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A complete heart block in a young male: a case report and review of literature of cardiac sarcoidosis

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Abstract Cardiac sarcoidosis is one of the uncommon causes of heart failure. Generally, it presents in the form of varying clinical manifestations ranging from asymptomatic to fatal arrhythmias such as ventricular tachycardia and complete heart block. It is difficult to make a diagnosis strictly based on clinical grounds. However, in the setting of extracardiac sarcoidosis and patients presenting with advanced heart block or ventricular arrhythmia, direct cardiac involvement should be suspected. The definitive diagnosis of cardiac sarcoidosis can be made from endomyocardial biopsy, but it is falling out of favor due to patchy myocardial involvement, considerable procedure-related risks, and advancement in additional imaging modalities. Once cardiac sarcoidosis has been diagnosed, management of the disease remains challenging. Steroids are considered the mainstay of therapy, and implantable cardioverter defibrillator therapy can be considered in a selected group of patients at greater risk for malignant ventricular arrhythmias.

Keywords Cardiac sarcoidosis · Complete heart block

Introduction

The clinical presentation of complete heart block varies based on the escape rhythm and heart rate in addition to accompanying comorbidities. The signs and symptoms commonly seen with complete heart block consist of hypotension, dizziness, syncope, and sudden cardiac death. In some cases, it may be asymptomatic and detected incidentally. The etiology for complete heart block includes infection, ischemia, drugs, autoimmune, and infiltrative conditions such as sarcoidosis. When a young adult is diagnosed with otherwise unexplained complete heart block, cardiac sarcoidosis (CS) should be considered among the differential diagnoses [1]. Complete heart block is often the initial presentation of CS and remains the most common conduction abnormality, affecting up to 30% of the patients [2]. Conduction disorders ensue when granulomas damage the atrioventricular (AV) node. Among the various non-invasive diagnostic modalities available, cardiac magnetic resonance imaging (CMRI) has a fairly high sensitivity and specificity when it comes to the diagnosis of CS [3]. The mainstay of treatment in these patients is corticosteroids. The 2008 ACC/AHA/HRS guidelines recommend consideration of implantable cardioverter defibrillator (ICD) implantation for primary prevention in patients with CS [4]. Additionally, those with high-grade conduction abnormalities invariably need pacemaker placement [4]. The basis of clinical presentation and treatment of CS requires an understanding of the pathogenesis. We present a case of CS presenting with asymptomatic complete heart block.

Case description

A 42-year-old African American male presented for an elective bronchoscopic evaluation of multiple lung nodules and mediastinal adenopathy. His past medical history was significant for hypertension, non-ischemic cardiomyopathy with left ventricular ejection fraction of 35%, sudden cardiac arrest, prior left-sided cerebrovascular accident, and stage 3 chronic kidney disease. His home medications included aspirin,

