Original Research Article

Spectrum of lesions encountered and accuracy of core needle biopsy of breast

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Abstract

Introduction: A wide spectrum of non-neoplastic and neoplastic lesions can affect the breast. Core needle biopsy (CNB) forms an integral part of the Triple test to evaluate breast lumps and is progressively replacing fine needle aspiration cytology(FNAC). The present study was planned to evaluate the accuracy of diagnosis and spectrum of lesions encountered on CNB.

Methods: A retrospective analysis of CNB received over a two year period was done. CNBs were categorized using the UK National Health services breast screening programme (NHSBSP) guidelines and correlated with subsequent excision wherever available.

Results: 68 CNB were received, 65/68 had a palpable lump. Malignant lesions(B5) were the most common (43%) followed by B1. Infiltrating duct Carcinoma (IDC- NST) was the most common malignancy. Proliferative and Non proliferative benign lesions, granulomatous and non-specific inflammation, Fibroadenoma and Phyllodes tumor were some of the other lesions seen. Overall concordance between CNB and final excision was 71.4%. 8/10 discordant CNB were from Category B1. For detection of malignancy overall sensitivity, specificity, positive predictive value(PPV), negative predictive value (NPV) and accuracy were 90.4%, 100%, 100%, 87.5% and 94.2% respectively. Sensitivity, specificity, PPV, NPV and accuracy in biopsies with more than 3 cores was 100%.

Conclusion: A wide spectrum of lesions can be diagnosed on CNB and CNB is accurate, sensitive and specific for preoperative diagnosis. Study of more than three cores per biopsy and a multidisciplinary approach with clinicoradiologic correlation will improve overall sensitivity and NPV.

Keywords: Core Needle Biopsy, Breast, Accuracy, Lesions

Introduction

Breast diseases can present with diverse clinical features like pain, lump, nipple discharge, mastalgia etc.; pain and lump being most common. Triple test combining clinical examination, radiological imaging (mammography, sonography) and pathology is the gold standard test in assessment of a breast lump.[1] Fine Needle Aspiration Cytology (FNAC) and Core Needle Biopsy (CNB) are an integral part of pathological examination in triple test. CNB has been progressively replacing FNAC in preoperative assessment due to its higher sensitivity (94–99%) and specificity (99–100%) compared to FNAC (sensitivity- 43.8–95.0%; specificity - 89.8–100%) and is also becoming the method of choice in the investigation of micro-calcifications without an associated mass lesion.[2] Ancillary immunohistochemical and molecular tests can more reliably and easily be done on CNB as compared to FNAC. In areas where resource constraints exist, definite indications for CNB include - Patients with suspected malignant or uncertain lesions by FNAC; Patients negative for malignancy with FNAC but with suspicious ultrasound and/or mammography findings; Patients in whom diagnosis is impossible due to inadequate samples collected by FNAC; breast lesions with microcalcifications.[2]

The present study was undertaken to evaluate the spectrum of lesions and diagnostic accuracy observed in our practice setting.

Material and Methods

This is a retrospective study of the core needle biopsies of breast received in the Histopathology division of a tertiary care and referral hospital over a period of 2 years.

Database of the Histopathology laboratory was searched for patients who underwent core needle biopsy of breast. All CNBs had been clinically guided and performed with the help of a 14 gauge needle. The data collected included age of the patient, clinical features, and investigations. Needle biopsy cores were fixed in 10% buffered formalin and submitted for routine processing; paraffin sections were cut at 2-3 microns thickness and stained with haematoxylin and eosin (H & E) stain. Lesions were classified from B1 to B5 categories as per the United Kingdom National Health services breast screening programme(NHSBSP) guidelines.[1] Special stains for mycobacteria and fungus were done wherever indicated. The histological diagnosis was correlated with the surgical excision specimen wherever available. The data was analyzed to assess the various histopathological lesions

encountered and to study correlation between CNB and subsequent excision specimen findings. Statistical analysis was performed using SSPS program.

Results

68 CNB were received in this period. Patients' ages ranged from 15-87 years, with 48.4 years being the mean age and the median age being 45. 41% of CNBs were from patients of age ≥50 years. On review of their clinical features, 50 patients had only a palpable lump while in 15 patients there was a palpable lump with other associated symptoms and/or signs; that included pain(5 cases), weight loss(3 cases), nipple discharge(2 cases), axillary lymphadenopathy(2 cases), retracted nipple(1case) and lump with ulcer(1case). One patient was a known case of malignant neuroendocrine tumor (NET) in thymus with a breast lump suspicious of metastasis. One patient presented with generalized body ache and was diagnosed as secondary myelofibrosis with metastasis from carcinoma of breast, on bone marrow biopsy. Subsequent clinical examination revealed a small breast lump which was then biopsied. In two patients no history was available.

