

Review article

Sarcoid heart disease: clinical course and treatment

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Abstract

Sarcoidosis is a rare granulomatous disease of unknown etiology that can affect any organ. Cardiac involvement, although uncommon, has a wide spectrum of clinical manifestations and is potentially fatal. Although there is no agreement upon a strategy for the diagnosis (which is difficult to make based on clinical information alone), the introduction of newer technology is promising and may be useful both for the early diagnosis of cardiac involvement and for the evaluation of response to therapy.

Early treatment is crucial in improving symptoms and prognosis. ICD implantation and cardiac transplantation may offer improvements in management, as steroid therapy and pacemaker implantation has led to improved outcomes over the past three decades.

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1. Introduction

Sarcoidosis is a multisystem, granulomatous disease of unknown etiology often seen in young adults. Age-adjusted annual incidence rate in the United States is 35.5 per 100,000 for blacks and 10.9 per 100,000 for whites with an overall prevalence rate of approximately 20 per 100,000 population [1]. Higher prevalence rates have been reported in Japan and some northern European countries such as Sweden.

Three separate clinicians initially described the disease in the 19th century in Europe [2]. In 1899, Boeck first used the word “sarkoid” to describe a cutaneous lesion because of the histological similarity (but favorable course) to sarcoma [3].

2. Etiology

The current evidence suggest that sarcoidosis results from an exaggerated cellular immune response to a variety of antigens or self-antigens which cause CD4 (helper-inducer) T-cell accumulation, activation and release of inflammatory cytokines eventually leading to granuloma

formation [4] (Figs. 1 and 2). The disease may affect almost any organ and is characterized classically by the presence of non-caseating granulomas composed mainly of an aggregate of epithelioid cells and Langhans or foreign body-type giant cells in the center, surrounded by lymphocytes, plasma cells and mast cells.

Although many infectious, environmental and genetic factors have been implicated, no clear relationship has been established. Kern et al. [5] observed a cluster of sarcoid cases in a group of firefighters who lived together, implicating an environmental factor. Hills et al. [6] reported a cluster of cases among nurses and persons who lived near a hospital.

Genetic factors also seem to play a part in the pathogenesis of sarcoidosis [7]; the disease is more common in monozygotic twins than dizygotic twins, and familial clusters of sarcoidosis occur in 19% of affected black families.

3. Cardiac sarcoidosis

Although the respiratory tract and the lymphatic system are most often affected, the clinical manifestation of sarcoidosis can be widespread and may involve any organ system. The first case of cardiac sarcoidosis was reported in 1929 when Bernstein described sarcoid granulomas involving the pericardium [8]. Since then a wide range of cardiac manifestations of the disease has been described including

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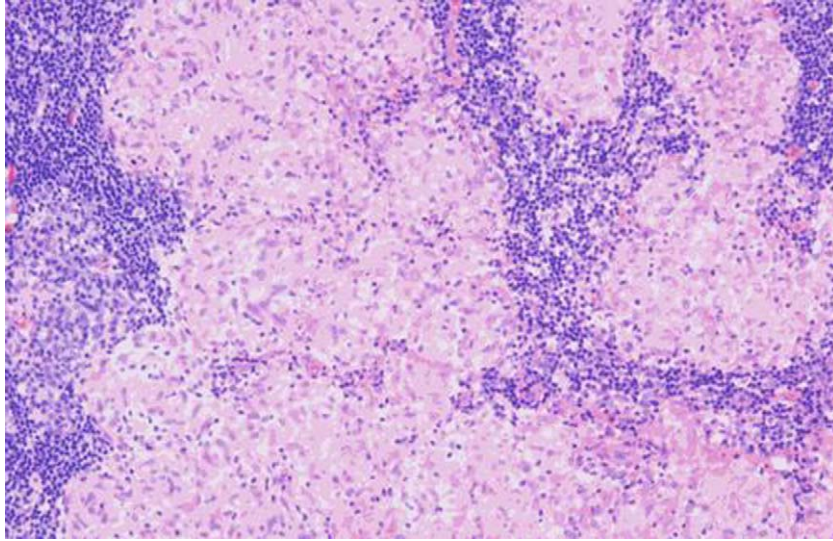


Fig. 1. Non-caseating epithelioid granulomas of sarcoidosis in a mediastinal lymph node (hematoxylin and eosin, $\times 100$).

conduction abnormalities, mitral regurgitation, congestive heart failure (CHF), ventricular aneurysms, pericardial effusion and tamponade, pericarditis, ventricular arrhythmias and sudden death.

