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CASE REPORT
Cardiovascular imaging

Cardiac sarcoidosis manifesting with atrioventricular block and intracardiac masses: case report and literature review

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Background Cardiac sarcoidosis (CS) typically manifests with atrioventricular block (AVB), ventricular arrhythmias, or heart failure. Intracardiac masses due to CS are rare, and there is both a paucity of evidence and guidelines of how manage them.

Case summary We describe a 45-year-old woman who presented with palpitations and dyspnoea on exertion found to have second-degree AVB. Further work-up noted two right atrial masses that, following excision and pathology, were identified as CS. Within several months of immunosuppressive treatment, imaging and device reports demonstrated mass resolution without arrhythmia recurrence.

Discussion Intracardiac masses are a rare manifestation of CS. Immunosuppressive therapy remains the mainstay of treatment, with consideration of mass resection for diagnostic purposes.

Keywords Case report • Cardiac sarcoidosis • Arrhythmia • Infiltrative cardiomyopathy • Intracardiac mass • Multimodality imaging

ESC curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 2.5 Nuclear techniques • 6.5 Cardiomyopathy

Learning points

- To review the various manifestations of cardiac sarcoidosis to expedite time to diagnosis.
- To identify medical and surgical management options for cardiac sarcoid masses.

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown aetiology that most commonly affects the lungs, skin, lymph nodes, and eyes. It has a large economic impact with estimated direct medical costs as high as $8.7 billion in the USA.[1] Cardiac sarcoidosis (CS) can occur either as part of systemic sarcoidosis or as an isolated entity. While CS is much less common, imaging and autopsy studies suggest that this may be because many cases are clinically silent and therefore go unrecognized.[2] Cardiac sarcoidosis most commonly causes either asymptomatic or symptomatic atrioventricular block (AVB), but other frequent presentations include ventricular arrhythmias and heart failure.[2,3] Notably, CS-related intracardiac masses are exceedingly rare.

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Summary figure

Date	Event
Day 1	She presents with palpitations and exertional dyspnoea. A 12-lead ECG shows second-degree AVB (*Figure 1*). She is admitted for further work-up and pacemaker placement.
Week 1	A CMR revealed two right atrial masses (*Figure 2A*). A subsequent base-to-skull FDG-cPET is performed and shows that the atrial masses are FDG-avid (*Figure 2B*).
Week 2	Two EMBs are performed but are either unremarkable or inconclusive.
Week 6	Both right atrial masses are removed. H&E stains reveal non-caseating granulomas (*Figure 2C and D*), and she is diagnosed with CS. Several days later, a dual-chamber ICD is placed. She is discharged with prednisone oral 30 mg daily.
Month 3	She receives the first dose of infliximab. A couple of weeks later, she starts methotrexate to prevent HACA formation.
Month 4	A device check is performed. It shows no atrial or ventricular arrhythmias.
Month 6	A repeat FDG-cPET shows no evidence of sarcoidosis, and the previously noted FDG-avid lesions in the atria are no longer present (*Figure 3*).

Presentation

A 45-year-old woman with a history of well-controlled Graves' disease presented with palpitations and dyspnoea on minimal exertion. Her family history was notable for a brother and sister with lupus, and her father has sarcoidosis. On presentation, she was normotensive, bradycardic with a heart rate of 38 b.p.m., eupnoeic, normoxaemic, and afebrile. Her cardiac exam noted bradycardia with an irregular rhythm but good pulses; pulmonary, musculoskeletal, neurologic, and cutaneous exams were unremarkable. She was admitted for further work-up.

A 12-lead ECG demonstrated a heart rate of 48 b.p.m. with second-degree AVB (*Figure 1*). She was admitted for further work-up and pacemaker placement for symptomatic bradycardia. A transthoracic echocardiography (TTE) demonstrated a left ventricular ejection fraction (LVEF) of 60–65% and suggested two intracardiac masses that were further characterized on cardiac magnetic resonance imaging (CMR) to be in the right atrium and have delayed gadolinium enhancement (*Figure 2A*). An ^{18}F-fluorodeoxyglucose-positron cardiac positron emission tomography (FDG-cPET) demonstrated that the atrial masses were FDG-avid (*Figure 2B*). She received an endobronchial lung biopsy plus a transbronchial needle aspiration of a left hilar lymph node, which were negative for malignant cells or organisms. Two subsequent endomyocardial biopsies (EMB) were either negative or non-diagnostic as well.

