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Case report

Refractory epilepsy accompanying acute encephalitis with multifocal cortical lesions: Possible autoimmune etiology

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Abstract

We report on a 14-year-old male suffering from acute encephalitis, whose clinical course met the criteria for acute encephalopathy with refractory, repetitive partial seizures (AERRPS). He presented with extremely refractory partial and secondary generalized seizures, and required high-dose barbiturate infusion therapy for 57 days under mechanical ventilation. Seven weeks after onset, the seizures were ameliorated by treatment with sodium bromide, carbamazepine, clobazam, and high-dose phenobarbital. Magnetic resonance imaging on day 14 of admission showed multifocal cortical legions scattered in the bilateral hemispheres; these disappeared on day 34. Diffuse and mild atrophy of the cerebral cortex, and moderate atrophy of the hippocampus, appeared by day 61. Serum anti-glutamate receptor ε2 autoantibodies were detected on day 2. The patient was discharged after 113 days of admission with intractable epilepsy, memory disability, and regression of intelligence. We discuss the etiological significance of the multifocal lesions, which are unusual findings on neuroimaging of AERRPS.

Keywords: Refractory seizures; Repetitive seizures; Status epilepticus; High-dose barbiturate; Multifocal cortical legions; MRI

1. Introduction

Awaya et al. [1] reported on children with a ''peculiar type of post-encephalitic epilepsy'', presenting with extremely refractory partial seizures during a prolonged acute phase and sequelae of intractable epilepsy. Approximately 40 similar cases have been reported in Japan. Sakuma et al. [2] proposed the terminology ''acute encephalitis with refractory, repetitive partial seizures (AERRPS)'' for this entity, with the criteria being: (1) prolonged acute phase of more than 2 weeks; (2) partial seizures of the same symptoms persisting from the acute phase to convalescence; (3) seizures frequently evolving into convulsive status especially during the acute phase; (4) marked intractability of seizures; and, (5) exclusion of related disorders such as known viral encephalitis or metabolic disorders. Additional features including responsiveness to certain antiepileptic agents, and the presence of serum anti-glutamate receptor antibodies were reported in some cases [1,3]. AERRPS is now an accepted clinical entity in Japan, based on these characteristics; however, this disease entity has not achieved worldwide consensus, despite recent reports of cases whose clinical features meet the criteria of AERRPS [4,5]. Here, we describe a patient whose clinical course was compatible with a diagnosis of AERRPS, in which multifocal cortical lesions were detected on magnetic resonance imaging (MRI). This finding is quite

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unusual in viral encephalitis, and suggests an autoimmune basis for the pathogenesis. Such a finding has also not been described in patients with AERRPS, and we discuss the associated nosological concerns.

2. Case report

2.1. Clinical course (Fig. 1)

A 14-year-old boy presented with fever and headache persisting for 3 days. Following a 5-day remission, the symptoms reappeared in association with vomiting and eruption, as well as generalized tonic convulsion. On admission, the patient was stuporous. Body temperature was 37.9 °C. Scarlet fever-like eruption was noted on the trunk, but otherwise there were no remarkable findings. Cranial computed tomography (CT) was normal. Routine assays of blood and cerebrospinal fluid (CSF) were within normal range, and electroencephalography (EEG) showed sporadic diffuse slow waves.

On the day of admission, he developed bilateral facial twitching and eyelid fluttering, which were controlled with a bolus infusion of diazepam and continuous intravenous administration of midazolam. He remained stuporous during the interictal period. On day 2, frequent twitching in the face, hand, and foot recurred, often evolving into generalized convulsions. Treatment with a suppository of phenobarbital (PB), as well as intravenous phenytoin, pyridoxine, and lidocaine were not effective. The seizures lasted for 0.5–2 min and appeared every few minutes, sometimes culminating in secondary generalized tonic–clonic convulsions, or an epileptic status. High-dose PB with a concentration of 150 μg/ml, or continuous infusion of thiamylal at 7 mg/kg/h under mechanical ventilation, did not suppress the seizures completely. High-dose immunoglobulin and steroid pulse therapy of 30 mg/kg/day methylprednisolone for 3 days also showed no beneficial effect. Ictal EEG showed focal rhythmic 5 or 10 Hz spikes in the bilateral frontal, central or occipital areas, with occasional generalization.

On day 27, the thiamylal was replaced by thiopental sodium (TP), which controlled the seizures when administered at a dosage of 2–6 mg/kg/h. At this time, the EEG showed a burst-suppression pattern. Under infusion of these barbiturates during the acute phase, we tried several oral antiepileptic drugs: sodium valproate, zonisamide, clobazam (CLB), sodium bromide (NaBr), and carbamazepine (CBZ). Only CLB produced any improvement in this acute phase.

The seizures ceased after 3 weeks of therapy with TP, which was gradually replaced by oral PB. Brief partial seizures recurred and persisted 0–5 times per day. Thereafter, the patient gradually recovered and was able to perform normal daily activities without aid. On day 113, he was discharged under treatment with PB, CLB, NaBr, and CBZ, which were effective to some degree at this stage of the illness. He had sequelae of intellectual regression with an intelligence quotient of 66, disability

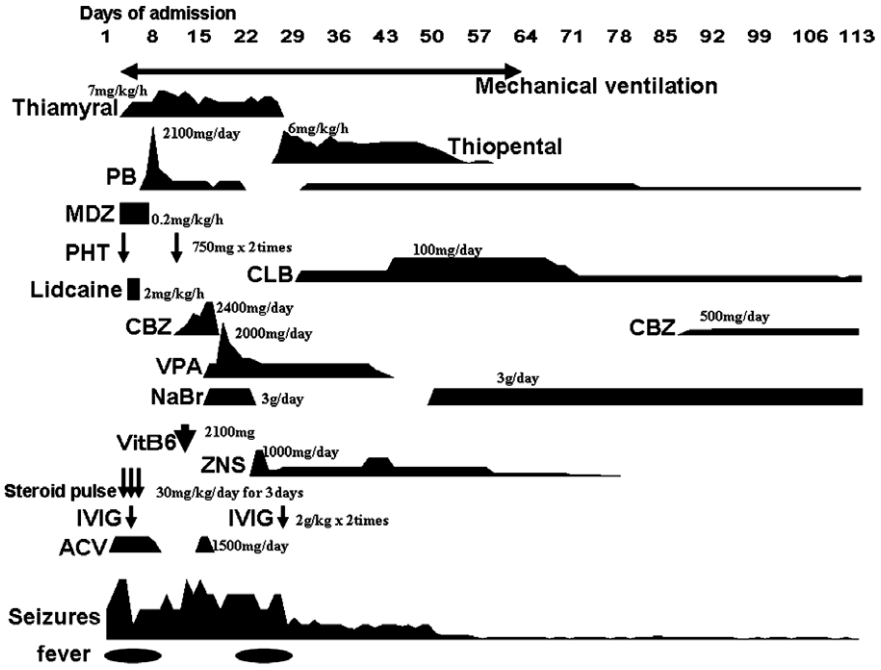

Fig. 1. Clinical course of the patient. Dosage of each drug refers to the maximum dose of continuous (thiamylal, thiopental, MDZ, and lidocaine) or one-shot (PHT, Vit.B6, steroid, IVIG, and ACV) intravenous injection or oral intake (PB, CLB, CBZ, VPA, NaBr, and ZNS). PB, phenobarbital; MDZ, midazolam; PHT, phenytoin; CLB, clobazam; ZNS, zonisamide; CBZ, carbamazepine; VPA, sodium valproate; NaBr, sodium bromide; IVIG, intravenous immunoglobulin; ACV, acyclovir.