

Serial Perfusion and Vascular Changes after a Prolonged Seizure

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Postictal hypoperfusion and hypoxia have been the proposed mechanisms of postictal behavioral dysfunctions such as postictal paresis, amnesia, and confusion [1,2]. Postictal perfusion changes can be detected using various arterial spin labeling (ASL) magnetic resonance imaging (MRI) techniques used to evaluate cerebral blood flow by magnetically labeled arterial blood [3]. Experimental animal studies suggest that postictal hypoperfusion may be mediated by arteriole vasoconstriction [1]. However, the evidence of accompanying vascular changes supporting this theory in humans is insufficient. In the present letter, we report a patient who presented with reversible hemispheric hypoperfusion on three-dimensional pseudo-continuous arterial spin labeling (3D-pCASL) with reversible vascular changes after a prolonged seizure, which may be the underlying pathogenic mechanism of postictal hypoperfusion.

A 7-year-old girl presented to the emergency room due to a seizure that lasted for 30 minutes. She had a generalized tonic seizure which stopped after administering intravenous (IV) lorazepam and IV fosphenytoin within 10 minutes of arrival. The initially focal onset or lateralized sign was unclear. The total seizure duration

was approximately 40 minutes. After the seizure termination, she was drowsy and ataxic. She had no fever, and no signs of meningeal irritation were observed. Her vital signs were as follows: body temperature 36.0°C, pulse rate 132 beats/min, respiratory rate 24 cycles/min, and blood pressure 100/60 mm Hg.

Written informed consent by the patients was waived due to a retrospective nature of our study.

She was born full term, and perinatal and developmental histories were unremarkable. This was her second seizure, her first one being an unprovoked seizure 9 months prior. Otherwise, she was healthy before admission. At arrival, venous blood gas analysis revealed respiratory acidosis (pH 7.16, pO₂ 56.3 mm Hg, pCO₂ 84.6 mm Hg, HCO₃⁻ 30.1 mmol/L, and SaO₂ 77.8 %), which resolved soon after treatment. Results of other blood tests were as follows: white blood cell counts, 12,600/μL; hemoglobin, 12.0 g/dL; platelet, 582 K/μL; sodium, 139 mEq/L; potassium, 3.9 mEq/L; calcium, 9.5 mg/dL; glucose, 145 mg/dL; magnesium, 0.71 mmol/L; alanine aminotransferase, 8 IU/L; aspartate aminotransferase, 30 IU/L; creatine kinase, 153 U/L; lactate, 0.8 mmol/L; and ammonia, 73 μmol/L. Other laboratory findings were unremarkable.

The patient's first MRI—which aimed to detect acute brain injuries causing the prolonged seizure—comprised 3D-pCASL, diffusion-weighted imaging (DWI), and phase contrast magnetic resonance angiography (PC MRA), performed 80 minutes after the seizure termination (Fig. 1A). The patient was sedated, but not hemiplegic. DWI revealed no visible diffusion-restricted lesion. However, 3D-pCASL revealed hypoperfusion in the right hemisphere (RH). The left hemisphere (LH) seemed relatively hyperperfused (Fig. 1A, left). Cerebral vascularity on PC MRA also decreased in the RH (Fig. 1A, right). A full sequence MRI including 3D-pCASL and time-of-flight (TOF) MRA was performed 4 hours after seizure termination (Fig. 1B). 3D-pCASL revealed

slightly improved but residual hypoperfusion in the RH and reduced hyperperfusion in the LH, suggesting a recovery phase (Fig. 1B, left). Vascular changes were not observed in TOF MRA (Fig. 1B, right). A third MRI, including 3D-pCASL and both PC MRA and TOF MRA, was performed 26 hours after the seizure termination (Fig. 1C). The asymmetric perfusion changes had disappeared (Fig. 1C, left). Subtle decreased vascularity in the RH was suspected in PC MRA but not in TOF MRA (Fig. 1C, middle and right). Electroencephalogram (EEG) on the second day of admission revealed occasional spike or polyspike and wave complexes in the right parieto-occipital and right temporal areas (Fig. 2).

