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The Role of Medical Thoracoscopy for the Diagnosis and Treatment of Unexplained Pleural Effusion: A Single Center Experience Over One Year

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Abstract:

Background: ***Medical Thoracoscopy (MT) is a minimally invasive endoscopic procedure that allows almost complete visualization of pleural cavity, collection of appropriate amount of samples and to do necessary work for the treatment of pathologies. MT is gaining popularity world-wide and few centers in Dhaka practicing it. Here, this study observed the utility of MT in a single centre in a single calendar year.***

Methods: ***It was a retrospective study done at respiratory medicine center of a tertiary care hospital, Dhaka reviewing records of all cases of medical thoracoscopy (MT) done as a diagnostic and/or therapeutic procedures over one year. After collecting data, we analyzed them to see the indications, pre- and post-procedural status, outcomes and safety of this procedure.***

Results: ***Total 16 patients with unexplained pleural effusion were undergone medical thoracoscopy (MT) last year in Square Hospital. All 16 had diagnostic MT and 7 had therapeutic MT as well. Among all 16 patient, 3 patients were from Oncology, 2 from intensive care unit, 1 from gastroenterology unit and 1 from nephrology unit, others were from our inpatients. MT revealed malignancy in 7 cases (43.75%), tuberculosis in 4 (25%), complicated multiloculated empyema in 3 cases (18.75%), hepatic and renal hydrothorax in 1 case respectively. Among malignant cases, bronchial carcinoma predominates, followed by breast cancer (1 patient) and uterus (1 patient). Pleural adhesionolysis and deseptation was done in 5 cases and pleurodesis by talc slurry or poudrage in 4 cases. There was no major adverse effect seen at or after the procedure. Pain due to chest tube was the main adverse-effect which was managed with simple analgesics. One patient had mild reperfusion pulmonary edema which was easily managed with perenteral steroid for 3 days. One patient had bronchopleural fistula which was managed with repeated tetracycline pleurodesis. All patients were managed effectively with only 2 patients shown to have minimal residual effect like pleural thickening.***

Conclusion: ***Medical thoracoscopy or pleuroscopy is a safe and very effective procedure for the diagnosis of the primary etiologies of unexplained pleural effusion and their management.***

Key words: ***Medical thoracoscopy, Unexplained Pleural effusion, Pleurodesis, Adhesionolysis***

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Introduction:

Pleural effusion is a common clinical problem in our daily practice. It's estimated that 40000-50000 patient suffers from PE in USA each year[1]. A lot of conditions lead to accumulation of fluid in pleural space. Common causes of pleural effusion are heart failure, chronic liver disease, pneumonia, tuberculosis and malignancy[2]. It is essential to find out the cause of pleural effusion for its effective management.

Simple thoracocentesis and pleural fluid analysis can give very important clues to explore the etiologies of pleural effusion especially in transudates[2,3]. It can be done at bed side based on clinical and radiological findings without any local anesthetics or analgesics.

Sometime, especially when pleural effusion is small or loculated, an ultrasonography can guide the procedure[4]. Most important distinction that can be made from pleural fluid analysis is whether fluid is transudate or exudative using to Light's criteria. Transudative pleural effusion had low protein and low LDH and found in cardiac failure, cirrhosis of liver, nephritic syndrome, malabsorption etc. Exudative fluids have high protein and LDH content and mostly found in TB, Malignancies, pneumonia. Pleural fluid cell counts could reveal predominance of lymphocytes or neutrophils or others. In pneumonia, neutrophils are and in TB or malignancy lymphocytes are the predominant cells. Adenosine Deaminase (ADA) which is an important enzyme released by lymphocytes is found elevated in TB, empyema or lymphoma, but normal in malignancies[5]. Malignant cell in pleural fluid cytology is a strong evidence of malignant origin and guide for further investigations to find out histological types and primary site of origin. Pleural fluid microbiological culture can provide important clues to antimicrobial treatment. Pleural fluid PCR can also provide important investigations. Thus simple thoracocentesis and fluid study can help to explore the etiologies of pleural fluid along with other clinical findings[6].

Closed pleural biopsy by Abrahms' or copes' needle (± USG guide) for histopathological study is an important diagnostic tool to establish the causes of pleural effusion[4,7]. This procedure is also a simple, outpatient procedure done under local anesthesia giving 1-1.5 cm incision without any stitch by using an Abrahms' needle or cope needle. It has revealed combined yield of diagnosis in 48% to 90% cases[7]. Tubercular pleural effusion demonstrates chronic granulomata with or without caseous necrosis and sensitivity shown to be 48% to 78%. Malignant pleural effusion shows histological type malignancy and sensitivity 31% to up to 90%. Variability on diagnosis depends on user expertise, image guidance etc[7].

Medical Thoracoscopy is a minimally invasive procedure that provides access to the pleural spaces for proper inspection of whole pleural cavity and to do necessary work for the diagnosis and treatment of the patient. It allows for the basic diagnostic (undiagnosed pleural effusion and thickening) and therapeutic procedures (pleurodesis) to be performed safely[8]. It's a day-care procedure done under local anesthesia and conscious sedation in an endoscopy suit. A medical thoracoscope has a flexi-rigid scope, a processor and a monitor. The processor and monitor is the same instruments that is used with bronchoscope or any other endoscope and flexi-rigid scope is a fibre-optic camera device that is introduced into the pleural space through a simple 2-3 cm incision made over the 5th to 7th intercostals space for inspection of whole pleural space[8]. This procedure is very useful to determine causes of undiagnosed unilateral pleural effusion and to do pleurodesis and/or pleural adhesionolysis. Major recent cardiac event or cardiogenic shock or use of anticoagulants is relative contra-indications for the procedure. Approximately 25% of all pleural abnormalities remain undiagnosed after thoracentesis and/or closed pleural biopsies[2,4]. The diagnostic yields for MT in undiagnosed pleural effusion is 99.5% with lung malignancy being the most common diagnosis (41%) followed by tuberculosis (31%)[9].

In contrast, video-Assisted Thoracoscopic Surgery (VATS) is done in operation theatre under general anesthesia with single lung ventilation usually through multiple ports[10] for major surgeries like lobectomy or segmental resection or decortications etc. It is a more invasive procedure that uses sophisticated access platform and uses multiple ports for separate viewing and working instruments to access pleural space, and for complete visualization of the entire hemithorax, multiple angles of attack to pleural, pulmonary (parenchymal), and mediastinal pathologies with the ability to perform both basic and advanced procedures safely.

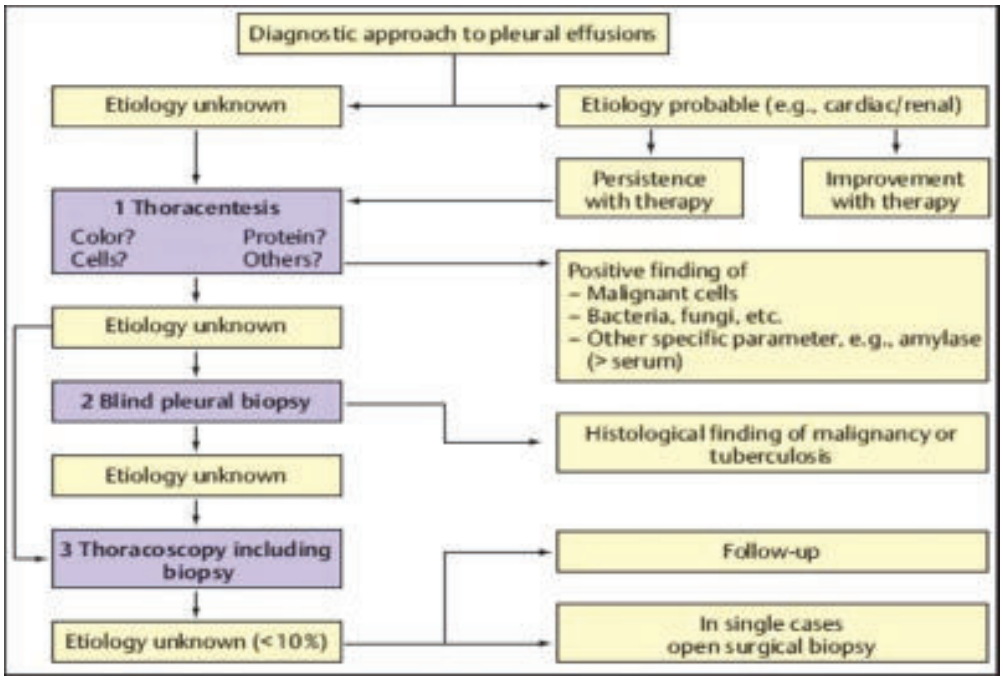


Table-1: Diagnostic Approaches to patients with Pleural Effusion

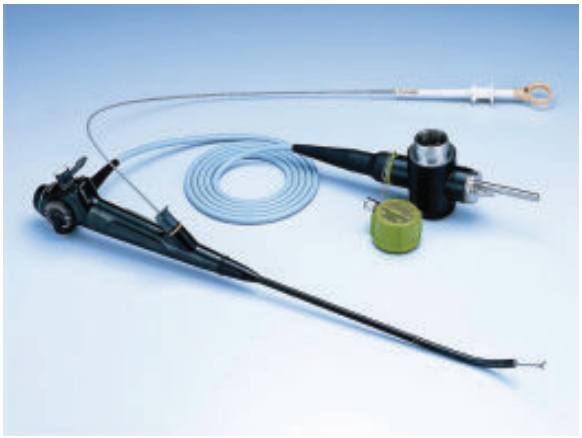


Figure-1: *Medical Thoracoscopy with Biopsy Forceps (pushed into the working channel with cutting end outside)*

