predictive value of 94.91%.

Twelve (12) cases among the 490 fine needle aspiration cytology reported as inadequate sampling (unsatisfactory) based on the presence of normal glandular cells on cytology. On repeat fine needle aspiration with ultrasound guidance all were reported as fibroadenoma. Patient underwent local excision of the tumor and histopathological confirmation later. Thus inadequate sampling rate was 2.45%. Accuracy rate of the needle tip in localizing the tumor in fine needle aspiration cytology was 97.55%.

Discussion

Breast is an important and popular site for fine needle aspiration cytology. In 1984, wanebo et. al. suggested fine needle aspiration in place of open surgical biopsy for the diagnosis of breast cancer[7]. There is an increasing tendency to confirm the diagnosis of the breast cancer at first consultation by some form of needle biopsy technique. This allows better investigation and wiser preoperative discussion than was possible when excision biopsy and frozen section confirmed the clinical diagnosis. The present series confirms the accuracy and clinical utility of fine needle aspiration cytology in the investigation of the patient with benign and malignant breast disease. The accuracy of the diagnosis in patients with malignant breast disease is in the range of 85 to 90% in most of the series[6].

In our study we had 373 benign lesions (76.12%) in FNAC, fibroadenoma being the most common benign lesion that presents for needle aspiration. This has been confirmed in other series also. Fibroadenoma form the 80% of the benign lesion aspirated for cytology. The fibroadenoma has been considered a significant cause for the false positive diagnosis. The over all activity of the epithelial cell in this tumor is probably the reason. We had no cases of false positive reports in our study.Breast carcinoma is one of the most common malignancies among women. The breast lump is usually discovered by the patient. In premenopausal women, up to 80% are benign; where as in patients over the age of 60 approximately 90% of the breast lumps are malignant. The fine needle aspiration cytology has become the investigation of choice for the diagnosis of the breast malignancy. The typical carcinoma presents a gritty resistance to the fine needle. The aspirate is usually copious and blood stained[6]. In our study we had 117 malignant lesions (23.87%) in FNAC (Figure-II).

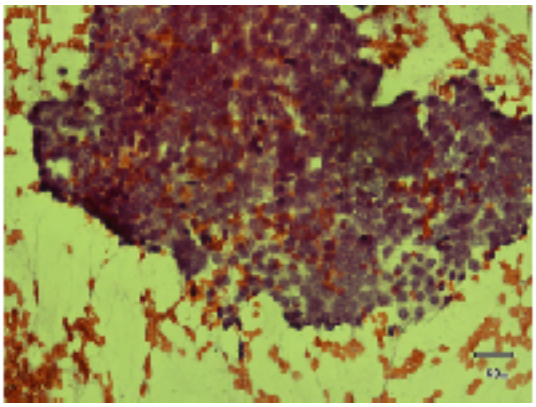

Figure II: FNAC Showing Clusters Of Malignant Cells With Hyper Chromatic Nuclei And Prominent Nucleoli - Diagnosed As "Carcinoma", Pap Stain, 400X

Infiltrating ductal carcinoma being the most common malignant lesion in histopathology (Figure-III). There was 1 case reported as lobular carcinoma in our study. Mainly diagnosed on histopathology, where as cytology was able to explain the presence of malignancy only. Lobular carcinoma can not be consistently differentiated from ductal carcinoma by cytology[8]. The present study confirms the accuracy and clinical utility of fine needle aspiration cytology in the management of benign and malignant breast diseases. The high rate of diagnostic accuracy and other predictive values in our study is similar to those in various other published series like the largest series conducted between 1982 and 2000 at Rush Presbyterian St. Lukes medical college Chicago, USA, where the sensitivity was 98%, specificity was 97%, positive predictive value was 99% and negative predictive value was 86%[9].

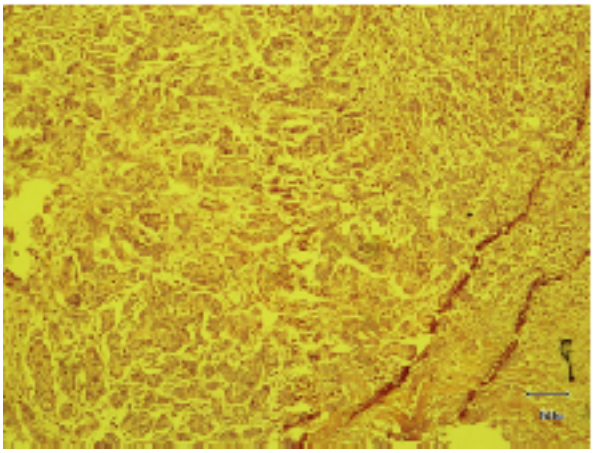

Figure III: Histopathology Showing Infiltrating Ductal Carcinoma. H & E Stain, 400X

Between September 1992 and may 1996 another study was conducted in department of surgery, St Joseph hospital, Denever, Colorado and concluded that the use of fine needle aspiration cytology for solid breast lesion is accurate and cost effective with 100% positive predictive value, 100% specificity, 87% sensitivity and 89% negative predictive value[10]. This high rate of accuracy in fine needle aspiration cytology permitted us for definite preoperative planning and discussion with the patient in whom the fine needle aspiration is positive or suspicious for malignancy. In another prospective study, use of fine needle aspiration cytology and core biopsy in the diagnosis of breast cancer which was carried out on patients attending an open access breast clinic by Dennison, et al. concluded that fine needle aspiration cytology and core needle biopsy is complementary in the accurate diagnosis of the breast cancer[11].