Following multidisciplinary discussions, the involved specialties agreed to pursue further tissue sampling. Given the failure of multiple EMBs,

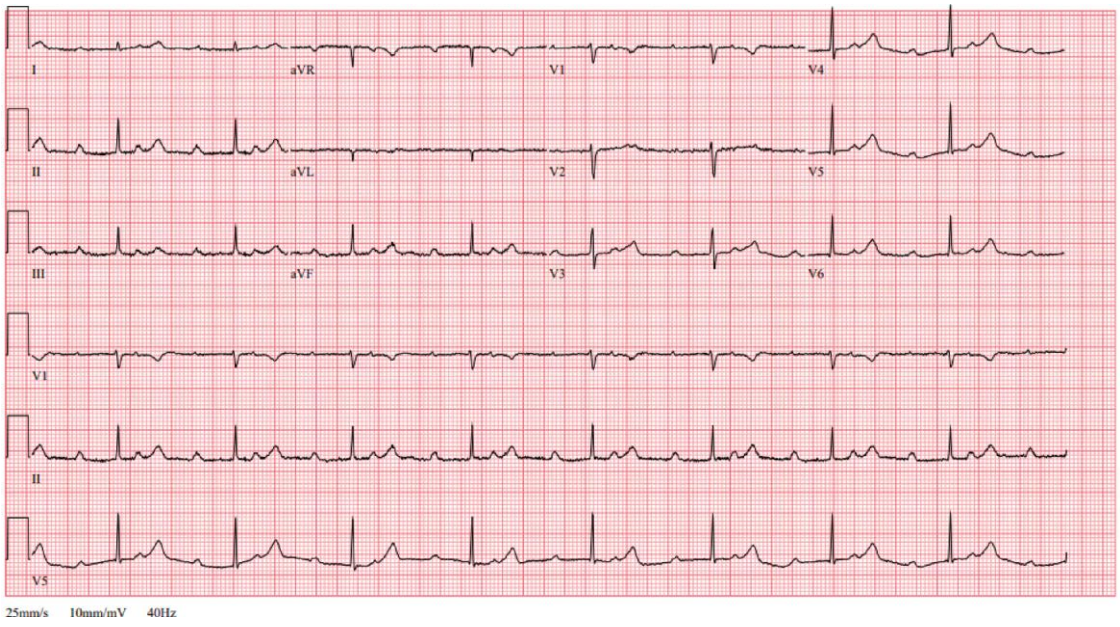

Figure 1 Initial ECG. ECG at initial presentation demonstrating HR 48 b.p.m. with second-degree AVB. AVB, atrioventricular block; ECG, electrocardiogram; HR, heart rate.

