A 16-year odyssey of cardiac sarcoid masquerading as idiopathic premature ventricular contractions and then arrhythmogenic cardiomyopathy

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Introduction

Cardiomyopathies can initially present with ventricular ectopy, which can be difficult to differentiate from idiopathic premature ventricular contractions (PVCs). Distinguishing cardiac sarcoidosis from arrhythmogenic right ventricular cardiomyopathy (ARVC) also can be challenging. We report the case of a patient who presented with benign PVCs that progressed to multiple recurrent ventricular arrhythmias over 16 years, was diagnosed as having ARVC, and eventually was found to have sarcoidosis.

Case report

A 44-year-old man with a diagnosis of ARVC was admitted for management of repetitive monomorphic ventricular tachycardia (VT) terminated by antitachycardia pacing from his implantable cardioverter-defibrillator. The patient's past history was remarkable for a diagnosis of idiopathic PVCs 16 years ago (Figure 1). Over the years, his PVCs had been highly symptomatic. Because the patient was intolerant of multiple medications, including beta-blockers, he underwent repeat electrophysiological studies (EPS) with ablation. Each was followed by symptomatic improvement but subsequent recurrent arrhythmias. Notably, he had no family history of cardiomyopathy or sudden death. The patient exercised routinely, including running, but he was not a competitive athlete. At his third EPS performed 4 years after initial presentation, the right ventricular (RV) voltage map was normal (no areas of electrograms <1.5-mV bipolar amplitude), and no sustained VT was inducible with programmed stimulation. Ablation targeted 3 different RV

KEY TEACHING POINTS

- In its early phase, cardiac sarcoidosis can present with isolated premature ventricular contractions, which makes the differentiation from benign premature ventricular contraction challenging.
- The clinical course of cardiac sarcoidosis can resemble that of arrhythmogenic right ventricular cardiomyopathy (ARVC), evolving over years.
- Myocardial scar in cardiac sarcoidosis can evolve with epicardial predominance, which also resembles ARVC.

PVCs. Cardiac magnetic resonance imaging showed possible thinning of the anterior RV, but no late gadolinium enhancement was observed. Six years later at the fourth EP study, again performed to ablate symptomatic PVCs, inducible sustained monomorphic VT was found, and a small low-voltage (<1.5 mV) area at the RV outflow region was noted. No ablation was performed at this time. Cardiac magnetic resonance imaging showed RV enlargement and severe hypokinesis. Late gadolinium enhancement was observed at the RV base to mid-free wall and mid-inferior wall but not in the LV. An implantable cardioverter-defibrillator was inserted. A positron emission tomography (PET) scan for sarcoid, RV endomyocardial biopsy, and genetic testing for ARVC were unrevealing. The fifth EPS performed 1 year later because of recurrent PVCs and VT revealed no inducible VT. Endocardial and epicardial mapping showed low-voltage areas (Figure 2, bottom), and substrate-guided ablation of these areas was performed. Symptoms improved, but frequent PVCs led to a sixth procedure 1 year later, targeting multiple morphologies of PVCs. The low-voltage endocardial scar was noted to have extended (Figure 2, middle). Symptoms again improved, but occasional symptomatic

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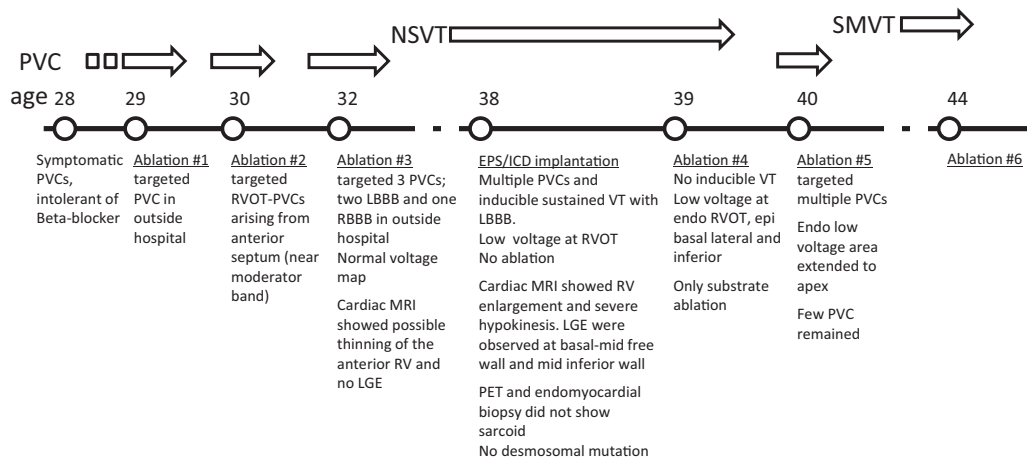
Figure 1   Time line of the disease. The patient had a history of 6 ablation procedures over 16 years with progression of arrhythmia over time. EPS = electrophysiological study; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LGE = late gadolinium enhancement; MRI = magnetic resonance imaging; NSVT = nonsustained ventricular tachycardia; PET = positron emission tomography; PVC = premature ventricular contraction; RBBB = right bundle branch block; RV = right ventricle; RVOT = right ventricular outflow tract; SMVT = sustained monomorphic ventricular tachycardia; VT = ventricular tachycardia.

