Echocardiographic Manifestations in Patients with Cardiac Sarcoidosis

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Background: Cardiac sarcoidosis is a life-threatening disease with protean clinical manifestations, including congestive heart failure (CHF), conduction disturbance, ventricular arrhythmia and sudden death. Nonetheless, it is difficult to diagnose cardiac sarcoidosis in the clinical setting. Some echocardiographic findings of cardiac sarcoidosis associated with other diagnostic tools (^{201}thallium scintigraphy, ^{67}gallium citrate scan, serum markers and others) may be helpful upon early suspicion and diagnosis of cardiac sarcoidosis.

Materials and Methods: Fifty-two patients (36 female) with cardiac sarcoidosis, with a mean age of 48 ± 14 years (range, 21–70 yr), underwent a series of echocardiographic follow-up (mean, 88 ± 48 mo) examinations, and important echocardiographic parameters and findings were recorded.

Results: There were left ventricular (LV) regional wall motion abnormalities (RWMAs) noted in 40 (localized in 16, multiple in 24), dilatation of the LV with impaired LV contractility in 28, thinning of the basal interventricular septum (IVS) in 27, thinning of LV free wall in 18, apical aneurysm in 12, apical thrombus in two, mimicking hypertrophic cardiomyopathy (HCM) in two, pericardial effusion (PE) in two (with cardiac tamponade in one), and LV wall thinning and aneurysm formation after steroid therapy for cardiac sarcoidosis in two of 43 patients.

Conclusion: Thinning of the basal IVS or LV free wall is a specific echocardiographic finding of cardiac sarcoidosis. Other echocardiographic findings of cardiac sarcoidosis may mimic coronary artery disease (LV RWMA or apical aneurysm), CHF, or HCM. PE and thinning of the LV wall after steroid therapy were also noted in rare situations.

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KEY WORDS: • congestive heart failure • apical aneurysm • regional wall motion abnormality • left ventricular free wall thinning • basal interventricular septum thinning

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Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology involving multiple organs, including lungs, lymph nodes, eyes, skin, heart, liver and others [1–3]. Cardiac involvement is documented in 20%–30% of patients with sarcoidosis on autopsy, but clinical cardiac manifestations are seen in only about 5% of patients. Cardiac sarcoidosis is definitively diagnosed histologically on finding typical noncaseating epithelioid granuloma cells, but the positive rate of endomyocardial biopsy is low (around 20%–30%) [4–8]. Cardiac sarcoidosis may lead to serious clinical events, such as ventricular arrhythmia, sudden cardiac death, conduction disturbance and refractory congestive heart failure (CHF). Morbidity and mortality due to CHF or ventricular arrhythmia are also high [9, 10]. Echocardiography in patients with cardiac sarcoidosis may have specific or nonspecific findings. The purpose of this study was to assess the incidence of abnormal echocardiographic findings of cardiac sarcoidosis in a single center and to determine the specific and nonspecific findings helpful for early suspicion or diagnosis of cardiac sarcoidosis.

Materials and Methods

Subjects

The records of patients who were diagnosed with cardiac sarcoidosis between January 1990 and June 2001 were analyzed retrospectively. We diagnosed patients with cardiac sarcoidosis according to the criteria proposed by the Specific Diffuse Pulmonary Disease Research Group, Sarcoidosis Division [11]. The diagnostic criteria were grouped histologically and clinically. (1) Histologic diagnostic group: endomyocardial biopsy or surgery revealed noncaseating necrosis with epithelioid granuloma cells in the myocardium. (2) Clinical diagnostic group: an organ other than the heart was histologically positive for sarcoidosis criterion A and at least one criterion from B to E. These criteria include: A) Electrocardiography (ECG) or 24-hour holter monitoring revealed right bundle branch block, left axis deviation, atrioventricular block, ventricular tachycardia, ventricular premature contractions (VPCs), ≥ Lown grade 2, abnormal Q wave or ST-T change. B) Echocardiography revealed left ventricular (LV) regional wall motion abnormality (RWMA), localized wall thinning or hypertrophy, or LV chamber dilatation. C) ^{201}thallium, ^{67}gallium citrate or ^{99m}technetium-PYP scintigraphy abnormality. D) Cardiac catheterization revealed abnormal intracardiac pressure or low cardiac output. Left ventriculography revealed RWMA or low ejection fraction (EF). E) Endomyocardial biopsy revealed nonspecific change and at least moderate grade interstitial fibrosis or cellular infiltration. (3) Clinically highly suspected group: Patients did not have a definitive histologic diagnosis but met criteria A to E, leading to a strong suspicion of cardiac sarcoidosis.

