Cardiac Sarcoidosis and Consequent Arrhythmias

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KEYWORDS

• Cardiac sarcoidosis • Ventricular arrhythmias • Sudden cardiac death • Atrioventricular block

KEY POINTS

- A cardiac electrophysiologist is an integral part of the multidisciplinary team taking care of patients with sarcoidosis because arrhythmias and electrocardiographic changes are the most common presentations indicating cardiac involvement.
- Inflammation and granulomatous infiltration of myocardium is the cause of electrocardiographic abnormalities, conduction disturbances, atrial arrhythmias, ventricular arrhythmias, and sudden death.
- Immunosuppression and catheter ablation can reduce arrhythmic burden in patients with cardiac sarcoidosis.
- An implanted cardiac defibrillator is indicated in most patients with cardiac involvement according to expert consensus based on observational research.

INTRODUCTION

Sarcoidosis is a systemic inflammatory disease of unknown cause, characterized by the formation of noncaseating granulomas and resultant scarring of affected organs. Myocardial involvement occurs in 20% to 30% of cases, though only roughly one-quarter of these patients are diagnosed antemortem.[1,2] This discrepancy is partly caused by the inherent difficulties in making the diagnosis of cardiac sarcoidosis (CS) and partly caused by the potential for the presenting manifestation of CS to be sudden cardiac death.[3]

Electrophysiologic (EP) findings are underrecognized in CS and are more common than congestive heart failure (**Table 1**). Electrocardiography and invasive EP testing are important components in the evaluation and diagnosis of CS. After myocardial involvement has been established, an implantable cardiac defibrillator (ICD) may be indicated. Many patients with CS will also have a pacing indication, given a high incidence of atrioventricular (AV) block in this population. Atrial and ventricular tachyarrhythmias are also common manifestations of CS and require management with antiarrhythmic therapy, immunosuppression, and/or catheter ablation. This article focuses on the EP manifestations of CS and the role of the cardiac electrophysiologist in the multidisciplinary team essential for screening, risk stratification, and management of patients with this rare disease.

ROLE OF THE CARDIAC ELECTROPHYSIOLOGIST IN DIAGNOSING CARDIAC SARCOIDOSIS

Electrophysiology Study

In patients with extracardiac sarcoidosis and unexplained palpitations and/or syncope, an EP study can identify an arrhythmic cause and potentially suggest cardiac involvement, particularly when imaging studies are inconclusive (**Box 1**). Inducible monomorphic ventricular tachycardia (VT) in these patients is a major diagnostic criterion for establishing cardiac involvement in the revised JMH (Japanese Ministry of Health) criteria and is

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Table 1
Incident arrhythmic presentation of CS

Arrhythmia	Prevalence in Study Series (%)
Atrioventricular block	26–67
Bundle branch block	12–61
Atrial arrhythmias	23–25
Ventricular arrhythmias	11–73
Sudden cardiac death	12–65
Congestive heart failure	10–30

Data from Refs.[1,14,15,26,27,39]

among the Heart Rhythm Society (HRS)/American College of Cardiology (ACC)/World Association for Sarcoidosis and Other Granulomatous Disorders' criteria for probable CS in the recently released consensus statement (**Box 2**).[4,5] Accordingly, ventricular stimulation with inducible VT is both a risk factor for sudden death and a potential path for the diagnosis of a CS in the absence of other criteria.[6,7]

Electroanatomical Mapping

Three-dimensional electroanatomical mapping (EAM) systems have proven to be invaluable tools in the mapping and ablation of complex arrhythmias. These systems are also able to reconstruct chamber dimension and demonstrate the presence or absence of viable myocardium by the recording of voltage with a roving mapping catheter. EAM has been used in arrhythmogenic right ventricular (RV) cardiomyopathy (ARVC) with excellent correlation to cardiac MRI[8] and likely has similar utility for CS.

In cases of isolated CS or when sarcoidosis is suspected despite negative-yield extracardiac biopsy, endomyocardial biopsy may be required to confirm the diagnosis. In these cases, there may also be a role for EAM. The yield of the endomyocardial biopsy may be improved when performed with the guidance of voltage mapping in the EP laboratory, where the bioptome is directed to the areas of reduced voltage (ie, abnormal myocardium) and biopsies taken at these sites (**Fig. 1**).[9,10]

Box 1
Indications for EP study in patients with sarcoidosis

- Rare unexplained palpitations
- Risk stratification for sudden death in patients with known CS
- Unexplained syncope
- Evaluation of His-Purkinje system disease

Clinical Overlap with Arrhythmogenic Right Ventricular Cardiomyopathy

CS can present with features that mimic ARVC, including repolarization and depolarization abnormalities on electrocardiogram (ECG) (including even the presence of an epsilon wave[11]), left bundle branch block morphology VT, abnormal signal-averaged ECG, and RV dilatation, among others. Taken together, CS can satisfy task force diagnostic criteria for ARVC.[9,11–13] Physicians should be aware that the conditions have overlapping clinical features and consider investigating for CS in the patients referred with possible ARVC in the appropriate clinical context.

Conduction system disease and sinus node dysfunction

In CS, granulomatous infiltration of the basal interventricular septum can cause injury to the various elements of the cardiac conduction system, resulting in a variety of conduction disturbances leading to bundle branch block or any level of AV block. Because of the progressive nature of CS, the level and severity of conduction block may also progress in untreated CS (**Fig. 2**).

Bundle branch block (right bundle branch block in particular) has been observed on surface ECGs in 12% to 61% of cases of CS, depending on study series.[1,14–16] Although neither sensitive nor specific, both right and left bundle branch block are seen more commonly in patients with CS than those with sarcoidosis without myocardial involvement[16] and should prompt further investigations.

Complete AV block (CAVB) is one of the most common findings in patients with clinically evident CS, with a prevalence of 25% in one retrospective analysis.[1] Although usually thought to be related to infiltration of the conduction system itself, granulomatous involvement of the AV nodal artery has also been described as a cause of AV block in CS.[15] CAVB often occurs at a younger age in patients with sarcoidosis than in individuals with complete heart block from other causes.

Treatment of patients with high-grade AV block with permanent pacing should be performed in accordance with published guidelines.[17] However, the presence of AV block likely signifies extensive myocardial involvement from sarcoid granuloma and portends a higher risk of future ventricular arrhythmias (VAs).[18] For this reason, the recently published HRS' expert consensus statement gives a class IIa recommendation for ICD implantation (regardless of left ventricular ejection fraction [LVEF]) for the primary prevention of sudden cardiac death in CS if patients meet an indication for pacing.[4]