Tuberculosis as the cause of recurrent pericardial effusion: a case report

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ABSTRACT

Background: Pericardial effusion (PE), affecting approximately 3% of the Western population, has diverse aetiologies including heart failure, malignancy, autoinflammatory, metabolic, or microbiological diseases, and can be induced by trauma or drugs. Guidelines suggest early tuberculosis (TB) testing in patients with PE. However, clinicians in Western Europe often overlook this diagnosis. Therefore, the aim of this report is to emphasize the importance of considering this diagnosis.

Case Presentation: A 72-year-old woman, with a history of aortic valve replacement, was referred for episodes of PE without diagnosis, severe tricuspid insufficiency, and an atrial flutter. PE resisted high-dose anti-inflammatory treatment for sterile pericarditis after ruling out cardiac, banal bacterial, malignant, and autoimmune causes. She underwent surgical tricuspid valve repair with isthmus ablation, and bilateral pericardiopleural windows were created. TB was confirmed via QuantiFERON test and polymerase chain reaction of the pericardial fluid obtained during surgery. Antibiotic and corticosteroid treatment for TB was started with outpatient monitoring. The symptoms decreased after the final antibiotic and corticosteroid therapy.

Conclusion: This case report emphasizes the importance of considering TB as a potential cause of unexplained, recurrent PE in an immunocompetent patient from a non-endemic area, as stated in the guidelines. Especially in an increasingly intercontinental world. Early testing can expedite the start of treatment, reducing complications, invasive procedures, and improving outcomes.

Keywords: Pericardial effusion, cardiac tamponade, tuberculosis, pericardiopleural window surgery, case report.

Type of Article: CASE REPORT **Specialty:** Cardiology

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Introduction

Pericardial effusion (PE), an excess of fluid in the pericardium, may lead to cardiac tamponade with hemodynamic instability if acute. PE has an incidence of 3% annually in the Western population [1]. Aetiologies include heart failure, infections (viral, bacterial, fungal), autoimmune disorders, neoplasms, metabolic disease, or drug-induced conditions, with cardiac surgery as a known risk factor [1-4]. In high-income settings, tuberculosis (TB) is a rare cause of PE and often leads to delayed diagnosis, even though TB testing is advised in the guidelines for patients with PE. TB remains the leading cause of PE in developing countries, particularly in immunocompromised patients [1,3-6].

Tuberculous pericarditis (TBP) typically presents itself with systemic symptoms like atypical chest pain, dyspnea, and hemodynamic instability due to cardiac constriction and inflammatory symptoms. Diagnostic tests include polymerase chain reaction (PCR) for mycobacterium tuberculosis, gamma interferon assays, acid-fast bacilli staining, microscopic examination, and bacterial culture testing of pericardial fluid. The Interferon Gamma Release Assay, known as the QuantiFERON test and imaging techniques (e.g., cardiac magnetic resonance imaging), can aid in the diagnosis of TBP [5,7].

TBP can be complicated by cardiac tamponade, and constrictive pericarditis, which leads to increased mortality. Treatment includes antibiotics, corticosteroid therapy, and pericardiopleural window surgery for refractory cases to enable drainage [8,9].

This case report aims to address the importance of considering TB as a cause of PE in patients with low epidemiological and clinical suspicion. Additionally, this report aims to raise awareness among physicians to routinely test for TB and to be compliant with the cardiology guidelines in diagnosing the cause of PE.

