Nonasthmatic Case of Churg-Strauss Syndrome with Rapidly Progressive Glomerulonephritis

Yasuyo Yamashita, Noriaki Yorioka, Yoshihiko Taniguchi, Michio Yamakido, Chigusa Watanabe*, Takeshi Kitamura* and Shigenobu Nakamura*

A 61-year-old man developed mononeuritis multiplex accompanied by eosinophilia in 1993. Approximately 3 years later, acute renal dysfunction, a subendocardial tumor, and a high peripheral anti-neutrophil cytoplasmic antibody titer were also detected. Renal biopsy revealed glomerular crescents and interstitial infiltration of eosinophils, so allergic granulomatosis and angiitis was diagnosed. These clinical abnormalities regressed with steroid therapy. He had no history of asthma. This was therefore considered to be an atypical form of Churg-Strauss syndrome with rapidly progressive glomerulonephritis.

Key words: allergic granulomatosis and angiitis, peripheral anti-neutrophil cytoplasmic antibodies, pauci-immune necrotizing glomerulonephritis

Introduction

In 1951, Churg and Strauss (1) proposed allergic granulomatosis and angiitis as a disease to be discriminated from classical periarteritis nodosa based on its clinicopathological feature of necrotizing vasculitis occurring exclusively in asthmatic patients. Therefore, allergic granulomatosis and angiitis is also referred to as Churg-Strauss syndrome and is characterized by bronchial asthma, eosinophilia, and several signs of vasculitis, such as peripheral neuropathy, extravascular granuloma and necrotizing granulomatous angiitis. In Churg-Strauss syndrome, peripheral anti-neutrophil cytoplasmic antibody (p-ANCA) is detected in 70% of patients (2), but rapidly progressive glomerulonephritis such as pauci-immune necrotizing and crescentic glomerulonephritis is relatively uncommon (3). It seems to be extremely rare for this disease to be detected in a nonasthmatic patient; there are still many aspects of its etiology and pathogenesis that remain unclear (4). Here, we report a nonasthmatic case of Churg-Strauss syndrome (allergic granulomatosis and angiitis) associated with rapidly progressive glomerulonephritis.

Case Report

The patient was a 61-year-old man. In late January 1993 (at age 58), he experienced muscular weakness and numbness of the extremities accompanied by a fever of 39°C. On February 1, 1993, he was admitted to a local hospital with these symptoms. At that time, hematology tests detected eosinophilia, and prednisolone (60 mg/day) was prescribed for suspected hypereosinophilic syndrome. Subsequently, his muscular weakness and eosinophilia were improved, although numbness of the extremities persisted. On May 6, 1993, the patient was transferred to the Third Department of Internal Medicine at Hiroshima University School of Medicine. He was then diagnosed as having mononeuritis multiplex. Since his neurological symptoms were subsequently alleviated, prednisolone therapy was tapered and then withdrawn. The patient was discharged on July 11, 1993. From May 1996, he developed pain in both knees and ankles as well as numbness and purpura of the right lower extremity. In June 1996, he had edema of the heel of the right foot, eosinophilia, anemia, and thrombocytopenia, accompanied by weight loss. He was admitted to the Third Department of Internal Medicine at our hospital on June 14. He had suffered from pleurisy at the age of 18 years and had occasional episodes of coughing from 10 years ago, but there was no history of bronchial asthma.

Findings on admission: The patient was 161 cm tall and weighed 43.5 kg, with a temperature of 37.4°C, a pulse rate of 72/min, and a blood pressure of 128/64 mmHg. There was
Yamashita et al

