



Eosinophilic myocarditis due to Churg–Strauss syndrome mimicking reversible dilated cardiomyopathy

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ABSTRACT

A 41-year-old woman with a history of asthma arrived at the emergency room of our hospital with dyspnea. The electrocardiogram showed no specific results. Echocardiography defects revealed an obvious decrease in the left ventricular systolic function and enlargement of the left chamber. We initially considered her condition to be dilated cardiomyopathy. However, she had eosinophilia in the peripheral blood and elevated cardiac enzymes. The coronary angiography showed normal coronary arteries. Single photon emission computed tomography (SPECT) showed infiltrative myocardial disease. She was then diagnosed with eosinophil infiltrations. Combined with peripheral nerve injury and lung involvement, she was diagnosed as having Churg–Strauss syndrome. After initiating prednisone treatment, her eosinophilia and rising cardiac enzymes recovered to normal, and both her echocardiographic abnormalities and symptoms noticeably improved.

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Introduction

Churg–Strauss syndrome (CSS) is a rare form of systemic vasculitis. Eosinophilia-mediated CSS can affect any organ, but cardiac involvement in patients with CSS has a poor prognosis. Eosinophilic myocarditis (EM) is one of the most common forms of cardiac involvement in patients with CSS. Recently, EM mimicking acute myocardial infarction has been the most commonly reported case. However, to our knowledge, this is the first report presenting a patient who suffered from suspected EM mimicking reversible dilated cardiomyopathy (DCM) complicated by CSS.

Case report

A 41-year-old woman was admitted to the emergency room because of progressive and exertional dyspnea for 2 months. Two months ago, for the first time, she felt dyspnea without any direct cause, but it worsened with slight physical activity. She had intermittent bilateral edema of the lower extremities. Occasionally, she felt chest pain aggravated by inhalation. She also felt numbness and pricking at the bottom of her feet. She had a long medical history of asthma. Several chest CT scans in 2011 showed migratory and transient pulmonary infiltration. She never smoked or drank.

On physical examination, her blood pressure was 110/70 mm Hg, with a regular pulse rate of 109 beats per minute. She looked

chronically ill on admission and was in poor nutrition. Her face was cadaverous and the skin was not yellow. Her jugular vein was distended. Her lungs produced no wheezes or rales, but had decreased breath sounds in the bilateral bases. Cardiac examination revealed a regular heart sound with no murmur, rubs or gallop, but her left heart border expanded toward the left.

A diagnosis of dilated cardiomyopathy was initially considered based upon her known symptoms and echocardiography. The latter showed normal interventricular septum thickness, but systolic dysfunction with an ejection fraction of 31% (Fig. 1A, B). The patient's left ventricular end-diastolic diameter was 58 mm and left atrium end-systolic diameter was 35 mm. Her right atrium and ventricle were normal in size and systolic function. Minor regurgitation of the mitral valve and mild pericardial effusion were detected. Electrocardiography revealed sinus tachycardia, poor R wave progression in precordial leads and nonspecific ST-T abnormalities. A chest X-ray showed a cardiothoracic ratio of 62% and an increase of markings and patchy shadows in the bilateral lungs. The results of a routine blood panel showed a leukocyte count of 13,600/ μ l (upper limit of normal = 10,000/ μ l), with 32.1% (upper limit of normal = 5.0%) eosinophils. The concentrations of hyper-sensitive cardiac troponin T (cTnT, upper limit of normal = 100 pg/ml) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP, upper limit of normal = 450 pg/ml) were elevated (711.4 pg/ml and 7062 pg/ml respectively). Rises in IgE concentration (6.65 mg/L, upper limit of normal = 0.36 mg/L), C-reactive protein concentration (10.5 mg/L, upper limit of normal = 3 mg/L) and erythrocyte sedimentation rate (84 mm/h, upper limit of

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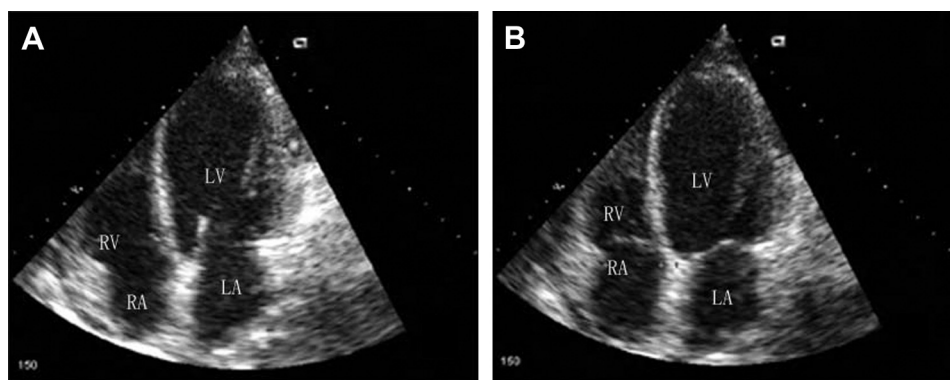


Fig. 1. Echocardiogram on admission showed left ventricle systolic dysfunction. A: echocardiogram in diastole. B: echocardiogram in systole.

normal = 20 mm/h) were also detected. Parasites, anti-neutrophil cytoplasmic antibody (ANCA) and tumor markers were negative, as were the tests for antibodies to viruses and a bone marrow examination. Neural electromyography showed that the first left lumbar nerve and fifth sacral nerve were impaired.

