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Cytopathological correlation of cell block in ultrasound guided fine needle aspiration cytology

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Abstract
Introduction: Despite many advantages, at times FNA does not yield enough information for precise diagnosis, the material remaining in the hub or extra material can be used in Cell Block preparation. Present study was done to assess utility of USG guided FNAC with CB preparation in increasing sensitivity and diagnostic accuracy of deep-seated lesions.
Methodology: One-year cross sectional study carried out in a tertiary hospital, on 50 patients referred for USG guided FNAC of deep-seated lesions after considering inclusion/exclusion criteria. Consent and detailed clinical history were taken. After making conventional FNAC smears, Fixed sedimentation method was used for cell block preparation by flushing residual material in needle hub and syringe in 10% buffered formalin. Centrifugation at 3000 rpm was done for 10 minutes to form pellets, supernatant was decanted, deposit was wrapped in filter paper and processed as regular surgical tissue. FNAC smears and Cell block sections were examined and results were correlated with histopathology.
Results: Of the 50 cases, Sensitivity, specificity, and diagnostic accuracy of deep-seated lesions considering histopathology as gold standard was 86.96%, 100%, 88.0% for FNAC and 95.65%, 100%, 96.0% for Cell block and 97.83%, 100%, 98.0% for FNAC+ CB combined respectively.
Conclusion: Cell blocks as an adjuvant to FNAC smears is highly effective technique in cytology for definitive diagnosis.

Keywords: Fine Needle Aspiration Cytology (FNAC), Cell Block (CB)

Introduction

The global burden of cancer incidence in India as per the GLOBOCAN 2018 is 1,157,294 and accounts for 784,821 cancer deaths [1]. Diagnostic cytology is the science of interpretation of cells; either exfoliated cells of sputum, vaginal scrapes, body fluids, etc., or examination of cells collected by brushing, scraping, abrasive techniques, or FNAC. Accuracy of cytologic examination from any anatomic site depends on the adequacy of sample, quality of preparation, staining, and expertise of both the aspirator and cytopathologist.

Fine Needle Aspiration (FNA)/Radiologically (CT/ USG) guided FNAC of superficial or deep-seated lesions is becoming a common practice. It is cost-effective, rapid, minimally invasive and safe diagnostic procedure for the initial evaluation of the patient. It eliminates the need of time consuming, costly diagnostic procedures.

Aspiration performed under image guidance can provide the desired material from the representative site. In addition to the routine smears, preparation of cell block (CB) can further aid in the cytopathological diagnosis. The CB provides high cellularity, better architectural patterns, morphological features and an additional yield of malignant cells, and thereby, increasing the sensitivity of the cytodiagnosis when compared with the FNA smears alone. CB is also useful for categorization of tumor, that otherwise may not be possible from smears alone.

Thus, FNA and CB together can have a major impact on the patient management and in many cases, avoid diagnostic surgical procedure and expedite the planning for therapy.

Aims and Objectives

1. To access the role of Cell Block as an adjunct to smears for establishing a more definitive cytopathologic diagnosis in deep seated USG guided FNACs.

2. To correlate the findings of Cell Block with ultrasound guided FNAC, radiological and histopathology findings wherever feasible.

Material and Methods

The present study was conducted in the department of Pathology, R.N.T. Medical College and Associated group of hospitals, Udaipur, Rajasthan.

Cell blocks of 50 patients with space occupying deep seated lesions referred for USG guided FNAC were made after considering inclusion and exclusion criteria in a period of one year.

Inclusion criteria

1. All patients referred with clinical, biochemical and radiological evidence of Space Occupying Lesion (SOL)
2. Patients with normal Bleeding Time, Clotting Time and Prothrombin Time were subjected to USG guided FNAC.

Exclusion criteria

1. Patients who refused to undergo the procedure.
2. The patients in whom the lesion was very deep seated so that the lesion was not approachable by maximum length of LP Needle.
3. Patients diagnosed radiologically with hemangioma and hydatid disease of liver.
4. Patients in whom material was inadequate for preparation of cell block.

Procedure & Technique

After obtaining the relevant details of clinical history, physical examination and USG findings and explaining the possible complication of the procedure, USG guided FNAC was done.

Under all aseptic precautions, aspiration was done using a 22G disposable spinal needle. The depth from the skin to the lesion periphery was measured by using the USG images and the appropriate length of needle was inserted and position of needle was confirmed by USG. The samples were obtained by using aspiration with a 10 ml syringe. After suctioning some material obtained was expelled on the slide and spreading done by spreader slide immediately to prevent clotting. The smears were air dried and fixed in methanol for Field's staining.

