Original Article

Thoracoscopic evaluation of 129 cases having undiagnosed exudative pleural effusions

Chetan Basavaraj Patil, Ramakant Dixit[1], Rakesh Gupta[1], Neeraj Gupta[1], Varna Indushekar

Departments of Pathology and [1]Respiratory Medicine, J.L.N. Medical College, Ajmer, Rajasthan, India

ABSTRACT

Background: Medical thoracoscopy is a minimally invasive procedure used in diagnostic and therapeutic applications for pleural diseases. In this study, we describe our experience in the outcome and analysis of thoracoscopy in undiagnosed pleural effusion presenting to our center. **Materials and Methods:** This is a prospective study conducted over last 2 years. We performed thoracoscopy in 129 cases of undiagnosed exudative pleural effusions using rigid thoracoscope. Clinical, radiological, cyto and histopathological data of the patients were collected prospectively and analyzed. **Results:** The overall diagnostic yield of thoracoscopic pleural biopsy was 110/129 (85.2%) in patients with undiagnosed pleural effusion, and 19/129 (14.8%) patients remained unexplained. Histopathological diagnosis confirmed malignancy in 66.4% patients (both primary and metastatic pleural carcinoma), tuberculosis in 28.2%, others including parapneumonic effusion in 4 cases followed by multiple myeloma, lupus pleuritis, and pulmonary langerhans cell histiocytosis in one case each. Procedure-related mortality was nil. Minor complications related to the procedure include hemorrhage, subcutaneous emphysema, etc. **Conclusion:** Thoracoscopy is relatively a safe and well-tolerated procedure with high diagnostic accuracy in undiagnosed pleural effusions, decreasing the need of formal diagnostic thoracotomy. Every chest physician must, therefore, consider this procedure to decrease the time lag in achieving the final diagnosis and to initiate the treatment as early as possible.

KEY WORDS: Pleural biopsy, pleural effusion, rigid thoracoscope

Address for correspondence: Dr. Ramakant Dixit, A-60, Chandravardai Nagar, Ajmer - 305 001, Rajasthan, India. E-mail: dr.ramakantdixit@gmail.com

INTRODUCTION

Medical thoracoscopy also referred to as pleuroscopy is an endoscopic evaluation of the pleural space. It is a minimally invasive procedure that was first invented in 1910 by Hans Christian Jacobeus, a Swedish internist[1] who is also regarded as the "father of thoracocopy." In the twentieth century, thoracoscopy was mainly used in the treatment of pulmonary tuberculosis (TB) and tubercular pleural adhesions.[2] In recent years, thoracoscopy has gained a lot of interest and popularity among pulmonary physicians mainly in etiological diagnosis of pleural effusions.

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The usefulness of thoracoscopy has also been extended in the evaluation of pneumothorax and empyema; in taking diagnostic biopsies from lung, diaphragm, mediastinum, and pericardium; for staging of lung cancers and malignant mesothelioma. Therapeutic procedures like pleurodesis and adhesiolysis may be done in preventing the recurrence of the pleural effusion and palliation of dyspnea.[3]

The concept of medical thoracoscopy is simplification of video-assisted thoracoscopic surgery, as it is done in conscious sedation under local anesthesia by trained pulmonologists. In Indian scenario, there are fewer studies

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that have been done on the role of tharacoscopy in cases of undiagnosed pleural effusion.[4-6]

In all the patients with pleural effusion, cytobiochemical analysis of pleural fluid is needed to establish the etiology; however, it is useful for diagnosis only in up to 60% of cases,[7] in around 20% of the cases, etiology often remains unclear even after extensive diagnostic workup.[8] So it is in this context that the thoracoscopy becomes an important investigation modality, where pleural cavity can be grossly visualized and appropriate representative sample can be easily picked up.

MATERIALS AND METHODS

This is a prospective, nonrandomized, and interventional study conducted at our center to establish the role of thoracoscopy in undiagnosed exudative pleural effusions.

All the cases, in of pleural effusion that remained undiagnosed after initial and repeated biochemical and cytological analysis of the pleural fluid were enrolled in this study at our institution. Definition of undiagnosed pleural effusion was considered as the failure to achieve an etiologic diagnosis by initial pleural fluid microscopic and biochemical analysis including protein, sugar, lactate dehydrogenase, Gram stain, acid fast *bacilli* (AFB) smear and culture, pleural fluid adenosine deaminase (ADA) levels, and at least three pleural fluid cytologies negative for malignant cells or other definite causes.

