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CASE REPORT
Cardiovascular imaging

An magnetic resonance imaging–pathology correlation case report of cardiac sarcoidosis mimicking arrhythmogenic biventricular cardiomyopathy

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Background Cardiac sarcoidosis (CS) is a granulomatous disease that can manifest as conduction defects, ventricular arrhythmias, and heart failure. The diagnosis of CS is inherently difficult due to variable presentations; as such, endomyocardial biopsy is often required but lacks sensitivity due to patchy myocardial involvement. Moreover, the diagnostic criteria of CS and arrhythmogenic cardiomyopathy overlap, particularly in right-side dominant or biventricular presentations, which further complicates an already challenging differential diagnosis.

Case summary A 53-year-old man with no prior chronic medical conditions presented with ventricular tachycardia (VT) and heart failure with reduced ejection fraction. He was found to have biventricular cardiomyopathy and late gadolinium enhancement on cardiac magnetic resonance imaging, resulting in an initial diagnosis of arrhythmogenic cardiomyopathy. Implantable cardioverter-defibrillator was placed, but he was readmitted for recurrent VT 2 months later. Despite an aggressive VT therapy (combination of antiarrhythmic drugs, epicardial and endocardial ablation, and stellate ganglion block), he continued with refractory VT and developed cardiogenic shock. Extra-corporeal membrane oxygenation was initiated as a bridge to heart transplantation. Pathology of the explanted heart revealed the underlying disease to be CS.

Discussion Cardiac sarcoidosis can mimic arrhythmogenic biventricular cardiomyopathy and may be difficult to distinguish by the proposed diagnostic criteria. High clinical suspicion and thorough investigation are necessary for an earlier diagnosis and initiation of treatment.

Keywords Cardiomyopathy • Ventricular tachycardia • Cardiac magnetic resonance • Imaging modalities • Case report

ESC curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 5.6 Ventricular arrhythmia • 6.5 Cardiomyopathy

Learning points

- To be able to make a differential diagnosis for causes of recurrent ventricular arrhythmias.
- To recognize the difficulties in differentiating arrhythmogenic biventricular cardiomyopathy from cardiac sarcoidosis and appreciate the need for thorough investigation to exclude cardiac sarcoidosis.

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Introduction

Differentiating between arrhythmogenic cardiomyopathy (ACM) and cardiac sarcoidosis (CS) is difficult as both can present similarly with ventricular arrythmias.[1–3] Diagnostic guidelines overlap, and CS diagnosis is especially challenging since clinical and imaging findings are not pathognomonic nor universally present and endomyocardial biopsy (EMB) has low sensitivity at only 36%.[4–8] We present a patient with ventricular tachycardia (VT) who was initially diagnosed with ACM. After heart transplantation, his explanted heart revealed CS, highlighting the complexities of differentiating CS from arrhythmogenic biventricular cardiomyopathy and the importance of thorough investigation to rule out a potentially treatable disease.

Summary figure

February 2022	The patient was admitted with VT. Left ventricular (LV) ejection fraction (LVEF) was reduced. Cardiac magnetic resonance (CMR) imaging showed biventricular cardiomyopathy and extensive right ventricular (RV) late gadolinium enhancement (LGE), leading to an initial ACM diagnosis. Implantable cardioverter-defibrillator (ICD) was placed.
March 2022	The patient presented with recurrent VT. He was cardioverted and placed on lidocaine and amiodarone but continued to have recurrent VT.
April 2022	The patient underwent epicardial and endocardial VT ablation but developed cardiogenic shock, requiring extra-corporeal membrane oxygenation (ECMO). He then underwent heart transplantation. The explanted heart revealed fibrosis of much of the RV and parts of the LV with some residual active granulomatous inflammation, confirming the diagnosis of CS.
January 2023	No recurrent granulomatous disease on post-transplant cardiac biopsies and patient has remained clinically stable.

