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CASE REPORT

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Pericardial Tuberculosis of Unusual Evolution in Immunocompetent Patient

Tuberculosis pericárdica de evolución inusual en paciente inmunocompetente

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ABSTRACT

Pericardial tuberculosis (TBP) is a rare manifestation of extrapulmonary tuberculosis (TB). It presents insidiously and nonspecifically, making diagnosis difficult and delaying treatment, leading to serious complications such as pericardial effusion with signs of cardiac tamponade or constrictive pericarditis.

The case of an 18-year-old female patient, pregnant, with a history of close contact with a relative with pulmonary TB is described; she consulted the Emergency Service for dyspnea.

Among the studies requested, the echocardiogram showed pericardial effusion with compression of cavities, requiring pericardiocentesis.

Pericardial fluid culture revealed *Mycobacterium tuberculosis* and antituberculous treatment plus corticosteroids were started. It evolved with a recurrence of effusion despite adequate medical treatment and the performance of a pericardial window.

Key words: pericardial tuberculosis; Medical treatment; Corticosteroid; Surgical treatment

RESUMEN

La tuberculosis pericárdica es una manifestación poco frecuente de la tuberculosis extrapulmonar. Se presenta de manera insidiosa e inespecífica, lo que dificulta el diagnóstico, retrasa el tratamiento, y lleva a complicaciones graves, como el derrame pericárdico con signos de taponamiento cardíaco o pericarditis constrictiva.

Se describe el caso de una paciente femenina de 18 años, embarazada, con antecedente de contacto estrecho con familiar con tuberculosis pulmonar, que consultó al servicio de urgencias por disnea.

Entre los estudios solicitados, el ecocardiograma evidenció la presencia de un derrame pericárdico con compresión de cavidades, por lo que requirió pericardiocentesis.

El cultivo del líquido pericárdico informó *Mycobacterium tuberculosis* y se inició tratamiento antituberculosis y corticoides. Evolucionó con recurrencia del derrame a pesar de tratamiento médico adecuado y realización de ventana pericárdica.

Palabras clave: Tuberculosis pericárdica; Tratamiento médico; Corticoide; Tratamiento quirúrgico

INTRODUCTION

Pericardial tuberculosis (PTB) is a rare disease (1-2 %); and its presentation is nonspecific and insidious. Therefore, it should be considered in patients with pericardial effusion in regions where tuberculosis (TB) is endemic.

Diagnosis relies on isolating the bacillus in pericardial fluid or biopsy. These procedures can be challenging or less accessible.

Treatment involves a regimen of antituberculous drugs combined with corticosteroids. However, some patients may require surgical intervention.

CASE REPORT

An 18-year-old female patient with a history of prophylactic treatment with isoniazid at the age of 8 due to contact with a cohabitant; G1 P0 A0 C0.

She presented to the hospital emergency department with symptoms that had begun with the pregnancy, characterized by general discomfort, a weight loss of 5 kg, dyspnea, thoracic pain, cough, and abdominal pain predominantly in the epigastric region. In the last few days, she had a subjective sensation of fever, progression of dyspnea to a score of 3 according to the mMRC scale (Modified Medical Research Council dyspnea scale), and persistent vomiting.

On physical examination, she had tachycardia, muffled heart sounds, hypoventilation, and bilateral pulmonary dullness. On gynecological examination, there was scant pinkish vaginal discharge, and the rest of the structures were consistent with the pregnancy. Laboratory results showed mild anemia without other abnormalities; and the PCR for COVID-19 was not detectable.

Obstetric ultrasound confirmed a 13.5-week pregnancy with cardiac activity and fetal movements present. The abdominal ultrasound revealed free periabdominal fluid, and the pleural ultrasound showed bilateral effusion.

A cardiac Doppler ultrasound was performed, revealing grade II diastolic dysfunction of the left ventricle, paradoxical movement of the septum, severe pericardial effusion with partial collapse of the right cavities, and a separation of 44 mm. No vegetations observed.

The patient was transferred to the Coronary Care Unit for a pericardiocentesis. 1950 mL of fluid with exudate characteristics were drained, with a pH of 7.20, protein content of 4.7, leukocyte count of 1590, and 60 % polymorphonuclear cells. Direct examination and culture for common pathogens, as well as bacilloscopy, were negative, and PCR for enterovirus was not detectable.

The cytological study reported an acute inflammatory process with abundant neutrophils. Treatment was initiated with non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and ampicillin + sulbactam.

Thoracentesis was performed. The pleural fluid showed characteristics of transudate. Direct examination and culture for common germs were negative, as well as the direct test for acid-alcoholic resistant bacilli (AARB) and cytology. Results of the culture for mycobacteria are pending. Serologies for HIV (human immunodeficiency virus), Chagas, VDRL (venereal research disease laboratory), HCV (hepatitis C virus), and HBV (hepatitis B virus) were negative, and the immunological laboratory results were negative. Thyroid hormones were within normal limits.