The total number of cores received for 68 CNBs were 196, with one core to seven cores per biopsy. 34% had just two cores while CNBs with number of cores <3 and ≥3 were equally distributed.

Table 1 shows the histopathologic diagnosis and NHSBSP categories encountered in the study, B5 and B1 were the most commonly encountered, accounting for 43% and 31% biopsies respectively.

21 cases were of Category B1, five showed only normal breast tissue and 16 were inadequate/non representative with presence of adipose tissue/ skeletal muscle.(Fig. 1A) Two of the five with only normal breast tissue were excised, one showed benign fibrocystic disease and the other showed a benign proliferative breast lesion - adenosis. Follow up of five inadequate CNBs were available. In two, a malignancy was detected in a repeat biopsy done elsewhere. In one case the lump was excised and was found to be a benign phyllodes tumor, one was a fibroadenoma and one was fibrocystic disease with foci of usual duct hyperplasia.

It was observed that in 75% of the B1 CNBs, the number of cores was less than three. Out of 16, seven CNB had only one core and five CNB had two cores.

Nine lesions were classified as benign lesions (B2) on CNB. As is seen in Table 1, five were proliferative and 4 were non proliferative. There were 3 Fibroepithelial Lesions; all three were labelled fibroadenomas on CNB. (Fig. 1B) Two fibroadenomas were confirmed on excision, while the third was diagnosed as a benign Phyllodes tumor. This was a 43 year old lady and her biopsy had shown epithelial elements and stroma with prominent hyalinisation with no hypercellularity or atypia in the stroma.

One CNB showed benign breast tissue with fibrocystic change however, it was a Phyllodes tumor on excision.(Fig. 1C) Of the three inflammatory lesions, two were granulomatous and one showed non-specific inflammation.(Fig. 1D) One case showed necrotising granulomas and a Mycobacterial ethology was suspected. Special stains were done for acid fast bacilli (AFB) and fungus in both cases but were found to be negative. Excision of the non necrotising granulomatous lesion showed lobulocentric granulomatous mastitis possible idiopathic granulomatous mastitis.

5 cases were allotted the category B3. All the five cases were fibroepithelial lesions and were reported as Phyllodes tumor or 'cannot rule out Phyllodes tumor' on CNB. (Table 2) (Fig. 1E, F) In 3/5 cases follow up was available and in all three a phyllodes tumor was confirmed.

Four CNBs were given as suspicious for malignancy (B4). Three lesions showed very few atypical cells, raising suspicion for malignancy however a definite diagnosis could not be made. Extensive individual cell necrosis and very occasional viable cells was observed in one of these lesions.(Fig. 2A) Follow up of only one case was available and showed Infiltrating duct carcinoma no special type (IDC-NST).

In 29 cases a malignancy was found. 27 were Infiltrating duct carcinoma - no specific type (IDC -NST) and one was a mucinous carcinoma.(Fig. 2 B, C, D) One case had a Thymic neuroendocrine tumor(NET) with secondary involvement of the breast, confirmed by immunohistochemistry. Follow up surgical excision specimen of 18 cases was available, 16 IDC and the Mucinous carcinoma was confirmed in the excision specimen while in one case only ductal carcinoma in situ (DCIS) was reported in the excision.

In all categories, a total of 35 cases had follow up and amongst these there were ten discordant diagnoses thus overall concordance was 71.4%. 8/10 discordant cases were in B1 category while two were in B2, as described above.

We considered B5 & B4 lesions as positive for malignancy on CNB and B3, B2 & B1 category lesions as negative for malignancy. Table 3 shows their final histopathology after excision. Thus, overall Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive value (NPV) and Accuracy for malignancy in CNB was 90.4%, 100%, 100%, 87.5% and 94.2% respectively.

