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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Cardiac Sarcoidosis With Prominent Epsilon Waves

A Perfect Phenocopy of ARVC

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ABSTRACT

Cardiac sarcoidosis (CS) overlaps in clinical presentation with arrhythmogenic right ventricular cardiomyopathy and shares phenotypic classification, including the presence of epsilon waves. The presence of conduction disease is seen exclusively in CS, as an important phenotypic difference. We present a case of ventricular tachycardia and epsilon waves due to CS, without conduction disease. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1097–102)

HISTORY OF PRESENTATION AND MEDICAL HISTORY

The patient was a 54-year-old Caucasian male pilot with no cardiac history who developed progressive dyspnea on moderate exertion with no syncope or awareness of any palpitations.

LEARNING OBJECTIVES

- To recognize the clinical overlap between the phenotypic classification of ARVC classification and CS.
- To recognize the absence of AV block or conduction system disease in the diagnosis of CS regardless of severity.
- To recognize that epsilon waves represent regions of late ventricular activation in infiltrative cardiomyopathies and are not pathognomonic of ARVC.

Presenting electrocardiography revealed sinus rhythm with a normal PR interval of 200 ms, QRS duration of 120 ms incorporating a post-ventricular excitation phenomenon consistent with epsilon waves, and prominent T-wave inversion (TWI) in leads V_1 to V_3 (**Figure 1**).

Subsequent electrocardiograms revealed salvos of ventricular tachycardia (VT) and premature ventricular complex left bundle branch block configuration and very delayed precordial R-wave transition (**Figure 2**). Echocardiography showed severe biventricular systolic dysfunction with a left ventricular ejection fraction of 15% to 20% and a severely dilated right ventricle. Coronary angiography showed moderate single-vessel disease without significant occlusion that would require coronary intervention.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included arrhythmogenic right ventricular cardiomyopathy (ARVC), pulmonary

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ABBREVIATIONS AND ACRONYMS

ARVC = arrhythmogenic right ventricular cardiomyopathy

AV = atrioventricular

CS = cardiac sarcoidosis

FDG = ^{18}F-fluorodeoxyglucose

PET = positron emission tomography

TWI = T-wave inversion

VT = ventricular tachycardia

embolism with biventricular failure, amyloid, and cardiac sarcoidosis (CS).

INVESTIGATIONS

Cardiac magnetic resonance imaging revealed biventricular systolic dysfunction with right ventricular dilatation and delayed hyperenhancement of gadolinium in the basal to mid septum of the right and left ventricles, extending to the epicardial left ventricular inferior wall (Figure 3). These imaging findings as well as electrocardiographic findings were initially suggestive of ARVC or left ventricular cardiomyopathy. Chest computed tomography did not reveal any mediastinal mass or lymph nodes.

MANAGEMENT AND FURTHER INVESTIGATIONS

Because of salvos of VT and frequent premature ventricular complexes, amiodarone was commenced, along with goal-directed medical therapy for heart failure and biventricular systolic dysfunction, and a dual-chamber implantable cardioverter-defibrillator was implanted for secondary prevention.

Genetic testing for inherited arrhythmia syndromes including an ARVC gene panel was performed, and the results were negative for all currently characterized ARVC genotypes.

Whole-body ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) was performed and showed nonspecific focal abnormal uptake in the visceral organs without radiographic correlate.

