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A girl with acute encephalitis followed by acute cerebellitis/cerebellopathy

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Abstract. – OBJECTIVE: The purpose of this study is to bring attention to a case of acute encephalitis not concurrent with acute cerebellitis.

CASE PRESENTATION: Five days after onset of common cold symptoms, a 17-months-old girl suffered convulsions, vomiting and respiratory arrest. On exam, she had pharyngeal inflammation, brisk deep tendon reflexes, respiratory acidosis, leukocytosis, negative rapid antigen tests, and segmental pneumonia. Brain CT and MRI/MRA were negative, and EEG was consistent with acute encephalitis. Following hypothermic therapy, methylprednisolone pulse therapy and cefotaxime, she recovered. Four days after discharge, she sustained limb and truncal ataxia associated with normal EEG, followed by bilateral intention tremor. Blood and CSF chemistry and cell counts were normal. Brain MRI revealed high intensity signals in the dentate nuclei and enhancement in the cerebellar white matter, suggestive of acute cerebellitis/cerebellopathy. SPECT imaging showed reduced blood flow in the cerebellum, right thalamus and brain stem. Following short-term administration of g-globulin and prednisolone, she regained her ability to sit and, eventually, to walk. Four months after initial presentation, her brain MRI was normal. No relapse has occurred in 5 years.

CONCLUSIONS: The uncommon sequential development of acute encephalitis followed by acute cerebellitis suggests an immune-mediated cerebellar ataxia.

Key Words:
Acute cerebellitis, Acute encephalitis, Ataxia, Children, Cerebellopathy, Immune-mediated cerebellar ataxia.

Introduction

Acute cerebellitis is a rare inflammatory syndrome with the majority of cases described in young, previously healthy children[1-3]. It can be a complication of systemic infections[1-7] and is characterized by acute onset of cerebellar signs and symptoms (such as ataxia, intention tremor or dysarthria) often accompanied by fever, altered mental status and characteristic imaging abnormalities of the cerebellum[1-3,8-10]. There is no established treatment, but some cases have been treated with intravenous immunoglobulin or steroids[1-3]. Some children presenting with acute cerebellitis are occasionally found to have concurrent inflammation in other parts of the brain (encephalitis)[11-17]. Herein, we present the rare and unique case of a young child with acute encephalitis who subsequently developed acute cerebellitis/cerebellopathy and was successfully treated.

Case Presentation

Patient was 17-months-old when she was admitted to the hospital for the first time suffering from an acute encephalopathy. She had no abnormalities at birth, and the family history did not show any prior complications. On day 5 after the onset of a common cold with no gastrointestinal symptoms, she suffered from partial convulsions followed by recurrent vomiting, which led to respiratory arrest for about 15 minutes. During her stay in the emergency department, her consciousness level was eye opening 2, verbal response 2 and motor response 3 in Glasgow coma scale. Later, she was admitted to the intensive care unit, and was kept under artificial mechanical respiration. Physical findings included injected pharyngeal mucosa and brisk accelerated deep tendon reflex in the upper and lower limbs. Blood gas and hematological analyses showed that the pH, PCO_2, WBC, and CRP values were 7.173, 63.4 mmHg, 21,600/mm^3, and 3.3 mg/dl, respectively. Rapid antigen test including influenza A/B virus, rota virus, group A *streptococcus* and mycoplasma were negative. A cerebrospinal fluid (CSF) test showed that the cell count and protein level were 52/3 and 15 mg/dl, respectively. Chest

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X-ray revealed right upper segmental pneumonia. Brain computed tomography did not reveal any abnormalities and brain MRI/MRA results were normal. Electroencephalograms (EEG) showed asymmetric high-amplitude d waves on both left and right sides, which was suggestive of an acute encephalitis (Figure 1). She was treated with 35.0 degree's mild brain hypothermic therapy combined with methylprednisolone steroid pulse therapy for 3 days (with a hypothermia duration of 72 hours). Continuous intravenous injection of midazolam, D-mannitol, cefotaxime sodium, and other needed agents was performed. 99m-Tc ECD single photon emission computed tomography (SPECT) did not reveal any abnormalities on day 12. MRI showed a slight atrophy in the frontal region on day 13. Improvement in the symptoms was observed, and the patient was discharged on day 14.

