

Cardiac sarcoidosis involving the papillary muscle: A case report



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Introduction

Sarcoidosis is a granulomatous multisystem disease that is thought to arise from a dysregulated immunological response. A total of 25% of those suffering from sarcoidosis have cardiac involvement on postmortem analysis, but it is clinically apparent in only 5%.¹ Isolated cardiac sarcoidosis (CS) has also been described.² It may manifest as conduction system dysfunction, ventricular arrhythmias, congestive cardiac failure, or sudden cardiac death.³ CS has a predilection for the ventricular myocardium and its clinical presentation may vary from no symptoms to sudden cardiac death.³

We report a case of isolated CS of the posteromedial mitral valve papillary muscle, which manifested as new-onset right bundle branch block (RBBB) and frequent premature ventricular complexes (PVCs), with subsequent electrocardiographic and radiographic recovery following immunosuppressive therapy.

Case report

Patient information

A 50-year-old white man with a 20 pack-year smoking history, known for persistent atrial fibrillation successfully treated by isolation of the pulmonary veins by radiofrequency ablation in 2015, obstructive sleep apnea, and a bicuspid aortic valve, was noted to have new RBBB and frequent PVCs on routine examination. There was no family or personal history of autoimmune pathologies. The patient reported no previous or current cutaneous, joint, abdominal, ocular, or oral symptoms, nor any B symptoms.

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Of note, except for a known bicuspid aortic valve, echocardiography before and after the radiofrequency ablation had been within normal limits, with no impaired left ventricular ejection fraction and no other valvular abnormalities.

Physical examination

Examination revealed an overweight patient (body mass index 28.3) with a new 2/6 systolic murmur, no clinical signs of heart failure, and a normal pulmonary examination. Cutaneous, oral, and anterior ophthalmologic examinations were normal. There was no lymphadenopathy. The blood pressure was 135/90 mm Hg and the heart rate was 75 beats per minute.

Diagnostic assessment

Repeat echocardiography showed normal biventricular function, new mild mitral regurgitation, and a moderately dilated left atrium. A Holter monitor confirmed the presence of >10,000 PVCs with an RBBB morphology and an rS pattern in the inferior leads and V₆, suggestive of a posteromedial papillary muscle origin (Figure 1).⁴ A cardiac magnetic resonance image (MRI) was therefore performed, which revealed a left ventricular ejection fraction (LVEF) of 51%, owing to anterior hypokinesia and akinesia of the anteroapical, apical, and inferoapical cardiac segments, not in keeping with a coronary territory. Postcontrast sequences showed subendocardial delayed gadolinium enhancement involving the inferoapical LV wall with mural extension >50% as well as enhancement of the whole mitral valve posterior papillary muscle. Prolapse of the mitral valve due to posterior papillary muscle dysfunction with a regurgitation fraction of 5% was also noted (Figure 2). Despite the hypokinesia and akinesia not corresponding to a coronary territory, invasive coronary angiography was performed, which ruled out the presence of significant coronary artery disease. The images were reviewed by 3 independent cardiologists, who confirmed the absence of atheromatous plaques. Given that ischemia had been excluded as a cause of the delayed gadolinium

KEY TEACHING POINTS

- Isolated cardiac sarcoidosis is an increasingly recognized disease that can affect any area of the heart.
- Cardiac sarcoidosis can cause conduction disturbances, arrhythmias, and ventricular systolic dysfunction. It needs to be considered when faced with a patient with frequent premature ventricular contractions of unknown origin.
- Delayed gadolinium enhancement on cardiac magnetic resonance imaging that does not fit with a coronary territory should encourage clinicians to consider inflammatory diseases and, where appropriate, should prompt further investigations.

enhancement, ^{18}F FDG positron emission tomography / computed tomography (PET/CT) imaging was undertaken. This revealed a focal uptake of the posteromedial papillary muscle (SUVmax 3.1), compatible with an inflammatory process (Figure 3). Focal uptake of the anteroapical (SUVmax 2.9) and laterobasal (SUVmax 3.2) LV segments was also noted, suggestive of active myocardial inflammation. Of note, there was no right ventricular, pulmonary, mediastinal, or abdominal inflammatory changes or lymphadenopathy, which suggested an isolated LV inflammatory cardiomyopathy.

