A case report and literature review of Churg–Strauss syndrome presenting with myocarditis

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Abstract

Background: Churg–Strauss syndrome (CSS) is a multisystem disorder characterized by asthma, prominent peripheral blood eosinophilia, and vasculitis signs.

Case summary: Here we report a case of CSS presenting with acute myocarditis and heart failure and review the literature on CSS with cardiac involvement. A 59-year-old man with general fatigue, numbness of limbs, and a 2-year history of asthma was admitted to the department of orthopedics. Eosinophilia, history of asthma, lung infiltrates, peripheral neurological damage, and myocarditis suggested the diagnosis of CSS. Transthoracic echocardiography revealed a dilated hypokinetic left ventricle (left ventricular ejection fraction ~40%) with mild segmental abnormalities in the septal and apical segments.

Conclusion: By reviewing the present case reports, we concluded that (1) the younger age of CSS, the greater occurrence rate of complicating myocarditis and the poorer prognosis; (2) female CSS patients are older than male patients; (3) patients with cardiac involvement usually have a history of severe asthma; (4) markedly increased eosinophil count suggests a potential diagnosis of CSS (when the count increases to 20% of white blood cell counts or 8.1 \times 10^9/L, eosinophils start to infiltrate into myocardium); and (5) negative ANCA status is associated with heart disease in CSS.

Abbreviations: ANCA = antineutrophil cytoplasmic antibodies, CK = creatine kinase, CPR = C-reactive protein, CSS = Churg–Strauss syndrome, G-MPI = 99mTc-sestamibi MIBI-gated myocardial perfusion imaging, MPO = antimieloperoxidase.

Keywords: Churg–Strauss syndrome, heart failure, myocarditis

1. Introduction

Churg–Strauss syndrome (CSS) is an eosinophil-rich necrotizing vasculitis of small-to-medium blood vessels that affects many organs including cardiac, pulmonary, renal, nervous, and vascular systems.[1] Symptomatic cardiovascular involvement occurs in as much as 27% to 47% of CSS cases and can present with eosinophilic vasculitis, pericarditis, pericardial effusion, valvular heart disease, cardiomyopathy, acute myocardial infarction, myocarditis, and acute heart failure.[2–4] Although uncommon, cardiac involvement is a major cause of morbidity and mortality in this disorder.

Here we report a case of CSS presenting with acute myocarditis and heart failure and review the literature on CSS with cardiac involvement.

2. Case report

A 59-year-old man with general fatigue, numbness of limbs and a 2-year history of asthma was admitted to the department of orthopedics in our hospital. Two days later, he was short of breath and unable to lie flat in bed. Inhaled corticosteroids were ineffective. Levels of troponin, myocardial enzyme, and B-type natriuretic peptide were elevated, and coronary heart disease was suspected. The patient was transferred to the cardiology intensive care unit for further diagnosis and treatment.

On admission to the unit, the patient had severe dyspnea and moderate edema of lower limbs, with body temperature 37.2°C, pulse 115 beats/min, and blood pressure 94/60 mm Hg. Auscultation of the chest showed diffused wheezing without crackles and cardiac examination revealed a muffled heart sound without murmur, rubs, or gallop.

Arterial blood gas analysis revealed pH 7.42, PaO2 51 mm Hg, PaCO2 28 mm Hg. White blood cell count was 18.6 \times 10^9/L with eosinophil cell count 7.6 \times 10^9/L (41% leukocytes), without anemia or thrombopenia. Hypersensitive C-reactive protein (CRP) level was 7.66 mg/dL (normally 0–0.35 mg/L). Serum IgE level was 2540 IU/mL (normally 0–100 IU/mL). Serum troponin I level was increased to 30.54 ng/mL (normally 0.0344 ng/mL), and levels of myocardial enzymes were all increased (aspartate transaminase 150 IU/L, lactate dehydrogenase 771 IU/L, creatinine kinase [CK] 252 IU/L, CK-MB 38 IU/L, hydroxybutyrate dehydrogenase 845 IU/L). B-type natriuretic peptide level was
847.3 pg/mL (normally < 76 pg/mL) and D-dimer level was 1810 μg/L (normally < 590 μg/L). Serum tests were negative for antinuclear antibodies, antimonyeloperoxidase (MPO), and anti-neutrophil cytoplasmic antibodies (ANCA). Serologic tests were negative for viruses (Epstein–Barr virus, cytomegalovirus, hepatitis B and C virus, HIV). Screening for parasites was negative. Blood and urine cultures were sterile. Electrocardiography revealed sinus tachycardia (Fig. 1). Transthoracic echocardiography revealed a dilated hypokinetic left ventricle (left ventricular ejection fraction ~ 40%) with mild segmental abnormalities in the septal and apical segments. The right ventricle was normokinetic and not dilated. Color Doppler ultrasonography revealed moderate regurgitation of the mitral valve. Mild pericardial effusion was present. Coronary CT angiography ruled out severe artery stenosis (Fig. 2). 99mTc-sestamibi MIBI-gated myocardial perfusion imaging (G-MPI) revealed multiple perfusion-decreased foci in the left ventricle, and left ventricular contractile function was impaired. CT scan revealed bilateral ground-glass nodular lung opacities and small pleural effusions. Renal function was normal, with serum creatinine level 67.33 μmol/L and estimated glomerular filtration rate 111.32 mL/min/1.73 m² (normally > 90 mL/min/1.73 m²). Urinalysis gave normal results. Electromyography revealed decreased nerve conduction velocity, representing peripheral neurological damage. Bone marrow testing showed reactive eosinophilia and thrombocytosis.
Table 1

