

Tuberculous pericarditis in adolescents: A case series

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Tuberculosis (TB) is one of the major causes of childhood mortality, especially in endemic areas. In 2013, the World Health Organization (WHO) estimated 550,000 new cases and 80,000 deaths due to TB among children. Around 70-80% of the cases were pulmonary TB, while the rest were extra-pulmonary TB.¹

Tuberculous pericarditis accounts for only 8% of all TB cases, however, tuberculosis is the main cause of pericarditis in high-TB-burden countries, including Indonesia.² The mortality rate reached 17-40% and is affected by treatment adequacy.³ Without adequate therapy, the mean life expectancy is 3.7 months, with only 20% surviving to the sixth month.⁴ A 2004 study reported that successful treatment of TB in children depends on several factors, such as treatment compliance, timing and accuracy of diagnosis, concurrent human immunodeficiency virus (HIV) infection and its clinical stage of disease, malnutrition, and drug resistance.⁵ Adolescents and young adults are at the highest risks of having TB.⁶ We report here on three cases of tuberculous pericarditis in adolescents and their outcomes following pericardiocentesis and medication. [Paediatr Indones. 2020;60:111-6 doi: <http://dx.doi.org/10.14238/pi60.2.2020.111-6>].

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Case 1

A 12-year-old boy presented with pallor and fatigue. He was suspected to have malignancy and congenital heart defect at the district hospital due to right pleural effusion, which was seen by chest X-ray (**Figure 1**, left). Pleural fluid aspiration was performed; and the cytology examination revealed predominantly lymphocytes and atypical cells with large nuclei and thin cytoplasm. Tuberculin skin test was negative. Hence, he was suspected of having a malignancy and was referred to our tertiary hospital for further examinations.

Upon admission, the patient presented with fever, breathlessness, and moderate malnutrition. Chest X-ray showed pleural effusion with marked cardiomegaly (**Figure 1**, right). He was then managed as having fever on malignancy and treated empirically with intravenous antibiotics (ciprofloxacin and ampicillin). Thoracic multislice spiral CT (MSCT) performed three days later confirmed bilateral pneumonia, bilateral pleural effusion, pericardial effusion,

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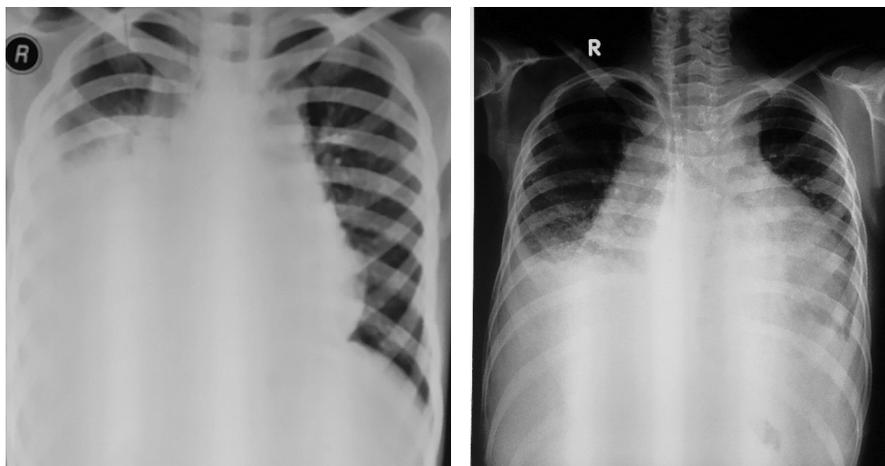


Figure 1. Chest X-rays of Case 1. Left: 2 months before admission to our hospital. Right: chest X-ray performed in our hospital.

and situs inversus (Figure 2). Pericardiocentesis was performed and 300 mL of serous fluid was aspirated. Pericardial catheter was inserted two days afterward, and fluid aspiration was done every 12 hours for the following 13 days. The cytology of pericardial fluid detected acid-fast bacteria, so anti-tuberculosis (anti-TB) drugs were started for tuberculous pericarditis with regimens of RHZE (rifampicin, isoniazide, pyrazinamide, and ethambutol) for 12 months, accompanied by prednisone at a dose of 1 mg/kg/day for the first two weeks, then tapered off.

