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CASE REPORT
Cardiac Imaging

Is positron emission tomography enough to rule out cardiac sarcoidosis? A case report

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Background Cardiac sarcoidosis (CS) is associated with poor prognosis, yet the clinical diagnosis is often challenging. Advanced cardiac imaging including cardiac magnetic resonance (CMR) and positron emission tomographic (PET) have emerged as useful modalities to diagnose CS.

Case summary A 66-year-old woman presented with palpitations. A 24-h Holter monitor detected a high premature ventricular contraction burden of 25.6%. She underwent two transthoracic echocardiograms; both showed normal results. Stress perfusion CMR did not show any evidence of ischaemic aetiology; however, myocardial lesions detected by late gadolinium enhancement (LGE) imaging raised suspicion for CS. While there was no myocardial uptake of fluorodeoxyglucose (FDG) in subsequent cardiac PET, high FDG uptake was seen in hilar lymph nodes. Lymph node biopsy confirmed the diagnosis of sarcoidosis.

Discussion Cardiac magnetic resonance and PET imaging are designed to evaluate different aspects CS pathophysiology. The characteristic LGE in the absence of increased FDG uptake suggested inactive CS with residual myocardial scarring.

Keywords Cardiac sarcoidosis • Cardiac magnetic resonance • Positron emission tomographic • Case report

Learning points

- Fluorodeoxyglucose positron emission tomography study identifies active myocardium inflammation; however, negative study result cannot completely rule out cardiac sarcoidosis (CS).
- Cardiac magnetic resonance has unique advantages in initial evaluation of CS as it can identify myocardium scar, detect active inflammation and oedema, assess left ventricular function, and exclude ischaemic aetiology in one single exam.

Introduction

Sarcoidosis is a granulomatous disease of unknown aetiology that involves multiple organs. Although cardiac involvement is clinically evident in only 5–10% patients with sarcoidosis, myocardial lesions can be identified at autopsy among ∼20–60% cases.[1] Importantly, patients with cardiac sarcoidosis (CS) appear to suffer from a worse prognosis than those without cardiac involvement.[2–4] Early diagnosis and close follow-up are crucial, but the clinical diagnosis of CS is often challenging in reality because of variable and non-specific clinical

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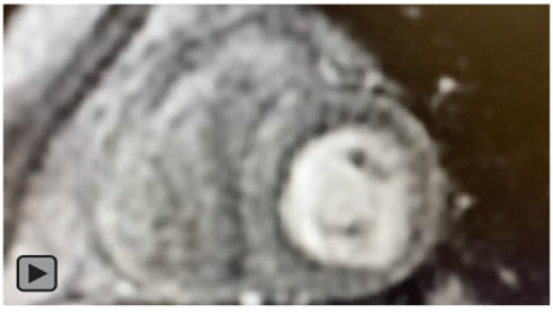
manifestation. Advanced cardiac imaging including cardiac magnetic resonance (CMR) and positron emission tomography (PET) have both emerged as useful non-invasive modalities to detect and diagnose CS.[3,5] However, each of these techniques has unique advantages and limitations, as they are able to detect different pathological attributes of the disease.

Timeline

Time	Events
Presentation	Presented with palpations Electrocardiography showed right bundle branch block
Month 1	A 24-h Holter monitor showed high premature ventricular contraction burden
Month 7	Transthoracic echocardiogram was normal
Month 8	Cardiac magnetic resonance imaging raised suspicion for cardiac sarcoidosis
Month 12	Positron emission tomography showed high fluorodeoxyglucose uptake in hilar lymph nodes instead of myocardium
Month 13	Mediastinal lymph node biopsy was consistent with sarcoidosis

