



Symptomatic Cerebral Hyperperfusion After Cerebral Vasospasm Associated with Aneurysmal Subarachnoid Hemorrhage

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Key words

- Cerebral aneurysm
- Cerebral blood flow
- Cerebral hyperperfusion syndrome
- Cerebral vasospasm
- Subarachnoid hemorrhage

Abbreviations and Acronyms

¹²³I-IMP: N-isopropyl[¹²³I]-p-iodoamphetamine

CBF: Cerebral blood flow

CT: Computed tomography

FLAIR: Fluid-attenuated inversion recovery

MRA: Magnetic resonance angiography

SAH: Subarachnoid hemorrhage

SPECT: Single-photon emission computed tomography

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INTRODUCTION

Cerebral hemodynamics dramatically change during the acute stage of subarachnoid hemorrhage (SAH),^{1,2} and the most common and devastating consequence is hypoperfusion due to cerebral vasospasm, which leads to delayed ischemic neurologic deficits.³ Conversely, cerebral hyperperfusion in the setting of SAH is a rare and overlooked condition. Hyperperfusion is defined as a significant increase in cerebral blood flow (CBF) relative to the homologous area of the contralateral hemisphere, which occasionally leads to cerebral hyperperfusion syndrome characterized by ipsilateral headache, seizures, and focal neurologic deficits.⁴ If

■ **BACKGROUND:** Cerebral hyperperfusion syndrome, which carries a potential risk of intracranial hemorrhage, is a rare and overlooked condition in the setting of subarachnoid hemorrhage (SAH).

■ **CASE DESCRIPTION:** A 72-year-old female presenting with SAH underwent clipping of a ruptured aneurysm of the left middle cerebral artery. On post-SAH day 7, the patient exhibited motor aphasia due to cerebral vasospasm of the left middle cerebral artery. After recovery from symptomatic cerebral vasospasm, the patient became restless and suffered from right hemiparesis on post-SAH day 12. Initially, recurrence of cerebral vasospasm was suspected; however, cerebral blood flow measurement using single-photon emission computed tomography revealed apparently increased perfusion in the same territory of the left middle cerebral artery. Hypertensive therapy was not induced during the postoperative period. Her neurologic symptoms and signs of cerebral hyperperfusion gradually improved with intensive blood pressure lowering.

■ **CONCLUSIONS:** This is the first report to describe posts ischemic cerebral hyperperfusion syndrome after symptomatic vasospasm detected using sequential single-photon emission computed tomography during the acute stage of SAH. Early diagnosis of this rare phenomenon is crucial given the necessity to lower blood pressure for preventing hemorrhagic complications, which is contrary to the usual management of patients with vasospasm.

not treated properly, cerebral hyperperfusion syndrome can result in severe brain edema, intracranial hemorrhage, and death. It is generally induced by the excessive resupply of CBF

after chronic or temporary ischemia with dysautoregulation of the central vascular system. Surprisingly, serial single-photon emission computed tomography (SPECT) measurements have revealed that >50% of

