

## **Tuberculous Pericarditis: A case report in South-East Nigeria**

### **Abstract**

Tuberculosis is a chronic infection and a common cause of chronic pericardial effusion. Approximately 1-2% of patients with pulmonary tuberculosis (PTB) develop tuberculous pericarditis (TBP) and it is less common in the developed world than in developing countries where active tuberculosis is endemic. In these countries with high endemicity, TBP is the most common form of pericarditis and is often associated with HIV. The clinical picture is usually that of a chronic systemic illness in a patient with pericardial effusion. The index case is that of a 24 year old male, who had presented to our medical outpatient clinic with a history of cough and chest pain of 9 and 2 days duration respectively. Diagnosis was made following echocardiography, electrocardiography (ECG), Chest X-ray (CXR) and culture findings which showed features in keeping with tuberculous pericarditis. His clinical condition improved significantly following pericardiocentesis and TB treatment was subsequently instituted. He was discharged for outpatient follow-up 5 days after pericardiocentesis. TBP can be difficult to diagnose and often goes undetected especially in resource poor countries. Accurate and early diagnosis is important as it is a dangerous disease if left untreated.

**Keywords:** Tuberculous Pericarditis.

### **Introduction**

#### **Background of the study**

Pericarditis is a relatively common disorder with multiple causes and presents in various clinical settings. Tuberculous pericarditis also known as pericardial tuberculosis is an uncommon complication of TB. In developing countries where TB remains prevalent, more than 50% of cases of pericarditis are related to TB, as against less than 5% of cases in developed countries where viral causes are responsible for 80-90% of cases. In these countries with low prevalence of TB, TBP has often been a disease of the elderly, where as it may affect any age group in developing countries with high endemicity. The majority of TBP cases have been reported to be in South African, Indonesia, Nigeria, Pakistan, India and China. This correlates with countries with a high burden of TB. It is worthy of note that TB accounts for up to 4% of acute pericarditis and 77% of cardiac tamponade cases. According to Hageman et al, TBP usually

affects individuals of the black race more, while a research by Rooney et al showed that men are more commonly affected than females.

### **Case Presentation**

We present the case of a 24-year-old male tertiary school graduate who was diagnosed with TBP. He presented to the medical outpatient clinic of Enugu State University of Science and Technology Teaching Hospital with a 9-day history of cough and 2 days history of chest pain. The cough was of insidious onset, productive of whitish sputum, which was not blood-stained, copious, foul-smelling or frothy. Cough was not position-dependent or worse at any time of the day and there was no aggravating or relieving factor. There was associated intermittent low-grade fever, slight weight loss evidenced by looseness of previously fitting apparels, dyspnoea and weakness. There was no history of night sweats. Chest pain was said to be central, also of insidious onset, sharp, non-radiating and worse on movement and deep stimulation. There was no relieving factor; there was no history of associated orthopnoea, paroxysmal nocturnal dyspnoea or leg swelling. He was not known to be asthmatic, diabetic or hypertensive. There was no contact with a chronically coughing individual. He was not known to use intravenous (IV) drugs and has never been placed in a correctional facility. The patient was not known to be HIV Positive and had no history of hospital admission in the past. He takes recreational drugs (cannabis) occasionally and about 16 units of alcohol weekly.

On physical examination, he was dyspnoeic, mildly pale. Had a pulse rate of 105bpm, small volume with occasional ectopics. Jugular venous pressure was raised and apex beat was diffuse, with a distant first and second heart sounds. Other aspects of the physical examination had essentially normal findings.

He was subsequently admitted into the medical ward of the hospital and started on Tabs Digoxin 0.25mg od, Furosemide 40mg od, Spinnolactone 25mg od and hematinuscs following an initial diagnosis of Dilated Cardiomyopathy in failure. He was requested to do CXR, ECG and echocardiography, amongst other routine investigations. On the second day of admission, patient's clinical slate remained the same.

The reports on the requested investigations were obtained on the third day of admission. HIV came out negative. CXR showed a globular heart and blunting of the left costophrenic angle. No

