Tuberculous pericarditis
An old acquaintance in an unusual site

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DOI: https://doi.org/10.36104/amc.2025.4365

Abstract

Tuberculous pericarditis is a rare but serious form of extrapulmonary tuberculosis. It is challenging to diagnose due to its nonspecific symptoms, requiring a combination of clinical findings, imaging techniques and laboratory tests. Direct microbiological confirmation is typically difficult.

We present two cases: an immunocompetent patient diagnosed indirectly through adenosine deaminase (ADA) testing, and an HIV immunocompromised patient with a positive molecular test of pericardial fluid. Both responded satisfactorily to antitubercular treatment.

Adenosine deaminase is a valuable tool that is quick and accessible when the presence of the bacillus cannot be proven by other means. Interferon gamma detection in pericardial fluid has shown an excellent diagnostic yield; however, this test has limited availability in our setting, as does pericardial tissue biopsy. **(Acta Med Colomb 2025; 50. DOI: https://doi.org/10.36104/amc.2025.4365).**

Keywords: *adenosine deaminase, pericarditis, Mycobacterium tuberculosis, extrapulmonary tuberculosis, polymerase chain reaction.*

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Received: 26/XII/2024 Accepted: 21/III/2025

Introduction

Tuberculous pericarditis (TP) is an extrapulmonary form of tuberculosis that accounts for approximately 1% of all tuberculosis cases and 1-2% of the extrapulmonary forms. In endemic regions, it constitutes 50-90% of effusive pericarditis cases, while in nonendemic areas it accounts for approximately 4%. Untreated, it can progress to cardiac tamponade, constrictive pericarditis, and even death (1, 2). It is also estimated that TP constitutes close to 4% of acute pericarditis cases, 7% of cardiac tamponade cases, and 6% of constrictive pericarditis cases (3).

Its clinical presentation is nonspecific, and symptoms vary depending on the rapidity of onset of the pericardial effusion, which is characteristically exudative (4, 5). The diagnosis is confirmed through identification of *Mycobacterium tuberculosis* on pericardial or pericardial fluid histopathology, maintaining a high index of suspicion when high ADA levels are found in the pericardial fluid (4).

Treatment is the same as for pulmonary tuberculosis, and corticosteroids may be added to reduce the incidence of complications.

This article presents two cases of TP: one in an immunocompetent patient and another in a patient with immunosuppression caused by human immunodeficiency virus (HIV). The objective is to highlight the various suspicious scenarios - which are not restricted to immunocompromised patients - and the importance of early diagnosis to begin treatment promptly.

Clinical case 1

A female patient in her 40s consulted due to six days of fever and nonproductive cough. She complained of moderate, non-radiating chest pain associated with grade 3 dyspnea on the MRC scale, orthopnea and bendopnea.

On physical exam, she had grade III jugular distension, rhythmic heart sounds and grade I lower extremity edema. A chest x-ray showed significant enlargement of the cardiac silhouette, with pericardial effusion confirmed on a transthoracic echocardiogram (Figure 1), which indicated severe global pericardial effusion with hemodynamic repercussions.

An emergency pericardial window was opened, obtaining sanguinous fluid. Pericardial fluid analysis showed polymorphonuclear exudate (Table 1) with negative PCR and cultures for *Mycobacterium tuberculosis*, but elevated adenosine deaminase (ADA) at 52.2 IU/L. The ELISA HIV test was negative. An interferon-gamma release assay (IGRA) was not performed because it was not available.

Based on the elevated ADA level, a presumptive diagnosis of TP was made, and antituberculous treatment was

