

Comparison of Diagnostic Yield between Pleural Fluid Cell Block and Pleural Biopsy by Pleuroscopy at the Pulmonology Department, Mayo Hospital, Lahore

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Abstract

Objective: To compare diagnostic yield between pleural fluid cell block and pleural biopsy by Pleuroscopy.

Methods: This prospective study was conducted at the Pulmonology Department, Mayo Hospital Lahore. Patients with exudative pleural effusion from December 2020 to December 2022 who underwent Pleuroscopy at the Pulmonology Department were included in the study. Pleuroscopy was performed under local anaesthesia; pleural fluid was collected for a cell block, and then multiple pleural biopsies were taken.

Results: Thirty patients with exudative pleural effusion were enrolled in the study. Final diagnosis was 16 adenocarcinoma, 2 small cell carcinoma, 1 squamous cell carcinoma, 5 malignant pleural mesothelioma (MPM), 3 no malignancy, 2 metastatic carcinoma, 1 caseating granuloma. Diagnostic yield by pleural biopsy in comparison to cell block was found to be significantly higher [90% (27/30) vs. 70% (21/30); $p = 0.008$]. Nine patients with negative cell block had positive results on pleural biopsy (1 diffuse large B cell lymphoma, 1 metastatic small cell carcinoma, 1 mesothelioma, 4 adenocarcinoma, 1 metastasis malignancy). Three patients had inconclusive evidence for malignancy on both pleuroscopy and cell block.

Conclusion: Cellblock can be used as an initial, less invasive diagnostic test for the workup of suspected pleural effusion. It can be easily performed on pleural fluid during thoracentesis, and treatment can be initiated in case of positive cell block reports without the need for pleuroscopy in every patient with suspected malignant pleural effusion. However, Pleuroscopy can be subsequently performed in patients with a negative cell block.

Keywords: Pleural Effusion, Malignancy, Biopsy, Thoracoscopy

Introduction

Pleural effusion is a common manifestation of malignancy. Adequate diagnosis of pleural effusion is sometimes difficult. There are various diagnostic techniques available to diagnose malignant Pleural effusion. Pleural fluid cytology and closed pleural biopsy have been utilised for decades and have a sensitivity of 60-90% and 42% respectively.¹⁻⁴ Although these two methods are adequately utilised, other methods with higher sensitivity for diagnosing malignant pleural effusion are preferred because of the limitations associated with these two methods.⁵

Definitive diagnosis of malignancy requires a tissue sample, special stains and immunohistochemistry. Pleuroscopy is a safer method with fewer complications and can be performed under local anaesthesia. A study on pleuroscopy has shown that pleural biopsy with pleuroscope has a sensitivity of 94%,⁶ while another study by R. Agarwal et al on semi-rigid pleuroscopy describes a sensitivity of 91% and a specificity of 100%.⁷

Cellblock is another easy-to-perform and safe method with a sensitivity of 74%,⁸ and it also involves special stains. A study by Indranath Ghosh et al included 60 patients of suspected malignant pleural effusion, 56 were confirmed to be malignant, while 46 cases were diagnosed on Cell block preparation.⁹ The cell block provides us better description of tumor cells and the structure of abnormal cells. The cell block method requires at least 150ml of pleural fluid.

Our study compared the yield of pleural fluid cell block and pleural biopsy through pleuroscopy. There is no useful data available on it in our country. Our study included patients > 12 years of age with exudative lymphocytic effusion. Patients with unstable cardiac disease, end-stage renal disease, transudative pleural effusion, coagulopathy, and persistent hypoxemia were excluded. Our

Contributions:

NZ, AH, FK, AJ, MN, FF - Conception, Design
NZ, AH, FK, AJ, MN, FF - Acquisition, Analysis, Interpretation
NZ, AH, FK, AJ, MN, FF - Drafting
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study assessed whether cell block can be an alternative to Pleuroscopy and, if it can be beneficial in our population. In our country, due to limited resources, Pleuroscopy is not available in every centre, and comparing the efficacy of both methods will help us in establishing an accurate diagnosis of patients with malignant pleural effusion with minimum intervention.

