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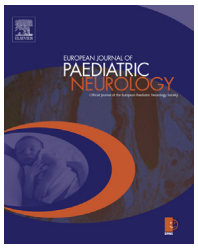

Original article

Clinical and neuroimaging findings in children with posterior reversible encephalopathy syndrome

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ABSTRACT

Objective: To clarify the clinical and radiological spectrum of posterior reversible encephalopathy syndrome (PRES) in children, and to identify the prognostic factors.
Methods: The records of 40 children with PRES were reviewed. Acute clinical symptoms, MRI including apparent diffusion coefficient (ADC) maps in the acute and follow-up periods and neurological sequelae, including epilepsy, were noted.
Results: Age at onset ranged from 2 to 16 years. Underlying disorders were hematological or neoplastic disorders ($n = 20$), renal diseases ($n = 14$) and others ($n = 6$). In the acute period, 31 patients had seizures, 25 had altered consciousness, 11 had visual disturbances and 10 had headache. Of 29 patients who had ADC maps in the acute period, 13 had reduced diffusivity as shown by ADC within PRES lesions. Of 26 patients with follow-up MRI, 13 had focal gliosis or cortical atrophy. No patients had motor impairment, and four patients had focal epilepsy. No clinical variables were associated with focal gliosis or cortical atrophy on

Abbreviations: PRES, posterior reversible encephalopathy syndrome; MRI, magnetic resonance images; ADC, apparent diffusion coefficient; DWI, diffusion-weighted images; FLAIR, fluid attenuated inversion recovery; EEG, electroencephalogram; T2WI, T2-weighted images.

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follow-up MRI, but lesional ADC reduction in the acute period was prognostic for focal gliosis or cortical atrophy on follow-up MRI ($p = 0.005$).
Conclusions: To the best of our knowledge, this is the largest cohort study to date involving PRES in children. Acute symptoms in pediatric patients are similar to those reported in adults, but altered consciousness was more frequent in children. Lesional ADC reduction in the acute period was common and was a good predictor of later, irreversible MRI lesions.

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological syndrome that is characterized by a potentially reversible vasogenic edema of white matter and cortex with a predilection for parenchyma supplied by the posterior circulation in the central nervous system. It was first described by Hinchey et al. in 1996.[1] A variety of clinical conditions can predispose individuals to PRES, including severe hypertension, eclampsia, organ transplantation, exposure to various immunosuppressants and cytostatic drugs, and systemic inflammatory conditions with impaired renal function. All of these conditions ultimately lead to endothelial dysfunction with failure of cerebral autoregulation and development of vasogenic edema.[1–4]

Previous studies[5–12] have demonstrated that the major symptoms of PRES are headache, decreased alertness, cortical blindness and seizures. Magnetic resonance images (MRI) typically show multiple regions of reversible high signal intensity on T2-weighted images (T2WI) and fluid-attenuated inversion-recovery (FLAIR) images. Recently, atypical neuroimaging findings, such as cytotoxic edema, infarction, hemorrhage and contrast enhancement, and non-reversible clinical course including subsequent epilepsy, have been highlighted.[8,9,13–16] However, the evidence for these atypical findings is primarily from studies of adults with PRES. Clinical and radiological characteristics of PRES in children are not well recognized. Thus, we conducted a retrospective multicenter study to identify the clinical and radiological spectrum of PRES in children. Additionally, we investigated predictive factors for later MRI abnormalities and neurological prognosis.

2. Patients and methods

We sent questionnaires to pediatric neurologists belonging to the affiliate hospitals of Nagoya University, Nagoya City University, Gifu University, Juntendo University and Fujita Medical University regarding children (patients less than 20 years of age) with PRES treated in their hospitals between 1999 and 2012. The diagnosis of PRES was made by pediatric neurologists in each hospital according to radiological findings, i.e., variable degrees of reversible vasogenic edema (represented by regions of high signal intensity on T2WI and FLAIR images) and clinical presentation compatible with PRES such as headaches, visual disturbances, altered mental functioning and seizures with an underlying etiology for instance hypertension, use of immunosuppressant. Two of the authors (H.Y. and J.N.) further reviewed all MRI and the clinical course of each patient to confirm the diagnosis. Patients without MRI in the acute period were excluded from this study.

The contents of the survey included underlying disorders, laboratory data, use of cyclosporine, tacrolimus or corticosteroids at the onset of PRES, clinical symptoms including headache, alteration of consciousness, seizure, visual disturbance, blood pressure at the onset of PRES, electroencephalogram (EEG) findings, MRI findings in the acute and follow-up periods and neurological prognosis. High blood pressure was defined as that in the 95th percentile of height according to the criteria of the National High Blood Pressure Education Program (NHBPEP) Working Group on High Blood Pressure in Children and Adolescents.[17]

MRI were obtained in each hospital using 1.5- or 3-T scanners. MRI obtained within 2 days of disease onset were regarded as acute MRI, and MRI obtained 1 month or more after disease onset were regarded as follow-up MRI. Two of the authors (H.Y. and J.N.) reviewed all MRI. Axial T1-weighted images, T2WI and FLAIR images were used to determine the location of lesions (frontal, parietal, occipital, temporal, striatum, pallidum, thalamus, hypothalamus, mesencephalon, pons, cerebellum, medulla oblongata or corpus callosum) and to determine if there was a hemorrhage in the lesion. Diffusion-weighted images (DWI) and ADC maps were evaluated if they were available. ADC maps were examined to determine if ADC was higher or lower at the location of the lesion than at other locations (Figs. 1b and e, 2b). Follow-up MRI were also reviewed to determine if atrophy (Figs. 1c and f; 2c) or gliosis (represented by hyperintense areas on T2WI and FLAIR images) were present. Neurological prognosis (motor impairment, mental impairment and epilepsy) was evaluated in patients who were followed for more than 6 months after disease onset by pediatric neurologists in the affiliate hospitals.

The associations between clinical variables or MRI findings in the acute period, especially ADC in the lesions, and neurological and radiological outcomes were evaluated using