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Original Research Article

Advantages of the cell block technique over the FNAC and correlation with histopathology of most prevalent breast lesions in the community at the tertiary care center

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ABSTRACT

Background: Breast lumps are a common cause of concern in both young and older women throughout the world. Fine needle aspiration of breast lesions is an important and widely practiced method of providing a preoperative diagnosis in women presenting with a lump in the breast. Cell blocks that are made from the aspirates help in preserving the architecture, and the nuclear morphology and help in preserving the material for immunohistochemical studies. The present study aims to highlight the role of FNAC and cell block in the diagnosis of breast lesions.

Materials and Methods: This was a two-year prospective study of 72 patients presenting with palpable breast lesions referred for FNAC to the Department of Pathology JJMMC, Davangere from 1st July 2015 to 30th June 2017. After a detailed history, general physical & local examination, informed consent was taken and FNAC was performed under aseptic precautions. A part of the aspirate was fixed, then processed as cell blocks, and stained with H&E. Wherever lumpectomy or radical surgery was performed the histopathology was correlated with cytomorphological findings.

Result: The present study showed a diagnostic accuracy of 85.71% in the FNAC diagnosis. The sensitivity and specificity of FNAC in diagnosing breast lesions were found to be 82.60% and 87.23%. PPV and NPV were 76% and 91.11% respectively. When cell blocks were used the diagnostic accuracy increased to 88.57%. Diagnosis by using cell block showed a sensitivity of 79% specificity of 93.47%, PPV of 86.36%, and NPV of 89.58%.

Conclusion: From the results of our study, it can be concluded that the accuracy of diagnosing breast lesions preoperatively can be increased when FNAC is combined with the cell blocks from the aspirates. The cell blocks also help to preserve the aspirated material for future reference and immunohistochemistry can also be applied for a more accurate diagnosis.

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1. Introduction

Breast cancer is a national health problem in India and a serious health concern in all countries. The early detection of breast cancer represents a major challenge for

oncologists, pathologists, and surgical oncologists.¹ Breast lumps are a cause for concern in both young and elderly women.² Fine needle aspiration cytology (FNAC) is a widely used preoperative diagnostic method that is quick, cost-effective, minimally invasive, and safe. But FNAC diagnosis comes with limitations in maintaining consistency and reproducibility of the findings.³

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Other limitations include difficulty in differentiating in situ and invasive carcinomas⁴ and classifying various proliferative breast disorders.⁵ These limitations can be overcome by using cell blocks. Architectural features can be better appreciated by using cell blocks and the classification of these lesions is easier. Acquiring an adequate sample material can be challenging for the preparation of cell block slides prone to having variable cellularity after processing which may or may not correlate with FNA slides.⁶ In addition, immunohistochemistry can be applied to these cell blocks to extend the accuracy of the diagnosis.

This study aimed at the advantage of cell block over the FNAC to study morphological features of breast lesions. However, it has been proved fact that the combined use of FNAC and cell blocks in the breast lesions yields better results.^{7,8}

2. Aims and Objectives

1. To study the cytomorphologic features of breast lesions on the cell block.
2. To correlate cytological diagnosis with histopathology whenever possible.

3. Materials and Methods

This was a two-year prospective study of 72 patients presenting with palpable breast lesions referred for FNAC to the Department of Pathology JJMMC Davangere from 1st July 2015 to 30th June 2017. After a detailed history and examination, FNAC was done under aseptic precautions using a 20-gauge needle & 10 ml syringe. Smears were stained with H&E and Giemsa. A part of the aspirate was clotted and fixed in neutral buffered formalin for 12 hours, then was processed as cell blocks and stained with H&E. Morphology of various breast lesions in cell blocks was studied. Wherever lumpectomy or radical surgery was performed the histopathology was correlated with cytomorphological findings.

4. Results

Cytomorphological features in cell blocks of various proliferating breast diseases were studied in 72 cases. Histopathology correlation was possible in 48 cases.

