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Tuberculosis and Cardiovascular Complications

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Abstract

Tuberculosis is one of the major life-taking diseases all over the world, with most of the victims from low- and middle-income countries. The etiology of this disease is primarily a bacterium called *Mycobacterium tuberculosis* (MTB). Although it normally affects the lungs, dissemination can occur in the lymphatic system, the central nervous system (CNS), the gastrointestinal system, and the cardiovascular system. Though the leading cause of death globally, cardiovascular diseases tend to be especially lethal as TB-related heart complications in these regions; hence, understanding and management of cardiovascular issues in TB patients are even more critical. TB can cause various cardiovascular complications, ranging from the more common pericarditis (inflammation of the lining around the heart) to rarer conditions such as myocarditis (inflammation of the heart muscle), coronary artery disease, and aortitis (inflammation of the aorta). These complications have a potential for the significant deterioration of the prognosis of TB patients; however, being mostly under diagnosed or missed, requires a high degree of clinicalawareness. This discussion addresses the complex interaction of TB and cardiovascular health.

Keywords: Tuberculous Aortitis, Tuberculous Myocarditis, Tuberculous Pericarditis, Cardiovascular Complications, Tb, Tuberculosis, Mycobacterium Bacterium.

Introduction:

Tuberculosis has continued to be one of the major global health challenges. It is estimated that *Mycobacterium bacterium* that causes tuberculosis
evolved around 150 million years ago. The name by which TB was referred has undergone several changes, with the ancient
Hebrews naming it " schachepheth", Greeks as " phthisis", English-speaking nations as " consumption", and " king's evil" in France. According to the Global Tuberculosis Report 2021 by the World Health Organization, despite centuries of medical advancement, TB is still among the major causes of death from infectious diseases, especially among people with compromised immune systems. In 2020, 9.9 million people were diagnosed with TB, and 1.3 million people died from it, representing 13% of those infected. The most common TB is within Southeast Asia, Africa, and the Western Pacific; men have more disease than women, 1.7:1 being the male-to-female ratio. Though deaths due to TB have reduced considerably in the last three decades because of the availability of treatments and public health interventions, it is still in a dire state, especially after COVID-19 further challenged efforts toward TB control.

TB is a communicable infectious disease that always results from *Mycobacterium tuberculosis* or MTB. The usual mode of spread of this bacterium among people is airborne when an infected person coughs or sneezes during active disease.

The immune compromised conditions such as DM and HIV, excessive alcohol consumption, smoking, and indoor air pollution are some of the risk factors that worsen the disease and hasten the disease's course. Furthermore, a study done by Shimeles et al. in Ethiopia also identified illiteracy, low household income, and absence of BCG vaccination scar as one of the major risk factors for TB. These findings reflect the broader socioeconomic challenges faced by many developing nations that result in a predisposition toward overcrowding and poor nutrition, conditions that encourage the spread and seriousness of TB.

TB usually begins with the lungs, from where it manifests symptoms of chronic cough, fever, night sweats, loss of weight, hemoptysis, and a loss of appetite. If left untreated, the infection may spread to other parts of the body by affecting organs like the lymphatic system, the CNS, the gastrointestinal system, especially the peritoneum, and the cardiovascular system. It highly predominantly affects the lymph nodes, and when it is a case of its necrosis, there's a high probability that TB could spread to other organs. According to a study carried out by Ohene et al, 21.8 % of the total 3342 diagnosed to have TB showed extrapulmonary tuberculosis or EPTB, in short, the disease affects quite a number of organs outside the lungs. This is a high percentage, and it points out that EPTB needs to be taken seriously since it complicates the management and prognosis of the disease.

Pathophysiology of Cardiovascular Involvement in TB

Generally, diseases like hypertension, diabetes mellitus, obesity, high levels of cholesterol, and smoking enhance the risk of heart disease. However, in the recent past, infection has also been proven to act as a factor for heart disease.

Studies have found a link between tuberculosis infection and cardiac disorders. Various theories have been advanced o n how TB would result in the development of cardiovascular disorders.

The immune response to TB involves the deployment of immune cells, including monocytes, macrophages, and lymphocytes, to attack the bacteria. In this process, these cells protect the body but at the same time may cause damage. The inflammation that results from the immune response leads to the deterioration of blood vessels and eventually the depositing of plaques in arteries. Even the TB bacteria could be hiding in such plaques, further damaging the blood vessels. The body, therefore, can potentially increase the chances of getting cardiovascular disea se as it attempts to fight off an infection.

