SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2014; 31; 71-75

An unusual manifestation of Cardiac Sarcoidosis

K. Ramanathan[1], D. Platts[2], Y. V. Apte[3], D. Muthalidas[4]

[1]Intensive Care Unit, Prince Charles Hospital, Chermside, Brisbane. Intensive Care Unit, Robina Hospital, Robina, Gold Coast; [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).

Received: 14 August 2013
Accepted after revsion: 26 November 2013
Correspondence: Ramanathan KR,
Department of Cardiothoracic Intensive Care,
National University Heart Centre, Singapore 138685.
Tel 006567727862, Fax 006567766475.
Email: ram_ramanathan@nuhs.edu.sg

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.

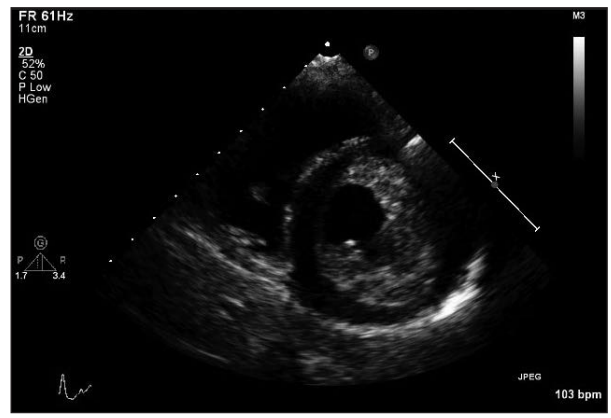

Fig. 1. Parasternal short axis TTE demonstrating an extensive left ventricular cavity mass, occupying much of the left ventricular chamber. Note also the clear tissue plane between myocardium and the mass.

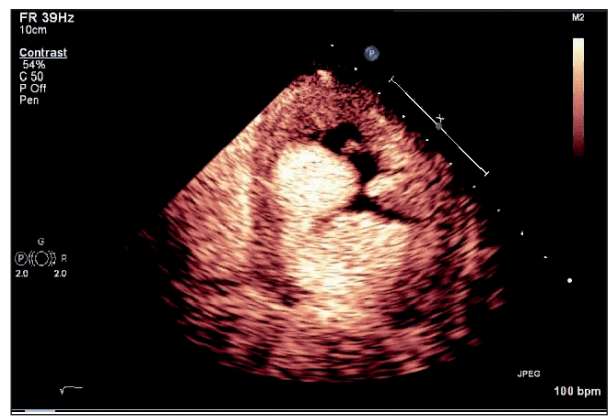

Fig. 2. Apical four chamber TTE using contrast enhanced left ventricular opacification imaging, highlighting the morphology of the ventricular apical mass with extension up the anterolateral wall.

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-

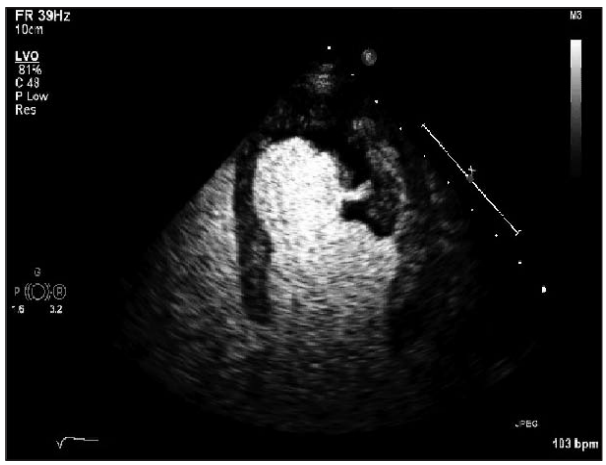

Fig. 3. Apical four chamber TTE using low mechanical index, myocardial contrast echocardiographic imaging, to enhance tissue characterisation. Note the region with no contrast signal (black area) indicating absent perfusion, consistent with inflammation/fibrosis/thrombotic material.

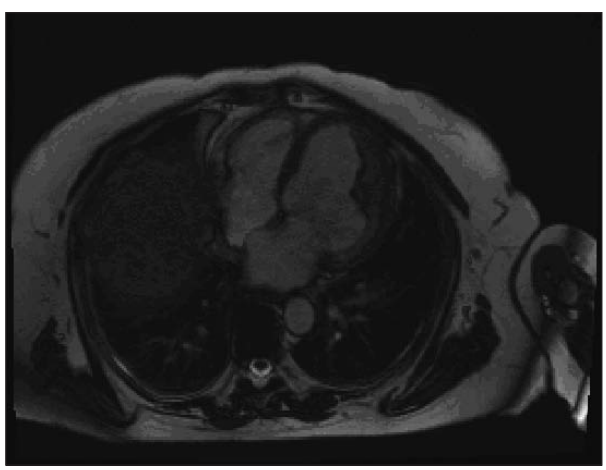

Fig. 4. Magnetic Resonance Image showing steady state free precession showing increased thickness of lateral wall [mid/apical segments] with irregular endomyocardial contour.