Materials and Methods:

It was a retrospective study done at respiratory medicine center of Square Hospital limited, Dhaka reviewing records of all cases of medical thoracoscopy (MT) done as a diagnostic and/or therapeutic procedures over one year. All patients who had MT at that time were studied by collecting the data from in-patient and OPD visit records. After collecting data, we analyzed them to find out the indications of MT, their presenting features, comorbidities, procedural events, after procedural complications and outcomes. Procedural events included the total time, local anesthetic agents and sedatives used, detailed findings of pleural fluid and cavity, on-table complications and post-event adverse effects were studied thoroughly. Lastly, at the time of follow-up, the patients' outcomes both clinical and radiological were examined the effectiveness of the procedure.

All medical thoracoscopies (MT) were performed in the endoscopy suit of the hospital by an expert pulmonologist under conscious sedation[12, 13]. Before MT, all patients were undergone CT scan of chest with contrast to locate puncture site and echocardiography to assess cardiovascular risks. Procedure duration was defined as time to start of skin incision to IT tube insertion. Pleural biopsies and fluid /pus collected for studies and recorded. Major and minor complications was studied along with their management protocols. Those had multiple bands and adhesions an attempt to remove those were done. Those had malignant PE, pleurodesis was done to close the space by talc slurry or poudrage. It was done when IT tube drainage became lesser than 100 ml for two consecutive days. Talc slurry was made by introduction of 50 ml normal saline into a talc powder vial and gentle shake mixed up the powder well. About 20 ml 2% lidocaine sulphate was injected 20

minute prior installation of talc mixture into the pleural space through IT tube. After Introduction of talc mixture, IT tube was kept blocked there for 1-2 hour. Then IT tube was removed and puncture site was closed tight with silk suture. Baseline characteristics also recorded and analyses here in this study.

Results:

During this one-year, total 16 patients had medical thoracoscopy (MT) including 11 diagnostic, 7 therapeutic purposes. Mean age of these patients was 52, ± 11 yrs. Male: Female ratio was 1.6: 1. Eight (50%) patients were from respiratory IPD; 3 patients from Oncology, 3 from ICU, 1 from gastroenterology and 2 from nephrology. 10 patients had ho smoking. 2 patient had previous malignancies.

Total VII cases (43.75%) had malignant PE, 4 cases (25%) tubercular, 3 cases (18.75%) empyema and 1 hepatic and 1 renal hydrothorax. Among malignant cases, bronchial carcinoma predominates, followed by breast cancer (1 patient) and uterus (1 patient). All empyema had turbid to yellowish fluid with varying degree of bands and adhesions. Tuberculous cases had small nodules on both pleura with multiple bands and adhesions. Malignant cases had larger nodules to masses that easily bleeds on touch and had hemorrhagic fluid. Renal and hepatic hydrothorax had shinny smooth pleural surfaces without any nodules or masses. Average procedure time was 40, ±24.3 minutes. Hospital stay was 48, ± 22 hrs in diagnostic MT.

Pleural ahesionolysis and deseptation was done in 5 cases; of them 3 for complicated empyema and 2 for tuberculous cases. For complicated empyema, post procedural fibrinolytics (Streptokinase) was used that was uneventful and helps in complete lung expansion. 4 patients were underwent pleurodesis by talc slurry or poudrage after/with the procedure. Each time, procedure was well tolerated and no patient reports for any problem.

During procedure, cough seen in 4 cases (25%) that had delayed the procedure for 5-10 minutes only. There was no arrhythmia other than sinus tachycardia (seen in 6 cases) at or after procedure. Post-procedural pain of variable severity was the main adverse-effect seen in 100% cases; which was managed effectively analgesics. One patient had mild reperfusion pulmonary edema which was easily managed with steroid for 2 days. One patient who had hydropneumothorax with HO recent needle aspiration initially found to have bronchopleural fistula after MT, was managed with repeated tetracycline wash/pleurodesis. There was no procedure related mortality (0%). One patient with parapneumonic effusion died of sepsis 3 weeks later for multi-organ failure (MOF) long after removal of IT tube.

Table-II

Characteristics of studied populations and MT procedures (n-16)

Characteristics	Value (n-16)
Age, yrs	52, ±11
Male sex	10 (16)
Smoking status	9 (16)
Current	5
Former	4
Never	7
History of TB	1/16
History of Malignancy	2/16
Sedation	
Fentanyl, mcg	50, ± 50
Midazolam, mg	3, ± 2
Propofol, mg	30, ± 20
Procedure time, minutes	52, ± 33
Fluid	
Straw	9
Hemorrhagic	5
Turbid	2
PE sided predominance	
Right	7
Left	9
Pleural cavity findings	
Small nodule	5
Large nodules	6
Fibrous adhesions	10
Loculations	6
No abnormalities	2
Chest tube drainage time, days	4, ± 6
Adverse Effects	
Mortality	0
Cardiac arrhythmia	0
Hypotension or shock	0
Pain	100%
Pulmonary edema	6.25%
Pneumothorax	0
Infection	0
Outcomes of PE, at discharge/Follow-up	
Complete resolution	14
Resolution with minimal abnormality	2
Not resolved	0

Parapneumonic Pleural Effusion and Empyema Thoracis

Among all 16 patients with MT, three patients had multiloculated parapneumonic effusion and empyema thoracis. All had hazy to turbid fluid with varying septations and loculations. After taking samples, all had adhesionolysis and deloculation by removal of septas which eventually revealed very effective in complete lung expansion and fluid drainage through chest tube. Thereby, ultimately complete recovery from complicated empyema.

Case:

Mr JM, 51 years old normotensive, non-diabetic, smoker gentleman got admitted into SHL with the complaints of high fever with productive cough with sputum production for 20 days. He was living in KSA and was working as field worker there. Immediately after getting sick there, he took some antibiotics and cough suppressants without any recovery and came to Bangladesh for proper treatment. Physical examination found that he had left sided moderate to large pleural effusion with chronic obstructive pulmonary disease.

Complete blood count of this patient was done at hospital and it showed Hb% 9.90 gm/dl; total while cell count was 21,900 cu.ml and Neutrophils were 84.0%; Lymphocytes 10.1%; Monocytes 4.00%; Eosinophils 1.30%; Basophils 0.60%; Platelet 795. CRP was 297.1; Procalcitonin (PCT) 0.35. At first, bed-side thoracocentesis was done and pleural fluid sent for study. It was mildly purulent; white blood cell count was 13380 with PMN 81.0%; Eosinophil 0.00%; Lymphocyte 18.0%; Macrophage 1.00%. Pleural Fluid Protein was 4.2 gm/dl, Sugar 87 mg/dl, ADA (Adenosine Deaminase Assay) 224. A CT scan of chest with contrast was done that showed left sided multiloculated moderate to severe pleural effusion with a thick walled cavitary lesion in right lung. Blood picture, fluid cytology and history favors complicated parapneumonic effusion, but high ADA, cavitary lesion on CT chest along with thickened pleura favors tubercular origin. Moreover, multiple septation and loculation had to indication for MT.

Finally, pleuroscopy was done that explored thick layers of purulent secretions throughout the pleural space including parietal and visceral pleura with multiple septations and loculations. Purulent fluid was evacuated and septas were removed as far as possible from pleural cavity and thereby disrupted the loculations. Chest tube was given to drain residual pleural fluids. Lastly on the next few days, 2.5MU Inj. Streptokinase was given in intrapleural space through chest tube once daily for 3 consecutive days along with parenteral antibiotics and other conservatives.

