Left Ventricular Aneurysm and Ventricular Tachycardia as Initial Presentation of Cardiac Sarcoidosis

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Abstract

Context: Cardiac sarcoidosis (CS) is a rare, potentially fatal disease. It has a wide range of clinical presentations that range from asymptomatic electrocardiogram changes to sudden cardiac death. Ventricular aneurysms and ventricular tachycardia are seen late in the disease, and are rarely the presenting manifestation of the disease. Diagnosis of CS is challenging and often missed or delayed. Case Report: We report a 35-year-old patient who presented with sustained ventricular tachycardia and ST-elevation on electrocardiogram. Cardiac catheterization showed normal coronaries and left ventricular aneurysm. Subsequent 2D-echocardiography showed an infiltrative disease pattern. Cardiac MRI was done and showed late gadolinium enhancement in the septum, apex and lateral wall. The patient was diagnosed with cardiac sarcoidosis and treated with immune suppression and antiarrhythmic agent. In addition underwent AICD implantation. Conclusion: Our case highlights the importance of suspecting cardiac sarcoidosis in young patients presenting with electrocardiogram changes, and present an atypical presentation of this disease.

Keywords: Aneurysm, Cardiac sarcoidosis, ST-elevation, Ventricular tachycardia

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Introduction

Sarcoidosis is a multiorgan, granulomatous disease of unknown etiology. Non-caseating granulomas are the pathological hallmark of this disease. Studies have suggested that it might be an immunological response to unidentified antigenic triggers. The highest incidence is reported in northern European and African individuals, especially in women. In the United States, the annual incidence is estimated to be 10.9 per 100,000 in whites and 35.5 per 100,000 in African Americans.[1,2]

Cardiac sarcoidosis (CS) can precede, follow, or occur simultaneously with other organs involvement. However, isolated cardiac involvement can occur. Symptomatic cardiac involvement is seen in around 5% of patients with sarcoidosis. Autopsy studies estimate the prevalence of cardiac involvement to be at least 25% of the patients with sarcoidosis.[3] Imaging studies with late gadolinium enhancement-cardiac magnetic resonance (LGE-CMR) show asymptomatic cardiac involvement in 19-25.9% of patients with extra-cardiac sarcoidosis.[3-5] CS alters the prognosis for those who are affected, and accounts for as many as 13-25% of deaths from sarcoidosis.[4]

Case Presentation

A 35-year-old African American female, with a history of pulmonary sarcoidosis, presented to the emergency department with a 1-hour history of palpitations and light headedness. No chest pain, shortness of breath, loss of consciousness, other significant symptoms, or similar previous episodes were reported. She was diagnosed with pulmonary sarcoidosis 3 years ago by mediastinal lymph node biopsy. She denied taking any medications. No history of smoking, drinking, or drug abuse was reported.
On examination, she was alert and oriented. Her vital signs showed a heart rate of 224 beats/minute, blood pressure of 138/92 mmHg, respiratory rate of 18, temperature of 98.2, and oxygen saturation of 99% on room air. No significant findings were found on physical examination. 12-lead electrocardiogram (EKG) showed a wide-complex tachycardia, ventricular rate of 225/minute, extreme axis, right-bundle pattern in lead V1, and Q-waves in the lateral leads. A decision was made to electively cardiovert the patient. Sinus rhythm was successfully restored, and amiodarone drip was started. Subsequent EKG showed normal sinus rhythm and ST-segment elevations in the lateral leads. Hence, a decision was made to send the patient for emergent cardiac catheterization. Coronary angiogram did not reveal any radiological evidence of coronary artery disease. Left ventriculography showed global left ventricular hypokinesis with an estimated ejection fraction (EF) of 35%. Additionally, an anteroapical segment aneurysm was identified [Figure 1].

2D-Echocardiogram showed dilated left ventricle with moderate concentric hypertrophy and an echogenicity involving the basal to mid septum, consistent with an infiltrative disease [Figure 2]. Due to the high likelihood of an underlying CS, a CMR with gadolinium enhancement was done and showed thickening of the left ventricular myocardium, seen particularly in the septum, and decreased EF of 40%. Delayed images showed diffuse, patchy, transmural and subepicardial gadolinium enhancement involving the septum, apex and lateral wall [Figures 3 and 4]. Additionally, an anteroapical wall ventricular aneurysm was seen [Figure 5].

