CASE REPORT

Sticky Fibrin Adhesion: Enlightenment from a Case of Tuberculous Pleurisy

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ABSTRACT

Introduction: Tuberculous pleurisy (TP) is the pleural inflammation caused by *Mycobacterium tuberculosis* (MTB) and a rare manifestation of childhood tuberculosis (TB). It is characterized by a large amount of fibrin, sticky adhesion, and even calcification. Pleural adhesion can significantly affect respiratory function and quality of life. Therefore, early detection, prompt therapy, and drainage of pleural effusion are crucial for preventing pleural adhesion. This case report is intended to enhance clinician awareness regarding avoiding and managing pleural thickening in TP.
Case: A 14-year-old child had shortness of breath, fever for 2 weeks, cough, loss of appetite, and no smoking history. The laboratory results showed anemia and non-reactive human immunodeficiency viruses (HIV), analyzed pleural fluid monocyte showed 72%, and glucose 58%. Adenosine deaminase (ADA) analysis showed a rise above 61 U/L. The tuberculin skin test was negative. The chest X-ray showed right pleural effusion, the chest ultrasonography revealed a right hemithorax echo-free plane, and the computed tomography (CT) scan showed right pleural effusion and pulmonary fibrosis. The thoracoscopy view showed fibrinous adhesion-producing tenting and vascularization in the base without multiple nodules. Water-sealed drainage was performed and produced approximately 3,450 ml with serous xanthochromia. Then the patient was diagnosed with TP and treated with anti-TB drugs and steroids.
Conclusion: Typical TP with fibrinous adhesions is an infrequent condition. This case report highlighted the importance of extensive screening using a thoracoscopy view and ADA analysis in patients with TP, especially in countries with a high TB burden.

INTRODUCTION

Tuberculosis (TB) is a serious global health issue that poses a significant challenge to disease control efforts. Indonesia is recognized by the World Health Organization (WHO) as a top-priority country for TB control due to its high number of cases.[1] Although extrapulmonary TB is present in about 30–40% of children, pulmonary TB is the most frequently observed in the pediatric population. Subsequently, tuberculous pleurisy (TP) is the most prevalent form of extrapulmonary TB in children and adolescents aged 3-5 years old, according to several studies from developing countries.[2] TP is one most common types of extrapulmonary TB and is the dominant cause of pleural effusion in endemic regions. Previous studies showed that pleural inflammation is not a common characteristic of primary pulmonary TB in young children and is more likely to be detected in adolescents and adults.[3] Furthermore, the diagnosis of TP remains a major challenge worldwide because the causal organism, namely *Mycobacterium tuberculosis* (MTB), is detected in the sputum, pleural fluid, or tissue with tubercles. Pleuroscopy is a minimally invasive and therapeutic procedure that can be used to observe the pleural cavity. Based on the study by Shah, *et al*. (2022), using this procedure in children is still very rare, with only a few studies.[3]

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TP can be a symptom of both primary and reactivated TB, with primary TB more frequently occurring in younger children and reactivated TB being more common in adults living in industrialized nations. The rupture of a subpleural caseous focus into the pleural space, which results in a type IV delayed hypersensitivity reaction and different cytokines that stimulate the macrophages' antimycobacterial activity, and is believed to be the cause of TB pleural effusion, causing pleural exudates. However, very few bacteria are often present in the pleural fluid, where they can cause a granulomatous reaction.[4] MTB should be identified by smear microscopy (Ziehl-Neelsen staining), pleural fluid culture, or pleural biopsy material, and clinical and imaging findings confirming pleural infection.[5] However, since MTB is difficult to identify in children, the diagnosis is frequently made indirectly using standardized epidemiological, radiological, clinical, and laboratory criteria.[2]

The tuberculin skin test is still a useful technique for diagnosing pediatric pleural TB because microbiological studies are rarely used to confirm cases. Although effective anti-TB therapy is easily accessible, childhood pleural TB may also progress into loculated effusion, pleural TB, which can enclose pathogenic organisms and impede pleural drainage. These loculation sites may eventually lead to persistent pleural sepsis.[6] Although intrapleural fibrinolytic therapy is successful in treating patients with loculated pleural effusion, a sizable percentage of patients continue to show no improvement. Furthermore, side effects like chest pain may make fibrinolytic therapy less accessible. In addition, the severity of the disease state can lead to treatment failure, requiring a second procedure. Therefore, surgical excision remains critical in treating children with loculated pleural effusion.[7,8]

We presented a case of a young boy from an endemic TB region in Banda Aceh, Indonesia, with a manifestation of right pleural effusion, undetected MTB in sputum, and a diagnosis of pleural TB based on a very characteristic pleuroscopy, and elevated adenosine deaminase (ADA) levels. It is very important to consider extensive examination and ADA pleural fluid testing in a case of pleural TB, especially in countries with a high burden of TB.

