Case Report/Series

A case report of tuberculous constrictive pericarditis as a sole manifestation of tuberculosis in a male adolescent

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ABSTRACT

Constrictive pericarditis is a rare type of pericardial disease that can be caused by various factors. Tuberculosis (TB) is one of the most common causes of this abnormality in Indonesia. Interestingly, tuberculous constrictive pericarditis can occur in the absence of acute pericarditis, pulmonary, or extrapulmonary TB. This case described a male adolescent with refractory right-sided heart failure symptoms who developed a rapidly progressive tuberculous constrictive pericarditis. Various imaging modalities, such as echocardiography, chest computed tomography (CT) scan, cardiac magnetic resonance imaging, and incidental PET/CT scan, were used to diagnose the pericardial abnormality. Histopathological findings in pericardial tissues confirmed the diagnosis. Complete surgical pericardiectomy, in conjunction with anti-TB drugs, diuretics, and colchicine, resulted in a significant clinical improvement.

KEYWORDS colchicine, complete pericardiectomy, constrictive pericarditis, right-sided heart failure, tuberculosis

Constrictive pericarditis is a relatively uncommon type of pericardial disease. This disease's prevalence remains unknown. Tuberculosis (TB) was and continues to be the leading cause of the disease in developing countries, followed by idiopathic, post-radiation, post-cardiac surgery, neoplasms, sarcoidosis, and uremia in developed countries.[1–3]

The main pathophysiology is related to damaged pericardial distensibility, which is associated with acute or subacute inflammation instead of fibrosis or calcification, which is commonly seen in chronic pericardial constriction leading to the development of fibrous thickening or calcification of the pericardium. Clinical manifestations result from right heart failure. Pericardiectomy can result in a significant symptom relief.[2,4]

We described a case of a 16-year-old male with an unremarkable medical history, good socioeconomic level, and no family medical history. He was diagnosed with TB-related constrictive pericarditis with no other organ manifestations. Furthermore, this was discovered in the absence of previous acute or effusive pericarditis.

CASE REPORT

For the previous 3 months, a 16-year-old male adolescent had orthopnea, progressive dyspnea on effort, bilateral lower limb edema, ascites, and weight gain of up to 25 kg. He had been admitted several times in the previous 2 months due to similar issues. He had multiple thoracocentesis and paracentesis procedures

