

Tuberculous Empyema Thoracis: Case Report

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Abstract: Tuberculosis is caused by bacillus *Mycobacterium tuberculosis*. The bacteria infected lung and many other organs such meninges, brain, and bone. Tuberculous empyema is a rare form extrapulmonary TB (EPTB). Two cases of tuberculous empyema presented in this case report. Both patients were males under 30th years old presented with shortness of breath, right side chest pain, and acute fever. Chest radiography show unilateral effusion with consolidation. The adenosine deaminase test is >300 IU/L for both cases which is very rare. Based on epidemiology, clinical presentation, fluid collected from thoracocentesis, laboratory result, and chest radiography, both cases diagnosed with tuberculous empyema. The patients got anti tuberculous drug and show improvement after 6 months therapy.

Keyword: Tuberculous empyema, adenosine deaminase, antituberculosis drug

1. Introduction

Until the coronavirus (COVID-19) pandemic, Tuberculosis still is the leading cause of death from a single infectious agent. TB is caused by acid-fast bacilli *Mycobacterium tuberculosis* which infects the lung as primary target organ and could spread to extra pulmonary organ by hematologic and lymphatic pathway. Almost a quarter of the world's population has been infected with *M. tuberculosis* bacteria, most of them are adults (90%) with the prevalence of male cases more than women.^{1,2} Indonesia is one of the 5 countries with the highest number of TB cases in the world, with an incidence rate of 257 cases / 100,000 population.² This disease can be treated, as many as 85% of people with TB will recover after undergoing treatment for 6 months.¹ Extrapulmonary tuberculosis cases are rare but increasing every year. In 2014 it was recorded EPTB case of 7.8 per 100,000 and grew to 25.4 per 100,000 in 2018 or 6.4% of all new TB cases in 2014 to 9.9% in 2018.³

One of EPTB cases is tuberculous empyema. Empyema is a condition where pus collects in the pleural cavity.⁴ Tuberculous empyema is an acute condition in chronic TB infection that arises in the pleural cavity. Management of this condition varies depending on the presence of bronchopleural fistula or empyema necessitates.⁵

The discovery of *M. tuberculosis* is the gold standard for diagnosing TB. However, in cases of extrapulmonary TB, it is sometimes difficult to collect tissue samples from the infected site. In addition, since the conventional smear microscopy has a low sensitivity with a range of 0%–40%, negative results cannot exclude the presence of TB. The results of *M. tuberculosis* culture vary from 30% to 80% with an average result obtained within 2-8 weeks, which is a very long time to make a diagnosis and start therapy.^{6,7} Therefore in cases of pleural effusion suspected TB infection, a simple, fast, and reliable examination is needed to establish the diagnosis namely adenosine

deaminase (ADA). ADA from pleural fluid sample with levels > 100 IU/L is only found in TB infection.⁸

2. Case Presentation

Case 1: A 23-year-old man admitted to the emergency department complaining of fever and cough since 1 day before admitted to the hospital and also complained of pain in the right chest. Upon arrival at the ER, the respiratory rate was monitored at 36x/minute with oxygen saturation of 94% of room air and body temperature of 39.1°C. The patient was given supplemental oxygen by nasal cannula at 4 lpm. Two RT-PCR swabs showed negative SARS-Cov2 and anti-HIV results were non-reactive. The results of a complete blood count revealed a white blood cell value of 46,440/ μ L with dominant neutrophils (93.1%), erythrocytes 4.76×10^6 / μ L, hemoglobin 14 g/dL, hematocrit 40.8%, and platelets 580×10^3 / μ L. Blood glucose is within the normal range of 113 mg/dL. The value of the erythrocyte sedimentation rate was obtained to increase at 40 mm/hour. The results of the chest X-ray showed a homogeneous consolidation in the lower zone of the right lung with a positive meniscus sign which was increasing after 3 days of receiving intravenous levofloxacin 1x750mg and cefoperazone-sulbactam 2x2gr. Thoracocentesis was performed after one week of treatment and purulent fluid was obtained with ADA (adenosine deaminase) test result of 347 IU/L. Examination of Gene Expert MTB/RIF from pleural fluid showed no *M. tuberculosis* was detected. The patient was diagnosed with tuberculous empyema and received metronidazole 3x500mg intravenously followed by oral for 5 days prior to antituberculosis drug waiting the ADA result. Antituberculosis regimen 2HRZE/4HR 1x4 tablets was given for 6 months. After 6 months of treatment, the chest X-ray showed an organized pleural effusion (Figure 1) with clinical improvement such as no cough, no shortness of breath, no fever and increasing body weight from 68 kg to 78 kg. Tuberculosis treatment was discontinued base on those examinations.

