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Case Report

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Eosinophilic Granulomatosis with Polyangiitis Presented as Acute Polyneuropathy and Cerebral Vasculitis

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Eosinophilic granulomatosis with polyangiitis (EGPA) is an immune related systemic disease that is caused by vasculitis affecting multiple organ systems. It is characterized by asthma, fever, eosinophilia, cardiac problems, renal injury, and peripheral neuropathy. In this report, we describe a patient with EGPA with concurrent cerebral infarction and acute polyneuropathy mimicking a Guillain-Barre syndrome (GBS). A 46-year-old man presented with rapidly progressing gait disturbance, muscular weakness, and tingling sensation in all four limbs. A nerve conduction study revealed sensorimotor polyneuropathy in all four limbs, and a test of the cerebrospinal fluid showed an albumin-cytologic dissociation. In addition, brain magnetic resonance imaging (MRI) using fluid-attenuated inversion recovery and diffusion weighted MRI revealed high signal intensity lesions with gadolinium enhancement on T1-weighted MRI in the right caudate nucleus. After performing laboratory tests, paranasal sinus computed tomography, and a nasal smear, the patient was diagnosed with EGPA and treated with high dose glucocorticoid and oral cyclophosphamide. In conclusion, our findings indicate that a diagnosis of EGPA should be considered when a patient presents with rapidly progressing polyneuropathy mimicking a GBS along with unusual systemic symptoms or brain lesions.

Key words: Eosinophilic granulomatosis with polyangiitis, Churg-Strauss syndrome, EGPA, vasculitic neuropathy, cerebral vasculitis, Guillain-Barre syndrome

INTRODUCTION

Eosinophilic granulomatosis with polyangiitis (EGPA) is an eosinophil-rich necrotizing vasculitis that involves small-to-medium blood vessels and was previously referred to as Churg–Strauss syndrome (CSS). EGPA can affect multiple organ systems, including the cardiac, pulmonary, renal, nervous, and vascular systems, and is characterized by asthma, fever, eosinophilia, pericarditis, pericardial effusion, myocardial infarction, acute heart failure, renal injury, and peripheral neuropathy [1-6].

Peripheral nerve involvement is caused by the degeneration of nerve axons due to ischemia that is secondary to damage of the vasa nervorum, and characterized by painful paresthesias and numbness, and later progresses to motor impairment and muscular atrophy [5, 7-9]. These features are sometimes similar to those of Guillain-Barre syndrome (GBS). The peripheral nervous system

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involvement of the EGPA is commonly presented, however, cerebral involvement such as stroke is rare, and furthermore a concurrent neurological complication involving acute polyneuropathy and cerebral infarction is extremely rare in the EGPA

In this report, we describe a patient with EGPA who presented with acute sensorimotor polyneuropathy mimicking a GBS and concurrent cerebral infarction.

CASE REPORT

A 46-year-old man visited our hospital with complaints of gait disturbance, limb weakness and a tingling sensation in the upper and lower limbs. Two weeks prior to his admission, weakness developed in both legs, and then rapidly progressed to all four extremities and also increased in severity. Furthermore, limb weakness and neuropathic pain progressed in a symmetric fashion, beginning with the feet and progressing up the limbs, and pain included shooting and sharp pain with tingling sensation in the distal legs. Given these symptoms, he experienced difficulties in gait, writing, handling chopsticks, and making a fist. In addition, he presented with mild fever accompanied by myalgia, headache, and dizziness.

He denied the history of relevant diseases, including hypertension, diabetes, hepatits and tuberculosis, and a familial history of neurological disease, smoking, and alcohol were not noted. Furthermore, he denied recent upper respiratory infection or diarrhea.

On admission, the patient was unable to walk independently, owing to severe muscle weakness in both lower extremities and intolerable neuropathic pain.

In a neurological examination, the patient was alert and his orientation was intact. Cognitive impairment was absent. There were no abnormal findings on an initial examination of the cranial nerves, except for mild slurring of speech and swallowing difficulty.

Motor system examinations using the Medical Research Council (MRC) grading scale revealed severe motor weakness in both the upper and lower extremities (distal lower limbs, MRC grade 1/5; proximal lower limbs, 2/5; distal upper limbs, 3/5; proximal upper limbs, 4/5). An examination of his sensory systems showed prominent hypoesthesia with painful paresthesia in the upper and lower limbs. There was a reduction in deep tendon reflex (DTR) responses in all limbs, and no signs of pathological reflexes, such as the Babinski and Hoffman reflexes. Initial brain magnetic resonance imaging (MRI) using fluid-attenuated inversion recovery and diffusion weighted MRI revealed abnormal high signal-intensity lesion lesions with gadolinium enhancement on T1-weighted MRI in the right caudate nucleus which was consistent with subacute cerebral infarction (Fig. 1A).

