Symptomatic arterial luminal narrowing presenting months after subarachnoid hemorrhage and aneurysm clipping

DOUGLAS KONDZIOLKA, M.D., MARK BERNSTEIN, M.D., F.R.C.S.(C), S. M. SPIEGEL, M.D., F.R.C.P.(C), AND KAREL TER BRUGGE, M.D., F.R.C.P.(C)

Divisions of Neurosurgery and Neuroradiology, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada

The authors describe three cases of clinical cerebral ischemia associated with angiographic evidence of cerebral arterial luminal narrowing presenting 7, 14, and 52 weeks after subarachnoid hemorrhage (SAH) and aneurysm clipping. Delayed vasospasm, in its usual time setting 1 or 2 weeks after hemorrhage, did not occur symptomatically in these patients. No evidence for aneurysm clip migration or rebleed was present. All patients responded favorably to volume expansion and elevation of blood pressure. This unusual occurrence of a very delayed vasospasm may further the understanding of the vasospastic process. The symptomatic onset of arterial luminal narrowing months after SAH may suggest that a proliferative vasculopathy more accurately explains the observed vessel narrowing, rather than conventional active constriction of vascular smooth muscle.

KEY WORDS • aneurysm • subarachnoid hemorrhage • vasospasm • delayed cerebral ischemia

Cerebral ischemia secondary to cerebral arterial luminal narrowing (vasospasm) complicates up to two-thirds of cases of subarachnoid hemorrhage (SAH), causing significant morbidity and mortality. The presence of blood and blood breakdown products in the cerebrospinal fluid (CSF) has been related to the etiology of vasospasm. A strong correlation between the amount of blood in the basal cisterns and the incidence and severity of spasm has also been observed. Delayed ischemia in association with vasospasm usually appears clinically and radiologically within the first 2 weeks after hemorrhage. Spasmogenic substances are thought to appear in the CSF during this time and cause arterial luminal narrowing. Correspondingly, the incidence and severity of vasospasm should decrease with time, as the concentration of these spasmogens also progressively lessens. Resolution of vasospasm in most cases occurs by Day 21 post-SAH. Weir, et al., suggested that vasospasm after 3 weeks is probably due to vessel stretching caused by edema, hematoma, hydrocephalus, repeat bleeding, or a static morphological change in the blood vessel wall.

This report is prompted by the recent management of three patients presenting with clinical and angiographic signs of arterial luminal narrowing, at 7, 14, and 52 weeks after SAH and successful aneurysm clipping. We were unable to find this phenomenon described in the literature. Various pathogenetic mechanisms for very delayed vasospasm are proposed.

Case Reports

Case 1

This 52-year-old previously healthy woman was gardening when she experienced a sudden severe headache followed by a tonic-clonic seizure. On arrival at the hospital she was mildly drowsy, but otherwise intact neurologically. Computerized tomography (CT) showed blood in the basal cisterns. On the day following admission, angiography showed a right 8-mm internal carotid-anterior choroidal artery aneurysm as well as a 4-mm left anterior cerebral aneurysm at the carotid bifurcation (Fig. 1 left). The right aneurysm was clipped with a curved Heifetz clip on the 3rd day post-SAH. There was evidence of recent hemorrhage from this aneurysm. The patient's recovery was unremarkable and she was discharged on the 10th postoperative day. It was elected not to clip the unruptured left anterior cerebral aneurysm.

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The rapid onset of weakness of the left arm and decreased vision in the right eye. A CT scan showed an area of decreased attenuation in the distribution of the right anterior and middle cerebral arteries, and no evidence of new SAH. Angiography revealed marked narrowing of the right anterior and middle cerebral arteries (Fig. 1 right) with no change in size of the other aneurysm. The rest of the intracranial circulation was unremarkable. There was no evidence of atherosclerotic arterial involvement from the common carotid to the supraclinoid internal carotid artery. No lumbar puncture was performed. The patient was treated with intravascular volume expansion for 7 days with marked clinical improvement.

Repeat cerebral angiography 7 months later (11 months post-SAH) still showed similar arterial narrowing (Fig. 2 left); however, angiography performed 17 months after SAH showed some increase in luminal size of the right internal carotid artery (Fig. 2 center). Four years after the original SAH, when the second aneurysm was clipped (the patient had refused clipping until this time), angiography showed further improvement in caliber of the right anterior and middle cerebral arteries (Fig. 2 right).

