Reperfusion injury after CAS

Post-Carotid Stenting Hyperperfusion Syndrome with Blood-Brain Barrier Disruption on Gadolinium-enhanced FLAIR MRI

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Abstract

After carotid revascularization, abrupt increase in the cerebral blood flow may disrupt the blood-brain barrier, resulting in hyperperfusion syndrome. This blood-brain-barrier damage may be reflected by subarachnoid enhancement on FLAIR MRI after gadolinium injection. We present two cases of post-carotid stenting hyperperfusion syndrome that showed hyperintensity in the subarachnoid spaces on T2 FLAIR MRI after gadolinium injection. These MRI findings may represent a marker for hyperperfusion syndrome after carotid revascularization.

Key words: hyperperfusion syndrome, carotid stenting, blood-brain barrier, MRI
Introduction

Mechanism of the hyperperfusion syndrome (HPS) occurring after carotid endarterectomy (CEA) or carotid artery stenting (CAS) may involve disruption of the blood-brain-barrier (BBB) induced by abrupt increases in the cerebral blood flow [1]. Patients with HPS present a variety of clinical manifestations, including headache, visual disturbance, confusion and other hemispheric symptoms [1,2]. Recently, the extravasation and stagnation of i.v. injected gadolinium (Gd) in the subarachnoid space has been suggested as an imaging marker for early BBB disruption in ischemic stroke. As such, it has been called a “hyperintense acute reperfusion marker (HARM)” [3]. We present two patients with post-carotid stenting HPS with HARM.

Case reports

Patient 1

A 67-year-old man with hypertension and diabetes mellitus was admitted because of transient aphasia. No acute infarction in the left hemisphere was revealed on a diffusion-weighted MRI (DWI) performed five hours after the onset of symptoms. MR angiography and conventional cerebral angiography revealed greater than 70% stenosis of the left proximal internal carotid artery (ICA) (Figure 1A). CAS of the left proximal ICA was successfully performed with a distal protection device seven days after the symptom onset (Figure 1B). Three hours later, he was disoriented, agitated and experienced sensory aphasia and drift of his right arm. Systolic blood pressure was maintained between 129 and 163mmHg, and diastolic blood pressure was maintained between 90 and 107mmHg. These values were slightly higher than the pre-stenting blood pressure. DWI obtained six hours post-stenting showed several small subcortical infarctions in the frontal subcortex probably associated with the stenting procedure (Figure 2B). Perfusion-weighted MRI (PWI) obtained six hours post-stenting showed a mildly increased perfusion on the time-to-peak map in the left hemisphere (Figure 2C). Immediate T2 fluid-attenuated inversion-recovery (FLAIR) MRI after Gd injection showed a diffuse leptomeningeal enhancement along the cerebral cortex in the hemisphere with hyperperfusion (Figure 3A) which was accompanied by signal changes on DWI (Figure 3B). The follow-up T2 FLAIR MRI obtained 18 hours after Gd injection showed subarachnoid hyperintensities in the left cerebral hemisphere (Figure 2D). He recovered in five days and experienced only mild dysarthria upon recovery. Subarachnoid hyperintensities were completely resolved on the follow-up FLAIR MRI (Figure 2E). Increased perfusion in the left hemisphere was nearly normalized on the follow-up PWI, which was obtained 24 hours after stenting.
Patient 2

A 66-year-old man with hypertension, diabetes mellitus was admitted for the intervention of the left proximal internal carotid arterial stenosis. He had a previous history of infarction in the territory of left middle cerebral artery (MCA) without any neurological deficits. MR angiography and conventional cerebral angiography revealed 70% stenosis at the bifurcation of the left ICA (Figure 1C). CAS of the left proximal ICA was successfully performed with a distal protection device (Figure 1D). His blood pressure was strictly controlled during and after the procedure. Five hours later, he was disoriented and agitated with aphasia. DWI obtained eight hours after stenting showed several small cortical infarctions in the left frontal subcortex (Figure 2G). PWI that was obtained eight hours after stenting showed no perfusion abnormality (Figure 2H). One day later, his aphasia was worsened. The follow-up T2 FLAIR MRI obtained 24 hours after Gd injection showed subarachnoid hyperintensities in the left cerebral hemisphere (Figure 2I). No additional new lesions were revealed on the follow-up DWI. He completely recovered in four days. Subarachnoid hyperintensities were completely resolved on the follow-up FLAIR MRI (Figure 2J).

