Sarcoid Heart Disease: A Case Report and Literature Review

Fayez EL Shaer¹²*, Shahd Al-Awad¹, Abdulmohsen Alghamdi, Amer AlFaqih¹
Hamdan Al Shehri¹³, Mostafa Alshimiri¹

¹King Fahad Cardiac Center, Department of Cardiac Sciences, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
²National Heart Institute, Cairo, Egypt.
³Assistant Professor of Internal Medicine, Najran University, College of Medicine, Internal Medicine Department, Saudi Arabia.

* Email: felshaer@ksu.edu.sa

ABSTRACT
Sarcoid Heart Disease (SHD), often misdiagnosed as tuberculosis is a potentially life-threatening condition. Cardiac manifestation of sarcoidosis is a challenging clinical condition as it is associated with pericarditis, heart block, ventricular arrhythmias, valve dysfunction, ventricular aneurysm, sudden cardiac death, and heart failure. This study presents a case of a syncopal attack due to complete heart block, which is the first indication of SHD. The study has also presented a literature review on the various management options employed for therapeutic and effective management of SHD. The study has proposed treatment approaches, such as Cardiac Magnetic Resonance (CMR), Magnetic Resonance Imaging (MRI), and Insertion of an Implantable Cardioverter Defibrillators (ICD) in patients with complete heart block to improve the quality of life and increase overall survival rates.

Key words: Arrhythmias, Cardiac Sarcoidosis, Cardiomyopathy, Heart Block.

INTRODUCTION
Sarcoidosis is a multisystem inflammatory disorder of unknown etiology characterized by the presence of tiny lumps of cells in organs known as granulomas. There are numerous sites involved in sarcoidosis including lungs, skin, eyes, parotid gland, spleen, liver, and heart. Granulomas are an aggregation of macrophages having an epithelioid like appearance surrounded by a rim of lymphocytes observed in response to various inflammatory triggers throughout the body organs [1]. Presentation of granulomas cannot be considered as the only symptom to diagnose Sarcoidosis, as many diseases such as Tuberculosis and Berylliosis also cause granulomatous inflammation [2-4]. Thus, Sarcoidosis requires correct clinical diagnosis and proper radiological and clinicopathological correlation in treatment [5].

Cardiac Sarcoidosis (CS) is found worldwide but most cases are reported in northern Europeans and African Americans, particularly in women [6]. However, the prevalence of sarcoidosis is potentially underestimated since many individuals with this disease have nonspecific symptoms. This disease affects patients from different regions and ages, with a prevalence of about 4.7 to 64 in 100,000 [6, 7]. The occurrence of sarcoidosis varies from the absence of symptoms demonstrating abnormal imaging to the heart failure and syncope due to arrhythmias resulting in sudden cardiac arrest [7]. It can also be presented in the forms of systemic complaints, pulmonary...
complaints, Löfgren syndrome (i.e., fever, bilateral hilar lymphadenopathy, and polyarthralgia) or dermatologic, ocular, and cardiac manifestations [5, 8].

Arrhythmia, also known as dysrhythmia results in either too fast, too slow heartbeat, or irregular heart rhythm [9]. Arrhythmia has two types: tachycardia (fast heartbeat) and bradycardia (slow heartbeat) [10]. SHD can result in both types of arrhythmias due to granuloma formation in the myocardium. This condition may result in a complete heart block (23-30%), bundle branch block (12-32%), ventricular tachycardia (23%), congestive heart failure (25-75%), and sudden death (25-65%) [11]. Sarcoi infiltration involves the cardiac structure, mainly myocardium in the left ventricular free wall and papillary muscle, basal septal wall, free wall of the right ventricle, and aria [12]. The diagnosis of cardiac sarcoidosis has improved with the development of cardiac magnetic resonance. In cardiac sarcoidosis, both atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are released indicating the presence of the disease. Approximately 25% of patients have non-caseation granulomas during autopsy with less than 5% having a clinical cardiac manifestation [13]. Ventricular tachyarrhythmia is a life-threatening condition with an incident of 15% per year. It can be managed by a corticosteroid in the early stage; while, intra-cardiac defibrillator (ICD) is required in advanced stage [14, 15].

More than 75% of the patients respond to symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs); while, patients with persistent pulmonary tuberculosis (15%) or extra-pulmonary tuberculosis (10%) require corticosteroid therapy [16]. These medicines can be administered by either one mg/kg per day or 40 mg per day dosage with tapering over several weeks [17]. Methotrexate (MTX) can be used as a corticosteroid-sparing strategy in chronic sarcoidosis for patients who are resistant to steroids or have side effects from steroids [18, 19]. Patients with SHD are monitored every 6-12 months to check their pulmonary function and chest radiography by an annual slit-lamp eye examination and ECGs [20]. This study has presented a case to examine the findings and management of a patient with sarcoid heart disease admitted to the cardiac center with a complete heart block.