Case 2

This 57-year-old previously healthy woman developed a sudden severe headache and vomiting while watching television. Lumbar puncture at a peripheral hospital revealed bloody CSF. On arrival at our institution, she was alert and neurologically intact. Angiography on the following day showed a right posterior communicating artery aneurysm. On Day 3 post-SAH, she underwent clipping of her aneurysm with a No. 12 Sugita clip. Recovery was uneventful, and she was discharged home on the 8th postoperative day. No early postoperative angiogram was performed.

The patient was well until 7 weeks later when she developed progressive weakness of the left arm, over a few days. Upon readmission, a CT scan was normal with no evidence of a rebleed. Angiography showed

FIG. 1. Right internal carotid angiograms, anteroposterior view, in Case 1. Left: Preoperative study showing an aneurysm (arrow) arising from the internal carotid-anterior choroidal artery junction 2 days after subarachnoid hemorrhage (SAH). There is no evidence of vasospasm. Right: Study 14 weeks post-SAH. The aneurysm clip is in place, and there is marked narrowing of the internal carotid (arrowhead), anterior, and middle cerebral (arrow) arteries.

FIG. 2. Right internal carotid angiograms, anteroposterior view, in Case 1. Left: Study 11 months after subarachnoid hemorrhage (SAH) showing that the arterial narrowing of the internal carotid, anterior, and middle cerebral (arrow) arteries is unchanged. Center: At 17 months post-SAH the right internal carotid artery (arrow) is slightly increased in size. Right: At 48 months post-SAH there is marked enlargement in the caliber of the right anterior and middle cerebral arteries (arrow). This photograph is × 1.5 compared to the previous angiograms.
marked luminal narrowing of the distal right internal carotid artery and the horizontal segment of the middle cerebral artery, with normal contralateral and posterior circulation. There was no atherosclerotic arterial involvement from the common carotid to the supraclinoid internal carotid artery. No lumbar puncture was performed. Treatment consisted of intravascular volume expansion for 10 days with moderate improvement of function in the left hand. Repeat angiography 7 days following treatment failed to show resolution of the arterial narrowing in spite of clinical improvement. The patient remained neurologically stable at her last follow-up examination 4 years later.

Case 3

This 36-year-old previously healthy woman had the sudden onset of a severe headache. She displayed meningismus, but otherwise had a normal neurological examination. A CT scan revealed a small amount of blood in the left sylvian fissure. Angiography showed a left posterior communicating artery aneurysm (Fig. 3 left). On Day 2 post-SAH the patient underwent surgery, and a Sundt encircling aneurysm clip was placed without incident. A temporary clip had been utilized during the operation. The postoperative angiogram on the 5th day after clipping (Fig. 3 center) showed moderate spasm of the left anterior and middle cerebral arteries, but no clinically associated deficit was present. The patient was later discharged home in excellent condition.

Fifty-two weeks later she awoke with right arm and leg weakness and progressive dysphasia. No headache or visual or sensory disturbances were noted. A CT scan was normal. Angiography disclosed complete occlusion of the left supraclinoid internal carotid artery (Fig. 3 right); there was no evidence of atherosclerotic disease in the neck. No lumbar puncture was performed. Treatment was begun with heparinization, intravascular volume expansion, and inotropic support for blood pressure elevation. A repeat CT scan 2 days later showed an infarction of the left middle frontal gyrus and subjacent white matter. After 1 week of treatment, a moderate right arm paresis persisted, but the right leg had regained full power and normal speech had returned. The patient was discharged to a rehabilitation facility.

Discussion

The appearance of clinical and arteriographic signs of cerebral arterial narrowing several months after SAH and aneurysm clipping must be considered an unexpected and puzzling occurrence. Two basic comments regarding the angiographic findings can be proposed. First, angiographic evidence of luminal narrowing might have been detected early in these patients, in the usual time setting of vasospasm, if angiography had been performed soon after surgery. This study was performed only in the third case, where evidence of vasospasm was noted, despite the lack of accompanying neurological deficit. If spasm had indeed been present early in all three cases, then the question arises as to
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why the onset of clinical deficit was delayed for several months. Second, it can be proposed that clinical and angiographic signs occurred simultaneously at 7, 14, and 52 weeks after SAH and surgery. Even in the third case, where a moderate degree of vasospasm was detected postoperatively, it is obvious that progression of luminal narrowing occurred, as evidenced by the complete internal carotid artery occlusion noted at 52 weeks when the neurological symptoms appeared. The reason for constriction of these arteries so long after SAH is not known. Various pathogenetic mechanisms are proposed.

