

Diagnostic Utility of Pleural Fluid Cytology versus Cell Block Technique: A Comparative Study

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ABSTRACT

Introduction: Categorization between benign and malignant pleural effusions most often create diagnostic dilemma. Categorization often requires clinical findings and morphological evaluation. Diagnostic possibility is increased if cell blocks are performed in addition to conventional cytology smears. This will help the clinicians in both treating the patient and determining the outcome of the disease process. **Aims:** The aim of this study was to compare the smears cytology with cell blocks sections in pleural effusions. **Methods:** This hospital-based cross sectional analytical study was carried out in Department of Pathology in Nepalgunj Medical College, Nepalgunj for one year. **Results:** The four criteria scored for each technique were amount of background blood, yield of diagnostic cellular material, degree of cellular degeneration as well as cellular trauma and architectural preservation. More amount of diagnostic material present and appropriate retention of architecture was more in cell block sections compared with smears cytology; whereas cellular degeneration as well as cellular trauma and background blood was less appreciated in cell block sections which scored more than the smears cytology. **Conclusion:** Cell block method especially in clinically, radiologically and cytologically suspected malignant cases should be routinely processed for cell block method.

Keywords: Cell block technique, pleural fluid cytology examination

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INTRODUCTION

Excess amount of accumulated fluid in pleural space is referred as pleural effusion.¹ Pleural effusion is an abnormal accumulation of fluid in the pleural cavity and presents as a major abnormality of pleural disorder.² Thoracentesis is a testing process for patients diagnosed with pleural fluid.³ Pleural fluid obtained by this procedure is sent in laboratory department for biochemical, microbiological, and cytological examination.⁴ In cases with pleural effusion, cytological analysis is one of the initial routine investigations especially in suspicion for malignancy. In addition to cytological analysis, pleural fluid can be further processed and examined with the cell block technique, which generally augments the diagnostic utility.⁵ Diagnostic problems arise in routine cytology practice to differentiate reactive atypical mesothelial cells and malignant cells by the routine conventional smear method for pleural fluid.⁶ Cell block method is cost effective as well as superior method of diagnosis in addition to cytological examination.⁷ Cell block diagnostic method has been less routinely used for pleural fluid diagnostic method in Nepal, which is mainly due to lack of required diagnostic tool.⁸ This study aims to find out current trend in diagnostic yield of cell block in addition to routine conventional pleural fluid cytological examination.

METHODS

This is a hospital based cross-sectional study and was conducted on patients with pleural effusions who underwent thoracentesis from April 2020 to March 30th 2021 at department of pathology, Nepalgunj Medical College, Nepalgunj. All samples were submitted for routine conventional pleural fluid cytology examination and portion of pleural fluid was also examined for cell block technique in histology. The results of cytopathological studies with reactive mesothelial cells and suspected malignant cases were compared to the final diagnoses of cell block histology.

Preparations of cell block technique: 2 to 5 ml of pleural fluid was centrifuged at 2,500 rpm for 5 min and supernatant was removed. One part of 40% formaldehyde (formalin) and nine parts of 95% methanol is used as fixative for formation of cell block method.^{9,10} Remaining fixed tissue kept in filter paper (Whatman) and was processed into a paraffin embedded block. A histological slide was cut and hematoxylin and eosin (H & E) staining was performed in cases with reactive mesothelial cells and malignancy. Samples were examined for cytology as well as cell block and scored according to

methodology described by scoring system of Thapar M et al and Mair S et al.^{10,11} After assigning the appropriate scores, the cases were divided into 3 categories, which consisted of “diagnostically superior” (score 6-9), “diagnostically adequate” (score 3-5), “diagnostically unsuitable” (score 0-2).

Statistical analysis

Data were entered in excel. Data was analysed using Statistical Package for the Social Sciences (SPSS) version 23.

Inclusion criteria: All pleural fluids collected during study period in pathology department were included in study.

Exclusion criteria: All other body fluids except pleural fluids were excluded from study.