Case Study
A 45-year-old man, working as a car maintenance technician, was presented at the emergency department with a history of syncopal attack, which occurred on the morning of the same day. The patient suffers from type II diabetes mellitus, hypertension, and is on regular medication; however, he was experiencing dizziness since the last 2 days. For the last 4 days, the patient had also experienced exertional chest pain, mainly in the left parasternal region characterized by heaviness with no radiation. The patient had also experienced shortness of breath (as per the New York Heart Association (NYHA), classification II), since the last 2 months.

Physical examination of the patient revealed the normal heartbeat with a regular heart rate of 43 b/m, no edema in lower limbs, intact peripheral pulsation; while, jugular venous pressure showed occasional Cannon wave.

<table>
<thead>
<tr>
<th>Table 1. Lab Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chest</strong></td>
</tr>
<tr>
<td>Abdomen</td>
</tr>
<tr>
<td>Vitals</td>
</tr>
<tr>
<td>Heart rate</td>
</tr>
<tr>
<td>RR</td>
</tr>
<tr>
<td>Blood Pressure</td>
</tr>
<tr>
<td>SpO2</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>Hemoglobin</td>
</tr>
<tr>
<td>Platelet</td>
</tr>
<tr>
<td>Na</td>
</tr>
<tr>
<td>Creatinine</td>
</tr>
<tr>
<td>Urea</td>
</tr>
<tr>
<td>Magnesium</td>
</tr>
<tr>
<td>Phosphorus</td>
</tr>
<tr>
<td>Ca</td>
</tr>
<tr>
<td>INR</td>
</tr>
<tr>
<td>Total CK</td>
</tr>
<tr>
<td>Lactic acid</td>
</tr>
<tr>
<td>ALT</td>
</tr>
</tbody>
</table>
Echocardiography (ECHO) showed a 3rd-degree atrioventricular (AV) nodal block at a rate of 43 b/m with a narrow QRS complex (Figure 1a). The patient was admitted as a case syncope due to complete heart block with uncontrolled hypertension. In the emergency room, the patient was managed by atropine and a transcutaneous pacemaker together, with intensifying oral antihypertensive medication. CXR showed bilateral hilar lymphadenopathy as well as small bilateral pulmonary infiltration that predominantly involved mid-upper lung zones (Figure 1b). This further strengthened sarcoidosis as a strong differential diagnosis.

Pulmonary function test (PFT) demonstrated a restrictive lung defect in which there was a decrease in FEV₁ and FVC, however, the FEV₁/FVC ratio was >80%, which further supported the preliminary hypothesis of interstitial restrictive lung disease. ECHO showed normal LV and RV cavity size, wall thickness, normal overall systolic function (estimated LVEF 55-60%), and impaired relaxation with no regional wall motion abnormalities (Figure 2). The echocardiography showed no significant valvulopathy or underlying restrictive cardiomyopathy.

Cardiac catheterization was conducted to rule out coronary artery disease revealing almost normal coronary angiography with no flow-limiting lesion (Figure 3). The exercise test was conducted to detect the response of the high-grade heart block, which revealed worsening of heart block with a widening of QRS duration and no increase in heart rate. Cardiac MRI showed basal septal gadolinium enhancement (Figure 4).

CT report of the chest showed multiple indeterminate lung nodules (Figure 5a). High-resolution CT thorax (HRCT) showed established patterns of fibrosis in a honeycombing pattern with reticular opacities. CT abdomen showed evidence of hepatosplenomegaly with multiple Granulomatous lesions involving the liver and spleen (Figure 5b). This is considered as the main diagnosis of sarcoidosis; however, other possibilities such as lymphoma or fungal infection may also be possible. Endobronchial ultrasound, transbronchial needle aspiration biopsy (EBUS-TBNA) was performed on the hilar nodes showing the evidence of non-caseating granulomatous inflammation. In addition, biopsy samples were sent to microbiology for culture and sensitivity to rule out any other possible infectious etiologies of granulomatous inflammation.

