

Sudden Death Due to Granulomatous Myocarditis: A Case of Sarcoidosis?

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Abstract

Introduction: We report a case of sudden death due to granulomatous myocarditis and propose that cardiac sarcoid could have been the underlying aetiology. This is the first case reported in Singapore. The differential diagnoses for granulomatous myocarditis including sarcoidosis and its cardiac manifestations as well as idiopathic giant cell myocarditis are discussed. **Clinical Picture:** A 53-year-old Indian woman died suddenly and autopsy revealed bilateral hilar adenopathy and myocardial infiltrates which proved to be granulomatous in nature. **Conclusion:** Sarcoidosis may not be a rarity here and it is important to recognise the different clinical manifestations.

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Key words: Giant cells, Granuloma, Heart, Sarcoid

Introduction

Granulomatous myocarditis and sarcoidosis are considered uncommon entities in our local community and sudden death due to either condition has not been described in local literature. Earlier local reports have alluded to the fact that sarcoidosis may be more common amongst Indian females and that more cases may be identified in the future. No large scale study has been conducted since to document its prevalence and natural history, perhaps reflecting the under-recognition of this disorder.

Case Report

A 53-year-old Indian woman had collapsed suddenly at home, became unresponsive and was brought in dead to the hospital. There was a medical history of type II diabetes for which she had been prescribed metformin and glibenclamide. The deceased had also recently attended hospital for treatment of left leg cellulites and a chest X-ray performed was normal. Physical examination at the emergency department revealed an old lower abdominal pfannenstiell incision scar. ECG monitoring showed asystole throughout. There were no other investigations done.

At the coroner's autopsy, it was found that the deceased was a well-nourished, late middle-aged, Indian female.

There were granulating ulcers over the left lower leg. A 12-cm lower abdominal scar was present, corresponding to previous hysterectomy and bilateral salpingo-oophorectomy. Internal examination also revealed a mildly enlarged heart that weighed 340 g. The coronary arteries were mildly atherosclerotic but patent. Significantly, there was a soft pale to creamy-white infiltrate over the lateral epicardial surface of the left ventricle which had extended transmurally to occupy an area measuring 3 x 2 x 1.5 cm (Fig. 1). The wall of the left ventricle at the mid septal level was also mildly thickened (1.6 cm) relative to the ventricular cavity diameter (1.5 cm). There was no myocardial infarction discernible grossly and the valves were normal. Both lungs were congested and oedematous but were otherwise normal. There was no evidence of pulmonary tuberculosis but several enlarged hilar lymph nodes were noted bilaterally. The liver was mildly enlarged and showed patchy fatty change. The left kidney was atrophic. All other organs were unremarkable. Myocardial tissue was retained for histology and blood was sent for toxicological analysis. No other organs were kept.

Microscopically, a granulomatous inflammatory infiltrate was seen in the myocardium, featuring 'sarcoid-type' non-caseating aggregates of epithelioid histiocytes, giant cells

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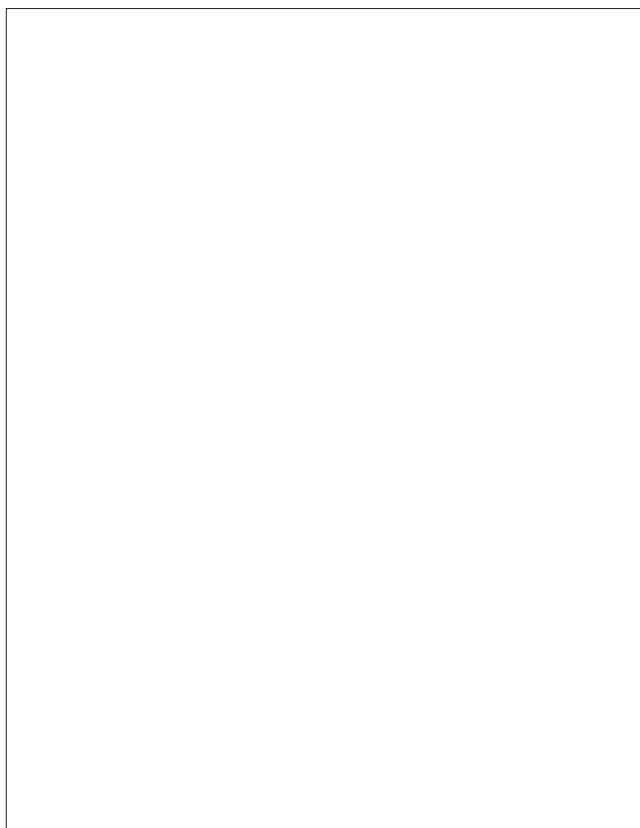


Fig. 1. Cross-section of the heart showing whitish left ventricular infiltrates (arrows).

and scattered inflammatory cells comprising predominantly of lymphocytes, and occasional plasma cells and eosinophils (Fig. 2). The giant cells were of the Langhans' and foreign body types. Fibrotic changes were noted. Cytoplasmic inclusion bodies including occasional asteroid bodies were seen within giant histiocytes (these by themselves were rather non-specific). No polarisable, birefringent material was identified and Hamazaki-Wesenberg bodies were not seen. Ziehl-Neelsen and fungal stains (Grocott methenamine silver and periodic acid-Schiff) failed to show acid-fast bacilli or fungi respectively. Toxicological finding of 7.1 mg/mL of paracetamol was well within therapeutic levels. The final cause of death was given as granulomatous myocarditis.