Characteristics of included studies.

| Study               | Age | Sex | WBC (10^9/L) | Eosinophils percentage (%) | Eosinophils count (10^9/L) | Extravascular eosinophils | CRP  | IgE  | ANCA | Renal involvement |
|---------------------|-----|-----|--------------|---------------------------|-----------------------------|----------------------------|------|------|------|-----------------|
| Courand et al[11]   | 22  | M   | 15.10        | 51.00                     | 7.70                        | Positive                   | N/A  | Positive | Positive | Negative |
| Chen et al[16]      | 41  | F   | 13.6         | 45.71                     | 6.21                        | Positive                   | Positive | Positive | Negative | Positive |
| Correia et al[13]   | 22  | F   | 21.4         | 68.30                     | 10.45                       | Negative                   | Positive | N/A | Negative | Negative |
| Tomoya[19]          | 67  | M   | 15.2         | 29.00                     | 3.30                        | Negative                   | N/A  | Positive | Positive | Negative |
| Masahiko[20]        | 60  | M   | 21.4         | 68.30                     | 10.45                       | Negative                   | N/A  | Positive | Negative | Negative |
| Hayashi et al[13]   | 26  | M   | 11.5         | 29.00                     | 3.30                        | Positive                   | Positive | Positive | Positive | Negative |
| Amaddie et al[1]    | 15  | M   | 13.50        | 26.00                     | 3.51                        | N/A                        | N/A  | N/A | N/A | N/A |
| Rabusin et al[8]    | 25  | F   | N/A          | N/A                        | N/A                         | Positive                   | N/A  | Positive | Negative | Negative |
| Goldberg            | 23  | F   | 28.20        | 39.32                     | 11.09                       | N/A                        | N/A  | N/A | N/A | N/A |
| Marno[23]           | 25  | M   | 11.5         | 29.00                     | 3.30                        | Negative                   | Positive | Positive | Positive | Negative |
| McAloney et al[4]   | 53  | M   | N/A          | N/A                        | 2.34                        | Positive                   | Positive | Positive | Negative | Negative |
| Puchal et al[21]    | 77  | M   | N/A          | N/A                        | 5.30                        | Positive                   | Positive | Positive | Negative | Negative |
| Merodriguez et al[16] | 16 | F | 19.00 | 42.73 | 8.12 | Positive | Positive | Positive | N/A | Positive |
| Bouiller[8]         | 63  | F   | 14.00        | 24.86                     | 3.48                        | Negative                   | N/A  | Negative | Negative | Negative |
| Petersen et al[24]  | 53  | F   | 28.80        | 60.00                     | 17.28                       | Negative                   | N/A  | N/A | N/A | Negative |
| Hervier et al[23]   | 42  | M   | 16.00        | 60.60                     | 9.72                        | Negative                   | Positive | N/A | N/A | Positive |
| Szczez[25]          | 59  | F   | N/A          | N/A                        | 12.00                       | Positive                   | Positive | Positive | N/A | Negative |
| Mano[17]            | 70  | F   | N/A          | N/A                        | 2.34                        | Positive                   | Positive | Positive | N/A | N/A |
| Kawano et al[20]    | 55  | M   | 5.00         | 60.00                     | 3.00                        | N/A                        | N/A  | N/A | N/A | Negative |
| Kawano et al[20]    | 53  | M   | 13.50        | 26.00                     | 3.51                        | Positive                   | Positive | Positive | N/A | N/A |
| Sharp[27]           | 77  | F   | 12.78        | 54.00                     | 6.90                        | N/A                        | N/A  | N/A | N/A | Negative |
| Tanaka et al[21]    | 43  | F   | 29.90        | 73.00                     | 21.83                       | Positive                   | Positive | Positive | Positive | Negative |

ANCA = anti-neutrophil cytoplasmic antibodies, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, WBC = white blood cell.