CASE

A 14-year-old boy complained of a fever with a temperature of 37.6°C without night sweats. The fever was felt almost every day for 2 weeks and was usually not very high. Furthermore, shortness of breath was felt for 1 week and worsened 3 days before admission to the hospital. Daily shortness of breath was felt due to light activity but without wheezing. These complaints made the patient rest more and reduced activity. Meanwhile, a non-productive cough was felt for 1 month, followed by a productive cough several weeks later, and there was no history of coughing blood. For 1 month, a decrease in appetite was felt, which led to weight loss, accompanied by nausea, but without vomiting. Additionally, the patient had no history of smoking.

Physical examination showed a weight of 43 kg and a height of 160 cm with a body mass index of 16.8, indicating underweight status. The movement of the right chest wall appeared to lag behind that of the left chest. There was a decrease in stem fremitus on the right chest, dullness on percussion, a decrease in vesicular breath sounds on the right lung, and no lymph node enlargement.

Table 1. Laboratory results at the time of admission to the hospital

Laboratory Test	Result
Leukocytes	8,600/mm^3
Hemoglobin	12.8 g/L
Hematocrit	37 %
Thrombocyte	504,000 mcL
Eosinophil	1 cell/mcL
Basophil	0 cell/mcL
Neutrophil	72 cells/mcL
Lymphocyte	15 cells/mcL
Monocyte	12 cells/mcL
Alanine transaminase (ALT)	113 U/L
Aspartate aminotransferase (AST)	71 U/L
Prothrombin time	18.00 second
Activated partial thromboplastin time	31.30 second
Glucose	113 mg/dl
Urea	26 mg/dl
Creatinine	0.80 mg/gl
Human immunodeficiency viruses (HIV) test	Non-reactive
Adenosine deaminase (ADA)	>61 IU/L
Pleural Fluid Analysis	
Color	Yellow
Purity	Turbid
Clot	Positive
Polymorphonuclear cell	28%
Mononuclear cell	72%
Leukocyte	472
Protein	5.4
Albumin	2.8
Glucose	58

Laboratory results showed normal leukocyte values, increased monocytes, increased liver function, normal coagulation function, normal liver function, and non-reactive human immunodeficiency viruses (HIV). Analysis of exudative pleural fluid showed a protein level of 5.4 g/dL, 72% monocyte cells, and a glucose level of 58 mg/dL. Furthermore, the ADA test increased to 61 U/L with a negative tuberculin test (Table 1).

Chest X-ray showed homogeneous opacity in the right lung field, trachea and heart deviation to the left side, both hila could not be evaluated, left broncho-vascular within normal limits, no infiltrate and nodules in the left hemithorax, sharp left costophrenic sinus, with the impression of massive right pleural effusion upon first admission to the hospital (Figure 1).