Four days after discharge (day 18), she suffered from ataxia of the limbs and trunk, EEG was performed but no abnormalities were detected. On day 23, we observed that patient was unable to maintain the sitting position while developing cerebellum symptoms. At the second admission, the consciousness level was normal, intention tremor on both hands was noted. Blood cell counting as well as blood biochemistry analysis were both normal. The CSF cell count was 32/3, and the protein level was 24 mg/dl. She tested negative for the oligoclonal band. Brain MRI results (T2-weighted FLAIR images) revealed a high signal intensity in the bilateral cerebellar deep white matter areas, at the dentate nucleus of the cerebellum, and in the subcortical white matter areas of the right parietal/occipital lobes. In addition, the cerebellar white matter and deep white matter, marked enhancement effects were observed (Figure 2A, B). Thus, the MRI findings suggested acute cerebellitis/cerebellopathy. At this point (on day 24) we administrated 400 mg/kg of g-globulin for 5 days alongside with 2 mg/kg/day prednisolone. The patient regains her ability to sit normally on day 29. SPECT results on day 37 showed a decline in blood flow in the cerebellum, right thalamus, and brain stem (Figure 2C, D). Thereafter, ataxia of the limbs and trunk symptoms were improved gradually. Patient was able to walk and was discharged on day 48. Four months after the initial onset, brain MRI confirmed the disappearance of all abnormal signal intensities in the cerebellum. There has been no relapse during 5 year of follow-up.

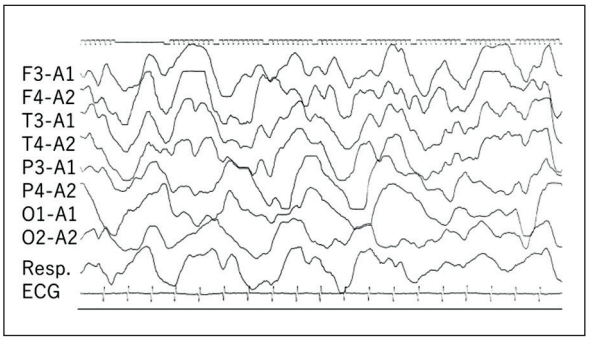

Figure 1. EEG recorded asymmetric high-amplitude d waves.

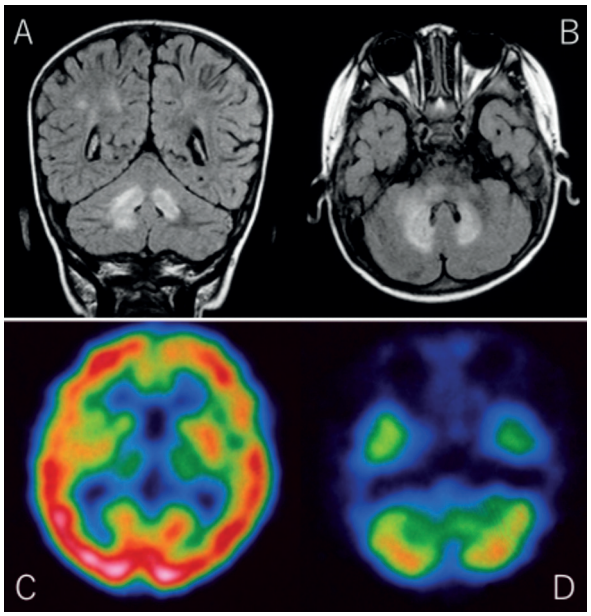

Figure 2. MRI and SPECT imaging. **A, B,** on day 23, MRI FLAIR images revealed high signal intensity in the bilateral cerebellar deep white matter, dentate nucleus and subcortical white matter of the right parietal/occipital lobes. **C, D,** on day 37, SPECT showed decreases blood flow in the cerebellum, right thalamus and brain stem.