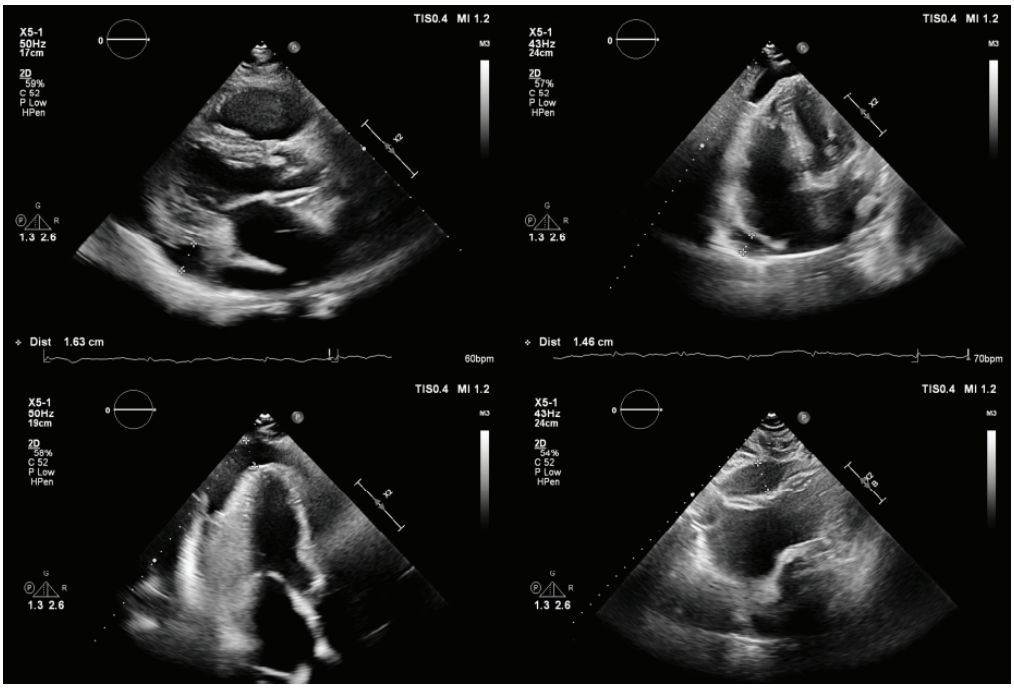

Figure 1. *Multiple transthoracic echocardiographic frames revealing PE.*

Case presentation

A 72-year-old Caucasian Dutch woman, with a medical history of arthritis, aortic valve replacement with a bioprosthetic valve, a Morrow procedure, and tricuspid insufficiency, was referred to our center for a second opinion regarding recurrent PE, severe tricuspid insufficiency, and an atrial flutter.

She initially presented to the referring hospital with progressive dyspnea, diarrhea, and a declining condition for 7 weeks. Physical examination revealed a heart rate of 105 bpm, blood pressure of 141/104 mmHg, a systolic murmur, without pericardial rub and pulmonary crackles. There were no other clinical signs indicative of TB. Blood tests revealed no infectious abnormalities. Electrocardiography indicated an atrial flutter with a delayed QT interval time (519 ms). Transthoracic echocardiogram (TTE) revealed relevant PE at all sides of the heart with a maximum of 24.1 mm (Figure 1). Exudative fluid was drained during pericardiocentesis, and malignancy was excluded (chemical properties in Table 1). After a brief febrile episode with elevated C-reactive protein (64 mg/l) values, the patient improved clinically and was discharged. In the absence of trauma, malignancy, or drugs known to cause PE, the differential diagnosis at the referring center was infectious disease (both of the pericardium and gastro-intestinal), or auto-immune disease. However, no bacterial cultures of the drained pericardial fluid had been obtained.

Four weeks later, she re-presented with recurring symptoms of dyspnea and a declining condition. Physical examination remained unremarkable, but a chest X-ray revealed an enlarged cardiac silhouette (Figure 2). Recurrent PE was confirmed by TTE. Pericardial fluid drainage revealed serosanguinous fluid with benign findings. Banal bacterial cultures (general bacteria, no TB) of the fluid were performed, which remained negative. Because the patient did not have any symptoms of auto-immune disease, no tests for this aetiology had been performed. The patient was treated for sterile pericarditis with high-dose acetylsalicylic acid and colchicine, and was discharged shortly after.

Table 1. *Chemical data results of laboratory research of the drained pericardial fluid.*

Parameter	Measured value	Unit
Cholesterol	2.9	Mmol/l
Hb	<0.01	Mmol/l
Leukocytes	0.2	$\times 10^9$/l
LD	217	U/l
Total protein	50	g/l

Over the next 6 weeks, the patient was re-admitted twice with recurrent dyspnea, increased PEs, and once with signs of tamponade. There was no fever during the episodes. Despite weakly positive rheumatic serology, autoimmune pericarditis was unlikely. A positive TB QuantiFERON test was noted, though general pericardial fluid cultures remained negative. A positron emission tomography scan was performed (Figure 3). PE and suppression of the myocardium were seen. However, no abnormal activity in the pericardium or lungs was observed. Additionally, no hilar or mediastinal lymphadenopathy was observed.