It is suggested that molecular mimicry and autoimmunity, in part, are critical elements in the cardiovascular complications arising in tuberculosis infection. This is with regard to the fact that heat shock proteins' system importantly relates to the immune response. Thus, about 40-

50% of the amino acid residues are identical in human HSP65 and MTB HSP65. HSP65 is expressed on the surface of endothelial cells after the body has been subjected to infection or other forms of stressors. This leads to the fact that the immune system will target it by producing antibodies against it. Due to structural similarities, the antibodies may cross-react with the body's own HSP60, leading to an autoimmune response.

Tuberculous pericarditis

Tuberculous pericarditis is one of the major causes of pericardial disease in the world, especially in developing countries. It is found in approximately 1-2% of all cases of tuberculosis. TBP may manifest as either pericardial effusion, constrictive pericarditis, or a combination of both. Symptoms include fever, malaise, chest pain, cough, breathlessness, night sweats, weight loss, and right upper quadrant pain due to liver congestion. Many of these symptoms are common in heart
failure and thus make diagnosis difficult. Thus, each case needs to be carefully evalu ated to identify the correct cause and administer appropriate treatment. In that respect, one can note among physical findings, rapid heart rate-predominating symptoms: tachycardia; hypotension or low blood pressure, pulsus paradoxus, or an abnormal fall of blood pressure on inspiration; pericardial knock, pericardial friction rub, muffling of the heart sounds; hepatomegaly or enlargement of the liver; ascites; and edema or swelling. Imaging studies typically used to make the diagnosis consist of echocardiography, co mputed tomography, and MRI. The imaging may also reveal fluid accumulation, thickening, or calcification of the pericardium, but most of these cases require a more invasive test in order to find the etiology, such as pericardiocentesis.

Imaging studies, including chest X-rays may also reveal pericardial effusion; in TBP, there could also be features of active TB that include lung nodules, cavitation, consolidation, or lymph node enlargement. In suspected TBP, samples for mycobacterium tuberculosis testing sho uld be collected on sputum and pericardiocentesis by microscopy, culture, or the Xpert MTB\RIF assay. Other useful tests include the measurement of ADA and IFNγ in pericardial fluid, both of which are good indicators of TB. These tests are also more expensive and less accessible than cultures. Finally, confirmation may be obtained by pericardial biopsy and histological examination.
The cornerstones of management for tuberculous pericarditis include treatment of the underlying tuberculosis infection, symptomatic relief related to fluid accumulation or constriction of the heart, and prevention of major complications. Before anti-TB treatments, the mortality rates were as high as 80-90%.
With current practices, this has been reduced significantly, with a reported mortality rate of approximately 26% in some populations.

In these cases, management usually includes at least four principal antitubercular drugs: rifampicin, isoniazid, pyrazinamide, and ethambutol. Even now, drugs poorly penetrate to the pericardium; in this respect, explaining still high mortality partly needs further searching for alternative medicine, a possibility of alterations in the actual level of drugs is required.
Symptoms may be treated not only with medicines but also with procedures, like pericardiocentesis, involving the drainage of fluid around the heart, which, in particular, could ease the symptoms of patients with cardiac tamponade, a condition where pressure on the heart develops owing to fluid accumulation. In severe forms, a pericardiectomy may be necessary surgically to improve heart function and alleviate symptoms of constriction. The role of corticosteroids in the treatment of tuberculous pericarditis remains controversial. Some studies have shown that they may be of benefit, while others have not reached a conclusion. In practice, corticosteroids are widely used to reduce inflammation and symptoms associated with the condition, despite the lack of clear consensus.

Tuberculous myocarditis and sudden cardiac death

Tuberculous myocarditis is a rare cardiac inflammatory disease and accounts for only 0.14-2% in some series of myocarditis.
It primarily affects young adults, predominantly those below 45 years, with a conspicuous male preponderance, the male-to-female ratio being about 2:1. It may be associated with pericarditis, presenting as myoperica rditis, or may present purely. The majority of individuals with tuberculous myocarditis are asymptomatic. Symptomatic ones may present condition problems such as ventricular arrhythmias and atrioventricular block, among others. Dilated cardiomyopathy, congestive heart failure, or even sudden cardiac death may be very serious complications arising from it.

The infection may reach the heart in various ways: it may be directly transmitted to the myocardium from the pericardium, extend posteriorly from infected lymph nodes, or be conveyed by the bloodstream.

The rarity of the condition, symptom-free cases, and predilection for younger individuals are some of the difficulties in earl y diagnosis of tuberculous myocarditis and can make it easy to overlook. Despite these challenges, the need to increase awareness of this condition is great, especially in regions where the incidence of tuberculosis is higher. In symptomatic tuberculous myocarditis, the prognosis remains very poor, with high mortality. That so many are diagnosed only at autopsy attests to the importance of timely recognition and intervention.
A transthoracic echocardiogram or cardiac MRI is usually indicated when there is a suspicion of tuberculous myocarditis in a pat ient. Imaging studies can delineate the valvular apparatus for any mechanical derang ement. An ECG is useful in the detection of a conduction abnormality, especially in symptomatic patients.

