Interventricular Septal Thickening as an Early Manifestation of Cardiac Sarcoidosis

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Summary

We report an unusual case of cardiac sarcoidosis demonstrated by interventricular septal thickening. A 64-year-old woman was diagnosed with sarcoidosis involving the lungs, eyes, and skin. Three years later, renal dysfunction was detected during a periodic examination and a renal biopsy revealed non-caseating granulomas. Electrocardiogram results were normal, but an echocardiogram revealed thickening of the interventricular septum. Abnormal accumulation of gallium-67 and a perfusion defect in technetium-99-methoxyisobutylisonitrile scintigrams occurred in the interventricular septum. Magnetic resonance images showed T2-high intensity in the lesion. We considered the thickening to represent cardiac involvement of sarcoidosis. Oral prednisolone therapy diminished the interventricular septal thickening. (Int Heart J 2014; 55: 181-183)

Key words: Interventricular septum

Sarcoidosis is a multisystem inflammatory disease of unknown etiology. Interventricular thinning is the most specific characteristic feature of cardiac sarcoidosis in echocardiograms, whereas interventricular septal thickening is extremely rare in sarcoidosis patients. Here, we report an unusual case of cardiac sarcoidosis that presented as interventricular septal thickening.

Case Report

In May 2008, a 64-year-old woman developed eye floaters and erythema on the forehead. A chest X-ray film and computed tomography scans revealed enlargement of the bilateral hilar and mediastinal lymph nodes and nodular shadows in the lung fields. She was admitted to our hospital for further examination. Her serum angiotensin converting enzyme (ACE) levels were normal (21.2 IU/L, baseline 8.3–21.4 IU/L), but her serum lysozyme levels were elevated (19.0 μg/mL, baseline 5.0-10.2 μg/mL). A gallium-67 scintigram revealed abnormal uptake in the mediastinal and bilateral hilar lymph nodes. An electrocardiogram, 24-hour Holter electrocardiogram, echocardiogram, and technetium-99-methoxyisobutylisonitrile scintigram revealed no abnormal findings. A transbronchial lung biopsy and a skin biopsy showed non-caseating granulomas. She was definitively diagnosed with sarcoidosis involving the lungs, eyes, and skin. Routine periodic examination with an electrocardiogram and echocardiogram revealed no abnormalities. Her serum creatinine, ACE, and lysozyme levels gradually increased after January 2011, and renal involvement of the sarcoidosis was suspected. In June 2011, she was admitted to our hospital again for further examination. Fine crackles were heard over both lung fields. Systolic murmurs were heard at the third intercostal space just left of the sternum. Laboratory data revealed elevated serum levels of ACE (26.5 IU/L, baseline 8.3–21.4 IU/L), lysozyme (27.4 μg/mL, baseline 5.0-10.2 μg/mL), and creatinine (1.95 mg/dL, 0.40 – 1.10 mg/dL). Histopathologic examination of kidney biopsy specimens revealed non-caseating epithelioid granulomas with giant cells, compatible with sarcoidosis. Electrocardiogram and 24-hour Holter electrocardiogram findings were normal, but an echocardiogram revealed thickening of the interventricular septum (33 mm) (Figure 1A). Cardiac magnetic resonance imaging (MRI) detected T2-high intensity in the thickened interventricular septum (Figure 2A,B). Gallium-67 accumulated in the lesion (Figure 3A) and technetium-99-methoxyisobutylisonitrile scintigrams showed a perfusion defect (Figure 3B,C,D). Thus, we diagnosed the interventricular septal thickening as myocardial involvement of the sarcoidosis, and initiated therapy with prednisolone (30 mg/day). The dosage of prednisolone was gradually reduced to 10 mg/day. The interventricular septal thickening gradually improved based on periodical echocardiogram examination and completely diminished after 5 months of steroid therapy (Figure 1B). Abnormalities on cardiac MRI and technetium-99-methoxyisobutylisonitrile scintigram had also resolved by the final examination.

Discussion

Cardiac involvement occurs in about 21.2% of Japanese patients with sarcoidosis. Only half of the patients with cardi-
Cardiac sarcoidosis show clinical evidence of myocardial involvement during their lifetime. Cardiac death is much more frequent in Japanese patients. Clinicians must determine the clinical findings of cardiac sarcoidosis in the early stages because steroid therapy is protective or therapeutic in the early stage of cardiac sarcoidosis, but not at later stages.