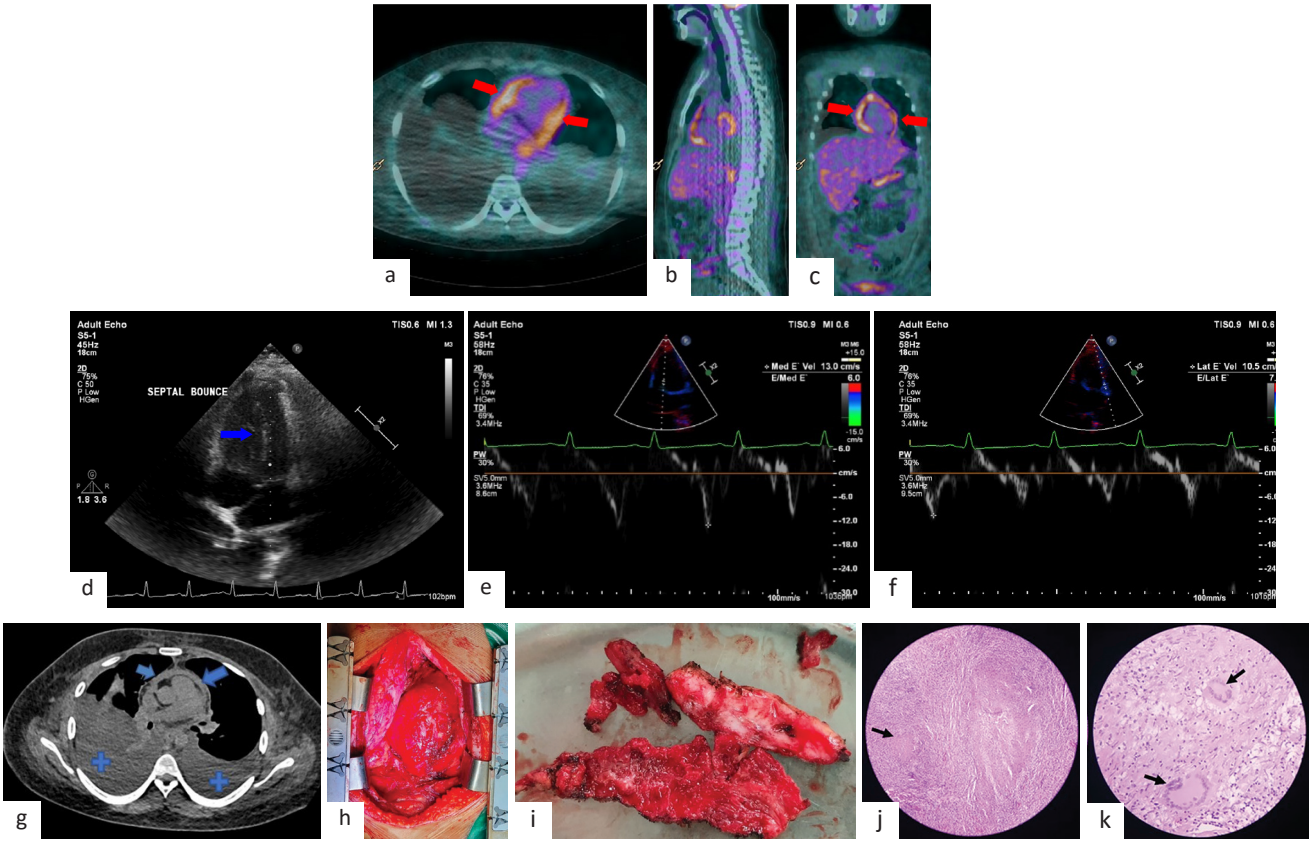

Figure 1. Examinations of the tuberculous constrictive pericarditis. (a–c) Positron emission tomography/computerized tomography (PET/CT) scan showed an active inflammation on the pericardium, along with significant thickening of the layer of the heart wall (red arrow); (d–f) echocardiography findings showed septal bounce during early diastole (d, blue arrow) and medial mitral annulus velocity (e) higher than the lateral mitral annulus velocity (f) indicating annulus paradoxus; (g) computed tomography (CT) scan showed thickened pericardium (arrow) with massive bilateral pleural effusion (+); (h & i) stiffened fibrous pericardium during open pericardiectomy; (j) 40× magnification and (k) 100× magnification of light microscope showing granulomas (black arrows) with epithelioid cells, multinucleated giant cells (Langhans), and caseous necrosis with hematoxylin and eosin staining

at various hospitals, but no clear diagnosis has been made. He was fit and active and had no notable medical history.

His physical examination revealed mild respiratory distress, persistent tachycardia, edema anasarca, dullness of the bibasilar lungs, tensed ascites, scrotal edema, and overall leg swelling. Nevertheless, he was hemodynamically stable, and no fever was recorded. There were no signs related to other manifestations of tuberculous infection, either pulmonary or extrapulmonary (neurologic changes, enlarged lymph nodes, arthritis, and cutaneous lesions). Pericardial knocking in the diastolic phase was easily heard by cardiac auscultation, whereas no murmur or friction rub was found.

The result of the laboratory test revealed leucocytosis with increased neutrophils but normal erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), mild hypoalbuminemia, hyponatremia, and hypokalemia. Notably, the repeated interferon-gamma release assay (IGRA) tests were positive. However, the analysis of pleural and ascitic fluid showed transudate with normal adenosine deaminase (ADA) levels. Autoimmune panels were negative. Chest X-ray (CXR) indicated a relatively normal size of the heart with bilateral large pleural effusion. Electrocardiogram (ECG) only demonstrated sinus tachycardia without other specific changes. Subsequently, a positron emission tomography/computerized tomography (PET/CT) scan was ordered in suspicion of malignancy as the underlying cause. However, the 18F-fluorodeoxyglucose-avid lesion was only detected around the heart, as well as significantly thickened pericardial layer, indicating an inflammatory pericardium (Figure 1, a–c). Thus, constrictive pericarditis was suspected.

Echocardiography (Figure 1, d–f) soon revealed the classical signs of constrictive pericarditis, including