After administration of anti-TB drugs, the boy's condition improved and the volume of effusion was markedly decreased. Echocardiography on the 15th day after the first pericardiocentesis showed remarkable improvement with minimal pericardial effusion. After aspirating 6 mL more of pericardial fluid, the pericardial catheter was removed. Chest X-ray after two weeks of anti-TB drugs confirmed the clinical improvement, hence, the patient was discharged on the next day. Due to the co-existence of pneumonia, the child was sent home with cloxacillin for two weeks, in addition to the anti-TB drugs. Echocardiography was performed one week after discharge at the outpatient clinic. It revealed moderate pericardial effusion. The anti-TB regimen was continued.

The patient completed the 12-month anti-TB regimen. Echocardiography at the end of the treatment revealed no pericardial effusion. No apparent complications such as cardiac tamponade or constrictive pericarditis occurred during our observation.

Case 2

Our second patient (a 17-year-old boy), was initially a referral case from a district hospital, with massive pericardial effusion. The patient mainly complained about a non-productive cough and breathlessness which had started around two weeks before hospitalization. The patient was diagnosed with acute pharyngitis by his general practitioner. However, heart enlargement was found on chest X-ray. Two weeks later, due to worsening symptoms, the patient was brought to the emergency room (ER) at a district hospital. Urgent echocardiography was performed which revealed massive pericardial effusion, hence, the patient was referred to our hospital (Figure 3). In our ER, emergency pericardiocentesis was performed and 1,150 mL of serohemorrhagic fluid was aspirated from the pericardial cavity. Routine pericardiocentesis was performed every 6 hours. Pericardial fluid analysis showed high protein with cellularity, predominantly lymphocytes. Pericarditis with pericardial effusion caused by non-specific bacterial infection and tuberculosis was suspected. The patient was treated empirically with antibiotics. During hospital care, routine pericardiocentesis yielded fluctuating volumes of pericardial fluid. Chest X-ray on the seventh day of care still suggested massive pericardial effusion (Figure 4, left). Sputum culture revealed the growth of *Enterobacter cloacae* and acid-fast bacilli (AFB) were detected in sputum staining. On the 8th day of care, adenosine deaminase

