

Evaluation of Fine Needle Aspiration Cytology in the Diagnosis of Suspicious/gray Zone Lesions in Breast Lesions and its Histopathological Correlation

Manas Madan*, Manisha Sharma, Sanjay Piplani, Mridu Manjari, Neha Sharma and Saloni Goyal

Dept. of Pathology, SGRDIMSR, Amritsar, Punjab, India

Keywords: FNAC, Malignant, Breast, Histopathology

ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) is an established tool in the diagnosis of palpable lesions. FNAC is a sensitive and rapid method in differentiating benign breast lesions from malignant ones. But there exist some gray areas in which this differentiation becomes difficult. Problem arises in categories C3 and C4 in which there exists significant interobserver variation in the diagnosis. The study was done to evaluate the usefulness of FNAC in diagnosis of C3 and C4 categories and correlate it with histopathological diagnosis.

Methods: This Study was conducted on 512 cases of breast FNAC in from January 2014 to December 2014. FNAC diagnosis of C3 and C4 categories were selected. The cytological diagnosis was compared with histopathological diagnosis in the cases where biopsy was done subsequent to FNAC diagnosis.

Results: C3 and C4 categories constituted 28 (5.46%) and 48 (9.3%) cases respectively. Histopathology was available in 13 cases of C3 (46.4%) and 30 cases of C4 (62.5%). Among C3 category, 10/13 cases showed benign lesions (77%) and 3/13 cases were malignant (23%). Among C4 category, 4/30 cases showed benign lesion (13.3%) and 26/30 cases were malignant (86.7%). There was a significant statistical difference between benign and malignant diagnosis of C3 & C4 categories ($p < 0.001$).

Conclusion: Clinicians and pathologists should understand the limitations of FNAC. C3 and C4 categories should still be continued with, as there was a statistically significant difference in benign & malignant diagnosis for these categories in our study.

***Corresponding author:**

Dr Manas Madan, 21 A, Sandhya Enclave Majitha Road Amritsar (143001), Punjab, India

Phone: +91 9888015365

Email: manasmadaan@gmail.com



Introduction

Fine needle aspiration cytology (FNAC) is an established tool in the diagnosis of various palpable lesions and it correlates well with histopathological diagnosis in most of the cases. The major utility of FNAC is in differentiating benign and malignant lesions of various tissues. Breast is one of the organs, which is routinely subjected to FNAC to diagnose malignant lesions. Breast carcinoma is the second commonest cancer among Indian females after carcinoma cervix and FNAC is a very cost-effective, sensitive and rapid diagnostic method in differentiating benign breast lesions from malignant ones.^[1,2] But there exist some gray areas in breast lesions in which this differentiation becomes difficult. Although needle core biopsy (CNB) is now being preferred over FNAC, FNAC still has a lot to offer as a first line diagnostic procedure, particularly in developing countries with economic restrictions. Moreover FNAC remains almost as accurate as CNB in determination of malignancies.^[1,2,3]

Breast FNAC diagnosis are characterized in to inadequate (C1), benign (C2), atypical, probably benign (C3), suspicious, favor malignancy (C4) and malignant (C5). These were recommended by the National Cancer Institute (NCI) to bring about uniformity in diagnosis of breast FNAC in a way similar to the Bethesda classification for reporting of thyroid cytology. Among these categories, C1, C2 and C5 do not pose much of a difficulty to the pathologists and leads to a good interobserver comparability. The shortcomings in FNAC are to differentiate invasive from in situ cancers and the presence of gray zone categories where definite diagnosis of benign or malignant is difficult. This problem arises in categories C3 and C4 in which there exists significant interobserver variation in the diagnosis, as no strict criteria are present for the diagnosis of these categories.^[1,2,3,4] Some authors have suggested the use of term "equivocal" for such inconclusive diagnosis (C3 & C4) on FNAC.^[5] The present study was done in order to evaluate the usefulness of FNAC in diagnosis of C3 and C4 categories and to correlate it with histopathological diagnosis.