Case presentation

A 66-year-old woman with a medical history of hypertension and diabetes mellitus presented to the cardiology clinic with palpitations. Electrocardiography showed sinus rhythm with right bundle branch block (RBBB). She had an unremarkable transthoracic echocardiogram (TTE) and nuclear stress test 1 year ago as part of the preoperative evaluation for hip surgery. A 24-h Holter monitor detected a high premature ventricular contraction (PVC) burden of 25.6%, with a predominant monomorphic morphology (*Figure 1*). A repeat TTE at this time showed normal right ventricular and left ventricular systolic function without any signs of regional wall motion abnormality. Given her high PVC burden, she underwent stress perfusion CMR to evaluate potential ischaemic aetiology, along with late gadolinium enhancement (LGE) imaging for myocardial scar assessment. Both ventricular size and systolic function were normal on CMR with an ejection fraction of 60–65%. There was no definite evidence of coronary artery pattern ischaemia on regadenoson stress perfusion test (*Video 1*). However, LGE detected two myocardial lesions. The first, the subendocardial enhancement, was located at the basal inferolateral wall with ≤25% of the myocardium segment involved. The second enhancement was noticed within the mid-myocardium of the basal inferoseptal wall (*Figure 2*). There was no definite increased in signal intensity detected by T2 imaging. Non-calcified enlarged hilar lymph nodes were seen on scout images. Cardiac sarcoidosis was considered as a possible diagnosis, and prior myocarditis was another differential diagnosis based on the LGE pattern. The patient underwent cardiac PET with sarcoidosis-specific protocol for further evaluation. Although there was no myocardial uptake of fluorodeoxyglucose (FDG), high FDG uptake was seen in the hilar lymph nodes. The results of PET imaging raised the suspicion of either lymphoma or extracardiac sarcoidosis (*Figure 3*). The patient subsequently underwent transbronchial biopsy of the mediastinal lymph nodes, which confirmed the presence of non-necrotizing granulomas, suggestive of sarcoidosis.



Video 1 Regadenoson stress perfusion imaging shows basal, mid, and apical short-axis segments of left ventricle, along with the two-chamber view. All those segments demonstrate normal gadolinium perfusion without signs of ischaemia.

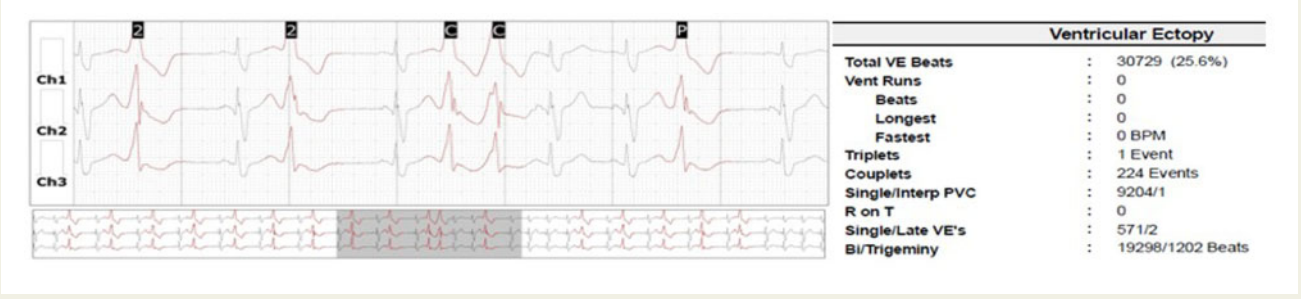


Figure 1 A 24-h Holter monitor shows a high premature ventricular contraction burden of 25.6%, with a predominant monomorphic morphology.