During admission, the patient developed two episodes of electrical pauses. The first one lasted 5.5 seconds while he was asleep; whereas, the second pause was for 7.8 seconds. The patient was completely asymptomatic despite these episodes. Cardiac sarcoidosis was diagnosed on a clinical basis with basal septal gadolinium enhancement, together with the presence of extra-cardiac manifestation, and exclusion of tuberculosis. The patient was started on Prednisone 60mg PO OD with GI prophylaxis, insulin for diabetes control, and angiotensin blocker combination with calcium channel blocker. The patient clinically improved but still was in a complete heart block. Thereafter, he developed a ventricular tachycardia while planned for permanent pacemaker insertion. Dual-Chamber ICD with pacing capability was implanted. Meanwhile, the patient had another attack of non-sustained ventricular tachycardia. Beta-blocker initiated together with the reprogramming of the ICD, while he continued on corticosteroid 60mg by the rheumatologist. The patient was then discharged and followed in the outpatient clinic by the rheumatologist for gradual tapering of steroids and electrophysiology clinic.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST</td>
<td>15</td>
</tr>
<tr>
<td>Troponin-I</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>APTT</td>
<td>39.20</td>
</tr>
<tr>
<td>PPD</td>
<td>&lt; 5 mm</td>
</tr>
<tr>
<td>Quantiferon test</td>
<td>Indeterminate</td>
</tr>
</tbody>
</table>

**Figure 1:** (a) ECG of the patient; (b) X-ray of the patient’s chest
Figure 2: An ECHO view; (a) An ECHO 2 chamber view; (b) An ECHO short axis view; (c); (d) An ECHO 4-chamber view

Figure 3: The cardiac catheterization of the normal coronaries

Figure 4: CMR gadolinium enhancement of the septum
DISCUSSION

Cardiac involvement in sarcoidosis is a challenging clinical condition with an unpredictable course and progressive chronicity. Approximately, 20-30% of sarcoïd patients have heart lesions; while, less than 5% of subjects are presented with clinical manifestations [19, 21]. Awareness about such cases is necessary due to the rarity of cardiac manifestation for rapid diagnosis and management. This requires a special strategy and specific algorithm to manage cost expenditure and shorten the length of hospital stay.

In the current case, the first presentation of sarcoïd heart disease was a complete heart block in a young patient. A number of different diagnoses were warranted before establishing the actual diagnosis to rule out ischemic heart disease, valvular heart disease, myocardial disease, and cardiomyopathy. Such cases with complete heart block initially require ECG examination followed by CMR examination, arrhythmia assessment using Holter monitoring and stress testing, and assessment of extra-cardiac and systemic manifestations [22].

Focal myocardial sarcoïd granuloma results in disturbed automaticity, which further causes the reoccurrence of tachyarrhythmia. The ventricular tachycardia (VT) is considered as the most common recurring kind of arrhythmia [23]. Roberts et al. [24] found that arrhythmia causes sudden death as a terminal event in sarcoïd heart disease in 67% cases. However, supra-ventricular arrhythmias occur in 15-17% of cases resulting in atrial dilatation and/or pulmonary involvement due to atrial granuloma. About 23-30% of patients were reported with complete heart block after granuloma of the basal septum with scar formation or ischemia, which involves the atroventricular nodal artery [11, 13, 25].

Around 25% of cases of cardiac sarcoïdosis are followed by progressive congestive heart failure. This occurs due to extensive myocardial involvement with the formation of a ventricular aneurysm, pulmonary hypertension due to pulmonary involvement (core Pulmonale), and valve regurgitation or a combination of all [26]. Other clinical presentations of sarcoïd heart disease vary from chest pain, impersonation of an acute coronary syndrome, acute pericarditis with pericardial effusion, and cardiac tamponade to constrictive pericarditis [27].

Laboratory tests have demonstrated many biomarkers of sarcoïdosis such as Serum Amyloid A (SAA), Angiotensin-Converting Enzyme (ACE), the Glycoprotein KL-6 and soluble interleukin-2 receptor (sIL-2R), Chitotriosidase (CTO), Lysozyme, etc. [28]. In addition, hypercalcemia is a common laboratory finding in sarcoïdosis resulting from non-caseating granuloma secreting excess 1,25-dihydroxy vitamin D3 [29]. Cardiopulmonary exercise studies are requested to assess the peak oxygen consumption in case of heart failure. This assists doctors to examine reasons for dyspnea and fatigue to precisely differentiate between cardiac and pulmonary disorders. It also helps to optimize the decision-making process and outcome prediction, while
determining targets for therapies [30]. ECHO is inefficient in determining which patient is more likely to develop high-risk arrhythmias, however, abnormalities can be detected in the advanced stage in 14% cases [11]. These abnormalities can range from diastolic dysfunction, systolic dysfunction with regional wall motion abnormalities, ventricular aneurysms, valve regurgitation, and pericardial effusion. Cardiac lesions can imitate hypertrophic cardiomyopathy as it may cause localized hypertrophy of the septal wall. However, it is missed at the early disease stage due to the lack of sensitivity of 2D echocardiography. Tissue characterization using backscatter that detects the acoustic character of the myocardium has a sensitivity of 75% in the early detection of SHD [31].