Case presentation

A 53-year-old man with no prior chronic diseases presented with sudden dyspnoea and lightheadedness from VT. Transthoracic echocardiogram showed reduced LVEF. Electrocardiogram showed wide-complex tachycardia with prolonged QTc, fusion beats, and left bundle branch block morphology (LBBB; *Figure 1A*). With CMR demonstrating biventricular cardiomyopathy, RV LGE, and history of sudden cardiac death in his father, ACM was clinically diagnosed and gene testing was planned. The differential also included CS, myocarditis, hypertrophic cardiomyopathy, infiltrative cardiomyopathy, and ischaemic heart disease. The patient underwent ICD implantation and was started on sotalol and metoprolol succinate but then presented to the local emergency department with recurrent VT. He was cardioverted, placed on lidocaine and amiodarone in addition to metoprolol, and transferred to our facility.

Transthoracic echocardiogram revealed severely enlarged RV chamber, moderately enlarged LV chamber, and severely reduced biventricular systolic function. Coronary angiogram demonstrated normal coronary arteries. Cardiac magnetic resonance (*Figure 2*; Supplementary material online, *Videos S1–S3*) showed biventricular LGE with increased extra-cellular volume by T1 mapping, consistent with interstitial fibrosis. In the LV, there was diffuse subepicardial LGE. The ventricular septum (on the RV side) showed anterior and inferior LGE in a bilayer or focally transmural pattern and patchy enhancement in the papillary muscles. In the RV (*Figure 3*; Supplementary material online, *Videos S4* and *S5*), there was diffuse near-transmural LGE of the entire free wall. T2-based sequences did not suggest significant active inflammation. Cardiac magnetic resonance confirmed an LVEF of 26% and RV ejection fraction of 21%. Prior to ablation, electrocardiogram demonstrated sinus tachycardia with first-degree atrioventricular block and extensive QRS fractionation, consistent with slow conduction and fibrosis (*Figure 1B*).

He underwent epicardial and endocardial VT ablation and stellate ganglion block but developed cardiogenic shock and respiratory failure, leading to ECMO cannulation and ultimately heart transplantation 2 weeks after admission.

The explanted heart showed biventricular dilatation and cardiomegaly. There was interstitial (replacement-type) fibrosis in a subepicardial and focally transmural distribution, involving the anterior, lateral, and septum of the LV and near the entirety of the RV (*Figure 4*). There was some residual active granulomatous inflammation involving the myocardium near the atrioventricular node. This confirmed biventricular CS primarily in a chronic, burnt-out phase, with minimal active disease. No pathologic variant was found on the cardiomyopathy gene panel.

The patient's post-transplant course was uncomplicated without recurrent arrhythmia or significant allograft rejection. A cardiac positron emission tomography (PET) showed no evidence of inflammation or fibrosis, and he did not exhibit extra-CS.

Discussion

Arrhythmogenic cardiomyopathy is a hereditable cardiomyopathy that manifests as ventricular arrhythmias due to myocardial fibrofatty replacement.[1] Arrhythmogenic cardiomyopathy can manifest as isolated RV, isolated LV, or biventricular involvement.[4] Diagnostic recommendations have been described by the 2010 Task Force Criteria and 2020 Padua Criteria.[4,5] With CMR indicating RV free wall akinesia, indexed RV end-diastolic volume of 132 mL/m^2, transmural RV LGE, reduced LVEF, multi-segment LV LGE, inverted T waves, possible epsilon wave in right precordial leads, and sustained VT of LBBB morphology and the inferior axis, this patient met three major and one minor Task Force Criteria, three major and two minor Padua RV Criteria, and two major Padua LV Criteria.[4,5] Thus, he would have been diagnosed with 'definite' ACM or arrhythmogenic biventricular cardiomyopathy, despite his later pathologically proven CS.

Sarcoidosis is a systemic granulomatous disease that usually involves the lungs but can impact any organ, including the heart.[2] Cardiac sarcoidosis tends to present with conduction abnormalities, ventricular arrhythmias, and/or heart failure.[2] Unfortunately, diagnosis of CS can be challenging. The 2014 Heart Rhythm Society recommendations for CS diagnosis require either histological diagnosis from myocardium or histological diagnosis of extra-CS along with a specific clinical presentation, such as unexplained sustained VT or LGE on CMR.[6] In 2016, the Japanese Circulation Society released guidelines that allowed for