Given that initial neurological examinations suggested that the patient had polyneuropathy such as GBS, a nerve conduction study (NCS) was performed using standard techniques of percutaneous supramaximal stimulation and recordings. These examinations revealed either a reduction in compound muscle action potential amplitude (CMAP) in bilateral ulnar nerve and the complete absence of action potentials in bilateral peroneal nerve, tibial nerve and sural nerve, which was indicative of axonal type sensory motor polyneuropathy. Cerebrospinal fluid (CSF) study showed elevated protein levels (67.4 mg/dl, normal value: 8~43 mg/dl) with a normal cell count. Consequently, the patient was diagnosed with rapidly progressing polyneuropathy and concurrent cerebral infarction. The patient also presented, however, with systemic manifestations, including fever, coughing, wheezing, knee joint pain, and a reddish skin color. These features led us suspect his condition as systemic disease that involved central and peripheral nervous systems and proceeded with systemic laboratory and radiological evaluations.

Laboratory investigations revealed normal hemoglobin levels, platelet cell counts, serum electrolyte levels, and renal and liver function. The results of tumor screening for alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and carbohydrate antigen (CA)-19-9 were normal. Additional evaluations of systemic vasculitis, which included tests for rheumatoid factor, fluorescent antinuclear antibody (ANA) titers, anti-dsDNA antibody, lupus anticoagulant, anti-cardiolipin antibody, anti-thrombin III, anti-Sjogren syndrome A and B (anti-SSA and anti-SSB) antibodies, complement 3/4, anti-jo-1 antibody, cryoglobulin, immunofixation electrophoresis/protein electrophoresis, anti-GM1 antibody, and anti-GD1b antibody, were all normal.

However, a few biochemical analysis showed elevated levels of erythrocyte sedimentation rate (41 mm/h, normal range <10 mm/h), C-reactive protein (119 mg/l, normal range <1.0 mg/l), anti-neutrophil cytoplasmic antibody (4.5), eosinophil count (5282 mm^3, normal range <300 mm^3) and differential eosinophil count (68.3 %, normal range <7.0 %). Furthermore, paranasal sinus (PNS) computed tomography (CT) revealed both sinonasal polyposis and sinusitis of the maxillary, ethmoid, and frontal sinuses. In addition, a nasal smear showed an eosinophilia of 100%.

In conclusion, the patient's recent neurological complaints of progressing polyneuropathy and his cerebral infarction were ultimately diagnosed as vasculitic complications caused by EGPA, and he was treated with a high dose steroid, cyclophosphamide, and antiplatelet therapy. After immune therapies and symptomatic management, the patient's symptoms of gait disturbance, limb