An extensive blood panel was within normal limits, including a full blood count, urea and electrolytes, liver function tests, corrected calcium, C-reactive protein, erythrocyte sedimentation rate, thyroid stimulating hormone, ferritin, adenosine deaminase, serum angiotensin-converting enzyme level, ANA, ANCA, rheumatoid factor, complement, and immunoglobulin levels. Testing for hepatitis, cytomegalovirus, Epstein-Barr virus, HIV, parvovirus B19, and tuberculosis was negative. Urine analysis and sediment revealed no abnormalities. NT-pro-BNP, LDL cholesterol, and triglycerides were within normal limits.

Because an isolated CS was suspected, immunosuppression was initiated with a combined treatment of methotrexate 15 mg once a week and prednisone 50 mg once daily, with a gradual weaning regimen. Owing to side effects, the methotrexate was later switched to mycophenolate mofetil, which was well tolerated. Because of the risk of worsening arrhythmias and/or conduction defects, we inserted an implantable loop recorder to allow a close surveillance. Six months following the introduction of immunosuppressive therapy, a follow-up ^{18}F -FDG PET/CT was performed. This revealed resolution of the abnormal uptake of the posteromedial papillary muscle, as well as a reduction of the uptake of the anteroapical segment. The abnormal FDG uptake of the laterobasal segment remains globally unchanged. Posttreatment Holter monitoring also confirmed disappearance of PVCs.

Discussion

Sarcoidosis is a granulomatous multisystem disease. Its incidence varies according to ethnicity and geography.¹ While



Figure 1 Electrocardiogram showing monomorphic premature ventricular contractions with a morphology pointing to an origin from the posteromedial papillary muscle of the mitral valve (right bundle branch block, superior axis owing to negative QRS complexes in leads II and III, R/S <1 in V₆).⁴

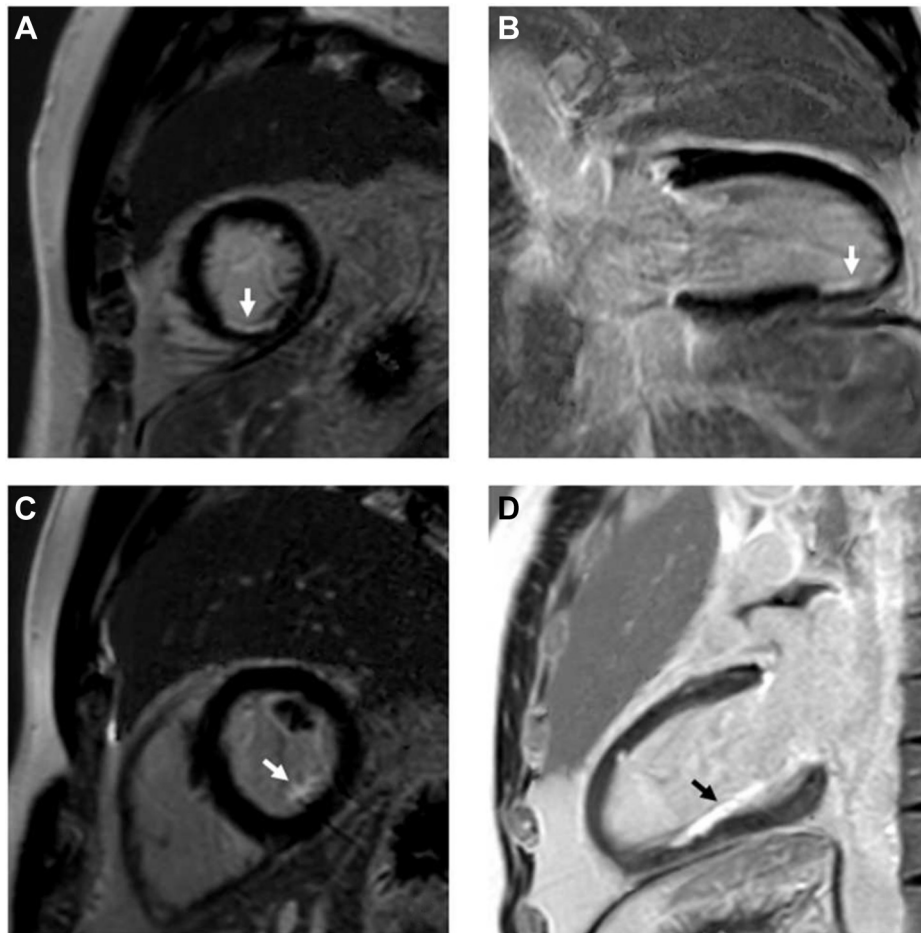


Figure 2 Cardiac magnetic resonance imaging. **A, B:** Subendocardial delayed gadolinium enhancement mimicking an ischemic scar (**A**, short-axis view; **B**, long-axis view). **C, D:** Delayed gadolinium enhancement of the posteromedial papillary muscle (**C**, short-axis view; **D**, long-axis view).

