

# A case of cardiac sarcoidosis with concurrent myocardial ischemia



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## Introduction

Sarcoidosis is a rare multisystem disease of unknown etiology affecting 10–40 in 100,000 population, characterized by granulomatous inflammation.<sup>1</sup> It has a diverse set of presentations ranging from diffuse to localized disease and can have either acute or chronic clinical course with multiple organ involvement.<sup>1</sup> Classically, lungs are the most commonly affected organ, but systemic, dermatologic, and cardiac involvement also occur. Specifically, 20%–30% of sarcoidosis patients have been observed to have cardiac involvement in an autopsy<sup>1</sup>; however, only about 5% have a symptomatic presentation with cardiac disease.<sup>1</sup> Cardiac sarcoidosis (CS) is a set of pathologies that occur owing to both active inflammation and granulomatous scarring in the heart. CS leads to arrhythmias, conduction abnormalities, and heart failure.<sup>1</sup> These abnormalities lead to significant morbidity and mortality, which is further undercut by challenges in diagnosing and screening CS. Early diagnosis of CS is essential to prevent such detrimental consequences. A definite diagnosis of CS remains difficult, especially in patients with confounding ischemic cardiac disease. We describe the case of a severe presentation of the rare condition, CS, that highlights the difficulty in diagnosis.

## Case report

The patient was a 62-year-old white man with hypertension, hyperlipidemia, type II diabetes mellitus, and biopsy-proven untreated pulmonary sarcoidosis diagnosed 2 years prior with minimal symptomatic lung disease. Prior electrocardiograms (ECG) and Holter monitoring had shown no evidence of ectopy or heart block. Five months before presentation, he was hospitalized for acute coronary syndrome, prompting a 4-vessel coronary artery bypass graft surgery. This consisted

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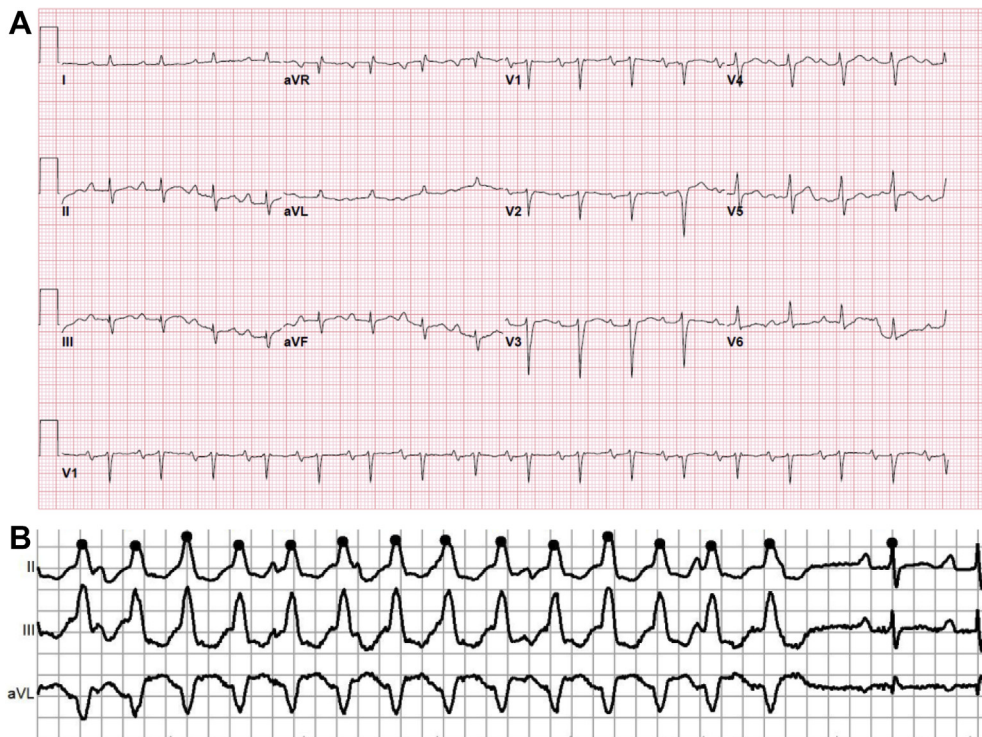
**Funding Sources:** The authors have no funding sources to disclose. **Disclosures:** The authors of this article have no conflicts to disclose. **Address reprint requests and correspondence:** Mr Eliot A. Rapoport, University of Illinois College of Medicine Peoria, 1 Illini Dr, Peoria, IL 61605. E-mail address: [erapopo2@uic.edu](mailto:erapopo2@uic.edu).