The patient underwent successful tricuspid valve repair, isthmus ablation, and bilateral pericardiopleural window creation in our center. Histology of the pericardial tissue revealed chronic fibrosing inflammation with

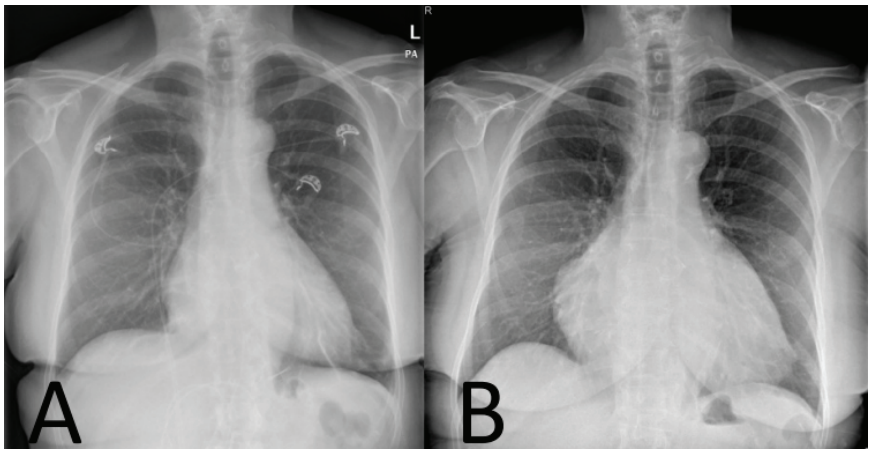

Figure 2. *(A) An older X-ray showing the normal heart figure of this patient. (B) The X-ray upon admission showing an increased heart figure and the absence of pulmonary TB.*

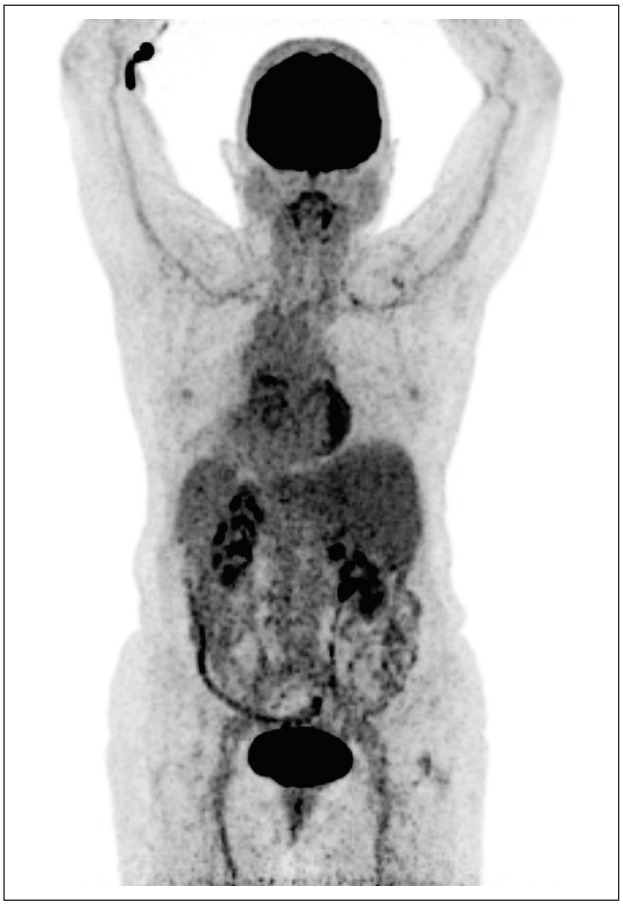

Figure 3. *Positron emission scan shown in coronal plane.*

prior hemorrhage, and PCR of the pericardial fluid tested positive for TB. However, tissue PCR and (myco)bacterial cultures were negative. Drug resistance could not be assessed. Mycobacterial cultures of the pericardial fluid remained negative as well.

