A “RARE” CAUSE OF PERICARDIAL EFFUSION – CASE REPORT

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A “RARE” CAUSE OF PERICARDIAL EFFUSION–CASE REPORT (Abstract): Although tuberculosis classically affects the lungs, lymphatic and hematogenous dissemination, as well as direct invasion of the pericardium from the adjacent pleura make Mycobacterium tuberculosis the most frequent cause of acute pericardial effusion in developing countries. We present the case of a 68-year-old patient presenting with acute cardiac failure due to large pericardial effusion, a week after undergoing drainage of a facial subcutaneous abscess. Pericardiocentesis followed by video-assisted thoracoscopic pericardial window were performed. Blood cultures were repeatedly negative, but the biochemical analysis of the pericardial fluid showed low glucose concentration and high protein levels, elevated adenosine deaminase and lactate dehydrogenase levels. Although bacterioscopy and pericardial fluid cultures were negative, we made a presumptive diagnosis of tuberculous fibrinous pericarditis and initiated appropriate therapy with rifampin, isoniazid, pyrazinamide, and ethambutol, with favorable clinical outcome. Our diagnosis was confirmed 22 days later, when the Mycobacteria Growth Indicator Tube cultures were positive for M. tuberculosis. Although tuberculosis is a rare cause of pericarditis in the Western world, in a country endemic for tuberculosis (such as Romania), the tuberculous etiology of fibrinous pericarditis should not be overlooked. Keywords: EXTRAPULMONARY TUBERCULOSIS, FIBRINOUS PERICARDITIS, PERICARDIAL TAMPOANDE, VIDEO-ASSISTED THORACOSCOPIC PERICARDIAL WINDOW, MYCOBACTERIA GROWTH INDICATOR TUBE.

Classic tuberculosis (TB) affects the lungs, but forms of extrapulmonary tuberculosis located in the genitourinary tract (1, 2), central nervous system (3), gastrointestinal tract (4), and skeletal system (5) have also been described. Tuberculous pericarditis is a severe form of extrapulmonary TB, being associated with a high 6-month mortality rate (17-40%) (6, 7). The incidence of TB pericarditis ranged from less than 4% in Western countries to 50-90% in developing regions, where tuberculosis is endemic (7, 8, 9). Although Romania remains endemic for tuberculosis, the number of extrapulmonary TB cases has gradually decreased during the past years, but 40-50 cases of TB pericarditis are still annually reported (10).

The most frequent clinical presentation of TB pericarditis is congestive heart failure (7). One of the most feared complications of TB pericarditis is constriction, which usually occurs within 6 months in 50% of cases in the absence of targeted
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anti-TB therapy (6, 7). This rate has been reduced to 17-40% with the help of aggressive anti-TB treatment and corticosteroid therapy (6). A noteworthy limitation of TB chemotherapy is the poor penetration of antibiotics into the pericardium (11).

CASE REPORT

A 68-year-old male patient was admitted to an otorhinolaryngology clinic for drainage of a frontal abscess of unknown etiology. A week after discharge, the patient developed fever (38°C) accompanied by chills and was referred to the infectious diseases department. Despite aggressive antibiotic therapy, he developed dyspnea on minimal exertion, palpitations, chest pain and exercise-related liver pain and was transferred to the local cardiology clinic.

The clinical exam revealed tachypnea, tachyarrhythmia (113 bpm), normal blood pressure, and right-sided heart failure. Routine laboratory evaluation showed inflammation (erythrocyte sedimentation rate 100 mm/hr., fibrinogen 948 mg/dL, elevated C reactive protein), thrombocytosis (663,000/mm³) and cardiac enzymes within normal range. Electrocardiogram revealed paroxysmal atrial fibrillation, managed with amiodarone and carvedilol. A throat swab culture revealed Candida albicans infection for which he received appropriate local treatment.

Echocardiography revealed circumferential pericardial effusion (34 mm) with fibrinous material and pericardial thickening (0.99 cm). Chest X-ray (radiography) showed pulmonary congestion and enlarged cardiac silhouette (fig. 1). The performed chest computed tomography (CT) (fig. 2, 3) detected multiple infracentimetric aortopulmonary lymph nodes with peripheral enhancement, but no active pulmonary or bone lesions. Although initial and repeated blood cultures were negative, the patient continued to present fever although he was on antibiotic therapy and nonsteroidal anti-inflammatory drugs.

Fig. 1. Chest X-ray - enlarged cardiac silhouette, pulmonary congestion

Fig. 2. Chest CT – pericardial effusion (maximum thickness 33 mm)

Fig. 3. Contrast enhanced chest CT – enlarged lymph nodes with peripheral enhancement
The patient began to show signs of incipient cardiac tamponade so he was transferred to the thoracic surgery department where pericardiocentesis and drainage of 100 mL serous fluid were performed. Pericardial fluid bacterioscopy and cultures were negative. Cytology was negative for tumor cells. Biochemical analysis revealed microscopic lymphocytic inflammatory reaction with high protein levels (46.8 g/L), high adenosine deaminase (ADA) - 71 U/L, high lactate dehydrogenase (LDH) - 849.2 U/L and low glucose (67.4 mg/dL) levels.

