

Cardiac Sarcoidosis Presenting as Constrictive Pericarditis

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In patients with cardiac sarcoidosis, the sarcoid granulomas usually involve the myocardium or endocardium. The disease typically presents as heart failure with ventricular arrhythmias, conduction disturbances, or both. Constrictive pericarditis has rarely been described in patients with sarcoidosis: we found only 2 reports of this association.

We report the case of a 57-year-old man who presented with clinical and hemodynamic features of constrictive pericarditis, of unclear cause. He was admitted for treatment of recurrent pleural effusion. After a complicated hospital course, he underwent pericardiectomy. His clinical and hemodynamic conditions improved substantially, and he was discharged from the hospital in good condition. The pathologic findings, the patient's clinical course, and his response to pericardiectomy led to our diagnosis of cardiac sarcoidosis presenting as constrictive pericarditis. In addition to the patient's case, we discuss the nature and diagnostic challenges of cardiac sarcoidosis. Increased awareness of this disease is necessary for its early detection, appropriate management, and potential cure. (Tex Heart Inst J 2014;41(3):319-23)

In the United States, one quarter of patients with systemic sarcoidosis have cardiac involvement,¹ which is the usual cause of sarcoid-related deaths.² The myocardium and endocardium are typically affected.^{1,3} Pure pericardial involvement, excluding the adjacent myocardium, is reported less frequently. Furthermore, sarcoidosis rarely appears to present as constrictive pericarditis.

We report the case of a man who displayed classic findings of constrictive pericarditis secondary to cardiac sarcoidosis (CS) with adjacent myocardial involvement, and we discuss the nature and diagnosis of CS.

Case Report

Key words: Cardiomyopathies/complications/diagnosis/pathology; diagnosis, differential; diagnostic imaging; myocardium/pathology; pericarditis, constrictive/complications/etiology/surgery; sarcoidosis/complications/diagnosis/pathology; treatment outcome

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In December 2010, a 57-year-old man presented with progressive exertional dyspnea and lower-extremity edema. He had been healthy until approximately 6 months before and reported no chest pain, orthopnea, or paroxysmal nocturnal dyspnea. His blood pressure was 120/90 mmHg, his heart rate was 70 beats/min, and he was afebrile. His jugular venous pressure was elevated (15 cm H₂O) with hepatojugular reflux. Cardiac auscultation revealed a normal S₁ and S₂ with no murmur, gallop, or rub. Lung auscultation revealed diminished air entry in the bases bilaterally, with no crackles. The patient had severe (4+) pitting edema of the lower extremities, extending to his thighs. A chest radiograph showed bilateral pleural effusion. A 12-lead electrocardiogram revealed sinus rhythm with low voltage. A transthoracic echocardiogram showed mild left ventricular (LV) hypertrophy with mild impairment of systolic function and interventricular septal bounce consistent with constrictive physiology. The cardiac valves appeared to be normal. A computed tomogram (CT) of the chest with contrast showed mild pericardial thickening with focal calcification, extensive mediastinal and bilateral hilar lymphadenopathy, and moderate left and large right pleural effusions. A diagnostic and therapeutic right thoracentesis yielded results consistent with transudative effusion. Right- and left-sided heart catheterization revealed nonobstructive coronary artery disease. The patient's hemodynamic data were consistent with constrictive physiology (Table I and Fig. 1). Simultaneous right ventricular (RV) and LV pressure tracings showed interventricular discordance, with diastolic equalization of the pressure in both chambers and a square root sign (Fig. 2). Pericardial calcification was noted on fluoroscopy. The diagnosis was constrictive pericarditis of unclear cause.