## KEY TEACHING POINTS

- Sarcoidosis may present in a clinical scenario with other myocardial pathologies. Presence of myocardial ischemia may not fully rule out the possibility of cardiac sarcoidosis.
- The mainstay of diagnosis in cardiac sarcoidosis is imaging with positron emission tomography with computed tomography (PET-CT) and cardiac magnetic resonance late gadolinium enhancement. Although these are both valuable tests, they may often be discordant, and they should be taken with the perspective of the entire clinical picture.
- PET-CT demonstrates the presence of active disease in the myocardium. This can be negative without ruling out inactive cardiac sarcoidosis, given that the primary arrhythmogenic mechanism is macroreentrant circuits around a scar.
- Cardiac sarcoidosis lacks a definitive treatment. Much of the available evidence is derived from observational studies. Corticosteroids and other immunosuppressants may have a role in the management of active granulomatous disease.

of saphenous vein graft to obtuse marginal 1 (OM1); radial graft to OM2; left internal mammary artery to left anterior descending artery; radial graft was anastomosed to a saphenous vein graft, which was then anastomosed to the right posterior descending artery (RPDA). He was placed on aspirin, clopidogrel, enalapril, metoprolol, and rosuvastatin. Following this event, he was found to have a left ventricular ejection fraction (LVEF) of 60% on a follow-up echocardiogram.

Five months later, the patient experienced 3 weeks of progressive exertional dyspnea, which culminated in the patient's developing cardiac arrest. The incident was witnessed by his wife, who promptly contacted emergency medical services and initiated cardiopulmonary resuscitation after about 2 minutes. Emergency medical services saw a



**Figure 1** A: Electrocardiogram (ECG) showing sinus tachycardia with first-degree atrioventricular block and anteroseptal infarct, age undetermined. B: Telemetry ECG showing episode of nonsustained ventricular tachycardia that provided evidence of severe cardiac dysrhythmia.

shockable rhythm—presumed to be a ventricular tachyarrhythmia. The patient was shocked 4 times and received in total 15–20 minutes of cardiopulmonary resuscitation before the return of spontaneous circulation. On admission physical examination, the patient had a temperature of 98.4°F, a heart rate of 106 beats per minute, blood pressure of 134/81 mm Hg, respiratory rate of 22 breaths per minute, SpO<sub>2</sub> of 91% on 6 liters of FiO<sub>2</sub> 60% by nasal cannula, and body mass index of 27.1 kg/m<sup>2</sup>. His cardiopulmonary exam was unremarkable, with a regular rate and rhythm, no murmurs, and lungs clear to auscultation. Laboratory studies showed a modestly elevated troponin of 0.036 ng/mL, brain natriuretic peptide 340 pg/mL, lactic acid 7.1 mmol/L. Electrolytes were unremarkable, and liver enzymes were elevated with AST 175 U/L and ALT 131 U/L.