Discussion

Acute cerebellitis is characterized by acute cerebellar ataxia or dysfunction attributable to a recent or concurrent infectious illness, or rarely a recent vaccination, associated with MRI evidence of predominant cerebellar inflammation[2]. It occurs in previously well children, usually under 6 years of age[2]. The clinical features of acute cerebellitis at presentation include in decreasing frequency (55%-15%) somnolence or

coma, ataxia, headache, nausea, vomiting, fever, dysarthria, mutism, gait disturbance, dysmetria and seizure[2]. The majority of cases are attributed to post infective inflammation based on the clinical presentation. Of the cases in which a pathogen was found, most were due to viral (e.g., rotavirus[11-15], Epstein-Barr virus, varicella zoster, influenza A and B[6]), bacterial (e.g., *Streptococcus*[7]) and mycoplasmal (e.g., *Mycoplasma pneumoniae*[5]) infections[1-4]. A minority of cases of postimmunization acute cerebellitis have been reported (e.g., vaccination for varicella, influenza) without evidence of systemic infection[2]. Also, the rates of cerebellitis after vaccination are much lower than in association with infection[18]. The pathogenic mechanisms through which systemic infections may cause specific neurological disorders have not been definitively established but are believed to be autoimmune[2,19]. An immune-mediated pathogenesis is also suggested by the paucity of causative pathogen detected in the patients' CSF. Auto-antibodies possibly involved in cerebellar inflammation have been detected in the serum and/or CSF of patients with acute cerebellitis and include antibodies against glutamate receptor delta 2 (predominantly expressed on cerebellar Purkinje cells)[7,20], gangliosides (in *M. pneumoniae* cases)[21,22] and centrosomes (pericentrin; in varicella cases)[23]. Clinically, the most sensitive imaging modality for assessing cerebral and cerebellar inflammation is MRI[1-3,8]. Various patterns of cerebellar inflammation have been reported, including inflammation of the dentate nuclei and hemispheres. Single-photon emission computed tomography (SPECT) imaging may reveal the presence of reduced cerebellar blood flow in acute cerebellitis[2,9,10]. Serology may demonstrate elevate infection or inflammation biomarkers, but CSF analyses and cerebral EEG are often non-contributory[1-3]. Most patients respond to medical management consisting of intravenous administration of immunoglobulins, steroids (e.g., methylprednisolone), antiviral agents (i.e., acyclovir) and broad-spectrum antibiotics[1-3]. The majority of patients improve within 2 weeks, but cerebellar ataxia may take months to resolve and long-term neurological disabilities and occasional deaths have been reported[1-3].

Some children presenting with acute cerebellitis are occasionally found to have concurrent inflammation in other parts of the brain (encephalitis). Examples of acute cerebellitis concurrent with encephalitis include cases of rotavirus gastroenteritis[11-15], rhinovirus[16] or with an unknown etiology[17]. In the present case, acute encephalitis with possible brainstem involvement developed first, as suggested by the patient's convulsion and respiratory arrest and EEG abnormalities without MRI evidence of cerebral or cerebellar inflammation. Only 4 days after her recovery and discharge did she demonstrate cerebellar signs and symptoms evidenced by limb and truncal ataxia, bilateral intention tremor, difficulty sitting and walking. Imaging abnormalities detected in the cerebellum by MRI and SPECT imaging were consistent with a diagnosis of acute cerebellitis/ cerebellopathy. Attempts at identifying the etiologic agent by rapid antigen test (influenza A/B virus, rotavirus and Group A *streptococcus*) and CSF oligoclonal band test were inconclusive. The temporal dissociation of acute encephalitis followed by acute cerebellitis suggests an immune-mediated cerebellar ataxia. Only in a report of two patients with rotavirus gastroenteritis have the symptoms of acute encephalitis subsided before the cerebellar signs (mutism, slow speech and dysarthria) became evident and a brain MRI showed cerebellar involvement[11]. However, the present case does not support rotavirus as the etiology and presents a different spectrum of cerebellar signs.

Conclusions

The sequential development of acute encephalitis followed by acute cerebellitis/ cerebellopathy in this child is uncommon. A process of immune-mediated cerebellar ataxia is supported by its response to immunoglobulin and steroid therapy.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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