CASE REPORT

Sudden Cardiac Death Associated With Churg-Strauss Syndrome

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A 60-year-old man who had suffered from bronchial asthma and diabetes mellitus (on dietary treatment) for the previous 2 years with a history of smoking, consulted the outpatient clinic with complaints of chest and right arm pain. He had undergone treatment for asthma and diabetes mellitus (on dietary treatment) for the previous 2 years with a history of smoking.

Churg-Strauss syndrome (CSS) is a multisystem disorder characterized by allergic rhinitis, bronchial asthma, and prominent peripheral blood eosinophilia, and was first reported by Churg and Strauss in 1951.1 It is also known pathologically as allergic granulomatous angiitis (AGA). Although its exact etiology is unknown, it is most likely related to an autoimmune system disorder. The lungs are the most affected organ, but other organ systems also can be affected, including the cardiovascular, gastrointestinal, renal, and central nervous systems. The diagnosis of CSS is suggested by the clinical findings and confirmed by biopsy of the clinically affected tissue. As long as it is diagnosed and treated appropriately, the prognosis is no poorer than for any other type of vasculitis. However, when CSS is associated with cardiac or gastrointestinal complications, its prognosis becomes worse. Manifestations of cardiac involvement in CSS include acute pericarditis (32%), acute heart failure (47%), and myocardial infarction,2 and these account for half of the causes of death associated with CSS. We report a case of CSS associated with eosinophilic myocarditis, coronary vasospastic angina, and unexpected sudden death.

Case Report

A 60-year-old man, who had suffered from bronchial asthma and diabetes mellitus (on dietary treatment) for the previous 2 years with a history of smoking, consulted the outpatient clinic with complaints of chest and right arm pain. He had never had any symptoms suggesting common cold associated with fever and diarrhea. However, no abnormal findings suggestive of any other disease were found. Two days later, his chest and arm pain recurred and did not resolve despite the application of nitroglycerin, and therefore, he was transferred to hospital. His general physical conditions were relatively good. The ECG revealed a down-slope type ST-segment depression in leads I, aV1, and V4–6 (Figure 1). Although there was a slight pericardial effusion, neither an asynergic portion of the left ventricle nor mitral regurgitation were observed on echocardiography. Laboratory examination of a blood sample showed increased white blood cell count and serum concentration of creatine kinase (CK)-MB (WBC: 21,400/μl; CK-MB: 77 U/L); however, the level of CK and both liver and renal function were within normal limits. He was diagnosed as suffering from acute coronary syndrome and emergency coronary angiography (CAG) was performed.

A spastic stenotic lesion was found in the left anterior descending coronary artery (LAD) and left circumflex branch (LCX) (Figure 2). After injection of 4 mg isosorbide dinitrate (ISDN) into the left coronary artery, the chest and arm pain resolved, and the LAD and LCX changed from a spastic to a normal appearance. Diltiazem (100 mg/day IV) was administered to treat his coronary vasospastic status. The results of blood examination on the next day revealed an elevated CK level, which peaked at 629 mg/dl (CK-MB: 107 mg/dl) and was regarded as the result of long-lasting vasospasm of the micro-coronary arteries.

Echocardiography was performed on the 3rd hospital day. Severe mitral regurgitation, an echo-free space of moderate grade and a collapsed free wall of the right atrium were observed.

He did not have any chest pain on the 2nd or 3rd hospital day, but did complain of numbness in his right arm. Brain MRI did not reveal any lesions suggestive of a cerebral infarction.

At 02.00h on the 5th hospital day, he had an episode of grand-mal chest pain with ECG findings of a down-slope-type ST-depression in leads I, aV1, and V4–6. The chest pain persisted despite the administration of sublingual nitroglycerin, and was slightly relieved by continuous intravenous injection of nicorandil. On the same day, CAG was per-
formed to investigate the cause of the chest pain and during the procedure he again began to complain of severe chest, arm, and leg pain, although CAG revealed normal coronary arteries. The symptoms did not disappear after an injection of ISDN and nicorandil, but all his pain disappeared after intravenous administration of morphine. Atrial fibrillation occurred, but was terminated by 50 mg pilsicainide administered intravenously. From the results of the CAG, it was unlikely that the chest pain originated from coronary vaso-spasms. Because gastrointestinal disease or aortic dissection may also cause serious chest pain, gastro-endoscopy and chest CT were performed on the same day; however, the results of both those examinations were normal. A blood test revealed hyper-eosinophilia, and so we concluded that his pain was related to some type of collagen disease, probably vasculitis. Even though the ANCA blood test was negative, the serum concentration of IgE and rheumatoid factor was 1,450 IU/ml and 230 IU/ml, respectively. Finally, we made the diagnosis of CSS.

On the 6th hospital day, physicians from the neurology...
department saw the patient. A neurological physical examination and neural conduction test showed that the numbness in his arms and legs was consistent with poly-mononeuropathy. Physicians from the collagen-disease department also saw him, and concluded that the disease might be CSS after considering his history and the medical findings. For the correct diagnosis, we planned to perform a biopsy of neurons from his arm and leg.

On the morning of the 7th hospital day, he suddenly had severe chest pain, and lost consciousness. The ECG revealed sinus tachycardia at 120 beats/min with a left-axis deviation, and no significant ST-T changes. Approximately 1 min later, he stopped breathing, no pulse could be palpated, and the ECG showed a conversion from bradycardia to electrical standstill. Despite cardiopulmonary resuscitation, death was confirmed approximately 60 min after the cardiopulmonary arrest.