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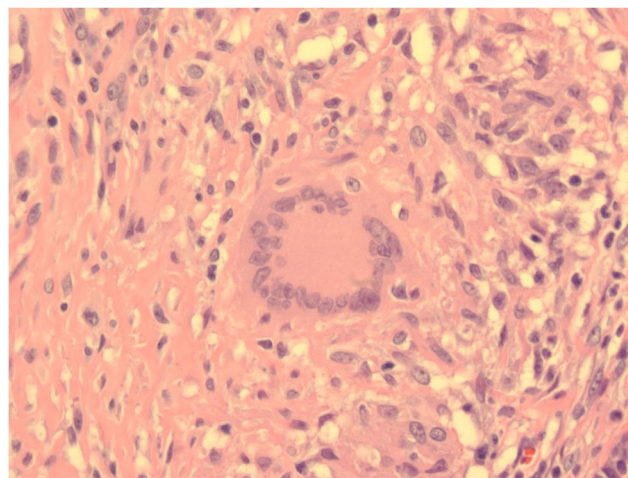2 Department of Pulmonary and Critical Care, Providence-Providence Park Hospital, Southfield, MI, USA
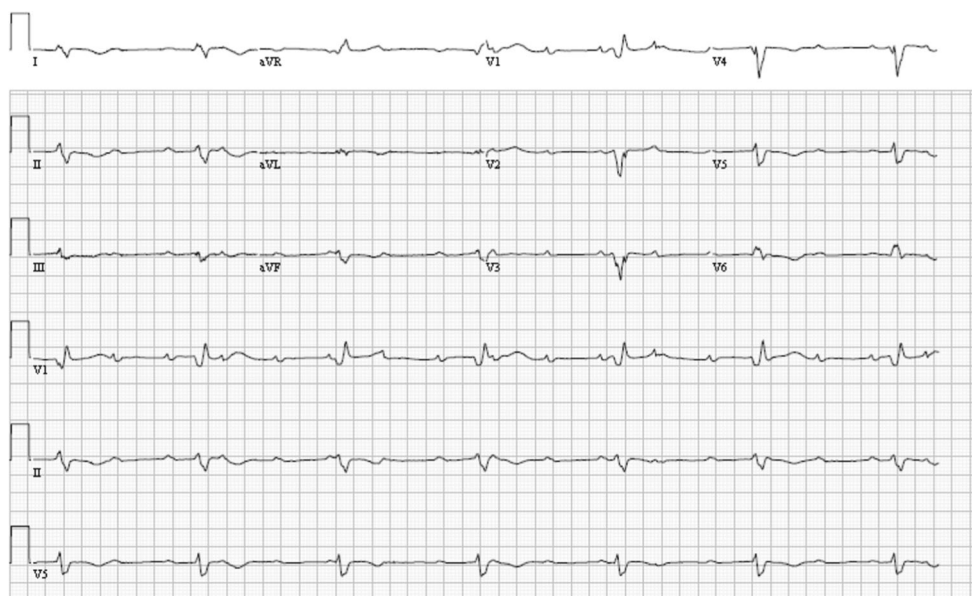
carvedilol, minoxidil, isosorbide mononitrite, levetiracetam, and baclofen. The patient's vital signs were a temperature of 97.7 F, pulse rate 53/min, respiratory rate 18/min and blood pressure of 147/87 mmHg, oxygen saturation 97% on room air, and body mass index of 33 kg/m^2. His cardiac exam was unremarkable. The patient developed a maculopapular rash that started on the forehead descending down to the upper abdominal area within 2 days of hospital admission. The electrocardiogram (ECG) revealed complete heart block (Fig. 1), and the patient underwent bi-ventricular ICD placement. The echocardiogram demonstrated severe concentric left ventricular and mild right ventricular hypertrophy, global impairment in LV contractility, and an ejection fraction of 35% with a small pericardial effusion. A biopsy of the left lung revealed multiple non-caseating granulomas consistent with sarcoidosis (Fig. 2). Histochemical stains for acid-fast bacilli and fungal organisms were negative. Based on extracardiac evidence of sarcoidosis, and the EKG findings of complete heart block at presentation, the patient was diagnosed with cardiac sarcoidosis (Fig. 3). Due to the ICD, an MRI could not be obtained. The patient was empirically treated with steroid with high index of clinical suspicion for cardiac sarcoidosis. During his stay in the hospital, the patient remained asymptomatic and in a paced rhythm. He was discharged on a taper of high-dose steroids.

Discussion

Epidemiology

Sarcoidosis is a disease associated with collection and progression of inflammatory cells in the form of granulomas
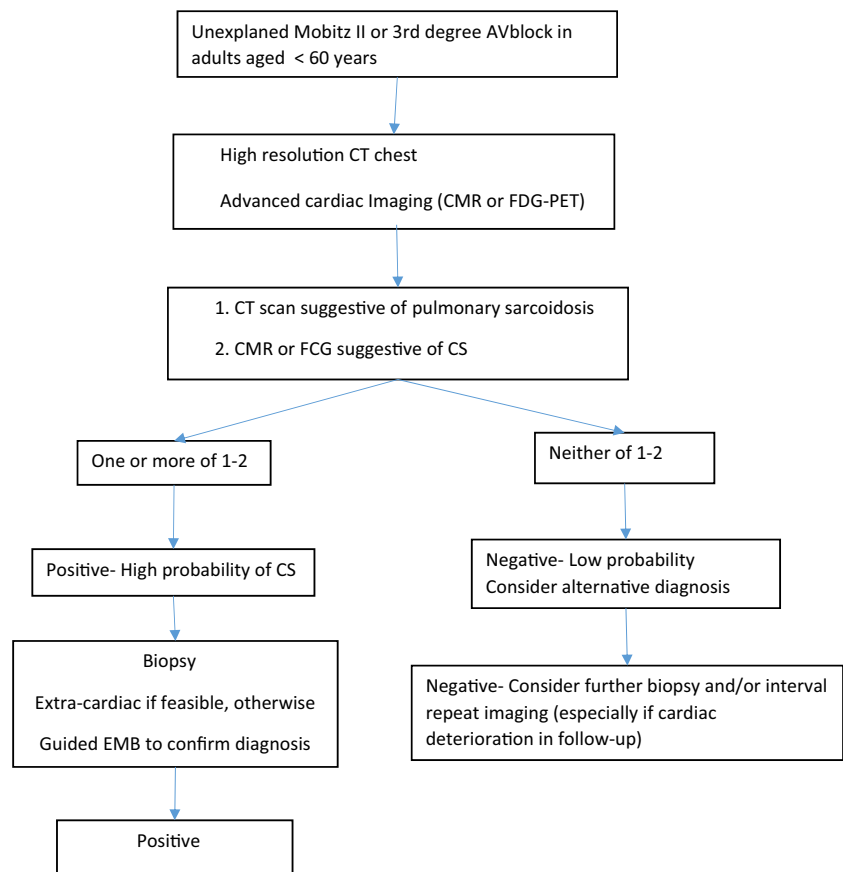
Fig. 2 Echocardiogram demonstrating global impairment in LV contractility with estimated ejection fraction of 35%