Lastly, the patient was followed up at 3 weeks, 6 weeks and after 2 months and found to have complete resolution of empyema with minimum residual effect (Chest x-ray given). In this way, MT play a vital role in diagnosis and treatment of complicated parapneumonic effusion and help to avoid possible surgical or VATS decortications.

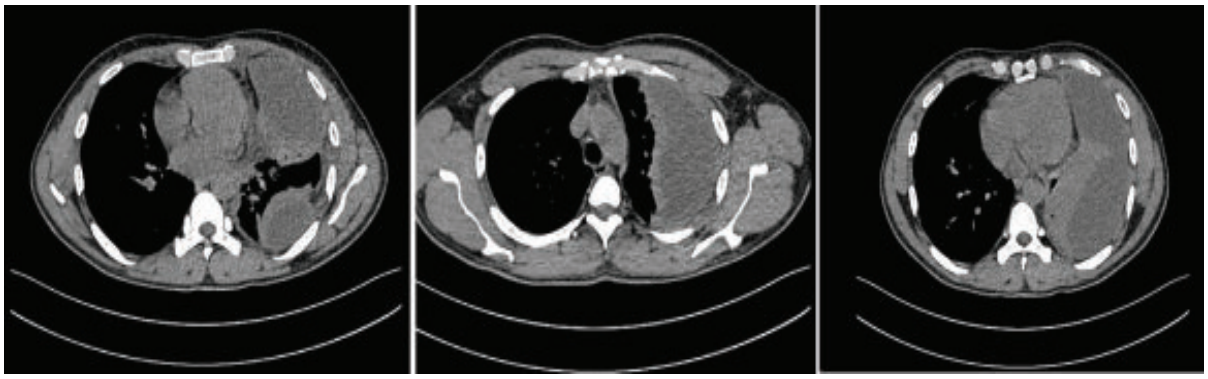


Figure-2: *CT chest with Contrast revealed left sided multi-loculated pleural effusion*

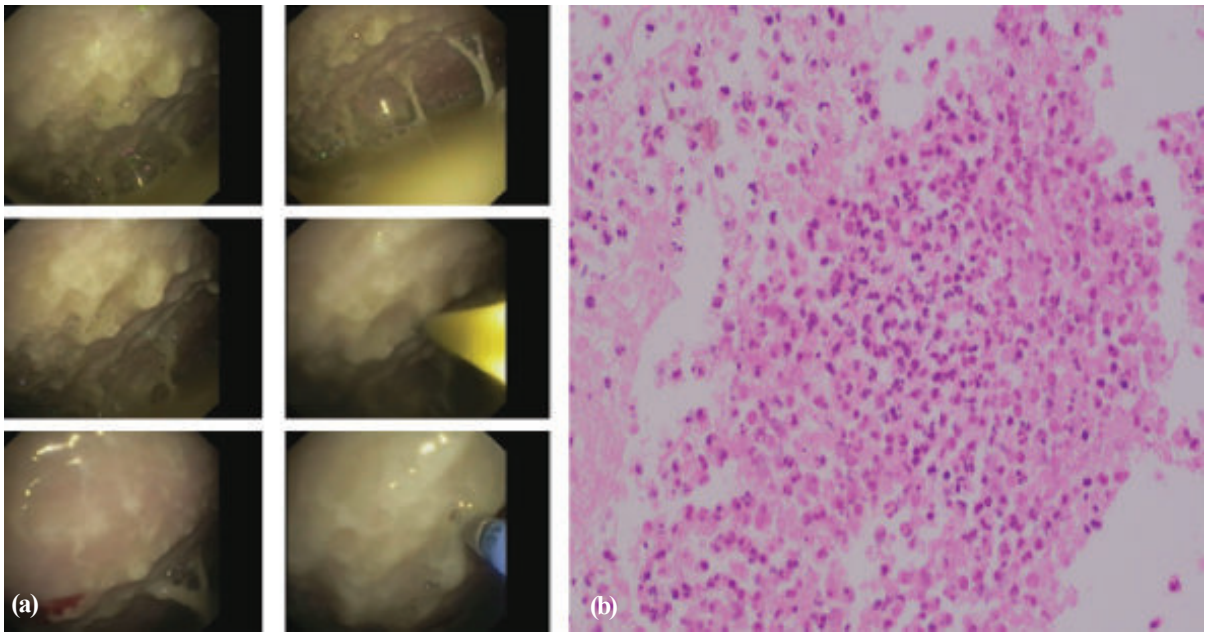


Figure-3: *(a) Medical Thoracoscopy report showing layers of purulent secretion on both parietal and visceral pleura with fibrous loculations. (b) Histopathology shows huge infiltration polymorphs.*

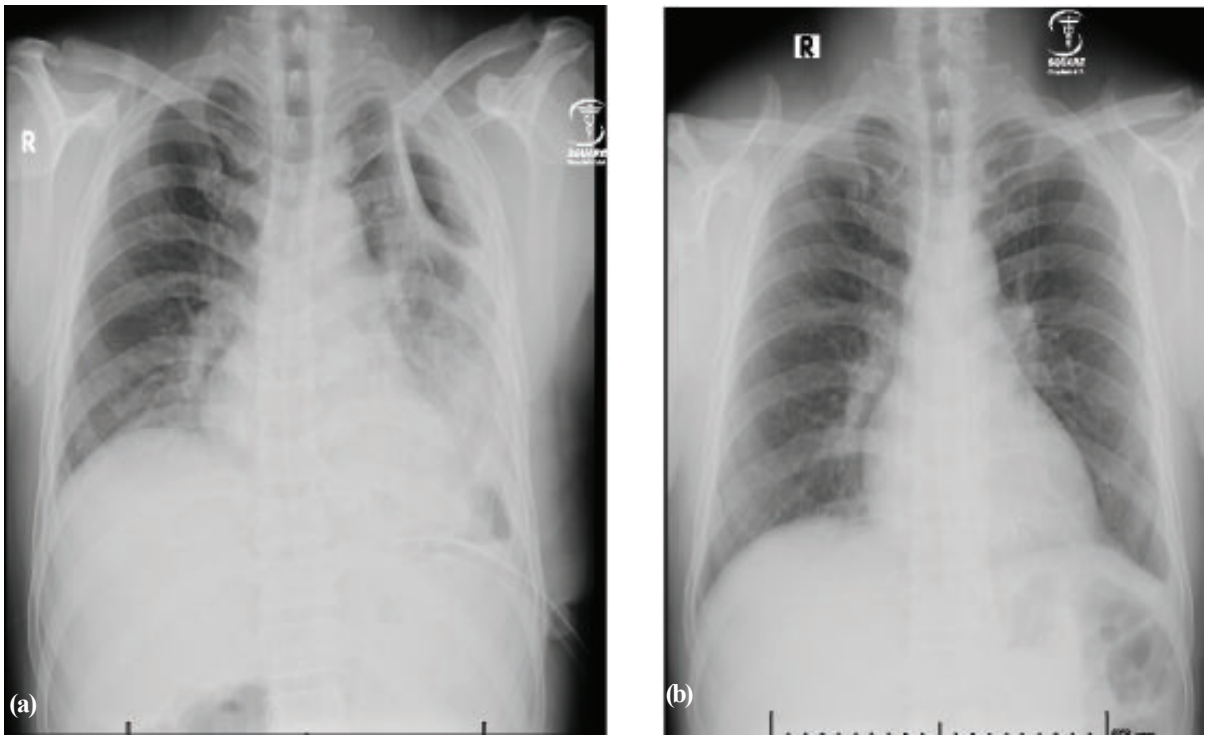


Figure-4: *Chest radiographs immediately after procedure (a) and after recovery (b)*

Malignant Pleural Effusion

Total 7 patients (43.75%) with malignant effusion were explored. Among them, bronchial carcinoma predominates, followed by breast cancer (1 patient) and uterine cancer (1 patient). Four patients were undergone pleurodesis by talc slurry (3 patients) and talc poudrage (1 patient). One patient had hydropneumothox and found to have broncho-pleural fistula during pleroscopy and was treated with repeated tetracycline solution wash. Here, this reported case had previous history of both breast cancer (2018) and thyroid cancer (2006) and pleuroscopy needed to explore the primary site.

Case:

Mrs. RS, 40 years young lady diabetic, normotensive got admitted into SHL through OPD for exertional breathlessness for 25 days and low grade fever for 15 days. Previously she had carcinoma of right breast diagnosed in 2018, for which she was underwent mastectomy followed by completed treatment with chemotherapy & radiotherapy. She had thyroid follicular carcinoma in 2006 and was underwent total thyroidectomy followed by radioactive iodine therapy. She had Laparoscopic Cholecystectomy (2014) and cesarean section thrice in her lifetime. Now after clinical evaluation, we found right sided moderate to severe pleural effusion and she had admitted for further evaluation and management.

