AN UNUSUAL MANIFESTATION OF CARDIAC SARCOIDOSIS

K. Ramanathan1, D. Platts2, Y. V. Apte3, D. Muthalidas4
1 Intensive Care Unit, Prince Charles Hospital, Chermside, Brisbane; 2 Dept. of Cardiology, Prince Charles Hospital, Chermside, Brisbane; 3 Intensive Care Unit, Robina Hospital, Robina, Gold Coast; 4 Dept. of Medicine, Robina Hospital, Robina, Gold Coast

Abstract. Non tropical, non hypereosinophilic endomyocardial fibrosis has been reported in literature and is a rare entity. Cardiac Sarcoidosis manifesting as non-tropical, non hypereosinophilic endomyocardial fibrosis is unknown, though it classically affects the left ventricle and is not associated with specific risk factors. We describe an atypical presentation of sarcoidosis as non-tropical non hypereosinophilic endomyocardial fibrosis in a middle aged female who presented to us with refractory heart failure. (Sarcoidosis Vasc Diffuse Lung Dis 2014; 31: 71-75)

Key words: Cardiac sarcoidosis, endomyocardial fibrosis, heart failure

Introduction

Endomyocardial fibrosis (EMF) is the most common cause of restrictive cardiomyopathy, and affects about 12 million people in the world. The disease is prevalent mainly in the tropical regions of sub Saharan Africa and also in India and Brazil. Cases have been reported from outside the tropics and the predisposing factors in this group of population seem different from the tropical ones. EMF mainly affects children and adolescents from the lower socioeconomic group. The etiology of this condition still remains uncertain. The pathogenic mechanisms of EMF seem to closely correlate with hypereosinophilic syndromes, certain tropical infections and autoimmune processes. It has been postulated that the disease has predisposition with heredity, ethnicity, diet, climate and socioeconomic status (1). EMF has been associated with helminthiasis, schistosomiasis, filariasis and malaria. Dietary ingestion of tapioca and cerium has also close correlation with the disease. Non tropical, non hypereosinophilic EMF has been reported in literature and is a rare entity.

The association of non-tropical, non hypereosinophilic EMF with sarcoidosis is unknown though it classically causes left ventricular EMF and is not associated with specific risk factors (2). Cardiac sarcoidosis can happen alone or alongside systemic sarcoidosis and the epidemiology and clinical presentation is influenced by geographical factors (3). The involvement of the heart may precede, occur concurrently or follow pulmonary sarcoidosis. Cardiac sarcoidosis may involve the pericardium, myocardium or the endocardium but conduction blocks and arrhythmias are the most common clinical presentations. It may manifest as frank heart failure but sudden cardiac death is the most feared complication of cardiac sarcoidosis and occurs in 30-65 percent of the patients. Interestingly in the first reported mortality due to cardiac sarcoidosis in 1937, Gentzen demonstrated giant cell granulomas in two patients with endomyocardial fibrosis (3).
We present a patient who had heart failure secondary to non-tropical non-hypereosinophilic endomyocardial fibrosis refractory to standard anti-heart failure medications. She had extra pulmonary sarcoidosis and her heart failure improved once she was started on steroids. Major causes of endomyocardial fibrosis were excluded and we believe sarcoidosis would have caused the pathology and contributed to her heart failure.

Case Report

A 51 year old female was admitted to our Intensive Care Unit (ICU) with septic shock secondary to nosocomial pneumonia. During the preceding 18 months the patient had experienced significant weight loss (20 kilograms), fatigue and pyrexia of unknown origin (PUO). Investigations for the PUO including autoimmune markers, infective serological markers for bacterial and viral infections, flow cytometry, serum Angiotensin Converting Enzyme (ACE), bone marrow biopsy as well as tumor markers were non diagnostic. The patient appeared frail and cachectic with severe muscle wasting. The patient was treated for a septic shock with antibiotics and vasopressor support.

Ultrasound imaging of the liver and biliary tract was normal and hepatic autoimmune markers were unremarkable. A liver biopsy revealed features suggestive of granulomatous hepatitis with an eosinophilic infiltration. CT imaging of the chest and abdomen revealed mildly enlarged lymph nodes in the mediastinum and abdomen but were considered too small (<1cm) for biopsy.

A transthoracic echocardiogram (TTE) was performed showing a left ventricular mass obliterating the apex with moderate mitral regurgitation and a restrictive filling pattern (Fig 1, 2, 3). The TTE findings were consistent with a diagnosis of left ventricular endomyocardial fibrosis. The patient was transferred to a tertiary cardiac centre for further evaluation, where a microsphere contrast TTE and cardiac MRI were performed (Fig 4 and 5). Both investigations correlated well with the findings on TTE.

The liver biopsy was reassessed and was labelled as being consistent with sarcoidosis. Further investigations for hypereosinophilic syndromes, tropical infections and protozoal infections turned out to be negative. A diagnosis of non-tropical endomyocardial fibrosis secondary to sarcoidosis was made. The patient responded dramatically to prednisolone and conventional heart failure therapy, including warfarin. Suitability for surgical excision of the mass is being performed.

Discussion

The incidence of sarcoidosis is reported to be around 4.4 per 100000 population in Australia. Cardiac sarcoidosis is rare in Australasia with no cases re-
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ported in a series of 122 cases of sarcoidosis reported in 2007 by Gillman and Steinfort (4). Twenty Australian patients with cardiac sarcoidosis have been reported by Allen (5) while Adamson et al reported 18 cases of cardiac sarcoidosis in Christchurch with a long term mortality of 11% (6). Non-tropical non hypereosinophilic endomyocardial fibrosis is very rarely encountered in the usual areas of sarcoidosis: Europe, North America, and Japan. In Africa, it is assumed that sarcoidosis may be under recognized because of misclassification as tuberculosis.