Given that myocarditis has non-specific causes, endomyocardial biopsy-a small sample of the heart tissue for observation-may be proposed as a method of diagnosis. On the other hand, some guidelines weakly recommend the procedure because there is limited evidence for its routine diagnosis. There is scant information about the standard treatment for tuberculous myocarditis mostly because of the rarity of the condition; nevertheless, the institution of anti-TB medications remains the main modality of treatment, since it can help improve a patient's immediate symptoms. It should be remembered, though, that while these medications may help in the short-term recovery of the patient, they do not lower the long-term risk of SCD. Long-term close followup is required in cases of tuberculous myocarditis for the control of persistent risk.

Tuberculous aortitis

Tuberculous aortitis is an uncommon but serious complication of tuberculosis, which was first described in 1882. Less than 1% of TB cases are complicated by aortitis, often as a part of widespread infection.
Of these, about half develop aneurysms, usually of the descending thoracic or abdominal aorta.
Inflammatory aortic stenosis may also occur.
The patients often present with symptomatology related to general TB symptoms, complemented by those due to the aneurysms: dysphagia, hoarseness of voice, or occasionally with severe complications such as rupture leading to hemodynamic instability.

Imaging for tuberculous aortitis is best done by CTA and CT angiography. The diagnosis should be suspected in patients with symptoms of systemic TB in combination with an aneurysm, particularly from TB-endemic areas. The usual treatments involve surgical removal of the aneurysm with aortic bypass, combined with a long course of anti-TB medications, sometimes extending for as long as one year. The prognosis, though generally poor with a mortality rate of around 50%, improves when medical therapy is combined with surgery. Other experts advocate for prolonged or even lifelong anti-TB therapy to prevent complications, such as prosthetic infections or aneurysm reoccurrence.

For patients with inflammatory aortic stenosis, the initial treatment involves anti-TB medications along with corticosteroids. Surgery is considered only if the patient's condition doesn't improve with this approach.

Tuberculosis and coronary heart disease

This becomes well elaborated, especially by explaining how the systemic inflammati on part in TB contributes to the atheroma formationone of the main conditions that are directly involved in the manifestation of CHD. Thereby, many similarities are extracted regarding the cause pattern for the condition s under scrutiny: how, specifically, active inflammation has evolved in accelerating at herosclerosis to trigger or exacerbate CHD. This inflammation in
TB, however, results in the immune response, which again is important in developing CHD. Also, being infected with HIV co-infection, particularly in low- and middle-income countries facing a bigger burden of the diseases, makes it even more inflammatory; t hat usually makes the consequences for a patient worse.
However, there is a relative paucity in the literature on how CHD management should differ in patients with TB compared to those without. In regard to drug therapy, all drugs prescribed for TB patients have to be considered with caution because of potential interactions with anti-TB drugs that can result in adverse effects, thus requiring close monitoring to avoid complications.

Tuberculosis and ischemic stroke

Ischemic stroke is a recognized complication of tuberculous meningitis. Various studies have reported that there indeed exists an increased risk of stroke in patients with the disease. For example, a retrospective review of 104 patients in New Zealand revealed that 33% of patients had a stroke as a complication of tuberculous meningitis. This trend was also evident in other studies suggesting a higher probability of stroke in patients diagnosed with tuberculous meningitis.

Various researchers have investigated an association between ischemic stroke and TB that does not involve the CNS. Among these, in 2009, Sheu et al. conducted a matched-cohort study wherein 2283 patients with TB were compared with 6849 patients without a diagnosis of TB. They found that TB patients, even without CNS involvement, were 1.52 times more likely to develop an ischemic stroke within three years of diagnosis. This may indicate that TB in itself, independent of any direct effects on the brain, increases the risk of ischemic stroke. However, information is still scant on this matter, and further studies should be done to fully understand the association. In terms of treatment, there are no specific management guidelines that highlight the stroke risk in TB patients. As such, the healthcare provider should focus on the effective treatment of the TB infection and promptly manage any ensuing ischemic stroke.

Conclusion:

Cardiovascular complications of TB are among the major causes of morbidity and mortality. This discusses the complications arising from
TB, considering various seminal studies and summarizing current epidemiological data on common and less common cardiovascular manifestations that sometimes go unnoticed in TB patients. It will also discuss the medical and surgical options available for the management of these complications.
The intersection of TB and cardiovascular diseases is a health challenge, as both are among the major causes of death in the world. This will try to put into perspective these complications to further improve patient care and reduce mortality. It emphasizes the need for a high level of clinical suspicion and a multidisciplinary team approach in managing such cases.
Cardiovascular complications often arise later, and thus even those patients who have finished treatment with active TB need to be continued on follow-up.

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