Cardiac involvement occurs in 20–27% of sarcoid patients in the United States and may be as high as 58% in Japan [9]. The majority of these patients are asymptomatic; clinical evidence of cardiac sarcoidosis is present in less than 5% of patients with sarcoidosis [10].

Isolated cardiac involvement with sarcoidosis has been described in few case reports but is extremely rare and usually preceded future systemic sarcoidosis. Nelson et al. [11] described three patients with conduction disorders found to have isolated cardiac sarcoidosis. Two of these patients developed clinical and radiographic evidence of systemic sarcoidosis after several years.

The clinical manifestations of cardiac sarcoidosis (Table 1) depend upon the location and the extent of the myocardium involved. In 1977, Roberts et al. [12] reported the result of 113 necropsy patients with cardiac sarcoidosis. They found that the left ventricular free wall is the most common location for granulomas and scars, followed by the intra-ventricular septum (Fig. 3).

The clinical presentation may include the following:

3.1. Conduction disorder

Conduction abnormalities ranging from benign first degree AV block to complete heart block are the most common clinical manifestation of cardiac sarcoidosis. In autopsy studies [13], virtually every patient with conduction abnormality had involvement of the basal intra-ventricular septum

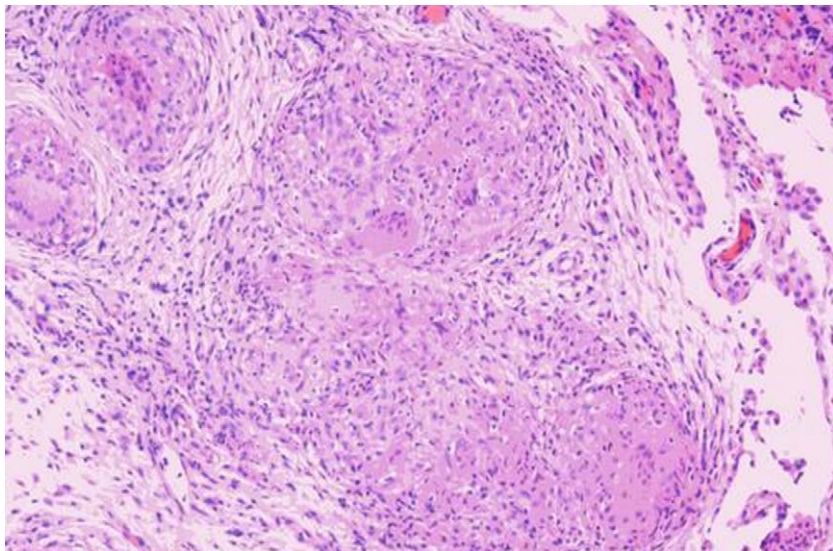


Fig. 2. Sarcoidal granulomas with multinucleated giant cells in a lung biopsy (hematoxylin and eosin, $\times 100$).

Table 1
The clinical manifestations in cardiac sarcoidosis

Author	Year	N	AV block (%)	BBB (%)	SVT/V-Tach (%)	CHF (%)	SD (%)
Matsui [9]	1976	42	62	48	14	10	41
Roberts [12]	1977	26	27	12	35	30	65
Fleming [14]	1981	300	26	61	73	24	26
Yazaki [15]	1998	95	45	NA	18	26	12

N, number of patients; AV, atrioventricular; BBB, bundle branch block; SVT, supraventricular tachycardia; V-Tach, ventricular tachycardia; CHF, congestive heart failure; SD, sudden death.

by sarcoid granulomas or scar tissue. Complete heart block occurs in 23–30% of patients; of these patients, 68% had episodes of syncope [12]. Right bundle branch block (RBBB) is more common than left bundle branch block, [14] and in one study RBBB was detected in 57% of patients with documented cardiac sarcoidosis [15]. Fleming noted that patients with cardiac sarcoidosis who develop complete heart block usually developed it at a much younger age than those with idiopathic heart block [16]. This observation is thought to be a clue to the presence of cardiac sarcoidosis in young patients who present with complete heart block.