After admission, the patient was alert and did not present further

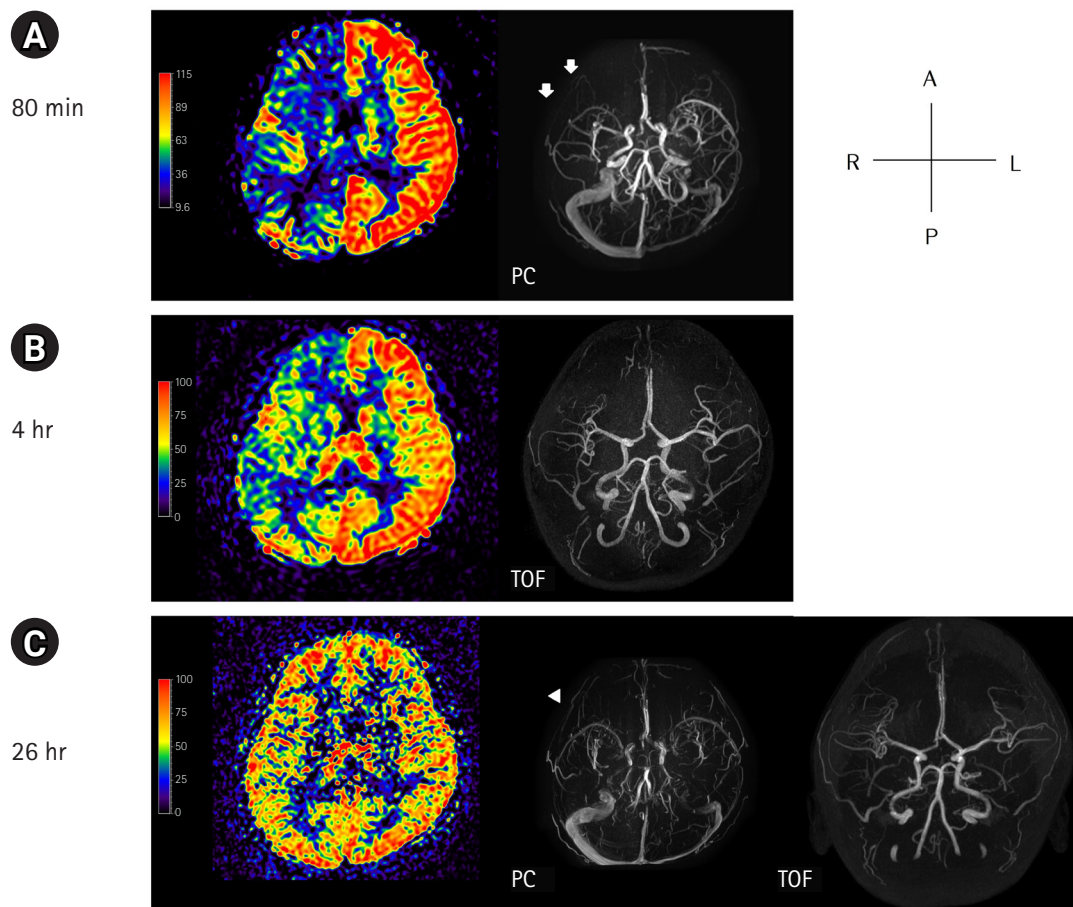


Fig. 1. Serial magnetic resonance imaging (MRI) with three-dimensional pseudo-continuous arterial spin labeling (3D-pCASL) and arteriographies of the patient. Mean cerebral blood flow (CBF). Mean CBF was calculated from 10 regions of interest (ROIs) of both the right hemisphere (RH) and left hemisphere (LH) (right and left prefrontal, frontal, temporal, parietal, periventricular areas, total area of ROIs: RH 14,838 mm², LH 14,843 mm²). The first MRI was performed 80 minutes after seizure. 3D-pCASL revealed hemispheric hypoperfusion on the RH and relative hyperperfusion in the LH (mean CBF: RH 41.4 cm/sec, LH 81.9 cm/sec) (A, left). Phase contrast magnetic resonance angiography (PC MRA) revealed decreased cerebral vascularity on the same side (arrows) (A, right). The second MRI was performed 4 hours after seizure termination. 3D-pCASL revealed slightly improved, but remaining hypoperfusion in the RH and decreased hyperperfusion in the LH (mean CBF: RH 44.1 cm/sec, LH 65.6 cm/sec) (B, left). The vascular change was not visible on time-of-flight (TOF) MRA (B, right). The third MRI was performed 26 hours after seizure termination, and asymmetric perfusion changes had disappeared (mCBF: RH 50.8 cm/sec, LH 50.6 cm/sec) (C, left). Subtle decreased vascularity was observed in PC MRA, but vascularity in TOF MRA was normal (triangle) (C, middle and right).



