Assessment of Myocardial Perfusion and Fatty Acid Metabolism in a Patient With Churg-Strauss Syndrome Associated With Eosinophilic Heart Disease

Nobuaki Shikama, MD; Tomoo Nakagawa, MD; Yasuo Takiguchi, MD; Nobuyuki Aotsuka, MD; Yoichi Kuwabara, MD*; Nobuyuki Komiyama, MD*; Takashi Terano, MD; Akira Hirai, MD

Churg-Strauss syndrome is characterized by asthma, eosinophilia and systemic necrotizing vasculitis; cardiac involvement (ie, eosinophilic heart disease) is the major cause of morbidity and mortality, although there are no reports of an association between left ventricular dysfunction because of eosinophilic heart disease and myocardial blood flow or myocardial fatty acid metabolism. A patient presented with Churg-Strauss syndrome associated with eosinophilic heart disease that had progressed to dilated cardiomyopathy. Coronary angiography, thallium-201 (201TI) and iodine-123 [1-]methyl-iodophenyl pentadecanoic acid (123I BMIPP) myocardial single photon emission computed tomography (SPECT) were performed to evaluate left ventricular dysfunction. Although coronary angiography was normal and 201TI SPECT showed no apparent image defect, 123I BMIPP SPECT showed diffuse decreased accumulation, excepting the apex. The left ventricular dysfunction in patients with eosinophilic heart disease is associated with impaired myocardial fatty acid metabolism rather than with impaired myocardial blood flow. (Circ J 2004; 68: 595–598)

Key Words: Churg-Strauss syndrome; Eosinophilic heart disease; Myocardial fatty acid metabolism; Myocardial perfusion; 201TI scintigraphy; 123I BMIPP scintigraphy

Case Report

The patient, a 71-year-old Japanese man, was admitted to hospital in September 2000, because of gait disturbance and eosinophilia. In June 2000, he had been diagnosed as having bronchial asthma, based on clinical symptoms. In the week prior to admission, he began to complain of low grade fever, muscular weakness and numbness of the lower extremities; his white blood cell count was 34,900 per mm3 with 53.8% eosinophils. Because of the symptoms and eosinophilia, he was referred to hospital for further evaluation.

Physical examination on admission revealed his body temperature was 36.6°C, blood pressure was 92/56mmHg, and his pulse rate was 74 beats/min. Erythema was observed on the dorsum of the proximal interphalangeal joints and metacarpophalangeal joints. There was no murmur, crackle or peripheral edema. A chest X-ray revealed an infiltrative shadow on the left middle lung field and mild cardiomegaly (cardiothoracic ratio: 51%) with no pulmonary congestion (Fig 1A). His electrocardiogram (ECG) showed sinus rhythm (heart rate: 83 beats/min), horizontal ST depression in leads V1–6 (max V6: –1.5 mm) and QS pattern and ST elevation in leads V1 and V2 (Fig 2A). An electromyogram (EMG) showed a neurogenic pattern in both sciatic nerve areas. He was diagnosed as having mononeuropathy multiplex, based on the EMG findings and physical examination. Laboratory data included the following: white blood cell count of 55,200/mm3 (with 84.0% eosinophils, 13.0% neutrophils, 2.0% lymphocytes and 1.0% basophils), red blood cell count of 3.68×106/mm3, hemoglobin concentration of 11.8 g/dl, hematocrit of 34.2%, platelets count of 23.3×103/mm3, total serum protein concentration of 7.4 g/dl, serum albumin concentration of 2.5 g/dl, 332 IU/L aspartate aminotransferase, 149 IU/L alanine aminotransferase, 851 IU/L lactate dehydrogenase, 14.4 mg/dl blood urea nitrogen, 0.9 mg/dl creatinine, 7.8 mg/dl C-reactive protein, 3,797 IU/L creatine kinase (CK) (with 5% CK-MB) and 348 U/ml IgE. Anti-nuclear antibody, anti-DNA antibody and C-antineutrophil cytoplasmic antibody were negative, but P-antineutrophil cytoplasmic antibody (266 EU) was positive. Troponin T (2.01 ng/ml), myosin light chain (122 ng/ml) and interleukin-5 (77.4 pg/ml) were elevated. The night of the admission, the dyspnea worsened and coarse crackles were auscultated in the bilateral lung fields. Initially, he was administered aminophylline (250mg) and...
hydrocortisone sodium succinate (100 mg) under the diagnosis of a bronchial asthma attack. The next day, a chest X-ray showed severe pulmonary congestion and cardiomegaly (cardiothoracic ratio: 55%) (Fig 1B), and echocardiography revealed diffuse hypokinesis of the left ventricle (ejection fraction 27.3%) (Fig 3). An ECG showed wide QRS tachycardia (complete right bundle branch block pattern; heart rate 145 beats/min) (Fig 2B). Based on the worsening of congestive heart failure (CHF) and laboratory findings, eosinophilic heart disease caused by CSS was diagnosed. The rapid progression of respiratory failure because of CHF was supported with continuous mechanical ventilation and treated with diuretics and inotropic agents. Simultaneously, pulse steroid therapy was started with methyl prednisolone at the dose of 1,000 mg/day for 3 days, followed by prednisolone at the dose of 60 mg/day for 3 weeks, after which the dose was tapered to attain a maintenance dose of 20 mg/day. On Day 7, the serum concentrations of eosinophilic cationic protein (ECP) (Pharmacia
ECP-RIA kit, Uppsala, Sweden) and major basic protein (MBP) (Mayo Medical Laboratories, Rochester, MN, USA) were measured by radioimmunoassay. ECP (13.3 μg/L) (normal value: <15.7 μg/L) was normal, but despite the pulse steroid therapy, MBP (11,755 ng/ml) (normal value: 421±56 ng/ml) was significantly elevated. Subsequently, his respiratory function improved and the congestive heart failure became compensated (Fig 1C), but the dilation of the left ventricle and reduction of the ejection fraction persisted. Therefore, 6 weeks after the start of prednisolone, left heart catheterization, coronary angiography, thallium-201 (201Tl) under resting conditions and iodine-123 ¹²³I-methyl-iodophenyl pentadecanoic acid (123I BMIPP) myocardial single photon emission computed tomography (SPECT) were performed to evaluate the left ventricular dysfunction. Left ventriculography showed diffuse hypokinesis (ejection fraction: 35%). The left ventricular end-diastolic pressure was 10 mmHg and the left ventricular end-diastolic volume was 79 ml/m². Although coronary angiography was normal and 201Tl SPECT showed no apparent image defect (Fig 4), 123I BMIPP SPECT showed diffuse decreased accumulation, excepting the apex (Fig 5).