14 days after admission, the absence of fetal cardiac activity was noted, and obstetric ultrasound confirmed the absence of cardiac activity and fetal movements. Fetal evacuation was performed without complications. A sample was sent for pathological anatomy, which reported an acute ischemic phenomenon with extensive areas of infarction, without morphological alterations suggestive of placental tuberculosis.

Twenty days after admission, the result of *Mycobacterium tuberculosis* isolation in the pericardial fluid sample was received. Treatment with isoniazid, rifampicin, pyrazinamide, ethambutol, and corticosteroids was initiated.

72 hours after the treatment began, a severe pericardial effusion compromising the patient's hemodynamic status was confirmed. A pericardial window was performed with drainage of 800 mL; and a biopsy sample was taken.

The pericardial biopsy reported a mixed inflammatory process, predominantly lymphoplasmacytic with histiocytes and amorphous fibrinoid material, and negative bacilloscopy.

Due to a favorable clinical evolution, five days after the pericardial window procedure, and with echocardiogram Doppler control showing no pericardial effusion, the patient was discharged from the hospital with antituberculous treatment and corticosteroids.

During outpatient follow-up, corticosteroid therapy was gradually discontinued, and the

patient transitioned to the second phase of antituberculous treatment with good tolerance and adherence.

Nearly three months after starting with the antituberculous treatment, the patient presented to the emergency department with pain in the left upper limb and epigastrium. On physical examination, the patient had muffled heart sounds, signs of right-sided heart failure, edema in the right upper limb, and a palpable left cervical cord. An echocardiogram revealed severe pericardial effusion with a separation of 20 mm and partial collapse of the right ventricle.

A cervical ultrasound showed signs of peripheral venous thrombosis. Anticoagulation therapy was initiated.

Several diagnostic possibilities were considered:

- Polyserositis secondary to autoimmune disease (due to disease progression despite antituberculous treatment and corticosteroid suspension), while the patient was still on antituberculous treatment and coinciding with the discontinuation of corticosteroids.
- Drug-resistant PTB.
- Obstruction of the pericardial window.

The immunological laboratory tests were requested again, and the results were negative. A Genotype MDR plus test was also requested for the culture sample of the pericardial fluid from the previous hospitalization to assess sensitivity.

The patient evolved with signs of cardiac tamponade, and had to be admitted to a closed unit for pericardiocentesis with total drainage of 740 mL of purulent fluid. Samples of that fluid were obtained for cultures of common germs, mycobacteria, and GeneXpert.

The follow-up Doppler echocardiogram revealed slightly dilated right cavities, mild pericardial effusion with fibrin tracts, and thickening of the parietal pericardium with echocardiographic signs of constrictive pericarditis.

Subsequently, the Genotype result confirmed sensitivity to rifampicin and isoniazid. The GeneXpert test on the new pericardial fluid reported detectable levels, sensitive to rifampicin.

These findings ruled out an autoimmune etiology and resistance to antituberculous drugs, so it was interpreted as obstruction of the pericardial window. Video-assisted thoracoscopy with pleuropericardial window and biopsy were performed.

The follow-up echocardiogram documented grade II diastolic dysfunction of the left ventricle, pericardial knock, increased pericardial thickness (5 mm), and minimal pericardial effusion.

The biopsy results reported fibrin, abundant AARB, and a negative Koch's culture.

Due to good clinical and hemodynamic progress, one and a half months after admission, the patient was discharged from the hospital with a plan to continue the second phase of treatment with isoniazid and rifampicin.

DISCUSSION

Tuberculous pericarditis is a rare but serious form of tuberculosis. Its definitive diagnosis is difficult and often delayed or even unattainable, leading to complications such as constrictive pericarditis with high mortality rates.[1]

The incidence accounts for 1 to 2% of all patients with *M. tuberculosis*[2] and varies depending on the endemicity of tuberculosis (TB) in the region.[4] HIV infection is the primary risk factor.[5]

Pericardial involvement develops through retrograde lymphatic spread of the bacillus from neighboring lymph nodes or hematogenous dissemination from a primary tuberculous infection.[3] Very rarely, it is due to the rupture and contiguous spread of a lesion in the lung or hematogenous dissemination from a distant infection.[3] It often corresponds to the reactivation of a previous infection without an apparent primary site.[1]

Four pathological stages are recognized: (1) Initial fibrinous exudate with abundant polymorphonuclear cells and bacilli, and early formation of macrophage granulomas and T cells; (2) Serosanguinous effusion with a predominantly lymphomonocytic exudate and foam cells; (3) Absorption of the effusion, caseating granulomas, pericardial thickening with fibrosis; and (4) Constrictive scarring: the parietal and visceral pericardium contracts into the cardiac cavities and may calcify, enclosing the heart, preventing diastolic filling, and causing constrictive pericarditis.[3]

Recent studies have demonstrated high bacillary loads of *Mycobacterium tuberculosis* in the pericardium, contradicting the commonly accepted concept that PTB is predominantly a paucibacillary localization.[4]

It can present as pericardial effusion, constrictive pericarditis, and effusive-constrictive pericar-

ditis.[3] The most common manifestation is pericardial effusion (79.5 %), regardless of the mechanism. These presentations manifest as heart failure and can be complicated by tamponade and shock.[4]

Among the diagnostic imaging tools, echocardiography is a precise and non-invasive method to diagnose the presence of pericardial effusion,[3] as well as computed tomography or magnetic resonance.[3] Chest X-ray shows enlarged cardiac silhouette in over 90 % of cases, characteristics of active pulmonary TB in 30% of cases, and pleural effusion in 40 % to 60 % of cases.