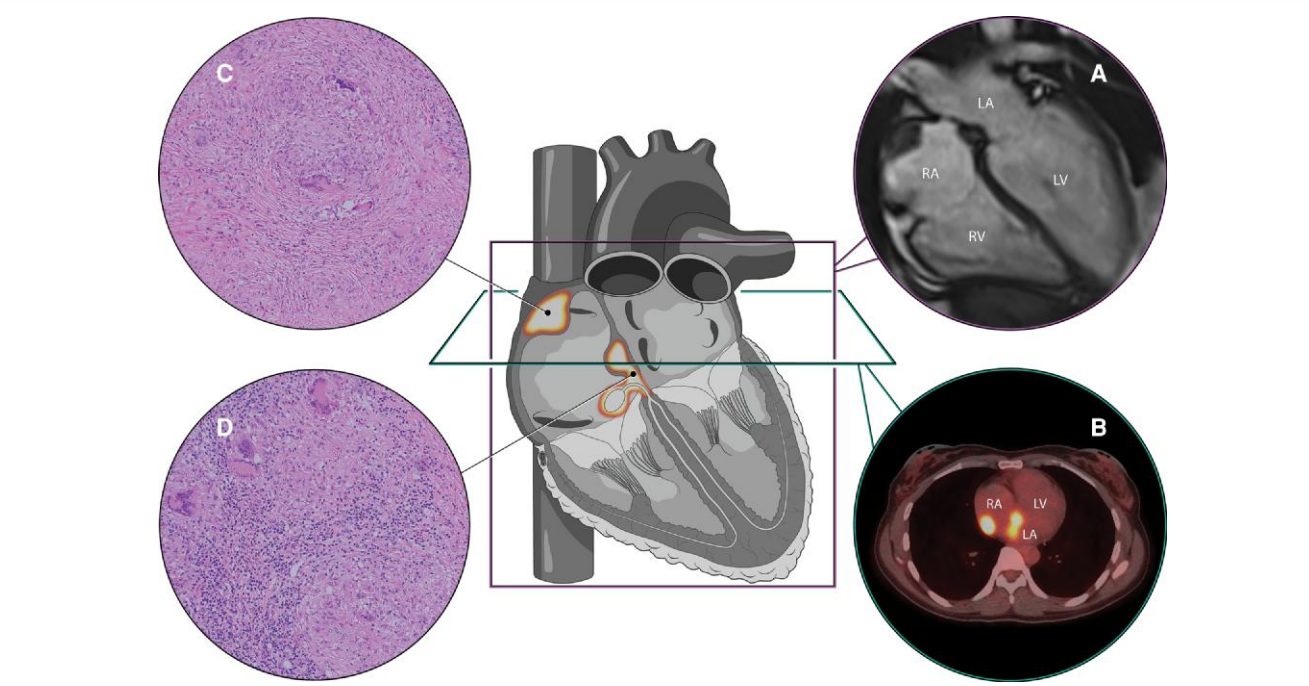

Figure 2 Anatomic representation of cardiac sarcoid masses. (*A*) Four-chamber gated CMR showing two right atrial masses—one in the interatrial septum extending towards the annulus of the tricuspid valve, the second located in the superior right atrial free wall. (*B*) FDG-cPET showing two foci of abnormally increased FDG uptake with CT correlates. (*C* and *D*) H&E stains of the right atrial samples under 10× magnification demonstrating extensive myocardial involvement by non-caseating granulomatous inflammation, suggestive of sarcoid granulomas. CMR, cardiac magnetic resonance imaging; H&E, haematoxylin and eosin; FDG-cPET, ^{18}F-fluorodeoxyglucose-positron cardiac positron emission tomography; RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

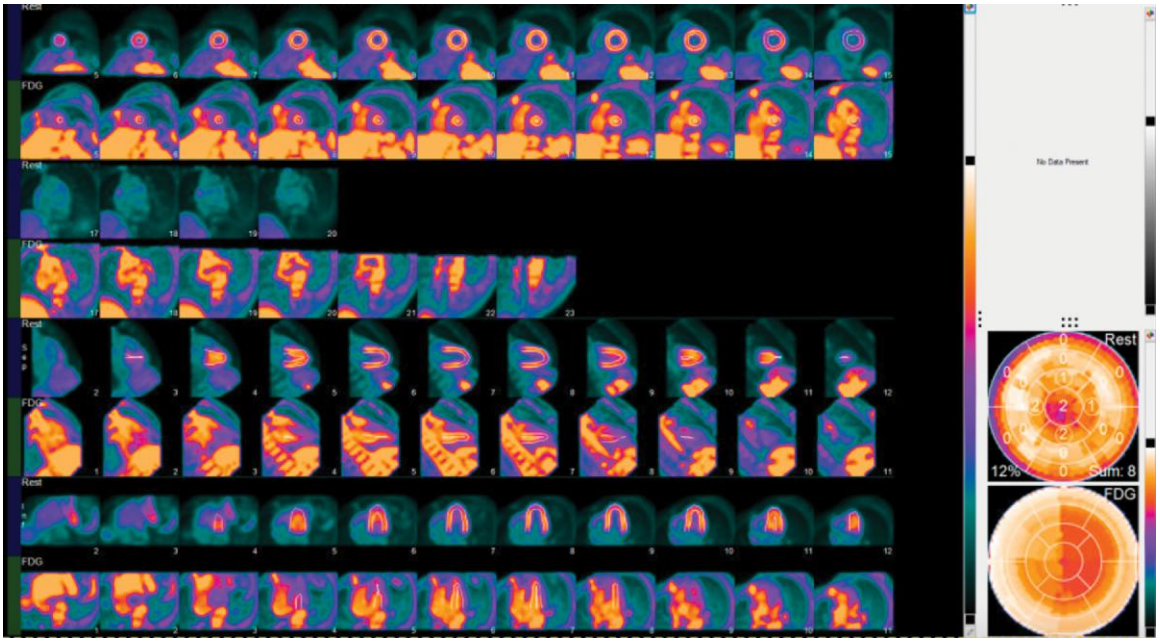

Figure 3 Follow-up FGD-cPET. A follow-up scan performed several months following the initiation of immunosuppressive treatment demonstrated that the initial FGD-avid foci in the right atria were no longer visible. FDG-cPET, ^{18}F-fluorodeoxyglucose-positron cardiac positron emission tomography.