focal lung lesion was seen and the pulmonary vasculature was not engorged. ECG showed sinus tachycardia and flattened Twaves in lead 1, avL, V5 and V6. Echocardiography showed functional pulmonary regurgitation (Vmax =135cm/s PG-7mmHg), right ventricular diastolic collapse suggestive of impending tamponade and thickened pericardium (parietal -8mm. visceral -11mm) with about 170mls of pericardial effusion. With these investigation reports, the diagnosis was reviewed to pericardial effusion (with impending cardiac tamponade) ?cause and Digoxin was discontinued. Pericardiocentesis and pericardial biopsy were considered and the Cardiothoracic Unit was invited. He had pericardiocentesis done under ultrasound guidance, with 1700mls of haemorrhagic effluent drained via the subxiphoid pericardial window. Samples of the effluent and biopsied pericardial tissue were sent for Gene X pert and culture, and these detected MTb and acid fast bacilli respectively. He was subsequently reviewed by the infectious disease unit and commenced on anti-tuberculous medications. He was discharged to out-patient care on the 9th day of admission following further observation. He was seen a week later at the out-patient clinic and remained clinically stable, he was then referred to see clinical psychologists on account of his use of recreational drugs (cannabis) occasionally and alcohol use of about 16 units.

## **Discussion**

For a patient presenting with tuberculous pericarditis, two important issues are treating for the immediate relief of symptoms present along requesting investigations relevant to the successful management of the case in order to save the life of the patient. The second is to determine other comorbidities.

TBP is the most common and significant manifestation of TB heart disease and is associated with significant mortality and morbidity. TBP is found in about 1% of all autopsied cases of TB and in 1-8% of cases of pulmonary TB. In developing countries with high prevalence of TB, TBP is the most common cause of pericarditis and is often associated with HIV infection.

In a large single center study from the Western Cape province in South African 69.5% (162 out of 233) of patients undergoing pericardiocentesis were found to have TB and over 50% of the

participants were infected with HIV. Mortality rate of TBP is as high as 40% have been described among ART naïve persons living with HIV/AIDS and it remains a significant treatable cause of heart failure in the same regions of the world.

TB spreads to the pericardium via three main mechanisms.

- a) Lymphatic spread; spread here is retrograde from mediastinal, peritracheal and peribronchial lymph nodes. This form of spread is seen mostly in immunocompetent hosts.
- b) Haematogenous spread; this usually occurs during primary TB and is the mechanism of spread in immunocompromised hosts.
- c) Direct contiguous spread from adjacent structures like the lungs, pleura and spine. This mechanism is not common.

TBP is usually restricted to the pericardial space in the immunocompetent hosts. Also, TBP in this host is frequently a paucibacillary condition in which the morbidity is related to the ferocity of the immune response it evokes and not to the virulence of the pathogen.

However, in patients with HIV, because TBP occurs more frequently as part of a disseminated process associated with TB bacteremia, the infection itself may have a greater impact on the morbidity and mortality.

In the pericardium, viable mycobacterial protein antigens presented by macrophages to CD4+ lymphocyte trigger activation of lymphocyte, macrophages and complement fixing antibodies, leading to pericardial inflammation, granuloma formation, cytolysis and production of a fibrinous exudate rich in inflammatory cytokines. HIV interferes with these processes via its alteration of the phenotype and function of CD4+ memory T cells within the pericardium, leading to a relative CD4+ T cell depletion and diminished granuloma formation systematically and within the pericardium.

TBP presents clinically in 3 forms; pericardial effusion (80% of cases), constrictive pericarditis (5% of cases) and effusive constrictive pericarditis (15% of cases). The index patient presented with pericardial effusion. TBP has 4 pathological stages.

- a) Dry stage – There is fibrinous exudation, initial polymorphonuclear leukocytosis, abundant mycobacteria and early granuloma formation with loose organization of macrophages and T- cells.
- b) Effusive stage- Serosanguinous effusion with a predominantly lymphocytic exudate with monocytes and foam cells are seen here.
- c) Adsorptive stage– In this stage, there is absorption of effusion and organization of the granulomatous caseation. There is also pericardial thickening due to fibrin deposition and collagen formation.
- d) Constrictive stage – This is a stage of constrictive scarring. The fibrosis forms between the visceral and parietal pericardium.

In the management of TBP, it is quite pertinent to decipher the source of infection while taking the history. Hence it is worthy to note the patient's occupation, as laboratory and health workers especially in this part of the world are more likely to be exposed to MTb. The patient's HIV status should also be noted and whether or not he is on anti-retroviral therapy (ART).

Other risk factors, e.g. presence of comorbidities like diabetes mellitus (DM), use of steroids, IV drug abuse, etc, should be explored. The predominant symptoms of TBP are cough, dyspnoea /shortness of breath and chest pain. These were all seen in the index patient. Other common symptoms include: Fever, weight loss, orthopnea, ankle/leg swelling and weakness.

Physical examination may show tachycardia, pulsus paradoxus, distended neck veins, distant heart sounds, pleural effusion evidenced by stony dull percussion note and hepatomegaly. Some of these signs were elicited in our patient.