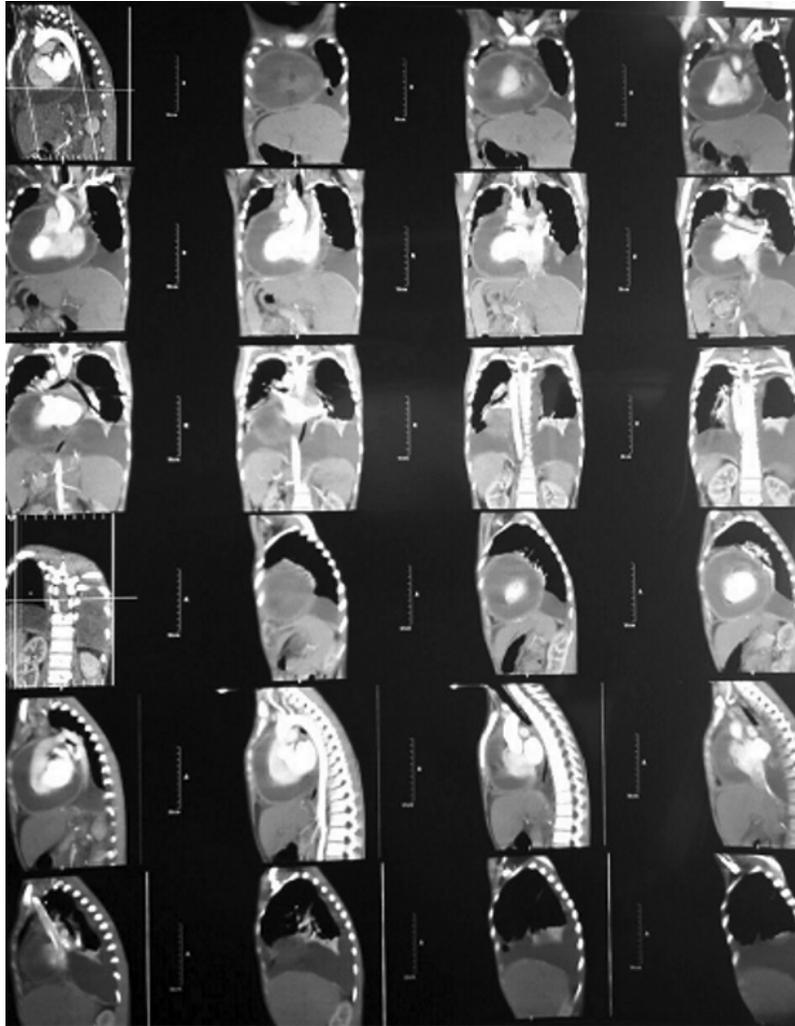


Figure 2. Thoracic MSCT of Case 1

(ADA) test resulted in of 90.1 U/L. GeneXpert assay detected *Mycobacterium tuberculosis* DNA in sputum. The patient was then treated for tuberculous pericarditis. Anti-TB treatment was started with the RHZE regimen. Corticosteroids were added at 1 mg/kg body weight (BW)/day for 2 weeks, then tapered off. Other comorbidities found were moderate malnutrition, hypoalbuminemia, electrolyte imbalance, and pneumonia caused by *Enterobacter cloacae* and *Candida tropicalis*. On the follow-up, the patient showed signs and symptoms of hemodynamic failure and emergency pericardiocentesis was performed. However, only 29 mL of fluid was extracted. Pericardial window was then performed on the 16th day of care, and after 27 days of hospitalization, the patient was sent home

with a substantially improved condition (Figure 4, right).

Case 3

A 17-year-old girl initially complained of fever for 14 days prior to admission, accompanied by a 10 kg weight loss in one month. The patient was brought to a public hospital one week later due to additional complaints of breathlessness, vomiting, and abdominal pain. No additional abnormal breath or heart sounds were heard on chest auscultation. A chest X-ray was performed as indicated, with slight cardiomegaly (Figure 5, left). The electrocardiography finding was only sinus tachycardia and laboratory results

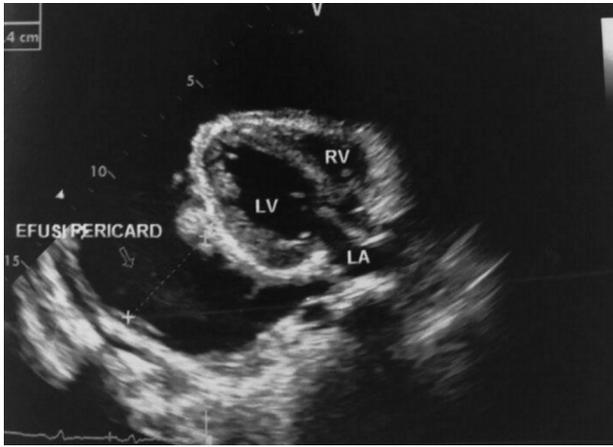


Figure 3. Case 2. Echocardiography at the district hospital revealed massive pericardial effusion

showed low hemoglobin level (7.7 g/dL). Abdominal ultrasonography (USG) revealed cystitis, ascites, and bilateral pleural effusion. The pleural effusion was suspected to be caused by either tuberculosis or non-specific bacterial infection. On the sixth day of care, due to unremarkable improvement of her condition, chest X-ray was re-performed, which revealed cardiomegaly with a water bottle shape and left pleural effusion (**Figure 5**, right). Urgent echocardiography showed massive circumferential pericardial effusion with signs of impending tamponade. The patient

was referred to our tertiary hospital for further management.

The patient presented to our ER with tachycardia, tachypnea, normal blood pressure, muffled heart sounds, and hepatomegaly with low voltage ECG. Echocardiography revealed massive pericardial effusion, right ventricular collapse, right atrial collapse, and swinging heart. Needle pericardiocentesis was performed and 460 mL xanthochromic fluid was extracted. A pericardial catheter was inserted and empirical antibiotics were administered. Fluid analysis revealed exudative fluid with polymorphonuclear dominance. Cytologic examination showed suppurative chronic inflammation with no malignant cells, but plenty of polymorphonuclear and mononuclear cells. No *Mycobacterium tuberculosis* or other bacteria were cultured from the pericardial fluid. No autoimmune marker was positive from the blood. However, ADA examination showed an elevated value of 52 U/L. The patient was then managed for massive pericardial effusion due to tuberculous pericarditis and was treated with anti-TB medication. Other comorbidities were moderate malnutrition and iron deficiency anemia. The patient showed remarkable improvement after treatment and was discharged after ten days of hospitalization.