3.2. Ventricular arrhythmias

Sustained or non-sustained ventricular tachycardia (VT) and frequent ventricular ectopy are detected in 23% of patients [12] and are the second most common presentation of cardiac sarcoidosis. VT is presumed to be the cause of sudden death in many of these patients; in others, complete heart block has been implicated.

The mechanism of VT in these patients is often myocardial reentry occurring through surviving myocyte bundles in

and around the scar, and is characterized by bundle branch reentry morphology [17]. While VT is frequently inducible at electrophysiological study (EPS), inducibility of VT is not associated with other measures of disease activity [18]. Anti-arrhythmic drug therapy of VT in these patients, even when guided with EPS, is associated with a high rate of arrhythmia recurrence or sudden death [19].

Involvement of the ventricular free wall and aneurysm formation is associated with higher risk of VT, and resolution of this arrhythmia has been reported with successful surgical resection of the aneurysm [20].

Ventricular fibrillation has rarely been reported [21,22] but is thought to be the final event in patients with sudden death.

3.3. Atrial arrhythmias

Supraventricular arrhythmias are less common than ventricular arrhythmias, with an incidence of up to 19% [10]. Atrial dilatation secondary to LV dysfunction or cor pulmonale due to pulmonary involvement are thought to be the possible cause of these arrhythmias, though direct atrial involvement by sarcoid granuloma may serve as a focus of ectopic atrial tachycardia, atrial flutter or fibrillation (Fig. 4). Sinus arrest secondary to granulomas involving the sinus node has been reported [23].

3.4. Pericarditis

Although a small, clinically silent pericardial effusion has been found in 19% of sarcoid patients during echocardiography [24,25], isolated pericardial involvement or symptomatic pericarditis are very rare. Both cardiac tamponade and constrictive pericarditis due to sarcoidosis are rare and have been described in case reports [26].

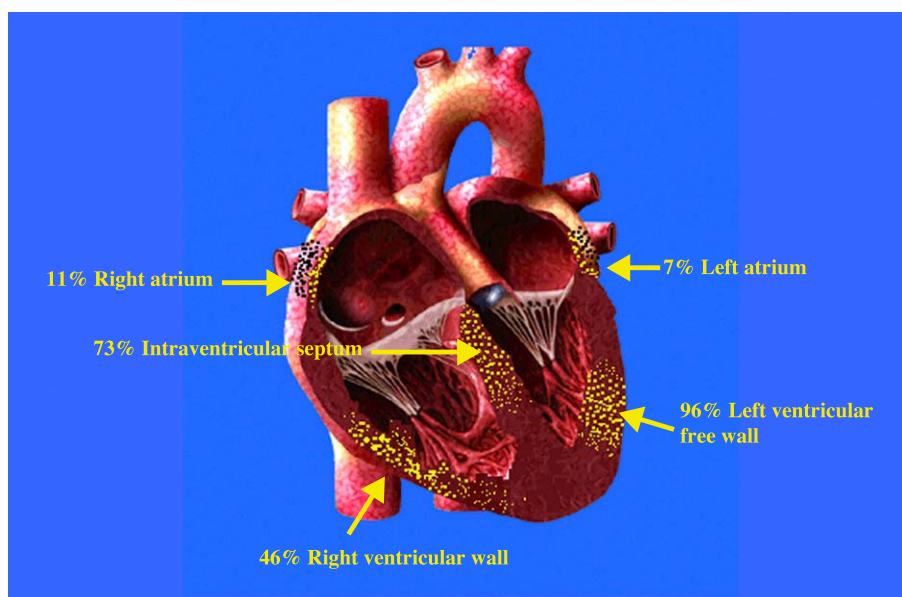


Fig. 3. A diagrammatic representation of the most common sites of sarcoid granulomas in the heart (modified from Roberts et al. [11]).

