



A Patient with Stenosis of the Cervical Internal Carotid Artery in Whom Hyperperfusion Syndrome Occurred after Staged Angioplasty

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Objective: We report a patient who underwent staged angioplasty (SAP) for stenosis of the cervical internal carotid artery (ICA), but developed hyperperfusion syndrome.

Case Presentation: The patient was an 84-year-old male. Stenosis of the left cervical ICA (pseudo-occlusion) related to cerebral infarction was observed. Emergency angioplasty was performed. At 9 days after the procedure, carotid artery stenting (CAS) was conducted. Restlessness was noted immediately after CAS. In addition, right hemiparesis and aphasia were exacerbated, and a convulsive seizure occurred 4 days later. MRI did not reveal the new onset of cerebral infarction. Single-photon emission computed tomography (SPECT) showed an increase in cerebral blood flow (CBF) in the left parietal lobe, leading to a diagnosis of hyperperfusion syndrome. An anticonvulsive drug was administered, and strict blood pressure control was performed. There was no hemorrhagic complication. The patient was referred to a rehabilitation hospital.

Conclusion: The present case developed hyperperfusion syndrome despite SAP was performed. Currently, there is no consensus for the interval; it is important to carefully determine the interval in each patient by evaluating cerebral perfusion status.

Keywords ▶ staged angioplasty, stenosis of the cervical internal carotid artery, hyperperfusion syndrome

Introduction

For surgery for stenosis of the cervical carotid artery, carotid endarterectomy (CEA) has been primarily performed, but carotid artery stenting (CAS) has also been increasingly conducted as an established procedure.

CAS can be non-invasively performed in a relatively short procedural time under local anesthesia. However, perioperative ischemic complications, puncture-site complications, and postoperative hyperperfusion syndrome

(HPS) may occur. In particular, more than two antiplatelet drugs are orally administered to most patients prior to CAS; postoperative HPS must be considered.

The incidence of HPS is reportedly 0.2–18%.¹⁾ HPS may cause headache, consciousness disorder, focal symptoms such as hemiparesis, and convulsion.²⁾ In addition, a study reported that the incidence of intracranial hemorrhage was 0.6%, and that the prognosis was unfavorable.³⁾

According to Ogasawara et al.,³⁾ strict blood pressure control after CEA was useful for preventing HPS-related intracranial hemorrhage, but not after CAS. Another study indicated that strict blood pressure control after CAS decreased the incidences of HPS and intracranial hemorrhage.⁴⁾ However, a consensus has not been reached. Recently, Yoshimura et al.⁵⁾ reported the usefulness of staged angioplasty (SAP) for the prevention of hyperperfusion after CAS.⁵⁾ Since then, SAP has been adopted in many institutions.

In this study, we report a patient in whom SAP for symptomatic stenosis of the left cervical internal carotid artery (ICA; pseudo-occlusion) was performed, but HPS occurred.

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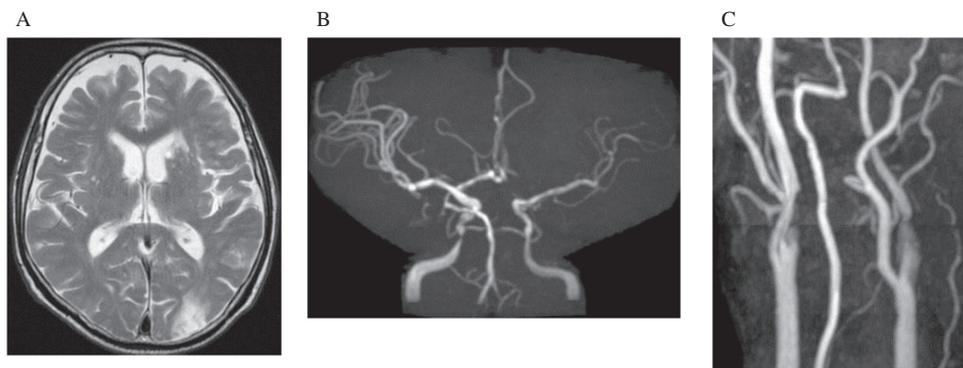


Fig. 1 (A) T2WI shows cerebral infarction in the left watershed zone. (B) MRA shows decline of intensity of the intracranial left ICA. (C) MRA shows severe stenosis of the left ICA. ICA: internal carotid artery; T2WI: T2-weighted images

Case Presentation

Patient: An 84-year-old male.

Medical history: Hypertension.

