Tuberculosis and the Heart

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KEYWORDS

• Tuberculosis • Tuberculous pericarditis • Tuberculous myopericarditis • Tuberculous myocarditis • Tuberculous aortitis

KEY POINTS

- Tuberculosis remains an important health problem of the developing world. Tuberculous heart disease is an important extrapulmonary manifestation of the disease.
- Tuberculous pericarditis occurs with higher frequency in individuals infected with the human immunodeficiency virus (HIV) and is characterized by differences in immune and clinical responses compared with HIV-negative individuals.
- A biomarker-based approach that uses pericardial fluid unstimulated interferon-γ, adenosine deaminase, and polymerase chain reaction offers a fast and reliable way of establishing the diagnosis.
- Four-drug antituberculous therapy is the mainstay of management for tuberculous pericarditis.
- Adjunctive steroid therapy has been shown to reduce hospitalization and progression to constrictive pericarditis, but not mortality; in HIV-positive patients, adjunctive steroids are associated with a higher incidence of malignancy.

Video content accompanies this article at http://www.cardiology.theclinics.com.

INTRODUCTION

Recognized since antiquity, tuberculosis (TB) still contributes significantly to the global burden of disease, with an estimated 9.6 million new cases of the disease worldwide in 2014.[1] This is especially true in the developing world where human immunodeficiency virus (HIV) infection and AIDS, socioeconomic deprivation, and poor health systems infrastructure interact to make TB a significant public health problem.[2] Although it remains primarily a disease of the lungs, the classic lesion of TB—the acid fast *Mycobacterium tuberculosis* (Mtb) bacilli in a necrotic core bound by aggregates of various inflammatory cells (granuloma)—can be found in virtually any part of the body (Fig. 1). Autopsy studies performed in the pre-HIV/AIDS era suggest that the heart is involved in approximately 2% of cases of patients who died from TB.[3] Similar studies of patients who died of TB and were coinfected with HIV demonstrate multisystemic dissemination in up to 80% of patients.[4,5] Of all the extrapulmonary manifestations of TB, involvement of the heart is second only to central nervous system TB in terms of its devastating morbidity and mortality.

It has been almost a decade since there was a comprehensive review of the main form of tuberculous heart disease.[6] That review focused on the pathogenesis, diagnosis, and management of tuberculous pericarditis and concluded by noting that there remained major gaps in our

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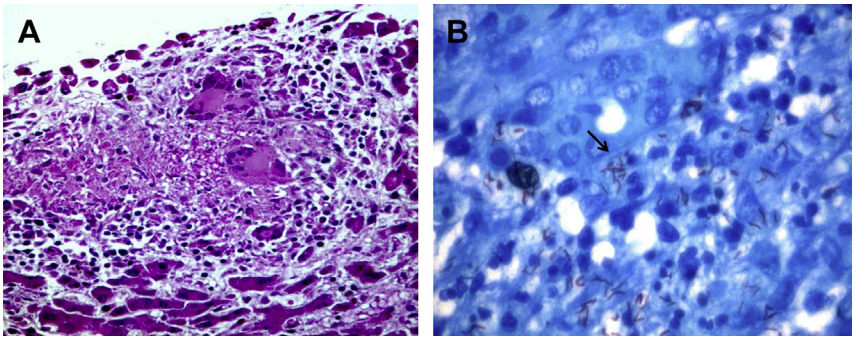

Fig. 1. *Mycobacterium tuberculosis*. Tuberculous granuloma (*A*) showing an aggregation of lymphocytes, monocytes, multinucleate giant cells with a central area of caseous necrosis. Ziehl-Neelsen stain (*B*) demonstrating acid-fast *M tuberculosis* (*arrow*). (*Courtesy of* Dr Craig Jamieson, formerly of Anatomical Pathology Department, University of Cape Town, Observatory, Cape Town, South Africa.)

understanding of the subject. The identified gaps included the need for improved diagnostic tools, a better understanding of the impact of HIV, and determination of the effectiveness of adjuvant therapy on clinical outcomes.[6] Since then, much data, predominantly from sub-Saharan Africa, have been generated to address some of these gaps. An updated comprehensive overview of TB and the heart with a summary of the new insights is therefore timely and hopefully of value to the general physician and cardiologist on the front lines of patient care.

The search strategy for this review involved a comprehensive search of MEDLINE, EMBASE and the Cochrane library of systematic reviews with the MeSH terms: "tuberculosis and the heart," "cardiac tuberculosis," "cardiovascular tuberculosis," "myopericarditis and tuberculosis," "tuberculous pericarditis," "tuberculous aortitis," and "HIV and the heart'' from January 2005 to December 2015. The reference lists of selected articles were searched for articles deemed to be of relevance to the subject. Appropriate English language studies were retrieved and reviewed.

There have been a number of important advances in our understanding of tuberculous pericarditis over the last decade. Most of the new information has been generated from sub-Saharan Africa and Asia, where TB is endemic, HIV is epidemic, and the majority of patients with TB are also coinfected with HIV.[2] The *I*nvestigation of the *M*anagement of *P*ericarditis in Afr*i*ca (IMPI) registry was a prospective observational cohort of consecutive patients with suspected TB pericarditis across multiple sites in sub-Saharan Africa. Important questions related to the immunopathogenesis, clinical manifestations, diagnosis, and outcomes of TB pericarditis in the HIV era were investigated in the registry.[7–18]

The IMPI immunotherapy trial was a double-blind, randomised control trial of 1400 patients with definite or probable TB pericarditis who were randomised to receive adjunctive corticosteroids or *Mycobacterium indicus pranii* versus placebo in a 2 × 2 factorial design.[19] These studies, which were conducted between 2004 and 2015, form the backbone of new insights gained since 2005.

There are 3 predominant clinical manifestations of tuberculous heart disease. In descending order of frequency, these include TB pericarditis, myocardial TB with or without aneurysm formation, and TB aortitis with or without mycotic aneurysms and pseudoaneurysms involving the aortic valve and/or sinuses of Valsalva. Important clinical, diagnostic, and management aspects of each are reviewed.

TUBERCULOUS PERICARDITIS

Tubercle bacilli access the pericardium via 3 main mechanisms. These include retrograde lymphatic spread from mediastinal, paratracheal and peribronchial lymph nodes,[20] hematogenous spread (dominant in immunocompromised hosts),[21] and, rarely, direct contiguous spread from adjacent structures such as the lungs, pleura, and spine.[20] In the presence of a competent immune system, tuberculous pericardial disease is usually localized to the pericardial space. It is typically a paucibacillary condition; tubercle proteins trigger a vigorous cell-mediated hypersensitivity response with T-helper cell (subtype 1) predominant cytokine release, leading to an inflammatory exudative effusion and its hemodynamic sequelae.[6] In patients with dysfunctional immunity as occurs in HIV/AIDS, there is evidence that mycobacterial replication is active, bacillary loads are high, and the