As the patient showed no clinical improvement after 2 days of conservative therapy he underwent a video-assisted thoracoscopic pericardial window performed on the left side. Pericardial biopsy confirmed our previous diagnosis of fibrinous pericarditis. A control chest X-ray was performed after the procedure (fig. 4).

We decided to initiate anti-TB chemotherapy with rifampin, isoniazid, pyrazinamide and ethambutol along with oral corticosteroids (prednisone). The diagnosis was confirmed after 22 days, when the Mycobacteria Growth Indicator Tube (MGIT) cultures detected *M. tuberculosis* susceptible to rifampin, isoniazid and ethambutol. The outcome was favorable with no evidence of constriction during the 4-month follow-up.

**DISCUSSION**

Our patient was admitted for rapidly progressive heart failure due to massive pericardial effusion. The following investigations were performed: chest X-ray (class I), inflammation marker panel (class I) and CT (class Ia). Although he did not meet the criteria for acute pericarditis (no pericarditic chest pain and friction rub, no ST elevation or PR depression), the current guidelines recommend managing pericardial effusions with positive inflammatory markers as pericarditis (7).

Our patient presented rapid clinical and biological decline after the drainage of a subcutaneous frontal abscess, so systemic staphylococcal or streptococcal infection with pericardial involvement was a possible cause of his current condition. Patient medical history was negative for TB and the CT scan did not detect any active pulmonary or bone lesions. However, he presented significant pericardial thickening, massive effusion with frond-like projections, and typical lymph node enlargement (hypodense center), all suggestive of TB etiology (7).

Since a bacterial etiology of the pericardial disease was suspected and our patient associated early signs of cardiac tamponade, pericardiocentesis (class I) (7) and drainage of 100 mL of serous fluid were performed.

Tuberculous pericardial effusions are usually cloudy and serosanguineous (12).
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The detection of acid-fast bacilli during microscopic assessment is diagnostic for TB but reported in only 40-60% of cases (12). Although in our patient the fluid analysis was negative for acid-fast bacilli, it documented lymphocytic inflammatory reaction with very high protein levels, both recognized features of tuberculous pericardial effusions (12). Increased pericardial interferon-gamma and ADA levels are associated with TB pericarditis (7,12). In our case, pericardial ADA levels were >40 U/L (a cut off value with 93% sensitivity and 97% specificity in diagnosing TB pericarditis) (12).

Per current guidelines, subjects with relapsing cardiac tamponade, repeated accumulation of pericardial effusion and those who do not improve with drug therapy should undergo surgical drainage. Pericardial biopsy is a class IIb indication for suspected TB pericarditis (7). As our patient’s clinical condition did not improve despite optimal drug treatment, we decided to perform a video-assisted thoracoscopic pericardial window.

The definite diagnosis of TB pericarditis requires the detection of M. tuberculosis in pericardial fluid or tissue through polymerase chain reaction (PCR) or cultures (6,7). Microbiological diagnosis can be augmented through cultures from extracardiac sites (pleural fluid, lymph nodes and sputum) (13). A possible diagnosis is based on successful response to TB chemotherapy or high ADA, unstimulated interferon-gamma or lysozyme levels in the pericardial fluid (7). Only 17% of cases meet the criteria for definite TB pericarditis (6). A study reported interferon-gamma measurement in the pericardial fluid as the best diagnostic tool, especially combined with ADA and cytology of pericardial effusion (13). Our patient’s CT scan was negative for active pulmonary lesions and superficial adenopathies, suitable for biopsy. The tuberculin skin test is not recommended in adults and we did not perform it in our patient. The guidelines recommend the use of interferon-gamma release assays in patients with probable TB, but the results are less specific in countries where tuberculosis is endemic (7).

The initiation of empiric anti-TB treatment in endemic regions is allowed as soon as other causes of pericardial effusion have been excluded (trauma, autoimmunity, cancer, uremia, purulent pericarditis), but it is not justified in countries where TB is not endemic and there is no clear evidence supporting the tuberculous etiology. Prevention of pericardial constriction requires 6 months of standard combined anti-TB treatment (class I). Intrapericardial urokinase reduces the risk of constriction. High-dose prednisolone can reduce the risk of developing constriction and has a class IIb recommendation in immunodeficiency virus-negative human subjects (7).

Our diagnosis of tuberculosis was based on clinical suspicion (endemic area for TB), echocardiographic and CT findings (pericardial thickening, fibrinous material) and high pericardial ADA and protein levels. The diagnosis was later confirmed by a positive response to empirical anti-TB treatment and positive MGIT cultures. Our patient should have regular follow-up as part of the screening for constrictive pericarditis, although he showed no evidence of constriction after 4 months of anti-TB treatment.

CONCLUSIONS
This case report proves that in a country endemic for tuberculosis, the differential
diagnosis of pericarditis should include *Mycobacterium tuberculosis* as one of the most frequent causes of pericardial effusion. We consider video-assisted thoracoscopic pericardial window along with pericardial and pleural biopsies to be valuable diagnostic and therapeutic tools for tuberculous pericarditis. Because of the high mortality rates associated with this condition, we chose to initiate aggressive anti-TB chemotherapy even in the absence of a definite diagnosis.

REFERENCES