

## CASE REPORT

### Cardiac sarcoidosis : two cases with autopsy findings

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#### Abstract

Cardiac sarcoidosis is a disease of young adults. In most cases it presents with sudden death, arrhythmias, conduction disorders, heart failure or cardiomyopathy. The authors describe two cases of myocardial involvement by sarcoidosis that lead to death of the patients. Case one was a 26-year-old Indian man who was previously well and presented with sudden death. Autopsy showed nodules of sarcoid granuloma involving the heart, lungs and lymph nodes. Case two was a 47-year-old Indian lady who complained of reduced effort tolerance. Echocardiography showed that she had restrictive hypertrophic cardiomyopathy with heart failure. Seven months after initial presentation, she developed worsening of heart failure and died. Autopsy revealed involvement of the heart, lungs and liver by sarcoidosis.

**Key words :** Heart, autopsy, sarcoidosis, sudden death

#### INTRODUCTION

Sarcoidosis is a rare multisystemic disease characterized by the presence of noncaseating granulomas. Geographical variation in its incidence is well known and young adults are the relatively largest group of patients.<sup>1</sup> Mediastinal lymph nodes, liver, eyes, and skin are commonly involved. Autopsy studies show that about 20 to 50 percent of patients with sarcoidosis have cardiac involvement.<sup>2,3,4</sup> The most common manifestation of myocardial sarcoidosis was sudden cardiac death.<sup>3</sup> In this report we highlight two cases who had cardiac involvement and death due to sarcoidosis.

#### CASE REPORT

##### Case 1

A 26-year-old Indian man, a factory worker, was found dead in his room by his sister one morning. He was last seen alive at 10.00 pm the night before. He appeared to have been well and did not complain of any symptoms. He had no significant past medical history. There was no history of taking any drugs of abuse including alcohol consumption or smoking.

At autopsy, there were no external injuries

noted. The cardiovascular system examination revealed the heart, weighing 320 grams, to have transmural circumferential whitish streaks of fibrous tissue involving the apical regions of both ventricular walls extending to involve the distal two-thirds of the left ventricle. The interventricular septum was also similarly affected with lesions extending proximally until 2 cm above the atrioventricular junction. The right ventricular free wall measured 1 cm in thickness and left ventricular free wall measured 1.8 cm and interventricular septum 2 cm in thickness which was measured at 1 cm distal to the atrioventricular junction. The left ventricle contained a mural thrombus. The valves were grossly normal. Coronary arteries showed mild atherosclerosis with no significant narrowing of the lumen. The aorta was unremarkable. The lungs, liver, right kidney and spleen showed numerous pale grey, firm, ill defined fibrous nodules measuring from 0.5 cm to 1 cm in diameter. A few hilar and mesenteric lymph nodes were seen. They were soft in consistency and their sizes varied from 1 cm to 2 cm in diameter.

Microscopical examination of the fibrotic areas at the apex of the heart showed replacement of the heart muscle by numerous nodules consisting of clumps of epithelioid cells and

multinucleated giant cells surrounded by dense fibrous tissue (Figure 1). No caseous necrosis was seen. Scanty lymphocytes were noted around the granulomatous nodules. Sections from the lung, liver, right kidney, spleen and lymph nodes showed similar islands of non-caseating granuloma. Ziehl-Neelson and Grocott-Gomori Methanamine silver stains did not reveal any acid fast bacilli and fungi, respectively. The pancreas, stomach, duodenum and brain showed no abnormality. A diagnosis of sarcoidosis was made.