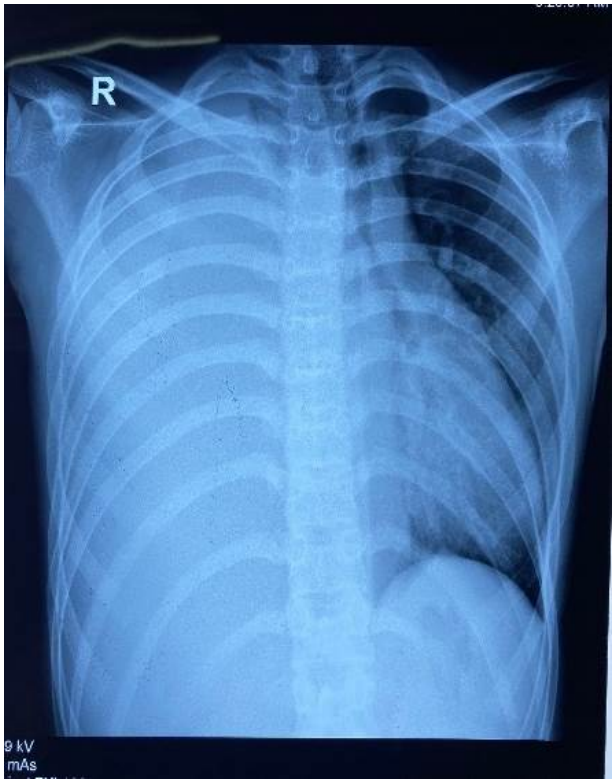

Figure 1. Right pleural effusion on admission

Thoracic ultrasound showed a homogenous anechoic shadow between the parietal and visceral pleura with an impression of right pleural effusion estimated at 5,000 ml. A chest tube was inserted using ultrasound (USG) guidance with a no. 22 trocar and about 3,450 ml of xerous xanthochromic fluid was drained during the first 5 days. After 5 days of installing water-sealed drainage, the homogenous opacity in the right lung field decreased, and pleural thickening was observed (Figure 1). Additionally, a USG evaluation showed a loculated pleural effusion (Figure 2a, 2b). Further evaluation with a thoracic CT scan showed a right pleural effusion and right lung fibrosis (Figure 3a, 3b).

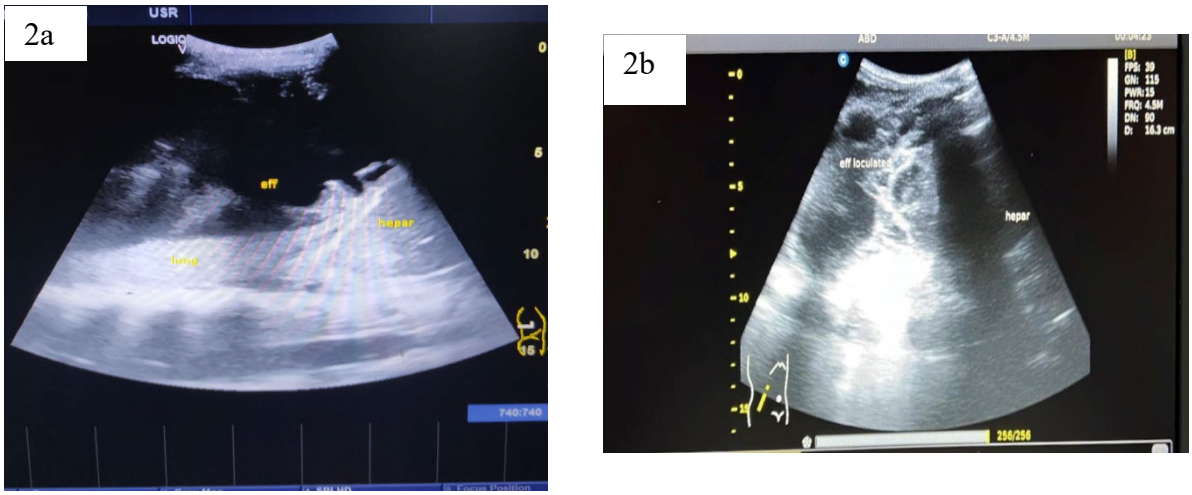

Figure 2. Chest ultrasound showed a homogeneous anechoic appearance. 2a) Massive pleural effusion. 2b) Pleural effusion loculated after 12 days of treatment.