A number of theories are available to explain the mechanisms for cerebral vasoconstriction following SAH. Spasmogenic substances within the CSF, resulting from blood breakdown or from the pharmacological response to hemorrhage, may interact with the vessel wall to cause narrowing. Mechanical stimulation due to the mass of the aneurysm, subarachnoid hematoma, or aneurysm clip may stimulate the vessel to constrict. Vasomotor constriction secondary to sympathetic stimulation may also occur. Iatrogenic injury to vessels at the time of aneurysm clipping may lead to reversible or irreversible luminal narrowing. Retraction injury to vessels or imperfect clip placement could compromise the vessel lumen in the area of the aneurysm.

Primary late narrowing should not be due to a CSF-borne spasmogen, since all possible substances should be progressively cleared from the CSF with time. No new spasmogens should be introduced unless rebleeding occurs. Zabramski, et al.,10 reported that rebleeding may be associated with an increased severity of vasospasm in patients who had previously suffered from spasm. None of our patients underwent late postoperative lumbar puncture to completely exclude a small rebleed. However, no clinical evidence (such as headache) or CT evidence for a rebleed was present. In the first case where the patient harbored a second aneurysm, no change in aneurysm size or shape was noted to suggest bleeding from this lesion. Of course, this does not definitely rule out a hemorrhage from this aneurysm. It is of note, however, that this second aneurysm remained stable until it was successfully clipped 4 years later.

The mass of the aneurysm and subarachnoid clot would also be expected to diminish after surgery and not be responsible for late vasoconstriction. However, the mass of the aneurysm clip and any associated histological change around the clip would remain in effect.

A number of studies have been undertaken to assess the degree of histological change around implanted aneurysm clips. An in vivo and in vitro study of the Sugita clip after implantation showed fibrosis immediately around the clip, but fair tissue compatibility was noted. A study of autopsy cases examined 6 days to 11 months after placement of Yasguril clips (seven cases) and Heifetz clips (five cases) as well as five control cases noted slight inflammatory reactions around the clip and the beginning of granulomatous change after 1 month. There were no cases of major adjacent vessel narrowing in either study. Mayfield and Kees, who implanted clips into the soft tissues of patients, noted no corrosion and only minimal foreign-body reaction. McFadden, however, has reported that “all metallic implants corrode.” Dujovny, et al., warned that aneurysm clips previously applied and reused may have blood in their blades and, despite sterilization, may evoke a significant inflammatory reaction if implanted into another patient. It has also been noted that a scratched clip, with some of the surface chromium oxide removed, is at greater risk for the development of corrosion.2

Temporary clipping, which was utilized in one of our cases, has been associated with endothelial cell damage, wall crater defects, and wall folding. Endothelial surface breaks, subendothelial platelet adherence, and cortical artery stenosis after extracranial-intracranial bypass. Degeneration of myelinated nerve fibers within the media of vessels from surgical clamping, leading to lack of autoregulation, has also been suggested.6

Conway and McDonald3 reported an autopsy series of 12 patients with prior SAH, and found intimal thickening from subendothelial granulation tissue in all patients surviving 4 weeks or more after SAH. In fact, in two of their cases where angiography was performed at 9 and 14 months post-SAH, they were able to demonstrate major vessel luminal narrowing. No correlation between the patient’s clinical status and angiographic plus pathological findings was made, nor did they explain why delayed angiography was performed.