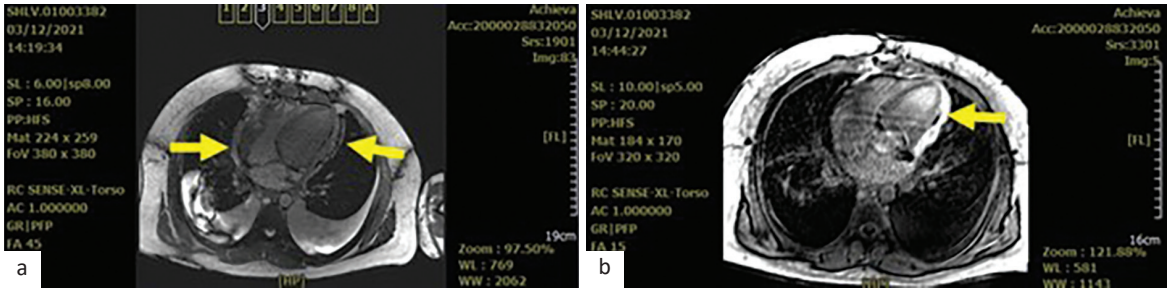

Figure 2. Cardiac magnetic resonance imaging (CMR) conducted 2 weeks after pericardiectomy. Inevitably residual parts of the thickened pericardium on the posterolateral region (yellow arrows, shown in different phases [a & b]). All cardiac chambers and functions appeared normal

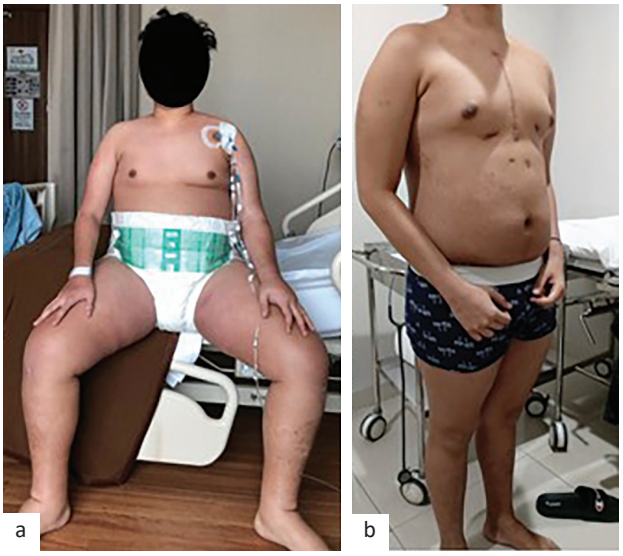

Figure 3. Clinical appearances of the patient. (a) At the initial hospital admission; (b) 2 months after successful surgical pericardiectomy. Peripheral congestion and ascites were significantly disappeared, as shown in the right picture

thickened pericardium without pericardial effusion, interventricular septal bounce during inspiration, respiratory variation of early mitral inflow velocity (E-wave) on pulse-wave Doppler, annulus paradoxes (E' medial>E' lateral) on tissue-Doppler interrogation, massively congested inferior vena cava, and bilateral large pleural effusion. No pericardial effusion was found. Then, a high-resolution chest computed tomography (CT) scan (Figure 1g) confirmed the diagnosis of constrictive pericarditis with diffusely and significantly thickened pericardium.

He was treated for 2 months with rifampicin 600 mg/daily, isoniazid 400 mg/daily, ethambutol 1,000 mg/daily, and pyrazinamide 1,500 mg/daily, followed by a rifampicin and isoniazid combination in same doses for up to 4 months. In addition, 62.5 mg/b.i.d. intravenous methylprednisolone was given to alleviate pericardium inflammation until he underwent open pericardiectomy in the following days. As a final treatment, a complete pericardiectomy via median sternotomy was successfully performed (Figure 1, h–k). During the procedure, extensive pericardial decortication was targeted, leaving merely a small region of the inflamed pericardium on the posterior part, which was technically difficult to evacuate. Pathology examination of the pericardial tissues demonstrated chronic inflammatory cells, tubercles with epithelioid cells, Langerhans giant cells, and some caseous necrotic spots, confirming the diagnosis of tuberculous pericarditis (Figure 2). He was discharged in the next 2 weeks after the surgery.

Moreover, the signs of right ventricle failure and peripheral congestion persisted in the first week of follow-up after discharge, requiring additional thoracocentesis, paracentesis, and high-dose oral furosemide. Further evaluation with cardiac magnetic resonance imaging (CMR) conducted 2 weeks after the surgery showed inevitably residual parts of the thickened pericardium with constrictive profiles, along with normal structures and functions of both ventricles (Figure 2). High-dose furosemide and anti-TB drugs consisting of isoniazid, rifampicin, ethambutol, and pyrazinamide were continued, while colchicine 0.5 mg/daily was added to reduce the remaining inflammatory pericardium. Two months after the surgery, a significant clinical improvement was achieved. He presented with no peripheral edema and a weight loss of up to 32 kg, resulting in milder symptoms daily and improved functional capacity (Figure 3). Following echocardiography and ultrasound, there was no evidence of pleural effusion or ascites. Low-dose furosemide 20 mg/daily, anti-TB regimen, and colchicine 0.5 mg/daily were among the most recent medications. This state was also seen at the next clinical visit 6

months after the procedure. Now, he could do daily activities and even light exercise without experiencing any limiting symptoms, despite continuing to take anti-TB medications.