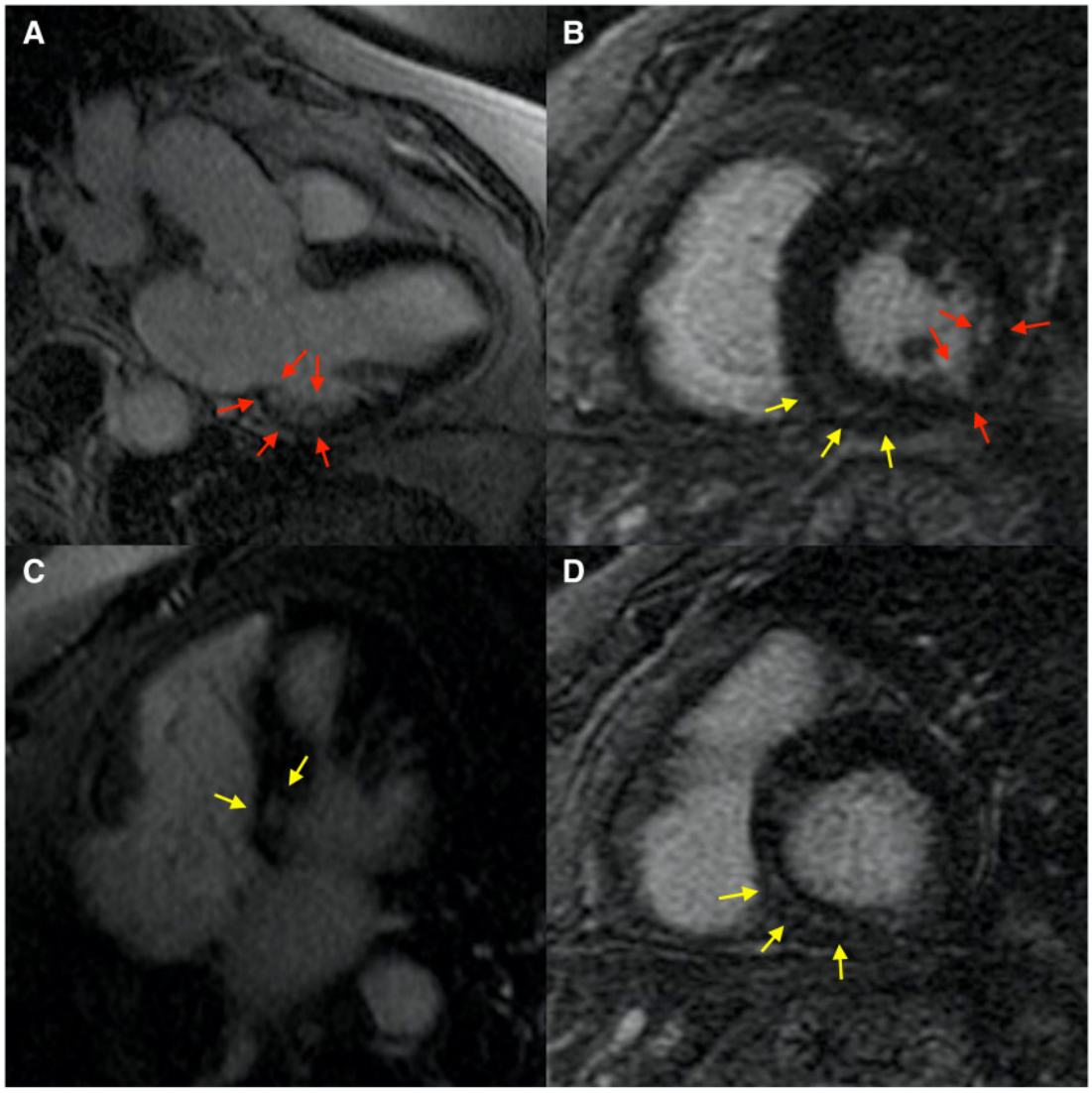


Figure 2 Cardiac magnetic resonance late gadolinium enhancement shows subendocardial enhancement at the basal inferolateral wall with ≤25% of the myocardium segment involved (red arrows). Patchy mid-myocardial enhancement at the basal inferoseptal wall with ≤25% of the segment involved (yellow arrows) [(*A*) long-axis three-chamber view; (*B*) short-axis at mid-cavity level; (*C*) long-axis four-chamber view; (*D*) short-axis view at basal level].

Discussion

There are three main manifestations of CS: conduction abnormalities; ventricular arrhythmias including sudden death; and heart failure.[2,3] In our case, the patient presented with palpitations, RBBB, and frequent monomorphic PVCs. However, none of those findings were specific, which makes diagnosis difficult, especially during the early stage of the disease. Although positive endomyocardial biopsy can confirm CS diagnosis, the diagnostic yield is ≤20% owing to the focal nature of the disease; hence, it is only indicated in patients with negative extracardiac biopsy result but high suspicion of CS.[2] Our patient fulfilled the clinical diagnostic criteria for CS based on the 2014 Heart Rhythm Society (HRS) expert consensus statement, which includes: (i) histological diagnosis of extracardiac sarcoidosis and (ii) LGE on CMR in a pattern consistent with CS.[3]

Positron emission tomography is widely used in the assessment of CS. ^{18}F-FDG is a glucose analogue taken up by macrophages in active myocardial inflammatory lesions. ^{18}F-FDG PET is helpful to detect myocardial inflammation and can therefore be used to diagnose active CS and monitor response to treatment. Focal and focal-on-diffuse are two characteristic FDG uptake patterns seen in the myocardium.[2,6] However, we should be aware that undetected myocardial FDG uptake cannot rule out cardiac involvement, because it only detects active disease, as seen in our patient.