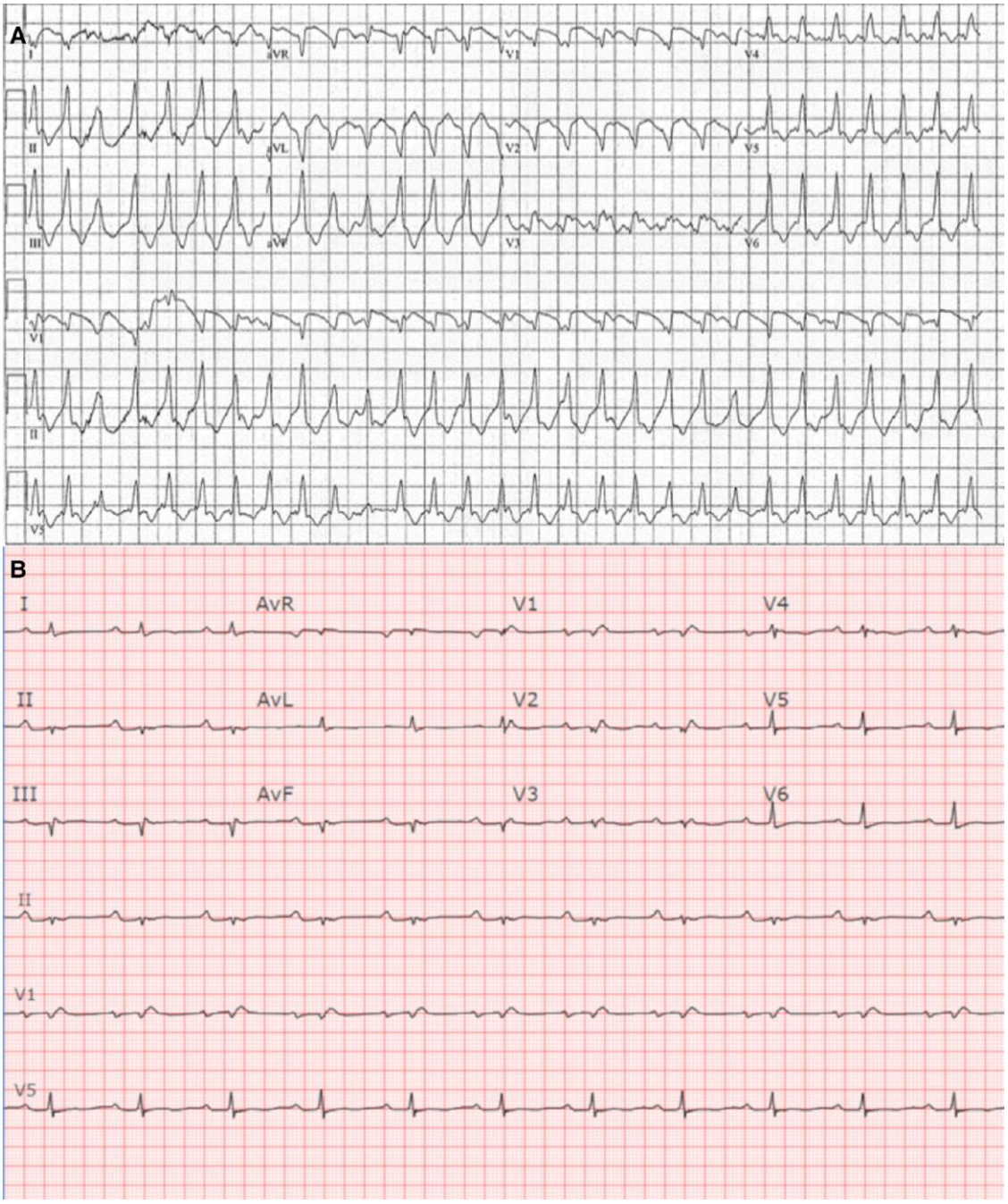

Figure 1 Electrocardiogram. (*A*) Electrocardiogram shows ventricular tachycardia with an inferior axis and left bundle branch block morphology. (*B*) Electrocardiogram shows sinus tachycardia with low voltage, fragmented QRS complexes, and delayed right ventricular activation with possible epsilon wave.