Present illness: In April 2015, dysarthria, aphasia, and right homonymous hemianopsia occurred. In another hospital, MRI revealed scattered cerebral infarction in the left frontal and parietal lobes and marked stenosis of the left cervical ICA. The patient was admitted, and medical treatment was performed. After discharge, the patient was referred to our hospital in May to undergo detailed examination and treatment for stenosis of the left cervical ICA.

Neurologic findings on the initial consultation were made in our hospital: The Glasgow coma scale (GCS) score was E4V4M6. Mild right hemiparesis, aphasia, and right homonymous hemianopsia were observed.

Carotid ultrasonography: The peak systolic flow velocity of the left ICA was 522.6 cm/s, showing a marked increase.

MRI: Scattered cerebral infarction was noted in the left watershed zone. Marked stenosis of the left cervical ICA was observed, and there was a decrease in intensity of the left intracranial ICA. Hypoplasia of the left anterior (A1) and posterior (P1) cerebral arteries was noted (**Fig. 1**).

Course: As a stenotic lesion of the left cervical ICA was symptomatic, we recommended CAS, but the patient wished to undergo medical treatment. Cilostazol, clopidogrel, and atorvastatin were orally administered, and follow-up was continued at the outpatient clinic. Neither regular carotid ultrasonography nor MRI revealed the progression of stenosis. In October 2016, the deterioration of dysarthria, aphasia, and gait disorder was observed, but the patient was followed-up at home. In November, regular MRI revealed new onset cerebral infarction in the left parietal lobe (**Fig. 2A**). On MRA, pseudo-occlusion of

the left ICA was suspected, and the patient was emergently admitted.

Cerebral angiography showed pseudo-occlusion of the left cervical ICA the following day (**Fig. 2B** and **2C**). Considering that single-stage CAS may induce HPS, SAP was selected. Emergency percutaneous transluminal angioplasty (PTA) was performed. Under local anesthesia, a 9 Fr OPTIMO balloon catheter (Tokai Medical Products Inc., Aichi, Japan) was navigated into the left common carotid artery (CCA), and a Carotid Guardwire PS (Medtronic, Minneapolis, MN, USA) into the left external carotid artery (ECA). CCA and ECA blood flow were blocked, and angioplasty was performed using a Jackal balloon catheter measuring 2.0×20 mm (Kaneka Medix Corp., Osaka, Japan) (8 atm, 2.0 mm, 30 seconds). However, recoiling was noted. Using a Sterling balloon catheter measuring 3.0×20 mm (Stryker, Kalamazoo, MI, USA), angioplasty was conducted (6 atm, 2.99 mm, 30 seconds), but sufficient dilation was not achieved. In addition, angioplasty was performed using a Sterling balloon catheter measuring 3.0×20 mm (10 atm, 3.25 mm, 60 seconds). Angiography after 15-minute waiting did not show any recoiling, and there was a marked improvement in left ICA blood flow (**Fig. 2D**). After the procedure, aphasia was improved, and the course was favorable.

Single-photon emission computed tomography (SPECT) with ^{123}I -iodoamphetamine (IMP) was performed 8 days after PTA. The left middle cerebral artery (MCA) territory cortex-to contralateral resting cerebral blood flow (CBF) ratio was 0.81 (**Fig. 3A**).

Considering the patient's age and risk of disuse syndrome, CAS was performed 9 days after PTA. Under local anesthesia, a 9 Fr OPTIMO balloon catheter was navigated into the left CCA, and a Carotid Guardwire PS into the left ICA while crossing the lesion site. CCA and ICA blood