Pallor of the palpebral conjunctiva, and decreased breath sounds at the bases of both lungs, but there was no asthmatic wheezing. Purpura (1–7 mm in diameter) were seen extending from the thigh to the lateral border of the calf on both lower limbs, and there was edema of the dorsum of the right foot. Neurological examination revealed mild muscular weakness in both arms and loss of the patellar tendon reflexes. There was reduced touch sensation on both palms and soles as well as numbness of both hands and the right leg. There was also decreased pain and heat sensation in the right calf. Laboratory findings on admission: Urinalysis detected protein (2+) and occult blood (2+), with urinary protein loss being 0.9 g/day. Hematology tests showed a white blood cell (WBC) of 12,900/mm³ (58.2% eosinophils), hemoglobin of 9.4 g/dl, and platelet count of 94,000/mm³, indicating anemia and thrombocytopenia. Biochemistry tests showed a blood urea nitrogen (BUN) of 35 mg/dl and a serum creatinine of 2.39 mg/dl, indicating pronounced renal dysfunction. His lactate dehydrogenase (LDH) was also high, at 966 IU/l. He had a high C-reactive protein level of 1.2 mg/dl and a high rheumatoid factor level of 515.21 IU/ml as well as high immunoglobulin levels (immunoglobulin (Ig)G was 2,250 mg/dl, IgA was 440 mg/dl, IgM was 237 mg/dl, and IgE was 719.11 IU/ml). Although his p-ANCA titer was high at 1,000 EU/ml, he was negative for c-ANCA, anti-nuclear antibody, anti-DNA antibody, anti-glomerular basement membrane antibody, and immune complexes. The chest X-ray film suggested pulmonary emphysema as well as bronchitis in the right lower lung field. Computed tomography (CT) scans showed overdistention of the lungs and infiltration along the thickened bronchial walls. Lung function tests gave the following results: vital capacity (VC), 4,120 ml (123% pred); forced expiratory volume in one second (FEV₁), 2,940 ml; and FEV₁/forced VC, 71.4%. The resting electrocardiogram showed no abnormalities, but exercise electrocardiography and thallium myocardial scintigraphy revealed transient ischemia of the cardiac apex and anterior septum. Echocardiography showed a subendocardial mass in the left ventricle (Fig. 1A). Peripheral nerve conduction testing indicated extensive axonal degeneration accompanied by demyelination. Bone marrow aspiration showed an increase of eosinophils (30%), but no heteroplasia. Renal biopsy was done at the Second Department of Internal Medicine of our hospital. Twenty glomeruli were obtained, with a cellular crescent being detected in one glomerulus and fibro-cellular crescents in 3 glomeruli. Mesangial proliferation and stromal growth were noted in all glomeruli. The interstitium showed infiltration by lymphocytes and eosinophils (Fig. 2). Fluorescent antibody staining of the biopsy did not detect IgG, IgA, IgM, C3, C4, or fibrinogen. There were no glomerular electron-dense deposits on electron microscopy. Based on these findings, a diagnosis of atypical Churg-Strauss syndrome associated with rapidly progressive glomerulonephritis (pauci-immune necrotizing glomerulonephritis) was made, and prednisolone (60 mg/day) was administered orally. The purpura, edema, fever and eosinophilia were improved immediately after the start of prednisolone therapy. However, the p-ANCA level remained high and symptoms of peripheral neuropathy were not improved, so steroid pulse therapy was administered. Because he also had a respiratory infection, methylprednisolone (500 mg/day) was used without a specific immunosuppressant. Subsequently, his renal function was improved (serum creatinine from 2.39 mg/dl to 0.82 mg/dl, and proteinuria from 2+ to +), and the p-ANCA level decreased markedly. The rheumatoid factor level decreased from 515.2 IU/ml to 6.0 IU/ml and the immunoglobulin level decreased gradually (IgG from 2,250 mg/dl to 859 mg/dl, IgA from 440 mg/dl to 146 mg/dl, IgM from 237 mg/dl to 132 mg/dl, and IgE from 719.11 IU/ml to 66.6 IU/ml). The subendocardial mass was also reduced in size on echocardiography (Fig. 1B). Prednisolone therapy was then tapered, although symptoms of peripheral neuropathy still persisted (Fig. 3).

Discussion

The present patient developed symptoms of mononeuritis multiplex with eosinophilia and a high fever, thus a diagnosis...
of hypereosinophilic syndrome (5) was suggested initially. Subsequently, skin lesions and renal dysfunction due to rapidly-progressive glomerulonephritis (pauci-immune necrotizing glomerulonephritis) also occurred, and a diagnosis of ANCA-associated systemic vasculitis was suggested. This type of vasculitis affects multiple organs, including the kidneys, lungs, skin, and peripheral nerves, mainly as a result of inflammation of the small vessels (6–8), therefore so Wegener’s granulomatosis, p-ANCA-associated crescentic glomerulonephritis, microscopic polyarteritis, and Churg-Strauss syndrome must be distinguished in the differential diagnosis (9). Wegener’s granulomatosis was initially excluded, because c-ANCA was negative and this is highly sensitive and specific for Wegener’s granulomatosis (10). Our patient had no history of asthma and showed rapidly progressive glomerulonephritis associated with p-ANCA (pauci-immune necrotizing glomerulonephritis). However, there were characteristic features of Churg-Strauss syndrome such as mononeuritis multiplex accompanied by eosinophilia (11) and renal biopsy showed granulomatous angiitis and interstitial eosinophilic infiltration. Moreover, the subendocardial mass in the left ventricle was suggested to be an extravascular granuloma because it decreased in size after steroid therapy, although this was not directly proved by pathological examination. Therefore, a diagnosis of Churg-Strauss syndrome (allergic granulomatosis and angiitis) associated with p-ANCA-related rapidly progressive glomerulonephritis was most strongly suggested. Nonasthmatic Churg-Strauss syndrome (allergic granulomatosis and angiitis) (4) and Churg-Strauss syndrome associated with rapidly progressive glomerulonephritis are reported to be rare (3), but with reference to these case reports, the present patient case was considered to have an atypical form of Churg-Strauss syndrome without asthma, but with rapidly progressive glomerulonephritis.

**References**