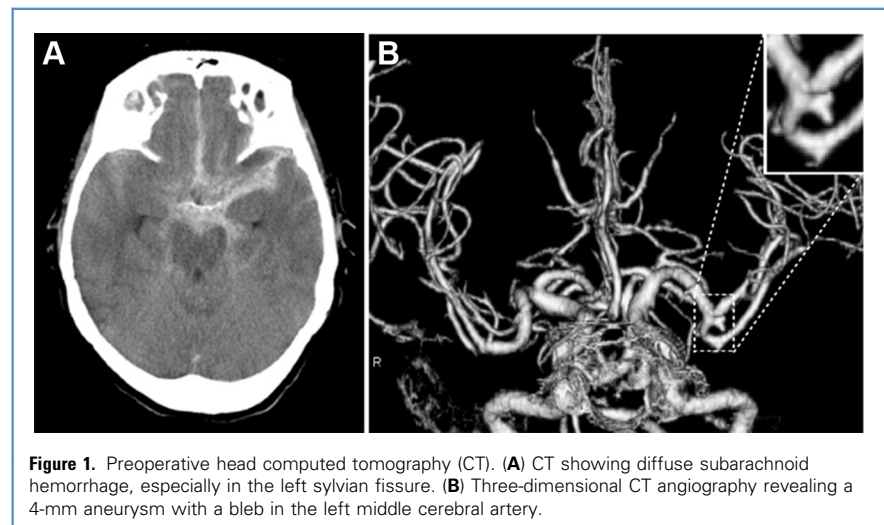


Figure 1. Preoperative head computed tomography (CT). (A) CT showing diffuse subarachnoid hemorrhage, especially in the left sylvian fissure. (B) Three-dimensional CT angiography revealing a 4-mm aneurysm with a bleb in the left middle cerebral artery.

patients with SAH experience regional mild hyperperfusion after initial hypoperfusion.¹ Moreover, 6% of patients with SAH suffer from hemorrhagic complications following cerebral vasospasm, although the causal relationship between intracranial hemorrhage and cerebral hyperperfusion syndrome is undetermined because of the lack of serial CBF measurements in previous reports.^{5,6}

Here we present a rare case of cerebral hyperperfusion syndrome following symptomatic vasospasm in a patient with SAH. Serial CBF measurements in this case led to the early diagnosis of cerebral vasospasm and subsequent symptomatic hyperperfusion, which was successfully treated by lowering blood pressure.

CASE DESCRIPTION

History and Examination

A 72-year-old female with a history of arterial hypertension presented with transient loss of consciousness followed by severe headache. She was drowsy and restless without focal abnormalities (Hunt and Hess grade III). Computed tomography (CT) of the head revealed SAH (modified Fisher grade 3) with a thick clot in the left sylvian fissure (Figure 1A). Three-dimensional (3D)-CT angiography revealed a 4-mm left middle cerebral artery aneurysm with a bleb (see Figure 1B).

Operation

On post-SAH day 1, the aneurysm was surgically clipped via left frontotemporal craniotomy. Temporary occlusion of M1 was performed for 2 minutes, 21 seconds under brain protection with edaravone and mannitol.

Postoperative Course

The patient awoke from anesthesia relatively soon without apparent neurologic deficits. Diffusion-weighted and fluid-attenuated inversion recovery (FLAIR) imaging on post-SAH day 3 showed no abnormalities. Postoperatively, her neurologic status was monitored closely with serial clinical examinations. On post-SAH day 2, she was started on intravenous fasudil hydrochloride, a Rho kinase inhibitor to prevent cerebral vasospasm. Induced hypertension was not performed