The 35 CNBs with follow up were divided into two groups. In one group there were less than 3 cores and in other group number of cores were 3 or more than 3. (Tables 4, 5) Sensitivity, Specificity, PPV, NPV and Accuracy for diagnosis of malignancy in CNBs with less than 3 cores was 80%, 100%, 100%, 77.7% and 88.2% respectively. Sensitivity, Specificity, PPV, NPV and Accuracy for CNBs with 3 or more than 3 cores was 100%.
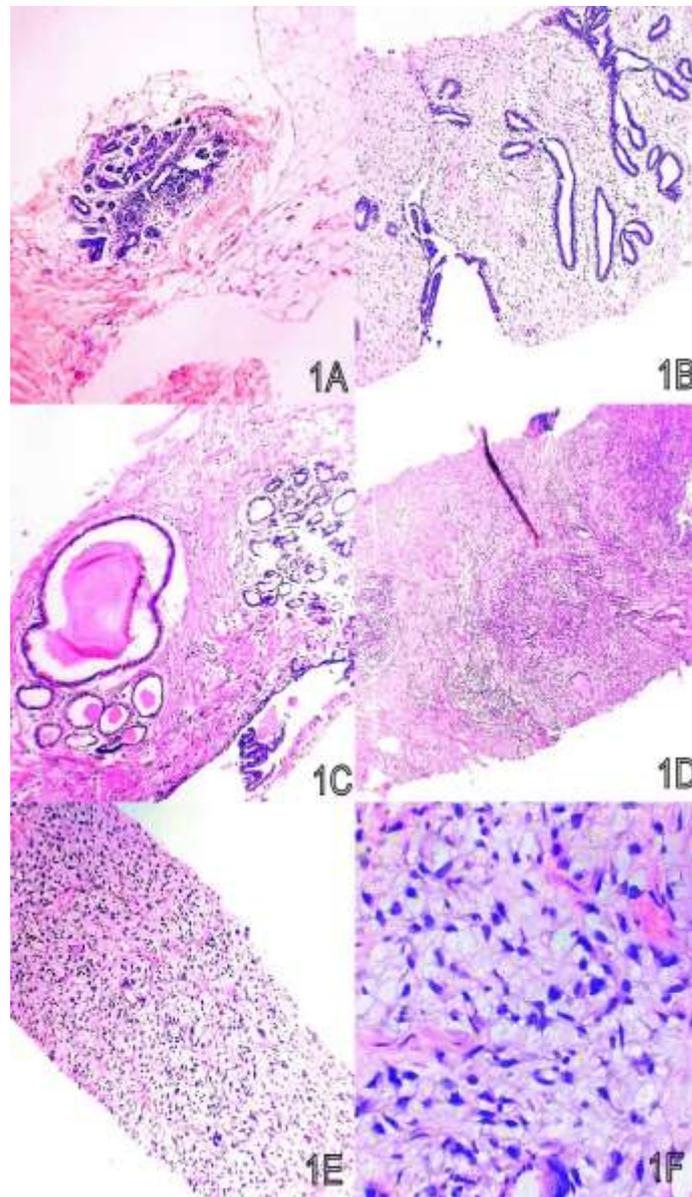
Fig. 1: A –CNB with normal breast lobule and fat(HE x100), B- Fibroadenoma showing biphasic proliferation (HE x 100), C- Fibrocystic change (HE x100), D - Granulomatous inflammation–Epithelioid granuloma with Langhans giant cell seen (Hex100), E, F–Phyllodes tumor showing cellular stroma in the core with plump spindle cells and no epithelium (HEx100, HE x400)
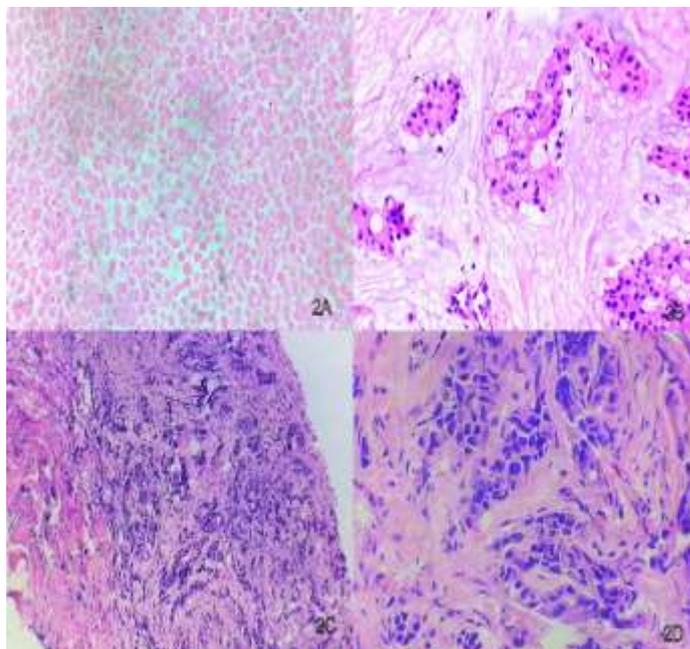
Fig. 2: A- CNB showing individual cell necrosis (HE x400), B- Mucinous Carcinoma showing small clusters of relatively bland cells in abundant extracellular mucin (HE x 400), C, D –IDC –NST showing irregular clusters and single malignant duct epithelial cells in a desmoplastic stroma. (HE x 100, HE x400)