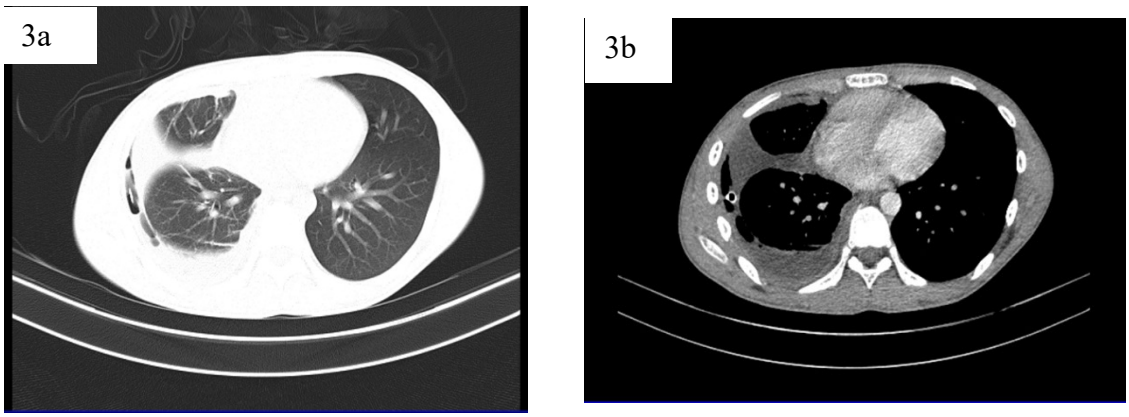

Figure 3. CT scan showing right pleural effusion and right pulmonary fibrosis. 3a) CT scan with lung window showing a shadow of fibrosis in the right pleura. 3b) Mediastinal window.

Thoracoscopy was then performed with a flexible bronchoscopy. Local anesthesia was applied laterally to the fifth intercostal space, and a 2 cm incision was followed by blunt dissection until the pleural space was reached. The flexible bronchoscope was inserted through a 7mm trocar, and supervision was performed using a monitor during the action. Thoracoscopy showed fibrin adhesions causing septations in the pleural cavity and vascularization at the base. However, no multiple nodules were observed (Figure 4).

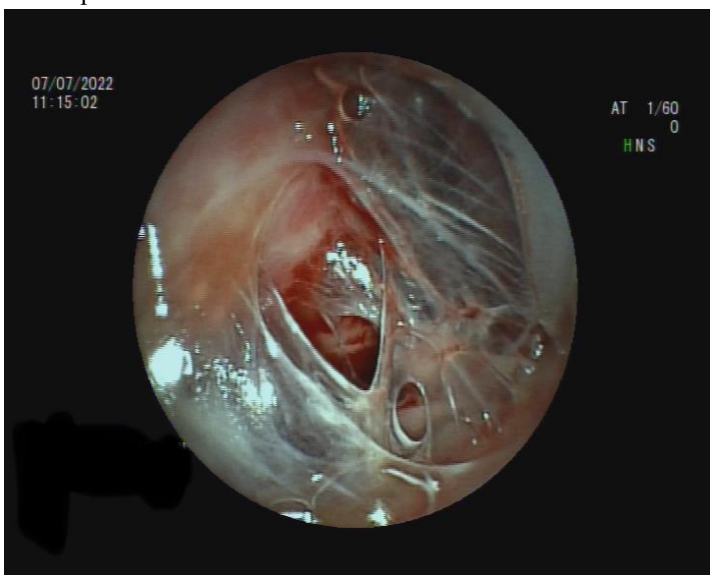

Figure 4. Fibrinous adhesion producing tenting and vascularization

The patient was diagnosed with TP based on the pleuroscopy findings and the increased ADA value. Furthermore, the patient was treated with anti-TB drugs adjusted to the weight, such as Rifampicin 450 mg, Isoniazid 300 mg, Pyrazinamide 1000 mg, and Ethambutol 750 mg, once daily. The patient also received 20 mg of oral steroids daily.

DISCUSSION

The diagnosis of TB is usually made based on careful clinical assessment, supported by relevant tests and investigations. In TB-endemic areas, TP, the second most common form of extrapulmonary TB, often leads to pleural effusion.[9] The incidence of TP is higher in young patients, but in non-TB endemic regions, patients tend to be old because reactivation dominates primary infection as a mechanism of disease development.[10] Due to the challenge of identifying MTB in children, the diagnosis is frequently established indirectly using standardized epidemiological, radiological, clinical, and laboratory criteria such as TB culture and the pathological picture. A study in Brazil showed that fever, coughing, and chest pain were the most prevalent signs of TP in children.[11]