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 etal 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.

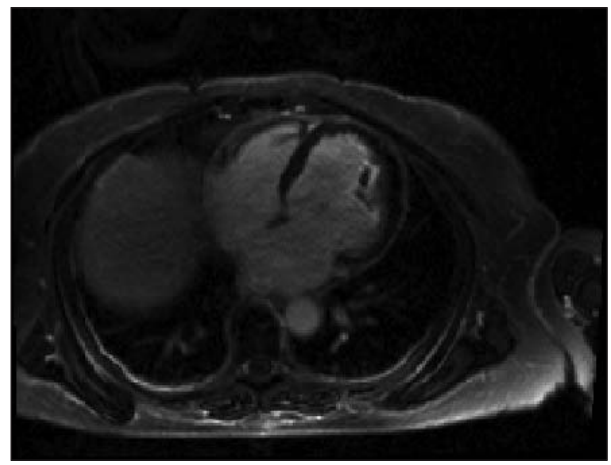

Fig. 5. Comparative post contrast Magnetic Resonance Image showing endomyocardial enhancement with overlying low signal thrombus as well as pericardial enhancement.

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

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 endo myocardial fibrosis does not usually respond to steroids and the treatment is usually symptomatic. 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

1. Mocumbi AO, Yacoub S, Yacoub MH. Neglected tropical cardiomyopathies: II. Endomyocardial fibrosis: myocardial disease. Heart 2008;94:384-90.
2. Hamilton-Craig C, Strugnell WE, Raffel OC, Porto I, Walters DL, Slaughter RE. CT angiography with cardiac MRI: non-invasive functional and anatomical assessment for the etiology in newly diagnosed heart failure. The international journal of cardiovascular imaging 2012;28:1111-22.
3. Sharma OP, Maheshwari A, Thaker K. Myocardial sarcoidosis. Chest 1993;103:253-8.
4. Gillman A, Steinfort C. Sarcoidosis in Australia. Internal medicine journal 2007;37:356-9.
5. Allen RK. Sarcoidosis in the sunburnt country. Internal medicine journal 2007;37:353-5.
6. Adamson P, Melton I, O'Donnell J, MacDonald S,CrozierI Cardiac Sarcoidosis: The Christchurch Experience, Internal medicine journal, Article in press.
7. Fahy GJ, Marwick T, McCreery CJ, Quigley PJ, Maurer BJ. Doppler echocardiographic detection of left ventricular diastolic dysfunction in patients with pulmonary sarcoidosis. Chest 1996;109:62-6.
8. Sun BJ, Lee PH, Choi HO, Ahn JM, Seo JS, Kim DH et al. Prevalence of echocardiographic features suggesting cardiac sarcoidosis in patients with pacemaker or implantable cardiac defibrillator. Korean circulation journal 2011;41:313-20.
9. Mocumbi AO, Ferreira MB, Sidi D, Yacoub MH. A population study

of endomyocardial fibrosis in a rural area of Mozambique. N Engl J Med 2008;359:43-9.
10. Sliwa K, Mocumbi AO. Forgotten cardiovascular diseases in Africa. Clin Res Cardiol 2010;99:65-74.
11. Salemi VM, Rochitte CE, Shiozaki AA, Andrade JM, Parga JR, de Avila LF et al. Late gadolinium enhancement magnetic resonance imaging in the diagnosis and prognosis of endomyocardial fibrosis patients. Circ Cardiovasc Imaging 2011;4:304-11.
12. Kim RJ, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445-53.
13. Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. Eur Heart J 2005;26:1461-74.
14. Barretto AC, Pileggi F. [Endomyocardial fibrosis: 100 cases, 10 years' experience]. Arq Bras Cardiol 1988;51:117-20.
15. Mady C, Barretto AC, Oliveira SA, Stolf N, Bellotti G, Pileggi F. Evolution of the endocardial fibrotic process in endomyocardial fibrosis. Am J Cardiol 1991;68:402-3.
16. Valiathan MS, Balakrishnan KG, Sankarkumar R, Kartha CC. Surgical treatment of endomyocardial fibrosis. Ann Thorac Surg 1987; 43: 68-73.
17. Moraes F, Lapa C, Hazin S, Tenorio E, Gomes C, Moraes CR. Surgery for endomyocardial fibrosis revisited. Eur J Cardiothorac Surg 1999;15:309-12; discussion 12-3.