DISCUSSION

We presented a case of tuberculous constrictive pericarditis with the profile of edema anasarca in a male adolescent without preceding known pulmonary or extrapulmonary TB. Chronic pericarditis can develop as pericarditis sicca with constrictive physiology, as shown in this case. Constrictive pericarditis is characterized by progressive exertional dyspnea, fatigue, persistent lower extremity edema, and abdominal distension with ascites. These symptoms may present in conjunction with other symptoms of right-sided heart failure, such as distended jugular veins, Beck's triad, the Kussmaul sign, pericardial knock, ascites, peripheral edema, organ congestion (especially kidney and liver), or cachexia. The thick and stiff pericardium traps the heart inside, hampering its contractility function and resulting in significant backward congestion and low forward cardiac output. Interestingly, ascites usually appear more prominent and earlier than bilateral legs edema in this pericardial disease, distinguishing it from the common heart failure syndrome.[5–7]

Making the diagnosis of tuberculous pericarditis in this case before surgery is challenging due to the lack of typical symptoms of TB, negative ADA findings at both pleural and ascites fluid, clear lung on chest CT scan, and low ESR and CRP. Although the IGRA test is generally associated with latent TB infection rather than acute infection, repeated positive IGRA results could be a clue to suspect TB.[8]

Clinical manifestation of constrictive pericarditis is often overlooked as a part of congestion in heart failure syndrome. Constrictive pericarditis should be suspected if echocardiography revealed normal cardiac with relatively normal ventricle functions. This ultrasound could demonstrate thickened pericardium, interventricular septal bounce during inspiration, respiratory variation of early mitral inflow velocity (E-wave), annulus paradoxes, congested inferior vena cava, and bilateral large pleural effusion.[3,7,9] These key signs were observed in this patient, supporting an initial diagnosis of constrictive pericardial involvement. Moreover, in the early stages of the disease, echocardiography may miss any cardiac and pericardial abnormalities. Multimodality imaging (advanced echocardiography protocols, chest CT scan, and CMR) is commonly required to confirm the diagnosis and potentially identify the underlying etiology.[6,10]

ECG changes in constrictive pathology are often minor, including nonspecific ST-segment, T-wave changes, and low QRS voltage.[3,6,7] Atrial fibrillation might also occur at a later stage.[3] Calcification on the pericardium might be detected in 20% to 40% of cases, particularly associated with a longer onset, and it is more common in tuberculous etiology.[3] The CXR of this patient was not typical, probably due to the shorter duration of the onset of his disease.

Cardiac CT and CMR are the most useful tools to confirm the diagnosis by both visualizing the pathologic pericardium and hemodynamic changes in the heart caused by the constricting sac. With the availability of a chest CT scan or CMR, PET/CT scan is rarely required in most cases. Interestingly, PET/CT scan incidentally found a pericardial inflammation in this case, although this test was initially meant to detect any malignancy process, particularly lymphoma, which potentially complicated the heart and lymph systems. Furthermore, CMR is sometimes required after pericardiectomy, particularly if hemodynamic disturbances and congestion symptoms persist, as presented in this patient. CMR could then assess the remaining thickened pericardium, residual right ventricle dysfunction, and even the presence of restrictive myocardial components.[3,9] Notably, myocardial hypotrophy/atrophy might develop in protracted constrictive pericarditis or delayed decision for pericardiectomy. This situation causes prolonged ventricular dysfunction, more commonly at the right ventricle, and persistent peripheral congestion as a further consequence after successful pericardiectomy.[9]

The diagnosis of TB involvement in this inflamed pericardium was confirmed by histopathology analysis of the pericardium tissue obtained during the open surgery. The features of tuberculous pericarditis in this case were granulomas structured by lymphocytes, epithelioid cells, Langhans giant cells, and caseous necrotic spots under hematoxylin and eosin stain. However, it is important to note that the diagnostic sensitivity of pericardial biopsy can range from 10% to 64%, especially if only small specimens are collected using a minimally invasive approach.[11]

The standard of anti-tuberculous therapy for at least 6 months is used to treat tuberculous pericarditis, and pericardiectomy is considered in patients who fail the initial conservative treatment.[11] This patient was initially given isoniazid, rifampicin, ethambutol, and pyrazinamide for 2 months. Following that, isoniazid and rifampicin were continued for the next 4 months to complete a total treatment period of 6 months, as recommended by the current guideline.[12] This approach provided a positive response to his condition, preventing re-inflammation of the remaining pericardial tissue following surgery.