### Case 2

A 47-year-old Indian lady presented with dyspnoea and reduced effort tolerance of seven months duration. Chest radiograph showed gross cardiomegaly with pulmonary congestion. Electrocardiography revealed complete heart block. 2D echocardiogram revealed concentric left ventricular hypertrophy with ejection fraction of 55%. The ventricular septum and the apex were hypokinetic with moderate mitral regurgitation. Angiogram showed patent coronaries. 24-hour Holter monitoring was within normal

limits. A temporary pacemaker was inserted which was later replaced by a permanent cardiac pacemaker. Patient showed improvement of symptoms subsequent to that. Five months later she was readmitted with acute pulmonary oedema. Repeat echocardiogram showed left ventricular hypertrophy with ejection fraction of 21%. There was global hypokinesia with mild tricuspid and mitral regurgitation. The cardiac chambers were not dilated and no intracardiac clot was seen. Computed tomography of the thorax did not reveal any mass, lymphadenopathy or pulmonary embolic disease. Two months later she was again admitted with symptoms of heart failure. In the ward her condition deteriorated. Her heart failure worsening and she developed renal failure that required dialysis and finally she succumbed to her illness.

Autopsy findings showed an enlarged and dilated heart weighing 430 grams with concentric thickening of the left ventricular wall and extensive but patchy myocardial fibrosis of both ventricles and interventricular septum (Figure 2). The right and left ventricular free walls measured 1 cm and 2.4 cm in thickness respec-

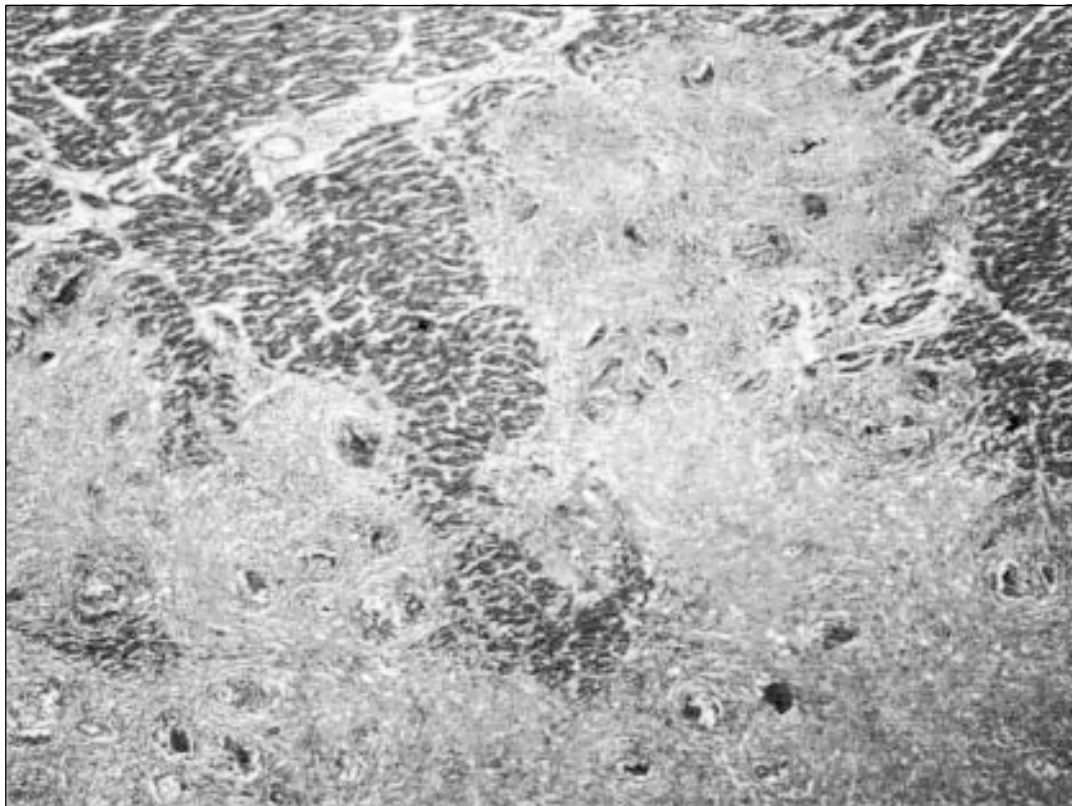


FIG. 1: Replacement of heart muscle by nodules consisting of clumps of epithelioid cells and multinucleated giant cells surrounded by dense fibrosis. H&E X 20.