PVCs still occurred and preceded the development of increasingly frequent sustained VT.

At the current presentation, the electrocardiogram (ECG) during sinus rhythm showed slight prolongation of the PQ interval of 210 ms, T-wave inversion in the inferior and precordial leads, and low-voltage QRS complexes (Supplemental Figure 1). The ECG of the current VT is shown in Figure 3. Echocardiography revealed significant dilation and wall-motion abnormalities of the RV, but left ventricular size and function were normal.
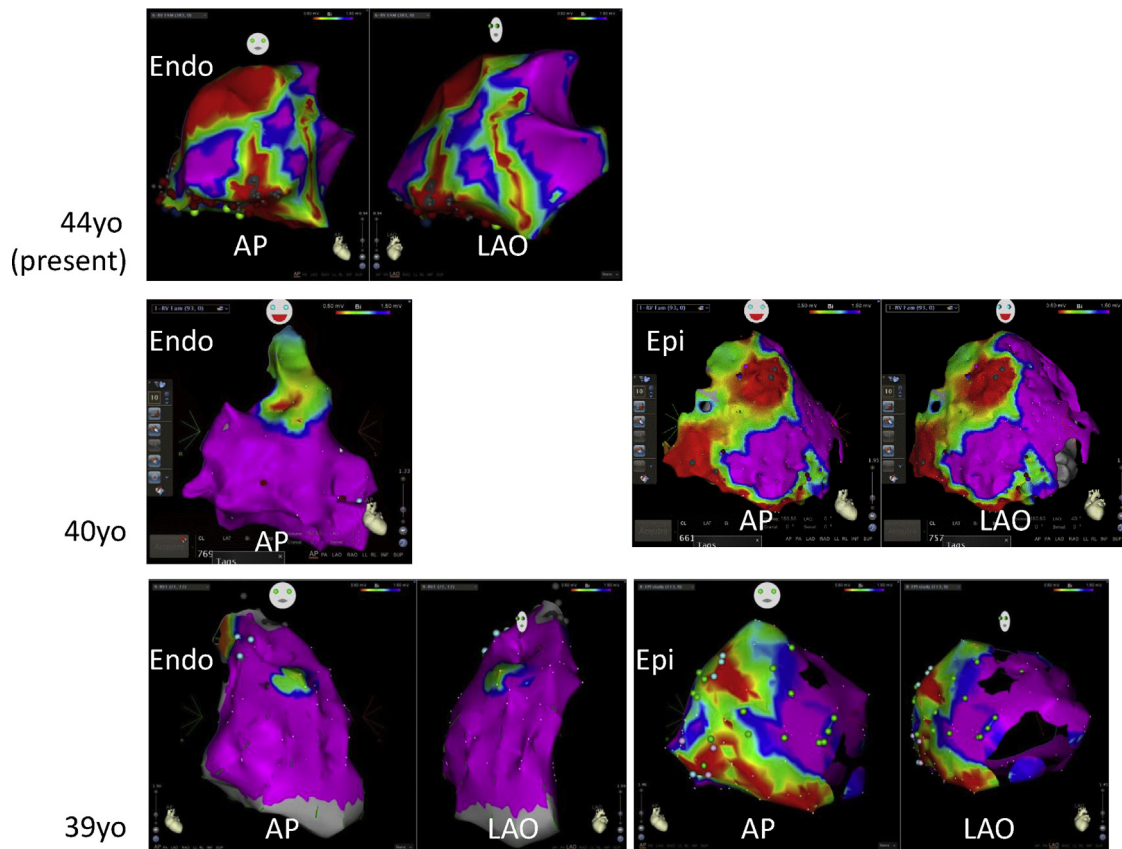
Figure 2   Electroanatomic sinus rhythm voltage maps in anteroposterior (AP) and left anterior oblique (LAO) projections. Normal voltage myocardium (>1.5 mV) is depicted as *purple*, and very low voltage (<0.5 mV) is depicted as *red*. Ablation sites are marked by *red circular tags*. **Top:** Low-voltage scar areas extend from the inferior to anterior free wall and inferobasal aspect of septum superiorly. Those areas showed normal voltage in previous endocardial mapping, whereas epicardial mapping showed low voltage in previous sessions (**middle, bottom**).
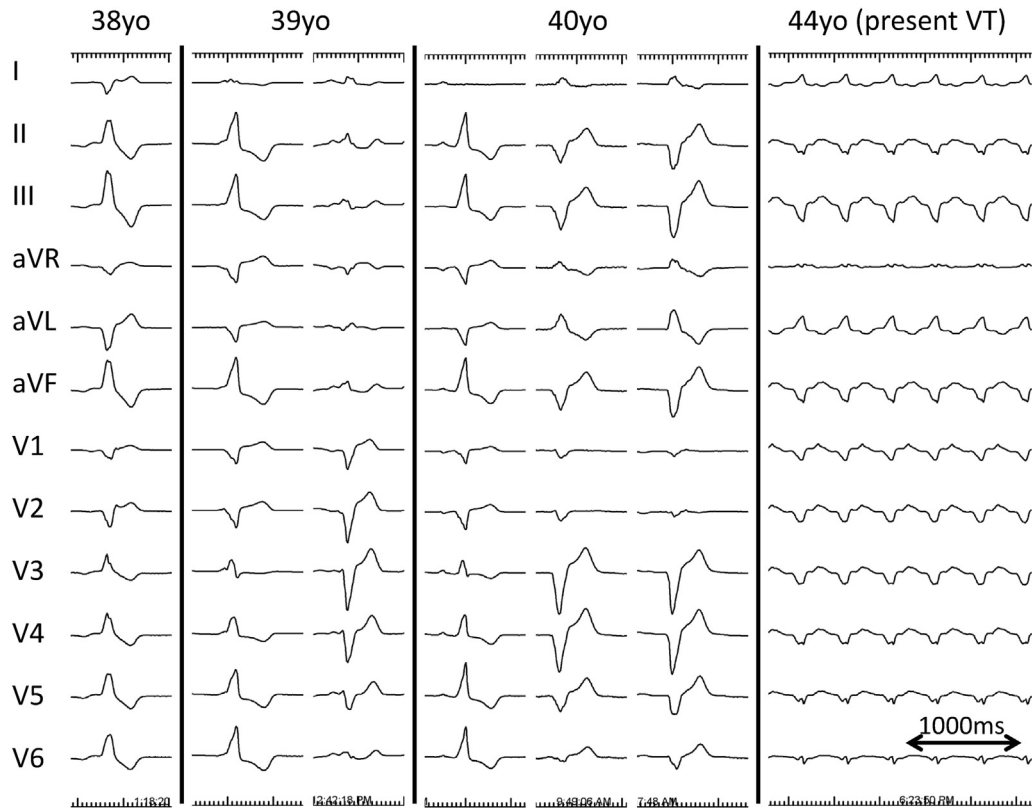
Figure 3 Electrocardiograms of ventricular arrhythmias. All arrhythmias had a left bundle branch block configuration in lead V_1 and different frontal plane axes consistent with a possible origin from the expanding low-voltage scar region over time. VT = ventricular tachycardia.