RESULTS

During the period of one year, there were total of 144 pleural fluids submitted for cytological examination. Among 144 cases which were included in study; 78 (54.2%) were male and 66 (45.8%) were female. The mean age for pleural effusion cases was 49.4 ± 29.4 years. Least age was of 7 years and highest was of 89 years. Most of the cases were in age group 61 to 70 years with male predominance and 29 (20.1 %) cases as in Table I.

Age group	Gender		Total
	Female	Male	
0 -10	0	3	3
11-20	7	3	10
21-30	12	17	29
31-40	9	5	14
41-50	7	2	9
51-60	12	14	26
61-70	7	22	29
71-80	9	9	18
81-90	3	3	6
Total	66	78	144

Table I: Age distribution according to gender

Among total 144 cases; 13 cases (9%) were diagnosed as negative for malignancy in cytology which comprises mesothelial cells only. Two cases (1.4%) were suspected for malignancy in conventional cytological techniques. Remaining 129 cases (89.6%) reveal inflammatory cells in pleural effusion.

Among 129 inflammatory pleural effusions; 103 cases (71.5%) were of lymphocytic pleural effusion, 23 cases (16%) were of neutrophilic pleural effusion and 3 cases (2%) were of eosinophilic pleural effusion.

Out of 144 cases, 35 pleural fluid cytology cases revealing reactive mesothelial cells and suspected for malignancy in cytology were further processed for cell block examination. Two cases which were suspected for malignancy in cytology

shows superior morphology in cell block preparation and were diagnosed as positive for malignancy.

	Cytology Diagnosis	CELL BLOCK			Positive for malignancy	Total
		Eosinophilia	Lymphocytosis	Neutrophilia		
Eosinophilia	3	0	0	0	0	3
Lymphocytosis	76	0	27	0	0	103
Negative for malignancy	13	0	0	0	0	13
Neutrophilia	17	0	0	6	0	23
Suspicious for malignancy	0	0	0	0	2	2
Total	109	0	27	6	2	144

Table II: Distribution of cases in cytology and cell block

Cytological smears in 35 cases revealing reactive mesothelial cells and suspected malignant cases which was further processed for cell block techniques were compared for their quality by using the point scoring system with reference to Thapar M and Mair et al.^{10,11} It was identified that 3% of the cytological smears and none of cell blocks among 35 cases scored 0 and was unsuitable for definitive diagnosis and was reported with final diagnosed as lymphocytosis in cytology and cell block examination (Table III). 34% of the smears and 29% of cell blocks were considered to be diagnostically superior (Table IV).

Criteria	Score	Cell blocks	Number	Cytology smears	Number
Minimal: Diagnosis easy.	2	26%	7	42%	15
Moderate amount: Diagnosis possible	1	74%	26	54%	19
Large amount of blood and clot: diagnosis greatly compromised	0	0	0	3%	1

Table III: Background blood in smears and cell blocks

Criteria	Score	Cell block	Number	Smears	Number
Abundant: Diagnosis simple	2	34%	12	29%	10
Sufficient for diagnosis	1	66%	23	71%	25
Minimal or absent: Diagnosis not possible	0	0	0	0%	0

Table IV: Amount of diagnostic material present in smears and cell blocks

Criteria	Score	Cell block	Number	Smears	Number
Minimal: Good preservation	2	37%	13	29%	10
Moderate: Diagnosis possible	1	63%	22	71%	25
Marked: Diagnosis impossible	0	0%	0	0%	0

Table V: Amount of diagnostic material preservation in smears and cell blocks

Criteria	Score	Cell block	Number	Smears	Number
Excellent architectural display closely reflecting histology	2	20%	07	17%	06
Moderate: some preservation e.g. follicles, papillae acini, syncytia or single cell pattern	1	80%	28	83%	29
Minimal to absent: Non diagnostic	0	0%	0	0%	0

Table VI: Retention of appropriate architecture and cellular architecture in smears and cell blocks

More amount of diagnostic material present and appropriate retention of architecture was more in cell block sections compared with smears cytology; whereas cellular degeneration as well as cellular trauma and background blood was less

appreciated in cell block sections which scored more than the smears cytology. Adequacy for diagnosis was compared and assessed for cytological and cell block techniques and diagnostically superior smears were shown by cell blocks as compared to cytological smears. The diagnostic yield was increased by cell block techniques in addition to examination of cytological specimens. Cell block technique increased the diagnostic yield as compared to cytological smear only.

