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Elevated cerebrospinal fluid IgG index in acute cerebellitis presenting with sudden onset headache

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Abstract

Acute cerebellitis is a rare inflammatory syndrome and is one of the important causes of acute cerebellar dysfunction in children. The cerebrospinal fluid (CSF) IgG index is most often tested clinically in the diagnosis of multiple sclerosis. However, it is not specific to multiple sclerosis, and can be elevated in a variety of neurologic diseases. A 7-year-old boy with acute cerebellitis presenting with sudden onset headache and subtle cerebellar dysfunction demonstrated an elevated CSF IgG index (1.1) and an absence of oligoclonal bands. On the seventeenth day, the follow-up CSF IgG index was 0.71. Two-month and one-year follow-up magnetic resonance imaging revealed cerebellar atrophy, although the patient showed no neurologic deficit. To the best of our knowledge, this case report is the first to describe acute cerebellitis accompanied by an elevated CSF IgG index and an absence of CSF oligoclonal IgG bands. These findings suggest that a breach in the blood-brain-barrier might occur in acute cerebellitis.

INTRODUCTION

In contrast to acute cerebellar ataxia, acute cerebellitis can be diagnosed when cerebellar lesions are detected on neuroimaging.[1] Although its typical clinical features are cerebellar dysfunction such as ataxia and dysmetria, it can also present with nonspecific neurologic symptoms such as headache and vomiting with minimal or no cerebellar signs.[2] Meanwhile, the cerebrospinal fluid (CSF) IgG index is most often used in the diagnosis of multiple sclerosis. However, it can also be elevated in various neurologic diseases, such as bacterial and viral central nervous system (CNS) infection and Guillain-Barre syndrome.[3,4] In the case reported here, a patient with acute cerebellitis presenting with sudden onset headache and subtle cerebellar dysfunction demonstrated an elevated CSF IgG index and was oligoclonal band-negative.

CASE REPORT

A 7-year-old male was admitted to our hospital due to a sudden onset headache. His headache began 5 days before admission and was accompanied by fever during the first 3 days. His fever subsided thereafter, but the headache remained. The patient sometimes complained of diplopia, but display no vomiting or unsteadiness. He had previously been healthy, and had no history of medication or head trauma. On physical examination, he exhibited no apparent abnormality, including of the skin and oral cavity. On neurologic examination, he was fully alert and oriented. All of his cranial nerves were intact. However, the patient showed subtle horizontal nystagmus, and his heel-to-shin test and tandem gait results were abnormal. The patient's CSF revealed white blood cells 420/mm^3, red blood cells 0/mm^3, protein 88.2 mg/dL, and glucose 52 mg/dL, with negative culture CSF. Brain magnetic resonance imaging (MRI) revealed diffuse T_2-weighted high signal intensity in the cerebellar hemispheres with mild compression of the brainstem, and pial gadolinium-enhancement along the cerebellar folia (Figure 1A, 1B, and 1C). There was no evidence of cerebral parenchymal lesion on the brain MRI. CSF polymerase chain reactions for herpes simplex virus 1 and 2, human herpesvirus 6, parvovirus B 19, and CSF reverse transcription-polymerase chain reactions (RT-PCR) for enterovirus all tested negative. Serologic antibody tests for Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, *Mycoplasma pneumoniae*, rubella, *Chlamydia pneumoniae*, and mumps produced negative results. The results for measles IgG and IgM antibody were positive (2.3 and 1.9, respectively; positive >1.1). However, the results of a culture

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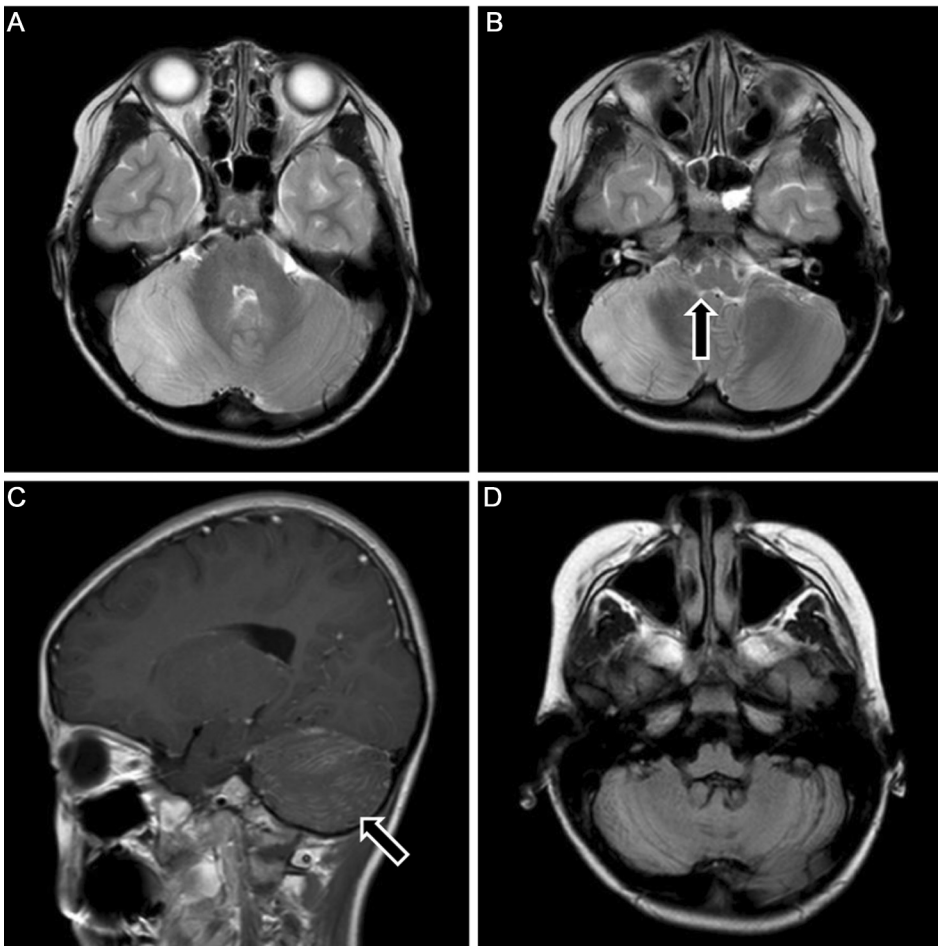