'suspected' CS diagnosis without EMB. These require fulfilment of clinical criteria along with imaging, such as ^{18}F-fluorodeoxyglucose-PET (FDG-PET), showing isolated heart involvement.[7] This patient would not have met CS criteria due to a lack of pre-transplant EMB, known extra-CS involvement, or whole-body sarcoid imaging. This illustrates the difficulty of differentiating ACM from CS, particularly in right-side dominant or biventricular cases.[8]

Immunosuppression with corticosteroids is the first-line therapy for sarcoidosis but not indicated for ACM.[2] Thus, in patients with suspected ACM, one should consider undergoing a careful investigation to exclude CS, including endomyocardial or extra-cardiac biopsy along with cardiac and whole-body FDG-PET. Certain LGE patterns on CMR could be more specific for CS, such as septal LGE with contiguous extension into the RV and intense non-contiguous multi-focal LGE in a non-infarct pattern.[9] However, various imaging features are commonly shared among CS and ACM, and clinical context and pre-test probability are critical in imaging interpretation. This patient had late-stage CS and immunosuppression at the time of presentation likely would not have changed his clinical course. However, diagnosis and treatment in early-stage CS cases could lead to reduction in morbidities. This was

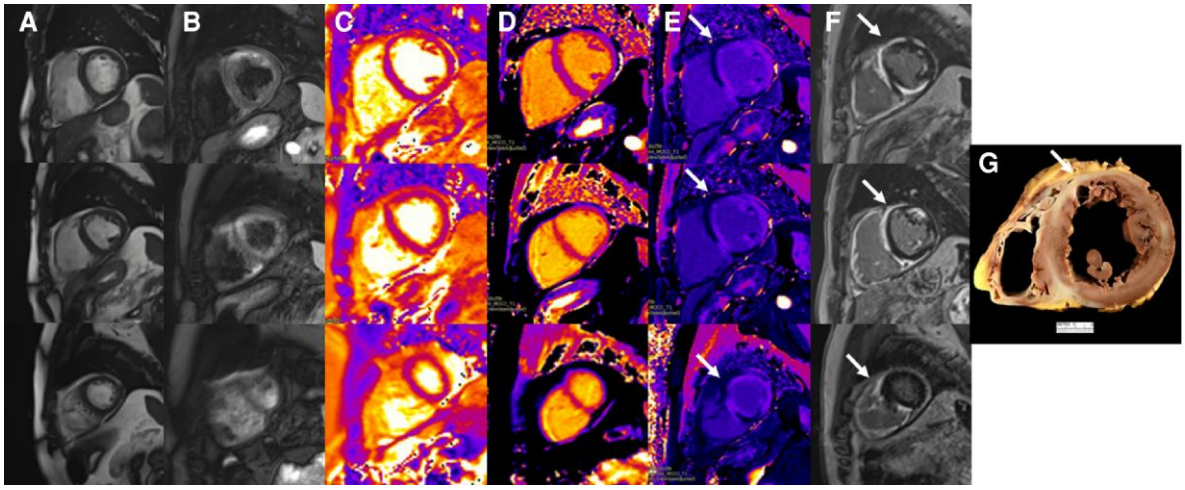

Figure 2 Magnetic resonance imaging (MRI) and pathology correlation. Cardiac MRI demonstrates increased biventricular size with reduced systolic function (Column A: cine SSFP of short axis slices, top: basal, middle: mid, and bottom: apical level), significant sub-epicardial scarring (arrows) of the interventricular left ventricular septum, basal left ventricular anterior and inferior walls, and entire right ventricular free wall (Column D: native T1 map; Column E: post-contrast T1 map; Column F: late gadolinium enhancement), without significant inflammation or oedema (Column B: T2 weighted series; Column C: T2 map), correlating with gross pathology (Column G).

