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Case Report

Transient dysautonomia in an acute phase of encephalopathy with biphasic seizures and late reduced diffusion

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Abstract

Paroxysmal sympathetic hyperactivity (PSH) is a dysautonomic condition that is associated with various types of acquired brain injuries. Traumatic brain lesions have been documented as the leading cause of PSH. However, detailed clinical features of pediatric PSH caused by intrinsic brain lesions remain to be elusive. We present a 3-year-old boy, who had been diagnosed as having cerebral palsy, developmental delay and epilepsy after perinatal hypoxia-induced brain injury. He developed status epilepticus with fever on the third day of respiratory infection. Whereas the seizure was terminated by systemic infusion of midazolam, consciousness remained disturbed for the next 48 h. Serial magnetic resonance imaging studies revealed that acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) evolved on 3 days after the seizure. Therapeutic hypothermia was immediately introduced, however, the brain lesion extended to the whole subcortical white matters on day 8. The intermittent bilateral dilation of pupils with increased blood pressure and tachycardia were observed until day 12. Real-time monitoring of electroencephalograms ruled out the recurrent attacks of seizures. The abnormal signs of autonomic nervous system gradually ceased and never relapsed after recovery from the hypothermia. PSH or a transient condition of dysautonomia may emerge and persist during the acute phase of AESD.

Keywords: Dysautonomia; Paroxysmal sympathetic hyperactivity (PSH); Therapeutic hypothermia; Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD)

1. Introduction

Paroxysmal sympathetic hyperactivity (PSH) is a severe dysautonomic condition that is associated with acquired brain injuries. Diagnosis of PSH is made on increase in blood pressure, heart rate, respiratory rate, hyperthermia with diaphoresis, mydriasis, and dystonia

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[1,2]. Traumatic brain injury is the leading cause of these dysautonomic symptoms, whereas detailed clinical features caused by intrinsic lesions, including acute encephalitis in childhood, remain to be determined [3].

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is the most common form of encephalopathy among Japanese children [4]. The diagnosis of AESD can be made on typical 'bright-tree appearance' with diffusion-weighted images, which usually arise in the subcortical white matter at 3–9 days of illness, and present unfavorable prognosis with severe neurological sequelae [4,5].

We herein report a case with severe AESD, who showed transient signs of dysautonomia during the therapeutic hypothermia. This study demonstrates that PSH or dysautonomic conditions may emerge in association with an excessive inflammatory condition of the brain in childhood.

2. Case presentation

The patient was a 3-year-old male. He was born to healthy, non-consanguineous parents at 41 weeks with 3,012 g of birth weight. Severe asphyxia was noted at birth with an Apgar score of 2 at 5 min. As a neurological sequela, he developed cerebral palsy and spastic quadriplegia. The developmental quotient was evaluated to be 45 at 18 months of age. He experienced the first attack of generalized convulsive seizure at 2 years and 4 months of age, and began to take valproic acid thereafter. He was brought to the emergency department of our hospital for right hemi-convulsions with a precedent episode of viral infection. The seizure was terminated by infusions of diazepam and midazolam, whereas his consciousness did not recover during the next 48 h (Fig. 1A).

Serial brain MRI scans started to show the bright-tree appearance at the left parieto-occipital region on the 3rd day, which extended to the whole subcortical regions by the 7th day (Fig 1**B**). With an immediate diagnosis of AESD, methylprednisolone (30 mg/kg/-day × 3 days) and immunoglobulin (1 g/kg/-day × 2 days) were used. Therapeutic hypothermia at 34 °C was introduced with systemic infusions of midazolam (0.1 mg/kg/hour) and thiamylal (3.6 mg/kg/hour). On the 6th day, he started to show bilateral dilated pupils to 5.5 mm, which lasted intermittently for 1–2 h per each event. Coincidently, heart rates were increased to 120–130 bpm, and the systolic/diastolic blood pressures fluctuated between 110/60 and 180/100 mmHg. These signs were repeatedly triggered by the stimulation of endotracheal suctioning, and recurred several times a day until the 12th day of admission. During therapeutic hypothermia, he was kept deeply sedated with thiamylal under the control of mechanical ventilation. Epileptiform discharges were absent in the real-time electroencephalogram (EEG) monitoring even when these symptoms were present. Thus, epileptic seizures were unlikely to cause these symptoms. Serial studies on head computed tomography and blood tests further excluded the possibilities of elevated intracranial pressure, infection, and metabolic disorders. He was therefore diagnosed as having either PSH or a similar condition of dysautonomia. Rewarming from extended hypothermia started on day 17, and was completed without problems. His cardiac, respiratory conditions and autonomic functions fully improved, whereas severe brain dysfunctions were left as sequelae of acute encephalopathy. Because he is currently bed-ridden, surgical gastrostomy and tracheotomy is indicated for long-term home care.

3. Discussion

This is the first report demonstrating that autonomic dysfunctions should be considered as one of neurological complications in the acute phase of severe AESD. The diagnosis of PSH can be typically made with episodic increases in heart rate, systemic blood pressure, respiratory rate, temperature, sweating, muscle rigidity, motor activity and mydriasis [3,6]. Compared to these symptoms, our case showed only milder signs of PSH, lacking fever, tachypnea, sweating and muscle rigidity. Thus, the autonomic signs of the present case might be properly referred to as transient dysautonomia rather than as PSH. Nonetheless, we regarded his signs as those of PSH, considering the onset around the fifth day after the brain injury, repeated episodes 5 to 6 times a day with approximately 30 min of duration. We speculated that therapeutic hypothermia and sedatives contributed to modifying the symptoms and severity of PSH.

PSH is a common complication in severe traumatic brain injury [2]. Overall, 8–33% of cases with traumatic brain injuries were reported to show dysautonomic conditions including PSH, where the prevalence rates widely varied with damaged areas and sizes [6]. Recent reports have also shown that PSH may develop in association with non-traumatic brain lesions in childhood (Table S1). PSH or PSH-resembling dysautonomia was identified in 29–31% of cases with anoxic injury [7]. Children with encephalitis or meningoencephalitis have been also reported to trigger the onset of PSH although details in their clinical profiles remain to be clarified [3].

Earlier studies have proposed the two hypothetic models for the pathophysiology of PSH. First, brainstem excitatory centers might be released from the cortical and subcortical control. Second, excessive excitatory-inhibitory ratio at the- brainstem and spinal cord levels may produce this condition [1,8]. Our report supports the former hypothesis because the present case showed broad inflammatory lesions in the cerebral cortex and subcortical white matter, but not in the