Diagnostic efficacy of thoracoscopy in recurrent undiagnosed pleural effusion

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Abstract
Background: Pleural effusion (PE) can occur as complication of many diseases. When pleural fluid is detected, an effort should be made to determine etiology. 20% of PEs remain undiagnosed even after all investigations. The study was to identify the different etiological conditions in recurrent pleural effusion using thoracoscopy. And to determine the etiology of undiagnosed recurrent pleural effusion by thoracoscopy.
Methodology: Prospective, observational study conducted in a tertiary care institute over a period of three years.
42 cases of undiagnosed recurrent pleural effusion were undergone thoracoscopy. Detailed history and physical examination, thoracocentesis and pleural fluid analysis were done in all cases. Ultrasound examination and computerized tomography done in all cases before thoracoscopy.
Results: Out of the 42 cases of recurrent pleural effusions, the most common type was Adenocarcinoma followed by tuberculosis. Three cases remained undiagnosed even after thoracoscopy.
Conclusions: Thoracoscopy is a simple, safe, less expensive technique with low morbidity and leads to early and quick diagnosis in recurrent pleural effusions. It was concluded in our study that thoracoscopy can establish the diagnosis in 92.85% cases of recurrent pleural effusion which were negative with pleural analysis there by decreasing morbidity and mortality due to pleural diseases.

Keywords: Biopsy; Malignancy; Pleural effusion; Thoracoscopy; Tuberculosis.

Introduction
Pleural effusion is an accumulation of fluid in pleural cavity which may result from as complication of many diseases. The cause of pleural effusion can be identified in majority cases by proper history, clinical examination and investigations. When pleural fluid is detected, an effort should be made to determine which among the conditions is responsible and is a challenge to the clinician as 20% of PEs remain undiagnosed even after all investigations [1]. The present study was to identify the different etiological conditions in recurrent pleural effusion using thoracoscopy.

Materials and Methods
Study Design
This study was a prospective cross-sectional study, performed in the department of pulmonary medicine at a tertiary care center in Andhra Pradesh, India, over a period of three years. An ethical committee approval and a written informed consent from study subjects was obtained.

Study Population
42 consecutive cases of recurrent pleural effusion who were undiagnosed by pleural analysis attending the department of pulmonary medicine above the age of 18 years during the study period, were selected by adhering to the inclusion and exclusion criteria.

Inclusion Criteria
People with clinical or radiological recurrent pleural effusion who are undiagnosed by either pleural analysis or pleural fluid for cell block in three samples and willing to undergo CT Chest, FNAC, biopsy and thoracoscope after written consent.

Exclusion Criteria
Patients with established cases of pulmonary malignancy, tuberculosis, haemothorax, hemodynamic unstable, anemia, poor general condition, HIV. One patient excluded after cardiac arrest before procedure. The study was approved by the institutional ethics committee.

Study Protocol
The selected patients after informed consent were admitted in the hospital for further evaluation by detailed medical history, clinical examination and investigations like Chest x-ray and routine blood investigations like complete blood picture, random blood sugar, serum urea and creatinine. All patients underwent pleurocentesis, pleural fluid analysis for Adenosine deaminase, protein, sugar, cell count, cell cytology and cell block connective tissue profile was done in suspected cases. In undiagnosed pleural effusions thoracoscope guided biopsy was planned. Before performing thoracoscope, every individual is subjected to CT/contrast-enhanced CT scan of the thorax for better anatomical delineation. After thoracoscopy, biopsy was taken from visible pleural nodules or from abnormal areas and sent for HPE. If any adhensions, thoracoscopic guided removal was done to allow proper visualization for pleural biopsy and intercoastal tube insertion was done to remove fluid. Repeat chest X-ray was done post procedure to see lung expansion and complications.

Results
Among 42 patients 29 (69.04%) were male and 13 (30.95%) were female with male: female ratio of 2.23:1.

Most common symptom was chest pain in 42 cases followed by breathlessness and cough in 37, weight loss seen in 24 patients, fever in 08 cases. Right side effusion was more common followed by left side. More than 80 percent cases presented with hemorrhagic effusions. Most common cause for undiagnosed pleural effusion in our study was malignancy followed by tuberculosis. Three cases remained undiagnosed even after thoracoscopy as shown in table 1.

