



Original Article

The diagnostic dilemma of an exudative pleural effusion and the emerging role of thoracoscopic pleural biopsy in these patients: A study from South India

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ABSTRACT

Objectives: Pleural effusion is one of the common presentations of several several diseases in clinical practice. The pathology behind a pleural effusion is often not clear on pleural fluid analysis. In developing countries like India, empirical antitubercular treatment is started assuming exudative pleural effusion to be tuberculosis. Over some time with more emphasis on evidence-based medicine, this is not a right approach. Thoracoscopic examination and biopsy visceral are a minimally invasive procedure which is underutilized in our practice. The study was conducted to evaluate the definitive etiological diagnosis of exudative pleural effusion and to analyze the diagnostic yield of thoracoscopic biopsy in the diagnosis of exudative pleural effusion.

Material and Methods: The study was conducted in the Department of Medicine and Oncology, Command Hospital Airforce, Bengaluru, India. All adult patients with exudative pleural effusion (according to light's criteria) reporting to the hospital from January 2019 to December 2020 were included and subjected for analysis.

Results: Out of a total of 100 patients who were included in the study, there was male predominance with 78 males and 22 females. Thoracoscopic biopsy remained conclusive in 100% of cases. Malignancy was the most common etiology with 48% of cases while tuberculosis was seen in 38%, 12% had inflammation, and 2 (02%) had mucormycosis. TB PCR sensitivity and specificity of TB PCR were 42% and 100%, respectively. MTB culture showed sensitivity of 11%. MTB culture of biopsy showed sensitivity of 26%. The specificity in both the methods was 100%.

Conclusion: Thoracoscopy is an ideal method for the diagnosis of pleural effusion with suspected exudative pathology. It gives an accurate diagnosis and helps differentiate between tuberculosis and malignancy which are the most common etiologies in India, thereby leading to early appropriate and specific treatment in such patients. Malignancy was the most common etiology in our study.

Keywords: Exudate, Pleural effusion, Thoracoscopy, Tuberculosis

INTRODUCTION

Pleural effusion is one of the commonly encountered problems in clinical practice of chest medicine. Pleural effusions usually occur in adults. However, they appear to be increasing in children, often in the setting of underlying pneumonia. Fetal pleural effusions have also been reported and, under certain circumstances, may be treated before delivery.^[1] Laboratory evaluation of patients with a pleural effusion is directed at first determining if the effusion is an exudate or a transudate.

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The etiology of an exudative pleural effusion is often not clear even after extensive analysis of the pleural fluid. There is a tendency to label most exudative effusion as tubercular and empirically ATT is started with no concerted efforts which are made to pursue the diagnosis. Often, the only diagnostic tests done are pleural fluid protein estimation, and pleural fluid cytology showing exudative pleural effusion with lymphocytic pleocytosis. However, nearly 20–27% of patients with pleural effusion undergoing pleural fluid analysis and closed needle pleural biopsy remain undiagnosed.^[2-4]

Tuberculosis is an important cause of lymphocytic effusions. However, malignancies, lymphoma, collagen vascular diseases, and chylothorax may have similar picture on analysis. Malignant pleural effusion is one of the leading causes of exudative effusion; studies have demonstrated that 42–77% of exudative effusions are secondary to malignancy. Majority are missed initially on pleural fluid testing and end up being detected later on after progressing on empirical ATT.^[5]

Pleural fluid analysis can tell us that the fluid is exudative, however to find a diagnosis still requires further evaluation. Pleural fluid cell blocks do have better chances for diagnosis but their role is limited because of technical expertise both at collection and preparation. Thoracoscopy is a cost-effective method for visualization and obtain effective tissue samples for diagnosing pleural diseases. Thoracoscopy is a method with which an optical system is used to gaze into the pleural cavity to examine and biopsy visceral and parietal pleura tissues surfaces, the lung parenchyma, and to perform other minimally invasive procedures within the chest cavity. The study was conducted to evaluate the definitive etiological diagnosis of exudative pleural effusion and to analyze the diagnostic yield of thoracoscopic biopsy in the diagnosis of exudative pleural effusion.

MATERIAL AND METHODS

The present study was conducted in the Department of Medicine and Oncology, Command Hospital Airforce, Bengaluru, India, during the period of January 2019–December 2020. The hospital is the largest tertiary care defense hospital in South India and caters to a large population of serving/retired defense personnel and their families. All 100 adult patients admitted to medical, respiratory, and oncology wards during the study period were included in the study. Those with exudative pleural effusion according to light's criteria were included and subjected for further analysis. The patients were enrolled after obtaining their informed consent. The patient's clinical history was taken and complete physical examination was performed. Investigations including complete blood count, coagulation profile, ADA level, pleural fluid analysis, TB PCR, and chest X-ray were conducted for all patients.