TABLE I. Hemodynamic Data from Cardiac Catheterization

Variable	Value	Observation
Right side		
Mean right atrial pressure, mmHg	24	Steep x and y descents, no evidence of significant respiratory variation, and increased right atrial pressure during deep inspiration (Kussmaul sign)
RV pressure, mmHg	40/24	—
Pulmonary artery pressure, mmHg	40/24	—
PCWP, mmHg	24	—
Cardiac output (Fick), L/min	3.58	—
Cardiac index, L/min/m ²	1.87	—
Left side		
Aortic pressure (mean), mmHg	95/65 (76)	—
LV pressure (mean), mmHg	83/11 (26)	—
LVEDP, mmHg	26	—
Simultaneous RV and LV tracings	—	Diastolic equalization present with square root sign, and RV–LV discordance

LV = left ventricular; LVEDP = left ventricular end-diastolic pressure; PCWP = pulmonary capillary wedge pressure; RV = right ventricular

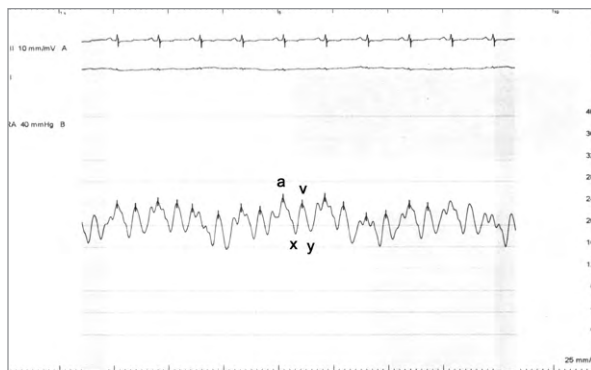


Fig. 1 Right atrial pressure tracing shows rapid x and y descent.

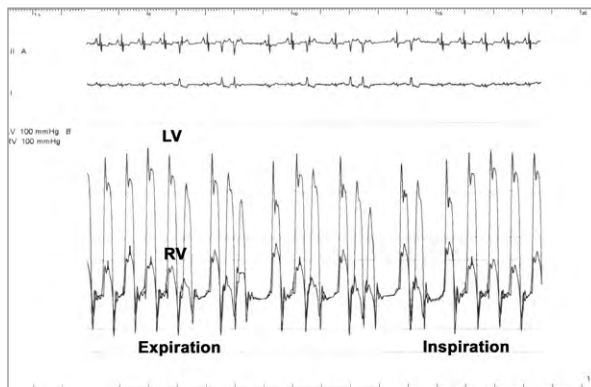


Fig. 2 Simultaneous recordings of left ventricular (LV) and right ventricular (RV) pressures show ventricular discordance. Note the decrease in RV systolic pressure during expiration (4th beat) and the marked rise at peak inspiration.

The patient was admitted to the hospital for treatment of recurrent pleural effusion, and he underwent right pleurodesis with biopsy of the mediastinal lymph node. His hospital course was prolonged and complicated by cardiogenic shock, severe anasarca, and respiratory and renal failure. After 6 weeks, he underwent extensive resection of the pericardium, which resulted in remarkable symptomatic and hemodynamic improvement. The excised pericardium showed pink-tan to purple-gray thickened fibrous tissue adhering to yellow, lobulated adipose tissue (Fig. 3). Histopathologic analysis of the excised specimens confirmed thickened pericardial tissue with dystrophic calcification, chronic inflammation, and no granulomas. The lymph node biopsy yielded nonnecrotizing and granulomatous inflammation and sclerosis (Fig. 4). Polymerase chain reaction analysis yielded no evidence of *Mycobacterium tuberculosis* complex DNA. Other diagnostic evaluations for infectious processes such as acid-fast bacilli and fungi produced no unusual results. Results of fluid cytology were negative for malignant cells. A cardiac magnetic resonance (CMR) image with gadolinium showed delayed enhancement involving the LV myocardium at the mid anteroseptal and basal inferolateral walls, consistent with infiltrative disease (Fig. 5). The final diagnosis was constrictive pericarditis caused by CS.

After 9 weeks total, the patient was discharged from the hospital, in good condition, on β -blocker and angiotensin-converting enzyme inhibitor therapy. He was prescribed oral prednisone, 30 mg/d for 6 weeks, with gradual tapering of the dosage over the following 8 weeks. As of June 2013, he had reported no cardiovascular symptoms during outpatient clinical visits.

