Bangladesh Crit Care J March 2026; 14 (1): 55-58

Case Report

Looking Beyond Fluid Analysis: An Atypical Presentation of Bilateral Tuberculous Pleural Effusion

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DOI: https://doi.org/10.3329/bccj.v14i1.88320

Abstract:

Background: *Tubercular pleural effusion (TPE) typically presents as unilateral exudative effusion. Bilateral involvement is uncommon and may delay diagnosis, particularly when pleural fluid microbiological tests such as GeneXpert MTB/RIF are negative.*

Case Presentation: *We reported the case of a 29-year-old male who presented with a one-month history of low-grade intermittent fever, shortness of breath, and a dry cough. He had a history of childhood asthma and was a non-smoker. There were no constitutional symptoms or any family history of TB. Chest radiography revealed mild bilateral pleural effusions. Two weeks prior, he had been admitted to a local primary care center in Malaysia and treated for atypical pneumonia. He also reported vague abdominal pain and was diagnosed with GERD and pangastritis. CT-thorax revealed moderate right pleural effusion with patchy alveolar opacities in the left apicoposterior segment of the left upper lobe and subcentimeter mediastinal lymphadenopathy without a tree-in-bud appearance. CT abdomen/pelvis revealed moderate ascites and small bowel wall thickening. A repeat CT thorax 2 weeks later demonstrated increasing right pleural effusion and minimal left pleural effusion, patchy ground glass changes in both upper, right middle, and both lower lobes along with mediastinal lymphadenopathy. Flexible bronchoscopy and medical thoracoscopy were performed. Bronchoalveolar lavage (BAL) and Pleural fluid MTB PCR and Gene Xpert were negative. Medical thoracoscopy revealed classical sago-like pleural nodules. A targeted pleural biopsy revealed caseating granulomatous inflammation that was consistent with tuberculosis.*

Conclusion: *This case highlights that pleural tuberculosis can present atypically, with bilateral effusion and a negative pleural fluid GeneXpert result. In such scenario, medical thoracoscopy remains the diagnostic cornerstone for early and definitive diagnosis.*

Keywords: *Bilateral pleural effusion, Medical thoracoscopy, Mediastinal Lymphadenopathy, Negative TB-PCR, Pleural tuberculosis, Tubercular pleural effusion.*

Introduction

Tuberculosis remains a major global health problem, with pleural tuberculosis accounting for a significant proportion of extrapulmonary cases. Tubercular pleural effusion (TPE) typically presents as a unilateral lymphocytic exudate, most often affecting young adults[1,2]. Bilateral pleural effusions are distinctly uncommon and may lead clinicians to consider alternative diagnoses such as renal failure, cardiac failure, nutritional deficiency[3.] Diagnosing Tubercular Pleural Effusion is frequently difficult because pleural fluid contains very few bacteria[4]. Although the GeneXpert MTB/RIF test has transformed tuberculosis diagnosis, its sensitivity in detecting the disease in pleural fluid remains limited[4,5]. Therefore, pleural biopsy obtained via thoracoscopy remains the definitive diagnostic method[6,7].

This report presents an unusual case of bilateral pleural tuberculosis with negative GeneXpert results in pleural fluid and bronchoalveolar lavage and illustrates the effectiveness of a medical thoracoscopic approach for definitive diagnosis.

Case Presentation

A 29-year-old gentleman presented with mild fever, shortness of breath, and dry cough for one month's duration. He had a history of childhood asthma, did not smoke, he had no prior history of tuberculosis or close contact. There was no history of hemoptysis or weight loss. 2 weeks earlier, he had been admitted and treated for atypical pneumonia and gastritis.

On examination, he was hemodynamically stable with intermittent low-grade fever spikes. Respiratory examination

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Received : January 26, 2026; Accepted : February 18, 2026

revealed reduced breath sounds over both lower zones, more pronounced on the right side. Other systemic examinations were unremarkable.