Fig. 2. Electroencephalography of the patient on the second day of admission revealed occasional spike or polyspike and wave complexes from the right parieto-occipital and right temporal areas (arrows) (time base 20 mm/sec, sensitivity 150 μ V/cm, high cut 70 Hz, low cut 1.0 Hz).

seizures. However, she developed mild fever (37.8°C) and respiratory symptoms; she received IV antibiotics and IV levetiracetam (10 mg/kg/day). On the second day of hospitalization, she was ataxic and presented severe headache, aggression, and irritability. Considering the possibility of levetiracetam-induced personality change, the anticonvulsant was changed to IV valproate (10 mg/kg/day). However, her behavioral changes lasted for another 2 to 3 days. Nasopharyngeal swab test for respiratory virus polymerase chain reaction identified parainfluenza virus. She gradually recovered by the fifth day of hospitalization and was discharged with a prescription of valproic acid. She had no residual neurologic deficit at discharge.

ASL is a safe, easy, non-contrast imaging study for tracking perfusion changes. Previous studies with ASL showed that postictal hypo-/hyperperfusion changes were co-localized to the seizure onset zone (SOZ) in 60% to 100% of patients [2]. However, the timing of ASL acquisition during the postictal period may be crucial in detecting perfusion changes. Most human studies were conducted during the interictal period with various acquisition timings.

In animal studies, postictal hypoperfusion was observed at the SOZ for up to 60 minutes [4]. In the recent prospective study of Gaxiola-Valdez et al. [2], ASLs were performed within 90 minutes after a habitual seizure, and hypoperfusion was observed in 71.4% of the patients. Moreover, the location of hypoperfusion was in accordance with the presumed SOZ in 80% of patients [2]. In the

present case, spike discharges from right parieto-occipital region were seen in the interictal EEG on the second day of hospitalization. Based on the results from Gaxiola-Valdez et al. [2], these areas are likely to relate to SOZ. However, the mild voltage attenuation in the left fronto-temporal area was not relevant to the findings on a concurrently conducted ASL.

The current study demonstrated postictal hypoperfusion in the hemisphere including SOZ with contralateral hyperperfusion and serial disappearance. Concomitant vascular changes were observed in PC MRA, which detected relatively slow blood flow. Thus, the decreased vascularity in PC MRA might be associated with vasoconstriction of smaller arteries, as compared to that of larger arteries observed in TOF MRA. The patient's prolonged behavioral changes might be attributed to the severe hemispheric hypoperfusion. Although levetiracetam may have caused the behavioral changes as an adverse effect, these changes persisted for a few days after stopping levetiracetam. The limitation of this study was that both PC MRA and TOF MRA could not be performed during the first MRI due to an emergency setting. Although it is not always feasible to perform an ASL MRI in emergency situations, it takes less time than a full sequence MRI. Performing ASL will provide more information on seizure-related changes. Additionally, concomitant PC MRA may suggest the underlying reversible vascular changes.

This study was approved by the Institutional Review Board of Hanyang University Guri Hospital (2020-11-009). Written in-

formed consent by the patients was waived due to a retrospective nature of our study.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Conceptualization: HLY, YJC, JHM, HJJ, and DWP. Data curation: HLY, YJC, JHM, HJJ, and DWP. Formal analysis: HLY, YJC, JHM, HJJ, and DWP. Methodology: HLY, YJC, and JHM. Project administration: HLY, YJC, and JHM. Visualization: HLY and JHM. Writing-original draft: HLY and JHM. Writing-review & editing: HLY, YJC, and JHM.

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