Case Report

Acute Coronary Syndrome Caused by Coronary Vasospasms Associated with Churg-Strauss Syndrome: Effects of Betamethasone Therapy

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Abstract

A 42-year-old woman with a history of aspirin-induced asthma was admitted with severe chest pain. Emergency coronary angiography revealed coronary artery spasms. The administration of vasodilators did not suppress the anginal symptoms, and the differential white blood cell count continued to show eosinophilia. The patient’s symptoms of aspirin-induced asthma, eosinophilia and other allergic states led to the diagnosis of Churg-Strauss syndrome (CSS). After starting betamethasone therapy, the eosinophilia and cardiac symptoms rapidly disappeared. Although coronary vasospasms related to CSS are rare, the present case suggests that a differential white blood cell count should be obtained in patients with refractory coronary vasospasms.

Key words: Churg-Strauss syndrome (CSS), coronary vasospasm, acute coronary syndrome

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Introduction

Churg-Strauss syndrome (CSS) is a rare systemic disease characterized by necrotizing vasculitis and peripheral eosinophilia. Although the overall prognosis is good, clinical studies suggest that cardiac involvement is associated with an adverse prognosis (1). The cardiac manifestations of CSS vary, including myocarditis, congestive heart failure and valvular disease, while coronary vasospasms are rare (2, 3). We herein report the case of a woman who presented with acute coronary syndrome caused by coronary vasospasms. The administration of vasodilators did not suppress the anginal symptoms, which suggested that the coronary vasospasms were related to the eosinophilia. The diagnosis of CSS was established based on the American College of Rheumatology Criteria for CSS (4). This is the first case in which a CSS patient exhibited severe coronary artery spasms without a provocation test.

Case Report

The patient was a 42-year-old woman. Although she had suffered from bronchial asthma during childhood, she no longer had symptoms and was not taking any antiasthmatic medications. Five years ago, she had taken aspirin and developed an acute asthma attack. At that time, she was diagnosed with aspirin-induced asthma. One year ago, she developed chronic sinusitis and nasal polyps. Six months prior to the current admission, she developed abdominal pain and consulted her primary physician, who noticed mild leukocytosis with an elevated level of eosinophils. Two months before admission, the patient developed chest pain that was not related to exertion. The pain lasted no longer than 30 minutes. Three weeks before admission, the chest pain attacks increased in number.

The patient was transported by ambulance to our hospital because she developed severe chest pain that produced unconsciousness. A 12-lead electrocardiogram (ECG) showed ST segment depression in leads V₂-V₅, and atrial fibrillation.
The sublingual administration of nitroglycerin promptly relieved the pain and normalized the electrocardiographic abnormalities. She had no cardiovascular risk factors. A blood analysis revealed a normal peak creatine kinase-MB fraction; however, troponin T was positive. The differential white blood cell count demonstrated an eosinophil count of 1,126/mm\(^3\), corresponding to 13.5\% of total leukocytes. Other laboratory data were almost normal.

Nine hours after admission, the patient developed recurrent chest pain. A 12-lead ECG immediately showed ST segment elevation in leads II, III and aVF and depression in leads I, aVL and V\(_2\)-V\(_6\). The ECG was obtained nine hours after admission.

We suspected that the patient had CSS. Four days after catheterization, we started treatment with betamethasone at a dose of 4 mg/day in combination with daily doses of 100 mg of diltiazem and 40 mg of isosorbide mononitrate. Following the initiation of betamethasone therapy, the eosinophil rate decreased to 1.7\% on the second day, and the anginal episodes disappeared. On the 6th day, the dose of betamethasone was reduced to 2 mg/day and isosorbide mononitrate was discontinued. On the 12th day, the administration of diltiazem was discontinued. At that time, the eosinophil rate was 0.1\%. On the 13th day, the dose of betamethasone was reduced to 1.5 mg/day, without the recurrence of symptoms. The patient’s symptoms of asthma, eosinophilia and other allergic states led to the diagnosis of CSS. At the 3-month follow-up, she remained free from angina pectoris. Cardiac catheterization revealed normal coronary angiography findings (Fig. 3). The dose of betamethasone was gradually tapered to a maintenance dose of 0.5 mg/day, without the use of antianginal drugs.

**Discussion**

We herein described a patient who presented with acute coronary syndrome caused by coronary vasospasms. Her symptoms of asthma, sinusitis, eosinophilia and allergic states, such as purpura and nasal polyps, led to the diagnosis of CSS. This is the first case in which a CSS patient exhibited severe coronary artery spasms without a provocation test. Cardiac involvement is frequently observed in patients with CSS and is the leading cause of mortality (1). Cardiomyopathy is a common complication of CSS; myocarditis, congestive heart failure and valvular heart disease are usually observed. Although coronary vasospasms are an unusual clinical manifestation of CSS, the present case suggests that coronary vasospasms should be suspected in cases of CSS.