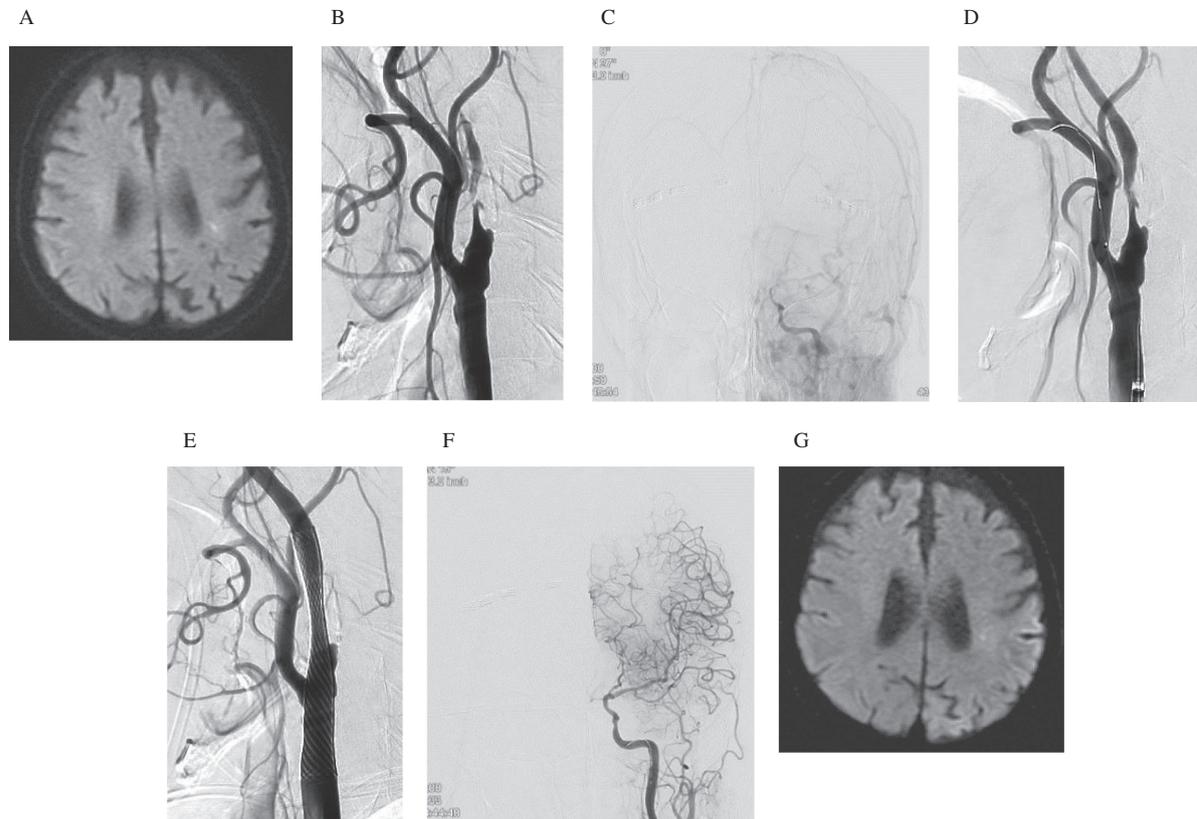


Fig. 2 (A) DWI shows a new hyper intensity in the left parietal lobe. (B and C) Left carotid angiography shows pseudo-occlusion of the left ICA. (D) After PTA, left carotid angiography shows partial dilation of the lesion and improvement of the left ICA flow. (E and F) After CAS, the lesion was dilated by stenting sufficiently and the left ICA flow was improved. (G) DWI shows hyper intensity in the left parietal lobe cortex. CAS: carotid artery stenting; DWI: diffusion-weighted image; ICA: internal carotid artery; PTA: percutaneous transluminal angioplasty

flow were blocked, and predilation was conducted using a Sterling balloon catheter measuring 3.0×20 mm (6 atm, 2.99 mm, 30 seconds). A Carotid Wallstent measuring 10×31 mm (Stryker) was deployed, and postdilation was performed using a Sterling balloon catheter measuring 4.0×30 mm (6 atm, 3.99 mm, 30 seconds). A further improvement in left ICA blood flow was achieved (**Fig. 2E** and **2F**). After the procedure, restlessness was noted, but there was no exacerbation of focal symptoms. The systolic blood pressure was strictly maintained at approximately 110–130 mmHg.

Right hemiparesis and aphasia were exacerbated, and a convulsive seizure occurred at 4 days after CAS. MRI did not reveal any new onset cerebral infarction in the left cerebral hemisphere. A diffusion-weighted image (DWI) showed a high-signal intensity in the left parietal lobe cortex, which was considered to be a post-convulsion change (**Fig. 2G**). Under a diagnosis of HPS, an anticonvulsive drug was administered, and more strict blood pressure control was performed. ^{123}I -IMP SPECT revealed an increase

in resting CBF involving the cortex of the left MCA territory (left MCA territory cortex-to-contralateral resting CBF ratio: 1.14) (**Fig. 3B**).

Subsequently, there was no convulsive seizure or hemorrhagic complication. ^{123}I -IMP SPECT 13 days after CAS showed a decrease in the laterality of resting CBF (**Fig. 3C**).

Although right hemiparesis and aphasia had been improved, the patient was referred to a rehabilitation hospital due to generalized weakness.