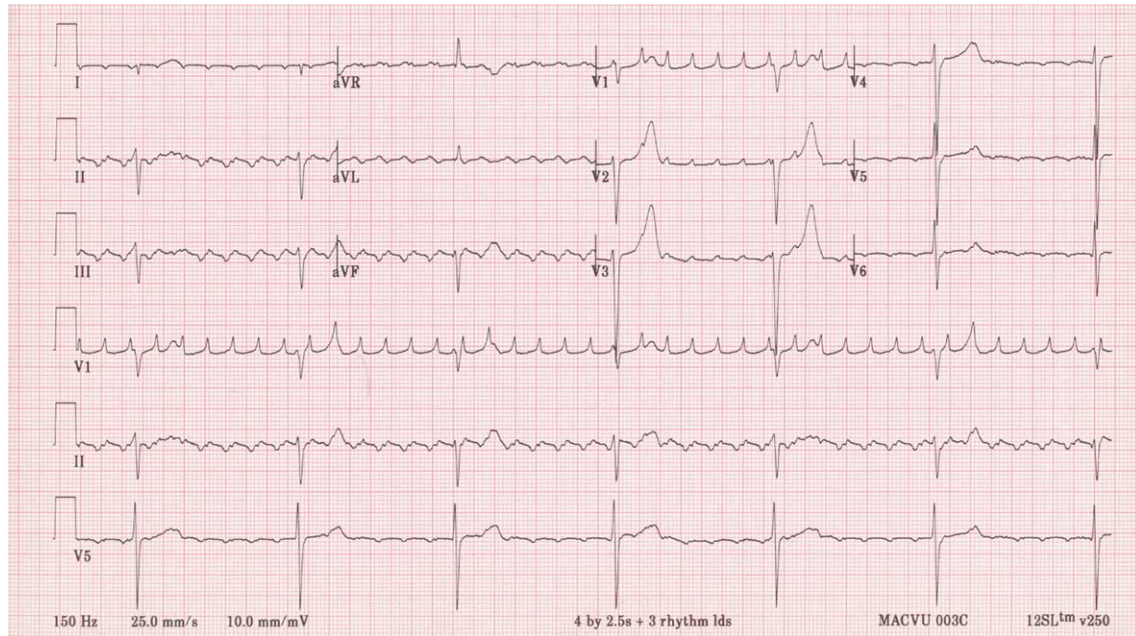


Fig. 4. 12-Lead ECG showing Atrial flutter with complete AV block in a 54-year-old man with pulmonary sarcoidosis diagnosed 20 years ago. The QRS complex shows right axis deviation with R/S ratio of less than one in leads V5 and V6 indicating right ventricular hypertrophy.

3.5. Valvular dysfunction

Mitral valve regurgitation (acute or chronic) is the most common valvular abnormality detected in cardiac sarcoidosis [27].

Valvular dysfunction due to papillary muscle involvement is more common than direct destruction of the valvular leaflets by sarcoidosis and has been observed in up to 68% of patients with cardiac sarcoidosis [28]. Patients may present either with the acute onset of mitral regurgitation and hemodynamic decompensation due to acute papillary muscle dysfunction or rupture, or with more insidious and chronic state characterized by left ventricular enlargement and compensatory eccentric hypertrophy.

Rare cases of sarcoid involvement of the aortic, tricuspid and pulmonic valves have been reported.

3.6. Congestive heart failure

CHF is the second most frequent cause of sarcoid-related mortality after sudden death. Cardiac infiltration by sarcoid granulomas may cause ventricular stiffness (diastolic dysfunction) or diminished systolic contractile function, or both. Fahy et al. [29] studied 50 patients with pulmonary sarcoidosis, 14% had diastolic dysfunction by mitral inflow pattern. In another study, Skold et al. [30] reported the presence of both systolic and diastolic dysfunction in patients with cardiac sarcoidosis documented by magnetic resonance imaging (MRI). Patients with CHF syndrome may show clinical features of restrictive and/or dilated cardiomyopathy. In patients with extensive fibrotic pulmonary sarcoidosis, secondary pulmonary hypertension may

develop and lead to right ventricular hypertrophy and eventually to right side heart failure.

Rare cases of cardiac sarcoidosis mimicking right ventricular dysplasia or hypertrophic cardiomyopathy have been described in the literature [31,32].

The presence of heart failure is an independent predictor of mortality and carries a very poor prognosis. Yazaki et al. [15] retrospectively studied 15 patients with LV systolic dysfunction from cardiac sarcoidosis and 30 patients diagnosed with idiopathic dilated cardiomyopathy (IDC). The sarcoidosis group had a statistically higher frequency of complete heart block (67% vs. 0%), RBBB (57% vs. 17%) and abnormal LV wall thickness (73% vs. 17%). Most importantly, the 3- and 5-year survival rates were significantly worse in the sarcoidosis group compared to the IDC group. In contrast to IDC, a recent study found that the transplant-free survival was better for patients with cardiac sarcoidosis than for patients with giant cell myocarditis at 5 years after symptoms onset [33].