Discussion

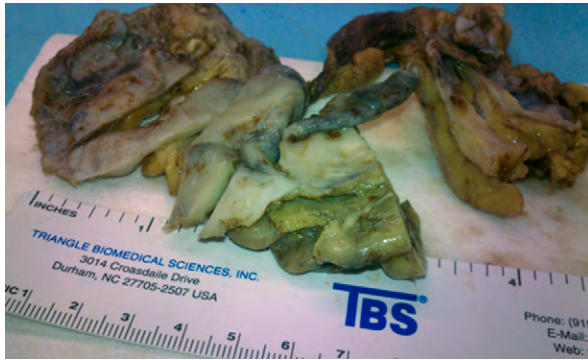


Fig. 3 Photograph of the excised pericardium shows pink-tan to purple-gray thickened fibrous tissue adherent to yellow, lobulated adipose tissue.

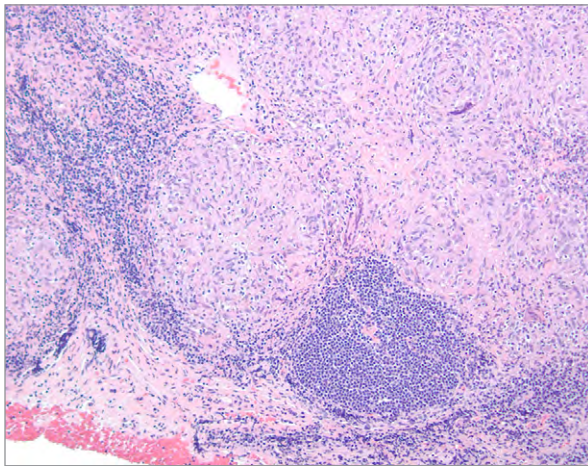


Fig. 4 Photomicrograph of the lymph node biopsy specimen shows nonnecrotizing and granulomatous inflammation and sclerosis (H & E, orig. $\times 100$).

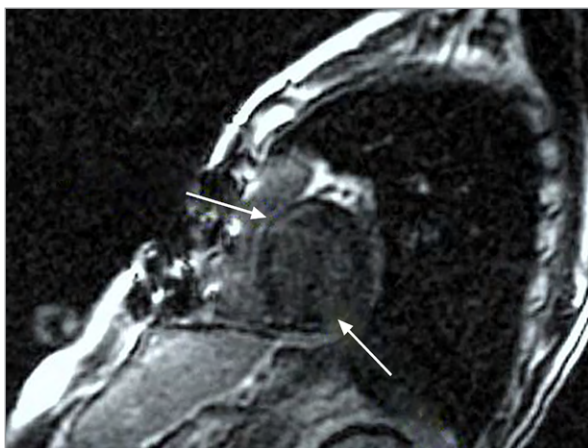


Fig. 5 Cardiovascular magnetic resonance image shows late enhancement in the anteroseptal and basal inferolateral segments of the left ventricular myocardium (arrows).

The clinical diagnosis of CS can be challenging because of the wide variety of clinical presentations, especially when the cardiac involvement precedes other manifestations of systemic sarcoidosis.⁴ Most often, patients present with conduction abnormalities and congestive heart failure. Other manifestations include valvular insufficiencies, myocardial infarction, recurrent pericardial effusion, and sudden death.^{1,5,6} Cardiac sarcoidosis should be part of the differential diagnosis in patients who present with refractory heart failure, conduction abnormalities, or ventricular arrhythmias.⁷ Pericardial involvement—especially constrictive pericarditis, as in our patient—appears to be an extremely rare clinical manifestation of this disease.

