A Case of Isolated Cardiac Sarcoidosis Diagnosed With Multimodality Cardiac Imaging

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INTRODUCTION

Sarcoidosis is an inflammatory granulomatous disorder of unclear etiology that can affect multiple different organ systems. Cardiac involvement is underrecognized. While it is thought that 5% of patients with sarcoidosis will demonstrate symptoms of cardiac involvement, the rate of subclinical cardiac sarcoid is believed to be much higher, with some estimates as high as 20%–25%.[1,2] Diagnosis of cardiac sarcoidosis (CS) can be difficult, even more so for cases with isolated cardiac involvement, and frequently a combination of imaging modalities along with biopsy is required. We report a case of a middle-aged man who presented with ventricular arrhythmia, was diagnosed with isolated CS with the use of multimodality imaging, and was treated successfully with oral steroids, guideline-directed medical therapy, and antiarrhythmic medications.

CASE PRESENTATION

A 54-year-old man with a medical history of well-controlled hypertension presented with fatigue of several weeks that limited his usual exercise routine. He was a long-distance runner who normally ran 5–8 miles per day but noticed that he was getting tired easily and had to walk instead of run. He denied chest discomfort, palpitations, lightheadedness, syncope, or shortness of breath. On examination he was afebrile with blood pressure 162/109 mm Hg and heart rate 145 beats per minute. He had no evidence of jugular venous distention and no peripheral edema. Lungs were clear to auscultation, and heart exam revealed an irregular fast rhythm without any murmurs or additional heart sounds. His electrocardiogram demonstrated an irregular wide complex rhythm with a right bundle pattern, superior axis, and a capture beat, consistent with ventricular tachycardia (Figure 1A). Laboratory workup, including troponin, was unremarkable. He was given intravenous metoprolol in the emergency department with successful conversion to sinus rhythm (Figure 1B), and he was admitted for further evaluation.

A transthoracic echocardiogram (TTE) showed moderately depressed left ventricular systolic function, with anterior, anteroseptal, anterolateral, and apical akinesis (Videos 1 and 2). Coronary angiogram showed mild coronary artery disease. Subsequent cardiac magnetic resonance imaging (MRI) revealed extensive late gadolinium enhancement (LGE) throughout the left ventricle and the free wall of the right ventricle with severe biventricular dysfunction (Figures 2A and B). He then underwent single photon-emitting computed tomography perfusion imaging, which demonstrated large resting perfusion defects in the anterior, apical, and basal inferoseptal segments of the left ventricle (Figure 3). This corresponded with marked fluorodeoxyglucose (FDG)-18 uptake in the same myocardial segments on FDG-18 positron-emitting tomography/computed tomography (PET/CT), consistent with CS (Figure 4A). Chest CT did not show parenchymal lung disease, and there was no subcarinal or hilar lymphadenopathy. The pulmonary team felt there was no clear target for transbronchial biopsy. Endomyocardial biopsy was also deferred due to overall low yield and convincing multimodality imaging. The patient underwent placement of an implantable cardioverter-defibrillator and was discharged on amiodarone and guideline-directed medical therapy for left ventricular systolic dysfunction, as well as prednisone 60 mg daily, with a plan for a slow taper over months.

Four months after the initial presentation, he was readmitted with recurrent ventricular tachycardia. On repeat imaging with FDG-18 PET/CT, he demonstrated complete resolution of FDG-18 myocardial uptake (Figure 4B). However, the left ventricular dysfunction and regional wall motion abnormalities remained unchanged on repeat TTE (Videos 3 and 4). He underwent ablation procedure for the ventricular tachycardia, which resulted in a lower burden of ventricular ectopy. On outpatient follow-up, he is doing well with continued remission of FDG myocardial uptake 9 months after his initial presentation. He is still on low-dose steroids.

DISCUSSION

Cardiac sarcoidosis is an uncommon entity, but it is thought to be underdiagnosed, perhaps in part due to the difficulty in recognizing the disease in early stages as well as previously unavailable imaging modalities that could provide tissue characterization.[1] The clinical manifestations of CS primarily include conduction abnormalities, ventricular arrhythmias, and heart failure. The most common rhythm disturbance is atrioventricular block.[1] The most common tachyarrhythmia is ventricular tachycardia and/or fibrillation,[1] which was the presenting symptom in our patient. The electrocardiogram abnormalities are neither sensitive nor specific for CS[2] and may include bundle branch block and/or fascicular block, ST/T wave changes, or pathological Q waves (pseudoinfarct pattern). Similarly, findings on TTE can be heterogeneous, although basal interventricular thinning may be a feature of CS. Other findings such as increased myocardial wall thickness, systolic dysfunction, diastolic dysfunction, wall motion abnormalities that do not follow a specific coronary distribution, and aneurysms are all associated with sarcoidosis.[2,3] A decrease in left ventricular global longitudinal strain is suggestive of myocardial infiltration.[2,3] However, this finding is not specific for the diagnosis of CS. Cardiac MRI offers regional tissue characterization and can demonstrate the edema associated with acute inflammation on T2-weighted

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Conflicts of Interest: None.