Discussion

An abrupt increase in the cerebral blood flow following revascularization has been identified as the direct physiological cause of HPS [1]. Impaired autoregulation of the cerebral blood flow and subsequent BBB disruption are conditions that may be associated with HPS [1,2]. Leptomeningeal enhancement on Gd-enhanced FLAIR MRI was observed in patients with meningitis, subarachnoid hemorrhage, leptomeningeal carcinomatosis or renal dysfunction [4,5]. Hyperintensities on FLAIR MRI after Gd enhancement has been suggested as a marker of reperfusion injury after thrombolysis [3,6,7]. Pre- and post-stenting serial Gd-enhanced FLAIR MRI studies in patients with CAS have revealed leptomeningeal enhancement after stenting [8,9]. Wilkinson et al reported asymptomatic leptomeningeal enhancements which were consequences of hemodynamic changes after CAS [9]. Because this study only involved patients with symptomatic carotid stenosis, the underlying disruption of the BBB by a previous ischemic injury might have resulted in the leakage of the injected Gd. The authors of this study recommended further studies using DWI to clarify these findings [9].

Our patients showed clinical symptoms of HPS. Post-stenting DWI showed only a few small ischemic lesions that were probably associated with the stenting procedure. However, the extent of the patients’ hemispheric symptoms cannot be fully explained by these limited lesions. Post-stenting cerebral blood flow
measurements by PWI showed mild hyperperfusion state on the time-to-peak map in patient 1. The T2 FLAIR MRI obtained immediately after Gd injection showed leptomeningeal enhancements along the cerebral cortex; this “on the spot” image might reflect Gd extravasation through the disrupted BBB during the hyperperfusion state (Figure 3A). Interestingly, DWI also showed acute high signal intensities along the cerebral cortex (Figure 3B). Focal disruption of the BBB in patients with acute ischemic stroke may be the cause of HARM in T2 FLAIR MRI. However, HARM in patients with HPS may be the transient reversible diffuse hemispheric disruption of the BBB. Although it is possible that multiple microembolic infarctions were present, cortical neuronal injury associated with hyperperfusion is a possible explanation for the lesions observed on DWI. Extravasated Gd appeared on the follow-up MRI as hyperintensities in the subarachnoid space. After four to five days, Gd washout was completed, and the clinical symptoms rapidly improved.

In the presence of concomitant acute infarcted lesion, where BBB was already broken, the meaning of post-stenting HARM may be quite limited, because it could be a simple consequence of Gd leakage through the broken BBB even in the normal perfusion state, not in the hyperperfusion state. Therefore, further studies considering multiple factors possibly related to the post-stenting HARM, such as presence of acute or chronic infarction, white matter hyperintensities, microbleeds, and clinical symptoms of hyperperfusion syndrome may be needed.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

HY Kim and HJ Cho designed the study, interpreted the data, and drafted the manuscript. YJ Kim and JH Lee participated in the design of study and helped to draft the manuscript. WJ Moon, HG Roh, and YI Chun participated in patient enrollment and interpretation of the data. All authors read and approved the final manuscript.
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References


**Figure legends**

Figure 1. Conventional cerebral angiography showed greater than 70% stenosis of the left proximal carotid artery (A and C). Carotid artery stenting was successfully performed (B and D). (A and B in patient 1; C and D in patient 2)

Figure 2. Serial follow-up T2 fluid-attenuated inversion-recovery (FLAIR) MRIs. Chronic ischemic white matter changes were observed in pre-stenting FLAIR MRI (A and F). Post-stenting FLAIR MRI obtained 18-24 hours after gadolinium iv showed hyperintensities in the subarachnoid space (D and I), which was resolved 4-5 days (E and J). Post-stenting diffusion weighted MRI showed few small subcortical lesions (arrowheads in B and G). Slightly increased perfusion on time-to-peak map in the left hemisphere was observed in patient 1 (C).

Figure 3. Immediate T2 fluid-attenuated inversion-recovery (FLAIR) MRIs after Gd injection showed diffuse leptomeningeal enhancements along the cerebral cortex of the left hemisphere (A) that was accompanied by signal changes on diffusion weighted MRI (B) in patient 1.
Figure 1
Figure 2