The diagnosis of CSS was considered according to the criteria (history of asthma, eosinophilia, neuropathy, and pulmonary infiltrates).[1] Immunosuppressive therapy, oral prednisolone 40 mg per day, was started on day 5 after admission to the cardiology unit. Apyrexia was achieved, and eosinophil blood count and CRP and troponine I levels quickly decreased to normal ranges. Symptoms of heart failure were gradually resolved.

After 2-week treatment, the patient’s condition improved. He no longer had shortness of breath and no numbness in limbs. The body temperature, eosinophilia, and cTrnT level all decreased gradually. The patient was discharged from hospital with treatment consisting of ramipril, bisoprolol, spironolactone, furosemide, and prednisone. On follow-up, the 6-min walking distance was 530 m. One month after diagnosis, the patient was still asymptomatic.

3. Systematic review of available data

3.1. Data search

MEDLINE via PubMed was searched for English articles by using the terms “Churg–Strauss Syndrome” AND “myocarditis”; 53 items were found. Articles were included if they (1) were a case report; (2) described a confirmed diagnosis of CSS complicated with myocarditis; (3) were published after 1990 because the diagnostic criteria for CSS were established in 1990; and (4) described no concomitant diseases such as intracranial hemorrhage or systemic lupus erythematosus. The search resulted in 22 articles (Table 1).

4. Results

Ten of the 22 reported cases involved females and the age at disease onset ranged from 2 to 77 years. Peripheral eosinophilia was reported in all 22 cases and extravascular eosinophil infiltration in 14 of 18 cases. The erythrocyte sedimentation rate was positive in 9 of 10 cases and CRP was positive in 10 of 12. Overall, in 8 cases, myocarditis was confirmed by biopsy and pathology and others were diagnosed by imaging. Two patients received leukotriene receptor antagonists and 3 steroids (1 by inhalation, 2 per oral) for asthma. Details are in Table 1.

4.1. Age

The mean age at diagnosis of CSS complicated by myocarditis was 42.77 years.[2] The incidence of myocarditis in CSS patients 20 to 30 years old (22.7%) was higher than that for other groups. Acute coronary syndrome in relatively young patients without classical cardiovascular risk factors is suggestive of myocarditis. More studies are needed for the cardiac manifestations of different ages. Given that patients under 20 years are few and the prognosis of pediatric CSS, such as the 2-year-old patient in the Rabusin report,[8] is poor, we propose that the younger the patient with CSS, the greater the occurrence rate of complicating myocarditis, and the poorer the prognosis.

4.2. Sex

Among the 22 patients were 12 males. The mean age of females was 46.67 years, 8.57 years older on average than males (38.10 years). The habits of males, such as smoking, likely have a synergistic effect with eosinophils on the heart.[5] As well, estrogen probably protects the female cardiovascular system from inflammation.[6] Further research is needed to verify and illuminate the protective effect of sex on CSS.

4.3. Eosinophils

White blood cell count increases sharply with the disease (mean = 17.4 × 10^9/L), probably resulting from the proliferation of eosinophils. The eosinophil percentage in all cases is >20%, much higher than the diagnostic standard (10%). Eosinophil...
count in 15 of 19 patients ranged from 2.5 to 12.5 × 10^9/L, with a mean of 8.1 × 10^9/L. Cardiac involvement, especially myocarditis, may be associated with a surge in eosinophils, which may suggest the pathogenesis of myocarditis in CSS patients. Extravascular eosinophil infiltration is due to the significant increase in intravascular eosinophils. When its count increases up to 20% of WBC counts or 8.1 × 10^9/L, eosinophils start to infiltrate into myocardium.