FIG. 2: Gross appearance of the heart showing concentric thickening of both ventricular walls and extensive myocardial fibrosis of both ventricles and the interventricular septum.

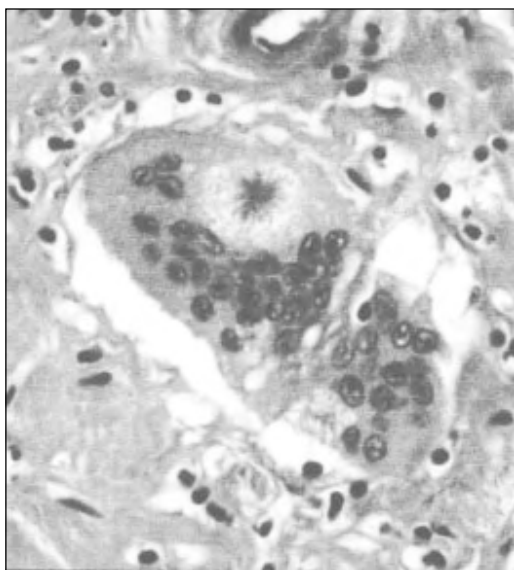


FIG. 3: Multinucleated giant cell containing asteroid body. H&E X 200.

tively and interventricular septum measured 2 cm at 2 cm distal to atrioventricular junction. Mural thrombus was seen in the right ventricular wall. The lungs showed oedema with no obvious nodules seen. There was pleural effusion and ascites noted. The liver was enlarged and showed a nutmeg appearance. The other organ systems appeared unremarkable.

Microscopical examination of the fibrotic

area in the heart showed mainly fibrous tissue with scattered multinucleated giant cells. Some of the multinucleated giant cells contained asteroid bodies (Figure 3). Scanty lymphocytes were noted around the nodules. No necrosis was noted. Special stains did not detect any acid fast bacilli or fungi.

Sections from the lungs showed fibrosis around the main vessels and bronchi near the hilar region with scattered non-caseating granulomas similar to the lesions in the heart. There was also evidence of interstitial pneumonitis with infiltration of lymphocytes and foamy macrophages in the alveolar septae. The liver showed focal areas of similar non-caseating granulomatous lesions. Centrilobular congestion with adjacent fatty change was also present.

### DISCUSSION

These two cases illustrate two different modes of death in patients with myocardial sarcoidosis. Sarcoidosis is a multisystemic granulomatous inflammatory reaction of unknown aetiology characterized by formation of non-caseating granulomas in affected tissues. Since other diseases including mycobacterial or fungal infections and berylliosis can also produce non-caseating granulomas, the histological diagnosis of sarcoidosis must be made by exclusion.<sup>5</sup>

Involvement of the heart by sarcoidosis is well established whether it occurs in isolation<sup>6,7</sup> or in association with systemic involvement. It

is estimated that the heart is affected in 20 to 50 percent of autopsied patients with sarcoidosis.<sup>2,3,4</sup> However, these figures represent a population bias as sudden death is a common manifestation of cardiac involvement, thus favouring autopsy of those patients with cardiac involvement. Clinical manifestation of cardiac sarcoidosis is uncommon, occurring in about five percent of cases.<sup>8,9</sup> The clinical presentation depends upon the extent of organ involvement and location of the lesions. In a great majority of cases, patients seek medical attention because of the insidious onset of respiratory symptoms (shortness of breath, cough, chest pain, hemoptysis) or constitutional signs and symptoms (fever, fatigue, weight loss, anorexia, night sweats). Fatal outcome is most significantly contributed by heart and lung involvement<sup>10</sup> as was seen in our two cases.