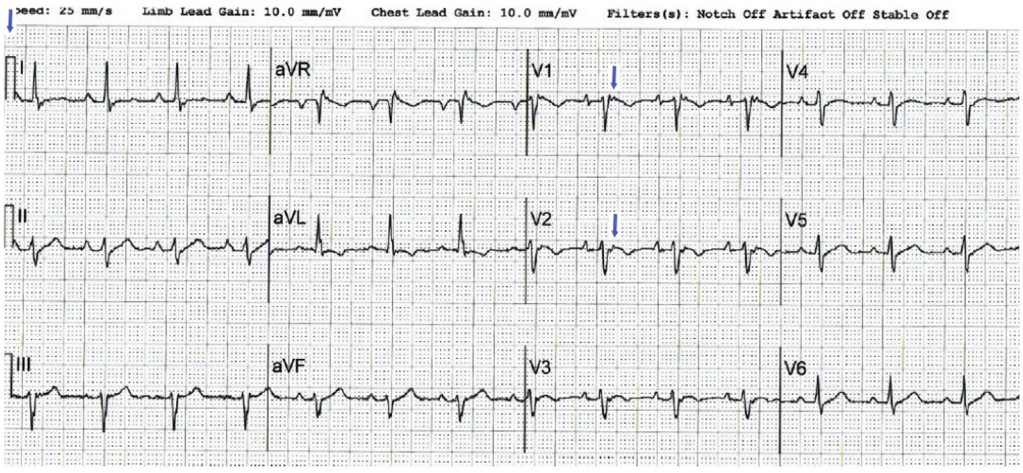
Cardiac FDG PET showed some scattered increased FDG uptake in the area of resting ammonia perfusion defect at the inferior-apical segments and basal inferior-septal segments, suggestive of active inflammation and scar in the same location (Figure 4). These findings are suspicious for but not specific to CS and could be seen in other inflammatory myocardial processes.

The patient subsequently developed recurrent and intractable ventricular arrhythmias after discharge from initial hospitalization, which prompted combined endocardial-epicardial VT ablation of 2 clinical VTs, with one originating from the anterolateral right ventricle extending from base to apex and the other localized to the basal inferolateral right ventricle (Figures 5A to 5C).

Four weeks after the initial VT ablation, the patient presented in electrical storm, with multiple device therapies and implantable cardioverter-defibrillator shocks that culminated in significant anxiety. Hypotension precluded escalation of his beta-blocker dose, and carvedilol was switched to propranolol to provide adjunct nonselective beta-blockade.

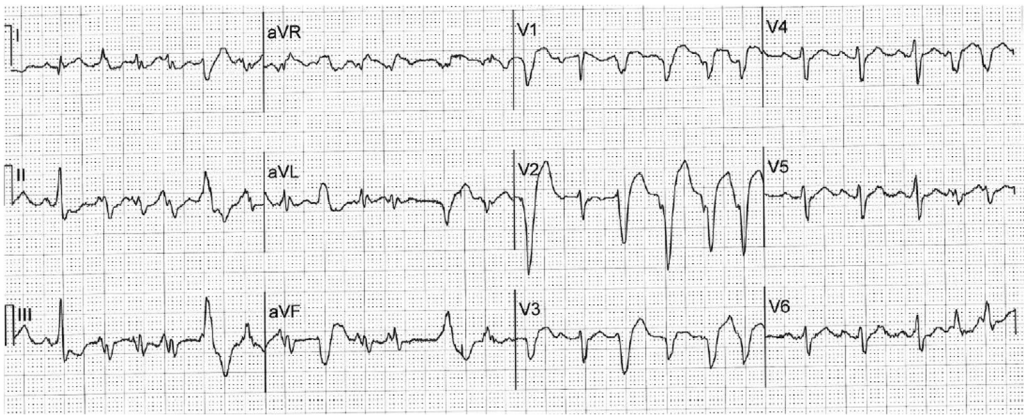
He then underwent surgical left cardiac sympathetic denervation (left stellate ganglionectomy) for better control of his ventricular arrhythmias. Lung

FIGURE 1 Presenting Electrocardiogram



Electrocardiogram showing sinus rhythm with normal PR interval, QRS duration of 120 ms that incorporated post-ventricular excitation consistent with epsilon waves **(blue arrows)**, and prominent T-wave inversion in leads V_1 to V_3.

FIGURE 2 Electrocardiogram Showing Salvos of Left Bundle Branch Block Ventricular Tachycardia and Pleomorphic Premature Ventricular Complexes



biopsy and lymph node biopsy were performed during the case, which revealed histologically normal lung (Figure 6) and discrete granulomata, respectively (Figures 7A and 7B).

DISCUSSION

Sarcoidosis is a multisystemic inflammatory disease characterized by histological evidence of non-caseating granulomas. There is a higher incidence of the disease among persons of North European and African descent, with a female preponderance (1). Although clinically evident cardiac involvement occurs in about 5% of patients with sarcoidosis, this can be the first manifestation of sarcoidosis in any organ. In addition, autopsy findings show cardiac involvement in up to 25% of sarcoidosis cases (2,3).