Total WBC count was 5.91 K/ýL, N 61.6%, L 31.0%, M 4.4%, Platelet 412 K/ýL, Hb 10.0 gm/dl, CRP 10, Creatinin 0.8 mg/dl. Pleural fluid total WBC 1021/cumm, L 94%, N 2%, Protein 5.1 gm/L, Sugar 120 mg/dl, ADA 25.7 U/L, no malignant cell found. MT was 08 mm. Pleuroscopy was done for diagnostic purpose and it revealed that there were multiple nodular lesions of variable size and shape in both parietal and visceral pleura with huge amount of hemorrhagic fluid throughout the pleural cavity. Total 1300ml pleural fluid was evacuated and 5 pieces of biopsy material taken from anterior pleura for histopathological study. Chest tube drainage was given. But patient had cough after procedure. A Chest radiography was done that revealed bilateral central haziness consistent with reperfusion pulmonary edema. Parentral dexametasone was given for 2 days and cough reduced gradually. Follow-up x-ray chest revealed disappearance of pulmonary opacities. and kept there for 5 days till collection is gradually decreased to less than 100ml for 2 consecutive days.

Histopathology showed malignant tumor composed of atpical cells arranged in cords or nests. Immunohistochemistry (TTF1, P63) shown metastatic carcinoma, favors metastatic ductal carcinoma. In view of ER+ ve, possible primary site is breast. Lastly, pleurodesis with talc slurry was done and IT tube was removed. Now she is haemodynamically stable and discharged with advice.

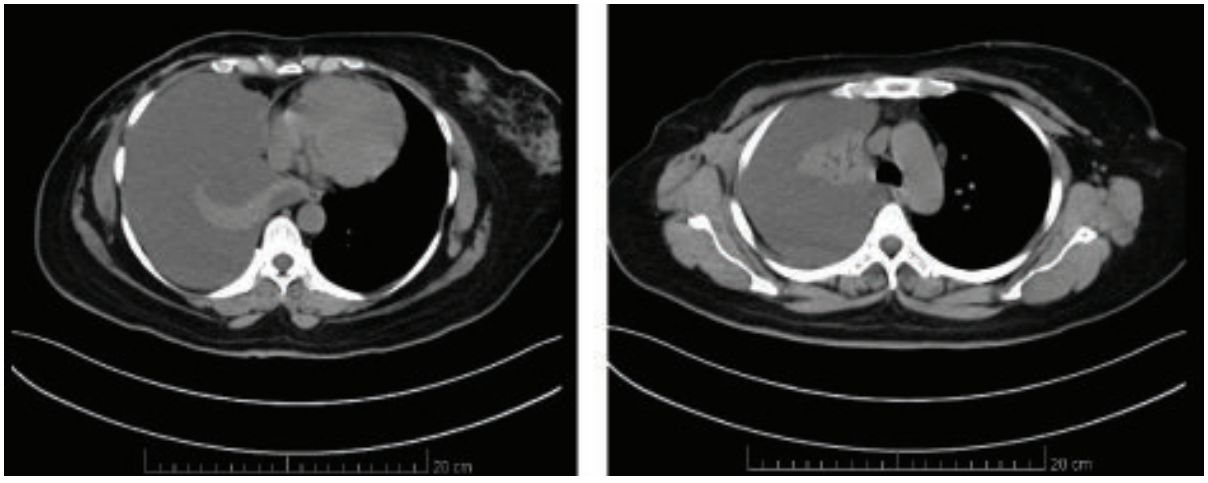


Figure- 5: *CT scan of Chest with Contrast revealed massive pleural effusion with complete collapse of adjacent lung*

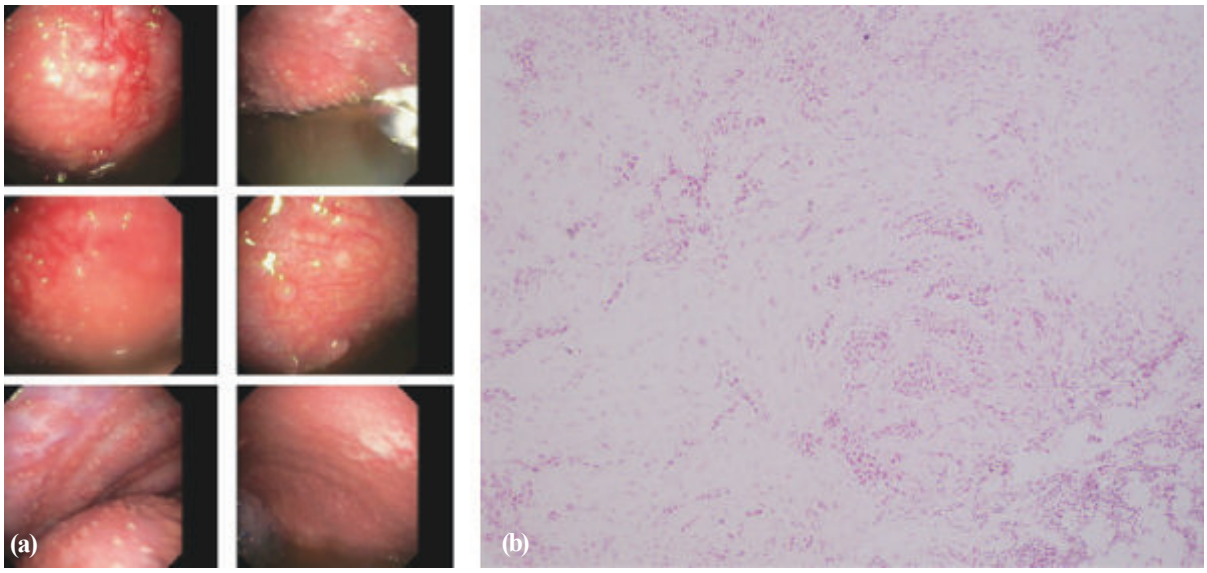


Figure-6: *(a) Medical Thoracoscopy shows multiple nodules with hemorrhagic fluid. (b) histopathology showing malignant cells arranged in nests*

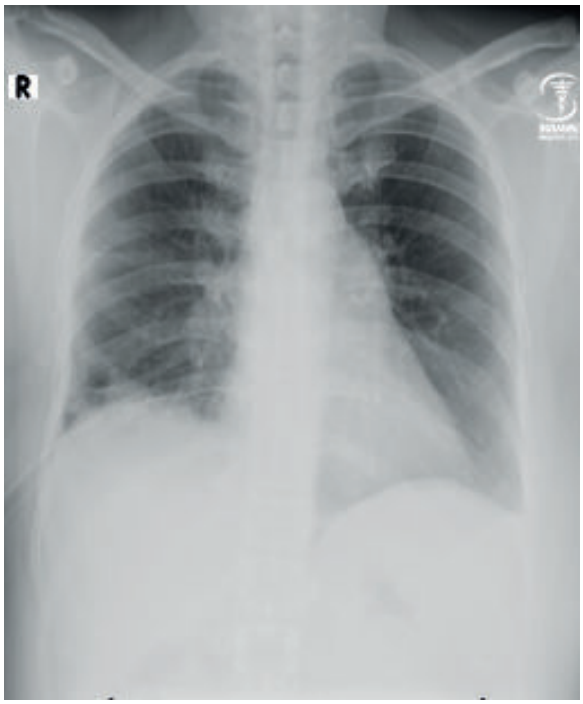


Figure-7: Chest radiograph after medical thoracoscopy revealed minimal pleural effusion with IT tube in situ

Tubercular Pleural Effusion

Four cases (25%) were found to have tuberculosis after MT. All the time, it revealed multiple nodules of variable size with varying degree of septas and adhesions. Three cases had straw colored fluid, one had mildly hemorrhagic. Deseptation and adhesionolysis was done in 2 cases, that shown to have positive outcomes.

Case:

Mrs. SA, 50 years old pre-diabetic, hypertensive lady hailing from cumilla got admitted into SHL through ER with the complaints of cough with sputum production for 20 days with chest pain & shortness of breath on & off for 7 days. She had no previous history TB or contact with smear positive TB. On clinical evaluation, we found right-sided massive pleural effusion with medistinal shifting with type 1 Respiratory failure (spo2 86% at room air) that was unusual for TB pleural Effusion. She was undergone pleurocentesis outside and found exudative (pleural fluid protein 32 gm/L), lymphocyte rich (67%) pleural fluid with no malignant cell and normal adenosine deaminase (17 U/L). Her CT scan of chest with contrast revealed right-sided huge pleural effusion with complete collapse of lower lobe and partial collapse of upper lobe of right lung and shifting of mediastinal structures towards opposite side.