that affect several organs of the body such as lungs, lymph nodes, reticuloendothelial system, skin, eyes, glands, heart, kidneys, and central nervous system. The lifetime risk of developing sarcoidosis in African Americans and Caucasians is 2.4 and 0.85%, respectively [5], and the disease is about 10–17 times more prevalent in African Americans than Caucasians [2]. The annual incidence of sarcoidosis in the USA has been estimated to be 10.9 per 100,000 in Caucasians and 35.5 per 100,000 in African Americans [6]. A large majority of the patients diagnosed with disease are between 45 and 75 years old with 30% of the cases presenting with extrapulmonary sarcoid. Roughly 5% of the patients have cardiac symptoms, but asymptomatic patients with cardiac involvement outnumber the former [7, 8]. Patients with CS are known to have a significantly worse prognosis than those without cardiac involvement [3]. Autopsy studies have detected cardiac involvement in as

Fig. 1 The ECG reveals bradyarrhythmia with widened QRS complex due to complete heart block and right bundle branch block

Diagnosis

There are no clear guidelines or definitive algorithms on approach to diagnosis of CS frequently leading to missing diagnosis or a delay in diagnosis and treatment. There lacks a consensus on the ideal non-invasive or invasive methods to assist in diagnosis, optimal timing of usage in clinical setting due to a general lack of large prospectively conducted trials in the disease population. Overall, a multitude of modalities may be used to diagnose definitive or presumed CS: endomyocardial biopsy or a combination of biopsy-proven extracardiac sarcoidosis with additional clinical, EKG, echocardiographic, and imaging data (Table 1). Though the latter approach suggests only the possibility of having CS, it is adequate to establish a diagnosis and initiate treatment [11]. Limited utility of myocardial biopsy is described later in the article. Even asymptomatic patients with proven extracardiac sarcoidosis could be tested for subclinical cardiac involvement.

high as 50% of the deaths attributed to sarcoidosis [9]. Some populations such as the Japanese have even reported higher rates of CS, with autopsy studies showing almost 75% of their sarcoid-related deaths to be cardiac in origin [10].

Pathophysiology

Although the exact etiology of sarcoidosis remains unclear, an interplay between environmental, genetic, infectious, and immunological factors is believed to play a role in the manifestation of disease. Genetic associations with polymorphism of HLA class II molecules and tumor necrosis factor α have been linked to CS [12]. There is a strong correlation between levels of MRP8/14, an inflammatory marker, and CS. The levels of MRP8/14 were significantly elevated in CS compared to idiopathic dilated cardiomyopathy or non-cardiac sarcoid patients [12].

The immune response is elicited by interactions among immune-modulatory cells and secretion of various cytokines that promote granuloma formation and chronic-associated changes on histology. Various cytokines such as transforming growth factor β, insulin-like growth factor 1, and interleukin 4 and 5 are believed to cause fibrotic changes in granuloma and scarring [13]. Involvement of cardiac myocytes is usually patchy, and over time, the granuloma fibrose affects the heart's contractility and conduction system. These fibrotic changes and inflammatory reactions act as a nidus for atrial and ventricular arrhythmias [1, 14, 15]. Myocardial infarct-induced fibrosis occurs chiefly in the subendocardial region and extends out, while the fibrosis in CS is more random in the absence of a pathognomonic pattern. The gross specimens of

Table 1 Japanese Ministry of Health and Welfare Criteria for cardiac sarcoidosis

1. Histological diagnosis

Cardiac sarcoidosis is confirmed when cardiac biopsy specimens demonstrate non-caseating epithelioid cell granuloma with histologic or clinical diagnosis of extracardiac sarcoidosis.

2. Clinical diagnosis group

Cardiac sarcoidosis is diagnosed in the absence of an endomyocardial biopsy specimen or in the absence of typical granulomas on cardiac biopsy when extracardiac sarcoidosis has been proven and a combination of major or minor diagnostic criteria has been satisfied as follows.

   1. More than two of four major criteria are satisfied, OR

   2. One of the four major criteria and two or more of the minor criteria are satisfied.

Major criteria

   (a) Advanced AV block

   (b) Basal thinning of the ventricular septum

   (c) Positive cardiac gallium uptake

   (d) Left ventricular ejection fraction less than 50%

Minor criteria

   (a) Abnormal electrocardiogram findings including ventricular tachycardia, multifocal frequent premature ventricular contractions, complete right bundle branch block pathologic Q waves, or abnormal axis deviation

   (b) Abnormal echocardiogram demonstrating regional wall motion abnormalities, ventricular aneurysm, or unexplained increase in wall thickness

   (c) Perfusion defects detected by myocardial scintigraphy

   (d) Delayed gadolinium enhancement of the myocardium on cardiac MRI scanning

   (e) Interstitial fibrosis or monocyte infiltration greater than moderate grade by endomyocardial biopsy

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AV atrioventricular, *MRI* magnetic resonance imaging

CS reveal a yellow, tan, light brown, or gray-colored tumor-like infiltrate within the myocardium. The characteristic pathologic finding in sarcoidosis is the non-caseating granulomas, containing lymphocytes, epithelioid cells, and macrophages that fuse to form a multinucleated giant cell. Conditions such as hypersensitive pneumonitis can also have non-caseating granulomas; however, granulomas in sarcoidosis are tense and track along lymphatic structures [5, 12]. Granulomas due to histoplasmosis and tuberculosis are typically tense but necrotizing; therefore, they are easily differentiated from sarcoid granulomas. CS most commonly affects the following (in descending order): the left ventricular free wall, septum, right ventricle, and atria [12].

