Single Case – General Neurology

Eosinophilic Granulomatosis with Polyangiitis Presenting with Myocarditis as an Initial Symptom: A Case Report and Review of the Literature

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Keywords

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Abstract

A 66-year-old woman with a history of bronchial asthma had shortness of breath and fatigue upon mild exercise. She was diagnosed as congestive heart failure. A blood test showed eosinophilia without the presence of anti-neutrophil cytoplasmic antibody (ANCA), and a myocardial biopsy specimen revealed eosinophilic infiltration in the myocardium. Eosinophilia was improved when she was administered short-term methylprednisolone. After that, she had numbness and pain in her lower limbs with re-elevation of eosinophils. She had dysesthesia and hypalgesia in the distal part of the limbs. Sural nerve biopsy revealed axonal degeneration and thickness of the arterial wall, indicating a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Two courses of steroid pulse therapy were performed, resulting in marked improvement of her sensory symptoms. ANCA-negative EGPA might be associated with myocarditis and peripheral neuropathy. A sufficient immunotherapy should have been considered to prevent rapid progression.

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Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is eosinophil-rich and necrotic granulomatous inflammation predominantly on the small- to medium-sized vessels associated with asthma and eosinophilia [1]. We experienced an EGPA case showing peripheral neuropathy after heart failure due to eosinophilic myocarditis. Anti-neutrophil cytoplasmic antibody (ANCA) was negative.

Case Report

A 66-year-old woman with a history of bronchial asthma developed a chronic cough. She had shortness of breath and fatigue upon mild exercise. She was diagnosed as congestive heart failure. Her cardiac function on admission was poor with a left ventricle ejection fraction (LVEF) of 36.2%. A myocardial biopsy specimen revealed eosinophilic infiltration, indicating eosinophilic myocarditis (Fig. 1). Laboratory test showed an elevated white blood cell count of 10,300/ μ L with eosinophilia of 55.7%. However, this was improved to normal white blood cell (8,100/ μ L; eosinophils 4.1%) when she was administered 250 mg of methylprednisolone for contrast media allergy during coronary angiography. Her heart failure did not progress further after treatment with a diuretic, angiotensin-converting enzyme inhibitor, and an $\alpha\beta$ blocker without treatment of steroids. One month later, she developed an abnormal sensation in the bilateral toes and was admitted to the neurology department in our hospital. On admission, there was no motor paralysis nor muscle atrophy. She had numbness and pain below her knees and hypalgesia in the distal part of the limbs with absence of her Achilles tendon reflexes. A complete blood count showed leukocytosis (35,800/ μ L; segmented neutrophils 9.5%, eosinophils 85.5%, and lymphocytes 5%). Serum autoantibody tests showed an elevated rheumatoid factor level of 1,101 IU/mL (0–15) and IgE level of 1,862 IU/mL (0–358). Proteinase-3-anti-neutrophil cytoplasmic antibodies, myeloperoxidase anti-neutrophil cytoplasmic antibody, anti-SS-A antibody, anti-SS-B antibody, and anti-nuclear antibody were all negative. Electrocardiography demonstrated a negative T-wave inversion in the V2–V4 lead. Echocardiography revealed poor wall motion and wall thinning in the posterior inferior wall with a decreased LVEF of 40%. A nerve conduction study indicated motor sensory axonopathy. A sural nerve biopsy specimen revealed the significant loss of myelinated nerves with multiple myelin ovoids (Fig. 2a). Although inflammatory cell infiltration was not observed, luminal obstruction due to the thickness of the arterial wall suggested previous inflammatory

Fig. 1. Histological findings of the myocardium. **a, b** Fibrosis and infiltration of lymphocytes and eosinophils are observed in the myocardium. Deposition of hemosiderin is seen in the section. Arrows indicate eosinophils (hematoxylin and eosin staining).

Fig. 2. Toluidine blue staining of a sural nerve biopsy specimen. **a, b** The nerve bundle of the sural nerve shows a loss of myelinated nerves, predominantly large fibers, and many myelin ovoids are present. **c** Inflammatory cell infiltration was not observed. The arrow indicates a luminal obstruction and recurrent findings in epineurial arterioles (toluidine blue stain).

occlusion of the arterioles (Fig. 2b). The pathological findings were consistent with ischemic peripheral neuropathy due to vasculitis. Two courses of steroid pulse therapy (methylprednisolone 1,000 mg/day $\times$ 3 days) were performed, and the oral administration of prednisolone 40 mg/day was started. Pain and abnormal sensations in the lower limbs improved, and the numbness in the lower limbs almost disappeared when she was discharged to her home.

Discussion

Notable clinical features of our case are the occurrence of eosinophilic myocarditis shortly before the appearance of typical EGPA. It was also characterized by the development of polyneuropathy immediately after the inadequate immunotherapy for myocarditis.

A previous study of 32 EGPA patients reported that 66% of patients had an abnormal ECG with decreased LVEF and abnormal wall movement by echocardiography compared with the control group [2]. Of note, the higher rate of complications with heart disease was shown in ANCA-negative EGPA patients compared with ANCA-positive patients (22.4 vs. 5.7%) [3]. Therefore, we should consider the presence of heart disease in EGPA, especially in ANCA-negative cases, because complications of heart disease may cause sudden death [4].

Another characteristic feature of our case is that while histologically demonstrating vasculitis, the clinical manifestations were symmetric polyneuropathy. Our case may have progressed to the acute vasculitic phase.

Complications of peripheral neuropathy are common in EGPA patients (65–75%) [5, 6]. Vasculitis was more present in ANCA-positive EGPA patients compared with ANCA negative (63 vs. 21%), and eosinophilic infiltrations in the epineurium were more present in ANCA

negative (0 vs. 36%) [7]. To prove the complexity of peripheral neuropathy observed in our EGPA case, 2 mechanisms might be involved: ischemic changes associated with vasculitis and inflammation by eosinophil toxicity. The following pathomechanisms are presumed as causes of these: IL-5 is a principal eosinophil-activating cytokine and is known to be involved in the pathogenesis of EGPA [8]. Cytotoxic granule proteins released from eosinophils cause small vessel vasculitis and neuritis [9]. The pathophysiology of EGPA is not yet fully understood, and further elucidation is expected in the future. Although steroid monotherapy was effective in our case, combination therapy with immunosuppressants or immunoglobulins should be considered because steroid therapy might be insufficient in a case with acute heart failure and rapidly progressive peripheral neuropathy [10].

Statement of Ethics

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

Kanako Kurihara wrote the first draft of the manuscript, which was reviewed by each author. Kanako Kurihara, Jun Tsugawa, Shinji Ouma, Toshiyasu Ogata, and Yoshio Tsuboi clinically cared for this patient as neurologists. Mikiko Aoki examined the pathological examination of the myocardium as a pathologist. Masatoshi Omoto and Takashi Kanda examined the pathological examination of the sural nerve as neurologists. All authors read and approved the final manuscript.

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