As a part of diagnostic work up, we recorded detailed history including occupation, drug intake (if any), smoking habits, significant past medical history, etc., All the necessary laboratory hematological and radiological investigations were done and thoracoscopy was performed in all eligible patients after taking informed consent and the procedure was video recorded.

Patients were kept nil by mouth for 6 hours prior to the procedure. Intravenous access was achieved in the upper limb opposite to the side of thoracoscopy. Patients were then made to lie in lateral decubitus position with affected side facing upward and both the arms were placed above and below the head. Patient's vital parameters such as electrocardiogram, blood pressure, and oxygenation were monitored continuously throughout the procedure. Thoracoscopy was carried out under local anesthesia by intercostal nerve block at the desired incision site and intravenous tramadol and midazolam were administered to increase patient's comfort without compromising respiration.

The port of site was usually 5th or 6th intercostal space in midaxillary line. 1–2 cm sized incision was made and the subcutaneous tissue and muscles were bluntly dissected to reach the pleural cavity. Then a trocar with cannula was inserted through the chest wall, pleural fluid was aspirated and systemic exploration of the pleura and pleural cavity was done by rigid thoracoscope Hopkins II (Karl storz Germany, 0°, 49003 AA). Site for second port for the purpose of pleural biopsies was made close to the first port; however, care was taken to avoid "fighting of instruments."

Typically 2–6 biopsies of the abnormal lesion inside the pleural cavity were taken by biopsy forceps. If no gross abnormalities were visible on parietal pleura, multiple biopsies were taken from different areas. A lateral "lift and peel" technique was used for taking the pleural biopsy. At the end of the procedure, a chest tube with underwater seal was placed via the thoracoscope insertion site, after removal of the port cannula. Chest tube insertion was undertaken as described in the British Thoracic Society Guidelines.[9] Second working port was sutured. Chest radiograph was taken 2 hours after the postprocedural period.

RESULTS

During the study period, a total 129 patients, out of whom 92 patients (71.3%) were male and 37 patients (28.7%) were female (Male:female ratio of 2.6:1); mean age of 54 ± 20.6 years (range 18–92 years) presented with recurrent exudative pleural effusion. The most common respiratory symptom was breathlessness in 87 patients (67.4%), followed by cough in 69 (53.4%). Seventy-four patients (57.3%) had a history of addiction, the most common being smoking in 46 patients. In this study population, 68 patients had right-sided pleural effusion (52.7%), 42 patients were left sided (32.5%), and bilateral effusion was present in 19 cases (14.7%) [Table 1].

Thoracoscopy yielded a definitive diagnosis in 110 out of 129 patients (85.3%), and 19 patients (14.7%) remained unexplained. The nature of pleural effusion in seventy-three patients (56.6%) was malignant, and non-malignant in 37 patients (28.7%). In patients with malignant effusion, metastatic adenocarcinoma lung (n = 27) was the most common followed by malignant mesothelioma in 19 patients. Other malignant conditions included squamous cell carcinoma in 7; small cell carcinoma in 4; metastatic carcinoma/sarcoma of other organs in 15 cases; multiple myeloma in one case. In patients with nonmalignant effusion, TB (n = 31) was the most common followed by parapneumonic effusion (n = 4) and 1 case each of lupus pleuritis and histiocytosis X [Table 2].

In the subset of metastatic carcinoma/sarcomas of other systems, carcinoma breast was the most common primary

Table 1: Characteristics of study population

Baseline characteristics	Subjects (*n*)
Total number of patients	129
Mean age (years)	54±20.6
Age range (years)	18-92
Male: female	2.6:1
Right side:left side:bilateral	3.6:2.2:1
Serosangunous fluid:hemorrhagic fluid:others*	11:9.5:1

*Others includes chocolate brown and pus

site in 5 cases followed by non-Hodgkin's lymphoma in 3 cases [Table 3].

Black anthracotic patches/plaques on either pleura were the most common gross thoracoscopic visual findings (n = 57), followed by thickened nonsmooth pleura (n = 53), and pleural nodules (n = 48) [Figure 1]. Other findings were pleura-parenchymal adhesions, smooth edematous shiny pleura, sago like granules [Figure 2], cauliflower-like growths [Figure 3], ulcerative pleura, etc. The mean duration of chest tube drainage after the thoracoscopy in all 129 cases was 5.26 days [Table 4].