Figure 1. Initial and follow-up brain MRI findings. Axial T_2-weighted MRI shows diffuse high signal intensity in the cerebellar hemispheres, much more prominantly on the right side (A), and mild compression of the right side in the brainstem (arrow) (B). Sagittal gadolinium-enhanced T_1-weighted MRI shows pial enhancement along the cerebellar folia (arrow) (C). In two-month follow-up brain MRI, axial fluid attenuated inversion recovery imaging shows diffuse atrophy of both cerebellar hemispheres and remaining subtle signal changes (D).

and RT-PCR for detection of the measles virus in the CSF, blood, urine, and a pharyngeal swab were negative. The patient's CSF IgG index was 1.1 (IgG in CSF: 12.84 mg/dL; albumin in CSF: 64 mg/dL; IgG in serum: 796 mg/dL; albumin in serum: 4,400 mg/dL). Oligoclonal band and myelin basic protein tests produced negative results.

On the second day, intravenous methylprednisolone (30 mg/kg/day) commenced, in addition to mannitol and empirical antimicrobial therapy. On the fourth day, the patient's headache improved significantly, and all of the cerebellar function tests revealed normal. The patient was discharged on the eleventh day. On the seventeenth day, follow-up CSF analysis revealed white blood cells 1/mm^3, red blood cells 760/mm^3, protein 39.2 mg/dL, and glucose 60 mg/dL. The CSF IgG index was 0.71 (IgG in CSF: 2.88 mg/dL; albumin in CSF: 25 mg/dL; IgG in serum: 728 mg/dL; albumin in serum: 4,500 mg/dL). The oligoclonal band results were negative. Two-month and one-year follow-up brain MRI revealed cerebellar atrophy, although no neurologic deficits were observed in the patient (Figure 1D). One-year follow-up results for measles IgG and IgM antibody were 1.6 and negative, respectively.

DISCUSSION

Acute cerebellitis is one of the important causes of acute cerebellar dysfunction in childhood. It is considered an inflammatory disease of the cerebellum caused by a direct infection or

postinfectious autoimmune mechanisms.[2] The infectious pathogens that have been reported to be associated with acute cerebellitis include varicella, measles, mumps, rubella, Epstein-Barr virus, cytomegalovirus, herpes simplex virus, influenza virus, poliovirus, coxsackie virus, *Salmonella typhi*, and *Mycoplasma pneumonia*.[2] In the case presented here, although the patient's serological antibody titer to measles was elevated, we could not confirm whether measles virus was the causative microorganism of acute cerebellitis.

The clinical presentation of cerebellitis is variable. The most common symptoms are truncal ataxia, dysarthria, dysmetria, tremor, and headache.[1,5] However, a recent review of the literature found that 50% (30/60) of patients with acute cerebellitis do not present with cerebellar signs.[5] Although the clinical course of acute cerebellitis is usually benign, life-threatening hydrocephalus resulting from cerebellar swelling with compression of the fourth ventricle has required neurosurgical interventions in some cases during the acute phase of the disease.[2,5] Regarding the long-term outcome in children with acute cerebellitis, one recent study demonstrated that neurologic sequalae, ranging from mild tremor to profound ataxia, and cognitive deficits are common.[6] In this case, however, the patient demonstrated favorable prognosis despite elevated CSF protein level and IgG index in conjunction with cerebellar atrophy.

The CSF IgG index is most often tested clinically in the diagnosis of multiple sclerosis, particularly in combination with oligoclonal bands. While the exclusive presence of oligoclonal IgG bands in the CSF when compared to the serum, indicate the production of IgG within the CNS compartment, the elevation of the CSF IgG index may reflect not only intrathecal production of IgG, but also a breach in the blood-brain barrier.[7] Meanwhile, elevated CSF/serum albumin ratio reflects the dysfunction of the blood-brain barrier.[7] In this case, the elevated IgG index, absence of the CSF oligoclonal IgG bands, and CSF/serum albumin ratio three times higher in the acute phase than in the convalescent phase (0.015 vs. 0.005) could suggest that there might be a breach of the blood-brain barrier during the acute phase of the disease, although the mechanism was unknown.

To the best of our knowledge, this case report is the first to describe acute cerebellitis accompanied by an elevated CSF IgG index and an absence of CSF oligoclonal IgG bands. Further investigations are necessary to elucidate the mechanism operating in the exclusive involvement of the cerebellum in patients with acute cerebellitis.

DISCLOSURE

Conflict of interest: None

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