Initially, we thought that our patient's clinical presentation might be due to systolic heart failure caused by dilated cardiomyopathy, so we performed coronary angiography to exclude ischemic causes.⁸ The patient's mild coronary artery disease did not explain his LV dysfunction. On the other hand, the additional diagnostic results were consistent with constrictive physiologic conditions: pericardial calcification (on fluoroscopy and chest CT), interventricular septal bounce (echocardiography), and elevated right-sided filling pressure (catheterization). On tissue biopsy, the presence of bilateral hilar lymphadenopathy and noncaseating granulomas helped to confirm the diagnosis of systemic sarcoidosis in the absence of tuberculosis or fungal infection.³

Most available diagnostic algorithms for CS arise from histologic or clinical criteria.^{9,10} In our patient, the presence of systemic sarcoidosis with LV asynergy, the intracardiac pressure abnormalities found during catheterization, and the CMR findings fulfilled the clinical criteria for the diagnosis of CS.¹¹ In addition, the diagnosis of sarcoid constrictive pericarditis was on the basis of the clinical presentation, the echocardiogram, and right-sided catheterization findings.

Congestive heart failure in patients with systemic sarcoidosis usually occurs after the sarcoid granuloma invades the myocardium or endocardium and causes dilated or restrictive cardiomyopathy.^{1,3} Conversely, pericardial involvement is thought to be infrequent without myocardial involvement. Small pericardial effusions have been found echocardiographically in up to 19% of patients with sarcoidosis; however, only a few cases of clinically significant pericardial effusion together with biopsy-proven CS have been reported. The effusion and CS can manifest themselves as pericarditis or pericardial tamponade.^{12,13}

Cardiac sarcoidosis usually presents as restrictive cardiomyopathy, and differentiating it from constrictive pericarditis requires careful attention to the hemodynamic effects and echocardiographic features of both entities.⁹ During cardiac catheterization, hemodynamic

data that support the diagnosis of constrictive pericarditis include prominent X and Y descent, absent variation of right atrial pressure during respiration, dip and plateau of the LV pressure waveform, and RV–LV discordance (Figs. 1 and 2).

Sarcoidosis is apparently an extremely rare cause of constrictive pericarditis. In the largest 2 series of constrictive pericarditis (from the Mayo and Cleveland Clinics), the most frequent causes were cardiac surgery, idiopathic pericarditis, and prior irradiation.^{14,15} We screened our patient for the rarer cause of tuberculosis.¹⁶

We found only 2 reports of constrictive pericarditis associated with CS. The first patient was a young man whose presentation was similar to that of our patient.¹⁷ The 2nd case of constrictive pericarditis was confirmed by means of RV and LV biopsy.¹⁸ Endomyocardial biopsy can be considered in patients whose clinical features suggest CS^{6,7}; however, the sensitivity of the test is low because of heterogeneous involvement.¹⁹ Cardiac imaging, including scintigraphy with technetium-99m, thallium-201, and gallium-67, had limited sensitivity and specificity in the diagnosis of CS.²⁰ Conversely, CMR, by showing enhanced signal intensity in the mid portion of the myocardium and epicardium, reportedly had a sensitivity of 100% and a specificity of 78%.²⁰

Evaluation of the pericardial tissue in our patient, as well as that in the first reported case of sarcoid constrictive pericarditis,¹⁷ yielded thickened pericardial tissue with dystrophic calcification, chronic inflammation, and no granulomas. Similarly, the most frequent histopathologic findings after pericardiectomy in patients with connective-tissue disease are nonspecific chronic inflammation, fibrosis, and calcification.^{18,21}

Management of Cardiac Sarcoidosis

Corticosteroids, the mainstay of therapy for CS, play a major role in preventing LV remodeling²² and they improve survival rates.^{5,23} However, pericardiectomy is considered to be the treatment of choice for most patients with constrictive pericarditis. This surgery serves as a potential cure with substantial improvement in symptoms (as in our patient), and it is associated with improved long-term survival rates.^{14,15}

Despite some controversy, we think that most clinicians would agree with implantable cardioverter-defibrillator (ICD) therapy for primary prevention of sudden cardiac death in CS. Cardiac sarcoidosis can be associated with life-threatening ventricular arrhythmias when the myocardium is involved. Placement of an ICD should be considered in high-risk patients, including those with a history of syncope, LV dysfunction, and spontaneous or induced cardiac arrhythmia during electrophysiologic studies.^{6,10,19,24} Increased awareness of CS and its challenges is necessary for early detection,

selection of the appropriate management strategy, and potential cure.

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