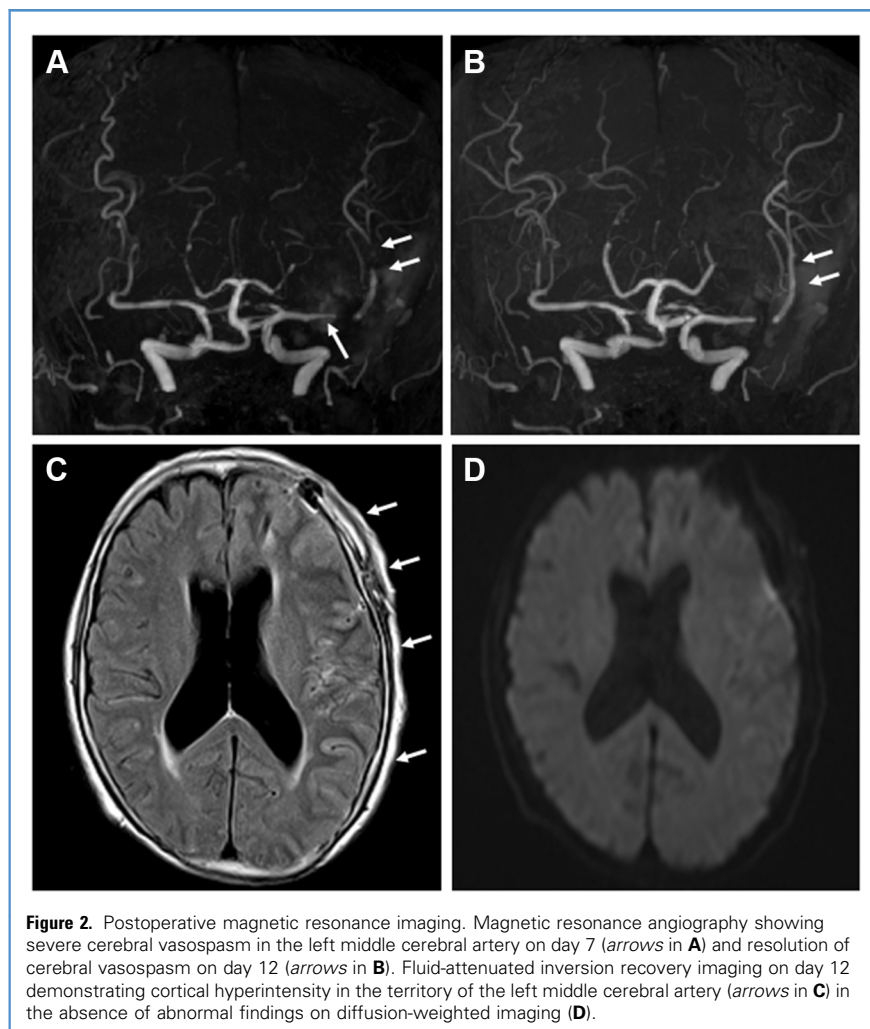
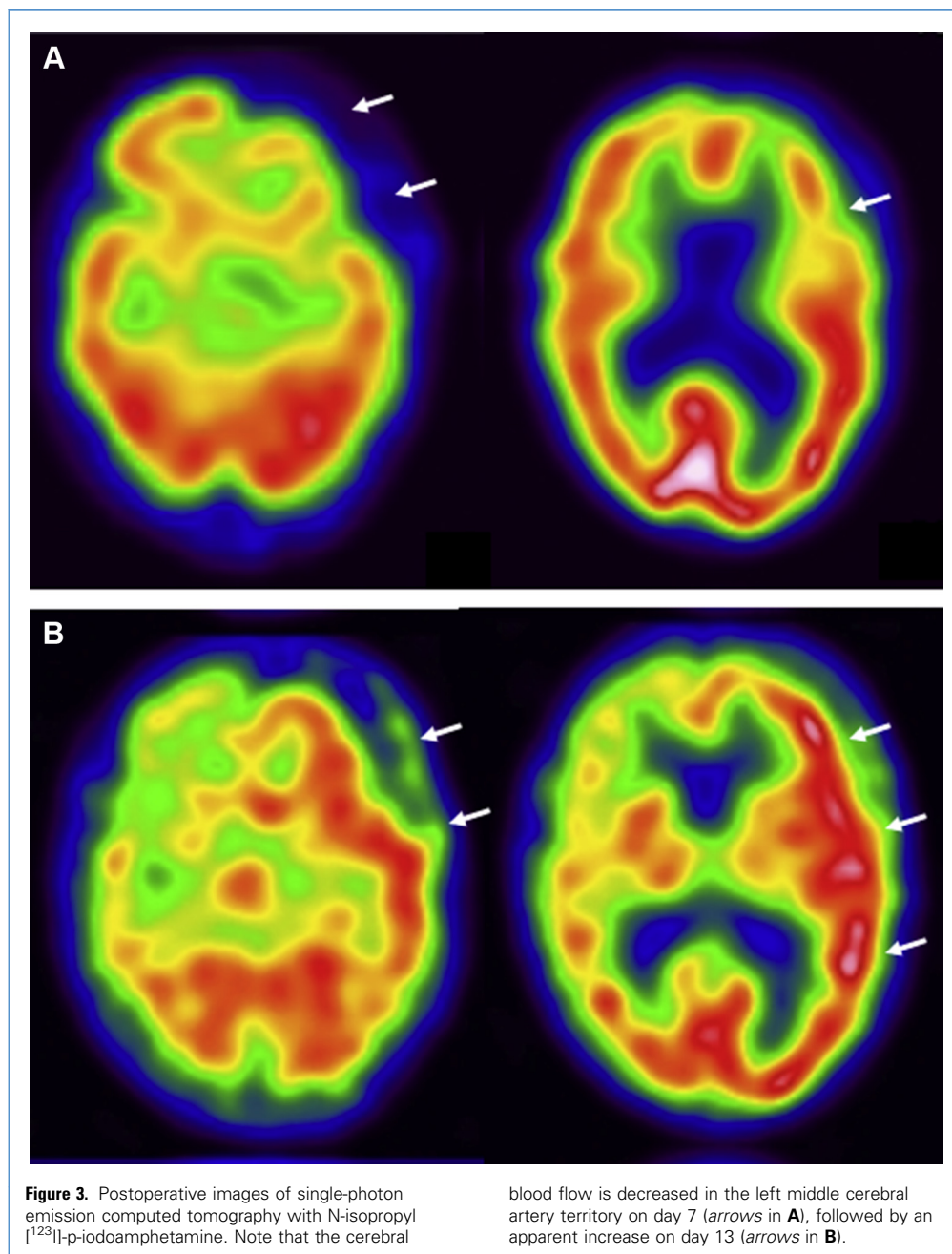