The patient was diagnosed with cardiac sarcoidosis complicated by ventricular aneurysm formation and ventricular tachycardia. She was switched to oral amiodarone and underwent AICD implantation for secondary prevention of life-threatening arrhythmias. The patient was discharged from the hospital with no further arrhythmias during her stay.

**Figure 1:** Left ventriculography, right-anterior-oblique cranial view: Anteroapical segment aneurysm

**Figure 2:** 2D-Echocardiogram, parasternal long axis view: Dilated left ventricle, moderate concentric hypertrophy. Echogenicity in the basal to mid septum

**Figure 3:** LGE-CMR, two-chamber view: Diffuse patchy transmural as well as subepicardial late gadolinium enhancement

**Figure 4:** LGE-CMR, shortaxis view: Diffuse patchy transmural as well as subepicardial late gadolinium enhancement
Discussion

The clinical presentations of CS are wide and variable; they can range from asymptomatic electrocardiographic changes to sudden cardiac death. The clinical manifestations are usually related to the location and extent of granulomas.

Electrophysiological abnormalities in cardiac sarcoidosis include conduction abnormalities and ventricular and supraventricular arrhythmias. Conduction abnormalities occur in up to 62% of patients during the disease course and usually present as complete heart block. Ventricular arrhythmias occur in up to 42% of patients during the disease course. They usually result from direct granulomatous involvement of the myocardium and might persist despite medical treatment.[2]

Unlike the conduction abnormalities that develop in the inflammatory phase of the disease, ventricular arrhythmias are not closely related to the disease activity, and frequently develop in the advanced stages.[6] Supraventricular arrhythmias occur less frequently than ventricular arrhythmias. They are usually the result of atrial dilatation due to left ventricular dysfunction, cor-pulmonale, or direct granulomatous involvement of the atria. Other findings on the electrocardiogram include pseudoinfarction patterns that mimic myocardial infarction and non-specific repolarization changes.

Heart failure occurs in 10%-30% of the patients during the disease course. Ventricular dysfunction can be systolic, diastolic, or both. Ventricular aneurysms result from direct myocardial involvement, which unlike ischemic aneurysms; do not follow a coronary artery distribution. Pericardial effusions are seen in up to 19% of patients. Rarely, symptomatic pericarditis, constrictive pericarditis, or cardiac tamponade can be seen. Mitral valve regurgitation is the most common encountered valvular lesion in CS, and is usually the result of papillary muscles dysfunction or direct granulomatous involvement of the valve leaflets.[3] Sudden cardiac death is the most feared cardiac manifestation of CS and usually results from either ventricular arrhythmias or complete heart block. It is the most common cause of death in CS and responsible for 24%-64% of all deaths in the USA.[21] Progressive heart failure is the second-most common cause of death and accounts for up to 25% of all the deaths in CS.[3] The most important independent predictors of mortality in CS are the New York Heart Association (NYHA) functional class, left ventricular end diastolic diameter, and presence of sustained VT.[8] Furthermore, patients presenting with ventricular aneurysm have been found to have a worse prognosis.[9]

The diagnosis of CS is challenging and often missed or delayed. Heart Rhythm Society expert consensus recommendations in July, 2014, identify CS by two pathways. The first requires the presence of non-caseating granulomas on histological examination of myocardial tissues with no other alternative cause. The second requires the presence of a histological diagnosis of extra-cardiac sarcoidosis, excluding other causes of cardiac manifestations, and one of the followings: steroid and/or immunosuppressant responsive cardiomyopathy or heart block, unexplained reduced LVEF (<40%), unexplained sustained (spontaneous or induced) VT, Mobitz type II second-degree heart block or third-degree heart block, patchy uptake on dedicated cardiac 18F-Flurodeoxyglucose-Positron Emission Tomography (FDG-PET), LGE-CMR, or a positive gallium uptake.[10]