Cardiac manifestation include conduction abnormalities, ventricular arrhythmias, sudden loss of consciousness due to cardiac arrest, atypical angina pectoris, pericarditis, ventricular aneurysms, cardiomyopathy, congestive cardiac failure and sudden death.<sup>4,5,8,11,12</sup> Fleming and others have observed that sudden death is the most common manifestation of myocardial involvement occurring in about 65 percent of patients with sarcoidosis.<sup>13,14,15</sup> The major causes of death in patients with cardiac sarcoidosis are arrhythmias or conduction block which occurred in the first case, and congestive heart failure as in second case.<sup>3,4,12</sup>

The most common sites of involvement in the heart are the interventricular septum base (conduction abnormality, heart block), the left free wall (aneurysms, heart failure, arrhythmias) and the papillary muscles (heart failure).<sup>11</sup> Sarcoid involvement of the conduction system has been reported, and some feel that the disease has an affinity for this area.<sup>12,16</sup> Therefore conduction system sampling in the region of sinoatrial and atrioventricular nodes should be performed in cases of sudden unexpected death in young persons in order not to miss the diagnosis. In both of our cases, proper examination and sampling for histology of the conduction system region were not done. However, in the first case the atrioventricular node was likely to be involved based on gross examination could have caused sudden cardiac death due to arrhythmia.

Ante-mortem diagnosis of cardiac sarcoidosis is often difficult to establish. In only 29% of cases was the antemortem diagnosis accurate.<sup>3</sup> Angiotensin converting enzyme (ACE) levels

are often elevated but are not specific for sarcoidosis. Echocardiography may demonstrate enhancement of the lesions that may give a clue to the diagnosis however it is also not specific. Changes on electrocardiogram may mimic myocardial infarction.<sup>11</sup> The most reliable method of diagnosis is endomyocardial biopsy in conjunction with biopsies of thoracic lymph nodes and other organs. However, because of the scattered nature of the lesions, the diagnostic rate achieved with biopsy in cardiac sarcoidosis is low.<sup>17</sup> Thus, a negative biopsy does not rule out cardiac sarcoidosis.<sup>2,8</sup> Since the procedure is invasive and not without significant risk it is done only in selected cases.

Visible lesions on gross examination of the heart are the exception. In a large autopsy series of sarcoidosis patients, gross myocardial lesions were found in only 17 percent of cases involved.<sup>4</sup> When seen, the areas are pale, white, infiltrative, and may be centered near the base of the left ventricle. In both cases in our report, gross myocardial lesions were seen as fibrous whitish streaks.

On microscopic examination, the granulomas are composed of epithelioid cells and multinucleated giant cells which are characteristically non-caseating. Commonly there are small numbers of surrounding lymphocytes and plasma cells (naked granuloma). The giant cells may contain asteroid bodies, Schaumann bodies or other microcalcifications which is classically seen but not pathognomonic for sarcoidosis and this was shown in the second case. With therapy, or by regression, fibrosis may be prominent, which may lead to ventricular aneurysm formation and may be misinterpreted as ischaemic fibrosis during autopsy.<sup>7</sup>

Cardiac sarcoidosis may have histological similarities to giant cell myocarditis. However, in giant cell myocarditis, myocytic destruction, macrophagic giant cells and eosinophils are present whereas cardiac sarcoidosis is an interstitial granulomatous disease without myocytic necrosis.<sup>18</sup>

Treatment in patients with cardiac sarcoidosis includes steroid therapy, anti-arrhythmic drugs, implantable cardioverter defibrillator and cardiac transplantation.<sup>13,15,19,20</sup> The overall prognosis of patients with myocardial sarcoidosis is poor. In the chronic type the one-year survival rate ranges between 25 and 75 percent.<sup>5,21</sup>

In summary even though myocardial sarcoidosis is rare, it should be considered as one of the causes of sudden cardiac death in young patients. The findings of restrictive cardiomy-



opathy with hypokinesia of the heart on echocardiogram in a patient should raise the suspicion of this condition.

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