These signs and symptoms may not be typical in HIV infected persons. Sometimes, they may even be asymptomatic. Thus a high index of suspicion should be placed on HIV patients with large pericardial effusion with or without the above features.

According to Miglioranza et al, following the ESC 2015 guidelines, the proposed diagnostic algorithm of TBP is as follows.

1. Confirmation of pericardial effusion.

Echocardiography is the best diagnostic method for pericardial disease as it allows for visualization of fluid in the pericardium, determine its volume and consequence of its accumulation eg collapse of the free (Right) ventricular wall in diastole. It can also be used to evaluate pericardial thickness.

CXR allows for visualization of PTB, pleural effusion and occasionally pleural calcifications, which are seen in the late stage of the disease and raises the suspicion of constrictive pericarditis. Cardiac CT can also be used to assess the volume of pericardial fluid, as well as the thickness and presence of possible calcifications.

Other imaging modalities include MRI and fluorideoxyglucose Positron Emission Tomography.

2. Establishing the choice of further diagnostic approach. This depends on the findings of the imaging.

In patients with signs of impending or overt cardiac tamponade, urgent decompression of the heart is needed.

In patients with recurrent cardiac tamponade after pericardiocentesis or unsuccessful pharmacotherapy, a pericardial drain can be placed surgically under general anaesthesia. Surgical treatment by the way of substernal pericardiotomy combined with pericardioscopy should be considered if there is no safe option to perform a percutaneous pericardial puncture.

For patients in whom pericardiocentesis is not feasible, the tygerberg score can be used. It is a clinical decision that can help in deciding whether or not pericarditis is due to TB. It takes into cognizance the following, Fever 1 point, Night sweats 1 point, Weight loss 2 points, Globin level  $>40\text{g/l}$  3 points. Peripheral leukocyte counts  $<10 \times 10^9/\text{L}$  3 points, a score of  $> 6$  points in the above scale is highly predictive of TBP in endemic regions. It has an 80% sensitivity and 85% specificity.

3. Confirmation of tuberculous aetiology. This can be direct via cultures direct staining and Gene Xpert of the pericardial fluid and biopsied tissue. The sensitivity of pericardial biopsy is low (10-64%) and a negative biopsy does not exclude TBP. The sensitivity of pericardial fluid culture ranges from 53-75%.

Indirect methods that can be used in establishing aetiology include; Adenosine deaminase, as levels may be elevated as it is a useful biomarker in the diagnosis of TB, interferon gamma (>50pg IL) and tissue lysozyme (> 6.5mg IdL).

Tuberculin skin test can be done to assess patient for latent TB.

Other investigations that can be carried out include, ECG. This may show sinus tachycardia, low voltage complexes, nonspecific ST Segment and Twave changes (2) full blood count (3) renal function test (4) viral serology.

According to the ESC 2015 guideline, the principle of diagnosing TBP is as follows.

(1) Confident diagnosis

- a. Positive direct staining of pericardial fluid or pericardial biopsy specimens for Mycobacteria and positive genetic test of MTb of pericardial fluid.
- b. Positive result of pericardial fluid or pericardial biopsy culture of MTb.
- c. Caseating granulomas in pericardial biopsy and positive genetic test for MTb.

(2) Probable diagnosis.

- a) Active tuberculosis of another organ, confirmed with positive culture and lymphocytic pericardial effusion with increased concentration of unstimulated interferon gamma, ADA activity or lysozyme activity.  
AND/OR
- b) Positive clinical response to anti-tuberculous treatment in endemic region.

### **Treatment**

Parts of the treatment have been described above. However anti-tuberculous medications should be commenced in every case of TBP, with adjustment of doses based on the presence or absence of comorbidities. It is recommended to start the patient on Rifampicin, Isoniazid, Pyrazinamide and Ethambutol administered for at least 2 months with a continuation of isoniazid and Rifampicin for the next 4 months. ART therapy is also required in TBP patients who have HIV co-infection. Steroid administration is an adjuvant therapy which lowers the risk of constrictive pericarditis and the necessity for hospitalization but does not reduce

mortality among patients with tuberculous pericarditis. However, administration of steroids in HIV positive patients increases the risk of developing secondary malignancies; therefore, adjuvant steroid therapy should be implemented with caution in this group of patients.

Fibrinolytic agents could be injected into the pericardium as a way of reducing the incidence of constrictive pericarditis in patients with large tuberculous pericardial effusion. However, there is insufficient scientific evidence to back this modality. It is still under investigation. Surgical pericardiectomy can also be performed in constrictive pericarditis, but it is associated with perioperative mortality depending on the centre, reaching 2.3-12%.

