Intracerebral Hemorrhage after Carotid Artery Stenting without Evidence of Hyperperfusion in Positron Emission Tomography

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Summary

A 75-year-old man with a recent history of transient left hemiparesis and dysarthria was referred to our hospital. Angiography showed right internal carotid artery (ICA) occlusion and left ICA 89% stenosis. Positron emission tomography (PET) showed decreased cerebral blood flow (CBF), and increased oxygen extraction fraction (OEF) and cerebral blood volume (CBV) in the right hemisphere.

In the left hemisphere, CBV was increased, but CBF and OEF remained normal. One month after the transient ischemic attack, left carotid artery stenting (CAS) was performed without complications. Diffusion-weighted magnetic resonance imaging (MRI) on the day after CAS showed no fresh ischemic lesion. PET on the second day after CAS showed increased CBF and decreased OEF and CBV in the right hemisphere as compared with those before CAS. In the left hemisphere, decreased CBV was observed and CBF was slightly increased as compared with those before CAS.

The postoperative course was uneventful, but on the fifth day after CAS, the patient suddenly showed a focal seizure and right motor weakness. Emergency computed tomography scanning showed massive intracranial hemorrhage with severe brain edema in the left hemisphere. Although CBF study is useful to predict the hyperperfusion syndrome, we cannot disregard the

possibility of intracerebral hemorrhage after CAS for carotid artery stenosis when there is no evidence of hyperperfusion on postoperative CBF study.

Introduction

Cerebral hyperperfusion is defined as a major increased ipsilateral cerebral blood flow (CBF) following revascularization for carotid artery stenosis by carotid endarterectomy (CEA) or carotid artery stenting (CAS). Hyperperfusion syndrome is characterized by unilateral headache, face and eye pain, seizure, and focal symptoms due to intracranial hemorrhage (ICH) or cerebral edema related to hyperperfusion¹⁻³. The signs or symptoms of hyperperfusion usually occur between three and eight days after revascularization for carotid artery stenosis. Hyperperfusion-induced ICH is associated with high mortality and morbidity rates¹⁻¹². The incidence rates of hyperperfusion syndrome and ICH are 0.6 ~ 3.1% and 0.3 ~ 1.2% following CEA, and 1.1 ~ 6.8% and 0.67 ~ 4.5% following CAS, respectively^{1-3,9-12}.

This phenomenon is attributable to the failure of normal cerebral autoregulation, secondary to long-standing decreased cerebral perfusion pressure^{3,4,6-8,10,12,13}. To investigate the failure of autoregulation, single-photon emission computed tomography (SPECT) is useful because it can quantitatively measure both

CBF and hemodynamic reserve as cerebrovascular reactivity (CVR) using acetazolamide challenge test^{3,6,7}. Otherwise, positron emission tomography (PET) is the most useful diagnostic modality to determine accurately the hemodynamic status of the cerebral circulation¹⁴. Powers et Al classified the hemodynamic status into three stages¹⁴. Stage 0 means that the cerebral perfusion pressure is normal. As the perfusion pressure falls, the first compensatory response is arterial vasodilation (stage 1). The cerebral blood volume (CBV) increases, but the oxygen extraction fraction (OEF) remains normal. As the perfusion pressure falls further, the capacity for compensatory vasodilation is overwhelmed and CBF begins to fall. At this stage, the cerebral oxygen metabolism is maintained by an increased OEF (stage 2), and autoregulation fails. Generally, hyperperfusion is defined as a CBF increase of 100% (that is, a doubling) or greater as compared with the preoperative values, and hyperperfusion-induced postoperative ICH occurs in this state^{3,7}. Evaluation of the pre- and postoperative CBF is useful to predict the postoperative hyperperfusion syndrome.

Recently, Ogasawara et Al have demonstrated that the patients who did not show immediate post-CEA hyperperfusion with SPECT never exhibit hyperperfusion or hyperperfusion syndrome afterward⁷. We present herein an interesting case of ICH on the fifth day after CAS without evidence of hyperperfusion in the postoperative PET study.