Table 1: Etiologies of undiagnosed recurrent pleural effusion

Etiologies of recurrent pleural effusion	No. of patients	percentage
Adenocarcinoma	23	54.76
Small cell carcinoma	01	02.38
Mesothelioma	05	11.90
Tuberculosis	07	16.66
Catamanial pleural effusion	01	02.38
Systemic lupus erythrematosis with effusion	02	04.76
Undiagnosed after thoracoscopy	03	07.14

During the study period, 42 patients with undiagnosed pleural effusion underwent thoracoscopy for diagnostic purposes. Most common presentation in thoracoscopy was pleural nodules, other presentations are septations, pleural thickening and hemorrhagic pleural fluid. The representative images of pleural abnormalities visualized during thoracoscopy and their histopathology from biopsy specimen are shown in the following figures [1-6].

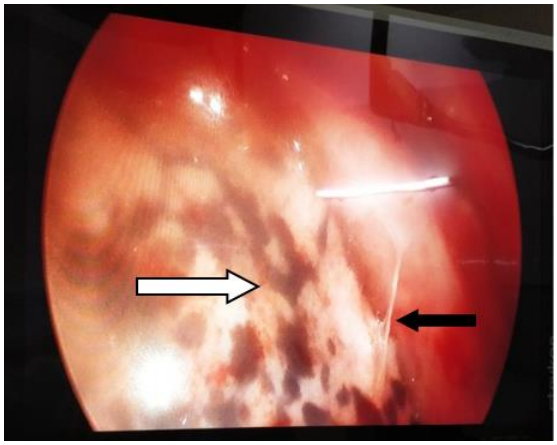

Fig. 1: Thoracoscopic view showing Nodular growth (white arrow) on parietal pleural with pleuro-parenchymal adhesions.

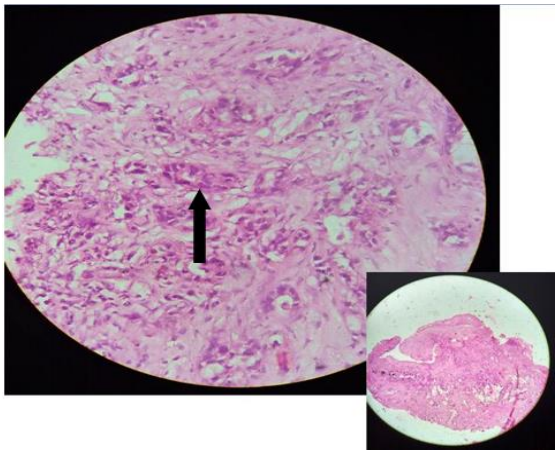

Fig. 2: Section study shows moderate cytoplasm with oval nuclei with prominent nuclei features of adenocarcinoma deposits H & E 40 X, with biopsy in 10X

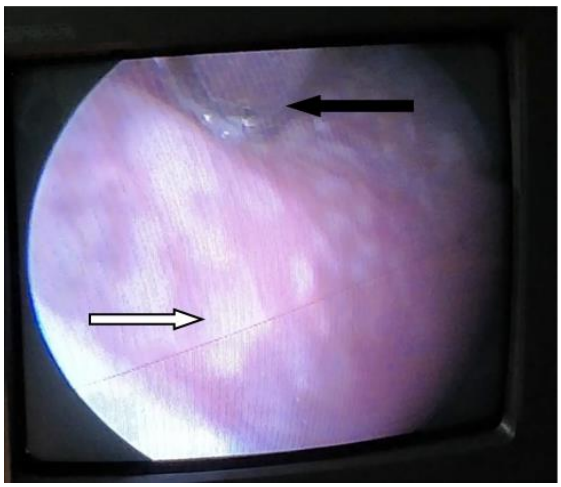

Fig. 3: Thoracoscopic view showing Sago granule (white arrow) appearance on the parietal pleura with biopsy forceps (black arrow).