Investigations

Laboratory Findings

- Complete Blood Count : Hb 12.4 g/dL, TWBC 3870/cmm, Platelet 241000/cmm
- Moderately elevated C-reactive protein (45.1mg/L)
- Remaining hematological and biochemical parameters were within normal limits.

Radiological Evaluation

Chest X-ray showed (Figure 1) moderate right-sided pleural effusion with no parenchymal lung abnormality. CT chest (Figure 2) revealed bilateral pleural effusions, more pronounced on the right side, along with areas of confluent patchy ground-glass changes involving right upper and lower lobes and left upper lobe mainly in the apico-posterior segment. No focal consolidation, cavitation, or lung mass was observed. Multiple enlarged mediastinal Lymph nodes were present at levels 2, 4, 6, 5, and 7, with the largest measuring 1.9 x 1.5 cm at level 4R and 1.5 x 1.2 cm node at level 7.

Given the lack of response to empirical antibiotics and persistent symptoms, further evaluation was undertaken.

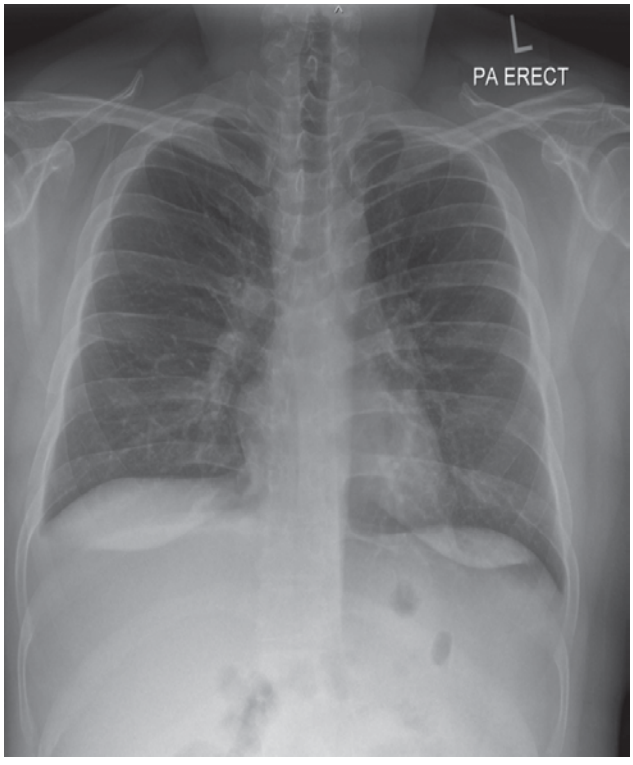

Fig 1: Initial Chest Radiography at the time of admission revealed only minimal obliteration of the right cardiophrenic angle, Minimal Pleural effusion on the right.

Bronchoscopy and Medical Thoracoscopy

Fiberoptic bronchoscopy (FOB) was performed under mild sedation and local anesthesia to evaluate the cause of ground glass opacities (GGO) in the lung parenchyma. Using a disposable 6mm bronchoscope, BAL was obtained from the apico-posterior segment of the left upper lobe, and sent for microbiological analysis. Thorough inspection of the airway revealed no endobronchial lesions or mucosal infiltration.

Immediately following FOB, thoracoscopy was performed under sedation and local anesthesia, in collaboration with a cardiothoracic surgeon. The patient was placed in the left lateral position and a 3 cm incision was made at the right 5th intercostal space along the midaxillary line, using a diathermy-cautery knife.

The subcutaneous tissue and the muscle layers were dissected until the pleural space was reached. The entry port was secured using an XXS-sized Alexis wound protector-retractor, which served as a better alternative to the disposable trocar. A flexible bronchoscope was passed through the stoma, and a thorough inspection was carried out from the apex to the base. Numerous sago-like nodules were observed on the parietal pleura [Figure 3], more prominent on the upper part of the right lung and scattered over the parietal pleura. Pleural fluid was aspirated and sent for standard testing, including TB, cytology, and ADA. Using a diathermy-cautery tool, an incision was made on the parietal pleura, and a large targeted 2 x 2 cm pleural biopsy specimen was obtained and sent for histopathology and Gene-Xpert/RIF.