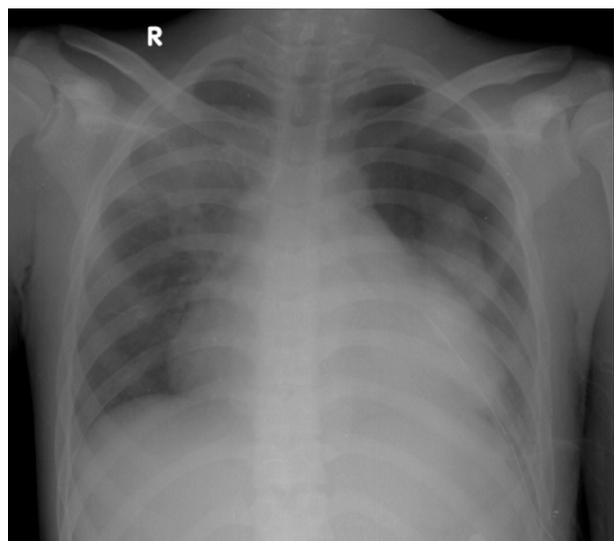


Figure 4. Case 2. Left: Chest X-ray at our tertiary hospital showed a water bottle shape indicating a massive pericardial effusion. Right: Chest X-ray on the 16th day of care after pericardial window showed marked improvement of effusion.

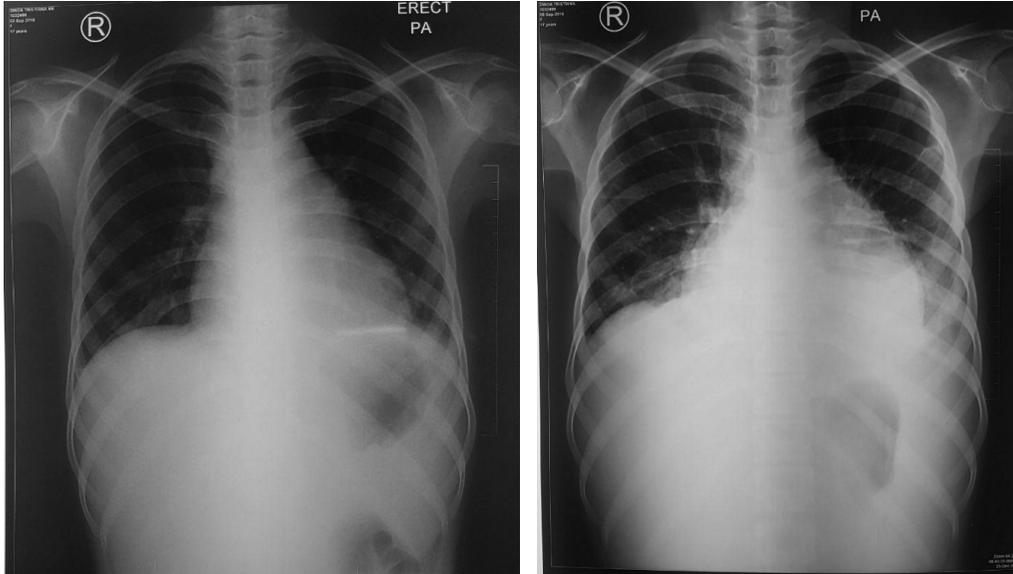


Figure 5. Case 3, Left: Chest X-ray on first day of admission at previous hospital. No abnormality was found except slight cardiomegaly with cardiothoracic ratio 0.56. Right: Chest X-ray on the sixth day of care. Cardiomegaly with water bottle shape and left pleural effusion.