Table 1 Literature search of CS masses from PubMed

	Age	Sex	Presentation	Mass(es) details	Cardiac manifestations	Extra-cardiac involvement?	Advanced imaging	Therapy (duration if specified)	Outcome
Joffe *et al.* 1995[4]	29	F	Weakness, light-headedness, and palpitations	Pericardial space, RA, and LV lateral wall	Sustained ventricular tachycardia	Mediastinal lymphadenopathy	None	Prednisone 60 mg daily	Reduction in size of masses
Scatarige and Fishman 2000[5]	33	F	Asymptomatic	RV along IVS	Ventricular tachycardia	Lungs	None	Not mentioned	Not mentioned
Abrishami, O'Connel, and Sharma 2004[6]	45	M	New-onset syncope	LA arising from the interatrial septum (34 × 38 mm)	Third-degree AVB, reduced ejection fraction (35%)	None	Gallium scintigraphy	Surgical resection	Not mentioned
Uchida *et al.* 2011[7]	39	M	Dyspnoea on exertion	Basal IVS	Third-degree AVB	None	CMR and gallium scintigraphy	Permanent pacemaker, prednisolone 30 mg daily for 4 weeks	Mass size reduction, AVB recovery to first-degree AVB
Deshmukh *et al.* 2012[8]	45	M	Palpitations and syncope	RV along IVS	Ventricular tachycardia	Para-hilar lymph nodes	CMR	Steroids	Arrhythmia resolution
Takahashi *et al.* 2016[9]	40	F	Asymptomatic with progression to presyncope	RA (12 × 12 mm)	First-degree AVB with progression to third-degree AVB	Lungs, liver, and spleen	CMR and FDG-PET	Prednisolone 40 mg daily tapered by 5 mg every two weeks	Not mentioned
Bertic, Tandon, and Wisenberg 2016[10]	33	M	Dyspnoea on exertion	RV free wall (50 × 17 mm)	Third-degree AVB	Not specified	CMR and FDG-PET	Not mentioned	Not mentioned
Fujimoto *et al.* 2018[11]	52	F	Dyspnoea on exertion	RV along IVS (16 × 25 × 28 mm)	First-degree AVB and complete RBBB with intermittent third-degree AVB	Eyes	CMR, FDG-PET, and gallium scintigraphy	Prednisolone 30 mg daily, tapered to 7.5 mg daily maintenance	Mass size reduction, resolution of AVB
Park *et al.* 2022[12]	20	F	Dyspnoea on exertion	IVS	Intermittent third-degree AVB	Mediastinal lymph nodes	CMR and FDG-PET	Prednisolone 30 mg daily	Mass size reduction, resolution of AVB
Asakura *et al.* 2022[13]	71	F	Not mentioned	IVS	Third-degree AVB	Lungs	FDG-PET	Permanent pacemaker, prednisolone 30 mg daily tapered to 7.5 mg daily maintenance	No change in mass size

Details of the 10 case reports identified.
AVB, atrioventricular block; CS, cardiac sarcoidosis; CMR, cardiac magnetic resonance imaging; IVS, interventricular septum; H&E, haematoxylin and eosin; FDG-cPET, ^{18}F-fluorodeoxyglucose-positron cardiac positron emission tomography; RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

she underwent surgical resection of both masses. The pathology report confirmed non-caseating granulomas (*Figure 2C and D*). Grocott's methenamine silver and acid-fast bacilli stains from the biopsy were negative. Infectious serology markers including rapid plasma reagin (RPR), HIV, Lyme, Interferon Gamma Release Assay (IGRA), and fungal antigens were negative. An ophthalmological evaluation showed no evidence of ocular involvement. She was therefore diagnosed with isolated CS.