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VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiogram, four-chamber apical view, demonstrating regional wall motion abnormalities with apical, apical lateral, and anterolateral akinesis. Left ventricular systolic function is moderately reduced.

Video 2: Transthoracic echocardiogram, short-axis view, demonstrating regional wall motion abnormalities and moderately reduced systolic function.

Video 3: Transthoracic echocardiogram, four-chamber apical view, obtained after treatment with steroids, demonstrating persistent regional wall motion abnormalities at the apex of the left ventricle and moderately reduced systolic function.

Video 4: Transthoracic echocardiogram, short-axis parasternal window, obtained after treatment with steroids, demonstrating persistent regional wall motion abnormalities involving the anterior wall of the left ventricle and moderately reduced left ventricular systolic function.

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imaging, as well as the fibrosis/scar of more chronic disease by LGE.[3] There is no specific pattern of LGE on cardiac magnetic resonance that is diagnostic for CS, although usually it is patchy and multifocal with sparing of the endocardial border. Despite the advantages and high negative predictive value of cardiac MRI,[3] these findings can also be present in several other cardiac diseases. An FDG PET/CT scan is useful in the diagnosis of active inflammation and can demonstrate focal or diffuse FDG uptake. It is useful as a disease activity marker and can be used to monitor CS therapy. Perfusion defects and abnormal metabolism on FDG PET are associated with higher mortality and more ventricular tachycardia.[4] FDG PET has a sensitivity of 89% and a specificity of 78% for cardiac sarcoid, using the 2006 criteria developed by the Japanese Ministry of Health and Welfare.[5] More recently, techniques such as hybrid PET/MRI have been developed that have shown a sensitivity of 94% in the CS diagnosis using the same 2006 criteria.[6] Endomyocardial biopsy may be required to confirm the diagnosis, but its overall yield is low due to the focal nature of disease. In patients with extracardiac manifestations, lung or lymph node biopsy is usually the first target.

Several guidelines for the diagnosis of CS have been developed over the years. The revised guidelines of the Japanese Ministry of Health and Welfare in 2006 offered a histological pathway via endomyocardial biopsy demonstrating granulomas or a clinical pathway in which there is histological evidence of extracardiac sarcoid and specific clinical criteria.[7] The Heart Rhythm Society in 2014 expanded on these criteria in its consensus statement for diagnosis, including typical findings on both cardiac MRI and FDG-PET/CT.[8] The Japanese Circulation Society provided updated guidelines for the diagnosis of CS in 2016, which incorporate multimodality imaging techniques as a reliable diagnostic tool. The most notable addition is the development of criteria for isolated CS. These have a histologic pathway but also a clinical pathway that requires high tracer uptake on FDG PET, in addition to meeting at least three of the other major criteria (high-grade atrioventricular block, basal thinning of the ventricular septum, left ventricular dysfunction, MRI with LGE of the myocardium).[9] In our case, successful use of multimodality imaging led to the diagnosis of isolated CS and shows that biopsy may not always be required to make this challenging diagnosis (Figure 5).

Treatment of CS remains a challenge. Steroid therapy is the mainstay of treatment, despite a lack of randomized trials to demonstrate efficacy.[2] Immunosuppressive agents are also commonly used in treatment of CS, but they too lack convincing data.[1] Methotrexate is often used as a second-line agent in refractory cases. The management of the arrhythmias associated with CS can be difficult as well. Steroid therapy has not shown a consistent effect on arrhythmias.[1] Antiarrhythmic therapy can be useful in patients with ventricular arrhythmias refractory to immunosuppressive therapy. Ablation of ventricular arrhythmias has modest outcomes, with a recurrence rate as high as 86%.[3] This is partially because the arrhythmias often originate in areas of myocardium that are difficult to reach with ablation.[2,3] It can be considered in patients with ventricular arrhythmias refractory to immunosuppression and antiarrhythmic therapy. An implantable cardioverter-defibrillator is a class I indication for patients with cardiac sarcoid with documented ventricular arrhythmia as well as for those with a left ventricular ejection fraction <35% despite treatment with guideline-directed medical therapy and a trial of immunosuppression.[8]

CONCLUSION

This case serves to highlight the challenges in identifying and managing isolated CS. High clinical suspicion should be maintained for patients presenting with new heart failure, ventricular tachycardia, or