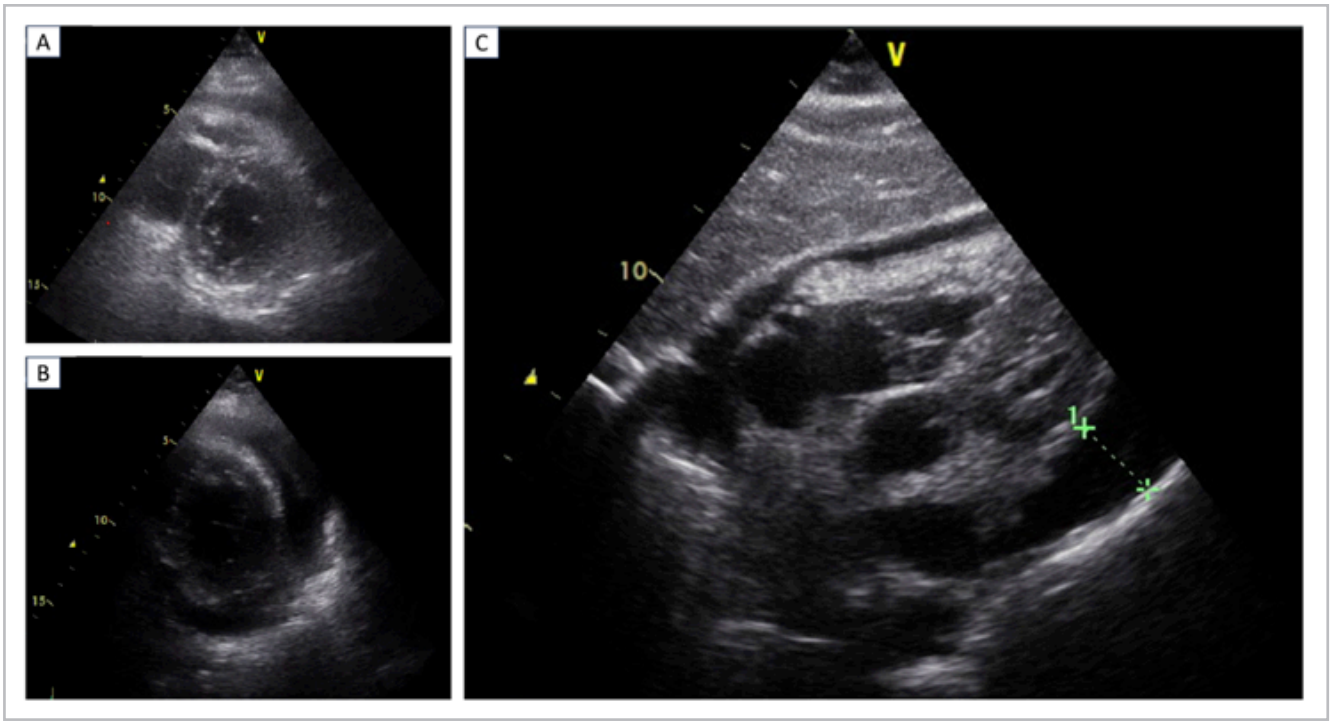

Figure 1. Transthoracic echocardiogram. **Case 1:** *A and B: thickened, reactive pericardium with large fibrin deposits. C: severe pericardial effusion measuring 2.8 cm.*

started with four-drug combination therapy (rifampicin, isoniazid, pyrazinamide and ethambutol [RHZE]), along with prednisolone.

Clinical case 2

A male patient in his 30s with a history of recent stage C3 HIV infection on antiretroviral treatment consulted with a complaint of dyspnea, nonproductive cough and predominantly nocturnal fever for the last eight days. He reported a more than 10 kg weight loss over the last two months, along with tachycardia, tachypnea and episodes of desaturation recorded with a home pulse oximeter.

On admission, his chest x-ray showed an enlarged cardiac silhouette and blurring of the costophrenic angles, and therefore bilateral pleural effusion secondary to pneumonic involvement in an immunocompromised patient was initially suspected. Antibiotic treatment with a fourth-generation cephalosporin (cefepime) was started, and blood cultures and a chest computed tomography scan were ordered (Figure 2) for a better description of the radiographic findings.