Figure 2. Postoperative magnetic resonance imaging. Magnetic resonance angiography showing severe cerebral vasospasm in the left middle cerebral artery on day 7 (arrows in A) and resolution of cerebral vasospasm on day 12 (arrows in B). Fluid-attenuated inversion recovery imaging on day 12 demonstrating cortical hyperintensity in the territory of the left middle cerebral artery (arrows in C) in the absence of abnormal findings on diffusion-weighted imaging (D).

during the postoperative period, and her systolic blood pressure ranged between 120 mm Hg and 140 mm Hg. However, on post-SAH day 7, she exhibited fluctuating motor aphasia. Diffusion-weighted and fluid-attenuated inversion recovery imaging showed no cerebral infarctions, whereas magnetic resonance angiography (MRA) demonstrated severe cerebral vasospasm at the left middle cerebral artery (Figure 2A), accompanied by hypoperfusion in the left frontal region confirmed by N-isopropyl[¹²³I]-p-iodoamphetamine (¹²³I-IMP) SPECT (Figure 3A). Delayed cerebral ischemia due to cerebral vasospasm was strongly suspected, and she was initiated on intravenous administration of edaravone and hypervolemic therapy, which led to the complete disappearance of motor

aphasia. However, on post-SAH day 12, the patient became restless and suffered from right hemiparesis. Initially, recurrence of cerebral vasospasm was suspected; however, ¹²³I-IMP-SPECT revealed apparently increased perfusion in the left middle cerebral artery territory (see Figure 3B), whereas resolution of vasospasm was observed in the left middle cerebral artery by MRA (see Figure 2B). FLAIR imaging demonstrated cortical hyperintensity in the left middle cerebral artery territory (see Figure 2C) without any abnormal findings by diffusion-weighted imaging (see Figure 2D). The neurologic symptoms and increased CBF were not caused by epilepsy because electroencephalogram showed no epileptic abnormal waves. These results suggested postischemic hyperperfusion