4. Diagnostic approach

Hugh Fleming, a cardiologist from England who specialized in the study of cardiac sarcoidosis, wrote in 1981 “the recognition of sarcoid heart disease . . . suggests that many of us have had, and many indeed still have, a blind spot for this diagnosis” [14]. More than 20 years passed since that statement and the diagnosis of cardiac sarcoidosis still a challenge for physicians.

To diagnose sarcoidosis in general, the American Thoracic Society (ATS) recommended the presence of a

compatible clinical picture, histological confirmation of non-caseating granulomas, and exclusion of other diseases capable of producing a similar clinical or histological picture [34]. Excluding fungal infection, tuberculosis or malignancy is essential especially if steroid treatment is being considered. Transbronchial lung biopsy is the most commonly recommended procedure and has a diagnostic yield of up to 90% when four to five biopsies are done [35]. However, more accessible locations like skin or lymph node lesions may be sufficient to make the histological diagnosis.

The Kveim–Siltzbach test is not as widely used today as it was in the past. This test consists of an intra-dermal injection of antigen prepared from the spleen of a patient with known sarcoidosis; a positive result is a development of a papule at the site of injection within 4–6 weeks [36,37].

Unfortunately, there are no definitive criteria to diagnose cardiac sarcoidosis. It is unclear if all patients with sarcoidosis should undergo non-invasive testing to further identify cardiac involvement considering that the majority of patients with cardiac sarcoidosis are asymptomatic and that sudden death usually occurs in the absence of a previous cardiac event [38].

In Japan, where cardiac sarcoidosis is more common than the United States, guidelines have been developed to diagnose cardiac sarcoidosis [39] (Table 2); these guidelines have not been validated by a controlled study and may not be applicable to patients in the United States.

The diagnosis of cardiac sarcoidosis is difficult to make and should be suspected when the clinical manifestations occurs in relatively young individuals, especially in the presence of multiorgan involvement.

The diagnostic work-up for patient with sarcoidosis should attempt to assess the presence of cardiac involve-

ment and, if present, the extent, severity, and prognosis of this involvement.

4.1. Electrocardiography

Every patient with newly diagnosed sarcoidosis should have an electrocardiogram (ECG) as part of the initial work-up, followed by periodic ECG testing regardless of the presence or absence of clinically apparent cardiac involvement. Electrocardiographic changes are found in up to 50% of patients with systemic sarcoidosis. The most common findings are non-specific repolarization changes, arrhythmias, conduction abnormality and pseudoinfarction pattern [40,41]. These abnormalities may well signal the presence of cardiac involvement and may warrant a more extensive testing. Tachibana et al. [42] reported the resolution of AV block and PVCs in follow-up ECGs in patients treated with corticosteroids, and recurrence when the steroid dose was reduced or stopped.

4.2. Holter monitoring

Twenty-four hour Holter monitoring can detect arrhythmias that are missed in a routine ECG. Suzuki et al. [43] compared the ECG findings of Holter monitor recordings in 38 consecutive patients with systemic sarcoidosis to 58 healthy individuals. It was concluded that the occurrence of PVCs of more than 100 per day showed a sensitivity of 67% and a specificity of 62% for indicating cardiac sarcoidosis. When the PVCs were of Lown's group IV (repetitive ventricular beats), the sensitivity was 67% and the specificity was 80%.

Holter monitoring is a simple non-invasive test that can be easily performed in outpatient setting and should be part of the routine work-up of patients who present with cardiac sarcoidosis.

4.3. Echocardiography

The evaluation of patients with sarcoidosis by echocardiography should include cardiac chamber dimensions, LV systolic and diastolic function, ventricular wall thickening, thinning and wall motion abnormalities, valvular evaluation, pericardial effusion and determination of PA pressure (if possible).

Cardiac granulomatous infiltration is initially seen as a mild thickening of the myocardium, especially the intra-ventricular septum, sometimes producing asymmetrical septal hypertrophy [32]. Later, as the disease progresses and scarring occurs, thinning of the myocardium and aneurysms may be noted [44].