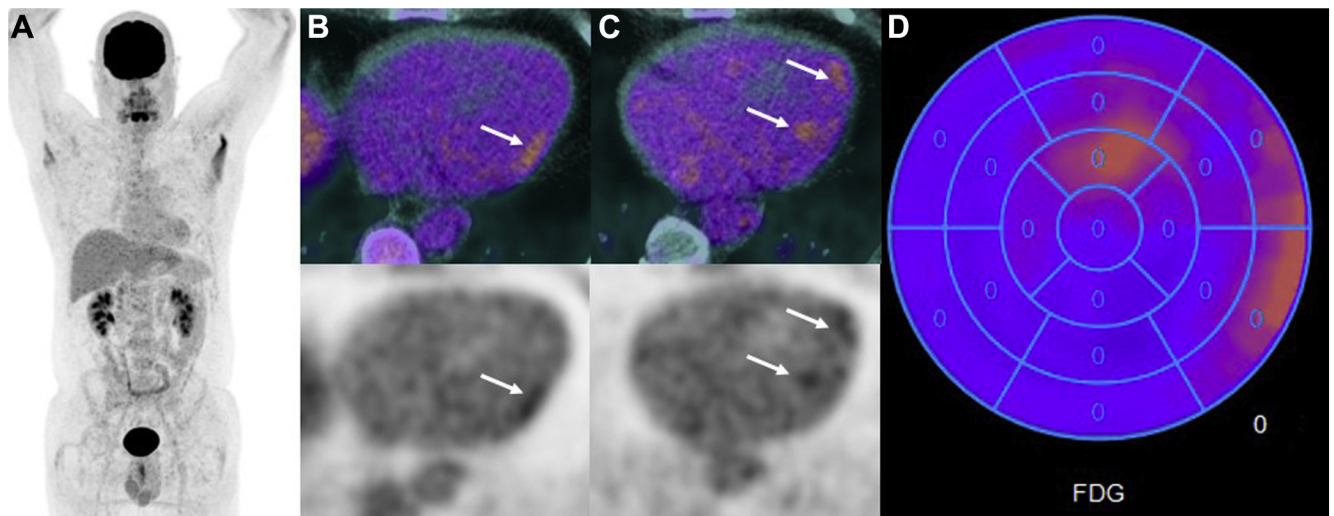


Figure 3 Cardiac ^{18}F -FDG positron emission tomography / computed tomography (PET/CT) before immunosuppression. **A:** Maximum-intensity projection view showing myocardial FDG uptake without any pathologic extracardiac involvement. **B:** Short-axis view of the fused ^{18}F -FDG PET/CT as well as the ^{18}F -FDG PET shows focal FDG uptake of the laterobasal segment. **C:** Short-axis view of the fused ^{18}F -FDG PET/CT as well as the ^{18}F -FDG PET shows focal FDG uptake of the anteroapical segment as well as the posteromedial papillary muscle. **D:** 17-AHA left ventricular (LV) segment representation shows the regional LV distribution of the FDG uptake, mainly at the inferolateral basal segment as well as at the anteroapical segment.

pulmonary sarcoidosis is the most commonly recognized phenotype, any organ can be affected.¹ Clinically evident CS is found in 5%–10% of patients with systemic sarcoidosis,⁵ but autopsy studies have identified cardiac granulomas in about 25% of patients with sarcoidosis.¹