The patients with exudative pleural effusion where diagnosis could not be made on pleural fluid analysis were subjected to thoracoscopy. All the eligible patients underwent a thoracoscopic pleural biopsy under LA/GA at our hospital. After creating an iatrogenic pneumothorax is created in the suspected lung, a midaxillary line vertical incision is made through the skin/subcutaneous tissue approximately 10 mm, parallel with and in the middle of the selected intercostal space. The trocar is inserted in a corkscrew motion until the sudden release of resistance (after passing the costal pleura) is felt. The trocar is removed leaving the cannula 1–3 cm within the pleural cavity; a thoracoscope is placed in the cannula and advanced into the pleural cavity under direct vision. The pleural fluid is removed with a suction catheter or directly through the working channel of the semi-rigid pleuroscope. The pleural space was inspected through the thoracoscope/pleuroscope, either directly or indirectly by video. Suspicious areas are biopsied through the working channel of the thoracoscope/pleuroscope. Multiple biopsies are taken. The area of the pleura to be biopsied was decided in most cases intraoperatively on visualizing the suspicious lesion in conjunction with CT scan findings. Two to six biopsies of a suspicious pleural lesion will establish the diagnosis and a chest tube is placed after the completion to inflate the lung. The patient was observed in hospital for complication post-procedure. Histopathology was reported at the hospital pathology laboratory.

RESULTS

A total of 100 patients were included in the study, 78 males and 22 females, in the age group of 22–75 years, with mean age of 46.62 years [Table 1].

Symptomatic analysis reported that chest pain was present in 64% of cases, breathlessness in 76%, fever in 60%, cough

Table 1: Distribution of the study population and characteristics.

Variables	Subvariables	n=100
Age group (in years)	21–30	20
	31–40	14
	41–50	32
	51–60	12
	61–70	14
	71+	08
Sex	Male	78
	Female	22
Symptoms	Chest pain	64
	Breathlessness	76
	Fever	60
	Cough	76
	Weight loss	70
	Hemoptysis	12

in 76%, weight loss in 70%, and hemoptysis was present in 12% of cases [Table 1]. On exploring the personal history, smoking was present in 44% of cases. Clinical and X-ray analysis reported that pleural effusion was present on the right side in 60% of cases, left side in 38% of cases, and bilateral in 2% of cases.

Thoracoscopic biopsy remained conclusive in all 100% of cases. Out of 100 cases, 48 (48%) cases were found to be having malignant pleural effusion, 38 cases (38%) as tubercular, 4 (04) had chronic non-specific inflammation and acute inflammation, and 6 (06%) was diagnosed as a case of fungal mucormycosis [Table 2].

Among the 48 malignancy patients, 30 (62.50%) were adenocarcinoma lung which was the most common histology while 4 (8.33%) were squamous cell carcinoma, 4 (8.33%) were non-small-cell carcinoma (large cell/carcinoid tumor), 2 (4.17%) was small-cell carcinoma, 2 (4.17%) was mesothelioma, 4 (8.33%) were secondary metastasis from an unknown primary carcinoma (later diagnosed from breast and soft-tissue sarcoma), and 2 (4.17%) was hemangioendothelioma.

The TB PCR results were correlated and compared with the thoracoscopic biopsy report. Eight cases were found to be true positive, 62 cases were true negative, 22 cases were false negative, and no case was false positive. The sensitivity and specificity of TB PCR was 42% and 100%, respectively, in our study. MTB culture of biopsy tissue came positive in 10 cases showing sensitivity of 26%. The specificity in both the methods was 100%. MTB culture came positive in only four cases showing sensitivity of 11%. MTB culture of biopsy tissue came positive in 10 cases showing sensitivity of 26%. The specificity in both the methods is 100%.

DISCUSSION

In our study from a tertiary care defense hospital, the thoracoscopic pleural biopsy was conducted in 100 patients who had exudative pleural effusion based on light's criteria. The mean age was 46.62 years with majority in the age group of 41–50 years of age. The study conducted in Kuwait and India also reported similar age incidence.^[6,7] Dyspnea, cough, and chest pain were the common clinical presentation in

our study and similar other studies conducted in India and Western countries.^[8-10]

The initial impression of finding the etiology of exudative pleural effusion was done on the basis of pleural fluid analysis but final diagnosis was confirmed by thoracoscopic pleural biopsy. The biopsy was conclusive in 100% of cases. The pleural fluid analysis had sensitivity and specificity of 58.33% and 88.46%, respectively, for diagnosing malignancy and sensitivity and specificity of 52.63% and 80.65%, respectively, for diagnosing tuberculosis. Gaur and Chauhan reported 68.4% sensitivity of pleural fluid analysis,^[11] the specificity, positive predictive value, and negative predictive value of pleural fluid cytology were 84.6%, 67.5%, and 78.6%, respectively. Similar studies conducted in the past reported sensitivity in the range of 60–90%.^[12-15]