There were 52 patients (16 men and 36 women), and their average age was 48 ± 14 years (range, 21–71). Of the 52 patients studied, 36 (69%) had positive histologic findings (noncaseating epithelioid granulomas) in the heart, lymph nodes, lung or skin. Sixteen patients (31%) showed positive right ventricular endomyocardial biopsy. Pulmonary involvement was noted in 12 (23%), skin lesions in 10 (19%) and eye involvement in 14 (27%) patients. Among these patients, echocardiography, ECG, myocardial perfusion scintigraphy, gallium scan, radionuclide ventriculography, cardiac catheterization with right ventricular biopsy, serum angiotensin converting enzyme and lysozyme levels, clinical cardiac events (chest pain, conduction disturbance, lethal arrhythmia, CHF and sudden cardiac death) and mortality were investigated during the follow-up period.

Ultrasound examination

All patients underwent a series of echocardiographic examinations during follow-up (mean, 88 ± 48 mo; range, 1–196) with commercially available ultrasound systems (SSD 870, Aloka, Tokyo, Japan; SSH-160A, Toshiba, Tokyo, Japan; or Sonos 2000, Sonos 5500, Hewlett-Packard, Andover, Massachusetts) and a 2.5-MHz imaging transducer. Thickness of IVS and LV posterior wall, LV end-diastolic diameter and LV end-systolic diameter were determined using M-mode echocardiography. LV end-diastolic and end-systolic volumes, and EF were also measured. Typical echocardiographic findings of cardiac sarcoidosis, including LV RWMA, thinning or hypertrophy of LV wall, thinning of the base of IVS and LV aneurysm were also recorded.

Definitions

The LV was divided into 16 segments and RWMA in each segment was evaluated (hypokinesia, akinesia,

dyskinesia). LV diastolic dysfunction was defined as reduced height of the E wave and increased height of the A wave, with an E/A ratio of less than one, accompanied by prolongations of the isovolumic relaxation time (IVRT) and deceleration time (DT). Pulmonary hypertension was defined as shortening of the pulmonary acceleration time (ACT), decrease of the ratio between the pulmonary ACT and pulmonary ejection period or tricuspid regurgitation (TR) pressure gradient measured by continuous wave Doppler plus 10 mmHg (right atrium pressure) more than 30 mmHg. Severity of mitral regurgitation (MR) and TR were measured using semiquantitative flow mapping scored as 1+ (mild regurgitation), 2 to 3+ (moderate regurgitation) or 4+ (severe regurgitation). Severe MR was associated with systolic reversal of pulmonary vein flow. Severe TR was associated with systolic reversal flow of hepatic vein flow). Hypertrophic cardiomyopathy (HCM) was defined as localized or generalized thickening of the IVS or LV free wall with (obstructive) or without dynamic obstruction of the LV outflow tract (LVOT). Cardiac tamponade was defined as diastolic collapse of the right ventricle (and right atrium). The Lown classification of VPC was as follows: grade 0 (no VPC), grade 1 (single or sporadic VPC), grade 2 (frequent, > 30 VPCs per min), grade 3 (multifocal VPCs), grade 4 (repetitive, two couplets or more than three continuous VPCs), grade 5 (VPCs with R on T phenomenon).

