

ORIGINAL RESEARCH

A Hospital Based Prospective Study to Evaluate the Role of Closed Pleural Biopsy in Diagnosing Exudative Effusions Not Diagnosed by Pleural Fluid Analysis at Newly Established Tertiary Care Center

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ABSTRACT

Background: Pleural effusion is a collection of fluid in the Pleural space. Determining the cause of a pleural effusion is greatly facilitated by analysis of the pleural fluid. Etiological diagnosis in of those cases is a diagnostic challenge to the clinician because even after all cumbersome work-ups some cases remain undiagnosed. Pleural effusion remains undiagnosed after routine tests in pleural fluid in many patients. so, we need a simple and safe investigative tool to evaluate undiagnosed effusion. This study is designed to diagnose the cases of undiagnosed effusions by a simple and safe investigative tool.

Materials & Methods: A hospital based prospective study done in 30 patients with exudative pleural effusion remain undiagnosed after pleural fluid analysis in department of respiratory medicine at government medical college, Bhilwara, Rajasthan during one-year period. Pleural fluid sent for basic biochemical and microbiological investigations. Pleural biopsy was performed using ABRAM'S pleural biopsy needle under strict aseptic precaution under local anesthesia and the specimen was sent for the following investigations such as histopathological examination, rt-PCR and culture for Tuberculosis by BACTEC.

Results: Histopathological examination diagnosed 46.66% of biopsy specimens as tuberculosis and 23.33% as malignancy. The rest 30% of case were left undiagnosed after histopathological examination of Pleural biopsy. Reverse Transcriptase Polymerase Chain reaction was positive in 16.66% of the cases and was negative in 83.33% of the cases. Our study shows that tuberculous pleural effusion is more common in the younger age group and malignant pleural effusion more common in the elder age in both males and females. There were no false positive results with histopathological examination, BACTEC & rt PCR making the specificity and positive predictive value as 100%. The sensitivity was 70%, 10% & 25% respectively and negative predictive value was 60%, 35% & 40% respectively in tuberculosis patients.

Conclusion: We concluded that combination of histopathological examination, BACTEC culture and rtPCR reaction in closed pleural biopsy has a greater diagnostic yield in diagnosing exudative effusions not diagnosed by pleural fluid analysis. Closed pleural biopsy can be used as a easy, quick, cost effective and relatively safe method.

Keywords: Pleural effusion, Tuberculosis, Malignancy, Undiagnosed, rt PCR, BACTEC, Histopathological examination

INTRODUCTION

Pleural effusion is a collection of fluid in the Pleural space. It is not a disease but rather a complication of an underlying illness. Effusion can occur for a variety of reasons. Normally fluid enters the pleural space from the capillaries in the parietal pleura and is removed via the lymphatics situated in the parietal pleura. Fluid can also enter the pleural space from the interstitial spaces of the lung via the visceral pleura or from the peritoneal cavity via small holes in the diaphragm. The lymphatics have the capacity to absorb 20 times more fluid than is normally formed. Accordingly, a pleural effusion may develop when there is excess pleural fluid formation (from the interstitial spaces of the lung, the parietal pleura, or the peritoneal cavity) or when there is decreased fluid removal by the lymphatics.¹

Determining the cause of a pleural effusion is greatly facilitated by analysis of the pleural fluid. Thoracentesis is a simple bedside procedure that permits fluid to be rapidly sampled, visualized, examined microscopically, and quantified. A systematic approach to analysis of the fluid in conjunction with the clinical presentation should allow the clinician to diagnose the cause of an effusion.²

The first step is to determine whether the effusion is a transudate or an exudate. A transudative pleural effusion occurs when systemic factors that influence the formation and absorption of pleural fluid are altered. The leading causes of transudative pleural effusions are left ventricular failure and cirrhosis. An exudative pleural effusion occurs when local factors that influence the formation and absorption of pleural fluid are altered. The leading causes of exudative pleural effusions are Tuberculosis, bacterial pneumonia, malignancy, viral infection, and pulmonary embolism. The primary reason to make this differentiation is that additional diagnostic procedures are indicated with exudative effusions to define the cause of the local disease.²

Exudative pleural effusions are frequently encountered in clinical practice of pulmonology. Etiological diagnosis in of those cases is a diagnostic challenge to the clinician because even after all cumbersome work-ups some cases remain undiagnosed. Given that 15-20% of exudative effusions remain undiagnosed even after extensive efforts³, invasive diagnostic procedures are needed for diagnosis in such cases, among which percutaneous needle biopsy of pleura is a cost-effective approach. By closed pleural biopsy, up to 49% of missed cases may be diagnosed.⁴ Closed pleural biopsy provides highest diagnostic yield in pleural tuberculosis and malignancy, which are the two most common causes of exudative pleural effusions.⁵

Pleural effusion remains undiagnosed after routine tests in pleural fluid in many patients. so, we need a simple and safe investigative tool to evaluate undiagnosed effusion. This study is designed to diagnose the cases of undiagnosed effusions by a simple and safe investigative tool.