Materials and Methods:

The study was a retrospective one conducted in the department of pathology SGRDIMS, Amritsar from January 2014 to December 2014 after taking the necessary approval from the institution. Slides of the entire breast FNAC conducted during the above period were surveyed and those fitting in to C3 and C4 categories were selected for study. The cytological diagnosis was compared with histopathological diagnosis in the cases where biopsy was done subsequent to FNAC diagnosis. The statistical

significance of benign and malignant lesions in both these categories was calculated.

Results

A total of 512 breast FNAC were done in the above-mentioned period. The age of the patients ranged from 16 to 87 years. The commonest age group was 21-30 years. Out of these, C3 and C4 categories constituted 28 (5.46%) and 48 (9.3%) cases respectively. All patients belonging to these two categories were females. Among these categories, the age ranged from 29-61 years. Histopathological diagnosis was available in 13 cases of C3 (46.4%) and 30 cases of C4 (62.5%). All the malignant cases in both these categories were infiltrating ductal carcinomas (29 cases). Benign histological diagnosis between both categories included fibroadenoma (07 cases), fibrocystic disease (03 cases) and proliferative breast disease (04 cases).

Among C3 category, 10/13 cases in which histopathological examination was available showed benign lesions (77%) and 3/13 cases were malignant (23%). Among C4 category, 4/30 cases available for histopathological examination showed benign lesion (13.3%) and 26/30 cases turned out to be malignant (86.7%) (TABLE1). There was a significant statistical difference between benign and malignant diagnosis of C3 & C4 categories ($p < 0.001$).

TABLE 1: CYTO-Histological Correlation.

HISTOPATHOLOGICAL DIAGNOSIS	FNAC C3	FNAC C4	TOTAL
BENIGN	10	04	14
MALIGNANT	03	26	29
TOTAL	13	30	43

Discussion

Breast FNAC is a widely accepted safe, rapid and an effective diagnostic modality for diagnosis of breast lesions especially malignancy. Out of the various diagnostic categories, C3 and C4 pose challenges to the pathologists and are also known as gray zone/indeterminate where a definite diagnosis of benign or malignant is difficult.^[1,2,3,4,5]

An interpretation of C3 is given when the aspirates show benign characteristics but have some features not present usually in benign aspirates. These include any or a combination of nuclear pleomorphism, loss of cell cohesion, nucleocytoplasmic changes resulting from treatment/hormonal influences and increased cellularity. C4 category diagnosis is given when the aspirates have cells with features of malignancy however the material is not very cellular to be diagnostic, poorly preserved or spread. These also include samples showing malignant

features of a greater degree than seen in C3 without the presence of overtly malignant cells. [2,4,5,6]

In this study, the age ranged from 29-61 years for both the above-mentioned categories and is comparable to many other studies conducted. [1,2] C3 and C4 categories combined constituted 76/512 (14.8%) cases subjected to breast FNAC during the study period. This percentage of C3 and C4 categories correlated well with various other studies, which give a range of 4-17.7% for both, these categories combined. [1,2,4,5,7,8] This is essential because there should not be erroneous overuse of these categories in reporting of breast FNAC.

In C3 category, where 13/28 cases were available for histopathological examination, 3 cases turned out to be (IDC) infiltrating duct carcinomas (3/13= 23%) and thus were considered false negative (FN). [Fig 1] This result also corroborated well with the range established by other studies (8.6-52%). [1,2,5,7,9] The reasons for these false negative cases can be sampling error, small tumor size. Low-grade tumor, less cellularity or low grade well differentiated carcinomas arising in cystic lesions. These 3 FN cases were again reviewed after histopathological diagnosis. All of these cases showed mainly cohesive sheets of ductal epithelial cells, bare nuclei with few clusters showing cellular crowding and lack of cohesiveness. Thus patients with C3 diagnosis need not undergo a surgical procedure if the proper clinical and mammographic correlation is done and they too suggest a benign lesion.