4.1. Fibrocystic disease

Fibrocystic disease was diagnosed in two patients using a cell block. The sections showed clusters of hyperplastic epithelial cells with a moderate amount of cytoplasm and hyperchromatic nuclei. Out of these, one cell block section showed a cluster of apocrine cells, foam cells, and stromal fragments and the other showed proteinaceous material in the background along with fibrofatty stroma. One case was confirmed as Fibrocystic disease by histopathology, other

case was diagnosed as IDC.

4.2. Fibroadenoma

Diagnosis of fibroadenoma was made in 34 cases by the cell block. Histopathology correlation was possible in 27 cases, out of which 21 cases were confirmed to be a fibroadenoma. Out of the remaining six cases, one was diagnosed as fibrocystic disease, three were phyllodes and two were diagnosed as Invasive ductal carcinoma. The cell block features of fibroadenoma were the presence of benign epithelial cells arranged in the form of round ducts and elongated ducts resembling the peri-canalicular pattern and intracanalicular pattern as seen in histopathology. The background in was composed of fibromyxoid stroma.

4.3. Phyllodes tumour

Cell block diagnosis of Phyllodes was made in two patients. Cell block sections showed numerous bundles of spindle cells and occasional clusters of benign cells. Histopathological diagnosis in both cases showed concordance with cytological diagnosis

4.4. Benign epithelial hyperplasia

Cell block sections of two cases had features suggestive of benign epithelial hyperplasia consisting of a cluster of epithelial cells intermixed with myoepithelial cells arranged in clusters. One case was diagnosed as fibroadenoma and the other as IDC by histopathology.

4.5. Atypical epithelial hyperplasia

Diagnosis of atypical epithelial hyperplasia was made in six patients using a cell block. Sections showed clusters of hyperplastic epithelial cells with a moderate amount of cytoplasm and hyperchromatic nuclei, surrounded by fibrofatty stroma. IHC was done on one of the cell blocks and it showed CK5 negativity and ER positivity. Histopathological study was possible in five patients, four were diagnosed with IDC and one patient with mucinous carcinoma.

4.6. Infiltrating ductal carcinoma

Infiltrating duct carcinoma was diagnosed in 26 cases using a cell block. Sections showed dyscohesive clusters of atypical epithelial cells with scant cytoplasm and hyperchromatic nuclei, nuclear pleomorphism, and mitotic figures background showed mainly hemorrhage in most of the cases. IHC was done on one cell block which showed features of IDC. It showed ER and PR positivity. Two cases of IDC could be further classified as IDC neuroendocrine type and IDC- medullary in the cell block sections. A cell block section showing sheets of uniform cells with scant cytoplasm and a nucleus showing salt and pepper chromatin

was diagnosed as IDC neuroendocrine type. IHC was done on the cell block section. It showed weak chromogranin positivity. This was confirmed by histopathology. Cell block sections of IDC with medullary type showed sheets of neoplastic cells having pleomorphic nuclei and scant to moderate amount of cytoplasm, surrounded by lymphocytic aggregates. IHC markers like ER, PR, and HER/2neu were done on these sections. It showed triple negativity and hence was confirmed as basal-like cancer. In one case cell, block sections showed benign epithelial and myoepithelial cells arranged in the form of ducts and hence were diagnosed as fibroadenoma. One case was diagnosed as benign epithelial hyperplasia. The other four cell block sections were unsatisfactory for evaluation. Histopathological diagnosis of nine cases correlated with the cytological diagnosis of IDC and out of these three were diagnosed as IDC with NOS, three as IDC with lymph node metastasis, two as IDC-Medullary type, and one as IDC-NEC type. Five cases were diagnosed as fibroadenoma in histopathology and one as usual ductal hyperplasia.