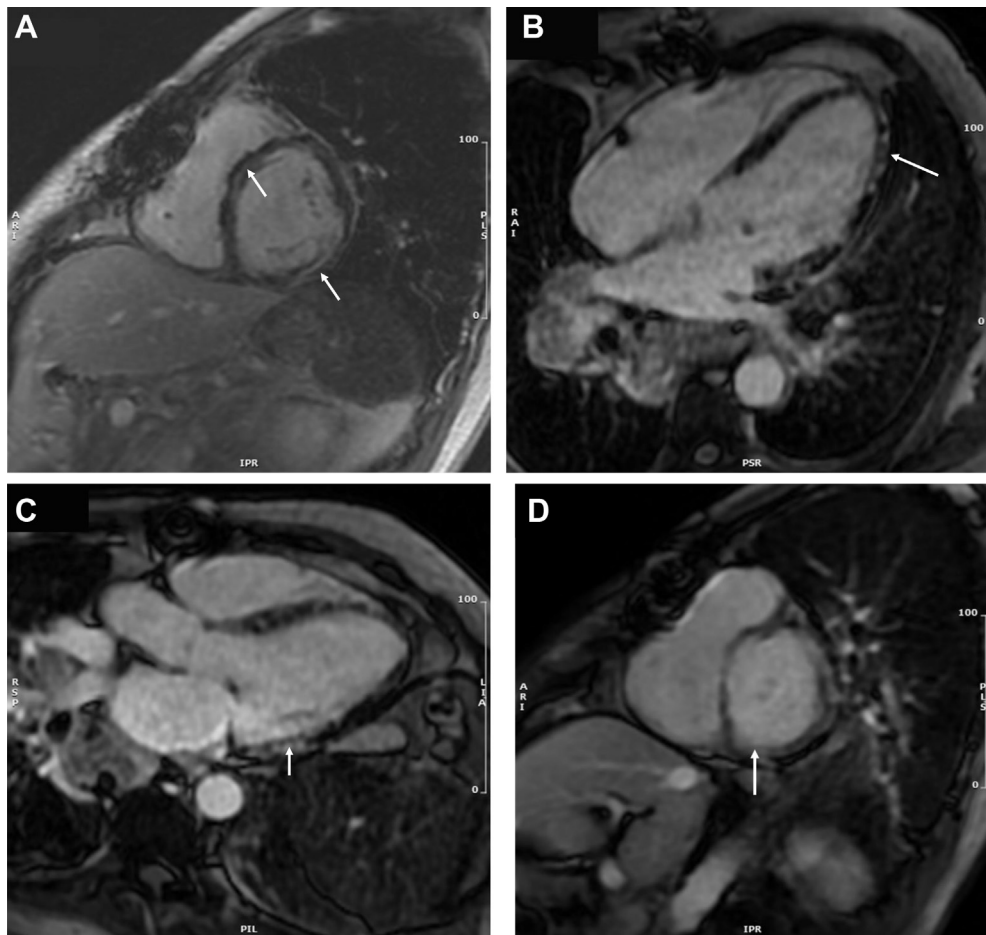
Initial ECG in the emergency department showed sinus tachycardia with first-degree atrioventricular (AV) block (Figure 1A). Bedside echocardiogram showed left ventricular dilation with normal thickness and global hypokinesia with an LVEF of 30%. Subsequent catheterization showed complete occlusion of the grafts to RPDA and OM1 with patency of the grafts to left anterior descending artery and OM2. A stent was placed in OM1. Because the radial graft to the RPDA was totally occluded and the distal right coronary artery was totally occluded with collateral formation, the decision was made to treat conservatively. During this procedure, the patient experienced an episode of nonsustained ventricular tachycardia while on prophylactic amiodarone (Figure 1B).