After admission, Total WBC 9.79 K/ýL, N 62%, L 29.7%, M 5.90%, Hb 10.4 gm/dl; CRP 42.3 mg/L, procalcitonin 0.06 nm/ml; sputum for AFB stain negative. Medical thoracoscopy was done that revealed multiple nodules of varying size and shape on both parietal and visceral pleura along with huge amount of straw colored pleural

fluid. Total 1100 ml straw colored pleural fluid was evacuated and four pieces of pleural tissue taken for histopathological study. Cytology (Cell Count) of pleural fluid was RBC: 2000; WBC: 2707; PMN 2.00; Eosinophil 0.00; Lymphocyte 96.0; Macrophage 2.00. Mesothelial cell less than 1% of all nucleated cells. Pleural fluid protein was 5.9 gm/L, sugar 151 mg/dl, LDH 166 U/L, ADA (Adenosine Deaminase Assay) was 87.3 U/L. Histopathology of biopsy specimen shows a fair number of granulomas composed of epitheloid cells, lymphocytes, histiocytes and giant cells. Caeseous necrosis was not seen. No evidence of malignancy was seen. Pleural fluid, cytology: Negative for malignant cell. Anti-TB regime (CAT-I) was started thereafter and her ICT was removed after 2 days. During follow-up after 1 month of treatment, we found almost complete resolution of effusion with minimal pleural thickening; but advised to complete6 months' anti-TB treatment.

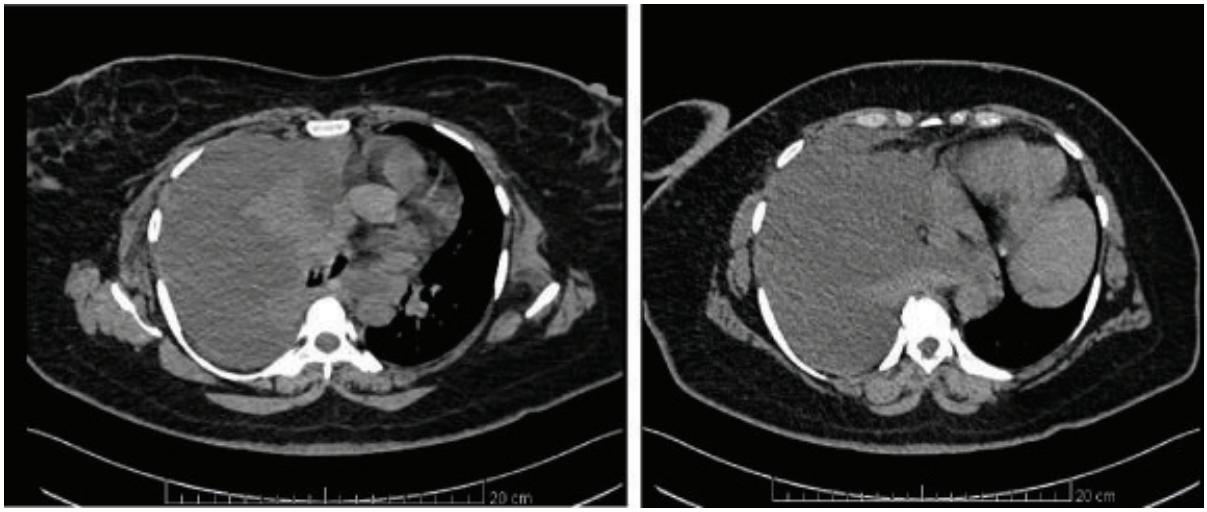


Figure- 8: *CT Chest revealed massive right sided pleural effusion with medistinal shifting.*

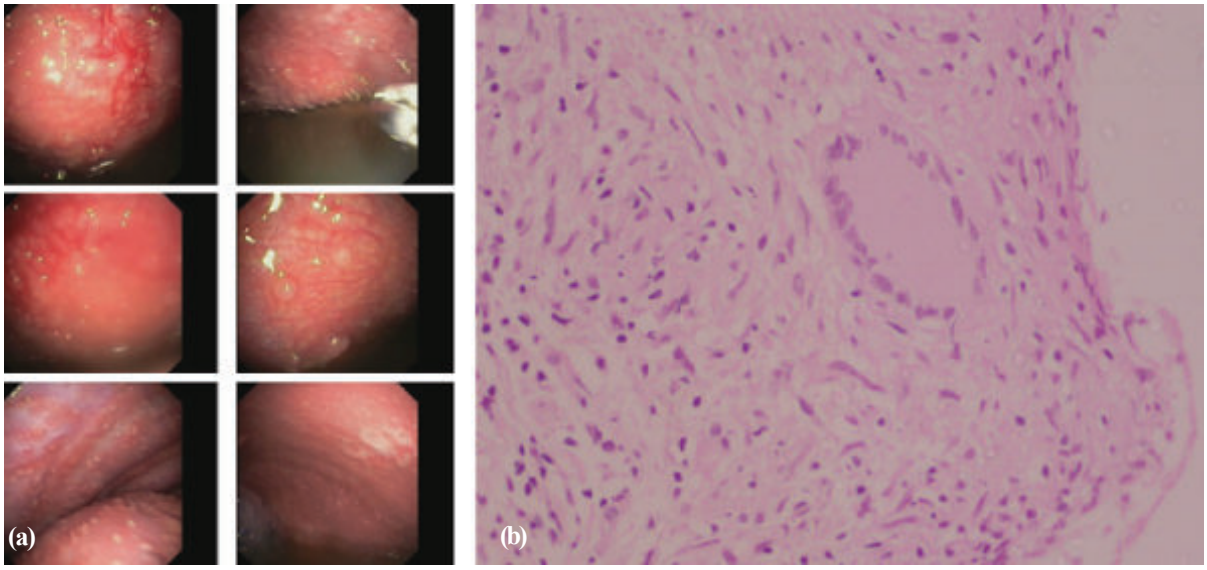


Figure-9: *(a) Pleuroscopic view of multiple nodular lesions in both visceral and parietal pleural with straw coloured pleural fluid. (b) Histopathology showing multiple granulomata with epitheloid cells.*

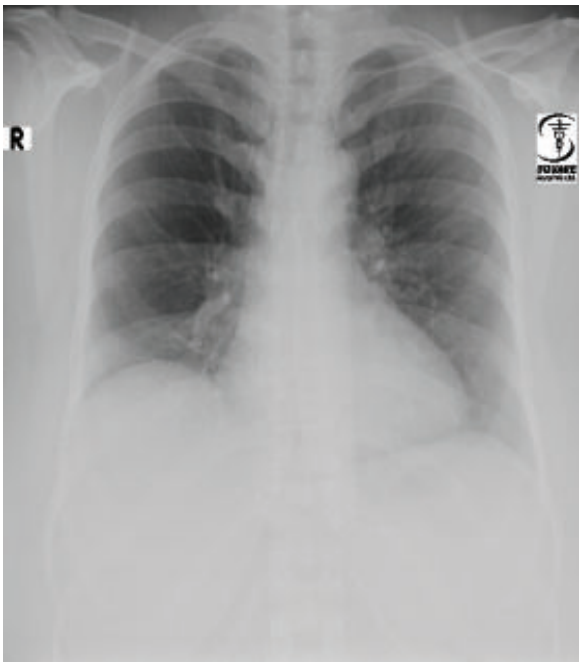


Fig-10: *Chest radiography revealed complete resolution of massive pleural effusion after 1 months' ATT*

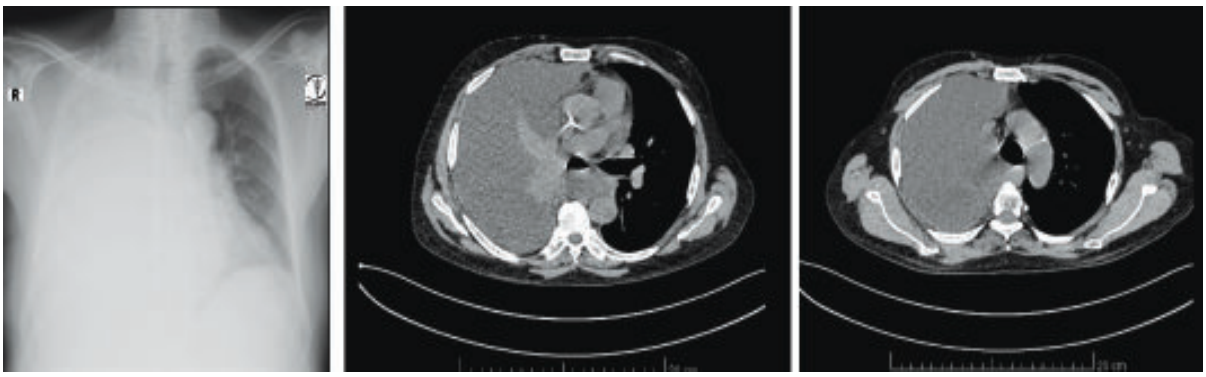
Hepatic hydrothorax:

Mr. KCB 64 years' old patient was referred to us who had chronic liver disease (NBNC) and hypothyroidism from GE-SHL with the complaints of severe respiratory distress and chest pain for 3 weeks. It was seen that he had massive right sided pleural effusion and pleural fluid was aspirated few days earlier in outside hospital and fluid analysis results were inconclusive. Patient had serious chest and upper abdominal pain and admitted to SHL for proper evaluation.