Cardiac magnetic resonance has unique advantages in the initial evaluation of CS, because it can identify detailed tissue

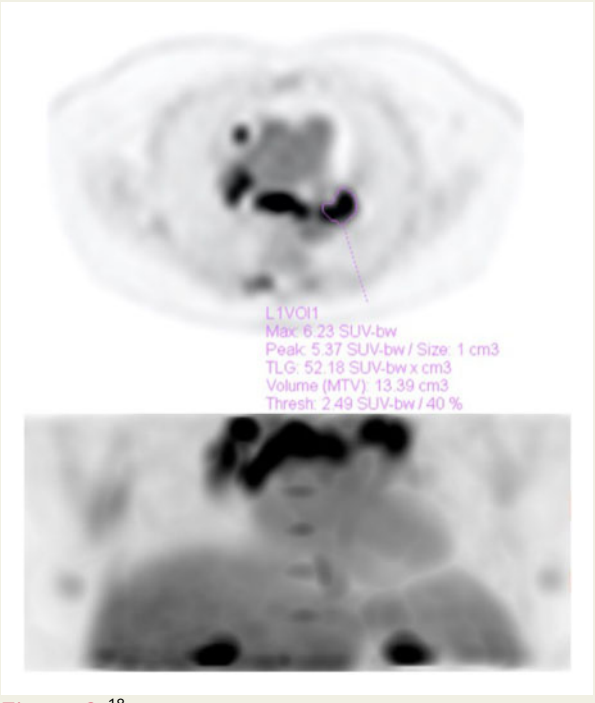


Figure 3 ^{18}F-fluorodeoxyglucose positron emission tomography shows hypermetabolism in the bilateral hilar and posterior mediastinal lymph nodes. There is no ^{18}F-fluorodeoxyglucose uptake in the myocardium.

characterization, accurately assess left ventricular wall thickness and function, and exclude ischaemic aetiology by stress perfusion imaging in one single exam.[7] The high resolution of LGE technique allows it to detect small-scale myocardial damage caused by CS at a very early stage. Patel *et al.*[1] showed that among 81 patients with biopsy-proven extracardiac sarcoidosis, LGE was more than twice as sensitive to identify cardiac involvement as the consensus criteria based on the modified Japanese Ministry of Health (JMH) guidelines. Although there is no specific pathognomonic LGE pattern for CS, it is usually described as patchy and multifocal, along with endocardial-border sparing and a non-coronary distribution. It is most commonly seen in basal segments, especially in the septum and lateral wall.[2]

Additional studies have shown that myocardial scarring in sarcoidosis patients diagnosed by LGE is associated with poor prognosis and is the best independent predictor of adverse and potentially lethal events.[8,9] In the same study conducted by Patel *et al.*,[1] patients with LGE-detected myocardial damage had a 9-fold higher rate of adverse events and an 11.5-fold higher rate of cardiac death than those without damage. In another study, Gowani *et al.*[10] followed-up 50 patients for 4.1 years. Late gadolinium enhancement was found to have higher negative predictive value for the development of ventricular arrhythmias than FDG PET (100% vs. 79%). There is growing consensus that CMR should be considered for sudden death risk stratification.[3]

In our case, myocardial lesions detected by LGE were located apart in the basal segments, including the one within the mid-myocardium, sparing the endocardium. This pattern was highly suggestive of non-ischaemic aetiology, which was further supported by normal stress perfusion test. Although myocardium damage from prior myocarditis may also have similar manifestation, the classic enhancement distribution and the lack of viral prodrome symptoms raised high suspicion for CS. Despite a normal myocardium on FDG PET exam, the clinical suspicion prompted further mediastinum lymph node biopsy. The result showed non-necrotizing granulomas consistent with sarcoidosis, which helped confirm the diagnosis of CS based on the 2014 expert consensus recommendations.[3]

This case was challenging to diagnose due to the unexpected cardiac PET findings. The hypermetabolism in the bilateral hilar and posterior mediastinal lymph nodes is classic for sarcoidosis, which was in line with our clinical suspicion. We expected to see focal or focal-on diffuse FDG uptake pattern in the myocardium to diagnose active CS. The characteristic LGE in the absence of increased FDG uptake in the myocardium suggested inactive CS with residual myocardial scarring. Despite suboptimal imaging quality owing to ventricular arrhythmia, this was also supported by the patient's T2 imaging as it did not show any convincing evidence of active inflammation.

The patient was started on metoprolol succinate with gradually titrating up and her palpitations significantly improved with the treatment.

Conclusion

Cardiac magnetic resonance and PET imaging expose different pathophysiological features of CS. Positron emission tomography scan is useful to detect ongoing inflammation and guide anti-inflammatory therapy, yet the scan alone is not enough to rule out CS as it may miss the inactive phase of the disease. It is reasonable to use CMR as the initial evaluation tool in cases of suspected CS, given its high diagnostic accuracy and prognostic value.

Lead author biography

Siyi Huang is a third-year internal medicine resident at the University of California, San Francisco, Fresno Program, USA. She graduated from Shanghai Jiaotong University, School of Medicine, China in 2016. She has special interest in advanced cardiac imaging. She is currently pursuing cardiology fellowship training.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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