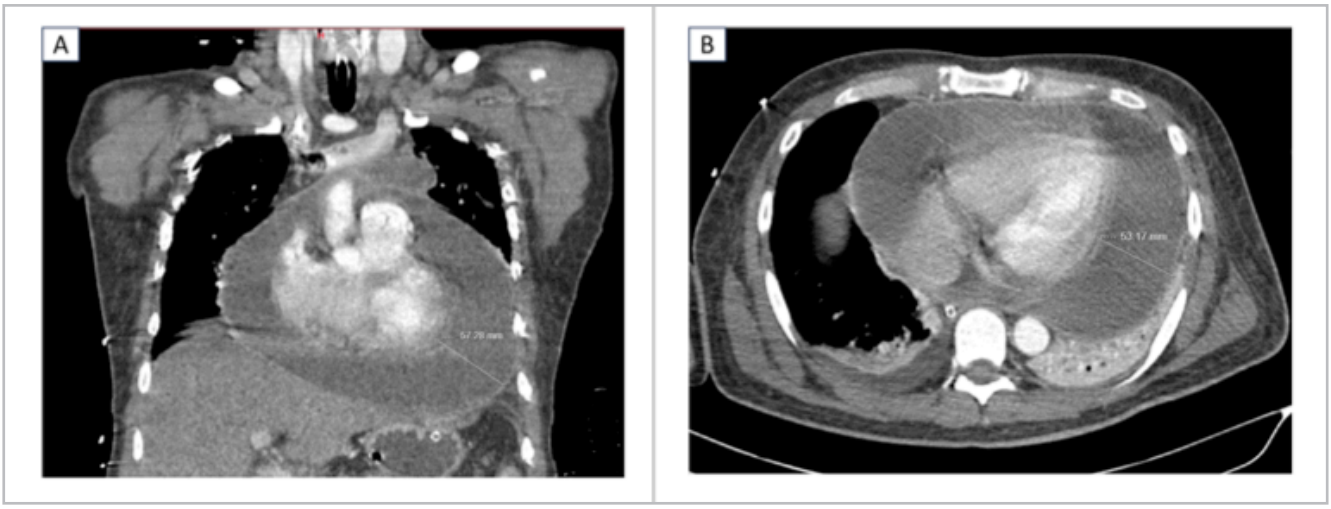

Figure 2. Computed tomography of the chest with contrast Case 2: *A: severe pericardial effusion measuring 57.28 mm, viewed in the coronal plane. B: bilateral pleural occupation and severe pericardial effusion measuring 53.17, viewed in the axial plane.*

Worsening of the patient's clinical condition suggested the possibility of sepsis, and antibiotic coverage was broadened with vancomycin and meropenem. The patient had to be intubated for invasive mechanical ventilation. An echocardiographic scan in the critical care unit showed severe pericardial effusion with hemodynamic repercussions and chamber collapse, which caused massive cardiac tamponade.

Emergency diagnostic and therapeutic pericardiocentesis was performed, obtaining 700 cc of citrine pericardial fluid. Samples were sent for testing. The cytochemical analysis showed cloudy, yellowish pericardial fluid with no leukocytes, abundant red blood cells, a negative culture for common microbes, and a detectable PCR for *Mycobacterium tuberculosis, sensitive to rifampicin and isoniazid, with no resistance* (Table 1).

Antituberculous treatment was started with RHZE along with oral corticosteroids, and his antiretroviral therapy was adjusted. A follow-up transthoracic echocardiogram seven days later showed a new severe septated anteroapical and posterior pericardial effusion, with no signs of cardiac tamponade (Figure 3), and therefore pericardiotomy was considered. The patient was referred to a hospital with a higher level of care for cardiovascular surgery, and the procedure was performed with no complications.

Discussion

Tuberculous pericarditis is a rare but potentially serious form of tuberculosis (1). It is challenging to diagnose due to its varied and often nonspecific signs and symptoms. Confirmation requires a combination of clinical findings, imaging techniques and, indispensably, laboratory tests (4, 5). Many times, the disease manifests acutely or sub-acutely, causing fever, chest pain, dyspnea and constitutional symptoms, and even signs of right-sided heart failure. Due to the wide clinical variety of cardiac or pulmonary conditions with which it may present, laboratory tests are strictly necessary for timely diagnosis (6). However, the clinical suspicion of pulmonary or extrapulmonary tuberculosis should remain high in areas endemic for the disease or in individuals with risk factors like immunosuppression and HIV infection (7).

Imaging techniques play a fundamental role. Echocardiography is generally the initial modality of choice for evaluating the pericardium, as it is highly sensitive for detecting indirect signs like pericardial effusion and thickening; however, these findings are not specific for tuberculosis. Cardiac magnetic resonance (CMR) imaging provides greater tissue resolution and may be useful for evaluating the extent of the disease and complications like pericardial constriction (6).