4.4. ANCA

ANCAs are reported in ~40% of CSS cases, the presence associated with increased risk of glomerular disorders, biopsy-proven vasculitis, and peripheral neuropathy and the absence related to heart disease. From our case and the literature, almost all cases with cardiac involvement are usually negative for ANCA (14 of 16), and 1 ANCA-positive case involves the myocardium. To conclude, our CSS patient with a predominant cardiac manifestation and without renal impairment lacked a characteristic ANCA pattern, which agrees with reported findings. Only 3 of 22 CSS cases were complicated by renal involvement, so myocarditis and renal involvement may be rarely present at the same time, which may be due to the ANCAs.

4.5. Other organ infiltration

According to the reports, 90% of CSS patients with myocarditis have asthma. Asthma is always present in CSS patients, not just those with myocarditis, and this finding helps differentiate it from other entities such as polyarteritis nodosa, granulomatosis with polyangiitis (formerly Wegener’s granulomatosis), or hyper-eosinophilic syndrome. In any patient with asthma, the diagnosis should be suspected when the case is complicated by at least one of three characteristics: difficult to treat, steroid-dependent, and late-onset disease.

5. Discussion

CSS has an extremely low incidence, ranging from 0.5 to 6.8 new cases per million patients per year and prevalence from 10.7 to 13 per million adults, varying by location and the diagnostic criteria applied. The mean age at diagnosis is 48 years, and both sexes are affected equally. We have little data on race distribution. The pathophysiology of CSS can be divided into 3 stages. The prodromal stage is characterized by asthma and atopic disease and can last a few years, even as long as 30 years, according to the report. In the next stage, eosinophils infiltrate into tissues such as lungs or myocardium. The final stage is usually the diagnosis and when necrotizing vasculitis appears. The pathogenesis of CSS is not detailed thoroughly. Genetics, environment, and their interactions all play important roles. Several inducing factors, such as infection, drugs, and especially leukotriene receptor antagonists (e.g., montelukast) and vaccinations, have been found responsible for the onset of CSS. Immune functional disturbance and dysregulated release of cytokines have been suggested to be associated with eosinophilic disorders.

Myocarditis is one of the most common cardiac manifestations in CSS, presenting from chest pain and palpitations to life-threatening cardiogenic shock and arrhythmia. Our data suggest that risk of myocarditis is increased in patients between 20 and 30 years old and cardiac manifestations occur later in females than males. CSS patients usually have asthma, whereas leukotriene receptor antagonists may be involved in the onset of CSS. Eosinophil count increases markedly to a level much higher than levels of other diagnostic criteria in patients with myocarditis, and the number of white blood cells also increases due to eosinophilia. Patients are positive for erythrocyte sedimentation rate and CRP level, indicating an inflammation response, whereas CSS patients with myocarditis are usually ANCA-negative.

CSS usually responds quickly to immunosuppressive therapy, associated with rather good prognosis. Corticosteroids are the first-line therapy, resulting in remission and improved survival. When recurrences are frequent or associated with a serious form of necrotizing vasculitis in organs such as the gastrointestinal tract or the heart, the use of cyclophosphamide is recommended. Such favorable outcomes might not apply to patients with organ system involvement that indicates poor prognosis. The French Vasculitis Study Group has recently revised 5 prognostic factors, the so-called 5-factor score (FFS). The new FFS comprises 4 factors that indicate poor prognosis (age >65 years, cardiac involvement, gastrointestinal manifestations and renal impairment characterized by serum creatinine level >150 mmol/L and 1 factor that indicates a better outcome (the absence of ear, nose and throat manifestations). According to the revised FFS, the presence of 0, 1 or 2 factors associated with CSS represents necrotizing vasculitis of medium and small vessels, typically characterized by asthma and hyper-eosinophilia. Multiple systems can be involved in CSS, which easily misleads doctors to other diseases.

We conclude that (1) the younger age of CSS, the greater occurrence rate of complicating myocarditis and the poorer
methods can improve the prognosis if diagnosed in time. Should not neglect the diagnosis of CSS. Effective treatment with oral steroids. In any patient with refractory asthma, we observe symptoms improved and eosinophil count was sharply reduced with oral steroids. In any patient with refractory asthma, we should not neglect the diagnosis of CSS. Effective treatment methods can improve the prognosis if diagnosed in time.

In summary, we report a confusing case of dyspnea and numbness finally diagnosed as CSS with cardiac involvement. Symptoms improved and eosinophil count was sharply reduced with oral steroids. In any patient with refractory asthma, we should not neglect the diagnosis of CSS. Effective treatment methods can improve the prognosis if diagnosed in time.

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