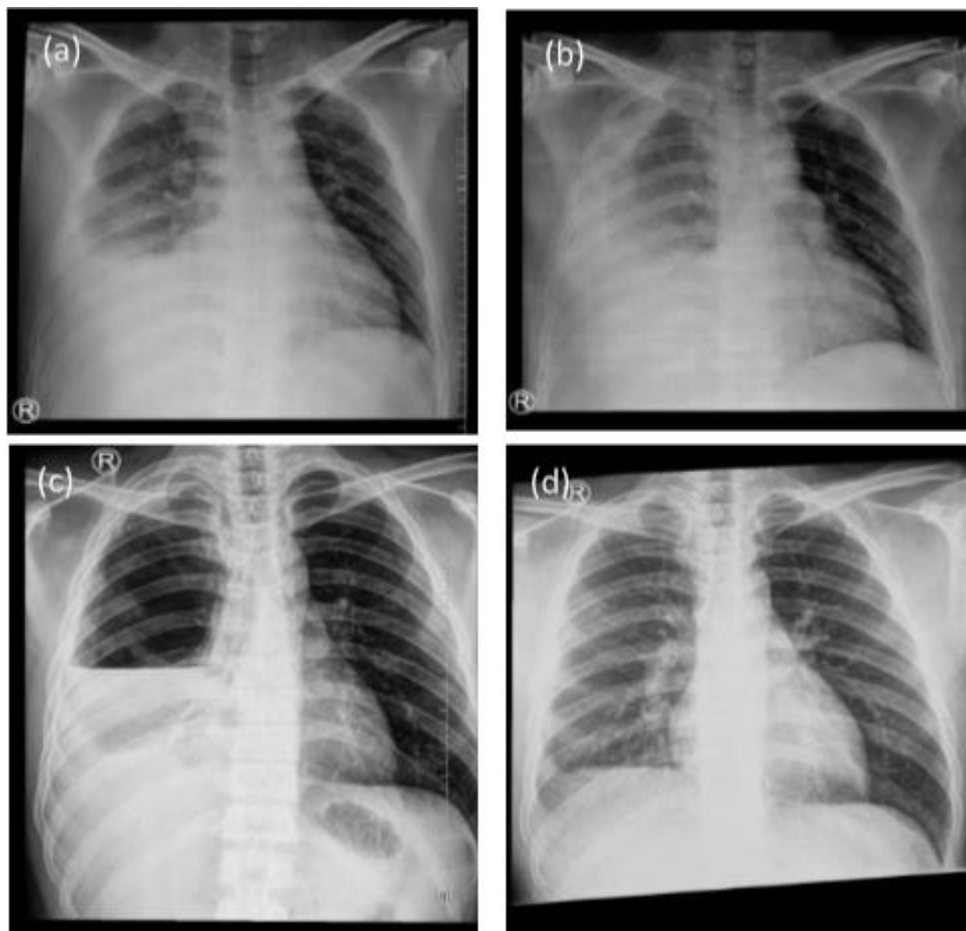


Figure 1: First chest X-ray (a) shows unilateral consolidation with a positive meniscus sign. (b) Chest X-ray on the 4th day of treatment with antibiotics showed an increasing pleural effusion. (c) and (d) Chest X-ray after receiving antituberculosis therapy.

Case 2: A man aged 28 years was admitted to the emergency department in February 2021 complaining shortness of breath since one week accompanied by right chest pain radiated to back and fever, the patient also complained weight loss since the last 2 weeks. The patient's respiratory rate was measured 38x/minute with oxygen saturation of 90% in room air, the patient was given oxygen assistance with a face mask. The results of the SARS-Cov2 PCR was negative and anti-HIV was non-reactive. Laboratory results showed the leukocyte value was 18.060/ μL with dominant neutrophils (89.4%), erythrocytes $3.68 \times 10^6 / \mu\text{L}$, hematocrit 31.8%, hemoglobin 10.5 g/dL and platelets $406 \times 10^3 / \mu\text{L}$. Blood sugar was 111 mg/dL. Chest X-ray showed consolidation in the right lung with right pleural effusion suggestive of pneumonia or pulmonary TB. The patient was given intravenous levofloxacin 1x750mg therapy. Thoracentesis was performed on the 2nd day of treatment and 100cc of purulent fluid evacuated. The patient was advised to do a decortication thoracotomy at the referral hospital but the