Laboratory tests are essential for diagnosis. Blood counts can show anemia and leukocytosis, while inflammatory markers like C-reactive protein and ESR are usually elevated. On a macroscopic level, the pericardial fluid tends to be a protein-rich bloody exudate, with a predominance of lymphocytes and monocytes (6). *Mycobacterium tuberculosis* can be identified indirectly in this fluid using Ziehl-Neelsen staining, or directly with molecular tests like Xpert MTB/RIF and microbiological cultures. These meth-

Table 1. *Laboratory parameters and microbiological tests of pericardial fluid (Cases 1, 2).*

Laboratory parameters	Case 1	Case 2
Pericardial fluid cytochemistry	Color: reddish Fibrin: none Appearance: clear, with a blood button pH: 8.5 Glucose: 63.4 (mg/dL) PF proteins: 6.04 (g/dL) LDH: 1297.0 (U/L) Leukocytes: 9,800 (cel/mm^3) Red blood cells: 2,000 (cel/mm^3) Others: 50% fresh 50% crenated	Color: yellow Fibrin: none Appearance: slightly cloudy with a red cell button pH: 7.5 Glucose: 71.5 (mg/dL) PF proteins: 5.00 (g/dL) LDH: 1786.0 (U/L) Leukocytes: 0 (cel/mm^3) Red blood cells: 1,000 (cel/mm^3) Others: 80% fresh 20% crenated
ADA	52.2 U/L	14.1 U/L
Mycobacterium tuberculosis PCR	Undetectable in the sample	Detectable in the sample
Identification of *Mycobacterium tuberculosis resistance*	Not applicable	Rifampicin: sensitive - no mutations found on the rpoB gene Isoniazid: sensitive - no mutations found on the katG/InhA gene
Culture for common microbes	Negative	Negative

ADA: adenosine deaminase. PCR: polymerase chain reaction. PF: pericardial fluid. LDH: lactate dehydrogenase. U/L: units per liter