In order to exclude non-ST-segment elevation myocardial infarction, the patient was also scheduled for coronary angiography, which revealed normal coronary arteries. On the tenth day of her hospitalization, the patient had a fever with a temperature of approximately 38.0 °C. The blood routine study showed 45.71% eosinophils which was rising quickly. Increases in hypersensitive cTnT (812.7 pg/ml) and NT-proBNP (9562 pg/ml) were also observed. Single-photon emission computed tomography myocardial perfusion imaging (SPECT) revealed a “patchy” distribution of radioactivity in the left myocardium, which is a sign of myocarditis. We discovered a high eosinophil count of 13.1% (upper limit of normal = 1%) in bronchoalveolar lavage fluid. A transbronchial lung biopsy showed remarkable eosinophilic perivascular infiltration in the lungs (Fig. 2). With the information available, a diagnosis of eosinophilic pneumonia was considered for our patient. A diagnosis of Churg–Strauss syndrome was then proposed based on a history of asthma, eosinophilia in peripheral blood, migratory and transient pulmonary infiltrations, and peripheral neuritis. According to the echocardiography defects and cardiac SPECT abnormalities, cardiac involvement-suspected eosinophilic myocarditis occurred in our patient with CSS. An endomyocardial biopsy was not performed because of the patient’s high left ventricular end-diastolic pressure.

The patient was then administered prednisone at a dose of 40 mg (1 mg/kg) per day. After one week’s treatment, her condition

improved. She no longer suffered from shortness of breath and had no numbness at the bottom of her feet. Her temperature, eosinophilia and cTnT had all returned to normal. A follow-up examination with our cardiology department 8 months later showed that her symptoms had improved significantly. The echocardiography showed that the pericardial effusion had disappeared, her left ventricular end-diastolic diameter was 48 mm, and the left ventricular ejection fraction (LVEF) had increased to 45% (Fig. 3A, B).

Discussion

Our patient primarily presented signs of chronic cardiac failure. Due to a combination of her symptoms, cardiac enlargement on physical examination, and the results of her X-ray and echocardiography, the patient was first diagnosed with DCM. However, we found a rise in cTnT, but a normal coronary angiography followed by a remarkably high eosinophil count in peripheral blood after hospitalization. Suspected eosinophilic myocarditis was then considered as a diagnosis for our patient. According to the guidelines of Japanese Circulation Society, EM is strongly considered when the following five criteria are fulfilled: (1) eosinophilia of more than 500/ul; (2) cardiac symptoms such as chest pain, dyspnea and palpitation; (3) elevated levels of cardiac enzymes such as CK-MB and Troponin T; (4) ECG changes; (5) transient hypertrophy or wall asynergy of left ventricle in ultrasonography. Coronary angiography is recommended to exclude acute myocardial infarction.¹ Our patient had a normal coronary angiography and met all five criteria, which indicate a high index of suspicion for EM. It is noted that if EM is clinically suspected, an endomyocardial biopsy should be done.² Although positive findings in lung biopsy are

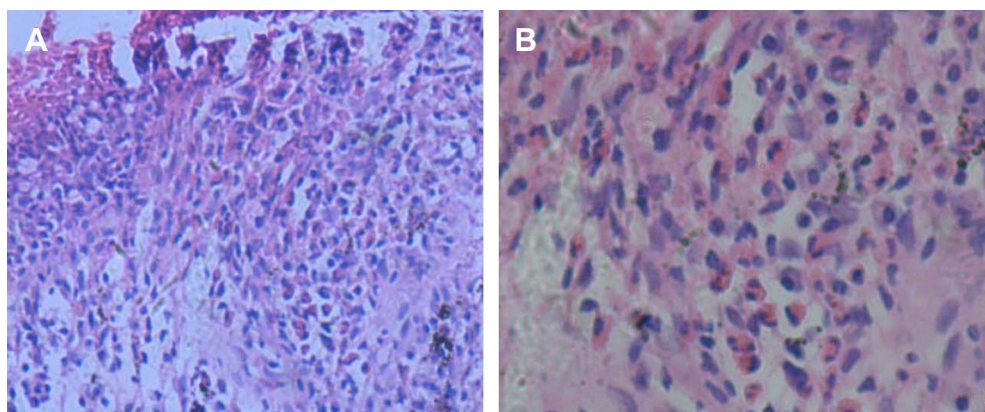


Fig. 2. Pathology of lung biopsy (hematoxylin and eosin staining) shows multifocal perivascular infiltration of eosinophils which is compatible with eosinophilic pneumonia. A: Under low magnification (×20). B: Under high magnification (×100).