Discussion

Tuberculous pericarditis is a rare form of extrapulmonary TB, with less than a tenth of all TB cases.⁷ Tuberculous pericarditis may occur due to spreading of infection from the mediastinal lymph nodes, lung, vertebrae, sternum, or miliary dissemination.⁸ Based on Wallgren's timetable of primary TB, tuberculous pericarditis that arises from miliary TB may occur approximately 12 months after the primary infection.⁹ Primary infection remains undiagnosed in the majority of cases, as symptoms are mild, non-specific, and usually self-resolving. The timing of primary TB and the sources of infection in our cases were unclear. Age and social environment might be considered as the most influential factors, since all our cases were adolescents. Adolescents were reported to be the most vulnerable population to contracting TB.⁶

All our cases had different signs and symptoms at the onset of illness, which commonly were not specific and might mimic other diseases. However, as the disease progressed, all developed fever and breathlessness. The major similarity of our cases was pericardial effusion as the main finding on echocardiography. Pericardial effusion is the most common manifestation of tuberculous pericarditis

(79.5%), followed by constrictive pericarditis with effusion (15.1%), and constrictive pericarditis without effusion (5.4%).⁸ The most frequent initial symptoms are fever and breathlessness (73-97% and 80-88%, respectively), whereas pericardial rub can be found in 37-84% of cases.⁸

Tuberculosis is not the only cause of pericarditis, however, it is the most common cause of pericarditis in developing countries.² A definitive diagnosis of tuberculous pericarditis is made if acid-fast bacilli are found in pericardial fluid or tissue. Probable diagnosis is made if at least one of the following three conditions is found: (1) pericardial effusion with confirmed TB in other organs, (2) exudative lymphocytic effusion with increased ADA level, and (3) treatment response to anti-tuberculosis drugs.⁷ Acid-fast bacilli were detected in our first and second cases, therefore, a definitive diagnosis could be made. The diagnoses were also supported by the increased ADA >30 U/L in pericardial fluid, which has sensitivity of 94% and specificity of 68% in establishing *Mycobacterium tuberculosis* as the cause of effusion.⁸ The third case showed only increased ADA, however, the patient was still managed for tuberculous pericarditis due to not finding any other possible cause of effusion. After the initiation of anti-tuberculosis treatment,

patient showed rapid improvement and discharged 10 days after.

Although all cases presented with effusion, each case showed different volumes and durations of fluid accumulation. Pericardiocentesis was performed in all cases, followed by insertion of pericardial catheter. Upon initial presentation, the largest volume of pericardial fluid was aspirated from the second case (1,150 mL). However, no tamponade signs were found. On the other hand, the third case suffered from impending tamponade before 460 mL of fluid was aspirated from her pericardial cavity. The risk of cardiac tamponade depends on the amount and duration of fluid accumulation. Acute accumulation of more than 100 mL of fluid can induce cardiac tamponade, while chronic accumulation can reach 2,000 mL of fluid without interfering with cardiac output.¹⁰

Anti-tuberculosis treatments were started in all cases during the hospitalization period. A 2004 study reported that successful treatment of TB in children depends on several factors, including therapy compliance, timing and precision of diagnosis, co-infection of HIV and its clinical stage, malnutrition, and drug resistance.⁵ Our first and third cases presented with moderate malnutrition as the comorbidity, and none of them suffered from HIV co-infection. Corticosteroids treatment were also given to reduce the inflammatory reaction that eventually lead to tissue damage. A double blind placebo-controlled study in patients with tuberculous constrictive pericarditis found a more rapid improvement and lower mortality rate in prednisolone group compared to placebo.¹¹ A meta analysis withheld in 2017 also found that corticosteroids decreased the risk of all-cause mortality [risk ratio (RR) 0.80, 95% confidence interval 0.59 to 1.09] and the need for repeat pericardiocentesis (RR 0.85, 95% CI 0.70 to 1.04) in HIV seronegative patients with tuberculous pericarditis.¹² Eventually all our cases improved with combination of anti-TB treatment and corticosteroid despite all the existing comorbidities, probably also due to high treatment compliance.

In conclusion, adolescents and young adults are the most vulnerable population to contracting tuberculosis. Tuberculous pericarditis may mimic other diseases at its initial presentation. Timing of diagnosis, pericardiocentesis, and anti-TB treatment compliance are major factors in determining outcomes.

Conflict of interest

None declared.

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