After admission, pleural fluid was aspirated twice here for both diagnostic and therapeutic purpose and each time, aspirated amount was more than 1 liter. Pleural Fluid Study Shown that is was transudative in nature; But Patient had recurrent rapid re-accumulation of huge pleural fluid within 2 days on that side only despite correction of serum albumin level by parental albumin. He had serum alpha- fetoprotein twice to exclude hepatocellular carcinoma and result was only 13 and 11. Other tumor Markers were also within normal limit. Fiberoptic bronchoscopy (FOB) was done to exclude underlying lung malignancy or pathology but it showed no endobronchial growth, only mild inflammation was seen at right lung. Bronchoalveolar lavage (BAL) revealed AFB stain was negative, gene x-pert also negative.

Pleuroscopy with biopsy was done on 20/01/2022 and about 1200ml pleural fluid was evacuated and sent for further analysis. There was no nodule or growth seen. Cavity was closed leaving a chest tube (28Fr) in situ. Histopathology pleural tissue revealed acute and chronic pleuritis. After 3 days of procedure, chest tube drainage was minimum (<100 ml) and follow-up x-ray chest shows complete lung expansion. Chest tube was removed and patient was discharged with advice.

Patient attended follow-up after 1 month and patient was found no cough, no respiratory distress and normal chest radiographs. This is the way, a refractory pleural effusion with CLD patient was managed with simple MT and chest tube drainage along with other conservatives.



Figue-11: *Chest Radiographs revealed massive right sided pleural effusion with complete collapse of adjacent lung (which is unusual in decompensated CLD)*

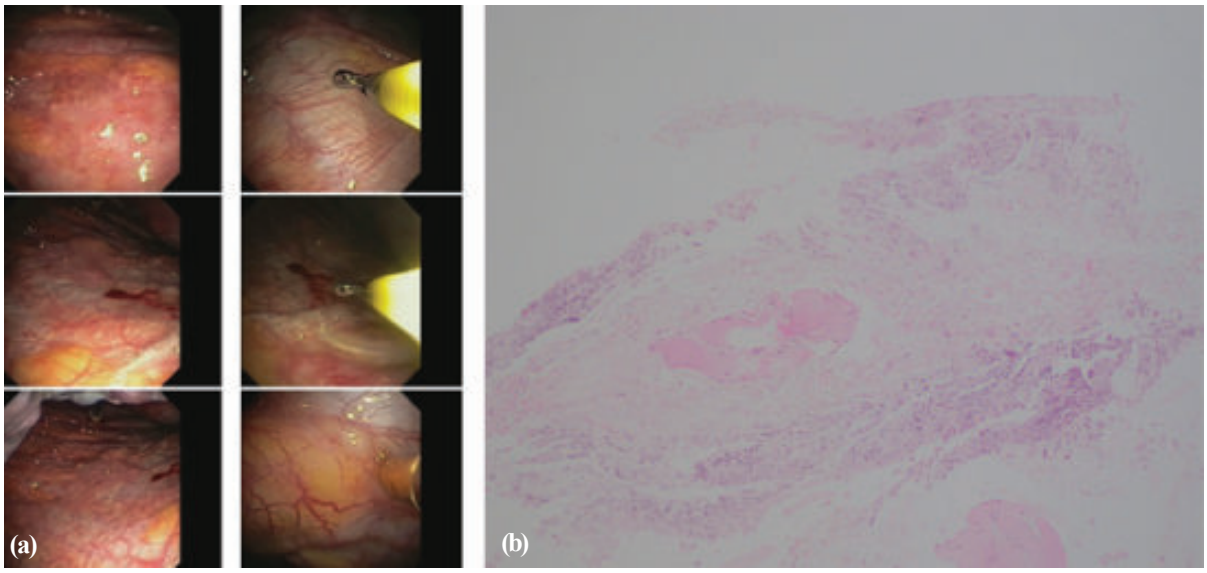


Fig-12: *(a) Pleuroscopic view of straw colored pleural fluid with shinny healthy cavity wall (b) Histopathology of biopsy sample showed acute and chronic inflammatory cell infiltrates.*

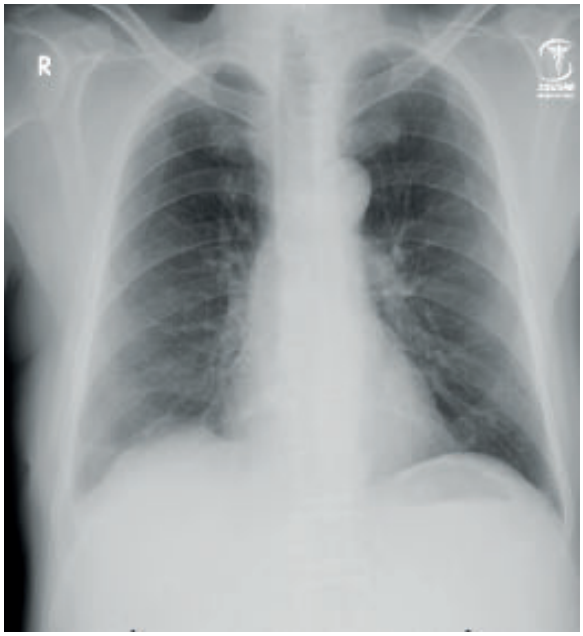


Fig-13: *Chest X-ray after Intervention at follow-up revealed complete resolution of Pleural effusion*

Renal Hydrothorax:

Mrs. MI 69 yrs old house-wife was admitted at nephrology unit for breathlessness and cough for 2-3 weeks. She had ESRD and was on hemodialysis under nephrology unit. She had Spinal TB and receiving anti-TB treatment (on continuation phase) for last 4 months. She had HO pulmonary/pleural TB 15 yrs back. She had HTN 10 yrs, T2DM for 6 yrs, BA, OSA. Immediately after admission, the patient was found to have left sided moderate pleural effusion without any fever or tenderness.

Total WBC count was 5.68 K/µL, N 66.4%, L 23.2%, M 6.2%, Platelet 255 K/µL, Hb 10.7 mg/dl. CRP was 24.9 mg/L, blood urea 37mg/dl, S. creatinine 3.5 mg/dl, s. albumin 4.6 gm/dl. CT scan of chest with 50 ml contrast was done and it revealed left sided moderate to gross pleural effusion with collapsed greater part of left lung and consolidation in aerated part of left lung, right lung nodules with minimum pleural effusion, bony destruction and soft tissue lesion at lower dorsal spine. USG of whole abdomen was done that revealed left sided gross pleural effusion with evidences of chronic renal parenchymal disease. Color doppler echocardiography revealed no wall motion abnormalities with EF 55%. CA-125 was 4.45 u/ml; CEA 89.4 U/ml; CA-19-9 35.8U/ml. Diagnostic and therapeutic thoracocentesis was done twice at nephrology unit and pleural fluid was shown protein 2.0 gm/dl and 2.9 gm/dl respectively, lymphocyte 80% and 93% respectively without having any malignant cell or raised adenosine deaminase (3.32 u/liter, 16.4 U/L). But pleural fluid re-accumulated repeatedly within short period and patient had dyspnea and needed 2 litre/min oxygen to maintain SpO2 >90%.

Lastly, pleuroscopy was done to explore the etiology that shown no nodular lesion or fibrous lesion seen, slightly hemorrhagic pleural fluid was seen with normal shinny pleural surfaces. Pleural fluid was sent for analysis and biopsy sent for histopathological study. Pleural fluid WBC was 79 mg/dl, L 93%, N 6%, Protein <2 gm/L, ADA 3.2 U/L, GeneXpert for MTB- negative,

malignant cell absent. Histopathology of biopsy specimen revealed fibro collagenous tissue focally lined by plumps of mesothelial cells with infiltration of chronic inflammatory cell including lymphocytes and histocytes. IT tube drainage was shown to be reduced in amount over few days and drainage tube was removed.

