Epileptic Ictal Hyperperfusion on Arterial Spin Labeling Perfusion and Diffusion-Weighted Magnetic Resonance Images in Posterior Reversible Encephalopathy Syndrome

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Background: The hemodynamic state of the posterior dominant vasogenic edema in posterior reversible encephalopathy syndrome (PRES) is controversial. The aim of this retrospective study was to examine the contribution of epileptic ictal hyperperfusion in patients with PRES using combined magnetic resonance perfusion imaging with arterial spin labeling (ASL) and diffusion-weighted magnetic resonance imaging (MRI). *Methods:* A detailed review of chronological MRI findings in 2 patients, including diffusion-weighted imaging (DWI) and ASL, with special reference to clinical and electroencephalographic findings, was performed. At the onset of PRES, both patients developed secondary generalized seizures. *Results:* At the first PRES episode in Case 1, ASL and DWI clearly depicted "ictal hyperperfusion" and prolonged epilepsy-induced cytotoxic edema in the left parieto-occipital lobe cortex, located around the vasogenic edema of the PRES lesion in the left occipital lobe (hypoperfused area). At the second and third episodes (2 and 7 months after the first episode, respectively), although recurrent PRES was ruled out, ASL and DWI clearly demonstrated ictal hyperperfusion in the left posterior temporal and parieto-occipital lobes associated with partial nonconvulsive status epilepticus, which developed around the PRES-related old hematoma lesion. In Case 2, peri-ictal MRI findings of ictal ASL hyperperfusion and cortical hyperintensity on DWI were also noted in the left parieto-occipital lobe, but were mild compared with Case 1. *Conclusions:* Combined use of DWI and ASL can provide information on hemodynamic state associated with epileptic ictal hyperperfusion in the various phases of PRES.
Key Words: Stroke mimics—ictal hyperperfusion—nonconvulsive status epilepticus—diffusion-weighted image—arterial spin labeling.

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological diagnosis characterized by rapid onset of headache, confusion, or depression in the level of consciousness, epilepsies, visual abnormalities, and posterior-predominant vasogenic brain edema.[1-3] Conditions commonly associated with PRES include severe hypertension or wide blood pressure (BP) fluctuation, autoimmune disorders, eclampsia, immunosuppressed state in patients with organ transplantation, and renal insufficiency.[1-3] Magnetic resonance imaging (MRI) studies typically reveal predominantly posterior subcortical

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vasogenic edema. Clinical and radiographic findings are generally reversible.[1-3]

There are 2 opposing hypotheses for the hemodynamic mechanisms of PRES, although they remain controversial. The current most popular theory suggests that severe hypertension exceeds the limits of autoregulation, with subsequent hyperperfusion, endothelial injury, and vasogenic edema. The earlier original theory suggests that vasoconstriction and hypoperfusion leads to brain ischemia and subsequent vasogenic edema.[1,2] These contradictory hypotheses are likely attributed to the limited methodology and different timing of measurement of cerebral blood flow (CBF) during the various phases of PRES. Evidence of focal hyperperfusion in PRES patients studied with technetium Tc99m-hexamethylpropyleneamine oxime single-photon emission computed tomography[4,5] and CT perfusion image with contrast medium has been reported,[6,7] and there is also evidence of hypoperfusion assessed by transcranial Doppler,[8] CT perfusion image with contrast or stable Xe,[9,10] and magnetic resonance (MR) perfusion image with contrast.[11]

Single-photon emission computed tomography and contrast-enhanced CT and MR perfusion imaging require an extrinsic radioactive tracer and contrast medium, respectively. Therefore, it is practically difficult to perform repeated examinations, although contrast-enhanced CT and MR perfusion imaging has the advantage of improved spatial resolution and can provide both morphological and hemodynamic information in a single investigation. By contrast, MR perfusion imaging with arterial spin labeling (ASL) provides a completely noninvasive measurement of CBF.[12,13] ASL relies on contrast by magnetically labeling blood water and detecting the signal intensity as an intrinsic tracer. Thus, repeated examinations can be made during the both acute and chronic phases of PRES.

Importantly, a number of reports of PRES cases have not examined the epileptic ictal hyperperfusion or postictal hypoperfusion during the acute phase of PRES,[14] despite epilepsy or status epilepticus (SE) being one of the most common symptoms in the clinical manifestation of PRES.[3,15,16] Recent MR studies demonstrated that combined use of diffusion-weighted MRI and ASL can provide dynamic pathophysiological information in the ictal or peri-ictal phase of epilepsy patients.[13,17-20] In prolonged partial epilepsy and partial SE, the epileptogenic cortex is in an electrophysiologically extreme state, and the activated cortex exhibits increased glucose and oxygen usage, thereby causing compensatory regional hyperperfusion.

Recent reports have described the appearance of "ictal hyperperfusion" with ASL.[13,19-23] When the hyperperfusion is no longer sufficient to supply the hyperactive cortical area, pathophysiological changes leading to cytotoxic edema in the epileptic cortical neurons can occur, which appear as an abnormal high signal in the cortical lamina (cortical hyperintensity) on diffusion-weighted imaging (DWI).[19,24-29] These MRI findings of high signals on DWI and low apparent diffusion coefficient (ADC) in partial SE resemble those of acute ischemic stroke, indicating changes attributable to cytotoxic edema.[17,19] Although these "ictal MR findings" on ASL and DWI are reversible in most cases,[18,19] the ictal MRI findings, especially ictal ASL high signal, persist postictally, likely depending on the magnitude and duration of the epileptic activities.[17,18,20] In the present study, using serial MRI including DWI and ASL and electroencephalogram (EEG) recordings, we demonstrated the contribution of epileptic ictal hyperperfusion in 2 patients with PRES.

Material and Methods

During 1 year from April 1, 2012, to March 31, 2013, 2 patients with PRES were admitted to our hospital. A detailed review of the chronological MRI findings, including DWI and ASL with special reference to clinical and EEG findings, was performed. Long-term follow-up over 2 years was also achieved.

MRI

Brain MRI with routine protocols and perfusion images was performed using a 3T-MR unit (Signa HDxt 3.0T version 23; GE Healthcare, Milwaukee, WI). Routine protocols included axial diffusion-weighted echo planar sequences (b value = 1500 seconds/mm^2, TR/TE, 6000/minute), T1-fluid-attenuated inversion recovery (FLAIR) sequences (TR/TE/TI, 2050/16.1/741), and T2-weighted fast spin-echo sequences (TR/TE, 4400/100) and T2-FLAIR sequence (TR/TE/TI, 9000/140/2120).

ASL was prepared using 3-dimensional spiral fast spin-echo sequence with background suppression for perfusion imaging covering the entire brain. A pulsed continuous scheme was employed. Other acquisition parameters were as follows: 4 arms with 1004 points in each spiral arm, phase encoding in the z direction = 32, section thickness = 4 mm, TR = 4728 seconds, post label wait = 1.525 seconds, and NEX = 3.

EEG

Routine EEG recordings were obtained from an 18-channel digital EEG machine (Neurofax; Nihon-Kohden, Tokyo, Japan) with electrode placement according to the International EEG 10-20 System. The EEG recordings were performed for at least 30 minutes for each patient in resting conditions.

Results

Case 1

A 55-year-old female received steroid pulse and maintenance therapy with the diagnosis of Vogt–Koyanagi–Harada disease. She developed headache in the morning