Results

Among the 52 patients undergoing echocardiographic examinations, LV RWMA were noted among 40 patients (Figs. 1 and 2). Sixteen patients had single localized and the other 24 had multiple RWMA. Dilatation of the LV with impaired LV contractility was also noted in 28 patients (Fig. 1). Among all 52 patients, echocardiographic findings of basal IVS thinning typical of cardiac sarcoidosis was noted in 27 (Fig. 2) and LV free wall thinning was noted in 18 patients (Fig. 3). LV apical aneurysm with dyskinesia was detected in 12 patients and two of them had apical thrombi (Fig. 4). Cardiac sarcoidosis mimicking HCM was noted in two (Fig. 5), pericardial effusion (PE) in two (with cardiac tamponade in one), and LV wall thinning and aneurysm formation in two of 43 patients after steroid therapy for cardiac sarcoidosis. LV diastolic dysfunction with early filling/atrial contraction (E/A) flow reversal was noted in 27 patients. Mitral regurgitation was noted in 33 patients (1+ in 18, 2 to 3+ in nine, and 4+ in six). Tricuspid regurgitation was noted in 26 patients (1+ in 11, 2 to 3+ in eight and 4+ in seven) and pulmonary hypertension detected by echocardiography was noted in 15 patients. The echographic findings are shown in the Table.

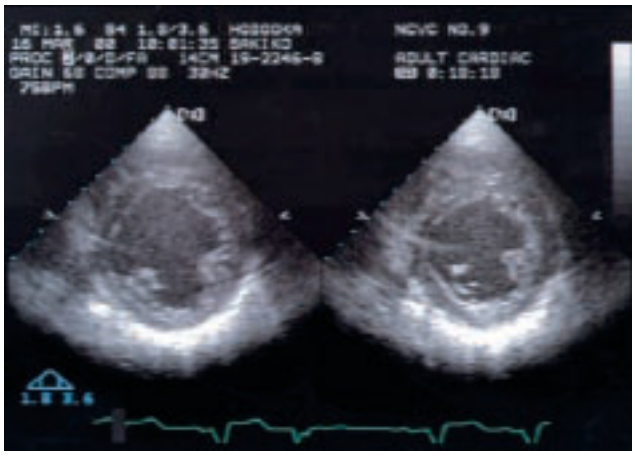

Fig. 1. *Parasternal short axis view in a 70-year-old woman with cardiac sarcoidosis. Left: diastolic phase. Right: systolic phase; poor left ventricular ejection fraction (25% by M mode calculation and 16% by modified Simpson's method) with inferoposterior wall akinesia and anteroseptal wall hypokinesia. Thallium scintigraphy also revealed multiple perfusion defects. Coronary angiography showed patent coronary arteries.*

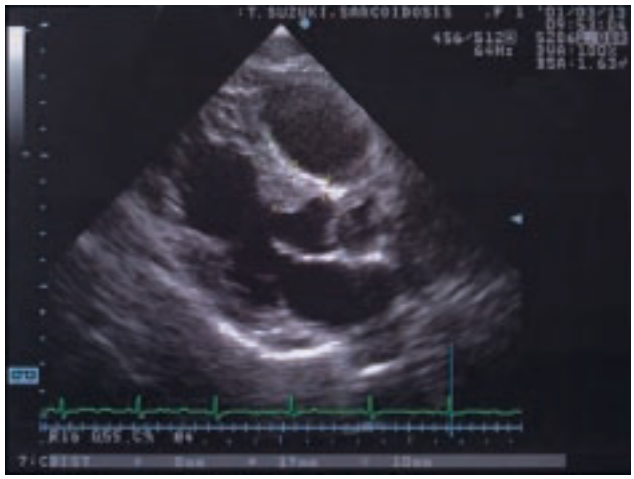

Fig. 2. *Parasternal long axis view in a 40-year-old woman with cardiac sarcoidosis. The figure shows typical thinning of the base of the interventricular septum.*

