Diagnosis of Right Ventricular Cardiac Sarcoidosis With Cardiac Magnetic Resonance in a Patient Presenting With Ventricular Tachycardia

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ABSTRACT Sarcoidosis patients often have myocardial involvement, however, very few have clinically significant cardiac disease and ventricular tachycardia as the initial presentation is exceedingly rare. We report the case of a middle-aged male with symptomatic but clinically stable ventricular tachycardia. Chest radiograph, computed tomography, and positron emission tomography demonstrated pulmonary and mediastinal abnormalities but no definitive etiology for his arrhythmia. Transthoracic echocardiogram revealed the nonspecific cardiac abnormalities of right ventricular dilation and septal flattening. Cardiac magnetic resonance demonstrated delayed enhancement and akinesia of the right ventricular free and inferior walls—virtually diagnostic of an infiltrative myocardial disease. The diagnosis was then verified with transbronchial biopsy showing noncaseating granulomas consistent with sarcoidosis. In conclusion, this case illustrates an unusual presentation of sarcoidosis and demonstrates how the diagnosis can be made using cardiac magnetic resonance alongside transbronchial biopsy.

INTRODUCTION Sarcoidosis is a multisystem disorder of unknown etiology characterized by the formation of noncaseating granulomas.1 Cardiac involvement is clinically apparent in less than 5% of patients with systemic disease2 but potentially fatal; historical studies have reported that cardiac involvement accounts for 13 to 25% of deaths from systemic sarcoidosis.3 Clinical manifestations of cardiac sarcoidosis include conduction abnormalities, syncope, congestive heart failure, and sudden cardiac death.4 Based on these findings, it is recommended that every patient with systemic sarcoidosis be evaluated for potential cardiac involvement. However, diagnosing cardiac sarcoidosis can be difficult for multiple reasons including its low prevalence, variable presentation, and unproven imaging techniques. Endomyocardial biopsy is often used as a reference standard despite a sensitivity of only 20 to 30% largely because of patchy myocardial infiltration.5

CASE PRESENTATION A 34-year-old African–American male without prior cardiac disease presented with a 3-week history of paroxysmal palpitations associated with substernal chest discomfort. Past medical history was notable for tobacco use and hypertension. His only medication was cyclobenzaprine for musculoskeletal pain. Family history was significant for pulmonary sarcoidosis in his mother and 1 maternal aunt.

Resting blood pressure was 103/59 mmHg and heart rate was 160 bpm. Examination of the heart, lungs, and abdomen was unremarkable. A 12-lead electrocardiogram (ECG) revealed monomorphic ventricular tachycardia (VT) (Fig. 1), and he was cardioverted with a procainamide infusion. Initial evaluation as to the etiology of the VT revealed no evidence of a metabolic or drug effect. Chest radiograph (Fig. 2) and computed tomography (CT) demonstrated bilateral upper lobe nodular consolidation, extensive pulmonary scarring in an upper lung zone distribution, and mediastinal and hilar lymphadenopathy (Fig. 3).

Transthoracic echocardiography revealed normal left ventricular function with an ejection fraction equal to or greater than 65%, mild to moderate right ventricular dilation, and a flattened septum (Fig. 4). Septal flattening was thought to be consistent with right ventricular pressure overload, possibly explained by the pulmonary findings.

Positron emission tomography with CT (PET-CT) demonstrated hypermetabolism within multiple hilar and mediastinal lymph nodes, and the right ventricular free wall (Fig. 5). This was suggestive, but not conclusive, of an infiltrative cardiomyopathy.

Cardiac magnetic resonance (CMR) proved far more revealing. In contrast to the techniques mentioned above, which were unable to accurately demonstrate and localize myocardial involvement, CMR demonstrated transmural delayed enhancement and akinesia of the right ventricular free and inferior walls (Fig. 6). CMR also confirmed the echo and PET-CT findings showing the precise location of many mediastinal and hilar lymph nodes.
Once the CMR results were known cardiac sarcoidosis was strongly suspected. Other considerations included arrhythmogenic right ventricular dysplasia and coronary ischemia. Arrhythmogenic right ventricular dysplasia is a rare genetic cardiomyopathy characterized by fibrofatty infiltration of the myocardium, predominantly of the right ventricle, which can present similarly but is not associated with pulmonary abnormalities. Ischemia was thought to be unlikely with a normal troponin, no evidence of ischemia or infarct on the postcardioversion ECG, and transmural rather than subendocardial myocardial enhancement on CMR.

