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Original Article

Thalamic Lesions in Acute Encephalopathy With Biphasic Seizures and Late Reduced Diffusion

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ABSTRACT

BACKGROUND: We aimed to assess the characteristics of thalamic lesions in children with acute encephalopathy with biphasic seizures and late reduced diffusion. **METHODS:** Using the Tokai Pediatric Neurology Society database, we identified and enrolled 18 children with acute encephalopathy with biphasic seizures and late reduced diffusion from 2008 to 2010. Using diffusion-weighted images, we identified patients with thalamic lesions and compared their clinical factors with those of patients without thalamic lesions. We analyzed the time sequence of thalamic, sucortical, and cortical lesions. To study the topography of thalamic lesions, we divided the thalamus into five sections: anterior, medial, anterolateral, posterolateral, and posterior. Subsequently, we analyzed the relationship between the topography of thalamic lesions and the presence of central-sparing. **RESULTS:** Seven children presented with symmetrical thalamic lesions associated with bilateral subcortical or cortical lesions. No statistical difference in the clinical features was observed between individuals with and without thalamic lesions. These lesions were observed only when subcortical or cortical lesions were present. In 5 children, thalamic lesions were present in bilateral anterior or anterolateral sections and were associated with subcortical or cortical lesions in bilateral frontal lobes with central-sparing. In the other two children, thalamic lesions were extensive and accompanied by diffuse subcortical and cortical lesions without central-sparing. **CONCLUSION:** Thalamic lesions in patients with acute encephalopathy with biphasic seizures and late reduced diffusion involve the anterior sections. The thalamocortical network may play a role in development of thalamic lesions in patients with acute encephalopathy with biphasic seizures and late reduced diffusion.

Keywords: acute encephalopathy, acute encephalopathy with biphasic seizures and late reduced diffusion, thalamic lesion, diffusion weighted image, thalamocortical system

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Introduction

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a newly proposed type of acute encephalopathy presenting with biphasic seizures and unique abnormality in diffusion-weighted images (DWI).[1,2] Typical AESD presents a unique time sequence of DWI. At

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the onset, prolonged seizures occur, but no abnormalities are observed on DWI; subsequently, the patient experiences late clustering seizures and impaired consciousness, and reduced diffusion in the subcortical white matter is observed on DWI. Subsequently, reduced diffusion in the cortex overlying the affected subcortical white matter appears, whereas the reduced diffusion in the subcortical white matter disappears within 1-2 weeks. A previous report demonstrated that reduced diffusion in the cortex may occasionally appear before the reduced diffusion in the subcortical white matter.[3]

There are several characteristic DWI features in AESD. Central-sparing lesions, which refer to the lack of reduced diffusion around the bilateral sylvian fissures, have been known as a significant neuroimaging feature of AESD.[4] In addition, several reports demonstrated that some children with AESD present with reduced diffusion in the thalamus as well during the acute phase of AESD.[3,5-7] Although thalamic lesions are frequently observed in AESD, fewer studies of thalamic lesions in AESD are published in the literature than studies of DWI abnormalities in the subcortical or cortical regions. Therefore, our aim was to assess the characteristics of thalamic lesions in AESD patients and analyze the time sequence and topography of the thalamic lesions and their relation to subcortical or cortical lesions during the acute phase of AESD.

Patients and Methods

Patients

AESD was defined as acute encephalopathy with seizure onset, biphasic clinical course, and widespread reduced diffusion in the subcortical white matter involving unilateral or bilateral hemispheres.[1,2] There is general consensus about typical AESD, although AESD has no definite diagnostic criteria thus far. Inclusion criteria for this study were consistent with previous reports: (1) neurologically normal before the onset of AESD; (2) AESD onset with seizure by the day after fever onset; (3) subsequent transient improvement in consciousness after the onset of AESD; (4) recurrence of seizure after ≥24 hours after the onset of AESD followed by impairment of consciousness; and (5) widespread reduced diffusion in the subcortical white matter involving unilateral or bilateral hemispheres marked at the time of recurrent seizure.[2,8,9] Between June 2008 and September 2010, we searched the Tokai Pediatric Neurology Society database and enrolled 18 children with AESD. The Tokai Pediatric Neurology Society consists of pediatric neurologists from Nagoya University, Juntendo University, Nagoya City University, and the hospitals affiliated with these universities. This study was approved by the Ethics Committee of Nagoya University Graduate School of Medicine.