Clinical presentation

Sarcoidosis is a multisystem disorder, and presentation depends on organ involvement and extent. It most commonly affects the respiratory system, but a majority of the patients are asymptomatic. Diagnosis is often via incidental findings, the most common respiratory symptoms being cough, fatigue, dyspnea, and fever. The skin, lymph nodes, eyes, liver, spleen, nervous system, parotid or salivary glands, heart, kidney, bone, and muscle are among the other involved organs.

As described earlier, sarcoidosis can affect the heart causing detrimental consequences, and patients tend to have a poorer prognosis [2]. It may present concurrently with other systemic manifestations or as an isolated event. Sarcoidosis can directly involve the myocardium, pericardium, heart valves, or conduction system. In many cases, patients present with atypical or non-specific symptoms. It can present as a cardiomyopathy with or without clinical heart failure, arrhythmias ranging from asymptomatic first-degree atrioventricular (AV) block to high-grade AV block, supraventricular arrhythmias, malignant ventricular arrhythmias, valvular dysfunction, coronary artery infiltration-related myocardial infarction, pericarditis, pericardial effusion, sudden cardiac death, and rarely in the form of a cardiac mass [15–18].

Supraventricular arrhythmias

Atrial arrhythmias may develop due to direct or indirect involvement of the atria. A review by Golwala et al. reported an incidence of atrial arrhythmias in roughly 19% of sarcoid patients [17]. Viles-Gonzalez et al. reported the prevalence of supraventricular arrhythmias to be 32% in CS patients, wherein atrial fibrillation was the most common arrhythmia (18%) [19]. The majority of patients (96%) in the study were symptomatic, and the presence of left atrial enlargement was associated in the patients with arrhythmias. Although coexisting heart failure, right atrial enlargement, mitral valvulopathy, and pulmonary diseases affect the left atrium, these were not associated with increased likelihood of supraventricular arrhythmias according to the study [19]. In general, supraventricular arrhythmias are less fatal than ventricular arrhythmias. Nonetheless, they can cause devastating consequences if they are not treated appropriately and in timely manner. Atrial involvement, though common in CS, is not as extensive as ventricular involvement [20].

Conduction disorders

The most common arrhythmia in CS is complete heart block that is reported in up to 30% of cardiac sarcoid patients and can be the initial presentation [2]. Patients with CS who present with conduction block do poorly than those with otherwise unexplained block [21]. The etiology behind complete heart block or high-grade AV block is scar formation in the basal septum which may involve the nodal artery supplying the conduit or directly destroy the conduction fibers [2]. When a young patient presents with unexplained complete or third-

degree heart block, sarcoidosis should always be considered in the differential diagnosis [22]. In one study, nearly 19% of the patients with complete heart block were diagnosed with CS and isolated cardiac involvement in two thirds of those cases [15]. Right and left bundle branch blocks may also be seen, with the former being more frequent than the latter [17]. Sudden death remains a large concern among patients with CS [23].

Ventricular arrhythmias

Ventricular arrhythmias (VA) are the second most common arrhythmias in CS. Inflamed foci and fibrosis induce abnormal automaticity and may disrupt ventricular activation and recovery, causing fast re-entrant ventricular arrhythmias [2]. They have been reported in 23% of the CS patients. Although monomorphic ventricular tachycardia (VT) is the most common form of VA, polymorphic VT can also occur in these patients [15]. Many reports on VA as an initial presentation of CS have been published. Interestingly, in a case report by Mohsen et al., CS presented as arrhythmogenic right ventricular cardiomyopathy [24]. VT can put the patients at risk of sudden cardiac death (SCD) [15]. Although the exact incidence of SCD is unknown in CS, it may be as high as 35% according to some reports [25].

Congestive heart failure

CS can cause both systolic and diastolic dysfunction. The etiology of heart failure commonly manifests as a dilated or constrictive cardiomyopathy [17]. Congestive heart failure (HF) may occur in 10–25% of CS patients and is the second commonest cause (25–75%) of death after sudden cardiac death [2]. The severity of heart failure is dependent on the extent of myocardial involvement from direct infiltration by granulomas [15]. The treatment of plan usually consists of standard heart failure regimen such as diuretics, angiotensin-converting enzyme inhibitors, and beta-blockers in addition to steroids [1].

In 10% of the cases, the fibrosed heart muscle becomes structurally weak and is prone to ventricular aneurismal formation especially in the case of untreated progressive disease. Steroids have also been associated with formation of ventricular aneurysms. One of the treatment options available in patients with a ventricular aneurysm is resection of the aneurysm [2].