An electrophysiology study showed a large right ventricular scar with inducible VT (Fig. 7). Catheter ablation was not successful in rendering the VT noninducible. An automatic implantable cardioverter-defibrillator (AICD) was implanted the following day. Final tissue diagnosis was made using transbronchial biopsy guided by CT, CMR, and bronchoscopic ultrasound, which verified noncaseating granulomas (Fig. 8).

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FIGURE 5. (A–D) PET-CT. Nonspecific multifocal nodular consolidative areas with robust 18F-fludeoxyglucose avidity are seen within the lungs, and there are sequelae of old granulomatous disease in the hilum and mediastinum. The axial view (B) shows nonspecific enlargement and abnormal accumulation of radiotracer in the right ventricular free wall (arrow) consistent with inflammation. The patient was studied on the Philips Gemini combined PET-CT scanner approximately 1 hour after the intravenous injection of 13 mCi fludeoxyglucose.

FIGURE 6. CMR. Four chamber (A) and sagittal (B) views with delayed hyperenhancement technique demonstrates persistent enhancement of the right ventricular free wall consistent with inflammation or fibrosis. A 1.5-T magnetic resonance imaging scanner was used in this study.

FIGURE 7. Electrophysiology study. Three-dimensional electroanatomical voltage map demonstrates large area of scar on the right ventricular basal inferior and free walls. Activation mapping of the VT found a large circuit involving this region and the inferior apex. Catheter ablation of an apparent critical isthmus was not successful in rendering the VT noninducible. There was no evidence of preexcitation of retrograde accessory pathway conduction.
DISCUSSION

Sarcoidosis is a multisystem disorder of unknown etiology characterized by the formation of noncaseating granulomas. These granulomas consist of both lymphocytes and phagocytes with the participation of a diverse range of cytokines mediating tissue inflammation and fibrosis. Intrathoracic involvement occurs in more than 90% of patients, but sarcoidosis can also be widespread with systemic manifestations affecting multiple organs including the eye, central nervous system, gastrointestinal tract, and kidneys. The heart is another organ that can be affected.

Although 25% of sarcoidosis patients in the United States have myocardial involvement at autopsy, less than 5% have clinically significant cardiac disease. The disease most frequently involves the left ventricle and septum, and is only rarely isolated to the right ventricle as in this case. Despite its low prevalence, cardiac sarcoidosis is often fatal; studies predating the widespread use of AICD devices reported that it accounted for 13 to 25% of deaths from sarcoidosis. In other cases, manifestations include conduction abnormalities, arrhythmia, syncope, and congestive heart failure. Although 23% of patients with cardiac sarcoidosis have VT, this is very rare as the initial manifestation of systemic sarcoidosis. The mechanism of VT is thought to be re-entry through both active inflammatory lesions as well as scarred and fibrotic tissue from old granulomas.

The initial presentation of stable VT because of underlying cardiac sarcoidosis, as seen in this case, is rarely reported, but may be underdiagnosed because of the challenges in its detection. Uusimaa et al established that sarcoidosis can manifest as VT without any detectable systemic findings in a case series of nine such patients. However, in this study eight patients were diagnosed by endomyocardial biopsy and the remaining patient was diagnosed by lymph node biopsy during mediastinoscopy 3 years after their initial presentation.

Here, we extend these findings by suggesting an effective diagnostic strategy using CMR and transbronchial biopsy and avoiding endomyocardial biopsy. In 2006, the most comprehensive guidelines for the diagnosis of cardiac sarcoidosis were updated by the Japanese Society of Sarcoidosis and Other Granulomatous Disorders (Table I). These guidelines were

### TABLE I. Modified Japanese Ministry of Health and Welfare Criteria for Diagnosis of Cardiac Sarcoidosis

<table>
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<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<td>a) Advanced atrioventricular block</td>
<td>a) Abnormal electrocardiogram findings include ventricular tachycardia, multifocal or frequent premature ventricular contractions, complete right bundle branch block, pathologic Q waves, or abnormal axis deviation.</td>
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<tr>
<td>b) Basal thinning of the ventricular septum</td>
<td>b) Abnormal echocardiogram demonstrates regional wall motion abnormalities, ventricular aneurysm, or unexplained increase in wall thickness.</td>
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<td>c) Positive cardiac gallium uptake</td>
<td>c) Perfusion defects detected by myocardial scintigraphy.</td>
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<td>d) Left ventricular ejection fraction &lt;50%</td>
<td>d) Delayed gadolinium enhancement of the myocardium on cardiac magnetic resonance image scanning.</td>
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<td>e) Interstitial fibrosis or monocyte infiltration greater than moderate grade by endomyocardial biopsy</td>
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a major step forward and can be very useful clinically, but are not be applicable to every patient. In this case, the guidelines would have failed to identify cardiac sarcoidosis because of the patient’s unusual presentation and nonspecific findings on all imaging modalities other than CMR.