The most common finding of cardiac sarcoidosis in echocardiograms is thinning of the interventricular septum. In contrast, interventricular septal thickening of sarcoidosis is quite rare and only 4 cases have been reported (Table). It is unknown whether interventricular septal thickening is an early or late manifestation of cardiac sarcoidosis. In the majority of patients with cardiac sarcoidosis, initial findings are arrhythmias, conduction disturbance, and congestive heart failure. In the 4 previous cases of interventricular septal thickening, 3 had an abnormal echocardiogram. Because our patient did not have arrhythmias, a conduction disturbance, or congestive heart failure, we considered that our patient was in the early stage of cardiac sarcoidosis. In the histologic analysis of fatal myocardial sarcoidosis, histologic classification is divided into 4 types and indicates the clinical course of sarcoidosis; 1) exudative type, 2) granuloma type, 3) combined type, and 4) fibrotic type. In the 3 previous biopsy-proven cases with interventricular septal thickening, one case was the exudative type and two cases were the fibrotic type. Although we could not obtain biopsy specimens in our case, the cardiac lesion was not detected at the periodic echocardiogram examination after the first diagnosis of sarcoidosis and appeared with worsening of the systemic disease. Moreover, as observed in our case, increased T2 high-intensity represents edema associated with the...
inflammation and granuloma in the myocardium as an early stage of cardiac sarcoidosis. 10,11 Thickening of the cardiac wall also could be observed in the ventricular free wall.12,13 In two cases with left ventricular thickening 12,13 and one case with right ventricular thickening,13 steroid therapy resulted in the normalization of atrioventricular block. The authors thus consider that cardiac hypertrophy would be the early stage of inflammation.

The severity of heart failure is one of the most significant predictors of mortality from cardiac sarcoidosis.13 In the case of interventricular septal thickening, the prognosis is unknown.2,3 Initiating corticosteroid treatment before the occurrence of systolic dysfunction results in an excellent outcome.2,3 Our case did not have cardiac systolic dysfunction, and steroid therapy diminished the cardiac thickening without the appearance of cardiac systolic dysfunction. Yazaki, et al reported that pulmonary involvement was associated with better survival, which will lead to earlier detection of cardiac involvement in patients with pulmonary sarcoidosis during the follow-up of pulmonary lesions.7 Periodic echocardiogram studies, especially when systemic disease activity is increased, could help to detect early findings of cardiac sarcoidosis and lead to early steroid therapy.

ACKNOWLEDGMENTS

The authors wish to thank Dr. Tomoko Nawata and Dr. Kazuhiro Shinozaki for their help with caring for the patients.

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Table. Clinical Profiles From Patients With Cardiac Sarcoidosis Presenting Interventricular Septal Thickening

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>ECG</th>
<th>IVS thickness (mm)</th>
<th>Ejection Fraction (%)</th>
<th>Extra-cardiac Lesion</th>
<th>Cardiac Biopsy</th>
<th>Therapy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>F</td>
<td>free</td>
<td>AV-block RBBB</td>
<td>18</td>
<td>70</td>
<td>Skin</td>
<td>Abnormal uptake in the anteroseptal region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>M</td>
<td>free</td>
<td>VPC</td>
<td>13</td>
<td>ND</td>
<td>Lung Eye</td>
<td>Abnormal uptake in the anteroseptal region</td>
<td>Myocyte hypertrophy Cellular infiltration Interstitial edema</td>
<td>PSL 60 mg/day</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>M</td>
<td>free</td>
<td>Normal</td>
<td>13</td>
<td>71</td>
<td>Lung Eye</td>
<td>Myocyte hypertrophy Cellular infiltration Fibrosis</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>F</td>
<td>Chest pain</td>
<td>RBBB</td>
<td>13</td>
<td>49</td>
<td>Eye</td>
<td>Myocyte hypertrophy Cellular infiltration Fibrosis</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Our case</td>
<td>67</td>
<td>F</td>
<td>free</td>
<td>Normal</td>
<td>33</td>
<td>69</td>
<td>Lung Eye Kidney Skin Medeistinal and bilateral hilar lymphnodes</td>
<td>Abnormal uptake in the intraventricular mass</td>
<td>ND</td>
</tr>
</tbody>
</table>

ECG indicates electrocardiogram; A-V block, atrioventricular block; RBBB, right bundle branch block; NS, not stated; ND, not done; and VPC, ventricular premature contraction.