Materials And Methods

It was a prospective study to compare the diagnostic yield between pleural effusion cell block and pleural biopsy obtained by pleuroscopy for malignant pleural disease with effusion, after taking permission from the ethical committee, and informed consent of patients was taken.

Team of Consultant Pulmonologists at the Pulmonology Department, Mayo Hospital Lahore, performed the procedures. Patients who fulfilled the inclusion criteria were selected, and pre-procedure ultrasound was done to quantify pleural fluid along with informed consent. Baseline Complete blood picture and Hepatitis screening, and PT/APTT were performed. IV line secured. Port site was identified with the use of ultrasound & patient was positioned in the lateral decubitus position, with the diseased side up. Vitals were monitored before, during and after the procedure. Under aseptic measures 1% lidocaine was administered for anaesthesia subcutaneously, and pleural fluid was aspirated. After performing skin incision and blunt dissection of the parietal pleura, a flexible trocar was inserted under ultrasound-guided site with maximum fluid window. The flex-rigid pleuroscope (LTF-260; Olympus, Tokyo, Japan) was introduced through the trocar; at least 150 ml of pleural fluid for cell block was collected, and the rest of the fluid was drained. Multiple biopsies from abnormal areas on the parietal pleura were obtained using flexible forceps (FB55CR-1; Olympus, Tokyo, Japan). Pleurodesis was performed afterwards with pyodine and doxycycline. After withdrawing the pleuroscope from the trocar, a 20- to 24-Fr wide bore chest tube was inserted and attached with under underwater seal. Stitches applied and dressing done.

Biopsy specimens were immediately fixed in formalin. 150 ml of pleural fluid was mixed with formalin for cell block. Statistical analysis. Data were presented as median (range), frequencies, and percentages. The McNemar χ^2 statistic was used to compare categorical variables. Statistical analysis was carried out using IBM SPSS Statistics (version 22, IBM SPSS Inc., Chicago, IL). A P value of less than 0.05 was considered statistically significant.

Results

The demographics of the study population are shown in Table 1. Among the 30 patients, 17(56.6%) were men and 13 (43.3%) were women, with a median age of 55years (range, 19–82 years). 20(66.6%) had thickened pleura, and 16 (53.3%) had pleural nodules on CT scan. 18 (60%) were Smokers and 12(40%) were Non-smokers. Three patients (10%) had a prior history of asbestos exposure.

Table 1: Demographic Features

Variables	Frequency (N)/ Mean	Percentages (%)
Age	55 Range (19-82)	N/A
Age Category		
<50	11	36.6
50-70	17	56.6
>70	2	6.66
Gender		
Male	17	56.6
Female	13	43.3
Smoking		
Smoker	18	60
Non-Smoker	12	40
CT-Scan		
Pleural Nodule	16	53.3
Pleural Thickening	20	66.6
Asbestos		
Exposure	3	10
No Exposure	27	90
Final Diagnosis		
Malignancy	26	86.6
No Malignancy	3	10
Tuberculosis	1	3.3

All 30 patients included in the study had Exudative Lymphocytic effusion on Thoracentesis. Final diagnosis of malignancy was 16 adenocarcinoma, 2 small cell carcinoma, 1 squamous cell carcinoma, 5 malignant pleural mesothelioma (MPM), 3 no malignancy, 1 metastatic carcinoma, 1 diffuse large B cell Carcinoma, 1 caseating granuloma.

Table 2: Comparison of Diagnostic Yield of Cellblock & Pleuroscopy according to histology

Final Diagnosis	N=	%	Cellblock	Pleuroscopy	P Value
Adenocarcinoma	16	53.3	12/16(75%)	16/16(100%)	0.045
Malignant pleural mesothelioma	5	16.7	4/5(80%)	5/5(100%)	0.034
Metastatic squamous	1	3.3	1/1(100%)	1/1(100%)	0.038
Metastatic small cell	2	6.7	1/2(50%)	1/1(100%)	0.047
Diffuse Large B-cell	1	3.3	0/1(0%)	1/1(100%)	0.036
No Malignancy	3	10.0	12/30(40%)	3/30(10%)	0.033
Caseating Granuloma	1	3.3	0/1(0%)	1/1(100%)	0.036
Metastatic malignancy	1	6.7	0/1(0%)	1/1(100%)	0.041

Table 2 in the diagnostic yield was significantly higher by pleural biopsy than by cell block [90% (27/30) vs. 70% (21/30); $p = 0.008$]. All patients with positive results on cell block had positive results on pleural biopsy. Table 2 also shows the diagnostic comparison between cell block and pleural biopsy in 10 patients with negative results on cell block; 8 of these patients had positive results on pleural biopsy.