Table 1: Spectrum of lesions and NHSBSP categories of lesions

NHSBSP	Diagnosis	No of cases	%
B1	Normal breast tissue	5	31
	Inadequate	16	
B2	Fibroadenoma	3	13
	Usual duct hyperplasia	1	
	Benign breast proliferation with focal Lactational change	1	
	Benign breast tissue with fibrocystic change	1	
	Granulomatous inflammation	2	
	Nonspecific inflammation	1	
B3	Phyllodes tumor	5	7
B4	Suspicious for malignancy	4	6
B5	IDC	27	43
	Mucinous carcinoma	1	
	NET (Neuroendocrine Tumor)	1	

Table 2: Phyllodes tumors on CNB (B3)

Age(yr)	Histological features	CNB diagnosis	Final HP(excision)
42	-Stromal predominance with very occasional epithelial cells -Cellular spindle cell stroma	Benign Phyllodes tumor	NA
45	-Cellular spindle cell stroma with stromal predominance	Phyllodes tumor	NA
42	-Loose fibromyxoid stroma with occasional atypical spindle cells and occasional mitotic figure	S/o Recurrent Phyllodes tumor (Prev h/o Phyllodes)	Recurrent Phyllodes tumor- Malignant
33	-Epithelial hyperplasia Fibromyxoid stroma, at place hyalinisation and stromal hyper-cellularity with periductal accentuation focally	Benign Phyllodes cannot be ruled out	Benign Phyllodes tumor
35	-Spindle cell stroma with focal stromal cellularity with plump spindle cells -No epithelial elements	i/v/o focally cellular stroma benign Phyllodes cannot be ruled out	Benign Phyllodes tumor

Table 3: Final Histopathology of lesions categorized as malignant on CNB

on CNB	Total	Final HP (Excision)	
		Malignant	Non-malignant
Malignant	19	19	0
Non-malignant	16	2	14
total	35	21	14

Table 4: CNB with less than 3 cores

CNB with cores<3	Total	Final HP (excision)	
		Malignant	Non-Malignant
Malignant	8	8	0
Non Malignant	9	2	7
Total	17	10	7

Table 5: CNB with 3 or more cores

CNB with cores ≥3	Total	Final HP (Excision)	
		Malignant	Non Malignant
Malignant	11	11	0
Non Malignant	7	0	7
Total	18	11	7

Discussion

The present study documents the CNBs done in our institute over a 2 year period. 95.5% (65/68) biopsies were performed in patients who presented with a palpable lump, in one case the lump was detected by the clinician and in two patients no history was available. As most of the patients coming to our tertiary care public hospital are from a poor socioeconomic status, the importance of screening is ill understood and a palpable lump is what directs majority of them to the hospital. We did not have any biopsy done for a screen detected lesion/micro calcification, unlike the western population where this indication is common. Breast lesions were assigned a specific category (B1-5) as per the NHSBSP classification and the biopsy was correlated with subsequent excision. The overall core biopsy and final surgical excision concordance was 71.4% and that for malignant lesions was 94.4%. In literature, the concordance rate for malignant lesions has varied from 84.4% to 100%.[3,4,5]

In our study, maximum lesions (43%) were in B5 category, in literature the percentage of B5 lesions varies from 14% to 45%.[6,7] As expected, IDC- NST was the most commonly encountered malignancy.[3,5] From the available follow up, all invasive ductal carcinomas were concordant with excision except one case which had been reported as DCIS; however slides/blocks of the excision were not available for review during the study. Mucinous carcinoma of the breast is a relatively rare entity and accounts for 2% all breast carcinomas. In our study, one (1.4%) mucinous carcinoma was found. Renshaw AA found 0.51% mucinous lesions on core needle biopsy.[8] The 100% concordance rate for mucinous carcinoma in literature was replicated in our study.[3,8] Mucinous carcinomas are usually associated with a better prognosis.