Table 1: Cell block and histopathology correlation

Cell block diagnosis	No of the cases that correlated
Fibroadenoma (37)	23
Phyllodes (3)	3
IDC (29)	16

5. Discussion

5.1. Fibrocystic disease

Cell block diagnosis of fibrocystic disease (Figure 2 A,B) was made in 2 cases. This diagnosis was confirmed by histopathology in one case, other case was diagnosed as invasive ductal carcinoma. This disparity may be because the focal area of fibrocystic disease was seen in the second case which may have masked the underlying malignancy. A similar problem was reported by Dey and Luthra in their study.⁹ Other reasons for this disparity are stated in a study conducted by Sankaye et al where they say that malignancy may be missed mainly due to hypocellularity of the smears or sampling done from a non-representative area.¹⁰

5.2. Fibroadenoma

Cell block features of fibroadenoma in the present study were the presence of cells arranged in the form of monotonous clusters or as small ducts showing intracanalicular and peri-canalicular patterns surrounded by fibromyxoid stroma. Similar features were described by Rafat et al who conducted a study on the use of FNAC and cell blocks in the diagnosis of breast lesions.⁷

The fibroadenomas were diagnosed more accurately with the help of cell block than just FNAC as the architecture of these lesions was preserved (Figure 3 A,B)

and characteristic histopathological morphology could be observed.

5.3. Phyllodes

Fibroadenomas and phyllodes tumors share common cytological features like the presence of a dimorphic cell population made up of stromal and epithelial components. (Figure 4 A,B) The features that favored the diagnosis of phyllodes tumor in the present study include the presence of stromal hypercellularity with well delineated stromal fragments along with bare nuclei.¹¹ Similar features were described by Scolyer et al. They proposed that the presence of hypercellular stromal fragments is the most useful in distinguishing phyllodes tumor from fibroadenomas and the presence of nuclear atypia is useful in separating malignant phyllodes tumor from benign ones.¹²

5.4. Benign epithelial hyperplasia

In the present study, the cell block of two cases showed the presence of benign epithelial cell stratification intermixed with a population of myoepithelial cells along with small slit-like spaces. (Figure 1 A,B) Similar cell block findings for benign epithelial hyperplasia were described by Andrew F Fischer.¹³

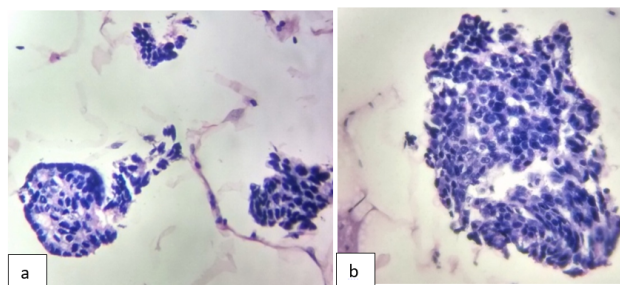


Fig. 1: A): Cell block sections of benign epithelial hyperplasia showing stratification of epithelial cells intermixed with myoepithelial cells (H&EX400); B): Cell block sections of benign epithelial hyperplasia showing stratification of epithelial cells intermixed with myoepithelial cells (H&EX400)

5.5. Atypical epithelial hyperplasia

In the present study, cell block findings of atypical epithelial hyperplasia were the presence of sheets or dyscohesive clusters of uniform cells with nuclear overlapping and a scant amount of cytoplasm with the absence of myoepithelial cells. (Figure 5 A,B) Andrew F Fischer described similar features in the cell blocks of atypical epithelial hyperplasia.¹³

In the present study, the histopathological correlation was possible in five patients, and all were diagnosed as malignancies in histopathology. This was comparable to the