The phenomenon of aneurysm clip-induced vessel wall fibrosis and luminal narrowing may be a reasonable explanation for the long delay in clinical and angiographic presentation. Treatment with intravascular volume expansion and hypertension may be effective depending on the degree of distensibility of the vessel wall. Permanent luminal enlargement would not be expected in these cases once intravascular therapy was discontinued, due to the static presence of the fibrosis. In Cases 2 and 3, this may explain why follow-up angiograms continued to show marked luminal narrowing. This phenomenon, however, does not help to explain the findings in Case 1. Although luminal narrowing was seen on angiography for up to 11 months post-SAH, the studies at 17 months and 4 years post-SAH displayed marked enlargement in luminal size. This cannot be caused by a progressive histological reaction-like perivascular fibrosis. The late onset of luminal narrowing in Case 1 followed by improvement in vessel contour suggest a phenomenon of very delayed vasospasm. In the absence of rebleeding, no specific etiology for vasospasm occurring this late is known. Histological and electron microscopic changes in vessels affected by vasospasm after SAH have been studied, and divided into groups with early and late onset, by Hughes and Schianchi.16 Late changes (those after 3 weeks post-
hemorrhage) are characterized by medial fibrosis and atrophy, as well as endothelial thickening. At this stage, narrowing of the affected arteries is likely to be irreversible. Early changes are probably compatible with reversibility and restoration of the premorbid caliber of the vessel lumen.

In the third case, the postoperative angiogram showed moderate luminal narrowing of the anterior and middle cerebral arteries in the region directly adjacent to the clip. Although this finding may represent physiological vasospasm, it is also possible that iatrogenic vessel impingement from clip placement had occurred. If clip placement had been the cause of vessel narrowing, then one would not expect to find luminal enlargement over time (as would be expected with true vasospasm). Local luminal compression in the area of the clip could lead to progressive thrombosis and/or arterial wall changes, and eventually to complete luminal obstruction. Dujovny, et al., suggest that endothelial irregularities, in addition to flow turbulence in the area of clip placement, could act to promote thrombogenesis.

Aneurysm clip migration has been associated with the production of major ischemic syndromes. This occurrence is usually seen in the immediate postoperative period. After 3 months postclipping, the amount of induced granulomatous change is thought to help anchor the clip and prevent migration.10 No evidence for clip migration was seen in these patients.

Cerebral thromboembolic disease can cause major cerebral ischemia. Vessel occlusion in areas of prior mild stenosis (due to the SAH and clip placement) from extracranial emboli may have caused the ischemic syndromes in these cases. However, none of the patients had angiographic evidence of extracranial atherosclerotic disease or cardiac disease, or prior history of other ischemic events.

The late onset of arterial narrowing in these cases should not alter the body of evidence supporting early aneurysm surgery.37 It seems unlikely, however, that early drainage of blood from the subarachnoid cisterns would prevent the onset of “vasospasm” months after SAH. There is no doubt that if vasospasm does occur, its treatment with intravascular volume expansion and induced hypertension is greatly facilitated by the early exclusion of the aneurysm from the circulation.17,22,24

What is the most appropriate terminology for the narrowing of cerebral arterial vessels seen months after SAH and aneurysm clipping? The term “vasospasm,” which remains in wide usage, is a clinical term attempting to explain narrowing of the vessel lumen, which may or may not be reversible. The term “prolonged cerebral vasospasm” was used by Simeone, et al., in regard to vessel narrowing lasting longer than 1 hour after a single experimental stimulus, in contrast to that lasting minutes from other stimuli. The term “delayed vasospasm” has been used to describe the onset of vasospasm within the first few weeks after hemorrhage.21,25 The onset of luminal narrowing several months after SAH may be labeled “very delayed vasospasm” in keeping with usage of prior terminology. This terminology, however, offers no pathophysiologic explanation for the luminal changes noted. “Vasospasm” also implies a knowledge of the ongoing dynamics of the process. Certainly, these dynamics are not presently known.3 The term “cerebral arterial luminal narrowing” does not presume any pathological knowledge that we cannot know clinically or radiographically. In our cases, whether the narrowing was iatrogenically induced at the time of surgery or secondary to the SAH itself is not conclusively known. It may be that, histologically, a proliferative vasculopathy more accurately explains the luminal narrowing, rather than active constriction of vascular smooth muscle.

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References


D. Kondziolka, et al.
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Address reprint requests to: Mark Bernstein, M.D., F.R.C.S.(C), 25 Leonard Avenue, Suite 211, Toronto, Ontario M5T 2R2, Canada.

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