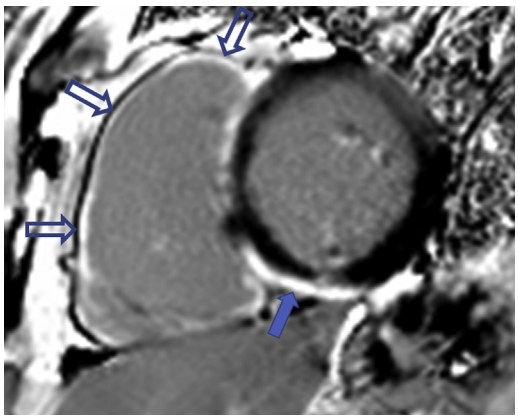
Epsilon waves remain an important tool and part of the diagnostic criteria for ARVC, but they have been shown to be less pathognomonic of ARVC, as this post-excitation potential can be seen, albeit rarely, in other infiltrative cardiomyopathies, such as CS (4).

In a retrospective study by Platonov et al. (5), the clinical overlap between phenotypic manifestations of CS and ARVC were well categorically differentiated by presence of some degree of atrioventricular (AV) block or conduction system disease in almost all the patients with CS identified, compared with ARVC. Our patient had none of these but rather more suggestive electrocardiographic features with repolarization abnormalities (TWI in leads V_1 to V_3) that was more consistent with ARVC, which made the initial diagnosis of CS more challenging at his first presentation.

In our case, the presence of epsilon waves, TWI in precordial leads V_1 to V_3 without any significant conduction delay or AV block, and severe biventricular systolic dysfunction affecting the right ventricle more than the left ventricle very effectively unified and camouflaged CS as a perfect phenocopy of ARVC.

Although genetic testing that was performed because of suspected ARVC phenotype was negative, this is not uncommon, as only 30% to 50% of patients with ARVC may be positive for currently identified genetic mutations of ARVC (6).

FIGURE 3 Cardiac Magnetic Resonance Imaging: 2-Chamber View



Circumferential late gadolinium enhancement (LGE) of the entire right ventricular wall and LGE of the basal inferior left ventricular epicardium **(arrows)**. Severe right ventricular enlargement is seen.

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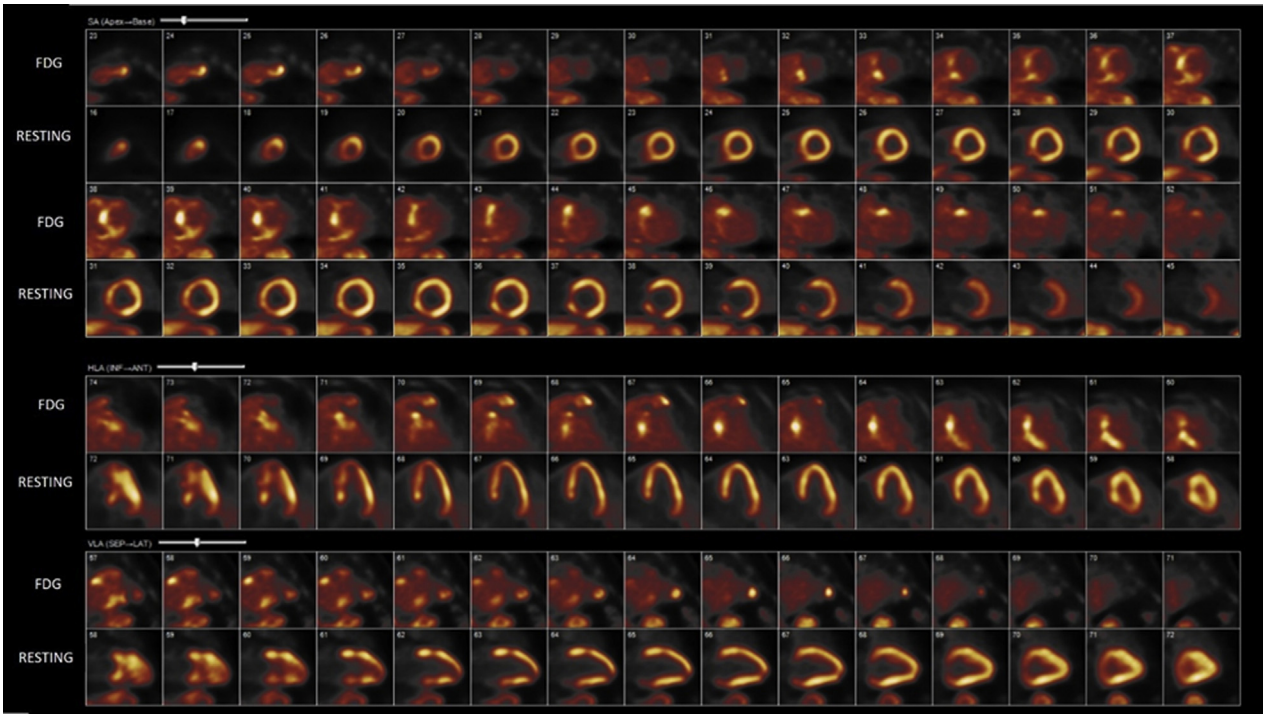
FIGURE 4 **Cardiac FDG Positron Emission Tomography**