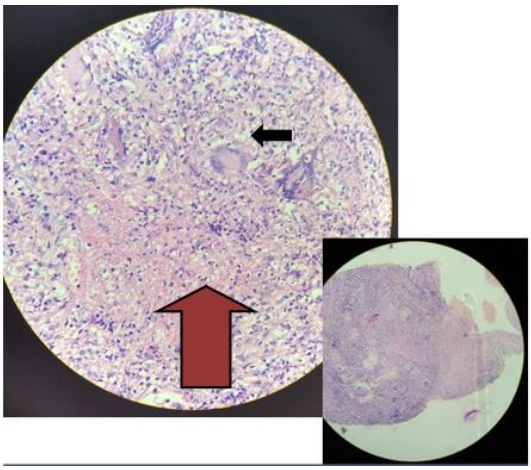

Fig. 4: Section shows inflammatory cells composed of lymphocytes, macrophages and foreign body giant cells (black arrow) along with necrosis (red arrow). H & E 40 X, with biopsy in 10X

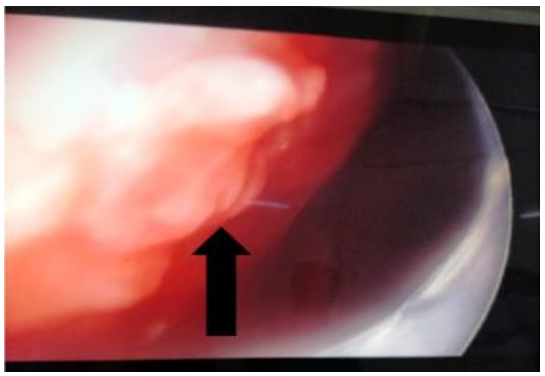

Fig. 5: Thoracoscopic view showing plaque like growth (black arrow) from pleura in mesothelioma with hemorrhagic effusion in pleural cavity.

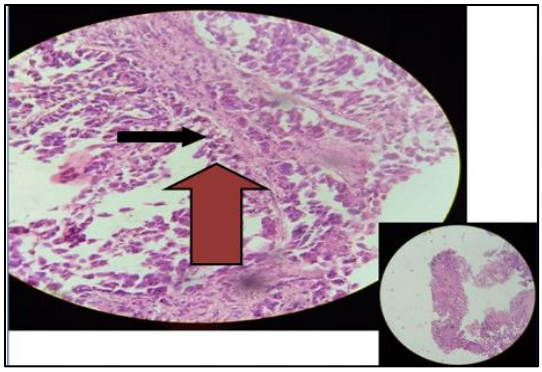

Fig. 6: Section shows proliferation of mildly pleomorphic mesothelial cells, mostly in the form of tubule-papillary patterns with intervening solid sheets (black arrow). Few foci show evidence of invasion into the underlying stroma with focal areas of necrosis, features suggestive of well differentiated malignant mesothelioma. H&E 40X, with biopsy in 10X

Of the 42 thoracoscopic procedures, two complications occurred, one case developed subcutaneous emphysema and other had persistent air leak. There were no instances of blood loss or shock during thoracoscopy procedure. One patient had cardiac arrest while giving short general anaesthesia, patient retrieved and kept in intensive care unit for observation and discharged without procedure.

Discussion

In tuberculosis pleural effusions, breathlessness and cough were the main complaints followed by chest pain, fever and weight loss, but in Berger and Mejia study [2], most patients with tubercular pleural effusions had cough, usually nonproductive, and many had chest pain, usually pleuritic in nature. In malignant pleural effusions, chest pain and breathlessness are the most common symptoms, weight loss was associated in 70% cases only. In Chernow and Sahn study, the most common symptom in malignant pleural effusions is dyspnea, which occurs in more than 50% and weight loss occurred in 32% [3].

The success of cytological analysis of pleural fluid by thoracentesis varies widely and is reported to be diagnostic in 45 - 96% of malignant effusions [4]. The diagnostic yield is lower in malignant effusion secondary to primary lung carcinoma compared with metastatic effusions. This may be due to the fact that effusions may occur as a result of lobar collapse, lymphatic obstruction, pneumonitis or severe hypoproteinaemia rather than pleural tumour involvement which may be the cause of three undiagnosed pleural effusions.