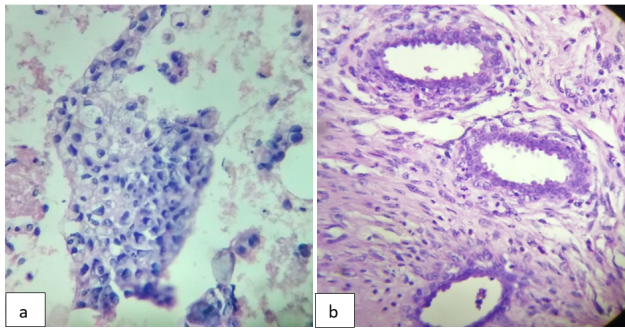


Fig. 2: **A):** Cell block section of fibrocystic disease showing foamy macrophages along with benign epithelial cells (H&E X400); **B):** Histopathology section of fibrocystic disease showing ducts lined by apocrine cells surrounded by fibrous tissue and chronic inflammatory infiltrate (H&E X400)

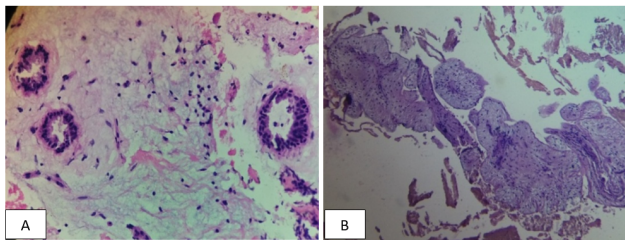


Fig. 3: **A):** Cell block sections of fibroadenoma showing peri-canalicular pattern of arrangement of benign epithelial cells surrounded by fibromyxoid stroma (H&E X400); **B):** Cell block sections of fibroadenoma showing fibromyxoid stroma compressing the benign epithelial cells (H&E X400)

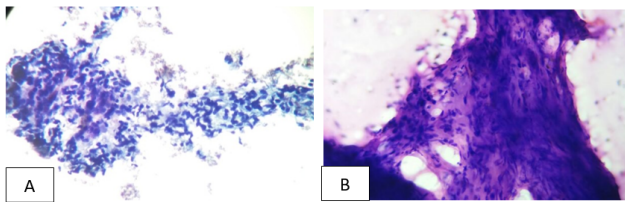


Fig. 4: **A):** FNAC smear of phyllodes showing stromal fragments (Giemsa X400); **B):** Cell block sections of phyllodes showing stromal fragments (H&E X400)

study conducted by Amrishi et al. who found a probability of 75% in finding malignancy in histopathology from cases having atypical findings in the cell block.¹⁴

5.6. Invasive ductal carcinoma

Cell blocks were used in the present study for further sub-classification of some of the malignant lesions. The cell block diagnosis correlated in 26 cases. The cell block features were like the FNAC features. They showed atypical ductal cells arranged in poorly cohesive clusters, with cells showing scant cytoplasm and hyperchromatic pleomorphic

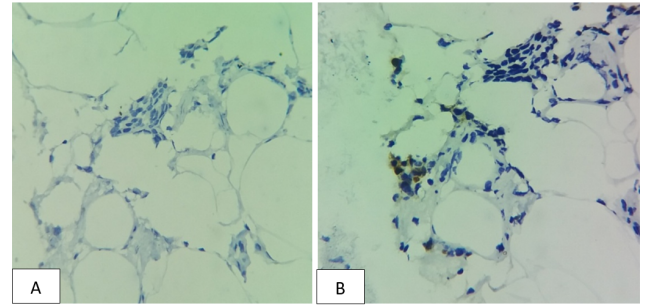


Fig. 5: **A):** Cell block sections of Atypical epithelial hyperplasia showing cells negative for CK-5 (IHC X400); **B):** Cell block sections of Atypical epithelial hyperplasia showing cells positive for ER (IHC X400)