Although it is an uncommon cause of heart failure in cardiac sarcoid patients, mitral valvulopathy, namely mitral regurgitation, can induce HF symptoms. It has been described that direct mitral valve or papillary muscle involvement or dilation of the left ventricle can impair mitral valve valvular function [2, 17].

Pulmonary hypertension

The association between pulmonary hypertension (PH) and CS has been acknowledged for years. According to the Dana point classification of pulmonary arterial hypertension, sarcoidosis is categorized in group 5 as a cause of pulmonary arterial hypertension [26]. One of the possible mechanisms of PH due to CS is involvement of the myocardium, causing pulmonary venous hypertension [27]. The pulmonary venous hypertension, in turn, leads to pulmonary arterial hypertension. Increased pulmonary arterial pressure causes strain on the right ventricle, and the patient develops right ventricular hypertrophy, tricuspid regurgitation culminating in progressive right-sided heart failure. The hypertrophy, enlargement of the right ventricle, and related stress results in elevated NT-pro-BNP levels. In a Japanese study by Handa et al., among sarcoid patients with PH, NT-pro-BNP levels were predictive of patients with cardiac involvement [28].

Non-invasive arrhythmia monitoring

There is limited data comparing the sensitivity and specificity of various screening tests for detection of CS, but a study by Mehta et al. showed the advantage of using a combination of history, electrocardiography, Holter monitoring, and echocardiogram to assist in the diagnosis with relatively high sensitivity and specificity [7].

Role of electrocardiography

Surface electrocardiography (ECG) is a ubiquitously used, high-yield, non-invasive diagnostic tool that assists in detecting several cardiac conduction and structural disease entities. The utility of ECG in CS extends beyond detecting conduction disorders and arrhythmias to detection of myocardial scarring and fibrosis. Fragmented QRS (fQRS) defined as the presence of an additional R wave (R′) or notching of S-wave nadir, or the presence of more than one R′ in consecutive leads, suggests myocardial fibrosis or scaring [29]. In a retrospective study, Brenyo et al. reported that fQRS has high predictive value for risk of sudden cardiac death. Based on their findings, the authors suggested that ICD placement in such high-risk patients could be valuable [30]. While fQRS does not point to a specific etiology for scarring or fibrosis, it acts as a marker to suggest further imaging in cases with suspected CS. Homsi et al. demonstrated fQRS to have 100% sensitivity, 80% specificity, 78% positive-predictive value, and 100% negative-predictive value in detecting cardiac involvement in sarcoidosis [31]. Involvement of the myocardium was confirmed using cardiac MRI in these patients.

Another method to detect myocardial scarring or fibrosis is the use of signal-averaged ECG (SAECG). It was initially

used for sudden cardiac death risk stratification in patients with prior myocardial infarction. It can also be utilized to detect fibrosis in non-ischemic cardiomyopathy and arrhythmogenic right ventricular dysplasia (ARVD) [32]. Schuller et al. discovered a correlation between SAECG and CS. Its sensitivity and specificity were 52 and 80%, respectively. They suggested that in patients with QRS <100 ms, a normal SAECG excluded CS.

In a case report, Strauss et al. reported how scar burden can be predicted by a QRS scoring system, where points were assigned based on Q-wave, R-wave, and S-wave morphology, duration, amplitude, ratio, and notch criteria in 8 out of 12 leads. They also reported that the calculated scar burden approximated cardiac MRI findings [33].

Echocardiography

In CS, echocardiography (Echo) serves an important role as the initial imaging modality. The ventricles may be globally hypokinetic or have regional wall motion abnormalities depending upon the extent of myocardial involvement. Thinning of the basal anterior septum in a young patient with dilated cardiomyopathy is highly suggestive of CS [1]. Typical findings on Echo include septal thinning or thickening, dilatation, and systolic dysfunction of the left ventricle with diastolic impairment although these abnormalities may be seen in a range between 14 and 67% of the cases [2, 9]. Overall, Echo is neither specific nor sensitive to diagnose CS, but the recent advent of ultrasonic tissue characterization with integrated backscatter has significantly improved detection [3].

Other imaging modalities

Thallium 201 (Ti) and technetium 99m (Tc) sestamibi is a radionuclide scan that can assist in distinguishing fibrogranulomatous myocardium from the fibrosis induced from ischemic coronary artery disease. When Ti or Tc is given to a patient, resting perfusion may display decreased uptake by affected myocardium. In contrast to ischemia-related fibrosis, a fibrogranulomatous myocardial defect may be reversed with exercise or vasodilators such as dipyradomole. In a small study, Tc has shown to have higher sensitivity than Ti for CS, the reported sensitivity and specificity for Tc being 64 and 100%, respectively, in another study [3]. Sestamibi single-photon emission computer tomography (SPECT) is another scan that is more sensitive than thallium but less specific for CS. Gallium scintigraphy has also been shown to be highly sensitive for CS due to its uptake by acutely inflamed foci. The gallium scan can additionally be useful in monitoring effectiveness of steroid therapy. A study showed that the combination of SPECT, gallium, and Tc had higher specificity for CS than either modality alone [2]. In 2012, Youssef