In this case, a flexible bronchoscope was used to navigate the pleural cavity, which is a modified version of the semirigid Thoracoscope. Medical thoracoscopy usually utilizes either a rigid thoracoscope or a semi-rigid thoracoscope, but in certain conditions, due to the unavailability of both the instruments, a flexible bronchoscope can be safely utilized to serve the purpose adequately [8].

A 24-French chest tube was placed after adequate drainage of the pleural cavity. The wound was closed with Vicryl sutures for subcutaneous tissue and the muscle layer, and skin closure was achieved using a V-Loc™ 180 absorbable wound closure device, and the chest tube was secured with 2-0 silk sutures, and a dressing was applied.

Pleural Fluid Analysis: Lymphocyte predominant fluid, exudative in nature as per Light's criteria with no malignant cells. Pleural fluid protein: 63 g/L. Glucose: 4.4 mmol/L. LDH: 369.1 U/L with negative pleural fluid MTB PCR and GeneXpert MTB/RIF. Pleural fluid ADA 79.3IU/L.

Immunological Testing: Positive QuantiFERON-TB Gold

Pleural Biopsy Histopathology: Multiple granulomatous areas composed of epithelioid histiocytes and Langhans-type giant cells with surrounding lymphocytic infiltrate and presence of central caseating necrosis in some granulomas (Figure 4). Moderate lymphoplasmacytic infiltrate within fibrous stroma was seen. Based on these findings, a diagnosis of pleural tuberculosis was confirmed.

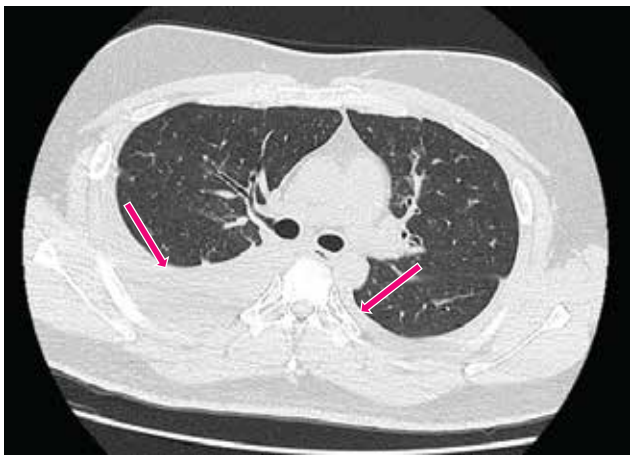

Fig 2: Axial section of the CT scan of the chest showing moderate right-sided pleural effusion and mild left-sided pleural effusion (arrows) and GGO on the left apicoposterior segment of the upper lobe.

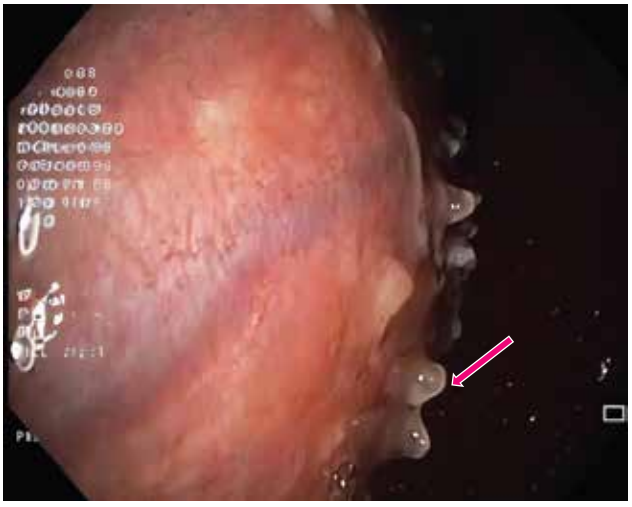

Fig 3: Thoracoscopic view of the pleural surface showing sago-like nodules.