Conventional cytological smear and cell block provided similar diagnostic yield. However, a combination of cytological smear and cell block gave a higher yield of diagnostic material especially in malignant cases compared to cytological smear alone.

DISCUSSION

Present study included all pleural effusion samples irrespective of the clinical or radiological findings of the patient. More of benign and inflammatory pleural effusions were identified in cytology and cell block. Study done by Joshi A et al and Miachio N et al also reveal similar findings.^{12,13}

Among 144 cases in present study, 13(9%) cases were reported as negative for malignancy in cytology. Similar findings were observed by Thapar M et al as among 190 cases, 26(37.2%) were showing features of negative for malignancy in cytology.¹⁰

2 cases out of 144 pleural fluid specimens (1.38%) were reported as malignancy. Only two cases of cancer in pleural effusion in our study were due to sample obtained from general hospital treating mainly non-cancerous patients. Similar low cases (3 out of 37 cases) were observed by Bista P et al.⁸ Nonmalignant cases were broadly categorized into reactive and malignant effusions as done by Bista P et al.⁸

Cytological smears stained with the giemsa and Papanicolaou technique yield adequate result of malignant cellular changes. In addition to cytological smears, cell blocks are helpful when cytological findings are misleading, especially in reactive mesothelial cells smears obscure with blood and inflammatory cells as well as in malignant cases.¹⁴

To augment and uplift the diagnosis from cytohistology of pleural fluid, the sediment from centrifuged pleural fluid can be processed as cell block for histology. Although cell block technique has been well established technique among pathologists, it is still underprescribed by clinicians. Therefore, this study was conducted this study to identify the benefits of cell block when assessed as a part of pleural fluid examination in routine clinical practice. Cell block was prepared with alcohol formal fixative which was followed by simple paraffin processing and similar procedure was used by Nathan NA et al.¹⁵ Cell blocks obtained from residual fluids in addition to smears aids on more definitive cytopathologic diagnosis.¹³

Age of the patients with pleural effusions ranged from the age of 7 to 89 years. This was similar to the age range in the study done by Davidson B et al.¹⁶ The majority of the patients were in the sixth decades of life. The male: female ratio of the studied

patients was 1.18:1. Similar male predominance was found in study by Shivakumarswamy U et al.¹⁷ Both cytological and cell block showed good cellular architecture in malignant cases but the overall findings in cell block in terms of cellular architectures like acini, cell ball, and papillary pattern also helped in giving idea and hint about the origin of the primary tumor. Similar findings were found in studies done by Mulkalwar M et al.¹⁸

One of the problems with the reactive effusion is the way some cell may appear or mimic malignancy which can lead to difficulty in diagnosis. We have encountered 2 such cases in cytology which were diagnosed as suspicious for malignancy. However on doing cell block and reviewing the slides the morphology were clearly malignant. Similar results were found in studies done by Santwani PM et al and Pal M et al.^{19,20}

LIMITATIONS

This study was conducted in one hospital setting; it would have been more informative if it covered other areas of the country as well. All 144 pleural fluid cases could not be processed for cell block examination. Also, a more detailed study in cell block method with immunohistochemistry could not be performed because of lack of immunohistochemistry procedure in Nepalgunj Medical College.

CONCLUSION

Lymphocytosis is the most frequent diagnosis in pleural fluid cytology. Cases for suspicious of malignancy are confirmed by cell block method. Considering the findings, it can be concluded that suspicion for malignancy in cytology can be confirmed by cell block method. Cell block method especially in clinically, radiologically and cytologically suspected malignant cases should be routinely processed for cell block method. Cell block preparation is simple, rapid and inexpensive technique for pleural fluids in which malignant cells can be reliably detected thus avoiding unnecessary invasive procedure in patient management. It is recommended medical personnel involved in treatment procedure for pleural fluid cytology as well as other fluid cytology to consider for cell block method with cell block histopathological diagnosis as a routine procedure.

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