Increased ^{18}F-fluorodeoxyglucose (FDG) uptake in inferior-apical and basal inferior-septal segments suggesting active inflammation and scar.

In addition, there was no mediastinal lymphadenopathy or other constitutional symptoms of chronic inflammatory disease that could have served as pointers. Results of lung biopsy were negative, and FDG PET pointed more at disease activity of active inflammation and could not have single-handedly predicted the diagnosis of CS (7).

The histopathologic presence of multiple noncaseating granulomas from the lymph node biopsy obtained during left stellate sympathectomy provided a crucial source to establish the diagnosis of CS when corroborated with the finding on all the imaging modalities and also engendered the opportunity to initiate an appropriate long-term management strategy for our patient, including early referral for cardiac transplantation evaluation.

FOLLOW-UP

Our patient was commenced on immunosuppressive therapy for CS with an initial good response. However, he had recurrent arrhythmias and worsening decompensated heart failure. He was successfully enlisted for cardiac transplantation and underwent successful transplantation with remarkable recovery and return of his quality of life.

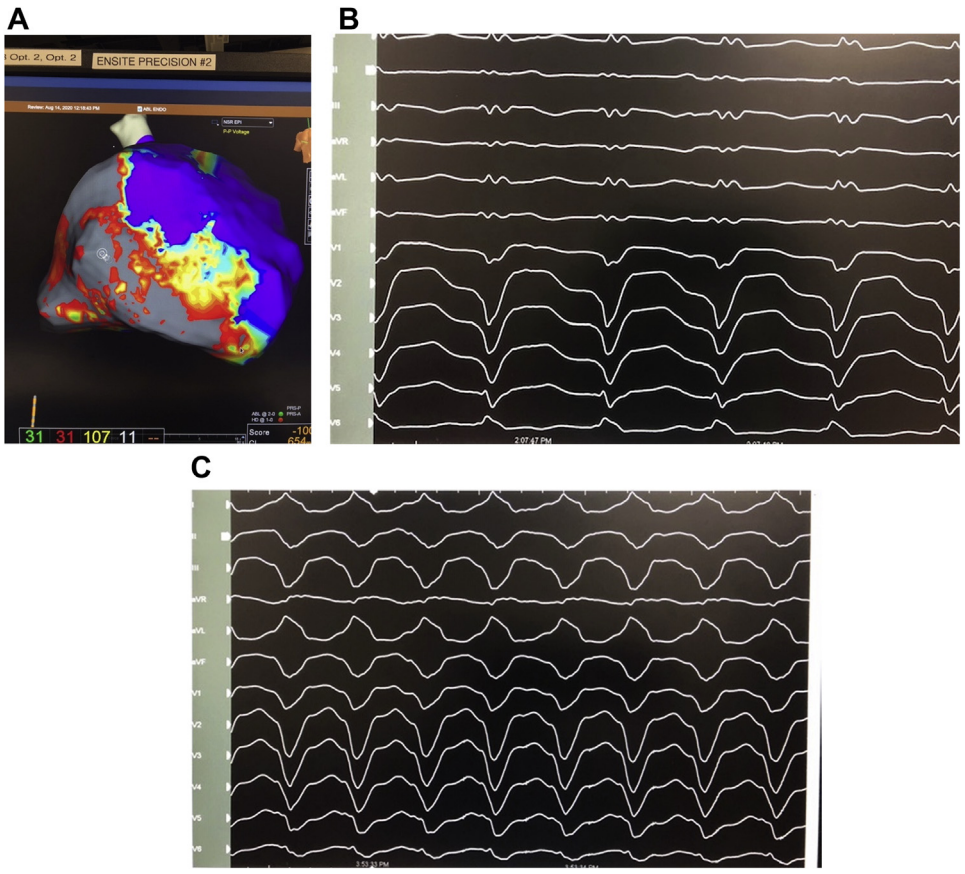
CONCLUSIONS

CS can overlap the clinical manifestation of ARVC and share a similar phenotypic classification as ARVC diagnosis.