CMR has an excellent sensitivity and specificity for the diagnosis of CS despite the lack of pathognomonic patterns.[10] The appearance of CS on CMR depends on the disease stage. In the acute setting, inflammation and edema are demonstrated by myocardial thickening and increased T2 signal with a subepicardial or midmyocardial enhancement patterns. In the chronic setting, granulomas cause focal areas of myocardial thinning resulting from scar formation.[11] This is mostly seen as delayed contrast enhancement in areas of granuloma and scar formation that is frequently patchy and nodular. The myocardial lesions are predominantly localized to the basal and subepicardial myocardium. This is atypical for myocardial infarction, which typically shows preferential hyper-enhancement of the subendocardial layer.[12] Similar to CMR, no pathognomonic findings for CS are seen on FDG-PET. CS is most typically associated with focal FDG uptake either in isolation or on a background of mild diffuse uptake with or without resting perfusion defects and wall motion abnormalities. Concomitant use of PET perfusion tracers can help exclude significant coronary
artery obstructive disease. In addition, FDG-PET can detect reversible stages of CS.

Lung or lymph node biopsies are usually done first in patients with extra-cardiac sarcoidosis due to their higher yield and lower risks. However, in cases of isolated CS or negative extra-cardiac biopsies, endomyocardial biopsy may be required to confirm the diagnosis. Non-caseating granulomas are found in less than 25% of patients due to the focal nature of the disease. Results can be enhanced by utilizing electrophysiological, PET, or CMR image-guided biopsies.[10]

Corticosteroids might halt the progression of cardiac disease and improve survival by slowing the progression of inflammation and fibrosis.[7] Superior results might be achieved if they are initiated early in the course of the disease.[5,8] They are most beneficial in CS patients with Mobitz-II or third-degree heart blocks,[13] frequent ventricular ectopy, non-sustained VT or sustained ventricular arrhythmias in the presence of an evidence of myocardial inflammation (Class IIa recommendations).[10,14] High dose prednisone (60-80 mg daily) is generally prescribed initially.[15] Nevertheless, lower initial doses (< 30 mg daily) can be used without affecting long-term prognosis.[8] Prednisone can be gradually tapered, once the disease is responding, over a period of six months and eventually discontinued.[15] Other immunosuppressive agents, such as infliximab, methotrexate, azathioprine, or cyclophosphamide, can be used in patients who can not tolerate or do not respond to prednisone therapy. However, data regarding their use is limited.[2]

Atrial and ventricular arrhythmias in patients with CS can be controlled with beta-blockers, calcium channel blockers, sotalol, dofetilide, and amiodarone. Class I agents are not recommended due to their adverse outcomes in patients with structural heart disease. Stepwise approach can be used in the management of ventricular arrhythmias; initial treatment with immunosuppression is followed by anti-arrhythmic medications, and finally catheter ablation in refractory or incessant cases (Class IIa recommendation).[10,14] VT/VF storm can be managed with combination therapy of anti-arrhythmic agents, usually amiodarone, and immunosuppression.

Cardioverter-defibrillator implantation is recommended in patients with spontaneous sustained ventricular arrhythmias, cardiac arrest, or in patients with LVED ≤ 35% despite optimal medical therapy and immunosuppression (Class I recommendation). ICD can be useful in patients with an indication for permanent pacemaker implantation, unexplained syncope or near syncope that is felt to be arrhythmic in origin, or inducible sustained ventricular arrhythmias (Class IIa recommendation). ICD can be considered in patients with LVEF of 36-49% and/or RVEF < 40% despite optimal medical therapy for heart failure and a period of immunosuppression (Class IIb recommendation).[10]

Heart failure due to CS is treated in the same way of that of other causes.[2] Patients with advanced heart failure or persistent ventricular arrhythmias not amenable to ablation might be considered for cardiac transplantation. Recipients show better one-year post-transplant survival when compared to cardiac transplant for all other indications. However, CS may recur in the transplanted heart.[15]

Screening for cardiac involvement is vital in patients with biopsy proven extra-cardiac sarcoidosis. This can be done initially by history, 12-lead electrocardiogram (Class I recommendation) and 2D-echocardiogram (Class IIa recommendation). Abnormalities can be investigated by advanced cardiac imaging with CMR or FDG-PET (Class IIa recommendation). Additionally, patients younger than 60 years with unexplained second-degree (Mobitz II) or third-degree AV block can be screened for CS with high resolution CT chest and/or advanced cardiac imaging (CMR or FDG-PET). Positive initial screening command extra-cardiac, if feasible, or image guided endomyocardial biopsies (Class IIa recommendation).[10]

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