A second sample for cytology can increase the yield by 17 - 22%, but further aspirations are unlikely to increase this yield. In these patients thorascopy as the procedure can be performed easily with low mortality. The diagnostic sensitivity of thoracoscopy in Menzies and Charbonneau [5] study in 102 patients obtained a definitive diagnosis in 94% of 95 patients. In this study, thoracoscopy was 96% accurate, with sensitivity of 91%, specificity of 100% and negative predictive value for pleural malignancy of 100%.

Now-a-days, the use of targeted therapies have led to an increase in survival of lung cancer patients with certain genetic alterations such as epidermal growth factor receptor (EGFR) activating mutations and anaplastic lymphoma kinase (ALK) rearrangements [6-8] for these a good biopsy specimen is needed which can be obtained by thoracoscopy as we can assess the pleura with minimal invasion and less mortality.

In our study diagnosis was established in 92.85% cases which was similar to Tscheikuna et al., [9] and higher then Kendall et al.,[10] and Mootha VK et al., [11] studies. Parikh et al., [12] found 100% success rate in diagnosis undiagnosed pleural effusion by thoracoscopy which may be due to proper selection of cases.

To conclude the etiological diagnosis of pleural effusion remains unchanged even after few decades in our country. Even after thorough investigations with the help of closed pleural biopsy, FOB, CT scan and CT guided FNAC, and others, 5.2% of cases could not be diagnosed. It has been also observed in another study by Light RW [1] where 15% cases remain undiagnosed as higher to our present study in 07.14% cases.

Ryan et al., [13] found that 61% of patients who underwent a thoracotomy for undiagnosed pleural effusions remained without a diagnosis during a follow-up of 1.5 - 15 years later these patients etiologies such as viral pleurisy or peri-pneumonic effusion are the probable cause.

In India studies by Thangakunam et al., [14] Dhooria et al., [15] and Prabhu et al. [16], diagnostic yield of pleuroscopy was found to be 67% 73%, and 97% in studies with sample sizes of 21, 45, and 68 patients, respectively. Among all the diagnoses, malignancy was the most common, and in those cases the most common variant was adenocarcinoma followed by tuberculosis which was similar to our study with carcinoma was found in 69% cases followed by tuberculosis in 16.66% cases of 42 patients.

In our study, systemic lupus associated pleural effusions resolved after starting oral steroids. In catamenial hemopneumothorax patient thoracoscopy view showed pleural nodularity with hemorrhagic effusion (Fig. 7) after thoracoscopy she underwent Pleurodesis and was put on long-acting GnRH agonist monthly.

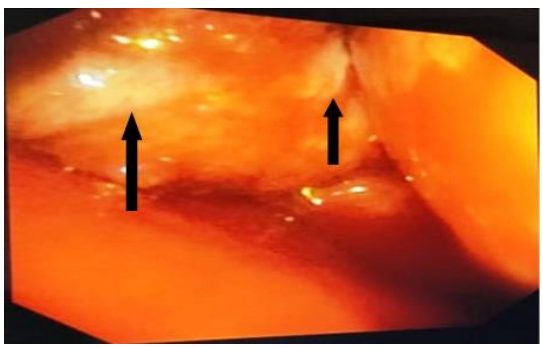

Fig. 7: Thoracoscopic view showing pleural nodules (black arrows) with hemorrhagic effusion in catamanial hemothorax.

In our study two complications occurred, one case developed subcutaneous emphysema which subsided by oxygen therapy and other case had persistant air leak which healed in ten days with conservative treatment.

Thoracoscopy is associated with a small probability (1.95%) of major complications and peri-operative mortality rates associated with diagnostic thoracoscopy range from 0% to 10% [3,5,17,18].

Conclusions

Diagnostic thoracoscopy is a useful modality with minimal complications for obtaining a diagnosis in pleural effusions where other investigative procedures have failed. Thoracoscopic pleural biopsy helps in early diagnosis and accordingly early intervention. In this era of targeted therapy, genetic mutations (eg. EGFR, ALK) can be diagnosed by obtaining adequate pleural biopsy tissue to give an individualized tailored treatment which gives better prognosis and cost effectiveness.

Conflicts of Interests: None declared.

Acknowledgements: None.

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