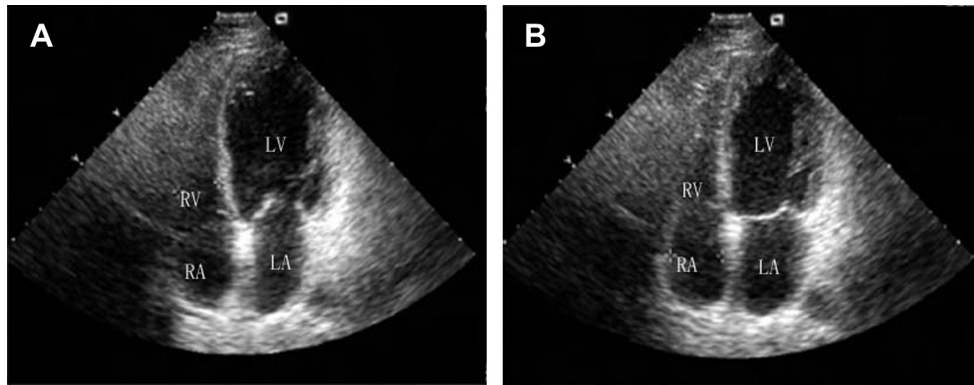


Fig. 3. Follow-up echocardiogram 8 months later showed the size of the left ventricle reduced and the ejection fraction improved. A: Echocardiogram in diastole. B: Echocardiogram in systole.

direct evidence of tissue eosinophilic infiltration, it still remains questionable if the patient truly had eosinophilic myocarditis. It is unfortunate that endomyocardial biopsy was not performed because of high left ventricular end-diastolic pressure in our patient. Thus, by elimination of all other possibilities, we make a diagnosis of suspected EM. Combined with a history of asthma, she was then diagnosed with CSS due to the rising eosinophil count and the involvement of several organs including her lungs, heart, and peripheral nerves. Therefore, we hypothesize that the presence of DCM in our patient with CSS is one of the forms of EM manifestation in the inflammatory progress.

Churg–Strauss syndrome (CSS) is a rare necrotizing vasculitis characterized by chronic rhinosinusitis, asthma and eosinophilia.³ CSS is typically divided into three phases which are overlapping mutually: asthma, tissue eosinophilia, and systemic vasculitis.⁴ In 1994, the American College of Rheumatology proposed six classification criteria for CSS: (1) asthma; (2) peripheral eosinophilia >10%; (3) neuropathy, mononeuropathy, or polyneuropathy; (4) migratory or transient pulmonary infiltrates; (5) paranasal sinus abnormality; and (6) evidence of eosinophilic infiltration on biopsy of extravascular organs.⁵ CSS is commonly diagnosed in the presence of more than four of six of these classification criteria. In our patient, hypereosinophilia and several associated symptoms such as asthma, paresthesia and pulmonary infiltrates were considered as the evidence in diagnosis of CSS. The prognosis of CSS with an overall 10 years survival rate of 81%–92%, is generally good.⁶ However, cardiac involvement in CSS is responsible for a dismal prognosis and is a leading cause of morbidity and mortality accounting for 50% in patients with CSS. Therefore, early recognition of cardiac involvement in patients with CSS and prompt treatment may play an important role in preventing progression of cardiac damage. Cardiac involvement includes eosinophilic endomyocarditis, eosinophilic myocarditis, coronary vasculitis, pericarditis, and valvular heart disease. EM, which is characterized predominantly by an eosinophilic infiltration into myocardium, is one of the most common forms of cardiac involvement complicated by CSS. It is noteworthy that myocardium hypertrophy is the main manifestation of EM because of eosinophilic granulocyte infiltration.⁷ However, presence of EM in patients with CSS can be quite variable. Recent reports show that EM in patients with CSS can also present like myocardial infarction, which may result in misdiagnosis.⁸ Herein, for the first time, we report a case of suspected EM in a patient with CSS that showed symptoms of DCM and without myocardial hypertrophy.

The management of EM includes eliminating the cause and starting standard therapy for heart failure. In addition, immunosuppressive treatment with a steroid, especially in patients with left

ventricular failure, has been shown to improve symptoms.⁹ However, treatment criteria for EM have not yet been established due to its scarcity and the majority of previously reported cases of EM were initially treated with prednisone at a dose of 1 mg/kg/day.¹⁰ In patients with CSS, a dose of prednisone at 1 mg/kg/day is recommended for one month, with a gradual taper for up to one year or until there is no traceable evidence of the disease.¹¹ After the diagnosis of suspected EM due to CSS, our patient was administered prednisone at a dose of 40 mg/day which was effective.

Conclusion

In conclusion, eosinophilic myocarditis complicated by CSS also can present like dilated cardiomyopathy. An early diagnosis of cardiac involvement in patients with CSS and subsequent adjunctive therapy is important for patients' prognosis.

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