MATERIALS & METHODS

A hospital based prospective study done in 30 patients with exudative pleural effusion remain undiagnosed after pleural fluid analysis in department of respiratory medicine at government medical college, Bhilwara, Rajasthan during one-year period.

Inclusion Criteria:

- Exudative effusion which is negative for malignant cells, Acid Fast Bacillus, Gram stain and Non-Tuberculous culture in Pleural fluid.

Exclusion Criteria:

- Exudative effusion positive for Malignant cells
- Exudative effusion positive for Tuberculosis in Pleural fluid smear
- Exudative effusion positive for Gram stain or Non-Tuberculous culture
- Parenchymal lesion in the X-ray suggestive of Tuberculosis or Malignancy or parapneumonic effusion
- Uncooperative patients
- Patients having coagulation disorders, uremia, empyema
- Dry pleural tapping

Study Procedure

Patients with undiagnosed exudative pleural effusion, fulfilling Inclusion criteria were admitted in Respiratory Medicine ward at Government General Hospital.

Investigations were done to rule out Renal diseases and Coagulation abnormality. Pleural fluid sent for basic biochemical and microbiological investigations.

Pleural biopsy was performed using ABRAM'S pleural biopsy needle under strict aseptic precaution under local anesthesia and the specimen was sent for the following investigations such as histopathological examination, rt-PCR and culture for Tuberculosis by BACTEC.

Method of Pleural Biopsy

The patient was positioned, and the site was selected either clinically or by image guidance. The skin was cleaned, and the local anesthetic was administered as for diagnostic thoracentesis.

Skin incision was made at the selected site to insert the Abram's pleural biopsy needle, the stylet was placed in the inner cannula, which, in turn, was placed in the outer trocar.

28 Once the tip of the needle is thought to be in the pleural space, the inner stylet was removed, and with the inner cannula in the closed position, a syringe was attached to the connection on the inner cannula. At this time, pleural fluid was aspirated for diagnostic studies.

The biopsy needle was then slowly withdrawn with constant aspiration until it hooked onto the pleura. When the needle hooks, one can be sure that parietal pleura was in the notch of the needle if pleural fluid can still be aspirated through the syringe. When the needle was hooked on the pleura, the outer trocar was held firmly with one hand while the inner cannula was rotated into the closed position with the other hand to cut off a small piece of parietal pleura.

Once the initial biopsy specimen was obtained, the needle can either be withdrawn from the pleural space in the closed position, the pleural biopsy specimen was found in the tip of the needle. Reinsertions of the needle are through the same tract, however, and are easier than the original insertion. The biopsy procedure can be repeated without removing the biopsy needle. Whenever the Abram's pleural biopsy needle was withdrawn from the pleural space, the biopsy tract was occluded with a finger immediately after the needle was withdrawn to decrease the likelihood of a pneumothorax.

At least six separate biopsy specimens were obtained. Four were placed in formalin and were taken to the pathology laboratory, and the other two were placed in a sterile container and sent to the laboratory for BACTEC culture and Reverse Transcriptase Polymerase Chain Reaction targeting 85B gene of Mycobacterium Tuberculosis.

Once the biopsy specimens were obtained, a therapeutic thoracentesis was performed through

the Abram's needle. The pleural fluid should be removed only after obtaining the biopsy specimens because the pleural fluid separates the parietal and visceral pleura, and increases the safety of the procedure. When the Abram's needle was withdrawn for the last time, the biopsy site was massaged for a short time to eradicate the needle tract. Then a small adhesive bandage was placed over the biopsy incision in a crosswise manner to act as a butterfly-type dressing. Chest radiographs were obtained on all patients after pleural biopsies.

RESULTS

Histopathological examination diagnosed 46.66% of biopsy specimens as tuberculosis and 23.33% as malignancy. The rest 30% of case were left undiagnosed after histopathological examination of Pleural biopsy. Reverse Transcriptase Polymerase Chain (rtPCR) reaction was positive in 16.66% of the cases and was negative in 83.33% of the cases. BACTEC was able to diagnose only 2 cases in the pleural biopsy specimens (table 1). Out of the malignancies proved in the study, adenocarcinoma topped the list with 42.85% followed by Squamous cell carcinoma with 28.57% and then by Lymphoma and Small cell carcinoma with 14.28% each.

Our study shows that tuberculous pleural effusion is more common in the younger age group and malignant pleural effusion more common in the elder age in both males and females (table 2).

