Cerebral Vasospasm With Infarction

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Abstract:
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A case of intense unilateral cerebral vasospasm with appropriate neurological deficit following rupture of a posterior communicating aneurysm was followed with serial angiography. Associated with the initially intense spasm was subsequent regional hyperperfusion with early venous filling which disappeared as signs of focal cerebral atrophy ensued. These angiographical findings can explain previous reported autopsy demonstrations of focal infarction in the distribution of aneurysm-bearing cerebral vessels. Laboratory cerebral blood flow studies in conjunction with experimental subarachnoid hemorrhage indicate that constriction of major cerebral arteries to less than one-half of their normal caliber is associated with reduction in regional cerebral blood flow to infarction levels.

Additional Key Words:
cerebral blood flow
subarachnoid hemorrhage
luxury perfusion

Constriction of major cerebral arteries is often observed angiographically after rupture of a cerebral aneurysm. This phenomenon is seen soon after the subarachnoid hemorrhage, and is present with variable and decreasing frequency on angiograms taken subsequently, up to eight weeks after the hemorrhage.1,2 Angiographical vasospasm may rarely accompany severe head trauma and meningeal infections.3 Clinical studies indicate that vasospasm after subarachnoid hemorrhage from an aneurysm is associated with a significant increase in subsequent mortality and morbidity.1,4 Other studies, however, suggest that vasospasm is not necessarily associated with a reduction in cerebral blood flow.5 Because angiographical arterial constriction has frequently been observed in patients who are alert and free of neurological deficit following aneurysmal rupture, some have questioned the effect of this phenomenon on cerebral perfusion. Gurdjian,6 in a comprehensive review of this problem, concluded, “Whether or not spasm can actively cause infarction is difficult to say at present.”

The following case, complemented by several serial angiograms, suggests that extensive cerebral infarction can be produced by severe arterial vasospasm.

Case History
V.C., a 38-year-old Negro female, was in excellent health until November 26, 1968, when she suddenly experienced violent bilateral retro-orbital pain which progressed to involve her entire head and the back of her neck. She presented to the emergency room of the Pennsylvania Hospital one hour later after a transitory loss of consciousness. On arrival her blood pressure was 180/110 and pulse 84. She complained of intense headache. Neurological examination was within normal limits with a suggestion of nuchal rigidity. A lumbar puncture demonstrated grossly bloody spinal fluid which did not clear in three tubes.

The following day four-vessel angiography was performed. This demonstrated an aneurysm at the left posterior communicating artery and mild spasm of the adjacent internal carotid artery (fig. 1). Because of mild vasospasm, surgery was deferred until December 3, 1968. At craniotomy, the left internal carotid artery was approached by retraction of the frontal and temporal lobes along the sphenoid wing. The aneurysm was found to be...
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FIGURE 1

Left carotid arteriogram which demonstrates an aneurysm at the posterior communicating artery-internal carotid artery juncture.

rather broad and its neck could not be isolated or occluded. During the procedure there was bleeding from the fundus of the aneurysm. The aneurysm was deemed inoperable from a direct approach, and the operation was concluded in favor of gradual common carotid occlusion at a later date. The internal carotid artery still appeared to be in some degree of spasm at the termination of the procedure.

The patient recovered promptly from surgery, but on the following morning weakness was noticed in her right arm and face. Speech difficulty ensued and by December 5, the patient was aphasic. On December 6, a left carotid arteriogram demonstrated intense constriction of the intracranial portion of the left internal carotid artery (fig. 2). The spasm was of such severity that the middle and anterior cerebral arteries on the left side were barely visualized. During the ensuing days, her neurological status remained relatively the same. By December 16, she was able to answer "yes" and "no," and she could write intelligibly with her left hand. On the following day, a left carotid arteriogram demonstrated considerable vasospasm of the internal carotid and middle cerebral arteries, though much less than was revealed on the previous study. There was a marked hyperemic area on the angiogram whose pattern was typical of the vascular "blush" seen a few days after a fresh cerebral infarction.1, 8 There was early venous filling through this region (fig. 3).

The patient's condition continued to improve, and on January 1, 1969, she was able to express herself in two-word and three-word sentences. However, the right hemiparesis remained fixed.