An autopsy was performed after obtaining consent from his family and the results were as follows. The heart weighed 385 g and was slightly hypertrophic.
The pericardial cavity contained a 90-ml effusion with fibrin. The surface of the heart showed opacity of the epicardium, including the coronary arteries. The entire myocardium exhibited an irregular fibrous change, and the papillary muscle connected to the mitral valve exhibited hemorrhagic changes, but had not ruptured (Figure 3). There was only slight atherosclerosis of the coronary arteries, and no significant stenotic lesions. The 2 main histological findings were as follows. (1) Vasculitis. Moderate or small-sized (80–500 μm) damaged arteries with inflammation were found. The findings were clearer in the relatively smaller arteries, and some parts were completely necrotic, blocked with thrombi, and filled with fibrillar material (Figure 4). In the moderate-sized arteries, inflammation of the adventitia and media was clearly observed, and some of the inflammation had damaged the inner elastic layers of the arteries and affected the inner membranous lining. We also observed severe infiltration of inflammatory cells, which consisted of lymphocytes and neutrophils. In the larger arteries, there was a slighter degree of inflammation, but severe inflammation with infiltration of lymphocytes into part of the outer layer was noted. In some of the larger arteries, inflammation with giant cells was observed. (2) Inflammation resulting from the vasculitis invaded towards the myocardium surrounding the arteries, and induced myocarditis with defluvium and fibrillar changes. Those findings were observed to be more severe on the endocardial side, especially on the papillary muscles, and the inflammation consisted of focal necrosis (Figure 5).

The autopsy report concluded that the findings were consistent with CSS, and that the main cause of death was vasculitis and eosinophilic myocarditis.

**Discussion**

Unfortunately, we were unable to save the patient reported here, despite correctly diagnosing CSS. We believe that there are 3 factors that made it difficult for us to quickly reach a diagnosis in this case.

First, the patient complained of right arm and right leg palsy, which is a serious complication of diabetes mellitus, so initially we did not recognize it as a symptom of CSS. Second, the patient actually had coronary vasospastic angina as the causation of the chest pain, which again distracted from CSS as the etiology. On the day of admission, CAG revealed that his chest pain arose from coronary vasospasm and so the elevated level of CK was considered to be the result of persistent vasospasm causing total occlusion of the coronary arteries. The reason why nicorandil relieved the chest symptoms despite the ineffectiveness of ISDN is unknown. Noguchi et al reported that intracoronary nicorandil can relieve refractory coronary spasm and they speculated that coronary spasm refractory to an exogenous nitric oxide might be responsive to a potassium opener such as nicorandil. We would like to suggest that the some synergistic effects of nicorandil, a hybrid nitrate and potassium-channel opener, could be a reason why nicorandil was able to relieve the chest symptoms in the present case. The CK elevation might also have been related to the myocarditis. As for the chest pain on the 6th hospital day, it might have...
been caused by the myocarditis as well, because ISDN and nicorandil were not effective in relieving it. Taira et al reported a case of vasospastic angina complicated by myocarditis, and Shimokawa explained that some cytokines might also cause coronary vasospasm. We deduce that the present patient was already suffering from the eosinophilic myocarditis at the time of hospitalization, in which case, large areas of the microvasculature might have been in vasospasm, although the ischemic findings on ECG was restricted to the LAD area. There might have been organic stenosis of the LAD combined with spasm of the microcoronary arteries. Furthermore, we consider that this patient did not suffer from coronary vasospasm prior to his transfer to hospital during the early stage of the myocarditis, and that he then had multiple attacks of coronary vasospasm resulting in ischemic asynergy of the left ventricle in the advanced stage of this inflammatory disease after admission to hospital. Third, it was not until the 4th hospital day that we noticed that the patient’s total eosinophil count had significantly increased. We had previously experienced sporadic cases of myocardial infarction or angina pectoris associated with a collagen disease. Therefore, we suggest that it might be prudent to check the blood plasma fraction as early as possible in patients with symptoms suggestive of cardiovascular events.

The diagnosis of AGA was made when the myocardial biopsy demonstrated findings compatible with that disease, which strongly suggested CSS. Therefore, in similar cases when vasculitis is considered as part of the findings, the patient should be started on steroids. A myocardial biopsy is a required examination for a definitive diagnosis of CSS, but imaging studies such as myocardial scintigraphy or cardiovascular MRI might be more useful.

It is well known that some drugs can induce eosinophilic myocarditis as a side-effect. However, in this case the patient had not taken any drugs for 6 months prior to the occurrence of this episode, and therefore, it is unlikely that it was drug-induced myocarditis. The essential etiology of this disease is vasculitis, and it is well known that the respiratory system is vulnerable to CSS. However, cases of CSS in which the most seriously damaged tissue is the heart are relatively rare. There have been several case reports in which CSS was associated with sudden cardiac death and eosinophilic myocarditis. In the present case, the relationship between CSS and myocarditis might be controversial. However, there were comparable vasculitis lesions associated with the eosinophilic infiltration of the myocardium in other organs such as peripheral neurons and bronchial arteries according to the histological examination. Therefore, we consider that the myocarditis in this case was related to CSS. Guillevin et al proposed the “5-factor-score” (createminemia, proteinuria, cardiomyopathy, gastrointestinal tract involvement, and central nervous system) for predicting the long-term prognosis of this disease.9 According to that scoring system, the present patient’s score was 1, suggesting a 5-year survival rate of 25.9%.

To the best of our knowledge, this is the first case of CSS associated with coronary vasospastic angina caused by eosinophilic myocarditis that resulted in sudden cardiac death.

References