Case Report

A 75-year-old man with a recent history of transient left hemiparesis and dysarthria was referred to our hospital. Diffusion-weighted magnetic resonance imaging (MRI) did not show any fresh infarction, but angiography showed right internal carotid artery (ICA) occlusion and left ICA stenosis. The degree of the left ICA stenosis was 89% as measured by the method outlined by the North American Symptomatic Carotid Endarterectomy Trial¹⁵ (figure 1A). Antiplatelet agents (aspirin 81 mg/day and ticlopidine 200 mg/day) were administered immediately. Systolic arterial blood pressure was between 120 and 140 mmHg without antihypertensive drug. PET showed decreased CBF and increased OEF and CBV in the right hemisphere (stage 2).

In the left hemisphere, CBV was increased, but CBF and OEF remained normal (stage 1) (figures 2, 3). One month after the transient ischemic attack, left CAS was performed via transfemoral catheterization under local anesthesia. After systemic anticoagulation with heparin, a distal protection balloon (PercuSurge GuardWire™ system) was carefully advanced across the stenosis. Pre-dilation was performed with a 3.5-mm controlled-compliant balloon catheter under distal protection. After pre-dilation, a self-expandable stent (SMART stent™) was deployed. Post-dilation was performed with a 4.5-mm controlled-compliant balloon catheter.

After sucking debris stuck out from the plaque in ICA, the distal protect balloon was deflated. Angiography showed good patency of ICA. (figure 1B) Administration of antiplatelet agents continued and intravenous argatroban was used for 48 hours after the procedure, but anticoagulation with heparin was not used. To control the hypotension and bradycardia after CAS, continuous intravenous administration of dobutamine and atropine was necessary for three days and the systolic arterial blood pressure was kept between 100 and 140 mmHg since then. Diffusion-weighted MRI on the day after CAS showed no fresh ischemic lesion (figure 4). PET on the second day after CAS showed increased CBF and decreased OEF and CBV in the right hemisphere as compared with those before CAS. In the left hemisphere, there was decreased CBV and CBF was slightly increased as compared with those before CAS (figures 2 and 3). There were no changes in neurological status after CAS during the first four days. However, on the fifth day after CAS, the patient suddenly showed a focal seizure and right motor weakness. Emergency computed tomography scanning showed massive ICH with severe brain edema in the left hemisphere, which was compatible to the finding of hyperperfusion syndrome (figure 5). Although strict control of the blood pressure and intracranial pressure under general anesthesia was achieved, the patient died of cerebral herniation on the 11th day after ICH.

Discussion

Hyperperfusion syndrome is thought to result from failed normal autoregulation of CBF, secondary to long-standing decreased perfu-

Figure 1 A) Left common carotid angiogram (lateral view) before CAS showing 89% stenosis at the origin of the internal carotid artery. B) Left common carotid angiogram (lateral view) after CAS showing good patency of the internal carotid artery.

sion pressure. This failure results in maximal dilation of the cerebral arterioles over a long period, with subsequent loss of their ability to constrict when the normal perfusion pressure is restored. Operative correction of stenotic lesions is expected to create sudden alterations in the blood flow patterns that were established by the relatively slow development of the atheromatous lesion. Excessive blood flow directed into a non-autoregulated vascular bed, as occurs following CEA or CAS of a highly stenotic carotid artery, may result in disruption of the small vessels with consequent hemorrhage into the brain parenchyma^{2,3,6,8,11-13}.

When autoregulation fails due to chronic reduction of the cerebral perfusion pressure, SPECT shows decreased CVR and CBF, and PET shows increased OEF and CBV and decreased CBF (stage 2).

This severe stage of cerebral hemodynamic failure has been termed "misery perfusion"¹⁴. Some previous studies suggested that the patients with preoperative hemodynamic failure have a definite risk for postoperative hyperperfusion syndrome^{2,3,7}. Preoperative decreased CVR observed by SPECT is a significant independent predictor of postoperative hyperperfusion^{6,7,13}. High-grade stenosis, poor cerebral collateral blood flow, and contralateral carotid occlusion are risk factors of postoperative hyperperfusion because their autoregulation usually failed^{1,2,7,9,11,12}. In our present case, angiography showed high-grade (89%) left ICA stenosis with contralateral ICA occlusion. Angiography revealed a potential risk of hyperperfusion syndrome after CAS in the left hemisphere. However, PET study did not exhibit misery perfusion (stage 2) in the left hemisphere.