In the study population of 129 patients, 19 were suspected having initial clinical diagnosis of TB and were on anti-TB treatment for a varying period (3 weeks to 5 months); however, only 5 (26.3%) among them proved to be TB following thoracoscopic biopsy. In 14 patients (73.7%) the final diagnosis was nontubercular etiology, which included malignancy in 9 cases (47.4%), chronic nonspecific inflammation in 3 cases, and one case each of lupus pleuritis and pulmonary langerhans cell histiocytosis (histiocytosis X).

Table 2: Distribution of study population according to histological diagnosis after thoracoscopy

Histological diagnosis	Frequency, *n* (%)
Benign/infective causes	*n*=37
Tuberculosis	31 (83.7)
Parapneumonic effusion	4 (10.8)
Lupus pleuritis	1 (2.7)
Histiocytosis X	1 (2.7)
Malignant causes	*n*=73
Adenocarcinoma lung	27 (37)
Malignant mesothelioma	19 (26)
Squamous cell carcinoma lung	7 (9.6)
Small cell carcinoma lung	4 (5.5)
Metastatic carcinoma/sarcoma*	15 (20.5)
Multiple myeloma	1 (1.64)

*Primary was present at sites other than lung and pleura

Table 3: Primary site of malignancy causing metastatic pleural effusion (*n*=15)

Primary origin of metastasis	Number of patients (*n*=15) (%)
Carcinoma breast	5 (33.3)
Non-Hodgkin's lymphoma	3 (20)
Carcinoma ovary	1 (6.6)
Carcinoma tongue	1 (6.6)
Carcinoma prostate	1 (6.6)
Synovial sarcoma	1 (6.6)
Osteosarcoma femur	1 (6.6)
Acute myeloid leukemic infiltration	1 (6.6)
Malignant melanoma	1 (6.6)

Table 4: Mean duration of the chest tube drainage in different etiologies

Histological diagnosis	Total number of patients	Meantime duration (in days)
Tuberculosis	31	2.8
Chronic nonspecific inflammation	18	3.4
Parapneumonic effusion	4	5.8
Metastatic pleural effusion (primary in lung and from other systems)	54	6.7
Malignant mesothelioma	19	6.9

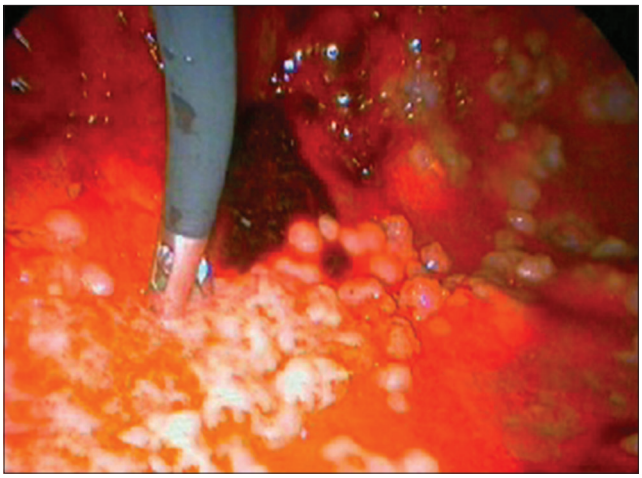

Figure 1: "Grape-like" distribution of nodules on parietal pleura in a case of epithelioid mesothelioma