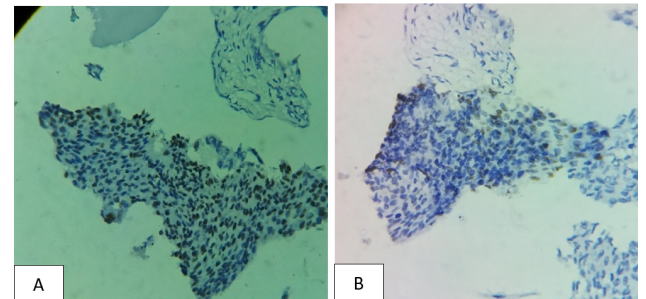


Fig. 6: **A):** Cell block section of ductal carcinoma showing cells arranged in poorly cohesive clusters showing ER positivity (IHC X400); **B):** Cell block section of ductal carcinoma showing cells arranged in poorly cohesive clusters showing PR positivity (IHC X400)

nucleus. Invasion of tumor cells into the surrounding stroma was seen in a few of the cell block sections. The invasion was identified by the presence of tumor cells in the adjacent stroma or adjacent adipose tissue either singly or in poorly cohesive clusters.

Similar features of invasion in cell blocks were described by Istvanic et al. who conducted a study on 40 rapid cell blocks of breast lesions. This study has also mentioned the criteria to diagnose invasion which includes the following—presence of malignant cells within the stromal tissue without adjacent myoepithelial cells, random pattern of arrangement of malignant cells concerning the surrounding tissue, and activation of the adjacent stroma.¹⁵

In the present study, the diagnosis of IDC- Medullary type and IDC- neuroendocrine type could be made using cell blocks that were earlier diagnosed as IDC by FNAC. The cell block sections of IDC- Medullary type (Figure 7 A) in the present study, showed the presence of syncytial growth pattern of tumor cells, high nuclear grade, lymphoplasmacytic infiltrate, and absence of tubular differentiation. Similar features were described by Ridolfi et al for the diagnosis of IDC- medullary type.¹¹ This

case showed triple negativity in IHC in the present study. (Figure 7 B,C,D)

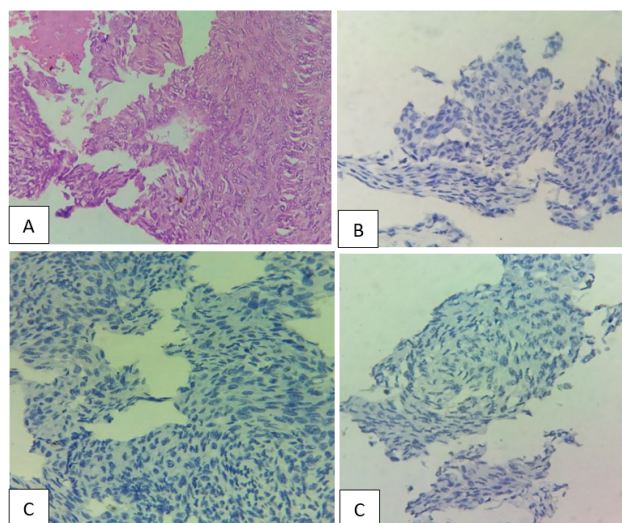


Fig. 7: **A):** Cell block section of Medullary carcinoma showing a syncytial pattern of arrangement of cells with high-grade nucleus (H&E x400); **B):** Cell block section of Medullary carcinoma showing which is negative for ER (IHC X400); **C):** Cell block section of Medullary carcinoma showing which is negative for PR (IHC X 400); **D):** Cell block section of Medullary carcinoma showing which is negative for HER 2 neu (IHC X400)

IDC-Neuroendocrine type was diagnosed in a 70-year-old female by cell block in the present study. The cell block features of the IDC-Neuroendocrine type in the present study included the presence of a monotonous population of cells arranged singly or in clusters with little variation in size and shape having cyanophilic cytoplasm and high nuclear to cytoplasmic ratio with granular chromatin and small nucleoli. (Figure 8 A) Sunita et al. have reported a case of primary neuroendocrine carcinoma of the breast in a 60-year-old female. Sunita et al in their study have used similar cytological criteria for the diagnosis of neuroendocrine carcinoma of the breast.¹⁶ IHC was done in the present study to confirm the diagnosis which showed chromogranin positivity. (Figure 8 B)