The finding of epsilon waves on electrocardiography is characteristic of ARVC but not pathognomonic of ARVC, as this phenomenon can be seen in other cardiomyopathies, such as CS.

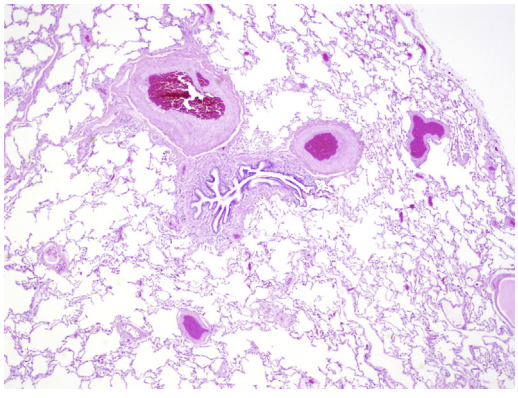
In the setting of phenotypic mimicry of ARVC by CS, although the presence of AV block and other electrocardiographic evidence of His-Purkinje system disease helps rule in CS, the absence of such conduction abnormalities does not necessarily rule it out, and this could make the diagnosis more challenging.

FIGURE 5 Combined Endocardial and Epicardial Ablation of Clinical VT



(A) Endocardial-epicardial ventricular tachycardia (VT) ablation map. **(B)** Basal to distal anterolateral right ventricular (RV) epicardial VT. **(C)** Basal inferolateral RV epicardial VT.

FIGURE 6 Normal Lung Histologic Findings



Although FDG PET and other imaging modalities provide important information about disease activity, the presence of a biopsy-proven diagnosis of sarcoidosis remains a useful correlation to differentiate this clinically important phenocopy of ARVC.

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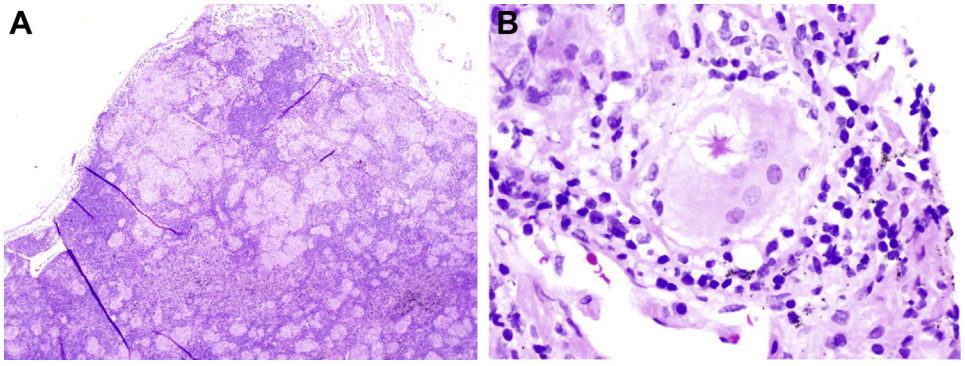
FIGURE 7 Lymph Node Biopsy Showing Histopathologic Findings Consistent With Sarcoidosis



(A) Low-power lymph node biopsy with granulomata. **(B)** High-power asteroid bodies in histiocytes.

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