In C4 category, 26/30 cases (86.7%) available for histopathological examination showed malignant

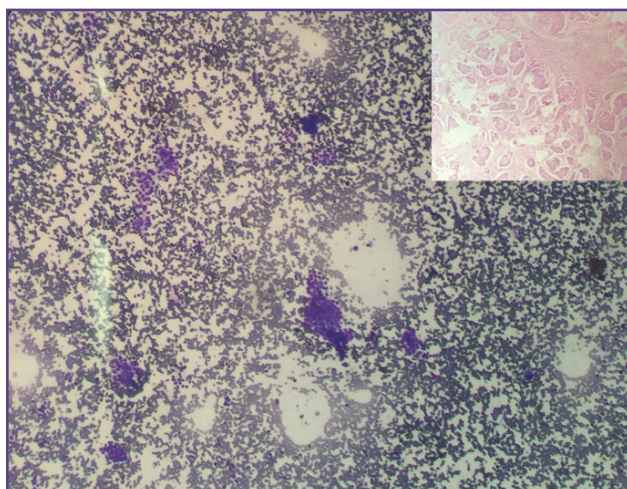


Fig. 1: FNAC diagnosis C3 showing clusters of ductal epithelial cells showing mild overlapping and pleomorphism along with few bare nuclei in the background (MGG 100X). Inset showing histopathology of the same case with features of infiltrating ductal carcinoma (H&E 100X).

pathology (IDC). 4/30 cases (13.3%) showed benign pathology on histopathological examination and were considered false positive (FP). [Fig 2a,2b] Of these 2 were highly cellular fibroadenomas and 2 were proliferative breast disease. These cases showed dyscohesive clusters, cellular overlapping and moderate cellular and nuclear pleomorphism. These results also correlate with the other studies, which show a range of 81-97% for malignancies in this category. [1,7,9,10,11,12,13] Some degree of atypia, dyscohesion and nuclear pleomorphism can be seen in fibroadenomas and along with increased cellularity can cause diagnostic difficulty. Most of these cases are conventional fibroadenoma although a few may be associated with proliferative lesions especially when atypical changes are present. Proliferative breast lesion is another gray zone lesion and can be called as the nightmare of the pathologists' especially radial scar and complex sclerosing lesions. These lesions can be hypercellular with dyscohesive cell clusters, atypia and absence of myoepithelial cells in few clusters. Thus all the patients with cytological diagnosis of C4 lesion on breast FNAC should undergo surgery, as the percentage of malignancies in these lesions is very high.

Thus to conclude, FNAC of breast is a simple, safe, rapid and inexpensive diagnostic modality and plays a very important role in diagnosis of breast lesions especially malignancies. However it is important that clinicians understand the limitations of FNAC. C3 and C4 categories should still be continued with, as there was a statistically significant difference in benign & malignant diagnosis for these categories in our study.

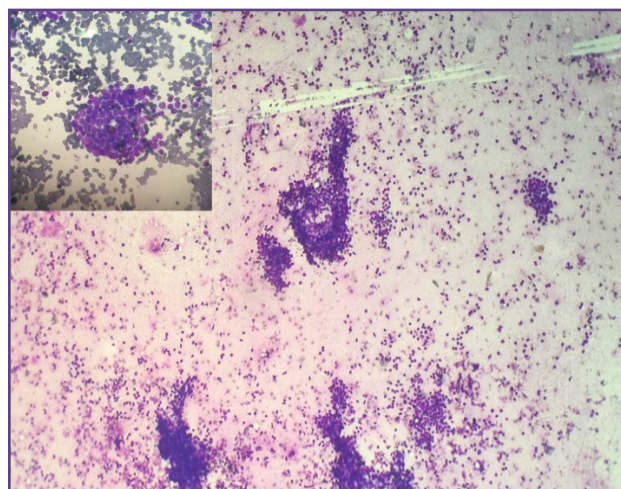


Fig. 2 (a): FNAC diagnosis C4 showing ductal epithelial cells arranged in groups (MGG 100X), inset showing overlapping cells exhibiting pleomorphism (MGG 400X). Note the lack of bare nuclei in background.