Several studies also showed the potential benefits of adjunctive steroid or non-steroidal anti-inflammatory drug therapy to reduce the development of pericardial constriction in tuberculous pericarditis, both in HIV-positive and HIV-negative patients. However, it is low-grade evidence based on the Cochrane study.[13–16] Otherwise, their role in treating constrictive pericarditis, which already existed, is unclear. In addition, steroids might worsen systemic congestion due to their effects on fluid retention.

Anti-inflammatory agents could be used to treat residual pericardial or mediastinal inflammation after pericardiectomy, and some evidence suggests that colchicine may be useful in this situation. Colchicine has anti-inflammatory properties by inhibiting motility, phagocytosis, and degranulation of leucocytes. It also inhibits interleukin (IL)-1 and IL-18, which are involved in recurrent pericarditis. A double-blind, multicenter, randomized, placebo-controlled trial in 2010 analyzed the effect of colchicine in 360 patients undergoing cardiac surgery.[17] All subjects received a loading dose of colchicine 1 mg/b.i.d on day-1 followed by 0.5 mg/b.i.d for a month (half dose to patients weighing <70 kg or had an colchicine intolerance). Lower doses (0.5 mg/daily) and weight-adjusted doses without a loading dose may reduce gastrointestinal side effects (diarrhea). They concluded that colchicine significantly reduced post-pericardiotomy syndrome after 12 months, as well as rehospitalization, recurrent pericarditis, cardiac tamponade, and constrictive pericarditis. Colchicine could be used as a treatment due to its ability to reduce inflammation in the pericardium and possibly the mediastinum.[18] It was suggested in the condition of active pericardial inflammation with high CRP and/or thickened pericardium (>3 mm) with late gadolinium enhancement of the pericardium on CMR.[2,18] Since this patient remained symptomatic and congested at the follow-up after pericardiectomy and relevant to persistent constrictive features viewed on CMR, colchicine 0.5 mg/daily was added to suppress the inflammation process of the mediastinum and left-over pericardium.

Pericardiectomy is the mainstay treatment for constrictive pericarditis in an advanced stage with a very thick pericardium, especially for the idiopathic group and miscellaneous constriction, including tuberculous pericarditis.[16,19,20] In most cases, around 40% of patients might have a dramatic improvement of hemodynamic and functional capacity in the early days or weeks after pericardiectomy, while the rest might only experience it late.[6,20] After consulting with the cardiac surgeon, pericardiectomy was recommended early in this patient because he had severe pericardium thickness, complicating protracted right ventricle failure. According to some studies, postponing surgery results in persistent right ventricle failure and a worse prognosis. This subsequence could be related to ventricular atrophy caused by prolonged compression and restriction of the tightening pericardium.[6,7]

Delayed or inadequate responses to pericardiectomy might result in persistent congestion and low cardiac output syndrome after the successful procedure. This condition is associated with myocardial atrophy or fibrosis, incomplete resection, and the development of recurrent cardiac compression by mediastinal inflammation and fibrosis.[6] Determining the primary cause of this residual problem is crucial to achieving an optimal treatment after the surgery. Multimodality imaging, particularly echocardiography and CMR, is essential to evaluate this matter further.

Finally, this patient responded well to the surgery and medication, with greater clinical improvement observed 2 months after the procedure. He claimed that he was nearly asymptomatic while performing daily activities. He no longer had leg swelling and taking the diuretics. He has been discharged from cardiology review but continues undergoing follow-up care with a pulmonologist for his TB treatment.

In conclusion, this case described a male adolescent with refractory right-sided heart failure symptoms who developed rapidly progressive constrictive pericarditis as an isolated manifestation of TB. Since there was no evidence of TB involvement in other organs, determining TB as the etiology of the pericardial involvement before collecting the specimens for

histopathology analysis was difficult. However, the initial diagnosis could be made by multimodality imaging above other hallmark signs obtained from clinical examination. Complete pericardiectomy was successfully implemented, followed by continuing anti-tuberculous regimens and diuretics after the procedure. In addition, colchicine might offer additional benefits in reducing inflammation of the mediastinum and the remaining pericardium.

Conflict of Interest
The authors affirm no conflict of interest in this study.

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