About 80% of cases were diagnosed when combining histopathological examination, BACTEC culture and Reverse Transcriptase Polymerase Chain reaction on pleural biopsy specimen. 20% of cases were left undiagnosed even after combining all the three tests. The study population was divided into two groups of tuberculous pleural effusion and malignant pleural effusion based on the final diagnosis and the yield of each test in tuberculous and Malignant effusion are discussed separately as follows.

There were no false positive results with histopathological examination, BACTEC & rt PCR making the specificity and positive predictive value as 100%. The sensitivity was 70%, 10% & 25% respectively and negative predictive value was 60%, 35% & 40% respectively in tuberculosis patients (table 3).

Table 1: Yield of HPE, rtPCR & BACTEC in Pleural Biopsy

Yield of pleural biopsy		Frequency	Percentage
Histopathology	Tuberculosis	14	46.66%
	Malignant	7	23.33%
	Undiagnosed	9	30%
Rt PCR	Positive	5	16.66%
	Negative	25	83.33%
BACTEC	Positive	2	6.66%
	negative	28	93.33%

Table 2: Yield of pleural biopsy in male and female in different age groups

Gender	Results	19-35yrs	35-50yrs	>50 yrs
Male	Tuberculosis	17	4	1
	Malignancy	0	1	5
	Undiagnosed	2	2	3
Female	Tuberculosis	1	0	1
	Malignancy	0	0	1
	Undiagnosed	1	1	0
Total		11	8	11

Table 3: Sensitivity, Specificity, PPV & NPV in tuberculosis patients with different diagnostic yield

Statistics	HP Examination	BACTEC	Rt PCT
Sensitivity	70%	10%	25%
Specificity	100%	100%	100%
PPV	100%	100%	100%
NPV	60%	35%	40%

DISCUSSION

Pleural effusion is one of the most common problems for which patients come to see a pulmonologist. Despite cytological, biochemical and microbiological studies of pleural fluid, 18% of cases remain undiagnosed. Needle biopsy of the pleura can establish the diagnosis of a malignant pleural effusion. The percentage of positive pleural biopsies in patients with malignant pleural disease ranges from 39% to 75%. In general, pleural fluid cytology is superior to pleural biopsy in establishing the diagnosis of pleural malignancy. According to various studies, the diagnostic yield of pleural biopsy in pleural effusion is about 60 to 80% in all cases.^{6,7} The diagnostic yield of Pleural biopsy in our study was 71% in Malignant cases.

Mycobacterial culture of pleural tissue was positive in 33.96% of patients with tubercular pleural effusions, which is much higher than in other published reports.^{8,9} This discrepancy may be attributed to small pleural biopsy specimen, single sample for mycobacterial culture and technical fault. One study has also revealed that more than one sample increased the diagnostic yield of pleural tissue mycobacterial culture.¹⁰

In our study Histopathological examination diagnosed 70% of Tuberculous effusion. Reverse Transcriptase Polymerase Chain Reaction diagnosed 25% of Tuberculous effusion. BACTEC diagnosed 10% of Tuberculous effusion, 80% of Tuberculous cases were diagnosed by combining all three tests. As there were no false positive results with any of the three tests (Histopathological examination, Reverse Transcriptase Polymerase Chain Reaction and BACTEC culture), they are highly specific in diagnosing both Tuberculosis and malignancy. Both the Specificity and Positive predictive value were 100% with these tests. As these tests are highly specific we can start treatment even when any of these tests is positive.

Nadia A. Hasaneen et al¹¹ concluded that PCR of the pleural biopsy was much faster in reaching diagnosis. PCR of pleural biopsy is a useful method when used in combination with the BACTEC cultures system and histopathologic examination of pleural biopsy to reach a rapid diagnosis of tuberculous pleural effusion.

Biswajit Chakrabarti et al¹² found that the overall diagnostic sensitivity of initial blind biopsy was 38% (rising to 43% when pleural tissue was obtained), with a negative predictive value of 40%.

Sudipta Pandit et al¹³ concluded that malignancy is more common than tuberculosis, particularly in elderly. When thoracoscope is not available, pleural fluid cytology and pleural biopsy can give definite diagnosis. Pleural fluid ADA ≥ 70 u/l is almost diagnostic of tuberculosis, where pleural biopsy is not recommended.

CONCLUSION

We concluded that combination of histopathological examination, BACTEC culture and Reverse Transcriptase Polymerase Chain reaction in closed pleural biopsy has a greater diagnostic yield in diagnosing exudative effusions not diagnosed by pleural fluid analysis.

Closed pleural biopsy can be used as a easy, quick, cost effective and relatively safe method.

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