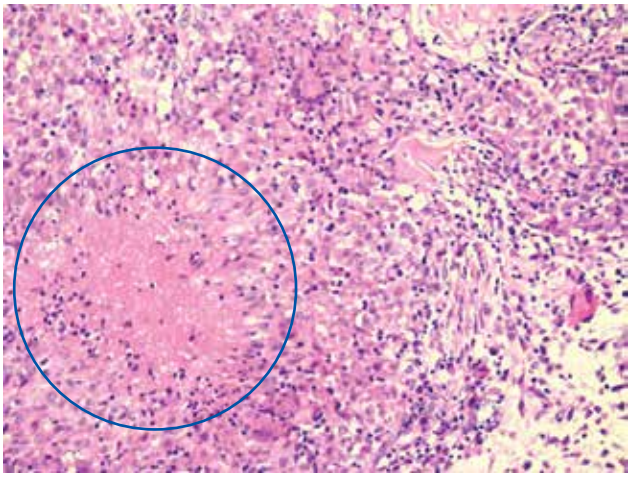

Fig 4: Histopathological slide showing Langhan's giant cells surrounded by epithelioid histocytes and chronic inflammatory cells. Caseation necrosis is present.

Discussion

Tubercular pleural effusion (TPE) is a common type of extrapulmonary tuberculosis and usually occurs as a delayed hypersensitivity response to Mycobacterium tuberculosis antigens in the pleural cavity[1,6]. Classically, TPE presents as an acute or subacute unilateral exudative pleural effusion in young, immunocompetent individuals[1,2]. Bilateral pleural effusion, as observed in this patient, is distinctly uncommon and is reported in a minority of cases[3]. Such atypical presentations may lead to diagnostic uncertainty and delay initiation of appropriate therapy. In this case, the patient had bilateral pleural effusions with minimal lung parenchymal haziness and failed to respond to empirical antibiotic therapy.

The diagnostic dilemma arose due to inconclusive and atypical radiographic presentations of tuberculosis, as well as the absence of risk factors for Tuberculosis. Bilateral effusions can occur due to other conditions, such as infections, malignancy, connective tissue disease, cardiac failure, or underlying autoimmune conditions, particularly in young patients without classical tuberculosis risk factors[2,3].

This case reinforces that pleural tuberculosis should remain a key differential diagnosis even in atypical radiological presentations. A major diagnostic challenge in pleural tuberculosis is the low sensitivity of pleural fluid microbiological tests. Pleural fluid is characteristically paucibacillary, as the effusion results from an immunological reaction rather than direct mycobacterial proliferation[4]. While nucleic acid amplification tests such as GeneXpert MTB/RIF have significantly improved rapid tuberculosis diagnosis, their sensitivity in pleural fluid is limited, with reported rates ranging from 20% to 30%. Consequently, a negative pleural fluid GeneXpert or MTB PCR result does not exclude pleural tuberculosis[5,6]. This case exemplifies this limitation, as both pleural fluid PCR and GeneXpert were negative despite definitive histopathological evidence of tuberculosis.

ADA (Adenosine Deaminase) plays an important role in establishing a diagnosis as it is a specific enzyme produced by lymphocytes through immune mediated response by the cells fighting against the mycobacterium tuberculosis[9]. ADA is further divided into two isoenzymes ADA-1 and ADA-2. ADA-1 is a general enzyme found in almost every cell in the body, but especially in Neutrophils and damaged tissue cells while ADA-2 is Tubercular specific enzyme found only in monocytes and macrophages[10]. When active infection caused by Mycobacterium tuberculosis bacteria survives inside macrophages as a defense mechanism, ADA-2 enzyme is released, and it is highly specific for tuberculosis[11]. Routine laboratory testing measures total ADA levels, which is excellent for TB with a sensitivity of ~92% and specificity of ~85%. The accepted cut-off for ADA is greater than 40 U/L[12] which favors the diagnosis of tuberculosis. However, high levels of ADA do not indicate only tuberculosis, they can be elevated in empyema, lymphoma, and inflammatory conditions like Rheumatoid arthritis[13]. In this case, the ADA level was elevated but the result was only available after 1 week, and the patient had already been started on Anti-tubercular therapy based on clinical presentation and histopathological findings.