At follow-up, patient haven't re-accumulated pleural fluid again, but had mild pleural thickening that was managed conservatively. Thus a patient with uremic pleurisy or chronic pleuritis of unknown etiology in a ESRD patient was managed uneventfully.

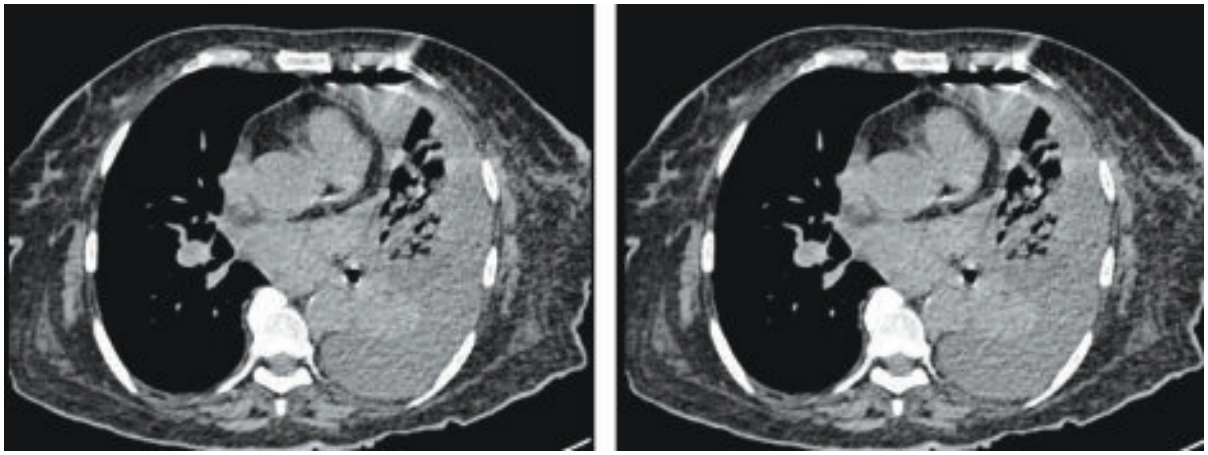


Fig 14: *CT Chest with contrast revealed left sided massive pleural effusion with loculations*

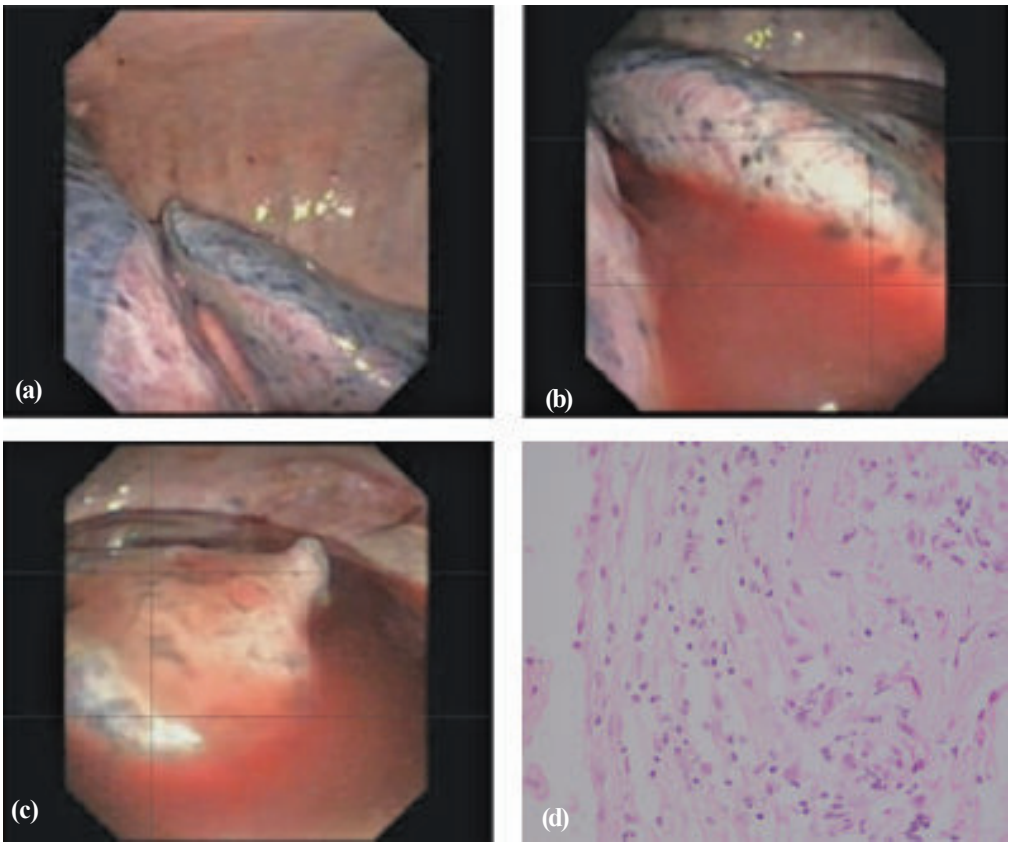


Figure-15: *(a-c) MT showing hemorrhagic fluid with normal looking parietal and visceral pleura. (d) pleural biopsy for histopathology demonstrated chronic pleuritis*

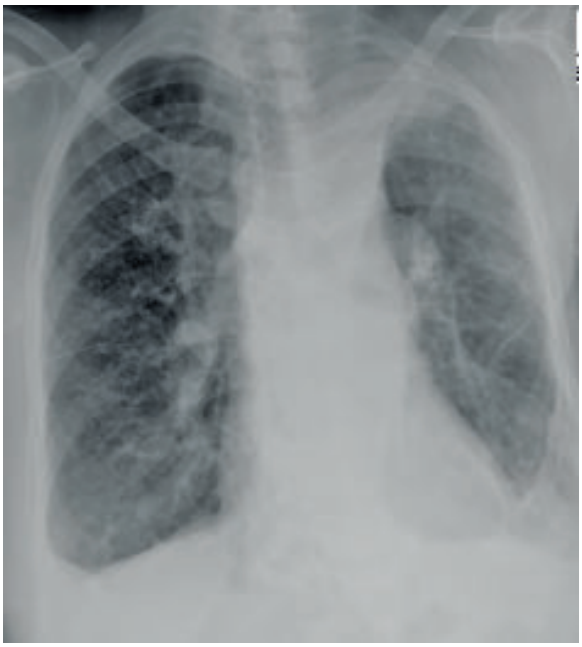


Figure-16: *Follow-up chest radiograph showed residual pleural thickening and upper lobe fibrosis (may be due to old PTB)*

Discussion:

Thoracoscopy was first performed by Francis-Richard Cruise in 1866, but the recognized "father of thoracoscopy" is Haus-Christian Jacobaeus, a Swedish physician from Copenhagen[11]. In 1910, Jacobaeus published a paper on laparoscopy and thoracoscopic surgery. In 1913, Jacobaeus used thoracoscopy to loosen the adhesion zone with the parietal pleura visceral layer to create a thorough artificial pneumothorax (APT), so that this technique is applied to the collapse therapy of tuberculosis, which is called "Jacobaeus surgery." Medical thoracoscopy was widely used in Europe in the 1960s, mainly for the diagnosis of pleural disease and for staging and the evaluation of efficacy and prognosis in lung cancer and malignant mesothelioma. It has gradually developed, especially in the past 10 years, with the birth of semi-rigid medical thoracoscopy, which greatly promoted diagnosis and treatment using medical thoracoscopy.

Medical thoracoscopy (MT) is a minimally invasive procedure, plays a very important diagnostic and therapeutic role for unexplained pleural effusion. This procedure allows visualization of almost entire pleural cavity and collection of appropriate and adequate biopsy samples for further studies and help to do necessary therapeutic interventions. It is usually done by a pulmonologist under conscious sedation with local anesthesia in a spontaneously breathing patient at endoscopy suit. It requires a single port of entry (15-20 mm size) into thoracic cavity and after the procedure, intercostals tube is place in situ for drainage of pleural fluid. In contrast, surgical thoracoscopy (popularly known as VATS) is done by a surgeon in an operating room under general anesthesia with selective intubation by at least three ports of entry into the thoracic cavity. Compared to surgical thoracoscopy, major advantages of MT include minimal invasion, cost-effectiveness and free of general anesthetic hazards.