The left-over material in the needle was used for Cell Blocks. For preparation of cell blocks the aspirated material was flushed into 10% neutral buffered formalin, pelleted by centrifugation, processed and embedded in the same way as routine biopsy specimens. Tissue sections were cut from cell blocks and stained with Hematoxylin and Eosin for morphological evaluation.

Histological correlation was carried out and considered as gold standard.

Results

All smears and corresponding CB were studied and a cytopathological diagnosis was made. The present study included 50 patients with mass in whom USG guided FNAC was performed. Out of the total 50 patients 21 were males and 29 were females with a male to female ratio of 0.72:1. The youngest patient was 13-year-old male child and oldest patient was 85-year female. The maximum number of patients were in the age group of 7th decade accounting to 26%. [Table 1]

The site wise distribution of lesion is shown in the [Table 2]. In our study, maximum number of cases were of liver origin. With both FNA and CB, cytopathological diagnosis was given out of which 16 were malignant lesions with 3 primary lesions (HCC) and 13 metastatic lesions. 1 Non neoplastic lesion was tumor like condition: regenerative nodule which showed sheets of hepatocytes with regenerative changes.

Rest of the cases were from other sites which included breast, ovary, deep seated lymph nodes, hypogastrium, kidney, soft tissue bone, retroperitoneum, gall bladder, lung, thyroid, left iliac fossa, left hypochondrium, paraspinous and mediastinal. The details of these cases with cytopathological diagnosis have been mentioned in the [Table 3].

Adequate material for FNAC and cell block was obtained in all 50 cases. On FNAC a definitive diagnosis was given for those with a sensitivity of 86.96% and on cell block with a sensitivity of 95.65%. With FNA cytology and cell block in combination a definitive diagnosis was given for 49 cases increasing the sensitivity to 97.83%. Table 4 and 5 shows the Statistical Analysis and results of Comparative evaluation of diagnostic utility of various methods in deep-seated lesions considering Histopathology as the gold standard.

Table 1: Age and Gender wise distribution of cases in the present study

Age (years)	Male (n=21)	Female (n=29	Total no. of cases (n=50)	Percentage %
Less than 10	1	2	3	06
21-30	2	1	3	06
31-40	1	1	2	04
41-50	3	7	10	20
51-60	5	7	12	24
61-70	7	6	13	26
71-80	2	4	6	12
>81	0	1	1	02

Table 2: Site of origin of abdominal masses

Site	No. of cases (n=50)	Percentage of cases
Liver	17	34
Breast	6	12
Ovary	7	14
Lymph node	5	10
Kidney	2	04
Gall bladder	1	02
Soft Tissue Bone	2	04
Hypogastrium	2	04
Lung	1	02
Retroperitoneum	2	04
Thyroid	1	02
Left Hypochondrium	1	02
Paraspinous	1	02
Left Iliac fossa	1	02
Mediastinum	1	02

Table 3: Diagnostic comparison of deep-seated neoplastic lesions: cytological diagnosis

Site / Organ	Diagnosis	FNAC Diagnosis (n=50)	Cell Block Diagnosis (n=50)	HPE Diagnosis (n=50)
Liver	Hepatocellular carcinoma (HCC)	3	3	3
	Metastatic carcinoma	13	0	0
	Metastatic Squamous cell carcinoma	0	3	4
	Metastatic Adenocarcinoma	0	9	9
	Regenerative nodule	1	1	1
	Non diagnostic	0	1	0
Kidney	Renal cell carcinoma	1	2	2
	Non diagnostic	1	0	0
Ovary	Cystadenocarcinoma Ovary	3	1	0
	Serous cystadenocarcinoma	1	3	4
	Mucinous cystadenocarcinoma	0	0	1
	Benign serous cystadenoma	1	1	1
	Benign ovarian neoplasm	1	0	0
	Teratoma	0	1	1
	Non diagnostic	1	1	0
Deep seated lymph node	Metastatic carcinoma	3	3	3
	Hodgkin's lymphoma	1	1	1
	Reactive lymphadenitis	1	1	1
Gall bladder	Malignant adenocarcinoma	0	1	1
	Non diagnostic	1	0	0
Soft Tissue Bone	Round cell tumor	1	0	0
	Metastatic carcinoma	0	1	1
	Osteosarcoma	0	1	1
	Non diagnostic	1	0	0
Hypogastrium	Malignant epithelial lesion	2	0	0
	Malignant Adenocarcinoma	0	1	1
	Squamous cell carcinoma	0	1	1
Lung	Inflammatory lesion	1	1	1
Thyroid	Follicular neoplasm	1	1	0
	Follicular carcinoma	0	0	1
Breast	Fibroadenoma	2	1	1
	Phyllodes	0	1	1
	Infiltrating ductal carcinoma	2	3	3
	Mastitis	1	0	0
	Granulomatous lesion	0	1	1
	Non diagnostic	1	0	0
Left hypochondrium	Malignant Adenocarcinoma	1	1	1
Paraspinous	Inflammatory lesion	1	0	0
	Plasma cell disorder	0	1	0
	Plasmacytoma	0	0	1
Retroperitoneum	Sarcomatous lesion	1	0	0
	Lipoma	1	1	1
	Undifferentiated Pleomorphic Sarcoma	0	1	1
Left iliac fossa	Malignant Adenocarcinoma	1	1	1
Mediastinum	Metastatic lesion	1	0	0
	Metastatic seminoma	0	1	1

