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Abstract

We report the case of a 57-year-old man with neuromyelitis optica spectrum disorder (NMOSD) presenting as acute eosinophilic encephalomyelitis. Magnetic resonance imaging revealed central nervous system lesions typical of NMOSD and anti-aquaporin-4 antibodies in the serum were identified; however, eosinophilia was evident in the cerebrospinal fluid (CSF) at the early stage of the disease. The number of eosinophils in the CSF decreased subsequently. Although activation of eosinophils is known to be an important factor in the development of NMOSD lesions, prominent eosinophilia in the CSF at the early stage of the disease has never been reported in patients with NMOSD.

(100 words)

Key words: neuromyelitis optica spectrum disorder; eosinophil; encephalomyelitis; anti-aquaporin-4 antibody; immunoglobulin E

Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is characterized by fulminant attacks of optic neuritis, acute myelitis showing long cord lesions, and the presence of anti-aquaporin-4 (AQP4) antibody in the serum [1]. Importance of eosinophil activation in the development of NMOSD lesions is described [2–4]. Eosinophilia causes encephalomyelitis in association with parasitic infection, malignant lymphoma, and allergic reaction. A case of recurrent encephalomyelitis showing elevated cerebrospinal fluid (CSF) eosinophil count with no evidence of anti-AQP4 antibody in the serum was reported [5]. Here, we report a patient with NMOSD showing apparent eosinophilia in the CSF during the early stages of the former disease.

Case report

A 57-year-old man developed acute-onset sensory disturbance beneath thoracic level 3 (Th3). Two days later, gait disturbance caused by paraparesis emerged. On admission, superficial and deep sensation was extinct beneath Th3. The lower extremities were

paraparetic with mild spasticity. Hyperreflexia was apparent with bilateral extensor plantar reflex. Autonomic dysfunction, including urinary retention, constipation, and impotence, presented. Optic nerve impairments were unremarkable. Blood eosinophil count was slightly elevated (8%; 968/μl; range: 0-6%), as was serum immunoglobulin E (IgE) concentration (762 IU/ml; range: 0-250 IU/ml). Antibody tests suggesting systemic vasculitis, collagen disease, viral infection, and parasitic infection were all negative. Pleocytosis was evident in the CSF (730/μl), and although most of the collected cells were mononuclear, 13.9% (88/μl) were eosinophils, as confirmed by Giemsa stain. An elevation of protein concentration (71 mg/dl) was apparent; however, IgG index was normal (0.52). No oligoclonal bands were detected. Spinal cord magnetic resonance imaging (MRI) revealed hyperintense lesions with no apparent gadolinium enhancement on the cervical and thoracic cord between vertebral levels C5 and Th6 (Fig. 1A). Brain MRI demonstrated multiple white matter lesions in the corpus callosum and left parietal lobe. These lesions showed no enhancement by gadolinium. Systemic investigation demonstrated no evidence of sarcoidosis, parasitic infections, or malignant

disorders. Subsequently, anti-AQP4 antibody was detected in the patient's stored serum, the latency of this result being due to the fact that the anti-AQP4 antibody test was yet to be established at the time of the first episode. We made a diagnosis of eosinophilic encephalomyelitis of unknown cause, due to the fact that information about the anti-AQP4 antibody was as yet unavailable. Intravenous methylprednisolone pulse therapy (1,000 mg/day for 3 days) improved the symptoms and radiological abnormalities.

Two months later, the patient was found to have a recurrent lesion in the thoracic cord followed by right optic neuritis and multiple cerebral white matter lesions (Fig 1B, C). Pleocytosis (199/μl) with elevated eosinophil count (7.1%; 43/μl) was then revealed in the CSF. An increased protein concentration (94 mg/dl) was apparent; however, IgG index was normal (0.63), and there existed no evidence of oligoclonal bands. Serum IgE levels were normal (160 IU/ml). After administration of intravenous corticosteroids, the number of brain lesions decreased. Eight months later, hypoesthesia of the sacral area emerged, and MRI revealed a deterioration of the thoracic cord lesions.

Although an elevation of serum IgE (393 IU/ml) was detected, mild pleocytosis (7/μl) with no evidence of eosinophilia was observed in the CSF. We administered interferon-β1b via subcutaneous injection. Fifteen months later, a recurrence of right optic neuritis was observed. During the associated admission, serum anti-AQP4 antibody was tested for the first time, leading to the diagnosis of NMOSD [1]. Six months later, dysarthria and dizziness presented with multiple cerebrum, brain stem and cerebellar lesions. Interferon-β1b administration was finally discontinued and followed by a small amount dose of oral corticosteroid therapy.