The degree of electrical dysfunction was thought to be out of proportion to the extent of myocardial ischemia seen on coronary angiogram. We therefore proceeded to evaluate for CS as a probable contributor to the high arrhythmic burden. Cardiac magnetic resonance imaging (CMR) showed mid-wall hyperenhancement in the basal inferolateral and the apical lateral segments. There were also multiple small areas of mid-wall hyperenhancement involving the septal, anterior, and inferior segments. Given a history of pulmonary sarcoidosis, these areas of hyperenhancement are most likely related to sarcoidosis rather than myocardial infarction (MI) (Figure 2). In addition, there was subendocardial hyperenhancement in the basal inferior segment, suggesting a primary MI. Follow-up positron emission tomography with computed tomography (PET-CT) showed abnormal uptake in the mediastinal and hilar lymph nodes and parenchymal lung nodules, but no uptake in the myocardium (Figure 3).

The patient's functional status began to improve to a point where he could ambulate without significant dyspnea. Prior to discharge, the patient had an implantable cardiac defibrillator placed and was treated with guideline-directed medical therapy. There were no further cardiac or pulmonary events noted at the 5-month follow-up. Follow-up echocardiography revealed LVEF remarkably improved to 52%.

## Discussion

CS is a rare condition for which treatment is vital to prevent life-threatening consequences. The pathogenesis of



**Figure 2** A: Short-axis cardiac magnetic resonance imaging illustrating mid-wall hyperenhancement in the septum and basal inferolateral wall (as seen by the arrows). B: Four-chamber cardiac magnetic resonance imaging showing apical-mid anterolateral wall late gadolinium enhancement. C: Three-chamber cardiac magnetic resonance imaging showing patchy mid-wall hyperenhancement of the basal inferolateral segment. D: Subendocardial basal inferior hyperenhancements consistent with a mild primary myocardial infarction.

