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Original article

Long-term outcomes in motor and cognitive impairment with acute encephalopathy

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Abstract

Background: Acute encephalopathy causes various sequelae, including motor disabilities and intellectual delays. Previous studies reported that cognitive impairments can also occur after acute encephalitis. Although the incidence of acute encephalopathy is high in Japan, there have been few reports on its sequelae.

Objective: To characterize the neurological outcomes of pediatric patients who sought motor rehabilitation for motor dysfunction after acute encephalopathy.

Method: Subjects were 26 children who were healthy before suffering from motor dysfunction following acute encephalopathy and were referred to our pediatric rehabilitation institute during a 9-year period (August 2007–April 2017). We examined subjects' neurological status and followed sequelae for at least 8 months.

Results: Of 26 individuals, 21 became ambulatory after several months or years during the observation period. Patients who could sit without support within 5 months after the onset of acute encephalopathy were able to walk within several months or years. Patients showing high intensity on T2-weighted sequences or "bright tree appearance" in the frontal region took an average of 7 months to develop walking, which was longer than other patients. Among ambulatory subjects, 16(76%) exhibited mild to moderate intellectual delay with a developmental quotient (DQ) under 70, and 20 (95%) exhibited cognitive impairment. There was a significant correlation between DQ scores and motor disability ($p = 0.013$, $r = -0.481$).

Conclusions: Although 80% of patients who had motor dysfunction caused by acute encephalopathy and visited out motor rehabilitation outpatient clinic were eventually able to walk, the time taken to develop walking ability depended on which region exhibited magnetic resonance imaging abnormalities. DQ scores and motor disability were significantly correlated.

Keywords: Acute encephalopathy; Sequelae; Cognitive impairment; Outcome

1. Introduction

Acute encephalopathy is defined as acute brain dysfunction with impaired consciousness, often accompanied by seizures [1]. Although the disease is common in Asian countries, including Japan, only a few cases have been reported outside Asia [2].

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In Japan, a research committee formed by the Japanese government studied the epidemiology of acute encephalopathy [3]. A total of 983 patients with acute encephalopathy were enrolled in the research study over 3 years. According to the syndrome classification, acute encephalopathy with biphasic seizures and reduced diffusion (AESD) is the most common syndrome (28.7%), followed by mild encephalitis/encephalopathy with reversible splenial lesion (MERS) (15.6%), and acute necrotizing encephalopathy (ANE) (4%). The influenza virus is the most common pathogen associated with acute encephalopathy (27%), followed by HHV-6 (17%) and rotavirus (4%).

Several previous studies have examined the sequelae of acute encephalopathy. Some studies have reported a relationship between blood tests and the outcomes of motor disability, and have investigated the prognostic factors underlying acute encephalopathy [4–7]. In a study of the time-dependent changes of acute encephalopathy, Nishiyama et al. administered the Pediatric Cerebral Performance Category (PCPC) at two time points (1 month after the onset of acute encephalopathy, and 12 months later) [8]. Their findings suggested that differences in PCPC scores were associated with the extent of sequelae. In addition, Lee reported that AESD patients with severe motor disability more frequently exhibited coma or involuntary movements, including dystonia and oral dyskinesia before the second phase, compared with a non-severe group [9]. To the best of our knowledge, few reports have examined time-dependent motor recovery in acute encephalopathy [8]. Moreover, although there have been reports on cognitive sequelae with acute encephalitis, none of these studies examined acute encephalopathy [10–13]. In the current study, we examined the characteristics and degree of cognitive impairments in addition to the timing of motor function recovery, to clarify the issues described above.

2. Subjects and methods

2.1. Setting and participants

Study subjects consisted of 26 pediatric patients who were referred to our pediatric rehabilitation institute over a 9-year period (August 2007–April 2017) with the chief complaint of motor dysfunction. Acute phase encephalopathy is not treated at our institute, so all patients were referred to us after initial treatment for acute encephalopathy once they were stable (i.e., more than 2 months after onset).

The study inclusion criteria were: 1) no evident neurological abnormalities before acute encephalopathy; 2) had suffered acute encephalopathy; and 3) exhibited motor dysfunction as neurological sequelae.

3. Determination of acute encephalopathy

Acute encephalopathy was diagnosed by: a) delayed recovery of decreased consciousness concomitant with fever or convulsion; and b) abnormalities in diffusion-weighted magnetic resonance imaging (MRI), such as bright tree appearance (BTA) [4]. When neurological manifestations suggest encephalitis but inflammatory cells are not found in the brain or cerebral spinal fluid (CSF), the condition is identified as encephalopathy [14].

We classified the syndrome types according to the following criteria [3]: 1) AESD; 2) acute encephalopathy following status epilepticus (SE) (in this case, the clinical course is monophasic); 3) hemiconvulsion-hemiplegia-epilepsy syndrome (HHES); 4) acute necrotizing encephalopathy (ANE); and 5) unclassified (absence of epilepsy but delayed recovery of consciousness and abnormalities on MRI) [3].

4. Measurements

Motor dysfunction severity was classified into three types, according to the following motor function ability criteria: 1) normal or mild disability (walking without support); 2) moderate (sitting without support); or 3) severe (bedridden) at the time the patients visited our institute, and during the follow-up period. We determined the type of acute encephalopathy and associated viral infection from medical charts. We also examined the clinical course of motor function and the presence/absence of cognitive impairment. If there was cognitive impairment, three experienced pediatric neurologists (YM, JS, or NO), an occupational therapist and a clinical psychologist diagnosed the impairment type. In addition, we determined the relationship between the severity of motor dysfunction and developmental quotient (DQ) scores. We measured DQ scores using the Enjoj infant analytical development examination table, the Kyoto scale of psychological development (2001), and the Tanaka-Binet intelligence test. We used the most recent DQ score and the most recent motor disability score measured during the follow-up period to analyze each relationship. We recorded the onset of acute encephalopathy, sex and follow- up period. The results are reported as the mean ± standard deviation and percentages.

This study was approved by the ethics committees of the Tochigi Rehabilitation center.

4.1. Statistical analysis

We analyzed the correlation between motor disability (1: mild, 2: moderate, 3: severe) and DQ scores. Motor dysfunction severity was treated as an ordinal scale measurement in the analysis. In the 21 ambulant patients, we also analyzed the relationship between the duration of

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