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Review

Sarcoidosis: Role of non-tuberculosis mycobacteria and *Mycobacterium tuberculosis*

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ABSTRACT

Sarcoidosis is a granulomatous inflammatory disease that is induced by unknown antigen(s) in a genetically susceptible host. Although the direct link between *Mycobacterium tuberculosis* (MTB) infection and sarcoidosis can be excluded on the basis of current knowledge, non-infectious mechanisms may explain the causative role of mycobacterial antigens. Ever since sarcoidosis was first described, its relationship with tuberculosis (TB) has been under-investigated. Whereas some researchers consider sarcoidosis and TB as two examples of the same disease process, others have rejected mycobacteria as playing any causative role in sarcoidosis. Whether they are linked causally or not, clinical evidence makes a differential diagnosis between the two conditions very challenging, particularly in countries with high burden of TB. The present study analyzes the relationship between sarcoidosis and TB and its implications in clinical practice. The coincidence of TB and sarcoidosis and the higher incidence of mycobacterial DNA in biological samples of sarcoid patients have been reported by many authors. In addition, new evidence of a similarity in MTB phenotype in sarcoidosis is provided. Overall, these observations suggest that TB and sarcoidosis may not only share the same etiology, but may even be different aspects of one disease.

Contents

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Introduction

The incidence of non-tuberculous mycobacteria (NTM) infection has been increasingly reported both in immunocompromised and immunocompetent patients. Pulmonary infections due to NTM and *Mycobacterium tuberculosis* (MTB) are also increasing worldwide [1]. Fast-growing NTM mycobacteria are ubiquitous organisms in the environment and may cause diseases in both healthy and immunocompromised patients. As such, they are a recognized cause of environmentally acquired diseases, including post-traumatic skin, soft tissue, and bone infections, pulmonary disease [2–4], disseminated infection [5] and cervical lymphadenitis [6]. Information about the risk factors for NTM disease is unclear given that the data comes from case reports and retrospective studies. Many factors have been involved in the increased susceptibility of NTM, such as pre-existing lung disease, immune suppression or genetic defects of cell-mediated immunity that may be playing an important role [7]. Sarcoidosis is an idiopathic, multi-organ, inflammatory disease which is characterized by the presence of epithelioid cell, non-caseating granulomas in various organs [8–10]. The lungs, lymph nodes, skin and eyes are the most commonly affected organs [11]. Yet the potential involvement of any organ system contributes to its myriad of clinical manifestations not well understood. The etiology of sarcoidosis remains unknown; its development is complex, with genetic susceptibility and environmental factors that may be playing important roles in the pathogenesis of diseases [12–14]. Furthermore, certain occupations and environmental exposures have been linked to the higher risk of sarcoidosis in some patients [15,16]. Since the lungs are the most commonly affected organ, the search for an etiologic agent has focused on airborne antigens and infectious or non-infectious bacteria [17,18]. The use of molecular tools and techniques demonstrating genomic or protein material of mycobacterial origin in sarcoidosis tissues, along with elevated humeral and cellular immune response to Mycobacterial antigens, may support the hypothesis that mycobacterial antigens may drive some cases of sarcoidosis.

In addition, there is much clinical evidence supporting the similarity between tuberculosis (TB) and sarcoidosis [19–24]. The present study provides a brief overview on the possible role of mycobacterium in the pathogenesis of sarcoidosis with a focus on the role of NTM. Finding a causal link between the concomitant occurrence of TB and sarcoidosis will be a challenge for the future, but will lead to the use of new therapeutic drugs for suppressing lung inflammation in these patients.

Sarcoidosis

The immunopathology of sarcoidosis remains elusive despite years of research into this multi-organ disease [25]. However, recent studies have provided new insights into the genetics and immune components involved in the clinical manifestation of the disease. Granulomatous inflammation is believed to be the host immune response to a persistent poorly degradable unknown antigen [25]. Although direct evidence

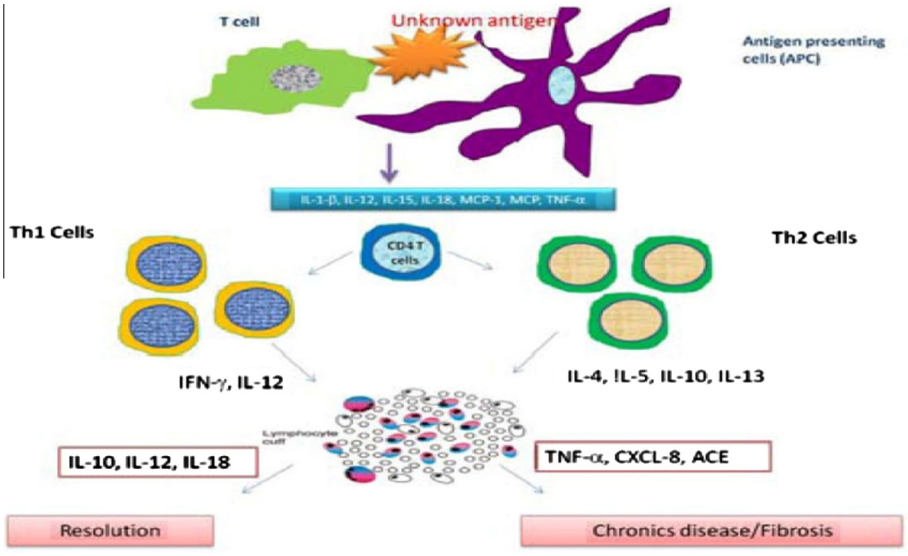

Fig. 1 – The cartoon indicating simple pathogenesis of Sarcoidosis Exposure of body to unknown sarcoid antigen leads to activation of the T cells and APCs which leads to releasing of cytokines. CD4 activation can skew the immune system to Th1 and Th2 response which in turn induces the granuloma formation. Formation of granuloma in later phases can end up to resolution or chronic status of diseases with fibrosis condition. Mortaz et al., Iran J. Allergy Asthma Immunol. 2014;13(5):300–6