Table 4: Statistical Analysis - Comparative evaluation of diagnostic utility of various methods in deep-seated lesions

	FNAC	Cell Block	FNC+ Cell Block	HPE
Neoplastic	40	44	45	46
Non- Neoplastic	5	4	4	4
Non- Diagnostic	5	2	1	0
Total	50	50	50	50

Table 5: Statistical analysis Results: of different diagnostic methods in diagnosis of guided FNAC lesions

	FNAC	Cell block	FNAC + Cell Block
Sensitivity %	86.96	95.65	97.83
Specificity %	100	100	100
Diagnostic accuracy%	88.00	96.00	98.00

Discussion

Despite many advantages, at times FNA does not yield enough information for precise diagnosis and the risk of false negative or intermediate diagnoses always exists. This may be due to poor spreading, air drying artifact, and presence of thick tissue fragments despite aspiration of adequate material [2].

Large amount of material remains in the needle hub after preparation of smears and this is generally discarded. The material that remains in the needle hub can be used in CB preparation, thus, increasing the sensitivity of diagnosis.

Doctor Leopold Koss has written: "The cell block technique should be used for processing all residual material remaining after completion of cytological preparations. This material often contains useful information" [3].

Cell block (CB) refers to the collecting of sediment, blood clots, or grossly visible pieces of tissue from cytologic specimens that are processed into paraffin blocks and stained mainly by hematoxylin-eosin [4, 5].

It offers many advantages over other cytological preparations. Architectural features, particularly of small tissue fragments, are best appreciated in a CB [6].

CB with on-site cytopathological evaluation of direct FNA smears can increase diagnostic yield, improve tumor sub classification and further molecular testing in solid organ tumors [7,8].

In the present study, the role of CB in guided FNA of deep-seated lesions was assessed in 50 patients. 26% of cases were in their 7th decade of age, which can be compared with the findings of Mathew EP *et al.* [9] (2017) in which maximum number of cases were between 61 and 70 years of age.

In our study the diagnostic sensitivity of smears alone was 86.96%. FNAC is an important diagnostic tool but CB was introduced to improve the accuracy.

In our study, out of 50 cases, 92% cases were reported as neoplastic and 8.0% as non-neoplastic. This is comparable to the study by Rastogi N *et al*., who had 89.47% malignant lesions [10].

In liver lesions cases, with FNA smears diagnosis of hepatocellular carcinoma was made but the CB sections showed distinct patterns like trabecular, solid and acinar. 13 cases were reported as metastatic carcinoma deposits to liver, out of which 9 cases were reported as metastatic adenocarcinoma. 4 were reported as metastatic deposits probably of squamous origin on HPE. CB played an important role in recognizing the architectural pattern and thus aided in arriving at a diagnosis in these cases.