et al. reported that pool sensitivity and specificity of ^{18}F-fluorodeoxyglucose (FDG) uptake with positron emission tomography (PET) in detecting active inflammatory regions in sarcoidosis were 89 and 78%, respectively [34]. Inflammatory cells have heightened glycolytic demand; thus, increased uptake in these cells can be differentiated from cells with normal metabolism [7]. Active inflammatory cells are arrhythmogenic, and it has found that positive FDG scan has been associated with ventricular arrhythmia and ICD firing [35]. The utility of FDG-PET significantly improves in conjunction with perfusion studies such as Tc. Increased FDG with normal perfusion is consistent with early phase of CS, while increased uptake in the background of poor perfusion suggests CS with myocardial damage. When the uptake and perfusion are decreased, it suggests scarring [36]. Figure 4 is an example one of our patients who was diagnosed with active cardiac sarcoidosis based on FDG-PET.

In comparison to the imaging modalities described above, CMRI offers both structural analysis and disease activity level determination. The more commonly described pattern in CS is ≥1 patchy regions of late gadolinium enhancement on CMRI that would be atypical for a myocardial infarction [37]. The presence and extent of gadolinium enhancement (GE) have been shown to correlate with the severity of disease and a worse prognosis including death, aborted sudden cardiac death, and ICD discharge [38, 39]. Early GE detects inflammation and edema, while late GE detects a combination of fibrogranulomatous and inflammatory status. In addition, CMRI may show wall motion abnormalities and wall thinning or thickening among other abnormalities. Late GE in patchy areas that do not follow a specific vascular territory is considered a hallmark finding of CS (Fig. 5).
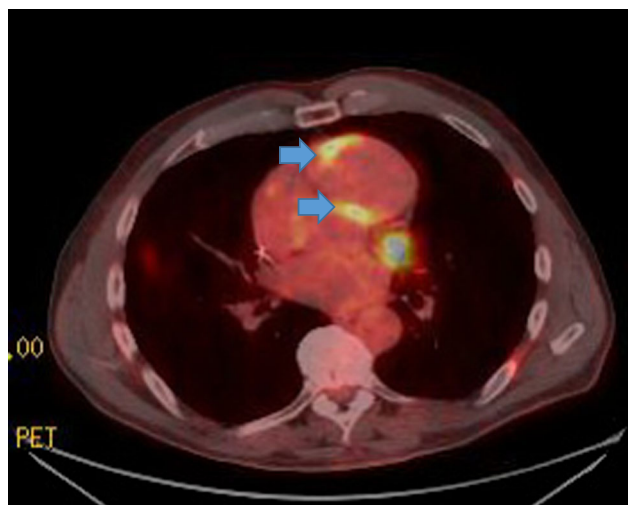
Fig. 4 This FDG-PET CT imaging shows patchy activity in the right ventricle (*arrows*) highly suggestive of cardiac sarcoidosis. *FDG-PET CT* ^{18}F-fluorodeoxyglucose-positron emission tomography

Fig. 5 These images show late gadolinium enhancement of patchy scars (*arrow heads*) from cardiac sarcoidosis
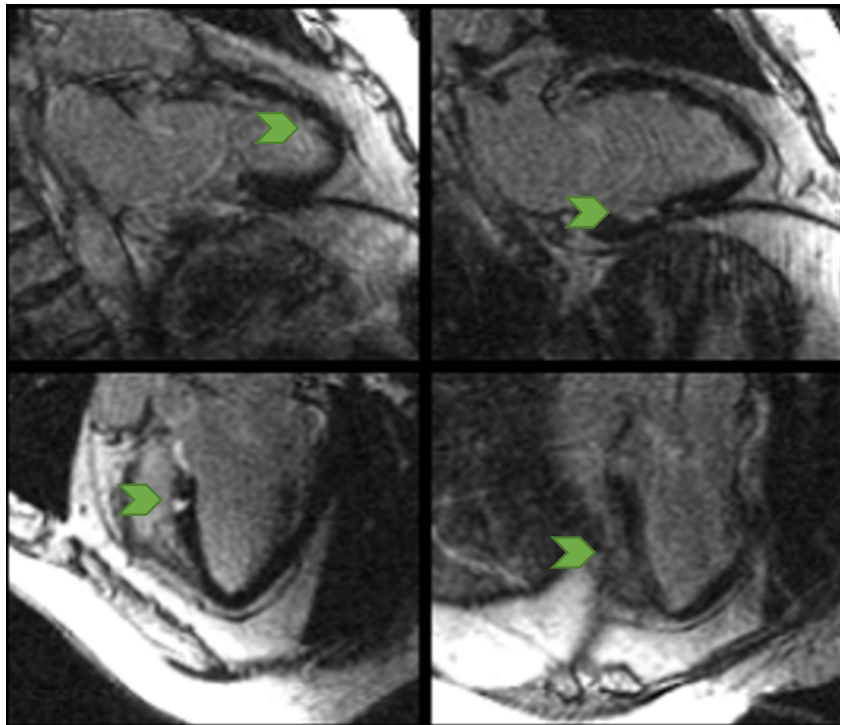
Endocardial biopsy