Pleural effusion manifests as paucibacillary mycobacterial infection within the pleural cavity, acquired from an initial parenchymal lesion and resulting in an increased immune response that increases pleural fluid formation and decreases pleural

fluid drainage.[12] Initially, a rapid neutrophilic inflammatory response within the pleura is symptomatic. This is followed by an immune reaction that produces prolonged lymphocytes, granuloma formation in the pleura, and the production of ADA.[13] Furthermore, the exudative fluid in TP contains a large amount of fibrin, which can accumulate in the pleura and obstruct lymphatic vessels. This often leads to the impediment of exudate absorption, production of pleural effusion, as well as thickening, adhesion, and calcification of the pleura.[14] Generally, pleural effusion is unilateral, with observational studies showing that TP accounts for 12% of massive pleural effusion.[15]

Clinical signs are usually chronic, with symptoms onset less than a month before diagnosis. The most common symptoms are similar to acute pneumonia. Most patients experience a non-productive cough (70%) and pleuritic chest pain (75%), preceded by cough and fever, while only 7 out of 49 patients (14%) do not experience fever. In the acute stage, symptoms are only mild chest pain, mild fever, non-productive cough, weight loss, and easy fatigue.[16] The patient in this study was diagnosed with a non-productive cough, chest pain, weight loss, and easy fatigue.

The characteristics of pleural fluid that indicates TB pleural effusion are exudative fluid with a protein level >5 g/dL, a lymphocyte percentage >50%, a glucose level, which may be low or normal, a pH >7.30, pleural fluid lactic acid dehydrogenase (LDH) > serum LDH, and mesothelial cells less than 5%.[17] Subsequently, ADA is an enzyme produced predominantly by T lymphocytes that catalyzes the conversion of adenosine and deoxyadenosine into inosine and deoxyinosine. The specificity of ADA for diagnosing TP is 92% and 90%, and this supportive test is useful in establishing the diagnosis of TB pleural effusion if the value is above 70 U/L. However, it is not the main modality for diagnosing TB pleural effusion, and clinical findings should also be considered.[18]

The diagnosis of pleuritis is based on the presence of MTB in pleural fluid and biopsy. The diagnosis can also be made based on increased levels of ADA or interferon-gamma (IFN-γ) in pleural fluid. Furthermore, it is one of the most commonly used markers in TP cases. Based on a meta-analysis of 63 studies involving 2,796 patients with TP and 5,297 patients with non-TB pleural effusion, the sensitivity and specificity of ADA for diagnosing TP are 92% and 90%, respectively. Thoracic USG examination is more sensitive and can help identify fibrin bands, septa, and loculated pleural effusion. USG can also determine the fluid volume more accurately than X-ray and the localization of membranous septa, pleural cavity, and pleural thickening.[19]

Upon admission to the hospital, the initial treatment for the patient with loculated TP involves thoracic drainage to remove the pleural fluid promptly. Early and efficient drainage can speed up the clearance of pleural effusion and minimize residual thickening of the pleura. The use of a tube thoracostomy is used to evacuate air and pleural fluid in the pleural cavity. The indications for using a chest tube include the placement, insertion technique, and available equipment, including the drainage system used for pleural effusion.[17]

Thoracoscopy is a safe, simple, and accurate tool for detecting pleural abnormalities. The combined histological and culture examination of thoracoscopic samples has a sensitivity of about 100% for TP. However, previous studies showed that a significant portion of patients with exudative pleural effusion and suspected TP remain undiagnosed.[20] Therefore, the widespread use of thoracoscopy can improve diagnostic outcomes and can also detect other pleural abnormalities, such as pleural thickening, caseous necrosis, and pleural nodules.[20]

Delays in the diagnosis and treatment of TP can lead to disruptions in fibrin regulation in the pleural space, which can cause fibrin deposition and accumulation of pleural fluid and interfere with the healing of effusion.[14] It is crucial to diagnose and treat TP in a timely manner to prevent further complications and improve overall patient outcomes.

CONCLUSION

A patient's medical history, clinical signs and symptoms, TB culture results, and pathological presentation are typically used to diagnose TP. Hence, extensive thoracoscopy might improve diagnosis and be utilized to identify other pleural defects such as pleural thickening, caseous necrosis, and pleural nodules. This case report highlighted the importance of thoroughly investigating pediatric pleural effusions to ensure proper diagnosis and prevent pleural damage.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Developed the case: BY and BB. Reviewed the manuscript: JA. Examined the patient's data: BY and BB. Supported data from any literature: JA.

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