Despite these challenges, it is still recommended that every patient with sarcoidosis should be evaluated for cardiac involvement. The diagnosis is difficult because of its rarity, variable presentation, and unproven imaging techniques. Without a gold standard, the most accurate diagnostic strategy likely involves a combination of ECG, imaging, and histological evidence. Generally, all patients should have at least one 12-lead ECG, if not a 24-hour ambulatory ECG. Echocardiography is also often recommended, although the spectrum and significance of echocardiographic findings is not fully known. Some have suggested, as was seen in this patient, that echocardiography may also lack the sensitivity to detect early myocardial involvement.

In the absence of a gold standard, the endomyocardial biopsy is often used as a reference standard despite significant limitations. Although the finding of noncaseating granulomas on biopsy is essentially pathognomonic for cardiac sarcoidosis, the test is not without significant risks, and is also criticized for its relatively low yield. This is largely attributed to patchy infiltration of the myocardium, which decreases the sensitivity to 20 to 30%. Biopsy also carries a risk of cardiac perforation which is theoretically greater in the thin right ventricular free wall. For these reasons as well as overwhelming evidence in support of the diagnosis from PET-CT and CMR findings, a biopsy was not indicated in this case as it would not have changed management.

Of the newer imaging techniques, PET-CT is unique in that it can provide both an indication of disease metabolic activity and measure the extent of myocardial infiltration. However, although small studies have reported PET to have a sensitivity of 85 to 100%, its specificity is much lower and may be as low as 38.5%. This is due to a similar uptake distribution in patients with dilated cardiomyopathy and in some cases of pulmonary hypertension as well as normal variation. CMR, another newer modality, is increasingly recognized for its accuracy in the evaluation of cardiac sarcoidosis, as was demonstrated in this case. Its sensitivity and specificity are reported as 75 to 100% and 77 to 78%, respectively. In a prospective trial of sarcoidosis patients by Patel et al, delayed enhancement CMR was proven to be nearly twice as sensitive for cardiac involvement as the consensus criteria in Table I. With these techniques, cardiac sarcoidosis is distinguished from ischemic cardiomyopathy by its lack of restraint to coronary artery distributions and lack of subendocardial predominance. Because of CMR’s superlative tissue resolution, it can also serve as a guide to help localize the ideal location for endomyocardial biopsy. If endomyocardial biopsy is to be avoided, as in this case, CMR also has the added benefit of accurately depicting the anatomy which could aid in preprocedural planning for noncardiac tissue biopsy via either mediastinoscopy or bronchoscopy.

An electrophysiology study was performed to further evaluate the electrocardiographic significance of the disease and to potentially eliminate the major focus of VT. Confirmation was made with bronchoscopy and transbronchial biopsy, which demonstrated noncaseating granulomas consistent with sarcoidosis.

Corticosteroids are the first-line therapy in patients with evidence of cardiac sarcoidosis. Although there is still considerable controversy about the optimal dose and duration, they have been shown to halt disease progression and are associated with improved survival. As was illustrated in this case, however, their effects on stopping VT are less conclusive. After corticosteroid therapy, repeat PET-CT, and CMR have both been used successfully to demonstrate suppression of disease activity and reduced tissue infiltration.

**CONCLUSION**

Cardiac sarcoidosis is a rare but potentially fatal condition and should be considered in all patients presenting with unexplained arrhythmia. Multiple imaging studies have recently been proposed to evaluate for this condition. Here we report an unusual presentation of cardiac sarcoidosis and show how CMR and transbronchial biopsy can effectively make the diagnosis without the risks associated with endomyocardial biopsy. This case adds further evidence that CMR could be considered the first-line imaging study when cardiac sarcoidosis is strongly suspected.

**REFERENCES**