Tuberculous pleural effusion is a common clinical problem, especially in TB endemic area like Bangladesh. TB pleurisy is common in primary TB; but can occur in secondary TB also by hematogenous, lymphatic or local spread. It is usually in primary TB, often remain unrecognized. But in secondary TB, it could be mild to moderate, sometime large or massive. After invasion of mycobacterium into pleural space, it causes formation of multiple nodules of variable size and shape, fibrous septas leading to loculations and pleural thickening and if remain untreated, could collapse the lung and pleural cavity. Medical thoracoscopy can also provide important scope for deseptation and removal of fibrous septas and loculation and adhesions and thereby reduce the chances of pleural complications. In our series, pleural tuberculosis was found in 25% cases. Jiang SJ et al evaluated the diagnostic value of MT in 2380 patients with unexplained pleural effusion and found that MT had explored tuberculous pleural effusion in 21.6% cases[14]. Nattusamy L et al explored 20.83% tuberculous pleural effusion cases among 48 unexplained PE cases[15]. These two study results are similar to our study, though we had less number of cases. Wang Z et al studied retrospectively the efficacy of MT in differentiating pleural TB from other lymphocytic pleural effusion patients over 9 yrs. He has found 333 of 833 pleural effusion patients to have confirmed tuberculous pleurisy. Among them, he found presence of mycobacterium tuberculosis ± presence of caseous granuloma in 99.1% cases. This study proved the high diagnostic value of MT for TB pleurisy. Xiong et compared the effectiveness of MT in three different form of pleural effusion- free flowing, multiloculated and organizing effusion with

USG guided pigtail catheter and large bore chest tube drainage. He found that MT had significant efficacy in multi-loculated and organized effusion rather than free flowing effusion[17].

Para-pneumonic pleural effusion is common clinical problem world-wide. Parapneumonic effusion occurs in 20 to 40% of patients who are hospitalized for pneumonia[19]. Complicated parapneumonic pleural effusions and empyema are a leading cause of morbidity in United States with over 1 million admission annually and mortality rate that remains high in spite of recent advances in diagnosis and treatment[20]. In our case series, 18.75% cases was complicated parapneumonic effusion or empyema which is near to expected level. The evaluation of parapneumonic effusion is divided into three progressive stages 1) exudative stage 2) fibrinopurulent stage and 3) organizing stage with pleural peel formation. In exudative stage, there is a rapid outpouring of fluid and inflammatory cells due to increased capillary permeability by the action of inflammatory cytokines. Fibrinopurulent stage is characterized by accumulation of fibrin clots and fibrin membrane within the pleural spaces leading to loculations and isolated spaces of fluid collection. The final organizing stage is characterized by fibroblastic proliferation and invasion lead to formation of thick pleural peel that lead to thick nonelastic pleural and trapped lung[21]. The first thoracocentesis is the most important diagnostic stage because it allows for a distinction between complicated and uncomplicated parapneumonic effusion[21]. Only complicated effusion need to be drained. Characteristics of patients that indicate that an invasive procedure will be necessary for its resolution include the following: an effusion occupying more than 50% of the hemithorax or one that is loculated; a positive Gram stain or culture of the pleural fluid; and a purulent pleural fluid that has a pH below 7.20 or a glucose below 60, or has a lactic acid dehydrogenase level of more than three times the upper normal limit for serum[19]. Drainage is most frequently achieved with tube thoracostomy. The use of fibrinolytics can play a role for the early use in complicated, loculated parapneumonic effusions and empyema, particularly in poor surgical candidates and in centres with inadequate surgical facilities[22]. Ravaglia C et al confirms that multiloculated pleural empyema could safely and successfully be treated with medical thoracoscopy while organizing empyema can be resistant to drainage with medical thoracoscopy, requiring video-assisted thoracic surgery or open surgical decortications[23]. Early adhesionolysis and drainage of fluid using medical thoracoscopy should be considered in patients with multiloculated complicated PPE after careful radiological (ultrasonography and CT) stratification, as a more cost-effective and safe method of management[24]. That is also found in our cases that MT with or without fibrinolytics play an important role is complete resolution of carefully selected complicated parapneumonic effusion cases. All three patients after adhesionolysis and deseptation during MT were recovered completely.

Malignant Pleural Effusion is an exudative effusion with malignant cells. It affects up to 15% of all patients with cancer and is the most common in lung, breast cancer, lymphoma, gynecological malignancies and malignant mesothelioma[25]. Jiang SJ et al revealed that MT had explored 37.8% MPE among 2380 patients with unexplained pleural effusion[14]. In this situation, closed pleural biopsy could help, but definitely medical thoracoscopy would be better to inspect the whole pleural cavity and take appropriate biopsy material for histopathological and immunohistochemical study. Moreover, medical thoracoscopy had important therapeutic role to relieve respiratory distress and providing important conduit for chemical pleurodesis thereafter.

Hepatic hydrothorax or pleural effusion due to chronic liver disease is a common clinical problem especially in decompensated CLD cases. It's the hypo-albuminemia and reduced osmotic pressure that leads to pleural effusion in CLD. It's usually mild to moderate; bilateral or right sided; transudative and can be managed easily by repeated paracentesis and albumin infusion. But in some clinical scenarios', pleural effusion in a liver disease patient have possibilities of TB, Malignancy or others illness and have to differentiate to manage pleural effusion. In these situations, medical thoracoscopy may play a very important role. Here, a patient in our case series had recurrent pleural effusion and atypical symptoms and could not be managed with albumin infusion and repeated thoracocentesis was managed with medical thoracoscopy and tube thoracostomy. Kumar s et al described that patients with refractory HH represent a therapeutic challenge and in selected group

of patients, medical thoracoscopy not only helps to establish the diagnosis but also can be used as an effective management strategy and a bridge to transplantation[33].

Renal hydrothorax or pleural Effusion in chronic renal failure patient is also common. It might be due to malignancy, TB, pneumonia and other causes, along with uremia itself. Simple paracentesis and albumin replace is enough for its management. But in some clinical situations, PE becomes difficult to explore the cause and manage. In that situation, medical thoracoscopy could play a crucial role. Here, a patient who had end stage renal disease (on mandatory hemodialysis) and Pott's disease (on anti-TB treatment) develop recurrent exudative pleural effusion. Primary work-out couldn't explore the cause and patient became dyspneic repeatedly. That time, MT played a very important role is resolution of dyspnea and PE. Ahluwalia G et al also describes the efficacy of MT in diagnostic evaluation and treatment of exudative pleural effusion in chronic renal failure patients[35].

Medical thoracoscopy is a very important therapeutic tool especially for pleurodesis in malignant PE. Treatment options for symptomatic MPE includes repeated pleurocentesis, pleurodesis via thoracoscope or chest tube, indwelling pleural catheter, mechanical pleurodesis at surgery or pleurectomy[32]. Pleurodesis is the preferred treatment for recurrent malignant effusion or benign effusion, and the use of talc is preferred over other sclerosing agents (e.g. mitozantrone and tetracycline). Talc pleurodesis had superiority over tetracycline or bleomycine regarding fluid clearance[32]. Talc poudrage via medical thoracoscopy is thought to be superior to talc slurry via chest tube. A RCT done by Batnagar R et al on 330 patients with 166/164 each group revealed no significant difference in terms of pleurodesis failure in 90 days[33]. In this case series, 4 pleurodesis was done and one with talc poudrage and other 3 had talc slurry. Success rate was not evaluated in this case series, but procedure was done safely and patient had no complaints post-procedural stage. Medical Thoracoscopy is a very safe and cost-effective procedure. Most of the studies done with MT revealed the procedure safe with a few complications[12, 14, 34]. Post- procedural pain for chest tube is common; but lung laceration, air embolism and re-expansion pulmonary edema was seen rarely in some case series. In our patients, one patient had re-expansion pulmonary edema which was managed easily with steroid within 2 days.

Conclusion:

Medical Thoracoscopy/ Pleuroscopy is a minimally invasive procedure, very effective diagnostic tool for unexplained pleural effusion to explore the etiology like malignancy, TB, parapneumonic effusion and so on. It is also a very effective therapeutic tool for adhesionolysis and deseptation in selected complicated parapneumonic effusion or tuberculous pleural effusion and for pleurodesis in malignant pleural effusion. In all the conditions, the procedure is very safe and had minimum adverse effects which can be managed easily.

Limitations:

It's a retrospective case-series study having a small sample size. A randomized prospective, comparative study with larger sample size would quantify the effectiveness and safety of MT over other techniques in the management of these patients.

Conflict of interest:

Nothing to declare

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