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Case report

Eosinophilic granulomatosis with polyangiitis localized to the central nervous system

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Abstract

A 73 year old man was admitted for epileptic seizure. Diffuse white matter lesions were observed in the bilateral occipital lobes, and left occipital lobe biopsy showed eosinophils and giant cells in the walls of medium to small blood vessels, fibrinoid necrosis, occluded blood vessels, and glia degeneration. Eosinophilic granulomatosis with polyangiitis (EGPA) was diagnosed. He showed consciousness disturbance at JCS 3, clumsiness, and cortical blindness. Because EGPA was observed in the central nervous system alone, we diagnosed this case as primary angiitis of the central nervous system. Prednisolone combined with immunosuppressant therapies improved his symptoms markedly.

Keywords: eosinophilic granulomatosis with polyangiitis, EGPA, Primary angiitis of the central nervous system

Introduction

Allergic granulomatous angiitis (AGA) is characterized by eosinophil infiltration, fibrinoid necrosis, and granuloma at blood vessels. The disease shows bronchial asthma, increased peripheral blood eosinophils, organ injury by angiitis, and frequent expression of MPO-ANCA. The disease was considered a subtype of ANCA associated angiitis [1], but was changed to eosinophilic granulomatosis with polyangiitis (EGPA).

Primary angiitis of the central nervous system (PACNS), proposed by Cravioto and Feigin *et al.*, is angiitis localized to the central nervous system (CNS) only [2]. Although diagnostic criteria have been proposed [3], the disease is diagnosed usually by exclusion. Here, we report the characteristics of a rare case of PACNS caused by EGPA.

Case

A 73 year old man was admitted for consciousness disturbance and epileptic seizure. He was treated for epileptic seizure from 16 years old. At 57 years old, he underwent chemotherapy for acute myeloid leukemia and achieved remission. He had no past history of asthma. He experienced a loss of consciousness in January, 200X. Diffuse white matter lesions were observed in the bilateral occipital lobes, and the consciousness disturbance deteriorated gradually. He was transferred to another hospital

in March, and a brain biopsy was performed. Pathological findings revealed angiitis and no tumor, and he was transferred to our hospital.

Consciousness disturbance (JCS I-3) and cortical blindness was recognized. There was no anisocoria, and light reflexes were quick bilaterally. Mild phonetic disorder was suspected and tongue protrusion was insufficient. There was no palsy, but left upper limb-kinetic apraxia was recognized. Tendon reflex was reduced at the lower limbs. Sense of vibration of both lower limbs was slightly disturbed.

Neuroradiological tests (Fig. 1a) revealed diffuse high intensity signals by T2WI in the bilateral occipital lobes. Diffusion-weighted imaging showed slightly high intensity signals with increased apparent diffusion coefficient (ADC) inside, and surrounding mild contrast enhancement was observed. MRA demonstrated no finding suggesting angiitis.

Blood tests showed only mild leukocytosis and increased IgE (10,995.3 IU/ml). MPO-ANCA was negative. Cerebrospinal fluid examinations revealed primary pressure at 160 mmH₂O, end pressure at 90 mmH₂O, cell count at 1/μl, protein at 93 mg/dl, and mild protein increase with the IgG Index at 0.72.

Nerve conduction studies revealed no findings of peripheral neuropathy. Chest and abdominal contrast X-ray CT, upper gastrointestinal endoscopy and colonoscopy, and

ophthalmological examinations showed no findings of EGPA.

Left occipital lobe biopsy was performed (Fig. 1c-f). Findings revealed an infiltration of eosinophils and giant cells to the walls of medium to small blood vessels, fibrinoid necrosis, occluded blood vessels, and glia degeneration. Direct Fast Scarlet staining demonstrated no amyloid deposits. Klüver-Barrera staining showed no findings of demyelination. Taken together, EGPA was diagnosed.

No EGPA findings were observed in other organs, and EGPA localized in the CNS was diagnosed. After steroid pulse therapy (IVMP), high-dose intravenous cyclophosphamide therapy (IVCY), high-dose intravenous immunoglobulin therapy (IVIg therapy: immunoglobulin at 0.4/kg/day for 5 days), and azathioprine at 50 mg/day were administered. Prednisolone at 60 mg/day was administered and reduced gradually to 30 mg/day. Symptoms and MRI findings (Fig. 1b) improved gradually, and he was able to walk with a cane and discharged in December.

Discussion

This case showed findings of EGPA pathologically. Systemic exploration showed angiitis in the CNS only, which satisfies PACNS diagnostic criteria [3]. This is the first report of EGPA localized in the CNS.

Diagnosis of PACNS is difficult, and the lesion in the CNS has been attributed to ischemia by angiitis. PACNS causes inflammation only in the blood vessels of the CNS. Pathologically, some cases show granulomatous change and vascular necrosis images, while others exhibit cellular infiltration to the vascular walls, suggesting various etiologies [4].

Granulomatous vasculitis, a disease entity included in PACNS, is often observed in amyloid angiopathy, but amyloid deposits were not detected by DFS staining in the present case. When CNS symptoms are observed in cases with systemic angiitis, potent preventive measures such as immunosuppression are usually taken, and angiitis findings in other organs may be overlooked. In addition, PACNS may have more disease mechanisms than have been reported.

To elucidate the pathogenesis of PACNS, it is important to accumulate cases that are accurately diagnosed pathologically. Identifying primary “EGPA” of the CNS, as reported here, is important for investigating disease mechanisms of PACNS and EGPA.

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Figure legends

Figure 1

a-b) Brain MRI (1.5T, FLAIR, TR 9000, TE 114).

a) On admission. b) After steroid pulse therapy.

c-f) Histological findings of brain biopsy

c,d) Hematoxylin-eosin staining. c) Bar = 500 μm . d) Bar = 50 μm . Infiltration of eosinophils and giant cells into the walls of medium to small vascular walls was observed, and occlusion of blood vessels by intravascular fibrinoid necrosis was recognized.

e) Klüver-Barrera staining revealed no demyelination in the white matter. Bar = 500 μm .

f) Direct Fast Scarlet staining demonstrated no amyloid deposit under polarizing microscopy, despite mild reddish staining. Bar = 100 μm .