The patient had no travel history or TB symptoms but reported a relative who visited TB-endemic regions. She was started on a TB regimen of rifampicin, isoniazid, pyrazinamide, ethambutol, and prednisone (dosage in accordance with the antibiotic blood level), consistent with current Dutch TB guidelines. Discharged a week post-surgery, she continued antibiotics with no recurrence of symptoms under close outpatient monitoring. The symptoms decreased, and self-reported therapy compliance and treatment tolerance were good.

Discussion

This case report illustrates TB as a potential cause of PE in immunocompetent, HIV-negative patients from non-endemic regions. Although TBP is rare in the Western world [5,6], intercontinental travel becomes easier and increasingly accessible for an increasing number of people from TB-endemic regions. This potentially increases the risk of TB infection amongst the Western population. Cases have been reported in which immigrants, from endemic regions, presenting with subtle symptoms, were ultimately diagnosed with TBP [10].

However, because of the current rarity in the Western world, the diagnosis is often delayed due to the absence of routine TB testing. This means the prevalence of TB, and particularly of TBP as its sole manifestation, which contributes to diagnostic challenges. Therefore, previous reports have similarly recommended routine TB testing in cases of unexplained PE [11,12].

While TB tests (e.g., QuantiFERON and PCR) are widely available in Western Europe, testing was deferred in this case, due to a delayed consideration of TB aetiology attributable to the region's low epidemiological prevalence and limited clinical experience with TB, leading to a delayed diagnosis and incompliance with the current guidelines [3,4]. Additionally, the systemic and more subtle symptoms of TBP with which it often presents itself [5] make clinical diagnosing more difficult. This is a well-recognized issue that has been previously reported and has posed challenges for other clinicians as well [12-14].

TB typically spreads to the pericardium via lymphatic pathways [8,9]. However, no lymphadenitis or enlarged

lymph nodes were detected in this case. A positive QuantiFERON-TB test, indicative of TB exposure or latent infection, should have prompted further investigation in recurrent, unexplained PE. Next to that, other potential causes (malignancy, bacterial infections, and autoimmune diseases) were excluded. European and American guidelines suggest considering TB testing in cases without an identified cause, even with low clinical suspicion [3,4]. Initial pericarditis treatment failed to address the underlying TB, resulting in recurrent symptoms.

Surgical interference (i.e., pericardiopleural window creation or pericardiectomy) should be considered as a last treatment option in refractory PEs because of the risk of complications involved [15]. However, in this case, an additional surgical procedure was required, which potentially could have been avoided with earlier diagnosis and targeted treatment. Additionally, because of the delayed diagnosis, there was a prolonged disease duration, which is associated with poorer outcomes [6,7,9]. The importance of early treatment has been highlighted in previous publications, given the significant risk of complications and fatal outcomes associated with TBP [12,13].

Conclusion

This case highlights the importance of considering TB in unexplained, recurrent PE, even with low clinical or epidemiological suspicion. Routine TB testing (as recommended in the European cardiology guidelines) should be integrated into local protocols as well, regardless of the epidemiological suspicion. This ensures compliance with current guidelines. In a progressively interconnected world, this becomes increasingly important.

Early TB diagnosis enables timely treatment and reduces the need for invasive interventions. Greater awareness and earlier testing can enhance treatment strategies and prevent unnecessary, potentially hazardous, extra procedures.

What is new

This case report highlights the importance of acknowledging and considering TB as a cause for PE. Especially in patients with low clinical or epidemiological suspicion in an increasingly global world.

List of Abbreviations

PCR	polymerase chain reaction
PE	pericardial effusion
TB	tuberculosis
TBP	tuberculous pericarditis
TTE	transthoracic echocardiogram

Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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None.

Consent for publication

Written informed consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	Patient (gender, age)	75 years, female
2	Final diagnosis	Mycobacterium tuberculosis infection of the pericardium
3	Symptoms	Recurring pericardial effusion and tamponade
4	Medications	None of significance
5	Clinical procedure	Pericardiopleural window surgery, antibiotic and corticosteroid therapy
6	Specialty	Cardiology

Timeline of Events