She was initiated on oral prednisone 30 mg daily along with trimethoprim–sulfamethoxazole three times weekly for *Pneumocystis jirovecii* prophylaxis. Prior to discharge, a dual-chamber implantable cardioverter defibrillator (ICD) was implanted. Over the next few weeks, prednisone was weaned and infliximab was added given the degree of cardiac involvement. Shortly after, methotrexate was added to prevent human antichimeric antibody (HACA) formation. She tolerated these medications well without any major adverse reactions.

At 4 months from initial presentation, her device was interrogated and demonstrated no atrial or ventricular arrhythmias. At 6 months, she had a repeat TTE and FDG-cPET, which demonstrated a LVEF > 65% and that the initial FDG-avid lesions in the right atria were no longer visible (*Figure 3*).

Discussion

Cardiac sarcoidosis masses are extremely rarely reported. Our search of PubMed using the Boolean phrases 'sarcoid* AND mass AND (cardia* OR atri* OR ventric*)' yielded an initial 103 results; however, only 10 of these items were true reports of CS masses (*Table 1*).[4–13] All of the patients in these cases presented with either AVB and/or ventricular arrhythmia, AVB being more common. The majority (60%) of masses involved the interventricular septum. All the cases that included their treatment approach utilized steroids, and one case performed surgical resection though no rationale was provided.[6] Of the cases that discussed treatment response, a majority (83%) demonstrated improvement either by reduction in mass size or resolution of AVB or arrhythmia.

The differential diagnosis for intracardiac masses includes vegetation, thrombus, primary neoplasms (especially myxoma or angiosarcoma), secondary neoplasms, CS, or implanted devices (e.g. device lead and prosthetic device). Like many intracardiac tumours, a definitive diagnosis of CS requires histopathologic confirmation. For CS, this means identifying the characteristic non-caseating granulomas in endo- or myocardial tissue and exclusion of other plausible causes.[14] Typically, EMB has low sensitivity of ~20% for CS because of the heterogenous distribution of the disease,[15] as evidenced by the two non-diagnostic EMBs we collected. Therefore, surgical resection may be the only mechanism to acquire a diagnostic myocardial sample and may be considered when the diagnosis remains elusive despite less invasive sampling methods.

There are no guidelines that discuss the management specifically of CS masses, and therefore data must be extrapolated from guidelines on CS. The mainstay therapy is oral glucocorticoids (GC), though there is significant heterogeneity in both the dosing and duration utilized.[16] Glucocorticoids have historically been first-line treatment, though recent guidelines suggest the addition of an oral steroid-sparing agent due to the long-term side effects of GC.[17] However, a recent meta-analysis found a relapse rate of about one-third in both GC monotherapy and combination therapy groups.[16] If the patient does not tolerate or fails GC therapy, the patient should try an oral steroid-sparing agent, most commonly methotrexate.[16] TNF-α inhibitors are reserved for further refractory disease,[17] and at least one recent study has shown that TNF-α inhibitor containing regimens decrease ^{18}F-FDG myocardial uptake while improving LVEF.[18] Our patient was transitioned to infliximab early in her treatment course due to the extent of her CS masses.

Following diagnosis of CS, it is unclear if there is a role for mass resection. In management of benign intracardiac tumours, resection is often performed due to the concern for tumour mass effect or fragmentation with embolization.[19] This resection is well tolerated with a good prognosis.[20] In our literature search of CS masses, there were no reports of these complications arising, which may in part be attributed to the good responses we identified of CS masses to immunosuppressive therapy. Taken together, these findings suggest that resection has limited therapeutic utility.

Conclusion

Cardiac sarcoidosis is a rare cause of intracardiac mass and should be considered when additional manifestations, especially AVB or ventricular arrhythmias, are present. A broad differential diagnosis may also include vegetation, thrombus, and neoplasm, and thus tissue sample is necessary for a definitive diagnosis. The mainstay of management is immunosuppressive therapy, with the primary role of mass resection being diagnostic as opposed to therapeutic.

Lead author biography

Noah Newman is currently a resident in internal medicine at Emory University in Atlanta, GA, USA interested in pursuing cardiology. He completed medical school at Wake Forest University School of Medicine in 2022.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been received from the patient in line with the Committee on Publication Ethics (COPE) guidelines.

Conflict of interest: None declared.

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Data availability

The data underlying this article are available in the article.

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