EPS was performed under general anesthesia, with mapping and ablation per our previously described methods.[1] Endo- and epicardial mapping were performed using a 3.5-mm irrigated-tip ablation catheter. The RV endocardial electroanatomic voltage map revealed an extensive low-voltage (<1.5 mV bipolar) area extending from the inferior to anterior free wall and inferobasal aspect of the septum (Figure 2, top), which was substantially more prominent than that seen at the ablation procedure 4 years ago. Interestingly, no sustained VT was inducible with up to 4 extrastimuli and burst pacing from the RV apex and RV outflow tract at baseline and during isoproterenol or epinephrine infusion. Therefore, an initial decision was made to start with ablation guided by voltage mapping and pace-mapping. Surprisingly, pace-mapping at the anterior inferior RV reproducibly induced sustained monomorphic VT (Figure 3). Limited mapping during VT with entrainment was consistent with a broad isthmus extending along the anterobasal RV along the tricuspid annulus, defined in part by regions of unexcitable scar that did not capture at 10 mA, 2-ms pulse width, in the mid-anterior RV (gray regions in Figure 2, top). Radiofrequency application in the isthmus region terminated VT. Additional radiofrequency lesions placed extending between the electrically unexcitable scar and the tricuspid annulus rendered the region unexcitable to pacing at 10 mA, 2 ms. No VT was then inducible by pacing, including that from the anterior RV with burst pacing.