To ascertain the patency of the aneurysm a final arteriographical study was performed on January 2, 1969. This demonstrated virtual complete resolution of the spasm. The vascular "blush" was gone, but in its place early venous filling through the infarcted area was visualized (fig. 4). The thalamostriate vein in the A-P projection indicated significant atrophic enlargement of the left lateral ventricle when compared to the preoperative study (fig. 5). The CSF pressure was normal and there was no clinical evidence of communicating hydrocephalus. The patient was discharged on March 22, 1969, for physical and speech therapy. At the time of discharge, she had developed proximal movement of her right arm and leg.

During the following three years, her condition has remained relatively stable. She has had occasional right-sided seizures. She is able to walk with a spastic gait, but has little right arm function. Her speech is restricted to short sentences.
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This is the last film of the angiographical series performed on the third postoperative day. There is intense spasm of the intracranial portion of the internal carotid artery (arrow) and poor filling of the other arteries.

Discussion

Because several angiograms were performed to determine the course of vasospasm and aneurysm filling here, a classical angiographical pattern of progressive cerebral infarction was demonstrated. One might reasonably assume that if serial angiograms were performed more frequently, instances of infarction secondary to vasospasm would be observed more commonly.

Focal infarctions in the distribution of major cerebral arteries have been observed during postmortem examination of the brains of patients who succumbed to ruptured cerebral aneurysms. Large cerebral arteries do not appear to be in spasm at autopsy, so a clear relationship between the vasospasm and infarction has not been observed. However, it is not infrequent to observe focal neurological deficit such as a hemiplegia or monoplegia when intense angiographical vasospasm of the contralateral internal carotid or middle cerebral artery is observed. Coma and death are commonly associated with angiographical demonstration of severe bilateral vasospasm following rupture of a cerebral aneurysm. It is similarly common to see angiographical narrowing of arteries without focal deficit or alteration in consciousness. This has led some to believe that vasospasm is not a symptomatic phenomenon. Similarly, Zingesser et al. found poor correlation between the angiographical appearance of cerebral vasospasm and cerebral blood flow. However, their study lacked cross-correlation in time between the performance of the cerebral blood flow studies and onset of symptoms. A few of their patients with the most severe angiographical spasm did show a reduction on the concomitant flow study.

Spasm commonly does not become symptomatic until 24 to 48 hours after spontaneous rupture or intracranial surgery on an aneurysm. Du Boulay found that relaxation of spasm could take as long as four weeks. However, during the latter interval patients were often asymptomatic. The presumed explanation for the apparently capricious nature of symptoms associated with cerebral vasospasm is probably a reflection of the degree of constriction as well as the length of vessel involved in constriction.
The capacity of cerebral vasculature to autoregulate is sufficient to maintain perfusion in the presence of modest proximal arterial constriction. However, when the arterial constriction becomes severe even the maximally dilated arterial bed cannot perfuse the brain adequately and symptoms develop. This hypothesis precludes the participation of the arteriolar bed in the vasospastic phenomena. Some skepticism of the role of spasm in the production of infarction lies in the demonstration of neurological symptoms following ruptured cerebral aneurysm in the presence of a subsequently normal cerebral angiogram. Here again, the angiogram must be performed during the onset of the symptomatology. Because of the waxing and waning character of this phenomenon, cerebral infarction may become established and remain symptomatic although the vasospasm has relaxed at the time of a later angiogram.

Pathological Studies
At autopsy Robertson noted that cerebral infarction occurred commonly after rupture of intracranial aneurysm. He observed microscopic infarctions in brains which appeared grossly normal or edematous. Frankel and Alpers found a softening of the brain in the distribution of the middle cerebral artery with middle cerebral aneurysms which had ruptured in the past. The findings were independent of destruction due to hematoma formation. Tomlinson and Smith similarly noticed ischemic lesions in the territory of aneurysm-bearing vessels. Birse and Tom found infarctions remote from the territory of the aneurysm-bearing vessels in six of eight autopsy specimens. Gross and microscopic examinations failed to reveal the cause. They did demonstrate marked constriction of the right anterior cerebral artery, immediately proximal to an anterior communicating aneurysm, and infarction in the distribution of this vessel in one case. Some of these observations were made before the angiographical phenomenon of cerebral vasospasm was appreciated. Subsequently, Schneck noted that infarcts were
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FIGURE 4

