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Original article

Clinical characteristics of acute encephalopathy with acute brain swelling: A peculiar type of acute encephalopathy

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Abstract

Objectives: Acute encephalopathy has been observed with acute brain swelling (ABS) that is characterized by rapid progression to whole-brain swelling. The objective of this study was to describe the clinical characteristics of ABS.

Methods: We encountered four patients with ABS and retrospectively investigated their clinical data with a medical chart review.

Results: Three patients had seizure clustering or status epilepticus in the clinical course. Signs of elevated intracranial pressure (ICP) appeared 3–9 h after the first convulsive attack in three patients. In all patients, signs of brainstem involvement appeared 1–8 h after signs of elevated ICP. Mild hyponatremia that progressed after signs of elevated ICP appeared was noted in three patients. Brain CT revealed mild brain swelling in the initial phase, which rapidly progressed to whole-brain swelling. No focal abnormalities were detected on brain MRI in one patient. Continuous electroencephalography was initially normal, but in two patients, high-amplitude slow waves appeared with rapid changes before signs of brainstem involvement. Although recovery was achieved without sequelae in two patients, outcome was fatal for the other two.

Conclusions: The pathogenesis of ABS has yet to be clarified, but clinical features in our patients are not consistent with any established subtypes of acute encephalopathy. Therefore, we believe that ABS should be recognized as a new type of acute encephalopathy.

Keywords: Acute brain swelling; Brain edema; Acute encephalopathy; Acute encephalitis; Hyponatremia; Electroencephalography

1. Introduction

Acute encephalopathy is a severe complication of common childhood infections such as influenza, exanthema subitum, and acute infectious gastroenteritis. It causes fever, seizures, and impaired consciousness and

Abbreviations: ABS, acute encephalopathy with acute brain swelling; ICP, intracranial pressure

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often shows abnormal findings in imaging studies. It frequently results in death or severe neurological deficits [1]. Acute encephalopathy with acute brain swelling (ABS) is a type of acute encephalopathy first proposed by Shiomi in 2003 [2]. Seizures and mildly impaired consciousness are observed in the initial phase. The next phase is characterized brain herniation that results in decreased blood pressure or respiratory arrest. Although brain swelling is reversible, patients may die of brain herniation if it progresses. When it responds to treatment, ABS can be cured without sequelae. However, the number of these case reports is small.

Here, we present the cases of four children with ABS who were treated in our center. This is the first report describing ABS in English. This paper has two aims: to establish ABS as a new subtype of acute encephalopathy by describing its clinical characteristics and to provide clinical information for early diagnosis and treatment.

2. Patients and methods

Based on medical records, we retrospectively examined patients who had been treated under an ABS diagnosis at our center between 2002 and 2011. The criteria for a diagnosis of ABS were as follows: (1) signs of elevated intracranial pressure (ICP) followed by signs of brainstem involvement within 24 h of neurological onset; (2) whole-brain swelling, including the cerebrum and cerebellum, without specific focal lesions on computed tomography (CT) or magnetic resonance imaging (MRI); (3) exclusion of similar diseases (i.e., known subtypes of acute encephalopathy or encephalitis, known metabolic diseases, or other conditions showing brain swelling caused by definite etiology). The following characteristics were supportive of an ABS diagnosis: (1) seizure clustering or status epilepticus following a viral febrile disease; (2) mild impaired consciousness after an initial seizure; (3) hyponatremia; (4) laboratory data showing no apparent hepatic or renal dysfunction or disseminated intravascular coagulation (DIC) before brain herniation; (5) complete recovery without sequelae or prognosis of death due to brain herniation. Signs of elevated ICP were a worsening level of consciousness, headache, vomiting. Signs of brainstem involvement were cerebellar ataxia, nystagmus, segmental myoclonus, tremor, cranial nerve paralysis, extension to pain, breathing abnormalities, pupillary dilatation, bilateral ptosis, and decerebrate and decorticate posturing [3].

Based on medical chart review, we retrospectively investigated clinical features, laboratory data, viral studies, neuroimaging data, electroencephalography, treatment, and prognosis of the patients with ABS. Informed consent for use and publication of clinical data was obtained from the parents of the patients.

3. Results

Four patients (1 male and 3 females) were diagnosed with ABS. Table 1 summarizes the clinical data. Ages ranged from 3 to 5 years (median: 4.5 years). Two patients had a history of simple febrile seizures, while one had a history of craniopharyngioma. Initial symptoms included fever in all patients, vomiting in two, and headache in one. Three patients had seizure clustering and/or status epilepticus in the clinical course. In Case 2, diazepam and midazolam (MDL) were intravenously injected to stop convulsive status epilepticus, and the patient subsequently fell asleep. In two patients, consciousness levels transiently returned to a Glasgow Coma Scale (GCS) level of 12–13 after the initial seizure. In three patients, signs of elevated ICP appeared 3–9 h after the first seizure. In Case 3, vomiting and headache had been already present when restlessness was suddenly observed. In all patients, signs of brainstem involvement appeared 1–8 h after signs of elevated ICP. Hyperosmolar therapy, invasive mechanical ventilation, barbiturate coma therapy and brain hypothermia therapy were performed for all patients. Two patients were monitored with insertion of ICP sensors and three were treated with intravenous methylprednisolone-pulse therapy, and one was treated with immunoglobulin therapy. Invasive mechanical ventilation was started at the onset of elevated ICP signs in Case 1, and at the onset of ventricular tachycardia and pulmonary edema in Case 3. In Cases 2 and 4, treatments were initiated after signs indicating brainstem involvement had appeared. Regarding outcomes, two patients with signs of brainstem involvement died, while the two were cured without sequela.

Regarding the initial laboratory data, mild hyponatremia was noted in three patients. Hyponatremia progression was observed in three patients after signs of elevated ICP appeared. Three patients showed increased white blood-cell count and C-reactive protein levels. Creatine kinase levels increased in two patients. No apparent hepatic or renal dysfunction was noted in the initial laboratory data of any patient. No patient developed hypoglycemia, hyperammonemia, or marked acidosis. Cerebrospinal fluid was examined in one patient and no abnormalities were detected. Influenza A in two patients and coxsackievirus B type 3 in one patient were detected as related pathogens. Repeated brain CT was performed on all children (Fig. 1). Three patients exhibited mild brain swelling in the initial phase that subsequently progressed rapidly to whole-brain swelling, with disappearance of the cistern around the brainstem and brain sulci. Case 3 already showed whole-brain swelling in the initial phase that resolved the next day. MRI was performed on one patient before signs of brainstem involvement. Although whole-brain swelling was observed, neither a diffusion-weighted image nor

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