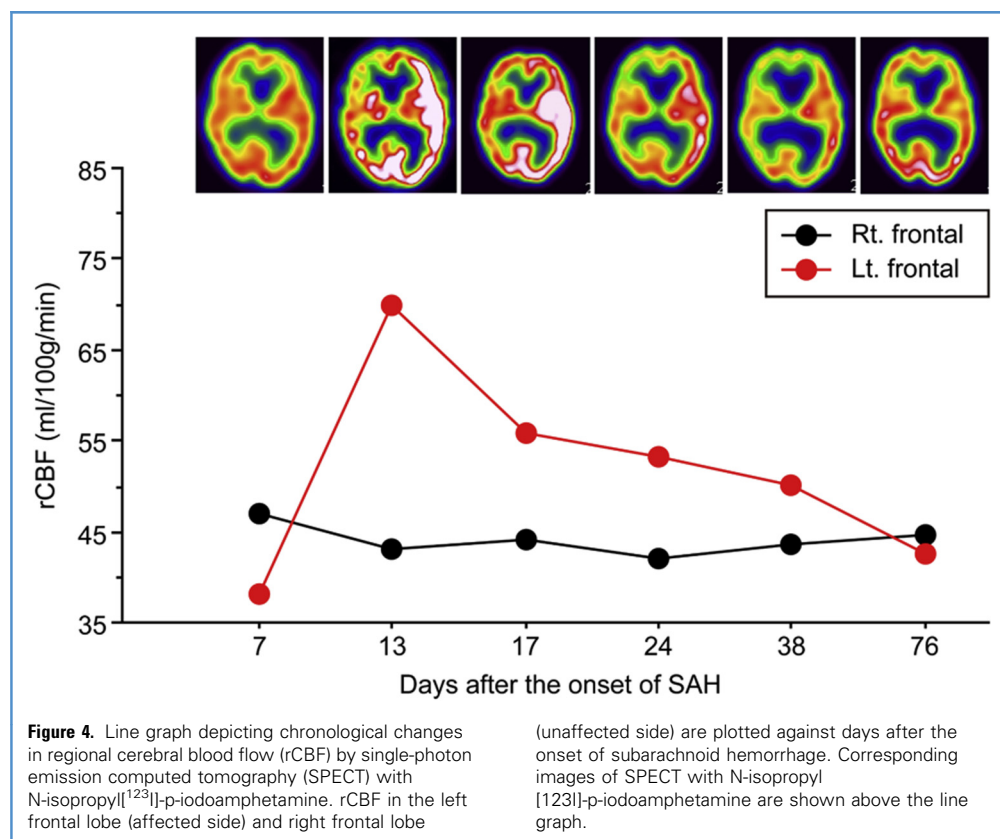


due to cerebral vasospasm-mediated ischemic insult led to the cerebral hyperperfusion syndrome.

Chronologic CBF data by ^{123}I -IMP-SPECT are shown in **Figure 4**. Briefly, CBF was quantified by autoradiographic methods, and the CBF in each subregion was automatically calculated by software for 3-dimensional stereotactic regions of interest templates provided by Daiichi

Radio-Isotope (Tokyo, Japan). The regional CBF of the left frontal lobe was decreased (ratio, 0.80) on post-SAH day 7 but suddenly increased prominently (ratio, 1.61) on post-SAH day 13. The systemic blood pressure was strictly controlled to stay in a range from 110 mm Hg to 130 mm Hg using continuous intravenous drip infusion of nicardipine hydrochloride. Hyperperfusion of the affected cortex

gradually improved and returned to normal on post-SAH day 76. The cortical hyperintensity on FLAIR imaging peaked between post-SAH days 12 and 17 and gradually decreased in intensity and returned to normal on post-SAH day 54. Neither hemorrhagic transformation nor atrophic changes were noted in the affected regions on CT scans and FLAIR imaging throughout the observation period.



Follow-Up

The patient's hemiparesis and restlessness gradually improved starting from post-SAH day 27. The patient had no neurologic deficits at the time of discharge from the hospital on post-SAH day 57.

DISCUSSION

Cerebral hyperperfusion syndrome in the setting of SAH is a rare phenomenon; however, recognition of this unusual complication is critical given the potential risk of intracranial hemorrhage.⁷ Previous reports found that the risk of hemorrhagic complications (6%) following cerebral vasospasm was relatively high possibly due to postischemic hyperperfusion, although the actual mechanism of hemorrhage remained unclear.^{5,6} In the present case, the serial CBF measurements by ¹²³I-IMP-SPECT have outlined the drastic change in cerebral hemodynamics during the acute stage of SAH, which aids in the potential identification of the trigger underlying cerebral hyperperfusion syndrome.