Fine needle aspiration cytology compliments clinical and radiological diagnosis; thus triple assessment has been reported to produce 99% accuracy for benign and malignant lesions. The diagnostic accuracy of clinical examination, mammography and fine needle aspiration cytology was compared with the definitive histological findings. Comparative study of all 3 diagnostic techniques in the diagnosis of breast tumor has shown that the accuracy of 99% can be achieved[12]. We had 3 false negative reports in our series. Although this can be regarded as a sampling error, the effect on management could be obvious. False negative rate in our series is 7.9%, which is comparable to various other series, which quoted false negative rate of 1 to 31% with average rage of 10%[13]. Great care must be taken to avoid false positive reports. Cellular fibroadenoma and papilloma bear a risk in this respect. (Figure-IV) We had no false positive cases in our study. Various other series have reported false positive reports with the range of 0 to 10%[13]. It must be reemphasized that proper clinical judgment should prevent an erroneous mastectomy being performed.

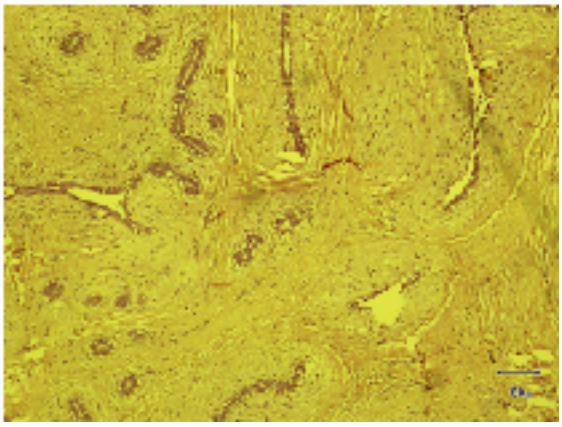

Figure IV: Histopathology Showing Proliferation Of Glandular And Stromal Components, Diagnosed As Fibroadenoma. H & E Stain, 400X

The accuracy of the needle tip in localizing the tumor in fine needle aspiration cytology was also studied in our series by comparing the normal glandular cell aspirate and inadequate aspitate with the tumor cell aspirate. The unsatisfactory (inadequate) sampling in which there was little or no cellular material reported, we believe, to be an error in the technique of aspiration. In our study we had twelve aspirations were reported as unsatisfactory, bringing the inadequate sampling rate to 2.45%. The unsatisfactory specimen rate for benign lesion was 3.22%, whereas for malignant lesion was 0%. The proportion of inadequate sampling as reported by different studies varies from 9 to 18%[14]. Our study result is comparable to study of Zarbo, et al.[14] who had reported that 17% of 2,254 aspirates in his institutional study were unsatisfactory for evaluation. Maintaining suction as the needle is withdrawn from the breast, leads to loss of cells in to the syringe at the time of withdrawal. This could probably be the common error done technically so as to produce an unsatisfactory material. Since inadequate sampling rate is 2.45%, the accuracy rate of needle tip in localizing the tumor in fine needle aspiration cytology is 97.55%. Repeat fine needle aspiration under ultrasound guidance was performed on the inadequate sampling specimen and that time it was reported as fibroadenoma, which was confirmed by histopathology after local excision.

By different studies also it has been concluded that accuracy of fine needle aspiration cytology in diagnosing the breast tumors increases by performing repeat aspiration in a lump for which previously been reported as inadequate sampling [14]. Apart from the high accuracy rate of fine needle aspiration cytology, this technique is quite attractive because of its rapidity of execution and interpretation, its low cost (compare to open biopsy of any type), and its low rate of morbidity. Some have raised questions about the possible dangers of cell implantation from the needle aspiration. These rare reports have largely resulted from the use of larger cutting needle (18 gauze) rather than fine needles (22 gauze). With this fine needle technique, there is essentially no danger of implantation with breast aspiration[15]. Franzen and Zajicek in a review of 3479 consecutive breast aspirates found no evidence of seeding along the needle tract[16]. This is not surprising as the needle tract is invariably removed with definitive surgery.

The use of fine needle aspiration cytology as the main and direct indicator for mastectomy (without biopsy) remains controversial. The major concern is the danger of a false positive diagnosis, leading to unwarranted mastectomy. Since the false positive report is very rare (in our study it is zero), in the centers where the surgical staff is accustomed to performing mastectomy on the basis of fine needle aspiration cytology for diagnosis of cancer, there is necessary for a high level of confidence in and rapport with the cytopathologyst. The danger of misdiagnosis of a cancer is studiously avoided by maintaining a cautious and conservative threshold for diagnosing a cancer. Any questionable diagnosis that is stated to be suspicious, an open biopsy is suggested where in centers an intraoperative frozen section analysis is not available.

Conclusion

FNAC is well recognised for its high accuracy and efficacy rate in investigation of breast lumps. Recently the fine needle aspiration cytology has become an increasingly popular technique utilized in the diagnosis of palpable breast lumps owing to it distinct advantages of being sensitive, specific, expedient, economical and safe. False results especially false positive results are very rare which can be further minimized with proper clinical correlation. Thus it is commonly used as a part of diagnostic triad in case of breast lump, which in addition to fine needle aspiration cytology, includes clinical breast examination and imaging.

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