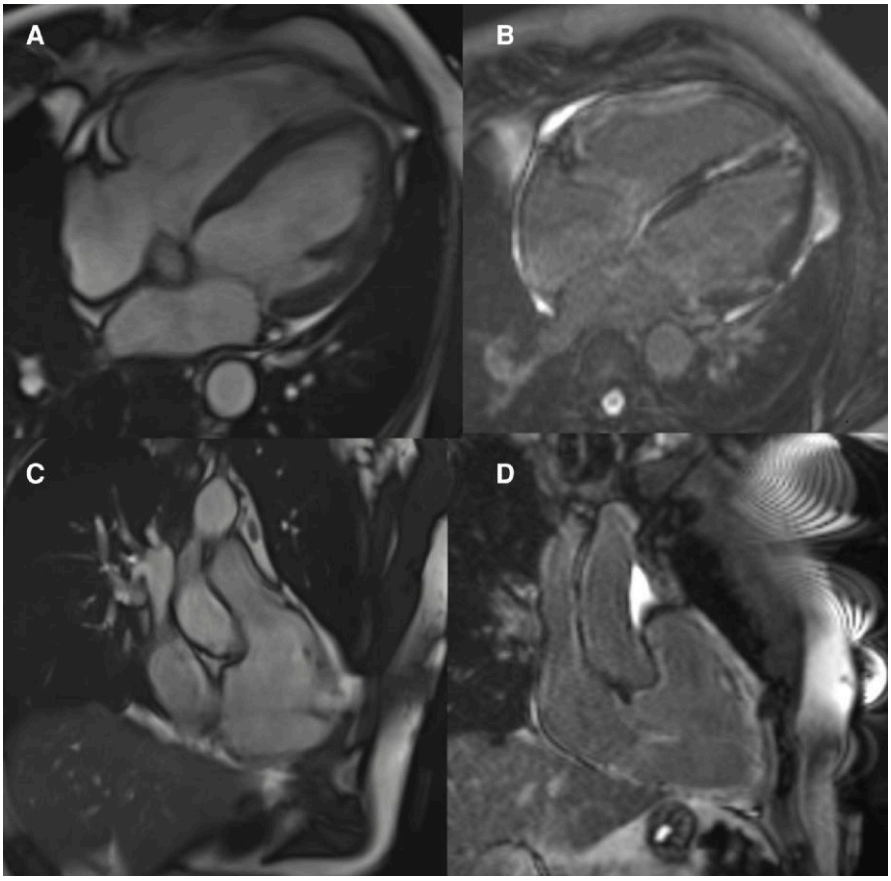

Figure 3 Magnetic resonance imaging (MRI). Cardiac MRI demonstrated increased right ventricular size and reduced right ventricular systolic function with akinetic mid to apical free wall [cine steady-state free precession, four chamber view (*A*) and right ventricular outflow tract (RVOT) view (*C*)] with corresponding diffuse late gadolinium enhancement of the right ventricular free wall [late gadolinium enhancement sequence, four chamber view (*B*) and RVOT view (*D*)].