The subtle ECG change with slight prolongation of PQ interval compared with the previous recording suggested an ARVC diagnosis. Before the ablation, a PET scan was performed with ^{18}F-fludeoxyglucose (FDG) imaging after a high-fat, no-carbohydrate diet to suppress cardiac glucose uptake and facilitate recognition of cardiac inflammation. The scan revealed multiple areas of ^{18}F-FDG uptake in the RV anterior wall and ventricular septum that were not present 6 years previously and were not attributable to catheter ablation (Supplemental Figure 2). Multiple ^{18}F-FDG–avid lymph nodes were now also present in the mediastinum and paratracheal area. Biopsy of a mediastinal lymph node revealed noncaseating granulomas. A diagnosis of cardiac sarcoidosis was made, and immunosuppressive steroid therapy was initiated. Over 6-month follow-up, the patient has been free from VT.

Discussion

This patient is remarkable for a course of RV arrhythmias that evolved over more than 15 years, initially diagnosed as idiopathic RV outflow tract arrhythmias, subsequently diagnosed as ARVC based on 3 major and 2 minor criteria for ARVC,[2] and then finally determined to be cardiac sarcoidosis. Although we cannot absolutely exclude the possibility that his initial PVCs were idiopathic, this seems unlikely given their multiple locations. Although he had undergone multiple ablation procedures, the areas of low-voltage scar that

evolved were more extensive than the ablation areas and un-likely were related to the procedures alone. A gradually progressive course of sarcoidosis seems most likely.

Cardiomyopathies can initially present with ventricular ectopy, and the ectopy sometimes arises from the outflow septum, making differentiation from idiopathic PVCs challenging.[3] After evidence of multiple RV arrhythmia sites and RV functional abnormalities was noted, a diagnosis of ARVC was made after a PET scan performed for sarcoidosis and endomyocardial biopsy was negative. It is well known that differentiating cardiac sarcoidosis from ARVC can be challenging, and there have been several case reports of sarcoid initially diagnosed as ARVC when RV enlargement was the only structural abnormality identified.[4–9] The suspicion of sarcoidosis is increased by the presence of lymphadenopathy, parenchymal pulmonary nodules, and conduction disturbances, but these are often absent, and the diagnosis may not be established until examination of the heart at necropsy or after cardiac transplantation.[7] Our patient had undergone 6 EPS over 15 years, with catheter ablation targeting symptomatic PVCs. During those 6 studies (the last performed 12 years from the start of symptoms), sustained VT was not inducible. Up to the first 4 sessions (10 years from the start of symptoms), endocardial mapping depicted no low-voltage area except for what was interpreted as postablation scar localized to the RV outflow tract. In the fifth and sixth sessions (4 and 5 years ago), endocardial mapping showed the same finding as in previous sessions. In contrast, epicardial mapping depicted a large basal and inferior low-voltage area extending to the apex. Those areas increased in size within 1 year, and the PVCs arising from this region became dominant (Figures 2 and 3). The present ablation procedure was performed 4 years after the last session. Endocardial low-voltage areas were now located opposite the epicardial scars seen at the previous session. It is noteworthy that scar expansion seemed to progress from the epicardium to endocardium over time, as is believed to occur in ARVC. In a previous series of sarcoid VT patients, we noted that the area of RV low-voltage scar was often larger in the epicardium than in the endocardium.[10] This seems to be another feature that can be common to both sarcoid and ARVC.

Conclusion

We report a case of cardiac sarcoidosis that can mimic idiopathic ventricular arrhythmias and ARVC, and can have a slowly progressive course that eludes diagnosis for years despite advanced imaging. The patient also demonstrated gradual myocardial scar progression in an epicardial to endocardial direction, demonstrating that this feature, commonly seen in ARVC, can also occur in cardiac sarcoid.

Appendix
Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2017.10.018.

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