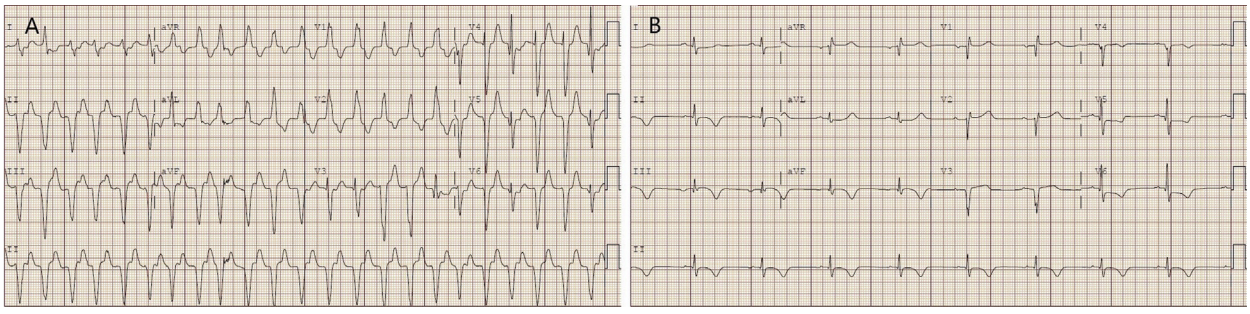

Figure 1 Electrocardiogram on initial presentation **(A)** demonstrating wide complex tachycardia with right bundle branch block morphology and superior access, as well as capture beats, consistent with ventricular tachycardia, alongside an electrocardiogram taken following administration of beta-blocker and amiodarone **(B)**, demonstrating sinus rhythm with diffuse repolarization changes.

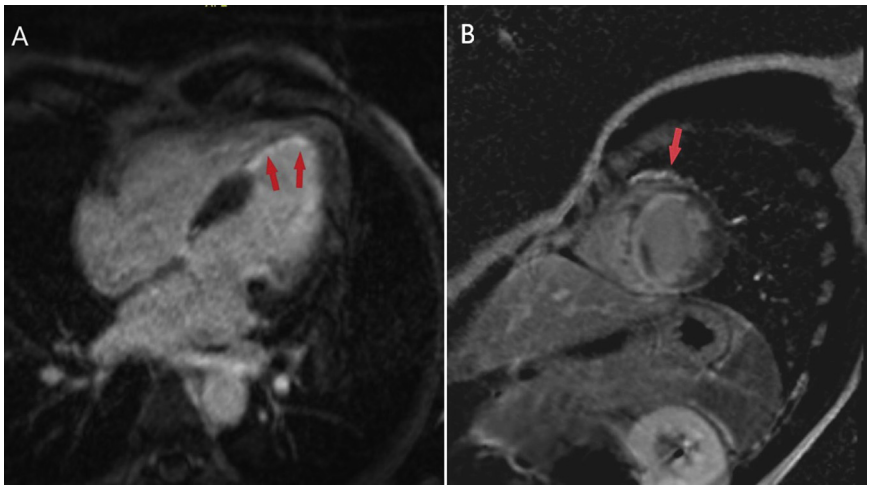

Figure 2 Cardiac MRI in the horizontal long-axis view **(A)**, revealing extensive LGE in the myocardium of the left ventricle (*red arrows*) and the short-axis view **(B)**, revealing LGE in the free wall of the right ventricle (*red arrow*).

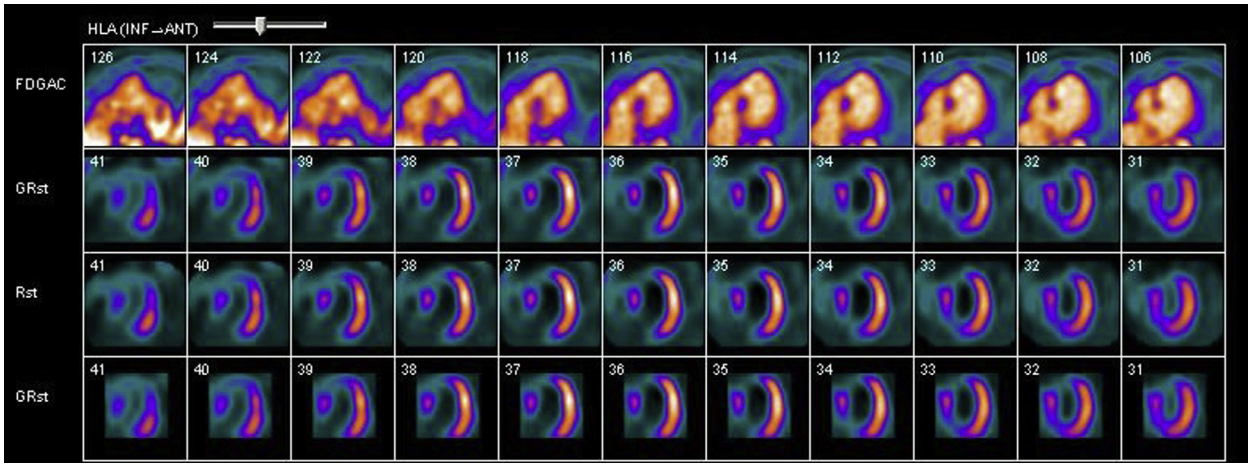

Figure 3 Single photon-emitting computed tomography images from the long-axis view, taken at rest, which demonstrate large resting perfusion defects in the anterior, apical, and basal inferoseptal segments of the left ventricle.