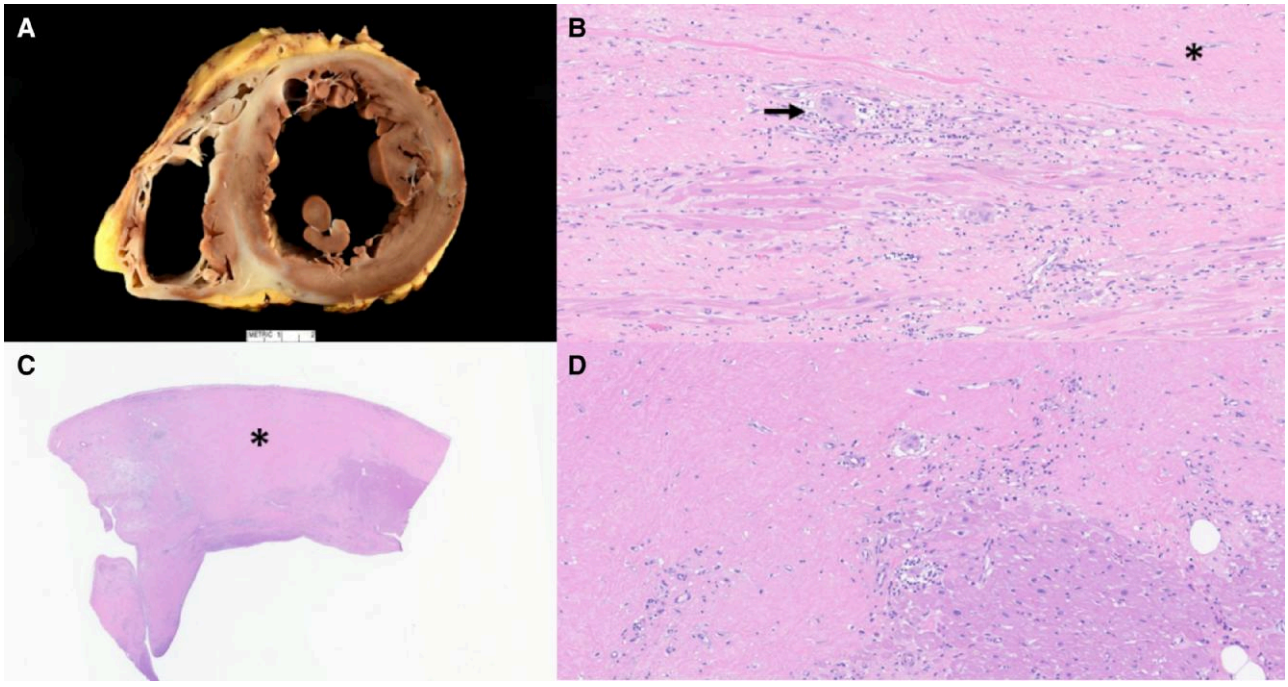

Figure 4 Explanted heart pathology confirming cardiac sarcoidosis. Short-axis, mid-ventricular slice of explanted heart (*A*) shows extensive grey–white scarring of the right ventricular wall, septum, and anterior left ventricular wall with associated right ventricular wall thinning. Haematoxylin and eosin-stained sections of the ventricular septum (*B*, ×200 original magnification) shows non-necrotizing granuloma (arrow) surrounded by fibrosis (*) and extensive fibrosis with multi-nucleated giant cells in the right ventricle (*C* and *D*; ×10 and ×200 original magnification, respectively).

a novel case in which the full explanted heart could be compared with imaging findings of a CS patient who thoroughly met arrhythmogenic biventricular cardiomyopathy criteria. Despite similar cases previously reported, heightened awareness remains necessary for diverse CS manifestations, especially in right-predominant cases such as this. Additional diagnostic tools are needed to improve the differentiation between these diseases.

Lead author biography

B. Michelle Kim, BS, graduated from Duke University with a Bachelor of Science in Biology and is currently a medical student at the Mayo Clinic Alix School of Medicine in Rochester, MN, USA. She has a strong interest in internal medicine and cardiology.

Supplementary material

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

Consent: The patient provided written consent for submission and publication of this case report in accordance with COPE guidelines.

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Data availability

The data underlying this article are available in the article and in its online Supplementary material.

References

1. Basso C, Corrado D, Marcus FI, Nava A, Thiene G. Arrhythmogenic right ventricular cardiomyopathy. *Lancet* 2009;**373**:1289–1300.
2. Birnie DH, Nery PB, Ha AC, Beanlands RSB. Cardiac sarcoidosis. *J Am Coll Cardiol* 2016;**68**:411–421.
3. Philips B, Madhavan S, James CA, te Riele AS, Murray B, Tichnell C, et al. Arrhythmogenic right ventricular dysplasia/cardiomyopathy and cardiac sarcoidosis: distinguishing features when the diagnosis is unclear. *Circ Arrhythm Electrophysiol* 2014;**7**:230–236.
4. Corrado D, Perazzolo Marra M, Zorzi A, Beffagna G, Cipriani A, Lazzari M, et al. Diagnosis of arrhythmogenic cardiomyopathy: the Padua criteria. *Int J Cardiol* 2020;**319**:106–114.
5. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. *Circulation* 2010;**121**:1533–1541.
6. Birnie DH, Sauer WH, Bogun F, Cooper JM, Culver DA, Duvernoy CS, et al. HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. *Heart Rhythm* 2014;**11**:1305–1323.
7. Terasaki F, Azuma A, Anzai T, Ishizaka N, Ishida Y, Isobe M, et al. JCS 2016 guideline on diagnosis and treatment of cardiac sarcoidosis—digest version. *Circ J* 2019is;**83**:2329–2388.
8. Markatis E, Afthinos A, Antonakis E, Papanikolaou IC. Cardiac sarcoidosis: diagnosis and management. *RCM* 2020;**21**:321–338.
9. Vita T, Okada DR, Veillet-Chowdhury M, Bravo PE, Mullins E, Hulten E, et al. Complementary value of cardiac magnetic resonance imaging and positron emission tomography/computed tomography in the assessment of cardiac sarcoidosis. *Circ Cardiovasc Imaging* 2018;**11**:e007030.