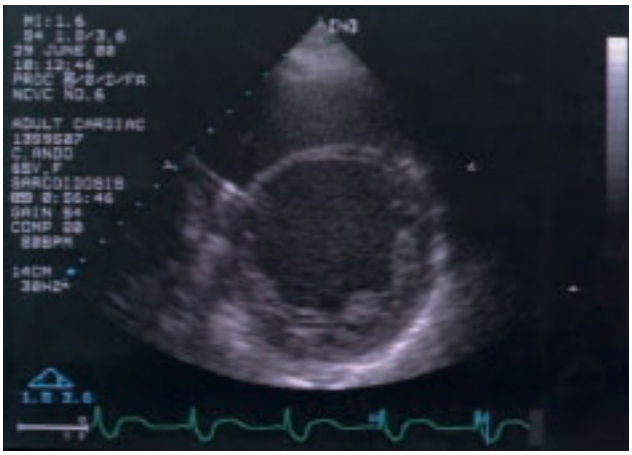

Fig. 3. *Parasternal short axis view in a 65-year-old woman with cardiac sarcoidosis. The figure shows thinning of the base of the interventricular septum.*

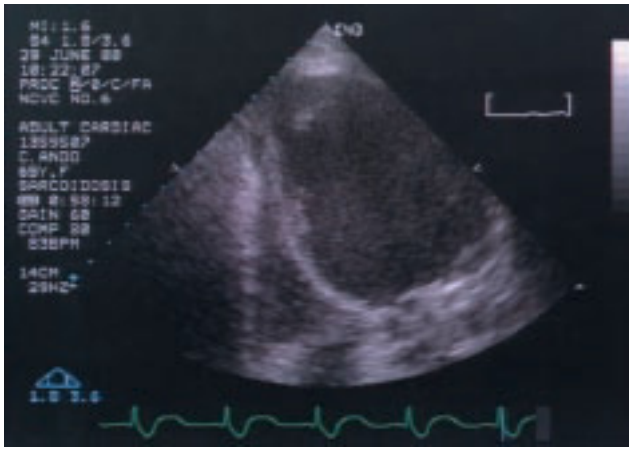

Fig. 4. *Apical four chamber view in a 45-year-old woman with cardiac sarcoidosis. The figure reveals apical dyskinesia of left ventricle with thrombus formation. Electrocardiography showed QS patterns in the precordial lead. Nonetheless, coronary angiography showed patent coronary arteries.*

Discussion

Cardiac sarcoidosis is a serious disease with severe morbidity and high mortality. Its clinical diagnosis is a challenging task. Cardiac sarcoidosis should be suspected in patients with clinical symptoms or signs of sarcoidosis along with abnormal echocardiographic or scintigraphic findings [12–16]. In patients with sarcoidosis, cardiac involvement is noted in 20% to 50% of patients. Moiseyev reported echocardiographic abnormalities in 33 of 90 patients with systemic sarcoidosis [17]. There were LV dilatation and impaired LV contractility in 21, LV wall thickening

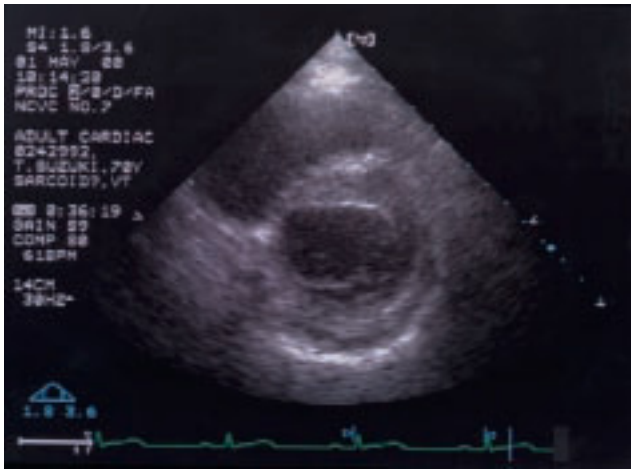

Fig. 5. *Parasternal short axis view in a 68-year-old woman with cardiac sarcoidosis. The figure reveals localized hypertrophy of anterior wall (thickness = 17 mm). No pressure gradient was noted in left ventricular outflow tract.*

in eight, LV wall thinning in seven and PE in five patients, according to his report. Burstow reported LV RWMA in 12 of 88 patients with systemic sarcoidosis [18]. Of these 12 patients, nine had a history of CHF. Valantine also emphasized that cardiac sarcoidosis should be highly suspected in patients with basal IVS thinning [19]. Echocardiography in our patients also had the same specific and nonspecific findings, suggesting cardiac involvement of sarcoidosis.