Isolated CS is an increasingly recognized disease. Two-thirds of CS cases have isolated myocardial involvement.⁵ Cardiac granulomas are most commonly found in the LV free wall and interventricular septum, often affecting the conduction system,¹ but cases of infiltration of the papillary muscles have also been described.^{6–8} Our patient had myocardial inflammation of the posteromedial papillary muscle of the mitral valve and the lateral LV. The typical clinical manifestation of CS usually includes impairment of ventricular function and arrhythmias.¹ Although our patient did not have a significantly impaired LV function, likely owing to early diagnosis, his LVEF decreased from 60% in 2015 to 51% in 2019. Furthermore, the presence of mitral regurgitation may have hidden the underlying LV dysfunction. Cardiac MRI revealed segmental hypokinesia in areas not corresponding to a coronary territory, arguing against an ischemic origin, while ¹⁸F-FDG PET/CT imaging revealed myocardial uptake at these locations, suggesting that the muscular dysfunction was due to inflammation. With regard to the effect of sarcoidosis on cardiac rhythm, electrocardiography revealed the development of conduction defects and ventricular ectopy, with a high incidence of monomorphic PVCs originating from the posterior-basal wall of the LV. This location correlated perfectly with the imaging findings of the posteromedial papillary muscle, namely the delayed gadolinium enhancement identified on MRI and the focal uptake identified on ¹⁸F-FDG PET/CT. Electrocardiography was suggestive of dysfunction of the conduction system conduction as evidenced by a new RBBB, a finding typical of CS.⁹

While we were unable to prove the diagnosis of isolated CS with histology, imaging findings showed the typical inflammatory changes seen in CS and all investigations pointed towards the same area of pathology, namely the posteromedial mitral valve papillary muscle. These changes regressed after immunosuppressive therapy, with a simultaneous disappearance of PVCs. A recent case series confirmed that half of patients with PVCs have evidence of underlying myocardial inflammation and that immunosuppression can reduce PVC burden.¹⁰ Further supporting the hypothesis of isolated CS was the absence of an alternative explanation on blood work. While the level of serum angiotensin-converting enzyme, often used for the diagnosis of systemic sarcoidosis, was within normal limits, this is elevated in only 60% of those with CS.¹

Endomyocardial biopsy is the gold-standard test for diagnosing CS,¹¹ but its diagnostic yield is limited¹² and is often deemed too risky. The risk of destabilizing the papillary muscle and valve was deemed high in our patient; therefore biopsies were not performed. The HRS expert consensus statement¹² proposed criteria for the diagnosis of CS, but these require histologic evidence (cardiac or extracardiac).

Recently, criteria for the diagnosis of isolated CS without histology have been proposed.¹³ They suggest that isolated CS can be diagnosed on clinical grounds if ¹⁸F-FDG PET/CT reveals abnormally high cardiac uptake and if 3 or more of the following major criteria are satisfied: high-grade atrioventricular block or fatal ventricular arrhythmia, basal thinning of the ventricular septum or abnormal ventricular wall anatomy, LVEF < 1%, and cardiac MRI revealing delayed gadolinium enhancement. Our patient fulfills 2 major criteria. Minor criteria for the diagnosis of CS include the finding of electrocardiographic abnormalities, including bundle branch block and frequent PVCs. While our patient does not fully meet these new criteria, he fulfills a number of major and minor criteria, strongly suggesting the diagnosis of isolated CS.

The prognosis for patients with proven cardiac involvement (gadolinium enhancement on MRI or uptake on ¹⁸F-FDG PET/CT) is significantly less favorable than those without. CS is the second commonest cause of death in sarcoidosis¹¹ and is associated with a risk of sudden death.¹⁴ The most important predictor of survival is related to the extent of LV dysfunction,¹⁵ but the presence and extent of myocardial delayed gadolinium enhancement is emerging as a potentially more important prognostic factor.¹³ A 2014 consensus¹¹ has proposed a risk stratification for patients with cardiac sarcoidosis who would benefit from implantable cardioverter-defibrillator (ICD). ICD is recommended in those with spontaneous sustained ventricular arrhythmias, prior cardiac arrest, and/or LVEF < 35% despite optimal medical therapy and a period of immunosuppression. Furthermore, ICD placement may prove useful in those with CS and another indication for pacemaker implantation, unexplained syncope or presyncope thought to be cardiac in origin or those with inducible sustained ventricular arrhythmias. Finally, ICD can be considered in patients with reduced LVEF (36%–49% and/or right ventricular ejection fraction < 40%) despite optimal medical therapy for heart failure, including a trial of immunosuppression. Our patient did not meet any of these above criteria. However, in the presence of clear disturbance of the conduction system and the extremely high incidence of PVCs, we opted for an approach with close and active surveillance by implanting a loop recorder.

In summary, we have presented a patient with worsening LV function, arrhythmia, and conduction system disturbance likely due to isolated CS predominantly affecting the mitral valve papillary muscle. While he does not fully meet the recently published criteria for isolated CS, imaging studies showed typical features of this disease with clear electrocardiographic and MRI evidence of improvement after immunosuppressive therapy.

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