With the advances in non-invasive imaging techniques mentioned above, the role of endocardial biopsy in diagnosis of CS has changed over time. Despite the very high specificity seen with endocardial biopsy, diagnosis of CS can be missed due to low sensitivity (20%) secondary to heterogenous involvement of tissue [2, 3]. Besides this, a cardiac muscle biopsy is an invasive procedure, putting patients at risk for bleeding, infection, and arrhythmias.

Treatment

The goals of treatment for CS range from treating active inflammation to prevention of scarring, fibrosis, or structural changes and downstream prevention of cardiac dysfunction and malignant arrhythmias with possibility for reversal. The anti-inflammatory properties of steroids with noted overall efficacy and clinical improvement in CS place them at the center of various treatment strategies. Despite the absence of large randomized trials, retrospective studies have shown a survival benefit in the steroid-treated group in those with preserved ejection fraction (EF) and improved ventricular function in those with an EF between 30 and 50% [40]. Patients with EF <30% failed to show any improvement even with treatment [3]. It is important to note the heterogeneity between studies and mixed results; there is disagreement on optimal oral dosing, but the current approach of starting with a high dose and gradual taper over months to years may be beneficial [1, 40]. Immunosuppressive drugs such as infliximab,

methotrexate, and antimalarial drugs have been shown to benefit patients with sarcoidosis, but data is limited. These medications can be reserved for those who cannot tolerate steroids [3]. Similarly, antiarrhythmic drugs such as amiodarone and sotalol should be considered in patients who experience recurrent shocks for ventricular arrhythmias in addition to ICD therapy. In patients with ventricular arrhythmias, studies have reported varying effects ranging from improvement to a lack of benefit and worsening of the arrhythmias with steroid use [41–44].

Another important treatment option for these patients is device implantation. Recommendations from the general device guideline documents do apply to this population. Since CS unpredictably affects the conduction system, affected patients should be considered for pacemaker implantation. A growing amount of literature suggests that these patients are at risk of developing ventricular arrhythmias and sudden cardiac death. In a retrospective trial, VT storms were more common in CS patients, and about 32% of patients received appropriate shock therapy from ICDs [45]. The 2014 HRS expert consensus statement on management of arrhythmias associated with CS published three class IIa recommendations in patients with advanced heart block. Refer to Fig. 6 for algorithmic approach. They recommended (a) pacemaker implantation in patient with CS and an indication for pacing even in the case of transient AV blocks, (b) use of immunosuppression in patients with Mobitz type II block or complete heart block, and (c) consideration for ICD implantation in patients with an indication for permanent pacemaker implantation [11]. An electrophysiology study (EPS) may be performed