Discussion

The incidence of HPS after CAS is reportedly 1.1%, and intracranial hemorrhage may occur in approximately 0.7% of patients, leading to an unfavorable prognosis.^{3,6)}

Various studies reported risk factors for HPS. A decrease in resting CBF before surgery and a decrease in cerebral vasoreactivity (CVR) are considered important.^{7–11)} In addition, Oshida et al.¹²⁾ indicated that the assessment of

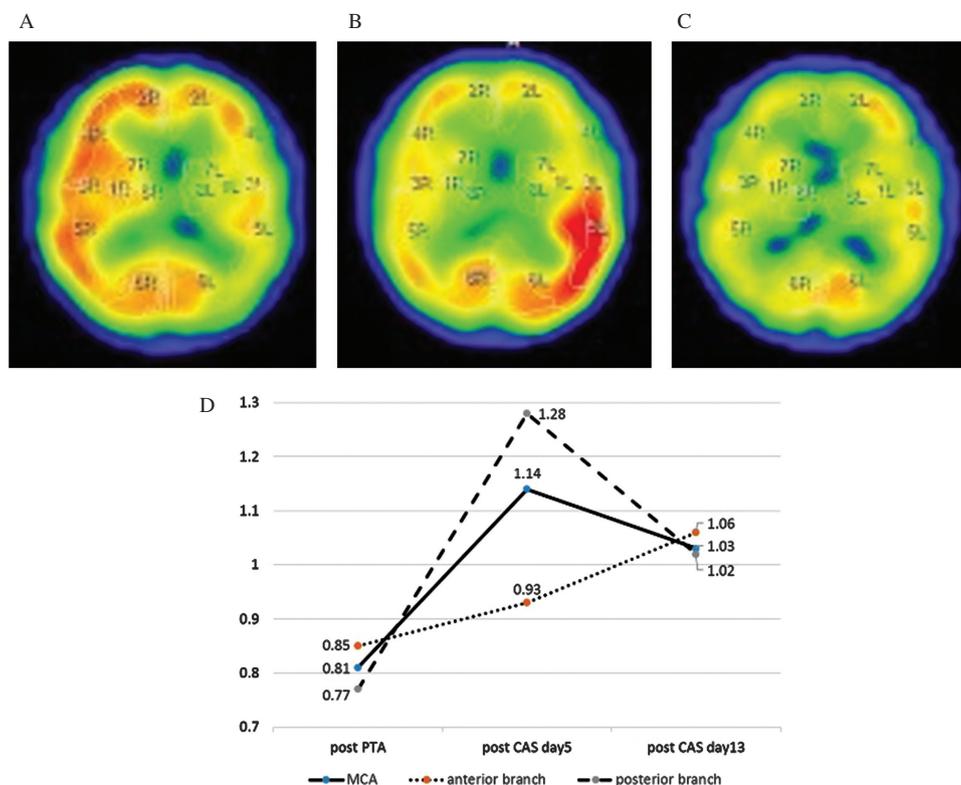


Fig. 3 Changes of rest CBF on ^{123}I -IMP SPECT. **(A)** CBF in the left MCA territory decreases 8 days after PTA. **(B)** CBF in the left MCA territory increases 5 days after CAS. **(C)** Crosswise difference of CBF decreases 13 days after CAS. **(D)** Changes of rest CBF ratio (affected side/unaffected side) in the whole MCA territory (solid line), MCA anterior branch territory (dotted line), and MCA posterior branch territory (broken line). CAS: carotid artery stenting; CBF: cerebral blood flow; MCA: middle cerebral artery; PTA: percutaneous transluminal angioplasty; SPECT: single-photon emission computed tomography; ^{123}I -IMP: ^{123}I -iodoamphetamine

CVR was more useful than that of resting CBF alone for the following reasons: among patients with a decrease in resting CBF, there are some patients with matched hypometabolism in whom CBF is decreased due to a decrease in cerebral metabolism,¹³⁾ whereas others show cerebral vasodilation even when resting CBF is maintained.¹⁴⁾

For post-CAS management in high-risk patients for HPS, it is initially important to prevent HPS. Even if HPS occurs, it may also be important to prevent deterioration to intracranial hemorrhage.