A gallium-67 scintigraphy test is positive when the disease is active as it will accumulate only in an area of active inflammation. It is useful to detect the presence or absence of inflammation and response to corticosteroid therapy [11]. Positron emission tomography (PET) 18F-FDG is more sensitive for myocardial involvement compared to thallium 201 SPECT and gallium-67 scintigraphy. The specification is not established as the heterogeneous uptake of FDG may occur in cases with idiopathic dilated cardiomyopathy [11]. CMR is highly sensitive in detecting early myocardial involvement, reliable in terms of assessing cardiac anatomy, function, inflammation, stress perfusion-fibrosis, aortic distensibility, and iron and fat deposition. Therefore, it constitutes an excellent tool for early diagnosis of cardiovascular involvement, risk stratification, treatment evaluation, and long-term follow-up of patients. Yazaki et al. [31] proved that a starting dose of 30 mg/day is enough for a better prognosis. After 2–3 months, the tapering should be discontinued if the disease is under control after the subsequent evaluation [11]. Subsequent evaluation is done after 1-3 months and if the disease is under control, the dosage is reduced to 5-15 mg daily to be continued for 9-12 months [37]. Studies also confirm that no difference between higher doses than 50 mg compared to doses of less than 30 mg daily. The patient should be followed for at least 3 years to rule out relapse and ensure complete recovery [38]. Corticosteroid therapy halts the deterioration of LV function and maintains the normal LV systolic function. It can also improve mild to moderate LV systolic dysfunction [38]. However, an observational study showed no improvement in severe LV systolic dysfunction; whereas, there was improvement in ejection fraction (<35%), with no improvement in milder LV systolic dysfunction [39].

Non-corticosteroid agents such as methotrexate, azathioprine, or cyclophosphamide can be used in refractory cases necessitating a high dose of corticosteroid complicated with an adverse effect [39]. Antiarrhythmic beta-blockers are used to treat tachyarrhythmia; however, there is no clear evidence-based medicine in patients with sarcoidosis. Amiodarone is used as a broad-spectrum anti-arrhythmic, however, it can cause lung fibrosis [11]. An intra-cardiac defibrillator is recommended in the case of non-sustained ventricular tachycardia as there is a high chance for recurrence despite anti-arrhythmic therapy and corticosteroid [24]. Similarly, an ICD with pacing...
capability was inserted for our patient for the high-grade AV block. Cardiac transplantation is very rare but still an option in end-stage heart failure with recurrent persistent ventricular tachycardia especially in younger patients [11].

Data related to mortality is relatively limited. In the United States, death tends to mainly result from end-stage lung disease and right-side heart failure [40]. Independent predictors of mortality are functional status class (NYHA), left ventricular end-diastolic diameter, and arrhythmias (VT). Poor prognosis occurs with the worsening of left ventricular systolic function and functional status [31]. Corticosteroid therapy is vital as it improves outcomes, decreases ventricular arrhythmias, and even lead to a complete recovery of atrioventricular conduction [41].

CONCLUSION

This study has presented a literature review and a case report providing a detailed account of SHD and its management. The study found that the diagnosis of cardiac sarcoidosis follows a procedure beginning from echocardiography; while, ending at either cardiac transplantation, ICD, or death. The asymptomatic condition or mixed symptoms are accounted for the limitation of the successful diagnosis of SHD.

With the high index of suspicion, it is highly recommended to follow a specific algorithm for diagnosis and management of cardiac sarcoidosis, which will be more cost-effective and shorten hospital stay. Both, cardiac and systemic magnetic resonance imaging should be done as early as possible when sarcoidosis was suspected. Corticosteroid should be started as early as possible upon establishing the diagnosis of sarcoidosis. Intra-cardiac defibrillator with pacing capability considered early when arrhythmia detected due to a high chance for sudden cardiac death. Follow up is required of these patients every 6 months by chest X-ray, pulmonary function test, electrocardiography, as well as annual Slit-lamp eye examination.

ACKNOWLEDGMENT

The author is very thankful to all the associated personnel in any reference that contributed in/for the purpose of this research. This research is not funded by any resource.

REFERENCES

7. Blankstein R, Stewart GC, McKenna WJ.: Clinical Manifestation and Diagnosis of Cardiac Sarcoidosis. 2018