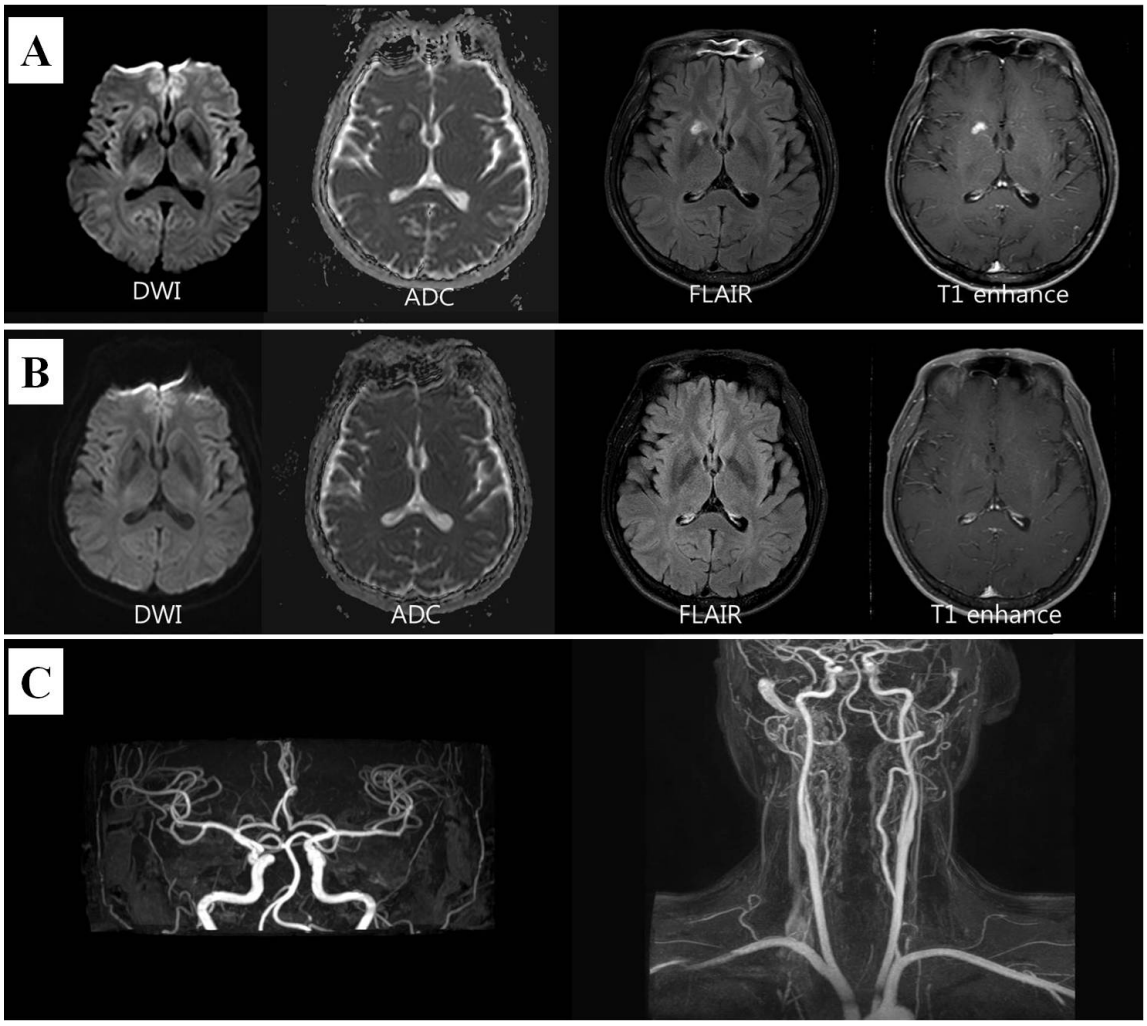

Fig. 1. Initial brain magnetic resonance imaging (MRI) using fluid-attenuated inversion recovery and diffusion weighted MRI revealed abnormal high signal-intensity lesion lesions with gadolinium enhancement on T1-weighted MRI in the right caudate nucleus which was consistent with subacute cerebral infarction. This cerebral lesions were diagnosed as vasculitic cerebral infarction caused by eosinophilic granulomatosis with polyangiitis (EGPA) (A). After immune therapy with a high-dose steroid and cyclophosphamide, a follow-up brain MRI showed marked improvement compared to the previous MRI (B). Intracranial MR angiography and neck angiography were normal (C).

weakness and sensory abnormalities gradually improved, and a follow-up NCS and brain MRI showed improvements when compared with previous results (Fig. 1B). The outpatient department has been continuously following the patient.

DISCUSSION

Herein, we described a patient with EGPA who presented with rapidly progressing polyneuropathy combined with cerebral infarction.

A diagnosis of EGPA is made in patients who have at least four of the following six objective features; 1) asthma, 2) eosinophilia greater than 10% on differential white blood cell count, 3) mononeuropathy (including multiplex) or polyneuropathy, 4) non-fixed pulmonoary infiltrates, 5) paranasal sinus abnormality and 6) extravascular eosinophils.

And our patient showed asthma, polyneuropathy, increased eosinophil counts and paranasal sinus abnormality, so he could be diagnosed as EGPA.

The patient's brain MRI using FLAIR and diffusion weighted MRI revealed high signal intensities with gadolinium enhancement on T1-weighted MRI in the right caudate nucleus, and it was compatible with subacute cerebral infarction. Prior to the brain MRI, the patient's neurological manifestations were thought to mimic a GBS with the unusual feature of axonal injury. GBS is a well-known, acute paralytic peripheral neuropathy that occurs after infection or another autoimmune reaction. Muscle weakness that is sometimes accompanied by sensory and cranial nerve ab-

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normalities progresses over 1 to 2 weeks and reaches a peak within 2 to 4 weeks [10].

In this case, the patient presented with acute sensory-motor polyneuropathy, which initially mimicked a GBS, however the etiology of polyneuropathy was determined to be vasculitic neuropathy caused by EGPA. Polyneuropathy associated with EGPA is usually caused by necrotizing vasculitis with vascular occlusion, which usually precedes multiorgan involvement and is typically characterized by axonal degeneration. Similarily, polyneuropathy in our patient showed predominant axonal features as well as albuminocytologic dissociation, and was responsive to high-dose steroids and cyclophosphamide treatment. Usually, elevated total protein concentration with normal CSF cell count (albuminocytologic dissociation) is a hallmark in acute and chronic inflammatory demyelinating polyneuropathies, however it has been also reported that a CSF protein might be elevated in the vasculitis involving peripheral nervous system.

Generally, systemic symptoms and the involvement of organ systems in EGPA are mediated by three major mechanisms: the presence of autoantibodies within organ systems, specific or nonspecific organ damage by inflammatory mediators, and antiphospholipid-related hypercoagulability and thrombosis [6-8]. EGPA commonly manifests in the prodromal phase, and then proceeds to the eosinophilic phase and the vasculitic phase [7]. The initial prodromal phase typically lasts months to years and includes arthralgia, myalgia, and fever. The eosinophilic phase is characterized by peripheral eosinophilia and the involvement of organs, including the lung, the heart, and the gastrointestinal tract. Finally, the vasculitic phase of EGPA is characterized by sensorimotor peripheral neuropathy and stroke. Therefore, we can conclude that our patient's case of EGPA had progressed to the acute vasculitic phase, as he presented with polyneuropathy and had experienced cerebral infarction.

In conclusion, our findings indicate that EGPA should be considered in the differential diagnosis of rapidly progressing polyneuropathy that mimics GBS with or without stroke at a young age. In addition, EGPA is likely to be rare and thus further evaluations for systemic manifestations are important in determining differential diagnoses of polyneuropathy.

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