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Original article

Differences between periventricular hemorrhagic infarction and periventricular leukomalacia

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Abstract

Purpose: To clarify the differences between infants with periventricular hemorrhagic infarction (PVHI) and those with periventricular leukomalacia (PVL). *Methods:* We retrospectively evaluated the clinical features, ultrasonography, and electroencephalogram (EEG) findings in 22 preterm infants with PVHI and 49 with PVL. EEG and cranial ultrasonography were serially performed in all participants starting immediately after birth. Acute and chronic stage EEG abnormalities were evaluated separately. *Results:* Gestational age and birth weight were significantly lower in infants with PVHI than those with PVL. EEGs were normal in the majority of infants with PVHI on days 1–2. However, EEG abnormalities appeared after ultrasonography abnormalities. The majority of infants with PVL showed acute-stage EEG abnormalities on days 1–2. The rate of infants with acute-stage EEG abnormalities decreased with age, whereas the rate of infants with chronic-stage EEG abnormalities increased with age. Normal EEG before ultrasonography abnormalities was more common in infants with PVHI than in those with PVL. However, deterioration of acute-stage EEG abnormalities was more frequent in infants with PVHI than in those with PVL. *Conclusions:* PVHI was presumed to cause mostly postnatal injury, whereas PVL was presumed to cause mostly pre-or perinatal injury.

Keywords: Periventricular hemorrhagic infarction; Periventricular leukomalacia; Electroencephalography; Gestational age; Timing of brain injury

1. Introduction

Advances in perinatal medicine have succeeded in improving survival rates in preterm infants. However, neurological and/or behavioral problems are not uncommon in survivors. Several studies have revealed the relationship between white matter lesions and neurological sequelae in preterm infants [1–5]. Two types of well-defined white matter injury in preterm infants are closely related to neurological sequelae: periventricular hemorrhagic infarction (PVHI) and periventricular leukomalacia (PVL). The cranial ultrasonography (US) findings in patients with PVHI and PVL are quite different. Periventricular intraparenchymal echodensity (IPE) occurs mostly 1–3 days after birth in infants with PVHI,

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whereas cystic changes in deep white matter are observed in infants with cystic PVL at 1–3 weeks following periventricular echodensities (PVEs) seen at 2–7 days of age. However, the differences in the pathogenesis of PVHI and PVL are incompletely understood.

Electroencephalography (EEG) is a powerful and sensitive tool for assessment of brain injury in preterm infants [6]. Several reports have shown that abnormal EEG findings are frequent in infants with PVHI and PVL [7–10]. Our previous studies showed that EEG abnormalities differ according to the time course of brain injury [6]; acute-stage EEG abnormalities (ASAs) reflect the suppression of EEG activities immediately after acute brain insults, and chronic-stage EEG abnormalities (CSAs) reflect irreversible brain lesions during the recovery phase [6]. Moreover, we investigated the timing of brain injury based on serial EEG findings beginning immediately after birth [11].

Although PVHI and PVL are both white matter injuries in preterm infants, differences in their pathogenesis can occur. We compared clinical and serial EEG findings between preterm infants with PVHI and PVL to clarify the differences between the two representative brain lesions, particularly in terms of the timing of brain injury.

2. Materials and methods

This study was approved by the ethical committee of the Nagoya University Graduate School of Medicine. From the parents of the infants, we obtained written informed consent for the clinical and research use of EEG, neuroimaging, and demographic data. We reviewed the hospital records of infants (gestational age, 23–32 weeks) with PVHI and cystic PVL who were admitted to Nagoya University Hospital and its four affiliated hospitals during 2000–2008. Because determination of the timing of brain injury was important, infants with PVHI were enrolled when at least one EEG had been recorded before the appearance of US abnormalities. Infants who had chromosomal abnormalities, multiple congenital anomalies, or both PVHI and cystic PVL were excluded. Finally, 22 infants with PVHI and 49 with cystic PVL were enrolled. Eighteen infants with PVL were included in our previous study [12].

PVHI and PVL were diagnosed based on US and MRI findings. PVHI was diagnosed when fan-shaped high echodensities continuing from an intraventricular hemorrhage were observed in the unilateral deep white matter. PVL was diagnosed when PVEs followed by cystic changes with a diameter $\geqslant 3$ mm were observed in bilateral deep white matter. PVEs were judged to be present when white matter was brighter than or of equal brightness to that of the choroid plexus. We routinely performed cranial US at least every 3 days during the first 2 weeks of life, and then once per week until discharge. US was performed by attending neonatologists or neurologists blinded to EEG data. Coronal and sagittal sections through the anterior fontanelle were examined using 7.5 Hz sector transducer. Follow-up magnetic resonance imaging (MRI) was performed at 1–2 years of corrected age in all patients who survived. We obtained at least axial T1-weighted, T2-weighted and fluid-attenuated inversion recovery images, and sagittal T1-or T2-weighted images. MRI findings were interpreted in experienced pediatric neurologists blinded to US and EEG findings. Porencephalic changes continuing in the lateral ventricle were observed in infants with PVHI. Ventriculomegaly, with irregular ventricular walls and abnormal high intensities on T2-weighed images in the surrounding areas, was seen in infants with PVL.

We collected the following clinical data: gestational age, birth weight, singleton or twin, Apgar score, mode of delivery, premature rupture of membranes, clinical chorioamnionitis (maternal fever accompanied by elevated maternal C-reactive protein and/or fetal tachycardia), mechanical ventilation, pH and base excess on initial blood gas analysis, and early death. The clinical, ultrasonographic, and EEG data were collected anonymously. EEG confirmed neonatal seizures were observed in 1 infant with PVHI and in 2 with PVL. In these infants, phenobarbital was administered after the EEG recording. No infants had received antiepileptic drugs or sedatives at least few hours before EEG recordings.

EEG is routinely recorded in our hospitals to assess brain injury. We obtained informed consent for EEG examinations. EEG was recorded polygraphically at the bedside for 40–90 min using bipolar montage with eight surface electrodes (AF3, AF4, C3, C4, O1, O2, T3, and T4), according to the international 10–20 system. All EEGs were performed during spontaneous sleep. AF3 and AF4 were located halfway between Fp1 and F3 and between Fp2 and F4, respectively. Generally, the first EEG was recorded within 48 h of life. When an infant was born on a weekend day or a holiday, the first EEG was recorded on the third or fourth day of life. The second EEG was obtained between days 5 and 14, the third between days 15 and 28, and subsequent EEGs were obtained at 4-week intervals until discharge. When profound deterioration of general condition occurred, additional EEG recordings were performed at the request of the attending physician. All EEGs were independently interpreted by at least two of experienced pediatric neurologists (TT, AO, HK, FH, TKu, KM, and TKa) blinded to US findings. When the interpretations of raters differed, EEG findings were determined by consensus.

ASAs and CSAs [6,12] (Fig. 1), were the EEG abnormalities evaluated in this study. When an acute and strong brain insult has occurred, EEG activity shows