Abnormal cerebral vasodilation in aneurysmal subarachnoid hemorrhage: use of serial $^{133}$Xe cerebral blood flow measurement plus acetazolamide to assess cerebral vasospasm

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A patient with cerebral vasospasm following subarachnoid hemorrhage (SAH) was investigated by serial measurement of cerebral blood flow (CBF) using the xenon-133 emission tomography method. The CBF was measured before and after acetazolamide injection. On Day 2 after SAH, there was early local hyperperfusion in the middle cerebral artery (MCA) territory, ipsilateral to the left posterior communicating artery aneurysm. The regional CBF of this arterial territory decreased slightly after acetazolamide injection, probably because of vasoplegia and the "steal" phenomenon, and thus surgery was delayed. A right hemiplegia with aphasia and disturbed consciousness occurred 4 days later (on Day 6 after SAH) due to arterial vasospasm, despite treatment with a calcium-channel blocker. The initial hyperemia of the left MCA territory was followed by ischemia. The vasodilation induced by acetazolamide administration was significantly subnormal until Day 13, at which time CBF and vasoreactivity amplitude returned to normal and the patient's clinical condition improved. Surgery on Day 14 and outcome were without complication. It is concluded that serial CBF measurements plus acetazolamide injection are useful for monitoring the development of cerebral vasospasm to determine the most appropriate time for aneurysm surgery.

Key Words • subarachnoid hemorrhage • vasospasm • vasodilation • acetazolamide • cerebral blood flow

Cerebral vasospasm from aneurysmal subarachnoid hemorrhage (SAH) can lead to disability or death. It occurs within the 1st week after SAH, and consequently delays aneurysm surgery. Changes in the morphology of the arterial wall are caused by SAH, resulting in tonic and long-lasting vasostriction of the cerebral vessels. The spastic arteries are no longer able to dilate normally, while the magnitude and duration of the induced vasoconstriction are exaggerated. Angiography, transcranial Doppler ultrasonography, and neurological examination are the main methods used to assess the extent and the consequences of the arterial vasospasm. Abnormalities of the cerebral vasodilation after SAH can be investigated by serial single-photon emission computerized tomography (SPECT) measurements of the cerebral blood flow (CBF) by the xenon-133 ($^{133}$Xe) method before and after intravenous injection of the cerebral vasodilator acetazolamide (Diamox). This procedure was used in the following case to monitor the development of cerebral vasospasm and to determine the appropriate time for surgery.

Illustrative Case

Seven days after giving birth to her first baby, this right-handed 27-year-old woman suffered a sudden onset of headache and faintness, followed by an epileptic seizure. She was admitted to the hospital 2 hours later. Examination showed slight obtundation, bilateral Babinski's sign, mild neck stiffness, and a body temperature of 38°C. She did not describe an unusual medical or surgical history. She was treated with anticonvulsant medication and the calcium-channel blocker nimodipine (10 mg/day intravenously). Computerized tomography showed SAH, and angiographic studies performed 24 hours after SAH demonstrated an aneurysm on the left posterior communicating artery (Fig. 1).
Abnormal cerebral vasodilation in SAH

Angiography also revealed a slight regular narrowing of the carotid trunk and of the origin of the anterior cerebral artery (ACA) and the middle cerebral artery (MCA). Follow-up evaluation was based on clinical examination and serial measurements of CBF using SPECT* after acetazolamide injection. Xenon-133 examination was used instead of transcranial Doppler ultrasonography because the patient lacked a temporal window. The changes in CBF with time are shown in Fig. 2. The first measurement of CBF was taken on Day 2 after SAH and was normal (47 ml/100 gm/min on the aneurysm side and 44 ml/100 gm/min on the other side), with hyperemia of the left MCA territory on the aneurysm side (Fig. 3a and b). The 7% increase in CBF in the right hemisphere after a 1000-mg injection of acetazolamide was subnormal (normal increase > 30%). The patient's headache, which had begun immediately after SAH, was aggravated by the acetazolamide injection. There was no change in the mean CBF on the aneurysm side, but the local hyperemia of the MCA territory disappeared, probably because of vasoplegia and the steal phenomenon. Vasospasm occurred 4 days later (on Day 6 after SAH), despite calcium-channel blocker treatment; the patient's clinical state deteriorated suddenly with right hemiplegia, aphasia, and aggravation of the consciousness disturbance. A second CBF study, performed on Day 6, showed a bilateral drop in blood flow and hypoperfusion mainly of the left carotid territory (ACA and MCA) (Fig. 3c and d), the territory where the previous hyperperfusion occurred. The 12% resting interhemispheric asymmetry increased to 30% after acetazolamide injection. The patient's clinical state began to improve on Day 9, and the interhemispheric CBF asymmetry decreased (Fig. 3e and f); however, cerebral vasodilation remained limited on the aneurysm side (12% vs. 43%).