Figure 2 Before CAS, the PET study showed decreased CBF and increased OEF and CBV in the right hemisphere (stage 2). In the left hemisphere, CBV was slightly increased, but CBF and OEF remained normal (stage 1). The cerebral metabolic rate of oxygen (CMR02) was slightly decreased in both hemispheres. On the 2nd day after CAS, the PET study showed increased CBF and decreased OEF and CBV in the right hemisphere. In the left hemisphere, CBV was decreased and CBF was slightly increased but not hyperemic.

Evaluation of the pre- and postoperative CBF study is useful to predict the postoperative hyperperfusion syndrome. Hyperperfusion after CEA is defined as a CBF increase of 100% (that is, a doubling) or greater as com-

pared with the preoperative values^{1,3,6,7}. Such an increase can be seen only when the cerebral autoregulation is impaired³. When the postoperative CBF increases >100 % after CEA or CAS, the risk of ICH in the patients with hyperper-

Figure 3 Cerebral hemodynamics and oxygen metabolism before (gray column) and after CAS (black column). Before CAS, the PET study showed decreased CBF and increased OEF (except in the parietal region) and CBV in the right hemisphere (stage 2). In the left hemisphere, CBV was increased, but CBF and OEF remained normal (stage 1). After CAS, PET showed increased CBF and decreased OEF and CBV (except in the occipital) in the right hemisphere as compared with those before CAS. In the left hemisphere, OEF and CBV were decreased and CBF was slightly increased.

(CBF, cerebral blood flow; CBV, cerebral blood volume; OEF, oxygen extraction fraction; CMRO2, cerebral metabolic rate of oxygen; F, frontal; T, temporal; P, parietal; O, occipital. The arrows indicate the average value of each parameter in our facility)

fusion is more than ten times that of the patients without hyperperfusion³.

Ogasawara et Al demonstrated that the patients who did not show immediate post-CEA hyperperfusion on SPECT never exhibit hyperperfusion or hyperperfusion syndrome afterward⁷. They advocated that SPECT between the first and third postoperative day was useful to predict the hyperperfusion syndrome. In our present case, the PET study did not show > 100% increase in CBF in the left hemi-

sphere on the second day after CAS and the patient did not have any typical symptoms of hyperperfusion syndrome. Nevertheless, ICH developed suddenly in the left hemisphere with a focal seizure and right motor disturbance on the fifth day after CAS. Most authors reported that hyperperfusion-induced ICH occurs between three and eight days after CEA or CAS^{1,5,7,10,11}. Piepgras et Al presented 14 cases of ICH after CEA³. Hyperperfusion caused ICH in 12 cases, and three patients did not

Figure 4 Diffusion-weighted axial MR image on the day after CAS showing no fresh ischemic lesion in the left hemisphere.

Figure 5 Computed tomogram on the 5th day after CAS showing massive ICH and edema in the left hemisphere.

have >100% postoperative increase in CBF³. ICH occurred after the first 48 hours in these three patients, and therefore the authors suggested that hyperperfusion might occur after 48 hours of CEA^{3,16}. They reported that eight patients showed hyperperfusion on SPECT immediately after CEA. A progressive increase in CBF was observed in two of the eight patients on the third day after CEA, and the hyperperfusion syndrome developed⁷. Although there was no >100% increase in CBF on the second day after CAS in our case, CBF probably increased continuously afterward and finally resulted in ICH.

Postoperative hypertension is reportedly important in the etiology of ICH after CEA, and strict control of the blood pressure is mandatory to prevent the hyperperfusion syndrome^{4-7,9,12,13}. Insufficient control of the blood pressure and insufficient bed rest after CAS are probable causes of the increase in CBF. Otherwise, there is a difference between CEA and CAS in the course of development of hyperperfusion syndrome.