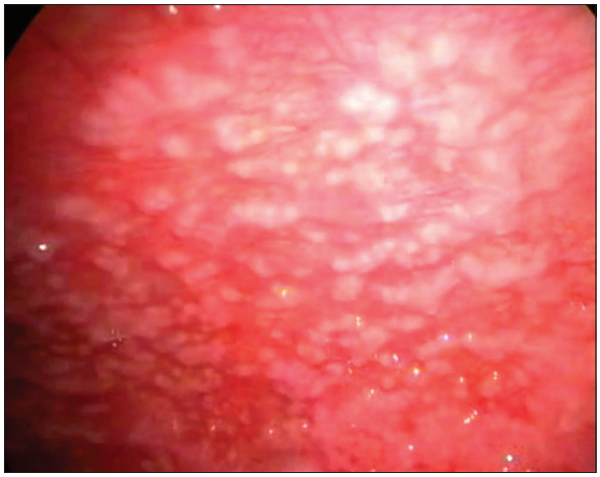

Figure 2: "Sago-like" granule appearance, typically seen in tuberculosis

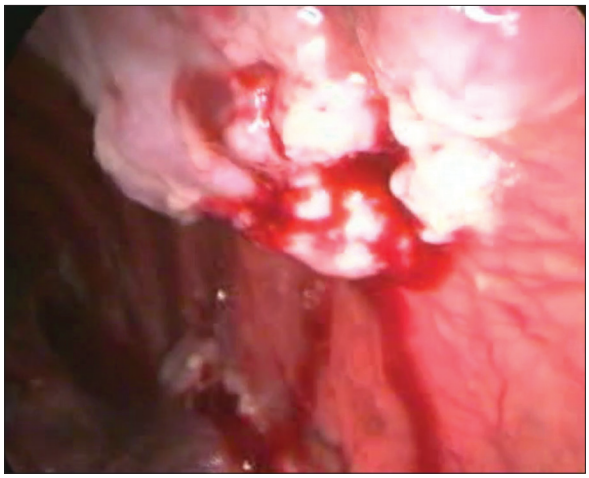

Figure 3: Cauliflower-like growth on parietal pleura which bleeds on touch in metastatic squamous cell carcinoma lung

There were no major complications. Minor complications observed were prolonged air leak in (4.6%), self-limiting subcutaneous emphysema (3.9%), empyema (2.3%), tract malignancy (1.5%), and cardiac arrhythmia and hypotension in 1 case each (0.7%). The procedure- related mortality was nil.

DISCUSSION

Main indication for thoracoscopy in this study was recurrent exudative pleural effusion, whose etiology remained unexplained after initial and repeated cytobiochemical analysis of pleural fluid. In this context, we needed pleural biopsy for histological confirmation. Since percutaneous blind needle pleural biopsy is having low sensitivity,[10] we chose thoracoscopy as it provides a positive diagnosis in a high proportion of pleural effusions in whom the diagnosis had not been achieved by conventional investigations. The major advantage of thoracoscopy is that it gives an opportunity to perform biopsy on suspicious looking pleural lesions and nodules on the surface of the lung under direct vision. It is also possible to get good views in loculated pleural effusions because of the ability to break down the loculi, either with diathermy or with biopsy forceps. In addition, it is possible to carry out chemical pleurodesis at the same time.[4]

In this particular study, we present the data of 129 patients who underwent thoracoscopy for undiagnosed pleural effusions. The overall diagnostic yield of thoracoscopic pleural biopsy in the study was 110/129 (85.3%). Similar experience with thoracoscopy was explained by studies across the globe. Hucker *et al*.[2] from England reported a diagnostic sensitivity of 80.3% in their study which included 102 patients, Mootha *et al*.[4] from India reported yield of 74.3% in 35 patients, Dhanya *et al*.[5] from Thailand could achieve diagnosis with pleural biopsy in 95.8% (91/95), and Hansen *et al*.[11] from Denmark were able to achieve diagnosis in 90.4% in a total of 147 patients of undiagnosed pleural effusion.

Pleural malignancies (either primary or secondary) being the most common histological diagnosis that was encountered in this study (n = 73; 56.6%), is comparable with the similar studies done in this field. Hucker *et al*.[2] reported malignancy in 59% of cases, Mootha *et al*.[4] reported 48.6%, Dhanya *et al*.[5] reported 55.8%, and Hansen *et al*.[11] reported malignancy in 62% of their study population.

Metastatic adenocarcinoma lung was being the most frequent primary lung carcinoma (71%) while most frequent metastatic carcinomas from other organs was breast carcinoma (33.3%), which is almost similar to the one reported by Hansen *et al*.[11] In our study, malignant mesothelioma was the diagnosis in 19 patients, other less common metastatic carcinomas from lung were squamous cell carcinoma (n = 7) and small cell carcinoma lung (n = 4). The possible reasons for the variation in diagnostic yield of thoracoscopic biopsy in different studies has been analyzed in depth by Loddenkemper and Boutin.[10] The important factors that contribute to this variation include paramalignant effusions, experience and skill of the thoracoscopist, inadequate sampling (underlooking of costovertebral gutter and diaphragm), pathological errors (not taking deeper cuts), fibrinous necrotic layer covering the actual pathological area, and the presence of dense adhesions.