ECG abnormalities are present in nearly all cases of tuberculous pericardial effusion, expressed as changes in the ST-T wave.[3]

Pericardiocentesis is recommended in all patients where TB is suspected as the etiology, with absolute indication in cardiac tamponade.[3]

Pericardial fluid is serosanguinous in 80 % of cases, typically exudative with a high protein and leukocyte content, predominantly lymphomonocytic.[3]

Alongside searching for the bacillus in the pericardial fluid, the presence of bacilli in sputum and lymph nodes should also be investigated.[3] The smear of pericardial fluid has a variable yield ranging from 0 % to 42 %.[3] Culture remains the most commonly used diagnostic test for PTB with a sensitivity ranging between 53 % and 75 %. However, it requires at least 3 weeks to obtain results.[4]

Biopsy has a sensitivity between 10 % and 64 %. Therefore, a normal pericardial biopsy sample does not exclude PTB.[3]

Although the culture of the fluid confirms TB more frequently than pericardial histology[3] when there are diagnostic doubts or when pericardial fluid is difficult to obtain, a pericardial biopsy may be justified.[4]

The GeneXpert MTB/RIF (Mycobacterium tuberculosis/rifampicin) has high diagnostic validity for detecting MTB in pericardial fluid, with a sensitivity of 72.2 % and a specificity of 100 %. The use of GeneXpert MTB/RIF provides additional information on drug resistance within a 2-hour timeframe and is highly recommended.[12]

Pericardial adenosine deaminase (ADA) activity has a specificity of 72 % and a sensitivity of 89 % for diagnosing PTB.[6] Lower levels were observed in HIV-positive patients.[3]

In areas with a high prevalence of TB, pericarditis is often considered of tuberculous origin unless there is an obvious alternative etiology.[3] Initiating treatment before bacteriological diagnosis[3] is recommended despite observational evidence indicating that empirical therapy is associated with increased morbidity and mortality.[4] However, in non-endemic areas, there is no justification for empirically starting antituberculous treatment.[3]

Antituberculous chemotherapy, consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol for at least two months, followed by isoniazid and rifampicin (a total of six months of therapy) is highly effective in treating patients with extrapulmonary TB, significantly increasing survival.[3] Treatment for 9 months or more does not yield better results and entails higher costs with poor compliance.[3]

The use of glucocorticoids for six weeks is associated with a reduction in the incidence of constrictive pericarditis and hospitalization. The beneficial effects are similar in both seropositive and seronegative patients.[8]

Constrictive pericarditis is one of the most serious sequelae of tuberculous pericarditis[3] and occurs in 30 % to 60 % of patients, despite the timely administration of medical treatment.[3] Although it has been considered a surgical disease, a subgroup of patients experiences the reversibility of pericardial inflammation with medical treatment, a condition referred to as “transient constriction”, defined as the absence of pericardial calcification. Computed tomography (CT) is the best modality for detecting pericardial calcification compared to plain X-rays or echocardiography.[11]

Pericardiectomy is recommended if cardiac manifestations don’t improve or deteriorate after 4 to 8 weeks of antituberculous treatment.[3] Pericardial calcification is an indication for surgery, which should be performed earlier under the cover of antituberculous medications.[3] The timing of pericardiectomy is controversial. Some authors recommend it once chemotherapy has been initiated, while others prefer to leave it for patients who do not respond to initial medical treatment.[3]

Limited pericardial resections (pericardial windows) should be avoided in the treatment of tuberculous pericarditis due to a recurrence rate of 33% and the subsequent need for a challenging second intervention.[2]

Effusive-constrictive pericarditis is a common presentation in Southern Africa which causes an

increase in pericardial pressure due to effusion in the presence of visceral constriction.[3]

Echocardiography can show pericardial effusion between thickened pericardial membranes, with fibrinous pericardial bands seemingly causing the loculation of the effusion.[3] The treatment of effusive-constrictive pericarditis is problematic, as pericardiocentesis does not relieve the altered filling of the heart, and surgical removal of the fibrinous exudate covering the visceral pericardium is not possible.[3]

CONCLUSION

Pericardial tuberculosis is a rare form of extrapulmonary tuberculosis. Pericardial effusion is typically the initial manifestation with signs of heart failure. Although imaging tests can help with the diagnosis, the diagnosis relies on demonstrating the bacillus in pericardial fluid or biopsy. Antituberculous treatment improves survival. Corticosteroids and pericardiocentesis prevent constriction, although some cases may still progress to constrictive pericarditis and require surgical intervention.

Pericardiectomy is recommended as a definitive treatment for constriction, as opposed to pericardial window, due to the recurrence rate and obstruction associated with the latter.

Conflict of interest

Authors have no conflicts of interest to declare.

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