Kaku et al explained that stimulation of the carotid baroreceptors with a balloon or carotid stent might play an important role in the development of delayed hyperperfusion syndrome.

Carotid baroreceptor stimulation induces transient, sometimes prolonged, bradycardia and hypotension; and the subsequent rebound arterial hypertension may induce cerebral hyperperfusion¹³.

In our present case, continuous intravenous administration of dobutamine and atropine was necessary for three days to control the hypotension and bradycardia after CAS, and ICH developed after the necessity of control of the hypotension was gone. We suspect that these subsequent rebound blood pressure and insufficient bed rest after CAS led to increase in CBF after the PET study, and consequently ICH developed.

Conclusion

Generally, hyperperfusion syndrome after revascularization for carotid artery stenosis is defined as a CBF increase of 100% (that is, a doubling) or greater as compared with the preoperative values, and the CBF study is useful to predict the hyperperfusion syndrome. However, we have to bear in mind the potential development of ICH after revascularization for carotid artery stenosis without evidence of hyperperfusion in the CBF study.

Reference

- 1 Henderson RD, Phan TG et Al: Mechanisms of intracerebral hemorrhage after carotid endarterectomy. *J Neurosurg* 95: 964-969, 2001.
- 2 Solomon RA, Loftus CM et Al: Incidence and etiology of intracerebral hemorrhage following carotid endarterectomy. *J Neurosurg* 64: 29-34, 1986.
- 3 Piepgras DG, Morgan MK et Al: Intracerebral hemorrhage after carotid endarterectomy. *J Neurosurg* 68: 532-536, 1988.
- 4 Kashiwazaki D, Kuroda S et Al: Normalization of cerebral hemodynamics and metabolism after carotid stenting in patients unfit for major surgery. *No Shinkei Geka* 31: 1315-1320, 2003.
- 5 Shinno K, Ueda S et Al: Hyperperfusion syndrome following carotid endarterectomy: evaluation using diffusion-weighted magnetic resonance imaging-case report. *Neurol Med Chir* 38: 557-561, 1998.
- 6 Hosoda K, Kawaguchi T et Al: Cerebral vasoreactivity and internal carotid artery flow help to identify patients at risk for hyperperfusion after carotid endarterectomy. *Stroke* 32: 1567-1573, 2001.
- 7 Ogasawara K, Yukawa H et Al: Prediction and monitoring of cerebral hyperperfusion after carotid endarterectomy by using single-photon emission computerized tomography scanning. *J Neurosurg* 99: 504-510, 2003.
- 8 Coutts SB, Hill MD et Al: Hyperperfusion syndrome: toward a stricter definition. *Neurosurgery* 53: 1053-1060, 2003.
- 9 Meyers PM, Higashida RT et Al: Cerebral hyperperfusion syndrome after percutaneous transluminal stenting of the craniocervical arteries. *Neurosurgery* 47: 335-345, 2000.
- 10 Morrish W, Grahovac S et Al: Intracranial hemorrhage after stenting and angioplasty of extracranial carotid stenosis. *Am J Neuroradiol* 21: 1911-1916, 2000.
- 11 Ouriel K, Shortell CK et Al: Intracerebral hemorrhage after carotid endarterectomy: Incidence, contribution to neurologic morbidity, and predictive factors. *J Vasc Surg* 29: 82-89, 1999.
- 12 Abou-Chebl A, Yadav JS et Al: Intracranial hemorrhage and hyperperfusion syndrome following carotid artery stenting. *J Am Coll Cardiol* 43: 1596-1601, 2004.
- 13 Kaku Y, Yoshimura S et Al: Factors predictive of cerebral hyperperfusion after carotid angioplasty and stent placement. *Am J Neuroradiol* 25: 1403-1408, 2004.
- 14 Powers WJ, Press GA et Al: The effect of hemodynamically significant carotid artery disease on the hemodynamic status of the cerebral circulation. *Ann Intern Med* 106: 27-34, 1987.
- 15 North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 325: 445-453, 1991.
- 16 Schroeder T, Holstein PE et Al: Hyperperfusion following carotid endarterectomy. *Stroke* 15: 758, 1984 (Letter)

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