Interferon-gamma release assays (IGRAs), such as QuantiFERON-TB Gold, reflect prior sensitization to M. tuberculosis antigens and may support the diagnosis in appropriate clinical contexts, although they cannot differentiate latent from active disease. In this patient, a positive IGRA result, in conjunction with lymphocytic exudative effusion and characteristic thoracoscopic findings, increased the pre-test probability of pleural tuberculosis.

Pleural biopsies were first performed in 1958 by Abrams; since then, they have been used to obtain samples blindly from the parietal pleura through the chest wall. This technique is utilized for the diagnosis of unexplained exudative pleural effusion, suspected tuberculous pleuritis, malignant pleural diseases, pleural thickening and other conditions. Overtime, advancements in diagnostic modalities have led to various techniques being used either alone or in combination to establish a diagnosis. Although closed pleural biopsy yields a moderately good result in tuberculosis, depending upon the technique, the risk of pneumothorax can be as high as 10%. The overall sensitivity of the Abrams needle procedure is about 60% with a specificity of 100% whereas medical thoracoscopy has a sensitivity and specificity of 93% and 100%, respectively[14,15].

Medical thoracoscopy remains the diagnostic gold standard for undiagnosed exudative pleural effusions[7]. Direct visualization of the pleural surfaces allows identification of characteristic features such as hyperemia, adhesions, and the classical "sago-like" nodules associated with tubercular pleuritis. Targeted pleural biopsies obtained under direct vision have a diagnostic yield exceeding 90%, particularly when histopathology demonstrates granulomatous inflammation with caseating necrosis, as seen in this case[7,8].

A flexible bronchoscope was used for pleural inspection through an Alexis® wound protector-retractor, which increases the viewing window for thorough inspection of the pleura, facilitates safe drainage of pleural fluid, and allowed diathermy-cautery tool to make an incision on the pleura. A large targeted pleural biopsy specimen was obtained with minimal bleeding. The use of a wound protector offered several advantages, including maintenance of access, protection of soft tissues, and ease of instrument manipulation.

Early thoracoscopic evaluation in this patient avoided further diagnostic delay, prevented unnecessary repeated pleural fluid sampling, and enabled prompt initiation of antitubercular therapy. This underscores the importance of timely escalation to thoracoscopy in patients with unexplained pleural effusions, especially when initial investigations are inconclusive.

Due to the disseminated tubercular disease, involving the lung parenchyma, pleural disease, mediastinal lymphadenopathy, and abdominal TB, the patient will be prescribed anti-tubercular treatment for an extended period of about 9 to 12 months, as per clinical assessment.

In summary, this case illustrates several important learning points: pleural tuberculosis may present atypically with bilateral effusions; negative pleural fluid GeneXpert does not exclude tuberculosis; and medical thoracoscopy remains indispensable for diagnosis. Furthermore, it demonstrates that innovative adaptations of thoracoscopic techniques using available tools can be safely and effectively employed.

Outcome and Follow-Up

The patient had an uncomplicated postoperative course. He was subsequently initiated on antitubercular therapy, and chest tube output was monitored. Once the fluid was less than 50 mL over 24 hours, the tube was removed after two days. Post-tube removal chest radiography showed near-complete resolution of pleural effusion. The patient showed significant clinical improvement.

Conclusion

This case highlights that pleural tuberculosis can present atypically with bilateral effusions and negative pleural fluid GeneXpert results. A high index of suspicion, combined with thoracoscopic evaluation and pleural biopsy, is essential for accurate diagnosis.

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