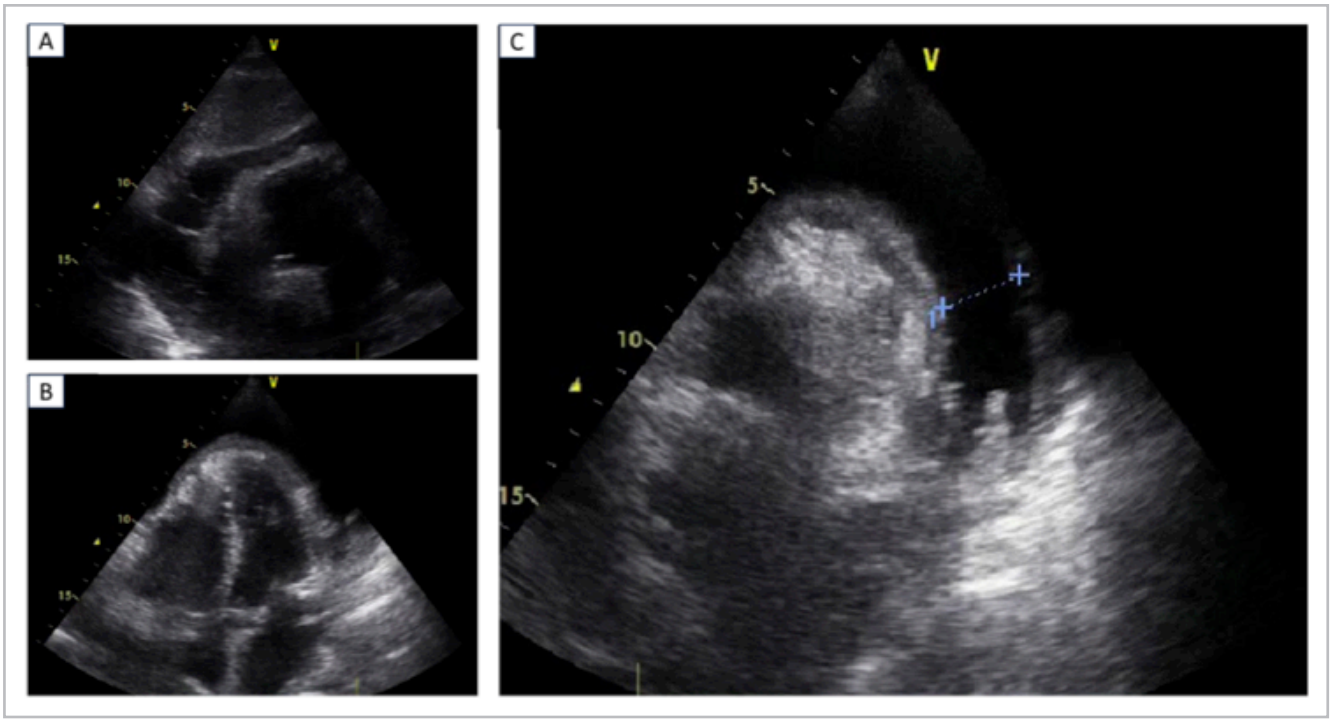

Figure 3. Follow-up transthoracic echocardiogram. Case 2: *A: severe, septated anteroapical and posterior pleural effusion. B: thickened, reactive pericardium with large fibrin deposits. C: severe pericardial effusion measuring 2 cm.*

ods can confirm the diagnosis; however, their sensitivity in pericardial tissue or fluid is low, under 80% in most cases (8–10). The lengthy culture time limits timely diagnosis and treatment (10, 11). In many cases, even in patients with HIV immunosuppression, these methods - especially culture - can be negative (9), which underscores the importance of other diagnostic modalities to confirm the disease promptly.

Other microbiological diagnostic tests include indirect techniques like adenosine deaminase (ADA) measurement, interferon-gamma (IFN-γ) detection in the pericardial fluid and serum interferon-gamma release assay (IGRA). Direct methods especially include pericardial tissue biopsy, which is considered the gold standard (12), although its yield varies depending on the phase of tuberculous pericarditis in which it is performed. Its sensitivity ranges from 10 to 64%, with a 13.3% increase when granulomas are found (8, 9, 11).

The ADA test of pericardial fluid is a useful, rapid and simple test for diagnosing TP. A cut-off value of ≥40 U/L achieves a sensitivity of 87-95.7%, although its specificity is limited, as it can also be elevated by other diseases, like viral or bacterial pericarditis (8, 10, 13). In Colombia, a value > 96 U/L is considered the adjusted cut-off point for suspected mycobacterial pericarditis (14). The ADA level was key in diagnosing the first reported case, and its usefulness has been highlighted in many articles. Páez Ardila et al. reported a young patient with cardiac tamponade secondary to TP and elevated ADA (70 U/L) in the pericardial fluid; while this test is not definitive, it has a critical diagnostic value in the clinical setting (15). Felipe-Reyes et al. documented another case of TP diagnosed and treated promptly in an endemic setting, with elevated ADA in an immunocompetent patient (4). Faria and Freitas highlighted its diagnostic usefulness in an immunocompromised patient with HIV, underscoring that high levels of ADA, even in immunosuppression, must be interpreted together with molecular biology and cultures to avoid false positives (16).

The detection of IFN-γ in pericardial fluid is another promising tool for diagnosing TP (9). High IFN-γ levels indicate a specific immune response against *Mycobacterium tuberculosis*, increasing diagnostic suspicion with a sensitivity and specificity of 95.77% and 96.3%, respectively, for values > 44 pg/L (10). A recent meta-analysis reported a sensitivity of 97% and specificity of 99% for this test (8), and some cases have recorded a sensitivity of 100% with values >200 pg/L. Although it is used less often than molecular tests, IFN-γ measurement in pericardial fluid can be especially useful when other microbiological tests are negative (8). However, its use in endemic areas is limited by its high cost (9).

Conclusion

Adenosine deaminase in pericardial fluid is a useful tool for diagnosing TP. Although its specificity may be limited, especially compared to other tests like IFN-γ or biopsy, it is a less expensive alternative that is quickly and easily accessible. It should be interpreted in conjunction with the clinical picture; new studies are needed in Colombian populations to readjust the cut-off points for greater and more efficient detection.

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