Fig. 6 Consensus recommendation for ICD implantation in cardiac sarcoidosis patients. *CMR* cardiovascular magnetic resonance, *ICD* implantable cardiodefibrillator, *LVEF* left ventricular ejection fraction, *RV* right ventricle, *VT* ventricular tachycardia. Reproduced with permission from *Heart rhythm: the official journal of the Heart Rhythm Society.* Jul 2014;11(7):1305–1323
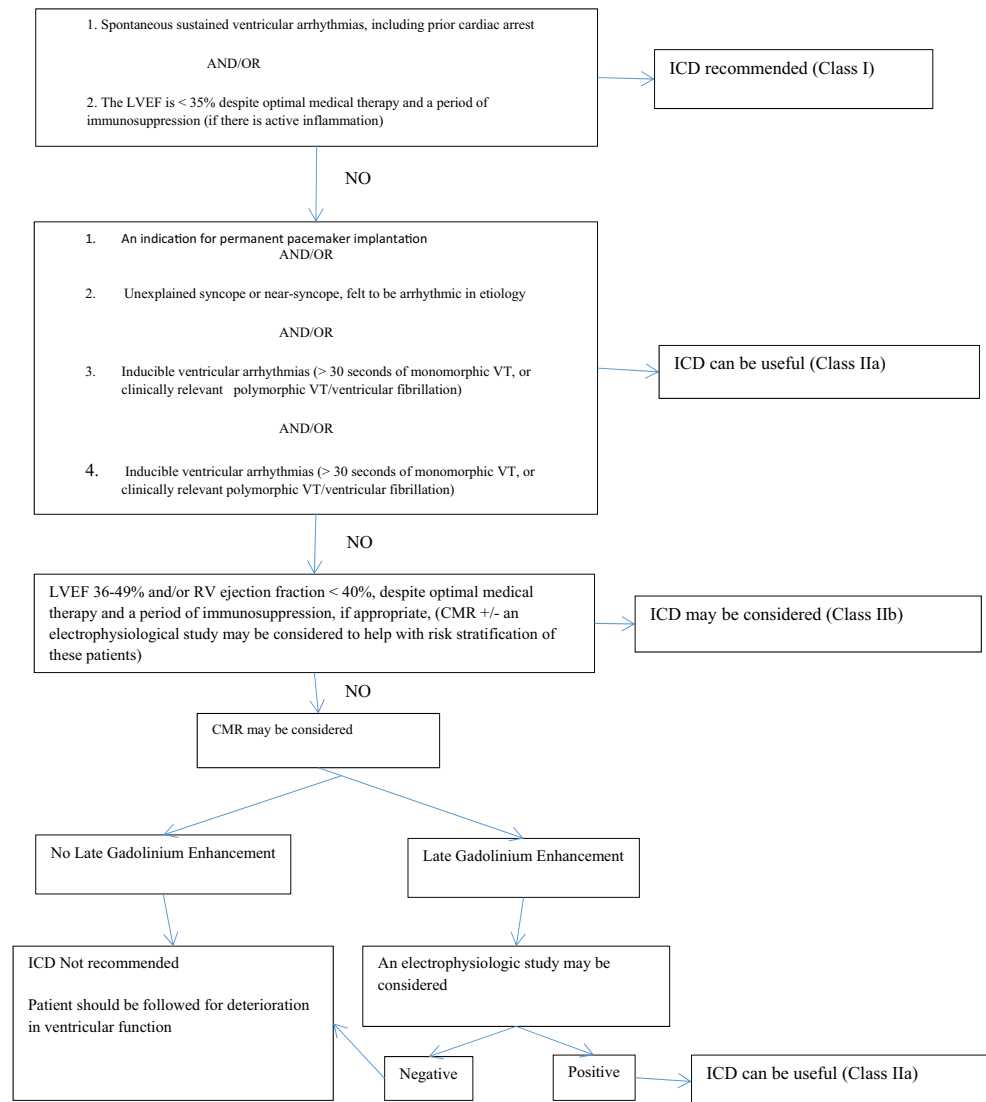
in first-degree AV block or fascicular block to define the level of conduction disease. They make a case for ICD implantation in all patients with left ventricular ejection fraction ≤35%. In addition, ICD implantation should be considered in the range of 36–49% and right ventricular ejection fraction <40%, while on optimal medical therapy and immunosuppressant. The role for EPS in screening patients at risk for ventricular arrhythmias is not well defined. The 2008 American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines also recommend that ICD implantation be considered in patients with CS without clearly defining the specifics of therapy [4]. In patients at high risk of VAs, ICD implantation prior to initiating immunosuppressant or during high-dose immunosuppressant can be undertaken [11].

Patients who fail the therapies described above, or have frequent VAs, catheter ablation (CA) could be an option with or without immunosuppressive therapy. In a multicenter registry report, 9 out of 42 patients had VAs uncontrolled with

medical therapy undergoing radiofrequency ablation. All patients had either a decrease or complete elimination of ventricular tachycardia during a mean follow-up of 19.8 ± 19.6 months [46]. If the circuitry was located intramurally and with advanced cardiac involvement, evidence suggests that it may be challenging to ablate those foci in affected patients [47, 48]. Despite mixed results, CA remains an option to eliminate or palliate disease symptoms in patients with recurrent VAs despite aggressive medical therapy.

As a final measure in rare instances, surgery may be used to treat valvular disease or resect a ventricular aneurysm to eliminate ventricular arrhythmias. In patients with refractory heart failure and ventricular arrhythmia, heart transplantation is also an option [2]. In patients affected by CS, symptoms of heart failure are common, and failure to diagnose CS early may lead to refractory heart failure. In theory, these patients may benefit from heart transplantation; however, the existing data available is not without controversy. In a retrospective review of

cardiac transplantation, 65 patients diagnosed with CS underwent heart transplant and had improved survival at 1 year compared to patients who underwent transplantation for other causes [49]. However, result in a smaller retrospective trial of 14 patients was contradictory to the former trial with worse outcomes among those with CS [50]. In contrary, another small study conducted by Perkel et al. showed that patients who has CS and underwent cardiac transplant, while maintained on low-dose steroids, had acceptable long-term outcome [51].

Conclusion

CS is a rare but potentially fatal disease. The incidence of CS is greater than previously reported. Evidence-based guidelines on screening patients affected by sarcoidosis are missing, and the best approach to diagnosis and treatment is still uncertain. The prognosis of disease is poorly defined, with incomplete guidance on the application of various postulated prognostic markers in actual clinical practice. We recommend that all patients with sarcoidosis be screened using a detailed history, physical exam, ECG, and echocardiography. Steroids are the mainstay of medical therapy, and ICD implantation should be recommended as a primary prevention in all high-risk individuals at a minimum. These recommendations are based on mostly observational and retrospective trials. The rarity combined with underdiagnosis of CS continues to remain a hurdle in conduction of large prospective, randomized control trial but should be encouraged.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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