Motor recovery was very satisfactory by Day 13, although aphasic signs persisted. The fourth CBF study showed a normal, symmetrical basal CBF and good vasoreactivity (26%) on the aneurysm side (Fig. 3g and h). Surgery was performed 1 day later (on Day 14 after SAH) and the outcome was uncomplicated. Neurological examination 1 week later showed only slight facial paresis and mild aphasia with no impairment of comprehension.

Discussion

This case demonstrates the presence of early spontaneous localized hyperemia preceding cerebral vasospasm after SAH. Several mechanisms could be responsible for this dilation. The initial epileptic seizure is unlikely to have produced this hyperperfusion since the first CBF measurement was taken 3 days after the convulsions. Similarly, "luxury perfusion," defined as a local, regressive vasodilation produced by the cerebral ischemia, can be eliminated as it follows the neurological deficit and generally corresponds to reperfusion. By contrast, the hyperemia in this patient occurred many days before the clinical impairment. The intense headache indicates that this unusual appearance is probably due to activation of the sensitive trigeminovascular system by SAH.

The time course of abnormal arterial vasoreactivity in SAH is well known. There is transient vasoconstriction within the first minutes after the entry of blood into the subarachnoid space, although for obvious reasons, this transient phenomenon is rarely observed in humans. There are early changes in the reactivity of the cerebral arteries to constrictor agents. The cerebral arteries narrow within the 1st week, when vasospasm

*Tomomatic 64 manufactured by Medimatic, Copenhagen, Denmark.
Fig. 3. (legend) →
Abnormal cerebral vasodilation in SAH occurs, and usually give rise to clinical symptoms of ischemia. This period lasts about 10 days before improvement and partial or complete recovery. During this time, the impairment of arterial vasoreactivity results in loss of autoregulation.10,11 Single-photon emission computed tomography7,12 is a noninvasive and more accurate method than transcranial Doppler ultrasonography10 for investigating the abnormalities of cerebral circulation that follow aneurysmal SAH and for monitoring the consequences of vasospasm. However, these measurements were not sensitized by dynamic vasodilation studies and did not provide enough functional information for planning surgery. The present case shows that early abnormalities of cerebral vasoreactivity in response to acetazolamide administration result mainly in the inability of the arterial territory that underwent vasospasm to dilate. We believe that these early abnormalities probably predict arterial vasospasm and indicate that aneurysm surgery should be delayed.9

This study shows that CBF measurement by 133Xe SPECT plus Diamo sensitization to assess cerebral vasoreactivity after SAH is a useful indicator of the intensity, extent, and development of cerebral vasospasm and can help in deciding the best time for surgery. The pathophysiological significance of the early abnormalities of cerebral vasodilation may lead to new ways of treating cerebral vasospasm.

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References


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← Fig. 3. Serial single-photon emission computerized tomography (SPECT) measurements of cerebral blood flow (CBF) before (left) and after (right) acetazolamide (Diamox) injection. Color key indicates CBF (ml/100 gm/min). a and b: Day 2 after subarachnoid hemorrhage (SAH). The hyperemia in the left middle cerebral artery (MCA) territory disappeared after Diamox injection because of a steal phenomenon following arterial vasospasia. The injection increased the headache noted at the first examination. c and d: Day 6 after SAH showing MCA vasospasm. The hyperemia was replaced by hyperperfusion of the left MCA territory. There was no vasoreactivity to the Diamox injection; however, the headache increased. The patient had right hemiplegia and aphasia at this time. The 12% interhemispheric asymmetry increased to 30% after Diamox injection. e and f: Day 9 after SAH showing continued interhemispheric asymmetry and lack of response to Diamox administration in the left MCA territory. g and h: Day 13 after SAH. The basal CBF became symmetrical, and the vasoreactivity of the aneurysm side to Diamox administration was almost normal.

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