This angiogram, taken 30 days after surgery, indicates almost complete resolution of the spasm and disappearance of the vascular blush. A small portion of the aneurysm still fills.

commonly found on the side of the brain contralateral to the aneurysm. He noted that among 51 patients who had angiography, 23 showed vasospasm on arteriograms taken sometime during their clinical course. Sixty-five percent of these demonstrated infarcts at autopsy. Of the remaining 28 patients in whom vasospasm was not mentioned, 23 had infarcts at 82% incidence. He concluded, "Vasospasm by itself, if it does occur spontaneously following aneurysm rupture, does not seem to be the most significant cause of cerebral infarction." He felt that, at most, it accounted for a small percentage of infarctions among the 105 brains he studied. In addition, he felt that vasospasm itself would be insufficient to cause infarction, though in combination with intracranial hypertension, systemic hypotension, diagnostic angiography and therapeutic procedures, the point of infarction could be reached. In a subsequent study, however, Schneck and Kricheff found that vasospasm was present angiographically in 62% of patients with infarctions, where only 38% without evidence of angiographical spasm had areas of encephalomalacia. They explained the variance on the discrepancy of the radiological interpretation. Instead of relying on a radiographical film report, a prospective study of the angiograms was done by one radiologist and more instances of vasospasm were found. They still observed that 62% of patients with infarcts had spasm whereas 52% of patients without infarcts also had vasospasm. However, they emphasized that spasm in cases with infarcts was always "marked" (that is, lumen narrowing greater than 60%) and diffuse. They described one case in which an angiographical "stain" was observed in an angiogram on a patient with a ruptured middle cerebral artery aneurysm. There was no angiographical evidence of spasm or occlusion; however, encephalomalacia was observed in this area at autopsy. On review of their original cases, they were more willing to accept the concept that cerebral vasospasm alone was capable of producing cerebral infarction, but they had no sequential angiograms to confirm this.

Crompton,18 1964, initially reported poor correlation between hypothalamic infarctions and spasm. Subsequently, he noted a high incidence of spasm judged "severe" by the
In the AP projection of the angiogram shown in figure 4, fine collateral channels in the arterial phase fill the thalamostriate vein which outlines an enlarged ventricle. The absence of shift or other signs of increased intracranial pressure suggests that this is an atrophic ventricular enlargement secondary to the infarction.

Spasm was induced in a monkey by puncture of the right internal carotid artery. Two days later the animal developed intense arterial constriction on the angiogram, associated with markedly reduced cerebral blood flow. Above is a radiograph of the brain made after the cerebral arteries were well perfused with barium during the spasm. Note the poor distal filling on the affected side (small arrows) and intense constriction of the right middle cerebral artery.

radiologist in brains demonstrating cerebral infarcts after death from ruptured cerebral aneurysm. In contrast, only one out of 33 brains without cerebral infarcts demonstrated "severe" angiographical spasm during life.

Laboratory Data
Subarachnoid hemorrhage has been produced in over 200 monkeys in our laboratories by puncture of the intracranial internal carotid artery with a fine needle. Subsequent angiographical studies determined that this technique produces angiographical spasm lasting from one hour to several days in more than two-thirds of these animals. Recently cerebral blood flow studies by the Krypton-85 washout method have complemented the angiographical assessment of spasm. Angiographical constriction of the internal carotid artery or middle cerebral artery of less than one-half of its control caliber was not associated with a significant (less than 25% below control) reduction in flow. When these vessels constrict to finer than half of their control diameter, a phenomenon which usually occurred later during progressive spasm, the regional blood flow decreased markedly. Although the length of the spastic vessel was not measured, most examples of spasm showed a uniform constriction throughout the involved vessel.

Figure 6 is a radiograph of an arterial barium cast made immediately after sacrifice of a monkey with intense unilateral spasm so produced. Note the poor distal perfusion which might well lead to infarction.

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