Thinning of the basal IVS or LV free wall is a typical and specific finding of cardiac sarcoidosis, and may be helpful for establishing early suspicion and diagnosis of cardiac sarcoidosis. It was a common finding and was noted in more than one-half of our patients on echocardiography. Nonspecific echocardiographic findings of cardiac sarcoidosis may mimic coronary artery disease (CAD), CHF or HCM. LV RWMA is the most common nonspecific finding of cardiac sarcoidosis detected by echocardiography. In our patients, most of them were young and did not have any risk factors for CAD. In addition, we found sarcoidosis in other organs in association with abnormal scintigraphic findings, abnormal serum markers for cardiac sarcoidosis (ACE or lysozyme) and patent coronary arteries on coronary angiography. Thus, we could rule out the possibility of CAD and thought it was granulomatous involvement in a single or multiple regions of the LV.

Table. Echocardiographic findings in patients with cardiac sarcoidosis

Echocardiographic finding	n (%)
Specific	
Thinning of basal IVS	27 (52)
Thinning of LV free wall	18 (35)
Nonspecific	
Impaired LVEF/chamber dilatation	28 (54)
LV RWMA	40 (77)
Apical aneurysm	12 (23)
Apical thrombus	2 (4)
Hypertrophic cardiomyopathy	2 (4)
Pericardial effusion	2 (4)
Cardiac tamponade	1 (2)
Mitral regurgitation	33 (63)
Tricuspid regurgitation	26 (50)
LV diastolic dysfunction	27 (52)

IVS = interventricular septum; LV = left ventricular; LVEF = left ventricular ejection fraction; RWMA = regional wall motion abnormality.

LV chamber dilatation with impaired LV function was the second most common echocardiographic manifestation of patients with cardiac sarcoidosis. Symptoms or signs of CHF were also noted in most of these patients. LV apical aneurysm with or without an apical thrombus mimicking anterior wall myocardial infarction (MI) also occurred in some patients. ECG of these patients can reveal ST elevation and QS patterns in the precordial leads, with echocardiography also showing LV dyskinesia. Nonetheless, the coronary arteries of these patients were all patent. Kosuge et al also reported a case of cardiac sarcoidosis with apical aneurysm [20, 21]. They thought that myocardial necrosis due to granulomatous inflammation was the main cause of apical aneurysm formation. In rare situations, cardiac sarcoidosis may present as an HCM-like manifestation on echocardiographic studies. We found localized or generalized thickening of three IVS or other portions of the LV, with or without a dynamic pressure gradient in the LVOT. Matsumori et al reported six cases of cardiac sarcoidosis mimicking HCM [22]. The manifestations of hypertrophy included IVS hypertrophy in four, asymmetrical septal hypertrophy in two, localized hypertrophy in one and apical hypertrophy in one. Yazaki et al thought that sarcoidosis mimicking HCM could be differentiated from true HCM by radionuclide image studies [23]. Because in cases of cardiac sarcoidosis mimicking HCM, thallium or gallium scan revealed perfusion defects or abnormal uptake in the hypertrophic myocardium.

LV diastolic dysfunction also occurred in over one-half of patients with cardiac sarcoidosis. It may have been due to impaired LV function, LV chamber dilatation, increased LV filling pressure or poor LV compliance. MR may be due to LV chamber dilatation, mitral annulus dilatation or papillary muscle involvement of cardiac sarcoidosis. TR and pulmonary hypertension may result from left heart failure or primary pulmonary sarcoidosis. In two of 43 patients undergoing steroid therapy for cardiac sarcoidosis, apical wall thinning and aneurysm formation were noted. The cause of aneurysm formation may be the result of steroid therapy or the natural course of cardiac sarcoidosis [21–23].

In conclusion, cardiac sarcoidosis may have various echocardiographic findings. IVS base and LV free wall thinning are typical and specific findings helpful for early suspicion and diagnosis of cardiac sarcoidosis. Other nonspecific findings may mimic CAD, CHF or HCM, and therefore, other diagnostic tools are needed to help establish the final clinical diagnosis. In rare situations, PE (with or without cardiac tamponade) is another echocardiographic finding.

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