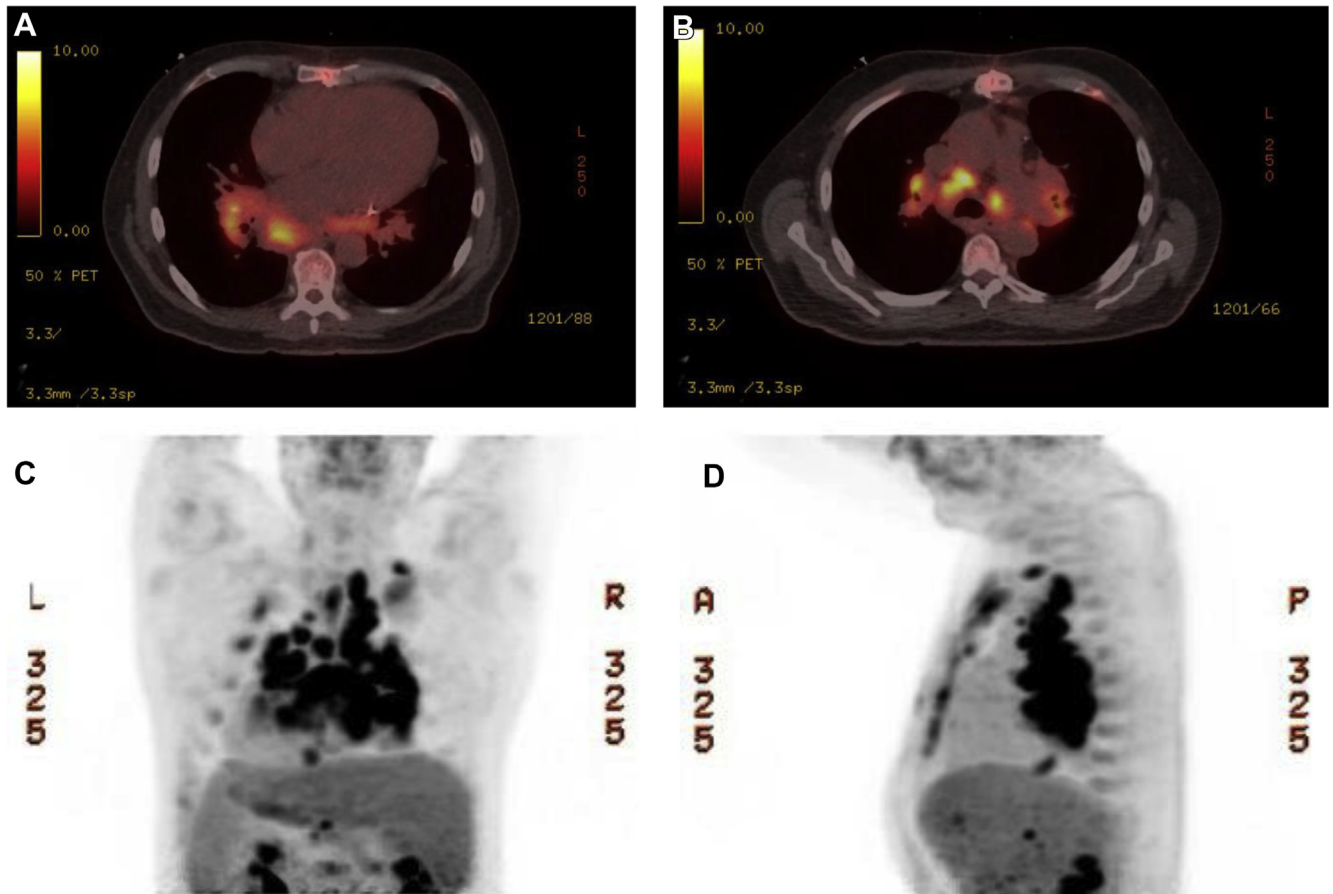
sarcoidosis is poorly understood, but the current hypothesis is suggested to involve largely unknown environmental antigens interacting with genetically predisposed individuals to create a granulomatous response.<sup>2</sup> When this occurs in cardiac tissue, it creates numerous pathologies. By pathology, CS most commonly affects the left ventricular free wall, with septal, right ventricular, and atrial involvement also seen.<sup>3</sup> These pathogenic granulomas and scars lead to conduction abnormalities through the formation of macroreentrant circuits and, less commonly, triggered arrhythmias from increased intracellular calcium release or activation of cells causing abnormal automaticity.<sup>2</sup> This causes clinically significant conduction abnormalities (23%–30%), ventricular arrhythmias (23%), heart failure (HF) (25%–75%), and sudden cardiac death (25%–65%).<sup>1</sup> The nonspecific cardiac symptoms of CS present challenges in differentiating it from other conditions. Notably, more common pathologies such as hypertensive heart disease, vascular disease, diabetes mellitus, and thyroid-related disease must be considered.<sup>4</sup>

While the definitive diagnosis for CS is endomyocardial biopsy showing noncaseating granulomas, this is rarely done in practice, as the procedure carries significant risk<sup>5</sup>

with a low sensitivity (~20%).<sup>6</sup> In lieu of this, imaging plays a crucial role in diagnosis. The 2 primary imaging modalities for CS are 18F-fluorodeoxyglucose positron emission tomography and CMR.<sup>6</sup> There is no pathognomonic finding for CS on CMR, but it typically displays a patchy pattern of late gadolinium enhancement (LGE) atypical for myocardial infarction (eg, mid-wall/epicardial enhancement sparing the subendocardium or basal heart enhancement, particularly in the septum or lateral wall).<sup>7</sup> The discussed CMR findings support the diagnosis of CS in this patient; however, LGE on CMR is a nonspecific finding also seen in cardiac amyloidosis, myocarditis, systemic sclerosis, and dilated cardiomyopathy.<sup>4</sup> To further clarify the diagnosis, the Heart Rhythm Society proposed that clinical diagnosis should include all 3 of the following: histologically confirmed extracardiac sarcoidosis, exclusion of other causes of cardiac dysfunction, and at least 1 imaging, ECG, or functional finding consistent with CS.<sup>8</sup>

This definition leaves ambiguity in the definitive diagnosis of this patient. The patient had previously histology-proven stage I–II pulmonary sarcoidosis as well as CMR findings consistent with CS and an unexplained episode of