In one CSS patient with recurrent episodes of unstable angina pectoris, the intracoronary infusion of acetylcholine induced multiple coronary artery spasms (2). In that patient, coronary angiography showed no anatomic stenosis before the infusion of intracoronary acetylcholine. The present patient exhibited severe coronary artery spasms in the right coronary artery; however, there were no anatomic stenotic lesions in the left coronary artery. It is possible that she would have developed multiple coronary artery spasms following the intracoronary injection of acetylcholine.

According to the American College of Rheumatology, a patient can be diagnosed with CSS if at least four of the following six criteria of the traditional format classification are met, with a sensitivity of 85\% and specificity of 99.7\%:
- asthma, eosinophilia>10\% on a differential white blood cell count
- mononeuropathy or polyneuropathy, non-fixed pulmonary infiltrates on roentgenography, paranasal sinus abnormalities or a biopsy containing blood vessels with extravascular eosinophils

A classification tree was also constructed using three selected criteria, with a sensitivity of 95\% and specificity of 99.2\%:
- asthma, eosinophilia>10\% on
Figure 2. Emergency coronary arteriogram obtained on the day of admission. (A) The left anterior oblique view of the left coronary artery (LCA) shows an extensive collateral supply to the right coronary artery (arrow). (B) The left anterior oblique view of the right coronary artery (RCA). Severe coronary artery spasms (arrows) are observed in both the proximal and distal segments. (C) Although the right coronary artery exhibited 35% narrowing, the intracoronary bolus administration of 0.2 mg of nitroglycerin immediately reversed the spasm and led to dilatation (arrow) of the epicardial vessels.

Figure 3. Coronary arteriogram obtained at the 3-month follow-up after the start of treatment with betamethasone. (A) No coronary artery spasms are observed in the right coronary artery. (B) The extensive collateral supply to the right coronary artery from the left coronary artery had disappeared.

LCA: left coronary artery, RCA: right coronary artery

differential white blood cell count and a history of documented allergies other than asthma or drug sensitivity (4). Among the criteria in the traditional classification, the present patient demonstrated asthma, eosinophilia and a paranasal sinus abnormality, although she failed to meet the other three criteria. We diagnosed her as having CSS according to the classification tree because she had asthma, eosinophilia and symptoms of allergies, such as a paranasal sinus abnormality, nasal polyps and purpura.

The major factors involved in the development of coronary vasospasms are endothelial dysfunction via abnormalities of nitric oxide (NO) synthase and its reduced bioavailability and hypercontractility of the vascular smooth muscle in spastic arteries. Vasodilators, such as calcium antagonists and nitrates, are effective in treating regular coronary vasospasms (5). In contrast, coronary vasospasms in patients with eosinophilia are often resistant to vasodilators and may be responsive to immunosuppressive agents (6). Our patient was initially treated with 4 mg of intravenous betamethasone, which corresponds to approximately 25 mg of predni-
While corticosteroids, such as prednisone, are used to treat vasculitis in CSS patients, betamethasone has not been previously used. The present patient had aspirin-induced asthma. Corticosteroid-induced bronchospasms are more commonly seen in asthmatics with a history of an allergy to aspirin, and betamethasone has been suggested to be an alternative agent in such patients (7, 8). After starting betamethasone, our patient’s eosinophilia and cardiac symptoms rapidly disappeared. This result indicates that the use of betamethasone can be considered in patients with CSS, particularly when a history of an allergy to aspirin is present.

The exact pathogenesis of CSS is unknown. Recent results suggest that eosinophil infiltration and ANCA-induced endothelial damage are likely the most important mechanisms in CSS (9). The differences between ANCA-positive and ANCA-negative CSS cases were recently emphasized (10). Similar to that observed in the present case, compared with ANCA-positive patients, ANCA-negative patients tend to have a high incidence of heart involvement (11). Activated eosinophils may be the major pathogenic factor in ANCA-negative CSS cases. The present patient’s symptoms and coronary artery spasms disappeared following the administration of betamethasone. This suggests that her coronary vasospasms were provoked by hypersensitivity or an elusive autoimmune mechanism based on eosinophil infiltration. It can be postulated that chemical substances released from eosinophils play a role in coronary vasospasms. For instance, leukotriene C4, a chemical mediator released from eosinophils (12), causes coronary artery constriction in miniature pigs at the level of small vessels (13). Therefore, eosinophilia may play an important role in coronary vasospasms. Further studies are needed to evaluate the relationship between coronary vasospasm and eosinophilia.

In this case of CSS-associated coronary vasospasms, vasodilators did not relieve the patient’s vasospastic angina; however, immunosuppressive therapy improved her symptoms. Several reports have suggested a possible link between numerous types of allergic diseases and coronary vasospasms (2, 3, 14). The reported patients were refractory to vasodilator treatment but successfully treated with immunosuppressive therapy. The outcome of the present case indicates that betamethasone may also be considered as a treatment choice in patients with refractory coronary artery spasms. A differential white blood cell count should be obtained in patients who are refractory to treatment with vasodilators to evaluate the possibility of CSS or other allergic states as potential differential diagnoses.

The authors state that they have no Conflict of Interest (COI).

References


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