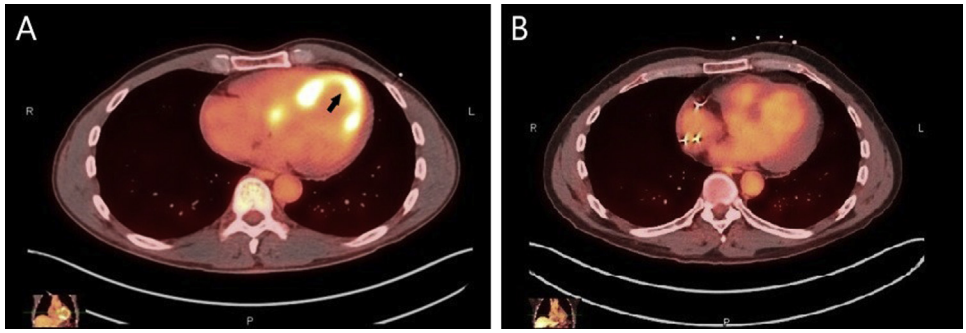

Figure 4 Fluorodeoxyglucose-18 PET/CT transaxial images at time of presentation **(A)** showing avid FDG-18 uptake in the myocardium of the left ventricle (*black arrow*) and following 4 months of treatment with oral steroids **(B)**, with complete resolution of FDG-18 uptake in the myocardium.

atrioventricular block. Echocardiography does not demonstrate specific findings, but the presence of basal interventricular thinning, wall motion abnormalities that do not follow a specific coronary distribution, and aneurysms may provide additional diagnostic clues. The use of multimodality imaging plays a pivotal role in the diagnosis of this entity. Cardiac magnetic resonance can demonstrate acute inflammation on T2-weighted imaging and fibrosis on LGE imaging, and FDG PET/CT can contribute to the diagnosis of the disease

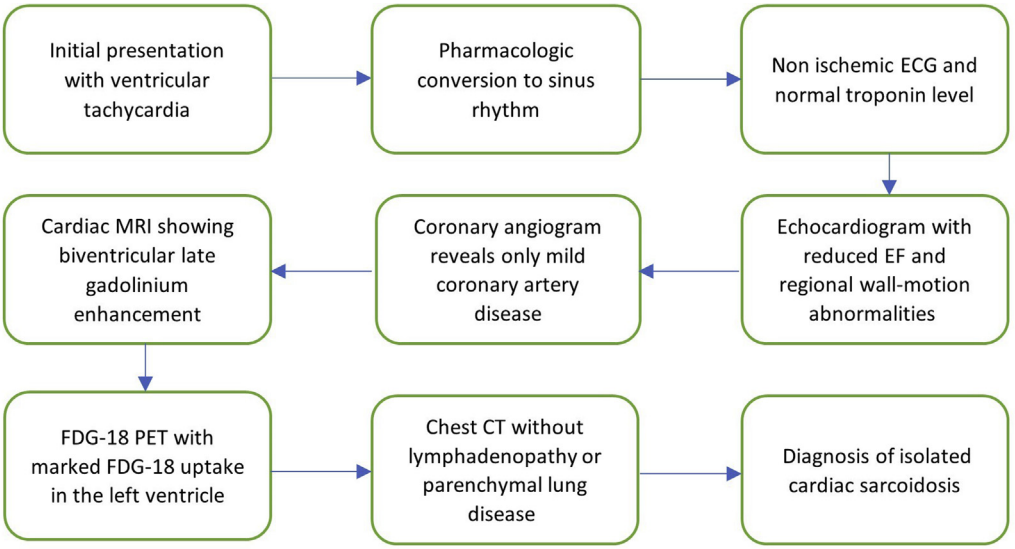

Figure 5 Flow chart illustrating the diagnostic workup for the patient in our case, starting with the presentation of ventricular tachycardia and culminating in the diagnosis of isolated CS, through successful combination of different cardiac imaging modalities.

and the monitoring of treatment and response to therapy. Management of isolated CS requires prolonged steroid therapy and sometimes immunosuppressive agents, along with guideline-directed medical therapy for patients with left ventricular dysfunction. Patients with ventricular arrhythmia are treated with steroids, antiarrhythmics, and placement of an implantable cardioverter-defibrillator.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2021.05.001.

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