The following clinical data were investigated: age at diagnosis, sex, past history or family history of febrile seizure, prodromal illness, presence of unclear consciousness 24 hours after onset, presence of status epilepticus at the onset, and the neurodevelopmental outcome. A status epilepticus was defined as a seizure lasting for 30 minutes or more. Neurodevelopmental outcome was considered poor when the patient had an intelligence or development quotient <50 or was unable to walk without support. For most patients, the intelligence or development quotient was clinically estimated by the attending pediatric neurologists, although in some instances, Wechsler Intelligent Scales for Children were used.

Examination of thalamic lesions

Individuals with thalamic lesions underwent further analyses using DWI. To analyze the time sequence of the thalamic lesions, all serial DWI taken within 20 days of the onset were analyzed. Each image was analyzed to detect the presence of reduced diffusion in the subcortical or cortical region and thalamus (Fig 1).

The topography of the thalamic lesion was divided into five sections:[1] the anterior section including the anterior nuclear group and ventral anterior nucleus,[2] the medial section including the medial nuclear group,[3] the anterolateral section including the lateral dorsal nucleus and ventral lateral nucleus,[4] the posterolateral section including the ventral posterior nucleus, and[5] the posterior section including mainly the pulvinar[10,11] (Fig 1). The atlas of Morel used in our study was also used in a previous pediatric study that analyzed thalamic lesions in neonates with total asphyxia.[12] Further thorough identification of the thalamic subnuclei was difficult because of the insufficient resolution of routine DWI. When the thalamic lesion was marked in more than one magnetic resonance imaging (MRI) series (in repeated MRI) within 20 days of the onset, the distribution of the thalamic lesion was analyzed using the MRI series, and the thalamic lesion was found to occupy the largest area. To evaluate the relation between the topography of the thalamic lesions and subcortical or cortical lesions, the lobes with reduced diffusion in the subcortex or cortex and presence or absence of central-sparing were marked.

Statistical analysis

Statistical analyses were conducted using the Mann-Whitney *U* test and the Fisher exact probability test and the SPSS software, version 20 for Windows (SPSS Inc, Chicago, IL). A *P* value <0.05 was considered statistically significant.

Results

Patient characteristics

Among the 18 children, thalamic lesions were identified on DWI in seven children (39%) during the acute phase. None of the patients presented with reduced diffusion in the cortex before presentation in the subcortical white matter. Characteristics of patients with and without thalamic lesions are listed in Table 1. The neurodevelopmental outcome was evaluated at a median of

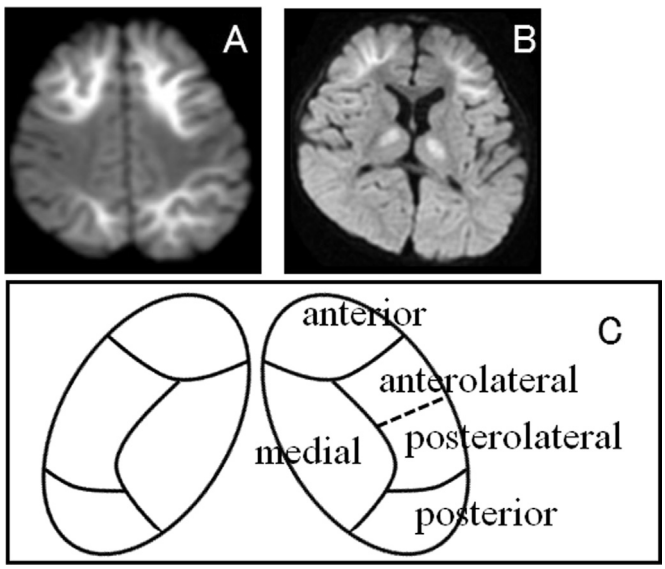

FIGURE.
Diffusion-weighted imaging (DWI) and the schema of Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD). (A) DWI depicts AESD with central-sparing. (B) DWI depicts AESD with thalamic lesions. (C) The schema presents the topography of thalamic lesions.