Thereafter, the patient's general condition and laboratory findings improved, and the eosinophilia disappeared; thus, we could taper the dose of corticosteroid to a maintenance dose of 10 mg/day. However, the left ventricular dysfunction (Table 1) and numbness of the lower extremities persisted.

**Discussion**

Eosinophilic heart disease may present in association with not only CSS, but a variety of diseases, including idiopathic and secondary hypereosinophilic syndromes! Moreover, patients with eosinophilic heart disease show various clinical cardiac manifestations, including eosinophilic cardiomyopathy, eosinophilic myocarditis, eosinophilic endomyocardial disease and eosinophilic pericarditis. Eosinophil granule proteins (eg, ECP5–7, eosinophil protein-X5 and MBP6–8) may play an important role in the develop-

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**Table 1 Time Course of Echocardiographic Findings**

<table>
<thead>
<tr>
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<th>Day 2 of admission</th>
<th>After 3 weeks</th>
<th>After 2 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVDd (mm)</td>
<td>49.5</td>
<td>52.6</td>
<td>52.6</td>
</tr>
<tr>
<td>LVDs (mm)</td>
<td>43.2</td>
<td>43.3</td>
<td>42.5</td>
</tr>
<tr>
<td>IVSd (mm)</td>
<td>9.4</td>
<td>6.9</td>
<td>7.2</td>
</tr>
<tr>
<td>LVPWD (mm)</td>
<td>9.4</td>
<td>6.9</td>
<td>6.1</td>
</tr>
<tr>
<td>EF (%)</td>
<td>27.3</td>
<td>42</td>
<td>39</td>
</tr>
<tr>
<td>MR</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>TR</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>E/A</td>
<td>–</td>
<td>2.33</td>
<td>0.58</td>
</tr>
<tr>
<td>DcT (ms)</td>
<td>–</td>
<td>101</td>
<td>133</td>
</tr>
</tbody>
</table>

LVDd: left ventricular diastolic dimension; LVDs: left ventricular systolic dimension; IVSd: interventricular septal wall thickness in diastole; LVWD: left ventricular posterior wall thickness in diastole; EF: ejection fraction; MR: mitral regurgitation; TR: tricuspid regurgitation; E/A: E to A ratio; DcT: deceleration time; –: no information available.
ment of acute cardiac dysfunction. The progress to dilated cardiomyopathy and acute cardiac dysfunction may be the result of interstitial and endocardial fibrosis, and to the possible continuous existence of eosinophil granule proteins in the myocardium. On the other hand, a previous study suggested that the extent of the abnormality of myocardial fatty acid metabolism assessed by $^{123}$I BMIPP in idiopathic dilated cardiomyopathy reflected the severity of hemodynamic deterioration and histopathological changes. In the present patient, myocardial fatty acid metabolism was impaired to a greater extent than myocardial blood flow, and the blood concentration of MBP was still high after pulse steroid therapy. It is possible that eosinophil granule proteins or cytokines released by eosinophils led to impairment of the energy metabolism of the mitochondria, and consequently, left ventricular function was impaired despite preservation of myocardial blood flow. Although we could not distinguish left ventricular dysfunction caused by eosinophilic heart disease from idiopathic dilated cardiomyopathy, based on the findings of myocardial scintigraphy, the findings reflected cardiac metabolic and histopathologic damage of the myocardium. Therefore, we suggest that the cause of left ventricular dysfunction in patients with eosinophilic heart disease might be impaired myocardial fatty acid metabolism induced by eosinophil granule proteins rather than an impairment of myocardial blood flow caused by the necrotizing vasculitis. However, the relation between myocardial fatty acid metabolism and the pathogenesis of eosinophilic heart disease remains to be verified.

References