Among cases with tubercular pleural effusion, ADA was in the range from 10.6 U/Lit to 88.3 U/Lit, with a mean value of 48.95U/Lit, and in the 48 cases of malignancy, ADA was found to be in the range of 0–50 U/Lit with mean of 19.65U/L. Similar study published in the past among 83 cases reported greatly elevated ADA levels in pleural fluid ranging from 30 U/Lit to 300 U/Lit, with a mean value of 77.20 ± 32.63 U/Lit at 37°C, and in malignant effusion, ADA value ranged from 20 U to 40 U/Lit with mean of 26.84 ± 6.92 .^[16]

MTB culture of pleural fluid had shown the sensitivity and specificity of 11% and 100% while TB PCR has sensitivity of 42% and specificity of 100% in our study. In the studies done by Berger and Mejia, Epstein *et al.* and Bueno *et al.* for the diagnosis of tuberculous pleurisy had shown that the sensitivity of pleural fluid culture is 10–35%.^[17-19]

Final diagnosis was made in all cases with thoracoscopic pleural biopsy on the basis of histopathology. According to tissue diagnosis, 48 cases (48%) were found to be malignant etiology, 38 cases (38%) as tubercular, 12 cases (12%) as inflammation, and 2 (2%) were fungal. Hence, a definite diagnosis was made in all 100 cases [Table 3]. Thoracoscopy is the ideal procedure available to directly explore the pleural cavity and visualize the malignancies in early stages, which are confined up to visceral pleura of lung. A study from China showed a 93% positivity rate of detection on thoracoscopy with a definite diagnosis being made in 50 out of 54 patients studied.^[20] A study published in Kuwait Med Journal in 2002 and showed the diagnostic accuracy of 91.67% of cases of pleural effusion.^[6] The diagnostic yield of thoracoscopy is between 90% and 100%, in contrast to 44% for closed pleural biopsy and 62% for fluid cytology.^[21] A study conducted in Mumbai, India, among 27 patients, who underwent thoracoscopy for an undiagnosed pleural effusion. The study reported that thoracoscopy was diagnostic in 24 of the 27 patients (four benign and 20 malignant).

Table 2: Histopathological diagnosis on the basis of thoracoscopic pleural biopsy.

Histopathological diagnosis	Number of cases (n=100)	% Age
Malignancy	48	48
Tuberculosis	38	38
Chronic inflammation	4	04
Mucormycosis	6	06
Acute inflammation	4	04

Table 3: Spectrum of malignancy in diagnosed malignant pleural effusion.

Malignancy	Number of cases (n=48)	% Age
Adenocarcinoma	30	62.50
Squamous cell carcinoma	04	8.33
Non-small-cell carcinoma (NOS)	04	8.33
Small-cell carcinoma	02	4.17
Mesothelioma	02	4.17
Metastatic carcinoma from another primary	04	8.33
Hemangioendothelioma	02	4.17

Our study also showed that the procedure was well tolerated, had a low pain score, and required only a low dose of midazolam. Only 17 patients required midazolam 1–3 mg intravenous injection. Local anesthesia thoracoscopy is a less invasive and less expensive, cost beneficial approach to thoracoscopy.^[21,22]

Thus, because of its high diagnostic accuracy, diagnostic pleuroscopy is an excellent option in exudates in which the etiology remains undetermined. Pleural biopsy by thoracoscopy under local anesthesia should be actively performed in patients with suspected malignant neoplastic lesions of the pleura, because the technique has a high diagnostic rate, and can be easily and safely performed with little burden on the patient.

CONCLUSION

Our study concludes that thoracoscopy is an ideal method for the diagnosis of pleural effusion in a suspected exudative pathology. It gives an accurate diagnosis and helps differentiate between infections and malignancy which are the most common etiologies in India, thereby leading to early appropriate treatment in such patients. Furthermore, in the era of evidence-based medicine, it would reduce the number of patients who may be empirically and unnecessarily treated with ATT for other non-specific infections and for sinister malignancies which are not picked up on pleural fluid analysis. It provides tissue for further mutational analysis in case of lung cancers which is mandatory in planning further therapy. Moreover, thoracoscopy may unearth a hidden primary tumor which may be picked up on histopathology. The sensitivity of TB PCR and MTB culture is low and usually unreliable in diagnosing tubercular etiology. Thoracoscopic biopsy should be the standard of care in all patients with exudative pleural effusion and has additional advantages in diagnosis confirmation and therapeutic planning.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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