Discussion

The presently discussed case showed acute encephalomyelitis, elevated serum IgE levels, and marked CSF eosinophilia at the early stages of the clinical course. Interestingly, CSF eosinophil count was normal at the time of the third episode of recurrence, and no CSF eosinophilia was detected subsequently.

The activation of eosinophils could be a key factor in the development of

NMOSD-typical lesions in the CNS. The infiltration of eosinophils, in addition to macrophages and B-lymphocytes, has been observed in autopsied tissues from NMO patients [2]. Furthermore, experimental models of NMOSD have demonstrated that the presence of both anti-AQP4 antibodies and eosinophils enhances NMOSD-like lesions [4]. Moreover, approximately 10% of NMOSD cases showed the presence of eosinophils in the CSF [3]. The relationship between eosinophil activation and the development of NMOSD lesions has not been elucidated in details. Nonetheless, the decreased CSF eosinophil count measured after our patient‘s third recurrence may suggest that eosinophil activation plays a crucial role in the development of NMOSD lesions during the relatively early stages of the disease.

Our patient demonstrated hyperIgEnemia in addition to eosinophilia. Atopic myelitis is a subtype of myelitis related to hyperIgEnemia, eosinophilia in the blood and CSF, and eosinophilic infiltration into the spinal cord [6]. As with NMOSD, some patients with MS have been demonstrated to possess elevated blood eosinophil counts; however, hyperIgEnemia has not been reported in patients with NMOSD or MS.

Further investigations are necessary to clarify the details of the relationship between NMOSD lesions, eosinophilic inflammation, and hyperIgEnemia.

(829 words)

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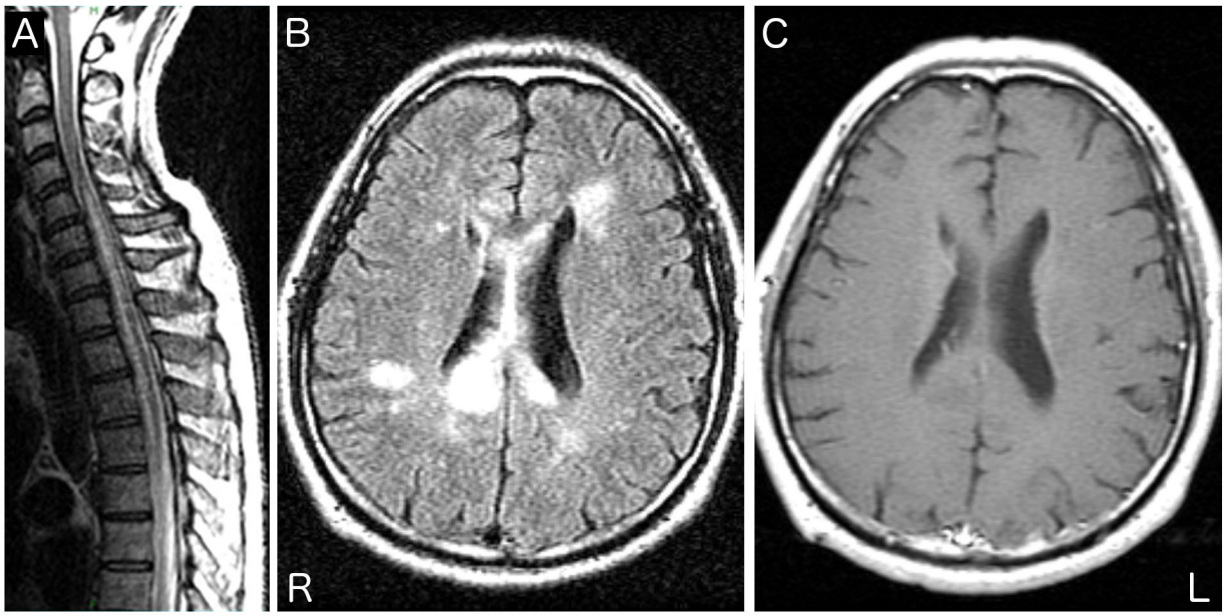
Captions to illustrations

Figure 1. Spinal cord and brain magnetic resonance images. Hyperintense lesions with spinal cord swelling are evident on T2-weighted sagittal image between vertebral levels of C5 and Th6 (A). Fluid attenuated inversion recovery axial images demonstrate multiple hyperintense lesions in the cerebral white matter and corpus callosum (B). No obvious enhancement by gadolinium is shown on the T1-weighted axial image (C).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