TBP can be complicated by cardiac tamponade, as in the index patient, pericardial constriction, hepatic congestion, cardiac arrest and death. Prognosis has been poor in TB endemic regions in sub-Saharan Africa, with few successfully managed cases, like in our patient. Mortality of 17-40% has been reported. This may be as a result of the disease condition being often overlooked and late presentation of patients. Unavailability of some investigative technique may also play a role. Prognosis is improved by early recognition of the condition, early intervention and availability of a tertiary center where pericardiectomy can be done if needed.

Intervention by clinical psychologists is important in the management of a case of tuberculous pericarditis who takes recreational drugs (cannabis) occasionally and about 16 units of alcohol weekly. The clinical psychologist was invited to identify all the risk factors for substance use, nature of cravings triggers in the patient. The clinical psychologist initiated psychotherapies to enhance preventions to re-exposure to those risk factors, as persistence of such risk factors will continue to predispose the patient to substance use, abuse and dependence. In the management of this patient, the clinical psychologists employ psycho-education, motivation interview and cognitive behaviour therapy to enhance recovery and relapses prevention.

## **Conclusion**

TBP is a rare form of extra pulmonary tuberculosis seen mostly in TB endemic regions. It is a disease with high morbidity and mortality, Cough, dyspnea and chest pain are its cardinal features, in addition to other symptoms of tuberculosis. Absence or atypical presentation may be seen in HIV infected person. Hence a high index of suspicion is necessary when evaluating HIV infected persons with large pericardial effusion, especially in sub-Saharan Africa and other TB/HIV endemic regions of the world. The most important treatment are anti-tuberculous medications and corticosteroid. The goal of preventing pericardial fibrosis and constrictive pericarditis is of importance. The European society of Cardiology (2015) has provided guidelines in the management of TBP, which have been of great assistance to clinicians in the treatment of this relatively rare disease.

### **Compliance with Ethical Standards**

#### **Statement of Informed Consent**

The participation was on voluntary basis and informed consent was obtained from the individual who participated in this case report.

### **References**

- Isiguzo G, Du Bruyn, Howlett P., Ntsekhe M. (2020). Diagnosis and management of Tuberculous pericarditis: What is New? *Curricardiol Rep.* 22 (2), 1254-1.
- Imazio M Spodick DH, Brucato A et al (2010). Diagnostic issues in the clinical management of pericarditis. *Int. J. Clini. Pract.* 64, 1384-1392.
- Imazio M, Brucato A, Mayosi BM, et al (2010), Medical therapy of pericardial diseases. Part I: idiopathic and infectious pericarditis *J. Cardiorasc. Med.* 11, 712-722.
- Oscar DL, Marlon MB, Juan CP et al, (2022). Tuberculous pericarditis- a silent and challenging disease: A case report. *World Journal of clinical cases*, 10(6), 1869-1875
- Mayosi BM, et al (2023), Rational and design of the investigation and the management of pericarditis (IMP) trial; a 2x2 factorial randomized double blind multianter trial of adjunctive prednisolone and mycobacterium tuberculosis with immunotherapy in tuberculosis pericarditis. *AM Heart J.* 165 (2); 109-15.

- Kishendree N, Mpiko N. (2020) Tuberculous pericardial disease; a focused update on diagnosis, therapy and prevention of complication. *Cardiovascular diagnose and therapy*, 10 (2). 289
- Malgorzata D, Katarzyna B, Juliusez G, Magdalena, K, Ewa A, et al. (2022) Tuberculous pericarditis –Owa Experience and Recent Recommendations. *Diagnostics (Based)* 12 (3): 619.
- Yehuda A et al., (2015). 2015 ESC Guidelines for the diagnosis and management of pericardial disease: The task force for the Diagnosis and management of pericardial Disease of the European society of cardiology (ESC) Endorsed by: The European Association for cardio-Thoracic Surgery (EACTS) , *European Heart Journal*, 36 (42), 29212964.
- Barbara WT, Rabih OD; (2001). Tuberculous pericarditis optimal Diagnosis and management. *Clinical infectious Disease*, 33 (7): 954-961.
- Ntsekhe M, Myosi BM (2013) Tuberculous pericarditis with and without HIV. *Heart Fail. Rev* 18: 367-373
- Nawaze S (2023) pathogenesis and treatment of tuberculous pericarditis. *Myiobac DIS*. 13.321.
- Wang S, Wang J, Liu J. Zhang Z, He J etal (2022). A case report and review of our literature: Tuberculous pericarditis with pericardial effusion as the only manifestation. *frontCardiorase Med*. 9:1020762. do,10.3389/ ferm.2022.1020672.