Cardiac Sarcoidosis

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KEYWORDS

• Cardiac sarcoidosis • Clinically silent • Clinically manifest • Atrioventricular block
• Ventricular arrhythmias • Heart failure • Sudden cardiac death

KEY POINTS

- Studies have suggested that clinically manifest cardiac involvement occurs in perhaps 5% of patients with pulmonary/systemic sarcoidosis.
- The 3 principal manifestations of cardiac sarcoidosis (CS) are conduction abnormalities, ventricular arrhythmias, and heart failure.
- An estimated 20% to 25% of patients with pulmonary/systemic sarcoidosis have asymptomatic cardiac involvement (clinically silent cardiac involvement).
- The prognosis of clinically manifest disease primarily relates to the extent of left ventricular (LV) dysfunction.
- Recently a consensus document detailed recommendations on the management of most aspects of CS.

EPIDEMIOLOGY AND CLINICAL MANIFESTATIONS

Studies have suggested that clinically manifest cardiac involvement occurs in perhaps 5% of patients with pulmonary/systemic sarcoidosis. Clinical features of CS depend on the location, extent, and activity of the disease.[1,2] The 3 principal manifestations of CS are (1) conduction abnormalities,[3–8] (2) ventricular arrhythmias,[9] and (3) heart failure.[2] Other data indicate that many patients with pulmonary/systemic sarcoidosis have asymptomatic cardiac involvement (clinically silent disease). For example, autopsy studies have estimated the prevalence of cardiac involvement to be at least 25% of patients with sarcoidosis in North America.[10–12] These incidence data from autopsy series are very consistent with recent data using modern late gadolinium enhancement–cardiac magnetic resonance (LGE-CMR) technology. These LGE-CMR studies in patients with extracardiac sarcoidosis found clinically silent cardiac involvement in 13%,[13] 25.5%[14] and 25.9%[15] of cases respectively.

DIAGNOSIS

In 2014, an international guideline for the diagnosis of CS was published (**Box 1**).[16] The international expert consensus statement was written by experts in the field who were chosen by the Heart Rhythm Society in collaboration with multiple other societies. Before this consensus document, the only published diagnostic guidelines were the Japanese Ministry of Health and Welfare criteria[17] and the National Institutes of Health's A Case

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Box 1
Expert consensus recommendations on criteria for diagnosis of cardiac sarcoidosis

There are 2 pathways to a diagnosis of CS:

1. Histologic diagnosis from myocardial tissue

   CS is diagnosed in the presence of noncaseating granuloma on histologic examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable)

2. Clinical diagnosis from invasive and noninvasive studies

   It is probable[a] that there is CS if

   a. There is a histologic diagnosis of extracardiac sarcoidosis and
   b. One or more of following is present
      i. Steroid +/− immunosuppressant responsive cardiomyopathy or heart block
      ii. Unexplained reduced left ventricular ejection fraction (<40%)
      iii. Unexplained sustained (spontaneous or induced) ventricular tachycardia
      iv. Mobitz type II second-degree heart block or third-degree heart block
      v. Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
      vi. LGE on CMR (in a pattern consistent with CS)
      vii. Positive gallium uptake (in a pattern consistent with CS)

      Plus

   c. Other causes for the cardiac manifestations have been reasonably excluded

[a] In general, probable involvement is considered adequate to establish a clinical diagnosis of CS.[24]

From Birnie DH, Sauer WH, Bogun F, et al. HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. Heart Rhythm 2014;11(7):1306; with permission.

Control Etiology of Sarcoidosis Study (ACCESS) set of criteria published in 1999.[18]

Role of Endomyocardial Biopsy in the Diagnosis of Cardiac Sarcoidosis

In patients with extracardiac sarcoidosis, lymph node or lung biopsy is typically targeted first due to the higher diagnostic yield and lower procedural risk. In cases of isolated CS or negative extracardiac biopsy, endomyocardial biopsy (EMB) may be required to confirm the diagnosis. However, EMB has low sensitivity due to the focal nature of the disease, revealing noncaseating granulomas in less than 25% of patients with CS.[19,20] To increase the sensitivity of the procedure, electrophysiological (electroanatomic mapping)[21] or image-guided (PET or CMR)[22] biopsy procedures have been described. Consensus guidelines recommend that EMB for investigation of a possible diagnosis of CS should always be guided.[16,23]

Screening for Cardiac Involvement in Patients with Biopsy-Proven Extracardiac Sarcoidosis

There are few data comparing the sensitivity and specificity of various screening tests for cardiac involvement in patients with sarcoidosis. Mehta and colleagues[25] studied 62 subjects with sarcoidosis. Those with symptoms (significant palpitations, syncope, or presyncope) or abnormal results (electrocardiogram [ECG], Holter monitoring, and echocardiography) were studied with CMR or PET scanning. The diagnosis of CS was based on abnormalities detected by PET or CMR. Subjects with CS had more cardiac symptoms than those without CS (46% vs 5%); and they were more likely to have abnormal Holter monitor findings (50% vs 3%, respectively) and trans-thoracic echocardiography findings (25% vs 5%).[25] It should be noted that the presence of 1 abnormal screening variable had a sensitivity of 100% and a specificity of 87% for the diagnosis of CS.[25] There are no data on whether interval rescreening is necessary in patients with an initial negative work-up.[16]

It is clear that larger studies are required to define the sensitivity and specificity (and cost-effectiveness) of various screening strategies/tests to detect clinically silent cardiac involvement. Also, research is required to look at other proposed screening tests or potential risk markers, including signal-averaged ECG and fragmented QRS.[26,27] Recent consensus guidelines have made recommendations for screening (**Box 2** and **3**, **Fig. 1**).