Discussion

Sarcoidosis, first described by Hutchinson, is a chronic, multisystem granulomatous disorder of unknown aetiology. Several infectious and non-infectious agents have been implicated but none substantiated. Lung disease and hilar adenopathy are common presentations. The liver, eyes and skin are other more commonly affected sites. The disease is said to have a female predilection and many times more prevalent among blacks than whites in the United States, yet in Europe it affects mostly whites. Among Southeast Asians, the disease is uncommon¹⁻³ but in 1985, Lee et al⁴

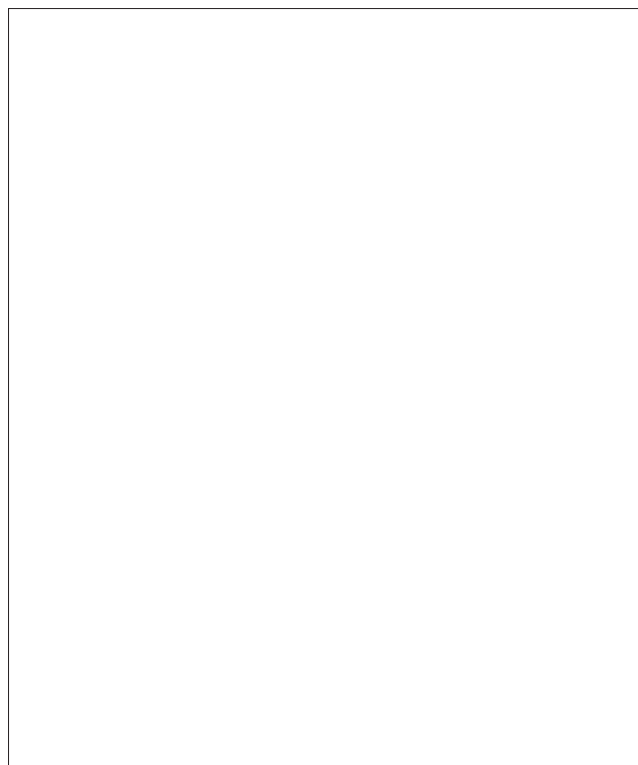


Fig. 2. Non-caseating granulomatous myocarditis (H & E, original magnification x 40). Inset shows asteroid body in giant histiocyte, x400.

looking at pulmonary sarcoidosis in Singapore noted that an increase in prevalence could be expected in the future. More recently, Sivakumar and Chee⁵ found 9 cases of sarcoidosis in Singapore over a 2-year period when they screened 262 cases of uveitis. The disease also seems to be more common among Indians in this region,⁶ although larger studies are needed to confirm this.

Cardiac sarcoid can be isolated or associated with systemic disease. As a cause of sudden death, it has been well described⁷⁻¹⁰ but we are unaware of any local report. Autopsy findings have shown that between 15% and 50% of patients with sarcoidosis have cardiac involvement,¹¹⁻¹³ although selection bias may have accounted for the high numbers. Besides sudden death, other cardiac manifestations include arrhythmias, papillary muscle dysfunction, congestive heart failure, pericardial effusion and ventricular aneurysm.¹⁴

Although sarcoidosis is a diagnosis of exclusion requiring clinical, histologic, biochemical and radiologic correlations for a firm diagnosis, we postulate, based on histology and autopsy findings of bilateral hilar lymphadenopathy, that a sudden fatal cardiac arrhythmia secondary to sarcoid myocarditis was the most likely cause of death for this Indian woman. Whenever a granulomatous myocardial lesion is encountered, diseases such as tuberculosis,¹⁵ fungal infection, rheumatoid arthritis, rheumatic fever, Takayasu's

aortitis, Wegener's granulomatosis and metastatic tumours with giant cells have to be considered. A few very rare causes of granulomatous myocarditis, such as Whipple's disease,¹⁶ silicosis¹⁷ and exposure to methyldopa¹⁸ and cornstarch,¹⁹ have also been reported in the literature. However, each of these differential diagnoses has its unique pathologic and clinical features which are absent in this case.

Another interesting entity that comes to mind whenever numerous giant cells are found in the myocardium is a rare and often fatal condition known as idiopathic giant cell myocarditis²⁰ (IGCM). This condition has been reported under various other names such as giant cell granulomatous myocarditis, Fiedler's myocarditis and myocarditis of the giant cell type. Histologic findings of seriginous necrosis with a polymorphous inflammatory infiltrate and numerous giant cells in the absence of sarcoid-like granulomas are said to be characteristic.²¹ The disease is associated with autoimmune disorders including diabetes mellitus, Hashimoto's thyroiditis, rheumatoid arthritis and myasthenia gravis. In the past, the existence of this condition as a distinct entity has been questioned but more recent findings of ultrastructural resemblance of the giant cells to degenerated myofibres²² as well as myocyte destruction by cytotoxic T cells and giant histiocytes²³ support the notion of IGCM as a distinct clinicopathologic entity. Cooper et al²¹ also found the disorder to be most prevalent among whites.

In conclusion, this case raises several learning points. The pathologist must bear in mind infiltrative myocardial diseases when whitish infiltrates are seen grossly in the myocardium, and not assume that they represent ischaemic fibrosis when concomitant coronary stenosis is also observed. Fibrosis is not an uncommon feature in genuine cases of cardiac sarcoid especially in the more chronic cases, but the whitish infiltrates representing granulomatous inflammation generally have a softer consistency. The recent fallout from organ retention scandals in Britain has highlighted the need for pathologists to be judicious in retaining human tissue and organ for routine analysis. This case illustrates the value of adopting a more liberal approach in select instances. For clinicians, the challenge is to recognise that sarcoidosis can manifest itself in different ways and that it is not a rarity.⁵ It is timely to conduct large-scale studies to document the epidemiology and natural history of this fascinating disease in our local community.

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