We speculate the mechanism underlying cerebral hyperperfusion syndrome post SAH as follows. First, loss of autoregulation (i.e., vasoparalysis) due to a preexisting ischemic insult is reported to induce postischemic hyperperfusion.^{8,9} Serial CBF studies revealed that vasospasm-induced hypoperfusion preceded symptomatic hyperperfusion in the corresponding area, which lends strong support for this possibility. Therefore ischemic damage caused by cerebral vasospasm potentially induced vasoparalysis in the affected cortex, resulting in cerebral hyperperfusion syndrome. Moreover, ischemic insult due to temporary clipping of a parent artery during aneurysm surgery is also known to lead to postischemic hyperperfusion, especially if the temporary clipping lasts for >20 minutes of the total duration.^{10,11} However, since the temporary occlusion time was <3 minutes, the influence of temporary clipping was considered minimal in the present case. Second, increased CBF at the epileptogenic site has been consistently reported during seizure

activity.¹² However, epilepsy-induced hyperperfusion is unlikely in the present case, since the electroencephalogram obtained immediately after the onset of symptoms revealed no epileptic abnormal waves. Third, hypertensive therapy for SAH-induced vasospasm was reported to cause hypertensive encephalopathy such as posterior reversible encephalopathy syndrome, resulting in symptomatic hyperperfusion.¹³ Indeed, hypertensive therapy was not induced in the present case throughout the postoperative period, and systolic blood pressure was maintained between 120 mm Hg and 140 mm Hg before the onset of symptoms. Therefore hypertensive encephalopathy might not be the trigger for symptomatic hyperperfusion. Taken together, postischemic hyperperfusion due to vasospasm-induced ischemic insult is considered the most reasonable trigger of cerebral hyperperfusion syndrome in the present case.

Because therapeutic strategies against symptomatic cerebral hypoperfusion and hyperperfusion are complete opposites,

accurate evaluation of cerebral hemodynamics before starting treatment is critical in patients who develop neurologic deficits in the acute stage of SAH. As treatment against cerebral vasospasm, including hypertensive therapy and administration of vasodilators, may lead to worsening of deficits and even permanent injury, the possibility of cerebral hyperperfusion syndrome should be considered during the postoperative period of SAH, especially in patients with preceding symptomatic vasospasm. In the present case, we performed repeat ^{123}I -IMP-SPECT imaging to assess cerebral hemodynamics after SAH, which led to the early diagnosis of cerebral vasospasm and subsequent cerebral hyperperfusion syndrome. Increased cortical intensity on FLAIR imaging in the affected area indicated reversible vasogenic edema caused by cerebral hyperperfusion syndrome.¹⁴ In addition, MRA served as a noninvasive and useful tool to determine whether worsening of the neurologic signs were due to cerebral vasospasm. Therefore serial angiography and CBF measurements are useful in identifying patients with hyperperfusion, as well as in distinguishing those with cerebral vasospasm.

Delayed intracranial hemorrhage due to cerebral hyperperfusion after revascularization surgery was reported previously⁴; therefore symptomatic hyperperfusion after SAH is considered to entail substantial risk of morbidity and mortality due to hyperperfusion. Therefore rapid counteraction of hyperperfusion is essential after the accurate diagnosis of cerebral hyperperfusion. Because intensive blood pressure lowering in patients with evidence of hyperperfusion by flow studies is the standard management of cerebral hyperperfusion after revascularization surgery for carotid artery stenosis, as well as Moyamoya disease,¹⁵ the systemic blood pressure in the present patient was managed strictly to stay below 130 mm Hg using continuous intravenous drip infusion of nicardipine hydrochloride. Postoperative use of a free-radical scavenger is an

acceptable additional approach to ameliorate secondary brain damage due to cerebral hyperperfusion, as reported in patients undergoing carotid endarterectomy.¹⁶ Fortunately, symptomatic cerebral hyperperfusion was resolved completely by blood pressure lowering and administration of a free-radical scavenger without the development of permanent neurologic deficits in the present case.

CONCLUSIONS

This is the first report to present post-ischemic cerebral hyperperfusion syndrome following symptomatic vasospasm detected by sequential ^{123}I -IMP-SPECT during the acute stage of SAH. Early diagnosis of this rare phenomenon is crucial given the necessity to lower blood pressure for prevention of hemorrhagic complications, which is contrary to the usual management of patients with vasospasm.

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