Valantine et al. [45] reported that thinning and wall motion abnormalities at the base of the intra-ventricular septum characterize the presence of cardiac sarcoidosis, although this findings can result from more common diseases (particularly CAD with prior myocardial infarction). Never-

Table 2
Guidelines for diagnosing cardiac sarcoidosis, the Japanese Ministry of Health and Welfare, 1993

• Histological diagnosis
Cardiac sarcoidosis is confirmed when histological analysis of operative or endomyocardial biopsy demonstrates non-caseating granuloma
Or
• Clinical diagnosis
In patients with a histological diagnosis of extracardiac sarcoidosis, cardiac sarcoidosis is suspected when item 1 and one or more of items 2–5 are present
1. Complete RBBB, left-axis deviation, atrioventricular block, VT, premature ventricular contractions (>grade 2 of Lown's classification of PVC), or abnormal Q or ST-T wave abnormalities on the ECG
2. Abnormal wall motion, regional wall thinning, or dilatation of the left ventricle in echocardiographic studies
3. Perfusion defects by 201 Tl-myocardial scintigraphy or abnormal accumulation by 67 Ga-citrate or 99m Tc-myocardial scintigraphy
4. Abnormal intra-cardiac pressure, low cardiac output, or abnormal wall motion or depressed LV ejection fraction in cardiac catheterization
5. Non-specific interstitial fibrosis or cellular infiltration in myocardial biopsy

theless, echocardiography is a cost effective, non-invasive technique that can detect cardiac abnormalities related to sarcoidosis and provide prognostic information [46].

4.4. Endomyocardial biopsy

The diagnostic usefulness of this test is limited by the patchy involvement of the disease and the higher incidence of granulomas in the basal ventricular septum and left side of the heart in comparison to the right ventricle where endomyocardial biopsies are usually performed. Hence, the sensitivity of this test is low. Biopsy findings of non-caseating granulomas were reported in 20–50% of patients with clinically diagnosed cardiac sarcoidosis [47–49]. Overall, a biopsy is not mandatory to make the diagnosis of cardiac sarcoidosis considering the poor sensitivity of the test and the advent of newer non-invasive diagnostic studies.

4.5. Radionuclide myocardial studies

Myocardial scintigraphy with thallium-201 has been used in patients with suspected cardiac sarcoidosis; segmental areas with thallium-201 defects correspond to areas of fibrogranulomatous replacement. Haywood et al. [50] showed focal LV myocardial perfusion defects at rest in 13% of patients with systemic sarcoidosis; all of these defects decreased in size on exercise stress thallium, a finding which helps to differentiate defects secondary to cardiac sarcoidosis from those caused by coronary artery disease.

Other studies, however, found nuclear imaging to be less helpful. Kinney and Caldwell [51] concluded that thallium scan findings in 52 sarcoid patients appeared to be too non-specific to be used as a diagnostic or screening test for the presence of sarcoid heart disease. They also found that myocardial scan abnormalities were not associated with survival outcome. The low yield of thallium imaging testing might be related to the inability to visualize the RV myocardium due to its low radioactive energy level, except in cases of excessive RV hypertrophy [52].

The combination of gallium-67 and thallium-201 improved the detection of cardiac sarcoidosis. Gallium uptake by the myocardium indicates areas of active inflammation, which is a useful finding in predicting the response to corticosteroids as shown in a small series of patients [53,54].

Technetium-99m-sestamibi has a higher radioactive energy compared with thallium or gallium and has shown in many studies to be of a better diagnostic yield for both LV and RV involvement in sarcoidosis, as high as 67% in one study [55,56].

No recommendations regarding the use of myocardial perfusion studies are available for screening sarcoid patients to diagnose myocardial sarcoidosis. Once cardiac symptoms developed, serial SPECT imaging might be a useful tool in following the response to treatment in patients with baseline abnormalities.

4.6. Magnetic resonance imaging (MRI)

The ability of MRI to provide high-resolution anatomic information as well as cardiac function has made it an effective modality for direct visualization of the myocardium and pericardium (Fig. 5). Although MRI has not been studied systematically in the diagnosis of cardiac sarcoidosis, its role is expanding. Regional myocardial enhancement represents focal scarring associated with the inflammatory process and post-inflammatory scarring. Regional and global LV and RV function can be quantified, and extracardiac involvement can be imaged [57]. Shimada et al. [58] showed the usefulness of gadolinium–diethyl triamine pentaacetic acid (DTPA)-enhanced MRI for diagnosing myocardial involvement in a small group of patients with sarcoidosis and for the evaluation of steroid therapy.