One secondary lesion in the form of metastatic NET was seen. Metastasis to breast is rare and comprises less than 1% of malignant breast lesions. Most of these are from contralateral breast or secondary lymphomas. NET metastasizing to the breast is diagnostically challenging. It frequently mimics in-situ or invasive breast carcinoma with or without neuroendocrine differentiation. Accurate diagnosis is essential for appropriate management. The clinical history and positivity for Synaptophysin and Chromogranin made it possible to diagnose the metastatic tumor accurately in our study. Perry KD et al in their study found 18 metastatic NET, of which 8 were initially labelled as primary breast malignancy on core biopsy.[9] Though majority of their patients had history of NET, it was not available at the time of interpretation of core biopsy. Hence, clinical history and a high index of suspicion is very important and it is important to rule out metastasis in neuroendocrine breast tumors.[9]

6% of lesions (4 cases) in this study were found to be suspicious for malignancy. The incidence in literature is 2-3%.[6,7] Extensive crushing artefacts and tumor necrosis with very few viable cells precluded a definitive diagnosis in these cases. Labelling such lesions as B4 indicates the need for a repeat biopsy or a diagnostic excision and the same should be communicated to the clinicians. This was seen in one case in our study wherein a repeat core biopsy revealed a malignancy, leading to therapeutic excision.

Five fibroepithelial lesions reported as either Phyllodes tumor or 'cannot rule out Phyllodes tumor' were included in B3. Two biopsies with stromal predominance and increased stromal cellularity were definitively labelled as Phyllodes tumor. In the other two lesions there was focal stromal hypercellularity with plump spindle stromal cells and hence the possibility of a Phyllodes tumor was considered though unequivocal stromal overgrowth and hypercellularity or mitoses was not seen. The patients were 33 and 35 years old and this added to the diagnostic dilemma. Subsequent excisions confirmed a benign phyllodes tumor.

Nine biopsies (13%) were assigned as category B2. Five were proliferative lesions consisting of fibroadenoma (three), usual duct hyperplasia (one) and benign breast proliferation with focal lactational change (one). Four were non-proliferative lesions- three inflammatory lesions and one benign breast tissue with fibrocystic change. In this category, follow up was available in 6 cases and in two cases the final excision did not match the CNB. In one the CNB was suggestive of fibrocystic lesion and the final excision showed a phyllodes. This CNB was probably not representative of the lesion and in a case like this, a multidisciplinary approach involving both the clinician and the radiologist would aid better management. Two CNBs showed granulomatous inflammation. In one of these lesions follow up was available and was suggestive of idiopathic granulomatous mastitis while the other showed necrotising granulomas and a mycobacterial ethology was suspected.

Granulomatous lesions of breast can be seen in infections, systemic granulomatous diseases, idiopathic granulomatous mastitis etc. Breast Tuberculosis is a rare disease with overall incidence of less than 0.1% of all breast lesions in western countries. In Indian series reported incidence of breast tuberculosis varies between 0.64 and 3.59%.[10]

31% (21/68) of lesions were in category B1 accounting for the second most common category. Percentage of B1 lesions in our study was significantly higher compared to previous study results where it was ranged from 5.9% to 20.5%.[6,7] More than two thirds were inadequate biopsies.

Cases in this category constituted 80% of total discordant lesions obtained.

Overall Sensitivity, Specificity, Positive Predictive Value, Negative Predictive value and Accuracy for malignant lesions on CNB was 90.4%, 100%, 100%, 87.5% and 94.2% respectively. The sensitivity in literature varies from 92.3 to 98.1% while the accuracy ranges from 93.4 to 99.3%.[4,11] The accuracy, specificity and positive

predictive value in our study is in concordance with literature however, the sensitivity and negative predictive value in our study is slightly lower due to the large number of inadequate biopsies.

It is suggested in literature that increased number of cores has a positive impact on diagnosis and a minimum of 3 cores per biopsy is recommended.[3,12] Impact of number of cores per biopsy on diagnosis was definitely established in our study as 75% of the inadequate biopsies had less than three cores per biopsy and the sensitivity and negative predictive value improved significantly with more than three cores per biopsy.

Conclusions

Core needle biopsy is an accurate, sensitive and specific test for preoperative diagnosis of breast lumps. A wide variety of inflammatory, proliferative and non-proliferative benign lesions as well as malignancies can be diagnosed on CNB. With improvement in technical expertise, study of a minimum of three cores per biopsy and a multidisciplinary approach there can be further improvement in the overall sensitivity and negative predictive value.

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