patient refused. The patient received additional therapy with metronidazole 3x500mg intravenously before the results of adenosine deaminase came out. The erythrocyte sedimentation rate value was obtained at 92 mm/hour with the result of the ADA test being 314 IU/L so that the patient started antituberculosis therapy after previously receiving levofloxacin 1x750mg and metronidazole 3x500mg therapy. The antituberculosis therapy given in 2-month regimen of rifampin, isoniazid, ethambutol, and pyrazinamide in the form of 1x4 tablet KDT according to the patient's body weight, followed by a follow-up phase given for 7 months with a regimen of rifampin and isoniazid 3 times a week. Evaluation of treatment with chest X-ray revealed a significant reduction in pleural effusion but a localized pneumothorax was seen (Figure 2). After 9 months of treatment with antituberculosis, the patient's body weight increased from 57.6 kg to 75.5 kg, cough and shortness of breath were not found, the erythrocyte sedimentation rate was 25 mm/hour so the tuberculosis treatment was discontinued.

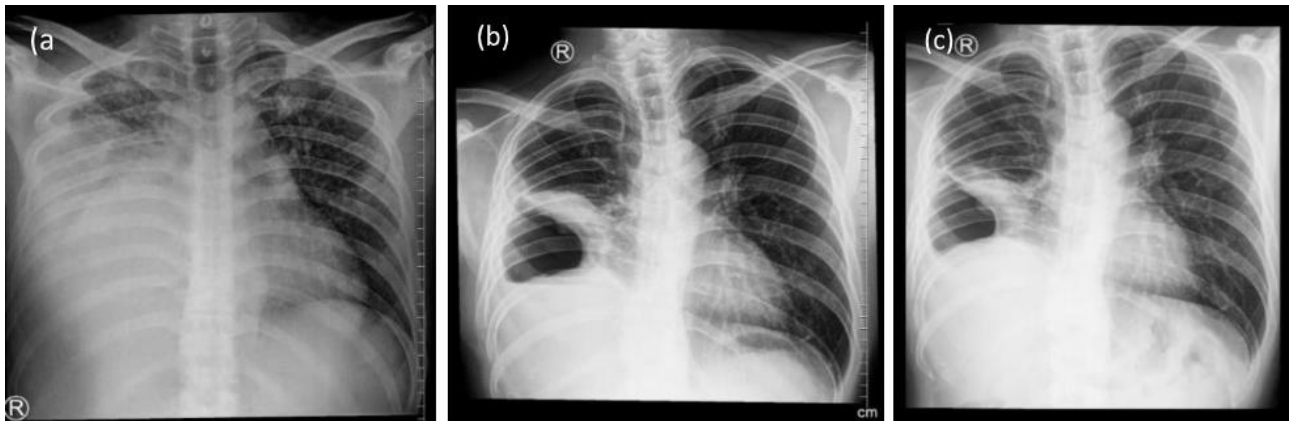


Figure 2: Chest X-ray of the patient during treatment. (a) When he was first admitted to the ED, he showed right and left suprahilar infiltrates with consolidation in the right lung midfield and right pleural effusion. (b) Formation of thick-walled cavity after 5 months of OAT treatment. (c) Loculated pneumothorax with organized pleural effusion in the end of treatment.

3. Discussion

Empyema is defined as a collection of pus in the pleural cavity. In the United States, there are approximately 32,000 cases per year. Empyema is associated with elevated morbidity and mortality, around 20% to 30% of patients affected will either die or required further surgery in the first year after developing empyema.⁹

TB is generally experienced by them in the productive age of 21-40 years. Extrapulmonary TB can be in the form of pleural effusion and empyema. TB was found to be the cause of empyema in almost 65% of cases in countries with a high prevalence of TB in the world.¹⁰ Indonesia is one of the 5 countries with the highest TB prevalence in the world along with India, China, Pakistan, and the Philippines. The number of new TB cases in Indonesia was 420,994 cases in 2017 (data as of 17 May 2018) with a male prevalence 3 times higher than female.^{2,4,10} In both cases, tuberculous empyema occurred in an adult male patient aged <30 years without HIV infection and diabetes mellitus. Both patients complained of fever, right chest pain (according to the location of the effusion on chest X-ray) accompanied by increased respiratory rate and decreased oxygen saturation. This is mostly complained by patients with tuberculous empyema.^{4,10} The initial diagnosis based on X-ray images is a unilateral pleural effusion with pneumonia. Where >95% of TB cases with pleural effusion are unilateral.¹¹ The etiology of pleural effusion and tuberculous emphysema is sometimes difficult to determine and requires clinical correlation and analysis of the pleural fluid. Only 40% of patients diagnosed with tuberculosis emphysema showed positive acid fast bacilli (AFB) sputum smears and fluid aspiration, most of which were only +1, making it difficult to find M. tuberculosis.^{10,11}

Empyema tuberculosis is an acute condition in chronic TB infection that attacks the pleural organs followed by migration of neutrophils into the pleural cavity.^{10,12} This situation can also be caused by rupture of the subpleural caseosa in the pleural cavity so that the M. tuberculosis antigen reacts with the sensitized T cells to form delayed hypersensitivity reaction that impairs capillary permeability and impairs drainage from the pleural space.