Pleural TB was present in 31 cases (24%) on histopathology. Only 3 patients had AFB positivity on pleural biopsy. Surprisingly, the mean ADA level in patients with tubercular pleural effusions was below borderline range (ADA value <40 in 21 cases, 40–60 in 8 cases, with mean value of 31.0 ± 5.5) except for 2 cases who had ADA of 98 and 102, respectively. Therefore pleural effusions cannot be designated as TB, solely based on the ADA values. Presence of either parenchymal lesion suggestive of TB or a histological confirmation is necessary before putting them on anti-tuberculosis treatment.

Other less common nonmalignant conditions were parapneumonic effusions (n = 4) and 1 case each of lupus pleuritis and histiocytosis-X. Mootha *et al*.[4] reported 22.9% patients havingTB, which is comparable with our study. Hansen *et al*.[11] reported only 2% cases of TB in their study and Hucker *et al*.[2] reported none. This gross difference in the incidence rate of TB is probably due to low prevalence of TB in Western countries.

In our study, the mean duration of chest tube drainage after the thoracoscopy was 2.8 days in tubercular effusions, 3.4 days in chronic nonspecific inflammation, 5.8 days in parapneumonic effusions, 6.7 days in metastatic pleural effusions, and 6.9 days in case of malignant mesothelioma with a total duration range of 2–27 days. These findings are in concordance with the findings of Hansen *et al*.[11]

In this study, 18 cases that had chronic nonspecific inflammation on pleural biopsy were allocated to the undiagnosed group since we could not initiate any specific treatment except keeping these patients under observation. However in the study conducted by Hucker *et al*.,[2] Hansen *et al*.,[11] *and* Blanc *et al*.[12] had included chronic nonspecific inflammation in the benign causes of pleural effusion and therefore they reported a relatively higher yield of thoracoscopic pleural biopsies. Hucker *et al*.[2] found 21 cases (20.6%), Hansen *et al*.[11] found 45 cases (31%), and Blanc *et al*.[12] observed 57 cases (38.2%) of chronic nonspecific inflammation. All of these patients were included in the benign causes of pleural effusion, thus making their diagnostic yield of thoracoscopic pleural biopsy closer to 100%.

Complication rate in our study was low. There were no major complications and procedure-related mortality was nil. Other minor complications were hemorrhage, which was seen in seven cases during the procedure.

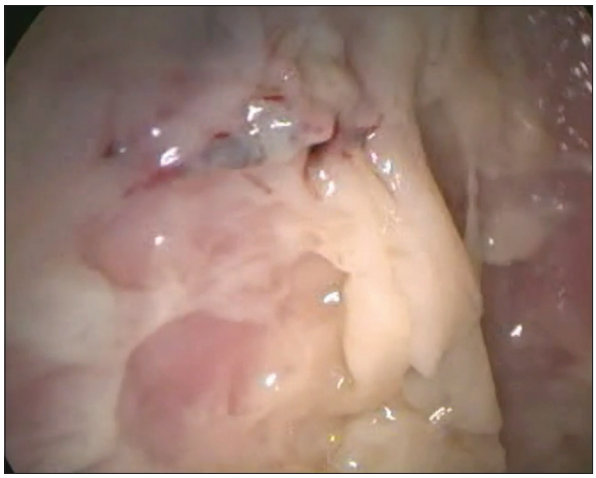

Figure 4: Thick necrotic pus debris in a case of empyema thoracis

A simple pressure application on the bleeding point with gauge peanut was sufficient. On rare occasions we used local hemostatic like intrapleural tranexemic acid or ferracrylum. Six patients had prolonged air leak of more than 7 days (4.6%), self-limiting subcutaneous emphysema in 5 cases (3.9%), empyema in 3 cases (2.3%) [Figure 4], tract metastasis in 2 cases (1.5%), and cardiac arrhythmia and hypotension were noted in 1 case each (0.8%) which was comparable with other studies like Hucker *et al*.,[2] Hansen *et al*.,[11] and Blanc *et al*.[12]

CONCLUSION

Our data suggests that pleuroscopy is a safe, well-tolerated procedure with minimal risk allowing the accurate diagnosis of indeterminate and undiagnosed pleural effusion in our setting. Besides the determination of underlying cause, it also affords the opportunity to provide unique therapeutic approaches to patients with malignant pleural effusions like pleurodesis or local chemotherapy. Therefore, thoracoscopy should be considered in patients with undiagnosed exudative pleural effusions, particularly those with lymphocytic predominant effusions where underlying malignant process is strongly suspected and where an initial clinical diagnosis was TB but showing poor response to specific therapy.

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Conflicts of interest
There are no conflicts of interest.

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