We encountered 5 cases where aspiration was non-diagnostic possibly because of tumor necrosis, failure of cytological interpretation, hemorrhagic / fluid like aspirate. However, cell block had enough material and a cytopathological diagnosis was given. 1 was a case from the kidney smears showed hemorrhage only while CB sections showed clusters of tumor cells with eosinophilic cytoplasm, hyperchromatic nuclei and a prominent nucleolus. Taking clinical, radiological and CB findings into consideration diagnosis of Renal cell carcinoma was made [Figure1, 2]. Another case of Gall bladder FNA smears showed only bilious material but was confirmed to be malignant adenocarcinoma on cell block. One case of breast showed only necrosis on FNAC was found to be Infiltrating duct carcinoma due to better preservation of cells by centrifugation for cell block. One case diagnosed as fibroadenoma on FNA was confirmed to be phyllodes tumor on cell block and HPE due to presence of abundant stroma and better architectural preservation. One case from paraspinous region was reported as inflammatory lesion on FNAC but was found to be plasma cell disorder on Cell Block and confirmed as Plasmacytoma on HPE. Another case from soft tissue bone which showed appearance of round cell tumor was diagnosed as metastatic carcinoma on cell block and confirmed by HPE based on clinical details, radiological and biochemical investigations. Case diagnosed as follicular neoplasm on FNAC, and Cell Block was diagnosed as follicular carcinoma on histopathology. One case of liver which was non diagnostic on cell block was reported as metastatic carcinoma on FNA smears.

One case which was non diagnostic on both FNAC and cell block was diagnosed as serous cystadenocarcinoma on HPE due to aspiration of serous fluid only. One case each from retroperitoneum and mediastinum could be accurately typed on cell block as undifferentiated pleomorphic sarcoma and metastatic seminoma and confirmed on HPE. [Figure 3,4]

Thus, an overall improvement in the final diagnosis was noted where smears were complemented by CB. With FNA and CB together, provided a definitive cytopathological diagnosis in 49 cases, increasing the sensitivity to 97.83%. When both the techniques were combined, the diagnostic accuracy reached to 98.0%. Patel MJ *et al.* [11] and Parate S *et al.* [12] also found complimentary use of cell block and FNAC to be beneficial. [Table 6]

Table 6: Statistical comparative diagnostic (FNAC + Cell Block) Analysis of deep-seated lesions (except thoracic) in different studies

Studies	Sensitivity%	Specificity%	Diagnostic Accuracy (%)
Patel MJ *et al.* (2018) [11]	96	100	96
Parate S *et al.* (2019) [12]	98.53	93.33	96.94
Present study (2019)	97.83	100	98.0

Conclusion

Cell block method allows recovery and processing of minute cellular material, facilitating better classification and increasing sensitivity and diagnostic accuracy for diagnosis of neoplastic lesions when cell block method is combined with conventional smears. Therefore, the routine preparation of the cell block improves the accuracy of fine needle aspiration cytology diagnosis. However, if cell block analysis is not possible for all aspirations, the technique should be used selectively in cases that are difficult to diagnose in smears.

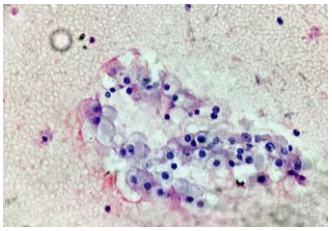

Fig 1: Cell Block preparation of Renal mass aspirate showing group of cells with clear cytoplasm, centrally placed round nucleus and granular nuclear chromatin suggestive of Clear cell Carcinoma Kidney. (H&E stain; X400)

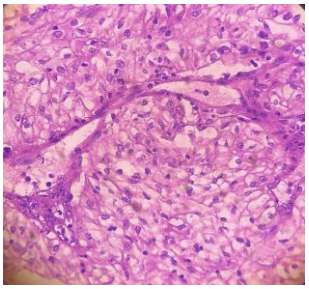

Figure 2: Corresponding Histopathological section of Renal mass showing nest and sheets of clear cells with centrally placed nucleus and indistinct nucleoli suggestive of Clear cell Carcinoma. (H&E stain; X400)

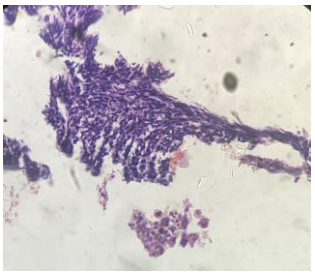

Fig 3: Cell Block preparation from Soft tissue Bone mass showing tissue fragment of malignant spindle cells with high grade nuclear features suspicious of Sarcoma. (H&E stain; X200)

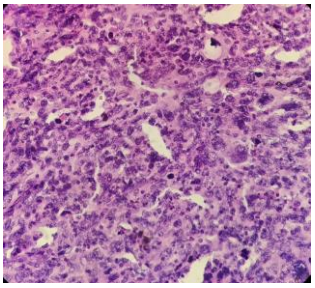

Fig 4: Corresponding Histopathological section showing spindle to epithelioid cells with marked nuclear pleomorphism and tumor giant cells suggestive of Undifferentiated Sarcoma. (H&E stain; X200)

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