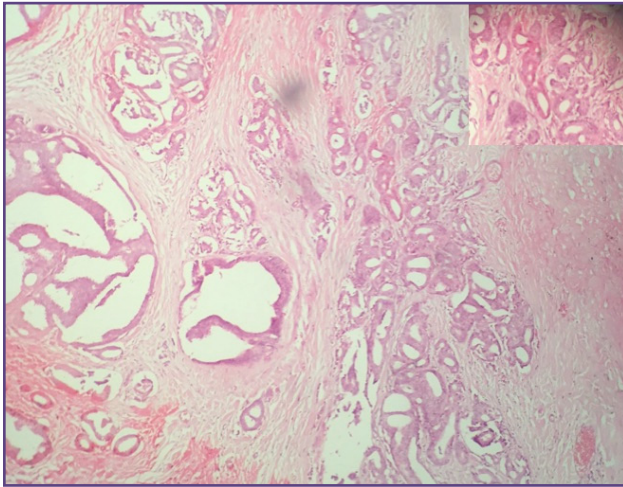


Fig 2. (b): Histopathology of same case exhibiting fibrocystic disease with epithelial hyperplasia (H&E 100X), inset showing high power of hyperplastic epithelium (H&E 400X).

Funding

None

Competing Interests

None Declared

References

1. 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;33:76-9.
2. Shabb NS, Boulos FI, Abdul-Karim FW. Indeterminate and erroneous fine-needle aspirates of breast with focus on the 'true gray zone': a review. *Acta Cytol.* 2013;57(4):316-31.
3. Chaiwun B, Sukhamwang N, Lekawanvijit S, Sukapan K, Rangaeng S, Muttarak M et al. Atypical and suspicious categories in fine needle aspiration cytology of the breast: histological and mammographical correlation and clinical significance. *Singapore Med J.* 2005;46(12):706-9.
4. Mitra S, Dey P. Grey zone lesions of breast: potential areas of error in cytology. *J Cytol.* 2015;32:145-52.
5. Goyal P, Sehgal S, Ghosh S, Aggarwal D, Shukla P, Kumar A et al. Histopathological correlation of Atypica; (C3) and Suspicious (C4) categories in Fine Needle Aspiration Cytology of the breast. *Int J Breast Cancer.* 2013;2013: 965498.
6. Yu YH, Wei W, Liu JL. Diagnostic value of fine-needle aspiration biopsy for breast mass: a systematic review and meta-analysis. *BMC Cancer.* 2012;25:12-41.
7. Kanhough R, Jorda M, Gomez-Fernandez C, Wang H, Mirzabeigi M, Ghorab Z, et al. Atypical and suspicious diagnoses in breast aspiration cytology-is there a need for two categories? *Cancer.* 2004;102:164-7.
8. Howell LP. Equivocal diagnoses in breast aspiration biopsy cytology: Sources of uncertainty and the role of "atypical/indeterminate" terminology. *Diagn Cytopathol.* 1999;21:217-22.
9. Deb RA, Matthews P, Elston CW, Ellis IO, Pinder SE. An audit of "equivocal" (C3) and "suspicious" (C4) categories in fine needle aspiration cytology of the breast. *Cytopathology.* 2001;12:219-26.
10. Lim JC, Al-Masri H, Salhadar A, Xie HB, Gabram S, Wojcik EM. The significance of the diagnosis of atypia in breast fine-needle aspiration. *Diagn Cytopathol.* 2004;31:285-8.
11. Yusuf I, Atanda AT, Imam MI. Cyto-morphologic correlation of equivocal C3 and C4 breast lesions. *Arch Int Surg.* 2014;4:131-5.
12. Tikku G, UMAP P. Comparative Study of Core Needle Biopsy and Fine Needle Aspiration Cytology in Palpable Breast Lumps: Scenario in Developing Nations. *Turk Patoloji Derg.* 2016;32:1-7.
13. Omi Y, Yamamoyo T, Okamoto T, Nishikawa T, Shibata N. Fine needle aspiration versus core needle biopsy in the diagnosis of the intraductal breast papillary lesions. *World Journal of Pathology.* 2013;2:11.