Brain & Development 38 (2016) 731–737

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Short and long-term outcomes in children with suspected acute encephalopathy

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Received 11 September 2015; received in revised form 21 February 2016; accepted 22 February 2016

Abstract

Background: The time-dependent changes that occur in children after acute encephalopathy are not clearly understood. Therefore, we assessed changes in brain function after suspected acute encephalopathy over time.

Methods: We created a database of children admitted to the pediatric intensive care unit at Kobe Children's Hospital because of convulsions or impaired consciousness with fever between 2002 and 2013. Clinical courses and outcomes were reviewed and patients who met the following criteria were included in the study: (1) 6 months to 15 years of age, (2) no neurological abnormality before onset, (3) treated for suspected acute encephalopathy, and (4) followed after 1 (0–2) month and 12 (10–17) months of onset. Outcomes were assessed using the Pediatric Cerebral Performance Category (PCPC) scale, with a score of 1 representing normal performance; 2, mild disability; 3, moderate disability; 4, severe disability; 5, vegetative state; and 6, brain death.

Results: A total of 78 children (32 male) with a median (range) age at onset of 20 (6–172) months were enrolled. Fifty-one cases scored 1 on the PCPC, 13 scored 2, three scored 3, five scored 4, one scored 5, and five cases scored 6 at discharge. Whereas seven of the 13 cases that scored a 2 on the PCPC recovered normal brain function after 12 months, none of the nine cases that scored a 3–5 on the PCPC recovered normal function.

Conclusions: Our findings suggest moderate to severe disability caused by acute encephalopathy had lasting consequences on brain function, whereas mild disability might result in improved function.

Keywords: Acute encephalopathy; Outcome; PCPC; Status epilepticus; Children; Sequelae

1. Introduction

Acute encephalopathy is one of the most serious causes of mortality and neurological sequelae in children [1]. In fact, the biggest epidemiological observational study ever conducted in Japan reported that 43.8% of

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http://dx.doi.org/10.1016/j.braindev.2016.02.011
0387-7604/

children with acute encephalopathy resulted in neurological sequelae or deaths [2]. On the basis of clinical, radiological, and pathological features, acute encephalopathy is classified into several syndromes, such as acute encephalopathy with biphasic seizures and late reduced diffusion (AESD), acute necrotizing encephalopathy (ANE), or hemorrhagic shock and encephalopathy syndrome (HSES) [1,3–5]. The prognoses associated with these different syndromes vary, with prognoses of ANE or HSES being serious in which the rates of sequelae are 67–86% or 81–90%, respectively [2,5–8]. The prognoses of children with AESD are also poor, as 71% of reported in the epidemiological observation resulted in neurological deficits, whereas 90% of children with clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) achieved a full recovery [2]. In these previous studies, the outcomes of acute encephalopathy were assessed in various ways; several studies were conducted without any scales [2,5,8], whereas the other studies were conducted with the Pediatric Cerebral Performance Category (PCPC) scale, which was developed for measurement of cognitive disability after critical illness or injury in children [6,9–11]. However, at present, the assessment of time-dependent changes in outcome using a scale to measure brain function after acute encephalopathy in children has yet to be established. The objective of this study, therefore, was to assess changes in brain function over time using the PCPC scale in children with suspected acute encephalopathy.

2. Subjects and methods

We created a database of children admitted to the pediatric intensive care unit (PICU) at the tertiary referral hospital, Kobe Children's Hospital, because of convulsion or impaired consciousness with fever between October 2002 and October 2013. Of the original cohort, we reviewed clinical courses and outcomes of children who were treated for suspected acute encephalopathy, including [12,13] those who (1) were aged between 6 months and 15 years, (2) had seizure with fever ($\geqslant$38.0 °C) with or without convulsions, and (3) exhibited refractory status epilepticus (RSE) and/or prolonged neurological abnormality and/or aspartate aminotransferase (AST) levels >90 IU/l within 6 h of onset. RSE was defined as a seizure or a sequence of intermittent seizures lasting 60 min or longer without fully regaining consciousness despite appropriate antiepileptic drug therapy. Prolonged neurological abnormality was established by a Glasgow Coma Scale (GCS) score of <15 or the development of hemiplegia 6 h after onset [13]. The subject group contained cases that had initially been suspected to have acute encephalopathy, but that had neither sequelae nor impaired consciousness lasting longer than 24 h. To assess brain function over time, we included children that were followed both after 1 (0–2) month and 12 (10–17) months of onset. Cases with a history of neurological issues (epilepsy, chromosomal abnormality, brain hemorrhage, hydrocephalus, history of intracranial surgery, or mental retardation) or cases with cerebrospinal fluid pleocytosis (>8/μL) including encephalitis or meningitis were excluded. Consequently, 78 children were included as subjects of this study.

We assessed outcomes of the subjects at discharge, as well as 1 and 12 months after onset. The period of 1 month after onset was defined as the range between 0 and 2 months, and the period of 12 months after onset was defined as the range between 10 and 17 months. In cases where children were assessed a few times in the same period, the closest time to 1 month or 12 months post-initial neurological symptom was reviewed. Neurological performances at each period were assessed by a pediatric neurologist using the PCPC scale [9,10], with a score of 1 representing normal performance; 2, mild disability; 3, moderate disability; 4, severe disability; 5, a persistent vegetative state; and 6, death. PCPC scores were obtained through direct questions about a child's ability to perform age-appropriate behaviors, as well as cognitive or physical disabilities. The validity of the score of PCPC was re-evaluated by two or more pediatric neurologists before being registered to the original database. Grading on the PCPC scale is difficult in infants, especially for scores of 2 or 3; therefore, we used the following indications to improve PCPC grading in this population: PCPC 2, children with some neurological problems but probably attend regular classes in the future; PCPC 3, children with difficult to attend regular classes; PCPC 4, children needing daily support such as tubal feeding. Cases with epilepsy and normal cognitive function were categorized as PCPC 2. Along with the record of PCPC at each point, we evaluated the concordance rate for outcomes at 1 and 12 months after suspected acute encephalopathy onset.

This study was approved by the local ethical committee of Kobe Children's Hospital, which stated that no patient consent was needed by nature of the observational design of this study.

3. Results

3.1. Baseline subject demographics

Of the 78 children, 32 were male (Table 1). The median (range) age of the children when they were admitted to the PICU at Kobe Children's Hospital was 20 (6–172) months. RSE and prolonged neurologic abnormality was observed in 45 and 71 children, respectively. The most common preceding infection was influenza virus, and the second was human herpes virus 6/7. Regarding treatment, the number of children that underwent