Although MRI is a promising non-invasive test and is being more widely accepted by cardiologists, its role in diagnosing cardiac sarcoidosis is yet to be established. The data available now is not sufficient to determine the sensitivity and specificity of the test [59].

4.7. Other diagnostic tests

Cardiac catheterization with coronary angiography is useful in patients who present with chest pain and abnormal ECG, abnormal myocardial imaging studies and CHF to exclude the presence of coronary artery disease. A normal coronary angiogram associated with an abnormal perfusion imaging study in a patient with sarcoidosis is a strong indicator of cardiac involvement [60,61].

EPS may be useful in selected group of patients for guiding short-term anti-arrhythmic therapy [62]. In general, the indications for coronary angiography and EPS are similar to those in the absence of cardiac sarcoidosis.

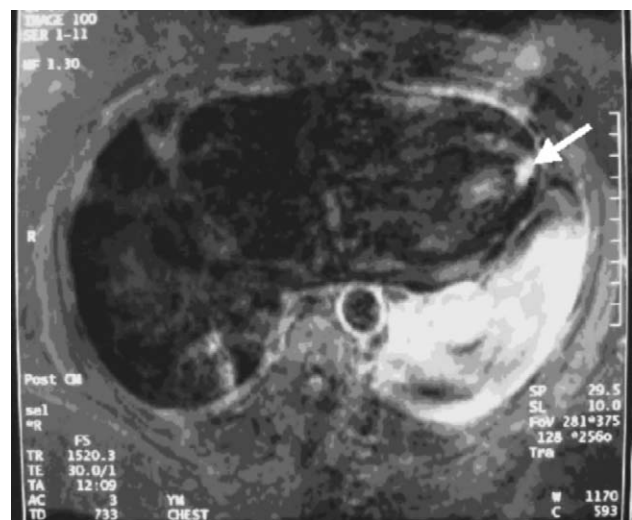


Fig. 5. Gated MRI in the transaxial view showed a 1-cm enhancing lesion in the LV apex in a 45-year-old patient with sarcoidosis. Note the left plural effusion.

5. Treatment

The treatment strategy of cardiac sarcoidosis should aim at relieving symptoms, controlling the inflammatory process, preventing further deterioration in myocardial function and preventing sudden death. Physicians should not wait until the onset of symptoms to start therapy; the treatment should be started as soon as the diagnosis is made.

5.1. Corticosteroids

Steroids are the mainstay of therapy in cardiac sarcoidosis and are the first line agents regardless of the clinical presentation. Despite the lack of well-controlled trials to show that these agents improve long-term outcome in pulmonary sarcoidosis [63], their role in cardiac sarcoidosis is well established and supported by a relatively large body of published clinical experience.

Early initiation of steroids as soon as the diagnosis of cardiac sarcoidosis is made and before the onset of heart failure is essential to prevent permanent damage and improve prognosis [64]. Resolution of electrocardiographic abnormalities [65], arrhythmias [66,67], conduction abnormalities [54,68,69] and disappearance of Q waves [70] have been reported with steroid therapy. Myocardial perfusion defects on thallium and technetium scans have improved or disappeared after a course of steroids [50,71]. Similarly, the enhanced areas were markedly diminished in size and signal intensity after steroid therapy in MRI studies [57,58]. Although LV systolic dysfunction might improve after starting steroid therapy [72], starting corticosteroids before the occurrence of systolic dysfunction results in excellent clinical outcome and is essential in treating patients with cardiac sarcoidosis [64].

There is no consensus about the proper dosing of steroids. An initial dose of 30 mg/day or 60 mg every other day has proven effective, and this dose can be tapered over a period of 6–12 months to a maintenance dose of 5–10 mg/day. Prolonged periods of treatment are often necessary as relapses are frequent in these patients [73]. No data are available regarding the discontinuation of steroid therapy, but earlier reports of sudden death following cessation of steroid treatment support the use of lifelong treatment.

While concern has been raised regarding the formation of cardiac aneurysms with the use steroids, it seems difficult to ascertain whether an aneurysm is simply due to the disease process itself or secondary to steroid administration. Most investigators believe that the treatment benefits outweigh the risk of aneurysm formation.

5.2. Immunosuppressive therapy

Other pharmacological approaches have been proposed in patients who cannot tolerate the side effect of steroids or whose disease is refractory to treatment with corticosteroids [74]. The efficacy of these drugs is not well established and

is not supported by well-controlled studies even in pulmonary sarcoidosis. Methotrexate, cyclosporine or cyclophosphamide may be used as corticosteroid-sparing agents in patients with sarcoidosis who require prolonged treatment [75–77].