Cardiac sarcoidosis can present anywhere from a benign incidental finding to sudden cardiac death. Cardiac sarcoidosis can manifest as conduction disorders, dysrhythmias, sudden death, cardiomyopathy, heart failure, valvular heart disease, or even myocardial ischemia. Complete heart block and ventricular arrhythmias occur with granulomatous infiltration of the conduction system and can lead to sudden cardiac death (3). Cardiac lesions can result in myocardial hypertrophy particularly at the ventricular septum or the left ventricular free wall and are rarely seen in the atrium or the right ventricle. Circumscribed myocardial involvement can cause local hypertrophy and may mimic hypertrophic cardiomyopathy. Granulomatous infiltration can further lead to dilated cardiomyopathy and severe heart failure secondary to systolic and diastolic dysfunction (7, 8). Healing granulomas can also lead to fibrosis of the myocardium. Various definitions and diagnostic approaches for cardiac sarcoidosis have been proposed, but there is no clear-cut consensus on the best diagnostic approaches that can monitor disease progression.

EMF is a specific disease entity that is characterized by specific epidemiological and diagnostic features and it involves fibrosis of the apical endocardium of the right ventricle (RV), left ventricle (LV), or both. The clinical manifestations correlate well with the consequences of restrictive ventricular filling, including left and right sided heart failure. Pathologically fibrotic tissue deposition happens in

![Fig. 3. Apical four chamber TTE using low mechanical index, myocardial contrast echocardiographic imaging, to enhance tissue characterisation. Note the region with no contrast signal (black area) indicating absent perfusion, consistent with inflammation/fibrosis/thrombotic material.](image1)

![Fig. 4. Magnetic Resonance Image showing steady state free precession showing increased thickness of lateral wall [mid/apical segments] with irregular endomyocardial contour.](image2)

![Fig. 5. Comparative post contrast Magnetic Resonance Image showing endomyocardial enhancement with overlying low signal thrombus as well as pericardial enhancement.](image3)
the endocardium of the inflow tract and apex of one or both ventricles. Fibrosis can also happen in the subvalvular apparatus and chords which leads to atrioventricular valve regurgitation. Progressive diastolic dysfunction leads to exercise intolerance and severe cardiac failure. Echocardiography is a first-line and the gold standard non-invasive technique for diagnosing EMF (9). It enables the identification of the disease in early stages, and the quantification of the degree of morphological and hemodynamic compromise. An echocardiographic grading of severity has been formulated based on major and minor criteria and is helpful in staging the disease and studying the progression (10). Endomyocardial biopsy is seldom helpful in the diagnosis in half these patients and carries the risk of embolisation. Cardiovascular magnetic resonance (CMR) provides detailed information on ventricular morphology and function, including excellent visualization of the ventricular apex (11, 12). Gadolinium usually tends to accumulate causing Late Gadolinium Enhancement (LGE) on CMR which in turn allows the evaluation of the presence of myocardial inflammation, fibrosis, and injury (12, 13). The characteristic features of non-tropical non hyper eosinophilic EMF on CMR include contracted left ventricular length, increased apical wall thickness, abnormal subendocardial fibrosis and presence of apical thrombus (2). Other conditions, such as Chagas disease, amyloidosis, sarcoidosis, and subendocardial infarction, could also cause sub endocardial LGE. The apical systolic inward motion is commonly preserved in EMF contrary to the dyskinetic motion of thrombotic apical obliteration occurring in patients with coronary artery disease or Chagas disease (13). LGE in cardiac amyloidosis often demonstrates global, inhomogeneous, subendocardial hyperenhancement associated with a global increase in wall thickness and systolic dysfunction. LGE in sarcoidosis will appear as areas of myocardial enhancement in regions with granulomas. These areas often show wall thinning and wall motion abnormalities. They are usually located in the septum but can affect other walls, with midwall, epicardial, or transmural involvement, whereas the RV wall is rarely affected (11).

Non hypereosinophilic endomyocardial fibrosis does not usually respond to steroids and the treatment is usually asymptomatic. Steroids are the mainstay of treatment in cardiac sarcoidosis despite lack of well-defined trials. However there is no clear consensus regarding the duration of steroid therapy, the initial dosing, optimal maintenance dosing, duration of treatment and the predictability of steroid responsiveness. Steroids can be tapered and eventually discontinued if the disease is dormant or stable but patients need to be followed up for relapse. Pacemakers and Implantable Cardioverter Defibrillators are used for patients with dysrhythmias.

Targeted endocardial resection combined with valve repair or replacement is the usual surgical treatment in EMF especially for patients in NYHA functional classes III and IV (14-16). Arrhythmias and low cardiac output syndrome contribute to early mortality in these patients while complications of prosthetic valves and permanent pacing account for the late mortality (16, 17).

Our patient had several unusual features. Endomyocardial fibrosis is quite rare outside the tropics. Sarcoidosis is well known to cause cardiac complications, but has been rarely associated with non-tropical non eosinophilic endomyocardial fibrosis. Cardiac sarcoidosis usually presents as rhythm disorders but our patient presented with features of heart failure secondary to endomyocardial fibrosis. She responded well to steroid therapy and is currently being considered for surgery.

References

9. Mocumbi AO, Ferreira MB, Sidi D, Yacoub MH. A population study