The result is a buildup of fluid in the pleural cavity in the form of pleural effusion.¹³ Pleural effusion will later evolve in 3 successive stages, the exudative phase (clear and sterile fluid, no bacteria found), the fibrinopurulent phase (thick purulent fluid containing bacteria), and the organized phase (formation of granulation tissue, pleural adhesions).^{13,14}

X-rays of the lungs in both cases showed the involvement of only the right lung (unilateral) with the meniscus sign and homogeneous consolidation on the lung which decreased after receiving antituberculosis therapy and antibiotics. Involvement of both lung fields in tuberculous emphysema is rare, >90% is unilateral.⁴

The results of aspiration in both patients obtained purulent fluid, with gene expert MTB/Rif from aspirated fluid showing negative results for MTB, while adenosine deaminase showed results >300IU/L in both cases. So the patient was diagnosed with tuberculous emphysema. Adenosine deaminase is a biomarker that has been widely used in the diagnosis of extrapulmonary TB using samples of body fluids such as pleural, peritoneal, and pericardial fluids. ADA is an enzyme involved in purine metabolism and is found in various tissues, especially from lymphocytes and monocytes in lymphoid tissue. The activity of this enzyme is increased in M. tuberculosis infection due to the stimulation of T lymphocyte cells by M. tuberculosis antigens. The sensitivity of this test for TB is 92% and specificity is 90%.^{7,12} In countries with a high prevalence of TB cases, the cut-off value for TB infection is 40 IU/L.⁷ In another study, ADA values >100 IU/L were found only on TB.⁸

The presence of respiratory symptom from an adult male patient in an area with a high prevalence of TB accompanied by a chest X-ray showing sign of a pulmonary infection with unilateral effusion, suspicion of TB disease arises. Accompanied by the results of the ADA test with a value of > 100 IU/L, both cases were confirmed as tuberculous empyema. Molecular rapid test results showed negative results, due to the low sensitivity of Gen Xpert MTB/Rif in pleural fluid (46.6%).⁷ Examination of high erythrocytes sedimentation is also a consideration for TB. ESR examination is not specific for certain infections, but the ESR value will increase in presence of chronic

infection, malignancy, kidney disease, and collagen disease. The mean value of ESR in extrapulmonary TB infection was 65.57 mm/hour.¹⁵

Treatment for tuberculous empyema consisted of drainage of pus (intercostal drainage or needle aspiration), antituberculosis drugs, and treatment of secondary infection in the pleural space.^{4,10} Both patients received antibiotic therapy with levofloxacin 1x750mg and metronidazole 3x500mg before finally starting antituberculosis therapy after the results of the ADA test were obtained. Antituberculosis was given in the form of a 2RHZE/4RH regimen as fixed dose combination package (KDT) according to body weight with a total treatment period of 6 months and 9 months. The average treatment for tuberculous empyema is 6-16 months.⁴

In both cases, because of the difficulty of obtaining pleural fluid specimens, response to treatment was assessed base on clinical improvement and chest X-ray. Both patients experienced improvement in clinical symptoms where shortness of breath and fever disappeared, weight gain and appetite improved, and chest X-ray improved with reduced infiltration and effusion. Antituberculosis treatment was discontinued at 6 and 9 months with an evaluation of the erythrocyte sedimentation rate which was in normal values, clinical and radiological improvement.

4. Conclusion

Tuberculous empyema is a rare case of extrapulmonary TB. In countries with a high prevalence of TB, any unilateral pleural effusion on a chest X-ray should be considered as an M. tuberculosis infection. Determining the etiology of a pulmonary empyema is sometimes difficult. Several diagnostic tools, such as examination of acid- fast bacilli smears, tissue culture, gen xpert tests sometimes fail to show the presence of M. tuberculosis infection. Assessment of the value of adenosine deaminase can be used to consider the presence of M. tuberculosis infection in the pleural fluid which of course needs to be combined with clinical, radiological features, disease epidemiology, and response to non-antibiotic therapy.

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