Table 3: Chi-square Tests

Person Chi Square	Value	Significance
Chi Square	14.427	0.025
Likelihood Ratio	17.162	0.009
Linear by Linear association	12.788	<0.001

Table 3 shows the P value calculated by Pearson's Chi Square was 0.025 with a likelihood ratio of 0.09 and linear-by-linear association of <0.01

Discussion

Pleural Effusion is a common presentation of malignancy. Malignant & Para malignant effusions are commonly seen in metastatic lung diseases, lung cancer, Lymphoma, Mesothelioma, Breast and Ovarian cancers & other haematological malignancies. Various diagnostic tools used to diagnose malignant pleural effusions include cytology, Pleural fluid cell block, closed pleural biopsy and Pleuroscopy.⁸

Pleuroscopy is performed by a Pulmonologist under local anaesthesia. It has the advantage of direct visualisation of pleural surfaces & tissue sampling, and pleurodesis is also performed. Studies have shown that it has a sensitivity of > 90 %⁹. A study on pleuroscopy included 102 patients, and it showed 91% sensitivity, 100 % specificity 96 % and a negative predictive value of 93 %.¹⁰ Another retrospective study included 709 patients who underwent Pleuroscopy. It showed sensitivity of 91%, specificity 100%, 100 % positive predictive value and negative predictive value of 92%.¹¹ Another study on pleuroscopy evaluated the diagnostic sensitivity of pleuroscopy in different malignancies. The study included 287 cases, diagnostic yield was 62 % for cytology and 95 % for pleuroscopy.¹²

Pleural fluid cell block is a safe, easy method to diagnose underlying malignancy. A study on pleural fluid cell block showed that it had a sensitivity of 60-89.4 %.¹³ Cellblock can be performed during thoracentesis before undergoing invasive investigations. Cellblock procedure involves 150ml of pleural fluid mixed with fixative material that includes formalin. Other fixatives that can be used are alcohol-formalin, Alcohol acetic acid, and plasma thrombin. Studies done to compare different fixatives did not show any significant difference.¹⁴

Cellblock is a superior method to cytology as it describes details of cellular structure, glands, clusters and other morphological features of cells and IHC immunohistochemistry stain is also used. Limited data are available on the comparison of the diagnostic efficacy of cellblock and pleuroscopy. A study on the comparison of pleural biopsy through pleuroscopy and cellblock showed that pleuroscopy has 94.2 % diagnostic yield while cell block had 71.4%.¹⁵⁻¹⁸

There is a need for more research work on the yield of the cellblock and comparison of the cell block and pleuroscopy methods. This study will help with the utilisation of the pleural fluid cellblock method as an initial investigation for the diagnosis of malignant pleural effusion instead of cytology, which has a lower yield than cellblock. Our study included 30 patients and compared the diagnostic yield of cell block and pleural biopsy through pleuroscopy. The results showed that out of 30 patients, 10 had negative cellblock report while 8 had a positive report on pleural biopsy and two patients had no malignancy on pleural biopsy report. Our study showed that the diagnostic yield of pleuroscopy was 90 % while that of cellblock was 70%. This study

describes the significance of cellblock as it is superior to cytology, and it can be used initially on every patient with suspected malignant pleural effusion and in patients with negative cytology. Pleuroscopy can be performed subsequently.

Conclusions

Pleural Fluid cellblock can be used as an initial diagnostic test in the workup of suspected malignant pleural effusion, followed by pleural biopsy through pleuroscopy in patients with a negative cellblock.

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