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Case Report

Epileptic spasms secondary to acute cerebral and cerebellar encephalitis

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Abstract

Background: Patients with infection-related acute encephalitis sometimes develop epilepsy in the chronic phase of the disease. Patients with postencephalitic epilepsy usually develop partial seizures due to the lesions generated by the encephalitis. We report a case who developed late-onset epileptic spasms after acute cerebral and cerebellar encephalitis.

Case report: A 5-year-old girl showed severe tremor, gait ataxia, partial or generalized tonic-clonic seizures, hyperactivity, and panic attacks after a mild enterocolitis. Her cerebellar symptoms disappeared until 3 months after onset, and her seizures were controlled with carbamazepine. However, the seizures reappeared as epileptic spasms 5 months after onset. The anti-NMDA-type glutamate receptor antibody concentration was significantly elevated in her cerebrospinal fluid at 8 days, 10 months, and 15 months after onset. The spasms were resistant to multiple antiepileptic drugs. High-dose methylprednisolone and high-dose immunoglobulin therapies did not show any benefits. Oral pranlukast hydrate was started 17 months after onset. After 3 weeks of the medication, her seizures disappeared, and her behavior also dramatically improved.

Conclusion: We presented a rare case of post-encephalitic epilepsy that manifested as epileptic spasms. Pranlukast significantly improved her seizures.

Keywords: Acute encephalitis; Acute cerebellitis; Postencephalitic epilepsy; Pranlukast hydrate; Anti-NMDA receptor antibody; Epileptic spasms

1. Introduction

Acute encephalitis/encephalopathy is often caused by viral infection. This condition is classified into several subtypes, including acute disseminated encephalomyelitis, hemiconvulsion-hemiplegia epilepsy, and febrile infection-related epilepsy syndrome [1–3]. Other subtypes of acute encephalitis/encephalopathy have

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been reported in East Asian countries [3,4]. In total, 6–16% of the children with acute encephalitis/encephalopathy develop postencephalitic epilepsy [1]. Half of patients with postencephalitic epilepsy show drug-resistant seizures that are refractory to multiple antiepileptic drugs [1].

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is a subtype of infection-related encephalitis. Its pathogenesis is mediated by specific autoantibodies to NMDA-type glutamate receptors. The clinical features of this disorder are stereotyped and include acute onset memory deficits, psychiatric symptoms, decreased consciousness, and hypoventilation [5–7]. The most commonly used therapeutic agents and treatments for this disease are intravenous immunoglobulins, plasma exchange, corticosteroids, rituximab and cyclophosphamide [7]. Encouragingly, approximately 75% of patients with anti-NMDA-type glutamate receptor antibodies recover or experience only mild sequelae [5,7].

We herein report a case involving a 5-year-old girl with acute cerebral and cerebellar encephalitis who then developed epileptic spasms without destructive cerebral lesions in the chronic phase of the disease. In both the acute and chronic phases of this patient's disease, antibodies to GluN1/N2B in serum and cerebrospinal fluid (CSF) were significantly elevated.

2. Case report

A 5-year, 4-month-old girl without a history of neurological disorders showed vomiting and mild diarrhea, which remitted within a day. Five days later, she presented with a severe tremor and gait ataxia and was transported to the hospital by ambulance because of generalized tonic-clonic seizures. Eight days after seizure onset, the protein and cell counts in her CSF were normal. She showed behavioral disturbances including hyperactivity, panic attacks, screaming, and incontinence. Fourteen days after onset, she developed tonic seizures in her left upper and lower extremities and secondary generalization. The seizures were controlled with carbamazepine. Until 3 months after onset, her severe tremor and cerebellar ataxia disappeared.

Our patient was discharged 3 months after onset despite some remaining behavioral symptoms. In the classroom, she was hyperactive and impulsive; she walked around the class during lessons and fought with her classmates despite her teacher's best efforts to control these behaviors. Her score on the ADHD Rating Scale-IV markedly increased to 54/54 (>99th percentile). Five months after onset, the seizures reappeared as epileptic spasms. Despite treatment with carbamazepine and valproate, the seizure frequency increased to a few times per day. Because of the refractory seizures, she was referred to the Comprehensive Epilepsy Center in Seirei-Hamamatsu General Hospital 8 months after onset. An ictal electroencephalogram (EEG) showed diffuse biphasic or triphasic slow waves followed by electrodecremental activity concomitant with epileptic spasms. We replaced carbamazepine with levetiracetam and lamotorigine. These partially reduced the seizure frequency. High-dose methylprednisolone therapy (30 mg/kg/day for 3 days) at 13 and 15 months after onset and high-dose immunoglobulin (2 g/kg) at 15 months after onset were ineffective. We began administering pranlukast hydrate at a dose of 7 mg/kg/d at 17 months after onset, and the seizures completely ceased within 3 weeks after starting the medication. Her hyperactivity and impulsivity gradually improved. At 22 months after onset, her score on the ADHD Rating Scale-IV decreased to 26/54 (94th percentile), and her behavioral problems in the classroom were markedly improved. Her intelligence quotient was 90 (WISC-IV) at 32 months after onset. We ceased her antiepileptic drugs other than lamotorigine. At the last follow-up 50 months after onset, she showed mild visuospatial memory impairments. Her Rey-Osterrieth Complex Figure Test score was 26/36 (<1st percentile). The EEG did not show any epileptic discharges. She remained free from seizures.

3. Antibodies against NMDA-type glutamate receptor

CSF antibodies against GluN2B (ε2, NR2B) -NT and -CT (N- and C-terminal domains, respectively) and GluN1 (ζ1, NR1) -NT, and glutamate receptor, ionotropic, delta 2 (GluD2, GluRδ2) -NT were elevated over 2 SD above controls at 8 days, 10 months and 23 months after onset. CSF antibodies against GluN2B-NT and -CT were also elevated over 2 SD at 15 and 23 months after onset. Serum antibodies to GluN1-NT were elevated over 2 SD at 10 months after onset.

4. MRI

Three days after onset, diffusion-weighted MRI showed a high signal in the left cerebellar cortex (Fig. 1A). At 8 (Fig. 1B) and 23 months after onset, MRI revealed that the region of the high signal cerebellar lesion had atrophied, but there were no changes in other regions.

5. Discussion

The patient developed cerebral and cerebellar encephalitis in the acute phase. She exhibited hyperactivity and postencephalitic epilepsy with epileptic spasms in the chronic phase of the disease. Anti-NMDA-type glutamate receptor antibodies might mediate postencephalitic epilepsy.

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