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Original article

Prognostic factors for acute encephalopathy with bright tree appearance

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Abstract

Objective: To determine the prognostic factors for encephalopathy with bright tree appearance (BTA) in the acute phase through retrospective case evaluation. *Methods:* We recruited 10 children with encephalopathy who presented with BTA and classified them into 2 groups. Six patients with evident regression and severe psychomotor developmental delay after encephalopathy were included in the severe group, while the remaining 4 patients with mild mental retardation were included in the mild group. We retrospectively analyzed their clinical symptoms, laboratory data, and magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) findings. *Results:* Patients in the severe group developed subsequent complications such as epilepsy and severe motor impairment. Univariate analysis revealed that higher maximum lactate dehydrogenase (LDH) levels ($p = 0.055$) were a weak predictor of poor outcome. Maximum creatinine levels were significantly higher ($p < 0.05$) and minimal platelet counts were significantly lower ($p < 0.05$) in the severe group than in the mild group. Acute renal failure was not observed in any patient throughout the study. MRS of the BTA lesion during the BTA period showed elevated lactate levels in 5 children in the severe group and 1 child in the mild group. MRI performed during the chronic phase revealed severe brain atrophy in all patients in the severe group. *Conclusions:* Higher creatinine and LDH levels and lower platelet counts in the acute phase correlated with poor prognosis. Increased lactate levels in the BTA lesion during the BTA period on MRS may predict severe physical and mental disability.

Keywords: Acute encephalopathy; Acute encephalopathy with biphasic seizures and late reduced diffusion; Bright tree appearance; Prognostic factors; Creatinine; Magnetic resonance spectroscopy; Lactate peak

1. Introduction

Acute encephalopathy with bright tree appearance (BTA), originally described by Shiomi et al. [1], is the most frequently diagnosed form of encephalopathy in Japanese pediatric emergency medicine. Two recent case

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studies reported acute infantile encephalopathy predominantly affecting the frontal lobes and acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) in non-Japanese patients; therefore, it seems that this clinical entity is not limited to the Japanese population [2,3]. Acute encephalopathy is typically characterized by a biphasic clinical course. It usually begins with status epilepticus and a mild symptomatic period of 2–3 days, followed by a cluster of seizures accompanied by a decreased level of consciousness. During this period, diffusion-weighted images obtained by magnetic resonance imaging (MRI) show strong signal intensities in the subcortical regions, referred to as BTA [1]. Few atypical types of acute encephalopathy with BTA have been described, including cases with altered consciousness but no status epilepticus or cases with a monophasic clinical course [4,5]. No standard treatment has been described for this entity, although glutamatergic excitotoxicity was proposed as its main pathomechanism [6]. Sequelae may include mild to severe motor and intellectual disability and epilepsy. The prognostic factors for acute encephalopathies, including one case with BTA, have been reported as a decrease in platelet count; an increase in aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase (CK), lactate dehydrogenase (LDH), and creatinine (Cr) levels; and abnormal blood sugar levels and clotting times [5,7,8]. Here we retrospectively examined the prognostic values of several serum markers, changes in these markers during the acute stage, and the findings of magnetic resonance spectroscopy (MRS) of the BTA lesion during the BTA period.

2. Methods

The participants included 10 patients with acute encephalopathy and BTA who were admitted to Osaka University Hospital from 2003 to 2012. Eight of the patients presented with fever and status epilepticus, which continued for over 30 min on day 0. MRS confirmed the presence of BTA from the 3rd to the 9th day of the illness. The other 2 patients did not present an obvious convulsive event; however, 1 of them presented with loss of consciousness, and BTA was confirmed in this patient on the 6th day. The other patient was transferred to the emergency room with loss of consciousness and respiratory arrest, and BTA was confirmed on the 8th day. For the 10 participants, we retrospectively examined the clinical history, clinical features, changes in different serum marker levels, and brain MRI findings.

Evaluation of clinical history included the patient's underlying condition, any past history of febrile convulsions, neurological status before encephalopathy, type of infectious disease, existence of a biphasic course, length of the latency period between fever onset and encephalopathic episode onset, duration of primary status epilepticus, specific medication used to cease convulsions and sedate, use of any prescribed antiepileptic agents during the acute phase, and history of specific treatment for acute encephalopathy. Neurological outcome was evaluated 1 year after the onset of encephalopathy. The intelligence or development quotient was not accurately estimated by developmental tests in most patients. Therefore, the severity of cognitive impairment was estimated and classified as follows: normal or mild if the patient could utter some meaningful words (for patients aged 12–24 months) or have a simple conversation (for patients aged >24 months), moderate if a patient could utter a few meaningful words (for patients aged >24 months), and severe if a patient could not utter meaningful words. For patients aged >12 months, the severity of motor impairment (MI) was estimated and classified as follows: normal or mild if the patient could walk without support, moderate if the patient could sit without support but not walk without support, and severe if the patient could not sit without support. The neurological status of patient 6, who presented with an underlying disease before encephalopathy, was not evaluated according to these criteria because the patient was aged <12 months. This patient could babble and hold the head upright but could not turn over unassisted before encephalopathy. We estimated that the patient had moderate mental retardation (MR) and MI. We divided patients into 2 groups according to the severity of encephalopathy, namely severe and mild groups, on the basis of the patient's neurological status at 1 year after the onset of encephalopathy. The mild group included patients with mild cognitive and/or mild motor impairment. The severe group included patients with a more severe neurological impairment. Therefore, 6 patients were included in the severe group and 4 patients in the mild group.

Blood samples were obtained during convulsions, immediately after the end of convulsions, or immediately after arrival at the hospital for patients without convulsions. We investigated the maximum and minimum values and any changes observed during the first 20 days in several serum marker levels. These markers included blood cell counts and AST, ALT, LDH, CK, blood urea nitrogen (BUN), Cr, sodium, potassium, chloride, total protein content, albumin, and blood sugar levels.

Brain imaging findings for the acute phase and chronic phase were examined >7 months later by performing MRI using a 1.5T Signa HD (GE Healthcare, Milwaukee, WI) system with a standard head coil. MRS [point-resolved spectroscopy sequence (PRESS): repetition time/echo time, 1800/136] was subsequently performed on BTA detection, and the region of interest was marked on the BTA lesion. Model information and condition of acquisition was not confirmed in patients 2 and 6. On MRS, we examined the peak of lactate and