**Figure 3** A: Positron emission tomography with computed tomography (PET-CT) fused transverse imaging showing minimal uptake in the cardiac tissue with some uptake in the mediastinal and perihilar lymph nodes. B: Fused PET-CT transverse imaging showing intense uptake in mediastinal lymph nodes. C, D: Non-fused PET images (anteroposterior and lateral, respectively) that emphasize the heterogeneous uptake.

ventricular tachycardia. The challenge appears with the requirement that other etiologies of cardiac symptoms be reasonably excluded. This patient previously experienced a severe degree of ischemic heart disease with reocclusion of grafts; additionally, CMR results showed evidence of a primary MI. This history of cardiac injury clouds the true origin of the severe symptoms observed, creating difficulty in forming a definitive diagnosis. Additionally, another potential cause of the decreased ejection fraction may have also been myocardial stunning secondary to a relatively long period of hypoperfusion. Given the significant CMR findings on LGE, we believe that CS was a significant inextricable contributor to the etiology of ventricular arrhythmia and reduction in left ventricular systolic function.

Another notable aspect of this case is the discordance of the CMR and PET-CT results. PET-CT showed no active myocardial disease. CMR and PET have sensitivities of ~75% and ~90%, respectively, with discordancy reported throughout the literature.<sup>6</sup> The negative PET-CT suggests that despite the background chronic CS, there was no active inflammation at the time of imaging. This is a beneficial finding, as positive PET-CT results are associated with poorer outcomes; however, it should be emphasized that the primary mechanism of arrhythmogenesis in CS is macro-

reentrant circuits around granulomatous scars.<sup>8</sup> This case, therefore, highlights the role of inactive sarcoidosis in symptomatic cardiac dysfunction.

Research into the treatment is limited and is largely based on observational evidence. A key aspect of treatment is the involvement of multispecialty teams, given the involvement of multiple organ systems. Management of HF plays a key role in the treatment of CS. LVEF is a strong predictor of overall survival in CS with a 10-year survival of 100% in patients with preserved LVEF, 67% in patients with mildly to moderately reduced LVEF (30%–55%), and 19% in patients with severely reduced LVEF (<30%).<sup>9</sup> Therefore, the mainstays of treatment for CS-related HF include guideline-directed medical therapy for heart failure, antiarrhythmic drugs, and implantable cardiac defibrillator placement if EF < 35%.<sup>8</sup> The role of steroids and other immunosuppressants in the treatment of CS, however, is less well established. Their primary use is for resolving active granulomatous damage and preventing the progression of disease.<sup>2</sup> This is especially useful in AV conduction blocks, with mixed evidence in ventricular arrhythmias.<sup>8</sup> Reports have emphasized the role of corticosteroids for conduction abnormalities even in the case of late initiation.<sup>4</sup> In heart failure, the role of corticosteroids also has insufficient study. There is some evidence

suggesting that corticosteroid use is most efficacious for the treatment of CS HF in patients with moderately reduced LVEF, whereas the role of immunosuppression in preserved LVEF and severely reduced LVEF is less established.<sup>2</sup> Additional therapies for CS include radiofrequency ablations for arrhythmogenic circuits, and in severe cases heart transplant may be considered.<sup>8</sup>

## Conclusion

Our case shows a very severe presentation presumed to be due to the rare disorder, cardiac sarcoidosis. The patient had mild pulmonary disease without cardiac involvement previously suspected. It highlights the difficulty in making a definitive clinical diagnosis of CS. In this patient, given the history of ischemic damage, it is difficult to conclusively rule out other cardiac etiologies. The confounding nature of this scenario is highlighted by the CMR results, which displayed characteristics of both CS and a small MI. Early diagnosis of CS is crucial to prevent detrimental consequences. A definite diagnosis of CS remains challenging.

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