Regarding CEA, a study reported that the preoperative administration of edaravone was useful for preventing postoperative hyperperfusion,¹⁰⁾ and another study indicated that strict blood pressure control was useful for the prevention of postoperative hyperperfusion-related intracranial hemorrhage.³⁾

Regarding CAS, a study showed that strict postoperative blood pressure control decreased the incidences of HPS and intracranial hemorrhage.⁴⁾ However, no method to prevent HPS has been established. A recent study

reported SAP,⁵⁾ in which only PTA is initially performed for high-risk patients for HPS, followed by CAS after a specific interval, suggesting its usefulness.

In the present case, emergency treatment was performed, and CBF before PTA could not be evaluated. However, the left ICA showed pseudo-occlusion, and it was expected that standard single-stage CAS might induce HPS. Therefore, SAP was selected. After PTA, the course was favorable, but early CAS was scheduled, considering the patient's age and risk of disuse syndrome. On ^{123}I -IMP SPECT 8 days after PTA, the left MCA territory cortex-to-contralateral resting CBF ratio was 0.81, exceeding the preoperative MCA territory cortex-to-contralateral resting CBF ratio 0.75, which reflects the risk of hyperperfusion after CAS,⁷⁾ and 0.80, which is a criterion for indicating SAP.⁵⁾ Therefore, CAS was performed 9 days after PTA, but HPS occurred 4 days after CAS. If SAP had not been conducted, more serious complications, such as intracranial hemorrhage, would have appeared. The results suggest the usefulness of SAP. On the other hand, the interval

between PTA and CAS was short (9 days), and sufficient resting CBF and CVR recovery was not achieved, which may have contributed to the onset of HPS. As another etiologic factor, insufficient PTA-related dilation may have led to the absence of CBF and CVR recovery. During PTA, the dilated vascular diameter was not confirmed using intravascular ultrasonography, but angiography showed a marked improvement in ICA blood flow, and there was no delayed circulation; the possibility of insufficient PTA-related dilation can be ruled out.

Regarding the interval between PTA and CAS, Yoshimura et al.⁵⁾ reported an interval of 4 weeks in 2009. In 2015, Uchida et al. and Sakamoto et al. presented favorable treatment results, with an interval of 2¹⁵⁾ and 3–6¹⁶⁾ weeks, respectively. However, a consensus has not been reached. Currently, it may be appropriate to establish an interval of more than 2 weeks.

In elderly or poor collateral circulation patients, a longer period may be required until resting CBF and CVR are sufficiently recovered after PTA, as demonstrated in the present case. Therefore, the interval until CAS should be determined based on the assessment of cerebral perfusion status after PTA. Oshida et al. indicated that decreases in resting CBF involving the cortex of the MCA territory and CVR on ¹²³I-IMP SPECT before CEA were predictive factors for postoperative hyperperfusion.¹²⁾ However, they reported that both the sensitivity and negative predictive value of CVR assessment were 100%, whereas those of resting CBF assessment were 84.3% and 97.3%, respectively.¹²⁾ Briefly, it may be impossible to predict hyperperfusion perfectly based on resting CBF alone; it is ideal to evaluate CVR in addition to resting CBF. In the present case, CAS was performed based on resting CBF alone, resulting in the onset of HPS. If CAS had been conducted after an adequate interval based on post-PTA CVR assessment, HPS could have been prevented. However, when evaluating CVR, adverse reactions to acetazolamide must be considered. The accuracy of resting CBF assessment is permissible, and whether CVR assessment should be conducted is controversial. Furthermore, in the present case, the left whole MCA territory cortex-to-contralateral resting CBF ratio after PTA was 0.81. However, when evaluating it with respect to the anterior and posterior branch territories of the MCA, the anterior branch territory cortex-to-contralateral resting CBF ratio was 0.85, and the posterior branch territory cortex-to-contralateral resting CBF ratio was 0.77. At the onset of HPS following CAS, the values were 0.93 and 1.28, respectively (**Fig. 3D**). Thus, the

above resting CBF ratio before CAS was lower in the posterior branch territory with hyperperfusion, suggesting that assessment with respect to branch territories improves the accuracy of resting-CBF-based examination.

Conclusion

We encountered a patient who underwent SAP for symptomatic pseudo-occlusion of the cervical ICA, leading to HPS. The interval between PTA and CAS was short (9 days); therefore, recoveries of CBF and CVR were considered to be insufficient. These factors may have contributed to the onset of HPS.

Regarding SAP, no consensus for the interval between PTA and CAS has been established; an adequate interval may differ among patients. Therefore, it is important to perform appropriate assessment of cerebral perfusion status after PTA and carefully determine the interval in each patient.

Disclosure Statement

There is no conflict of interest regarding this article.

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