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Case report

Overlapping MERS and mild AESD caused by HHV-6 infection

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Abstract

We report the case of an overlapping encephalopathy syndrome consisting of clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) and a mild form of acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) caused by human herpesvirus-6.

A previously healthy 17-month-old girl was admitted to our hospital as a precaution because of seizures that had developed more than 25 hours (h) after fever. Brain diffusion-weighted images (DWI) showed high signal intensity in the central splenial region on Day 2. She regained consciousness 16 h after the second seizure. On Day 6, she had a secondary cluster of partial seizures. DWI showed resolution of the splenial lesion and revealed reduced diffusion in the fronto-subcortical white matter. She regained consciousness 36 h after the secondary cluster of seizures without any sequelae. A third DWI performed on Day 15 showed that the fronto-subcortical white matter lesions had completely disappeared. Based on the clinicoradiological findings, we diagnosed the patient with overlapping MERS and mild AESD.

Our case, together with previous reports, suggests that patients can develop combined encephalopathy syndromes as a phenotype. Many encephalopathy syndromes have been established and classified; however, some may not present as independent syndromes.

Keywords: Overlap; Human herpesvirus 6; Clinically mild encephalitis/encephalopathy with a reversible splenial lesion; Acute encephalopathy with biphasic seizures and late reduced diffusion

1. Introduction

Human herpesvirus-6 (HHV-6) is the second most common pathogen causing acute encephalopathy in Japan [1]. Among encephalopathy syndromes associated with HHV-6, acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most frequent, followed by acute necrotizing encephalopathy (ANE). Clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS), hemorrhagic shock and encephalopathy (HSES) syndrome, and limbic encephalitis are rare [1].

Patients develop various types of encephalopathy syndromes with phenotypic differences; however, the

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mechanisms underlying the development of different encephalopathy syndromes from the same virus are unknown. Although each encephalopathy syndrome is established to some extent, it is unclear whether encephalopathy syndromes are completely independent from one another.

This report presents a rare case with overlapping MERS and mild AESD caused by HHV-6 infection and specifically focuses on the clinicoradiological findings.

2. Case report

A 17-month-old girl, the first child of healthy Japanese parents, was born at term by vaginal delivery and had no previous developmental problems. There was no family history of neurologic disease. The patient had a 3-minute (min) long generalized tonic–clonic seizure, which stopped naturally. Because we estimated that the seizure, which developed 25 hours (h) after fever onset, did not have the typical clinical course of febrile seizure, we judged that she required admission to the hospital for a follow-up as a precaution. On admission, she was alert without any neurological abnormalities. Routine hematological studies, blood gas analysis, and almost all biochemical studies were normal. Her serum sodium level was 134 mmol/L (standard range of institute: 135–147 mmol/L) on Day 1 of admission. Four hours after the first seizure, she had a generalized tonic–clonic seizure lasting 4 min. Although the second seizure also stopped without treatment, midazolam was administered by intravenous injection for persisting rigidity of the lower limbs. In addition, diazepam suppositories were given twice for recurrent seizures (Fig. 1). The results of a routine cerebrospinal fluid (CSF) examination were normal. Brain diffusion-weighted images (DWI) acquired using magnetic resonance imaging (MRI) showed high signal intensity in the central splenial region on Day 2 (Fig. 2). She regained consciousness 16 h after the second seizure. We diagnosed the patient with MERS based on the clinicoradiological findings [2,3]. Her fever was reduced on Day 5, and she had a rash on Day 6.

On Day 6, she had a cluster of three tonic–clonic seizures that occurred over 3 h, each lasting 5–6 min. Although all seizures stopped naturally, a diazepam suppository was given for irritability after the first seizure, and after the third seizure, midazolam was administered by intravenous injection, and phenobarbital suppositories and oral valproate sodium were administered regularly for preventing recurrent seizures. The second blood and CSF examinations were normal. DWI on Day 6 showed resolution of the high-intensity signal in the central splenial region identified on Day 2, and revealed reduced diffusion in the fronto-subcortical white matter (Fig. 3a–c). Under a diagnosis of AESD, methylprednisolone pulse therapy (30 mg/kg per day) and gamma-globulin treatment were administered. She regained consciousness 36 h after the secondary cluster of seizures. After the treatment was administered, the patient's consciousness improved rapidly without seizures, and she had fully recovered by Day 8. EEG findings appeared normal on Day 9. A third brain MRI (DWI) performed on

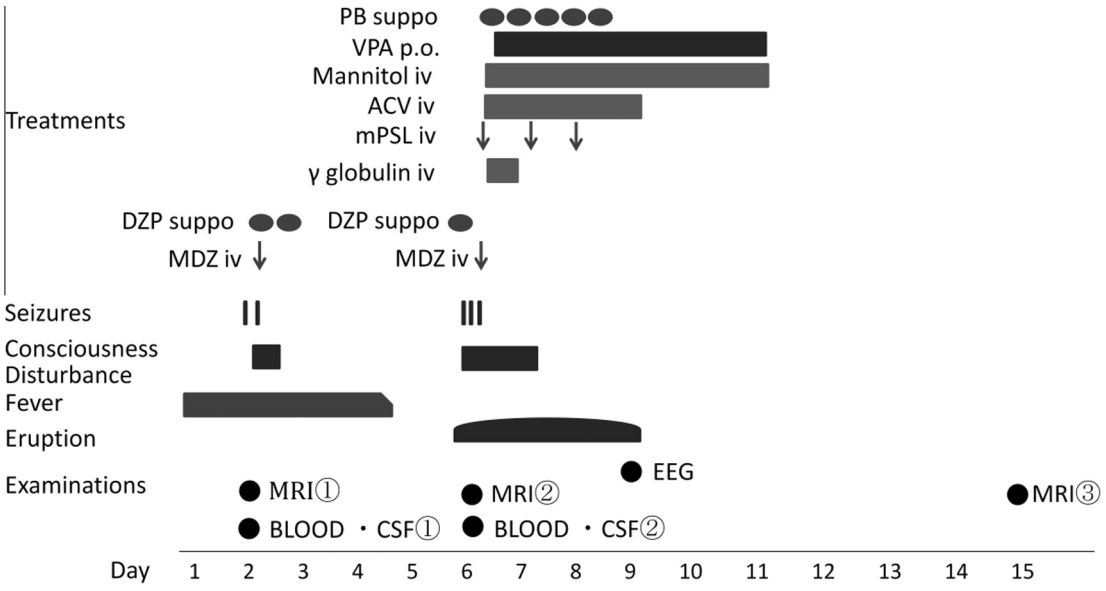

Fig. 1. Clinical course. EEG, electroencephalogram; BLOOD, blood examination; CSF, cerebrospinal fluid examination; MRI, magnetic resonance imaging; DZP, diazepam; suppo, suppository; MDZ, midazolam; PB, phenobarbital; VPA, valproate sodium; p.o., per os; iv, intravenous injection; ACV, acyclovir; mPSL, steroid pulse therapy.