5.3. Other pharmacological therapy

The medical management of heart failure due to cardiac sarcoidosis is similar to management in patients with heart failure due to other causes. Angiotensin converting enzyme inhibitors, diuretics, digoxin, spironolactone and beta-blockers should be used in patients with LV systolic dysfunction.

The role of anti-arrhythmic drug therapy for recurrent VT has not been defined clearly. In a series of 15 patients reported by Stein, the combination of prednisone and quinidine appeared effective in controlling ventricular arrhythmias [78]. In many case reports, other anti-arrhythmic medications have been used successfully in the treatment of patients with ventricular arrhythmias. Amiodarone use in this group of patients may be limited by the occurrence of pneumonitis and pulmonary fibrosis in 5–15% of cases; the drug-induced changes are indistinguishable radiographically from pulmonary sarcoidosis and may further compromise the pulmonary status of patients with sarcoidosis [67].

Winters et al. [17] reported the result of anti-arrhythmic therapy in seven patients with cardiac sarcoidosis and sustained VT. They found that even when the therapy was guided with programmed ventricular stimulation, patients had high rate of arrhythmia recurrence or sudden death.

5.4. Device therapy

The indications for permanent pacing are similar to those in patients without cardiac sarcoidosis. Permanent pacing has been shown to be effective in the prevention of sudden cardiac death and improving prognosis in sarcoid cases with advanced AV block and other bradyarrhythmias [79].

Because sudden cardiac death can be the initial presentation of cardiac sarcoidosis and ventricular arrhythmias may recur despite anti-arrhythmic medications, implantation of an ICD should be strongly considered once the diagnosis of cardiac sarcoidosis is made as a primary prevention of sudden cardiac death [80,81]. No firm guidelines are present now regarding the implantation of ICD in cardiac sarcoidosis, although many physicians believe that an ICD might be a cost-effective therapy in this high-risk group of patients. Patients with terminal illnesses and projected life expectancy ≤ 6 months, including drug-refractory heart failure patients who are not candidates for cardiac transplantation, are not candidates for ICD therapy [82].

5.5. Cardiac transplantation

Heart transplantation for cardiac sarcoidosis has been performed rarely and the total number of cases probably is

less than 20 patients worldwide, so far [83,84]. There have been case reports of patients with cardiac sarcoidosis undergoing heart transplantation who developed recurrence of sarcoidosis in the cardiac allograft after transplantation [85]. One study even showed that transmission of sarcoidosis via heart transplantation was possible [86], indicating that the disease was transmissible with human tissue and supporting the infectious theory of the disease. In summary, heart transplantation may improve the prognosis and quality of life for symptomatic advanced heart failure (NYHA Class IV) in patients with sarcoidosis that is limited to the heart.

7. Prognosis

The natural history and prognosis of sarcoidosis is difficult to determine due to the variable clinical presentations and severity of the disease, other organ involvement, the waxing and waning nature of the disease, and variable responses to steroid therapy in individual patients.

In the absence of cardiac involvement, the mortality rate of sarcoidosis is about 1–5% per year [73,87]. Cardiac involvement associated with poorer prognosis and the mortality rate may exceed 40% at 5 years and 55% within 10 years [64,88].

Over the last few decades, due to steroid therapy and pacemakers, the prognosis has improved and the main cause of mortality has shifted from sudden death to death from CHF [79].

Yazaki et al. [64] analyzed clinical findings and survival rate in 95 patients with cardiac sarcoidosis in an attempt to determine the significant predictors of mortality. During a mean follow-up of 68 months, there was no significant difference in survival of patients treated with a high initial dose and a low initial dose of prednisone. One of the most significant predictors of mortality was the severity of heart failure and NYHA functional class. Patients with LVEF >50% had a survival rate of 89% at 5 and 10 years, while those with LVEF <50% had a survival rate of 59% at 5 years and 27% at 10 years. Other independent predictors of mortality were LV end-diastolic diameter (hazard ratio 2.6/10 mm increase), sustained VT (hazard ratio 7.2).

The presence of pulmonary involvement was associated with better survival, probably due to earlier recognition of the disease and appropriate follow-up.

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