The sensitivity and specificity of cell block diagnosis of malignant lesion and atypical lesions in the present study was 77.77% and 82.85% (Table 2) compared to the study by Rafat et al, who evaluated the importance of the combined use of FNAC and cell block in diagnosing various breast lesions on 307 patients. They showed that the diagnosis by cell block had a sensitivity of 94% and specificity of 98%. PPV and NPV were also comparable to the study of Rafat et al. Sensitivity was slightly lower in the present because only a few cases had a histopathological correlation and, in a few cases, the cell block material was unsatisfactory for evaluation. The diagnostic accuracy of cell block was higher than FNAC in diagnosing malignant and atypical

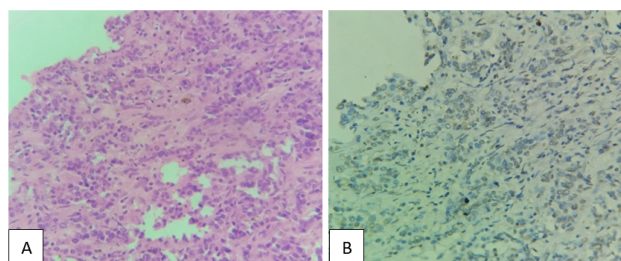


Fig. 8: **A):** Cell block section of IDC- NEC showing nests of uniform cells with round nuclei and stippled chromatin (H&E X400); **B):** Cell block section of IDC- NEC showing weak cytoplasmic positivity for chromogranin (IHC X400)

lesions.^{7,17,18}

Table 2: Diagnostic accuracy of cell block in comparison with other studies to diagnose malignant and atypical lesions

	Rafat et al ⁷ (2014)	Present Study (2017)
Sensitivity (%)	94	77.77
Specificity (%)	98	82.85
PPV (%)	94	70
NPV (%)	98	87.87
True positive (No of cases)	46	14
True negative (No of cases)	255	29
False positive (No of cases)	3	6
False Negative (No of cases)	3	4
Diagnostic accuracy (%)	98	81.13

6. Limitations of the Study

Due to the limited duration of the study, the sample size is smaller than expected and more sample size would have made the study more effective and authentic with an increased number of histopathological correlations. In addition, it was challenging to obtain adequate material for cell blocks. We have not performed IHCs in a greater number of cases due to financial restrictions and a lack of fully equipped lab facilities.

7. Conclusion

Breast masses are a source of anxiety for women especially of younger age as it has a risk of cancer and because of cosmetic disfigurement following surgery. Hence, there is a need for an accurate diagnosis of these breast lumps. FNAC of the breast is a minimally invasive, cost-effective, rapid, and simple technique to assess breast lumps. It has decreased the risk of morbidities like pain, infection, and hematoma as compared to other techniques like core biopsy.

We conclude that when FNAC is combined with a cell block the diagnostic accuracy has been increased. The cell block can be used to appreciate the architectural features that may not be possible using FNAC and ultimately makes the pathologist's job easier. Cell blocks have been shown to preserve nuclear architecture. It can characterize and recognize ductal proliferation. It can be used to detect the invasion of the malignant cell into the adjacent stroma. Cell block helps to overcome the limitation of breast FNA by its ability to diagnose invasion in ductal carcinoma of the breast. Cell block bridges the gap between cytology and histopathology by its property to complement FNA smears. Cell blocks also allow immunohistochemistry to be applied which increases the accuracy of the diagnosis further, in addition, can help to subtype certain tumors and find a primary site in case of metastasis.

8. Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary material. Raw data that support this study is available from the corresponding author upon reasonable request.

9. Source of Support

None

10. Conflict of Interest


None declared.


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