Reversible Cerebral Segmental Vasoconstriction

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Vasoconstriction is not recognized as a cause of cerebrovascular disease except in the vasospasm seen following subarachnoid hemorrhage and possibly in migraine. However, we found four patients to have transient, fully reversible vasoconstriction and dilatation prominently involving arteries around the circle of Willis. All four patients were evaluated for severe headaches and fluctuating or recurring motor or sensory deficits. No cause for the clinical syndromes and angiographic abnormalities was found. Similar patients are reported in the literature under various nosologies. This newly recognized clinical-angiographic syndrome should be differentiated from other known causes of vessel constriction and dilatation; the precipitants of reversible vasoconstriction may then be better defined. (Stroke 1988;19:1159–1170)

The pathophysiology of constriction of the cerebral vasculature is largely unknown. A reversible form of constriction, called vasospasm, has been shown to follow subarachnoid hemorrhage from a ruptured saccular aneurysm.1 Vessel constriction followed by dilatation is a postulated mechanism for migraine, although there is no definitive evidence for this.2 Aside from these two conditions, reversible constriction of arteries is not a recognized cause of cerebrovascular disease.

We describe the clinical and angiographic syndrome of four patients with reversible constriction of the cerebral vasculature. We also review some of the relevant literature and discuss the nosology of this only recently recognized condition.

Case Reports

Case I

A 48-year-old woman was admitted to the hospital because of a severe headache that was associated with a sense of spinning, nausea, vomiting, and blurred vision. Headaches were unusual for her, and there was no personal or family history of migraine.

Initially, her blood pressure was 200/100 mm Hg, but it quickly fell to the 120/65 mm Hg range without medication; other vital signs were normal. Her neck was supple. The general physical examination was normal. The neurologic examination was unremarkable except for a left Babinski's sign.

Complete blood count (CBC) showed a leukocytosis of 14,000/mm 3. Sedimentation rate was 20 mm/hr. Electrolytes and other blood chemistries were all normal. Cranial computed tomograms (CT scans) with and without contrast were normal. A lumbar puncture was traumatic and showed an opening pressure of 170 mm; the fourth tube of cerebrospinal fluid (CSF) was clear and colorless and contained 92 erythrocytes and no leukocytes. Protein content was 38 mg/100 ml and glucose content was 64 mg/100 ml. Meperidine relieved her headache for several hours; it then recurred, beginning a pattern of daily throbbing headaches that waxed and waned.

On Day 3 of hospitalization she had a focal seizure involving her left face, arm, and leg; a residual mild left hemiparesis slowly resolved over several days and she was started on phenytoin. On Day 4 a cerebral angiogram showed slight irregularities in the caliber of several leptomeningeal arteries; she was started on 60 mg/day prednisone. On Day 12 her gait was wide-based and unsteady. On Day 14 her legs felt numb. On Day 15 her right arm and leg became weak, and a right Babinski's sign appeared; a repeat cranial CT scan was normal. On Day 16 a cerebral angiogram showed segmental narrowing of intracranial arteries, particularly the posterior cerebral artery, which filled on both carotid and vertebral injection (Figure 1, top). Smaller leptomeningeal branches were less involved (not illustrated). A repeat lumbar puncture yielded clear, colorless CSF containing two erythrocytes and...
no leukocytes; protein content was 61 mg/100 ml and glucose content was 81 mg/100 ml.

On Day 18 she complained of blurred vision. On Day 19 she stated that she was blind; examination disclosed a right homonymous hemianopsia, left superior quadrantanopsia, a slight right hemiparesis, and bilateral Babinski's signs. The retinas were normal. A repeat cranial CT scan showed low-density lesions bilaterally in the occipital and parietal lobes.

Her vision improved during the next 2 days. On Day 22 she was started on 200 mg/day cyclophosphamide and 2 inches nitroglycerin paste every 3 hours and the prednisone was increased to 80 mg/day. During the next 2 weeks, her neurologic examination improved remarkably and her headaches decreased in frequency and severity. On Day 37 a repeat angiogram showed normal vessels (Figure 1, bottom). At discharge on Day 40 her only abnormalities were bilateral central scotomas, a right inferior quadrantanopsia, and a mild right hemiparesis; she no longer had headaches. Her medications were continued as an outpatient. Seven weeks later she was admitted again because of recurrent headaches, numbness, and weakness of her right arm. Examination was the same as on discharge. An angiogram at this time was normal, and she returned home.

Headaches recurred 6 months after her original admission, and she was admitted again. Another cerebral angiogram showed minimal irregularities of the caliber of the intracranial arteries bilaterally (not illustrated), particularly of distal branches of the inferior division of the middle cerebral artery. A
middle cerebral branch cortical artery 1 mm in diameter was biopsied through a small craniotomy at a site corresponding to an angiographic abnormality; the meninges and underlying cortex were also biopsied, as were the superficial temporal and occipital scalp arteries. These structures appeared grossly normal, and all microscopic studies were normal.

The patient was discharged home with a right inferior quadrantanopsia and mild right hemiparesis. She has remained otherwise well and free of further symptoms for 3 years. The prednisone, cyclophosphamide, and nitroglycerin were gradually discontinued.

Case 2

A 37-year-old woman was admitted to the hospital after losing consciousness. She was well until the evening of admission, when she developed a severe left-sided headache and minutes later was seen to slump to her left; there were no movements suggesting a seizure.

History was remarkable for 10 years of recurrent left hemicranial headaches with a visual prodrome. The headaches occurred about twice a year and were treated with acetaminophen and an ergot preparation.

In the hospital she regained consciousness over several hours. She complained of headache, tingling in her left fingers, blurring in her right visual field, and difficulty in swallowing. Vital signs and general physical examination were normal, and her neck was supple. There was moderate weakness of her left face, arm, and leg, with brisk reflexes and a left Babinski's sign. The sensory examination was normal.

CBC, blood electrolytes, and blood chemistries were normal; sedimentation rate was 20 mm/hr. A cranial CT scan of the brain without contrast was normal.

She was treated with nadolol, dexamethasone, aspirin, dipyridamole, and nifedipine, and her headaches slowly abated over 6 days. On Day 3 a lumbar
puncture yielded an opening pressure of 240 mm; the CSF was clear and colorless and contained 10 erythrocytes and no leukocytes; protein content was 51 mg/100 ml and glucose content was 60 mg/100 ml. On Day 5 a repeat cranial CT scan was normal. The patient’s hemiparesis was improving when on Day 8 she awakened with a severe headache, nausea, and vomiting; she became lethargic and developed dysarthria and increased left-sided weakness. These changes resolved in about 3 hours. On Day 9 a cranial CT scan showed a low-density lesion in the right basis pontis. On Day 12 a cerebral angiogram showed irregularities of the caliber of arteries adjacent to the circle of Willis, particularly the basilar artery (Figure 2), which were initially thought to represent standing waves or fibromuscular dysplasia (FMD).

Her last headache occurred on Day 16. She was discharged on Day 25 with a mild left hemiparesis.

An angiogram 1 month later, nearly 2 months after the original study, showed the basilar artery to be normal (Figure 3, right). Her medications were gradually discontinued. She has remained free of further symptoms for nearly 3 years.

Case 3

A nineteen-year-old man was in good health until he awoke one morning with a severe frontal and bitemporal headache associated with nausea and vomiting. He was seen in an emergency room, treated with analgesics, and discharged. His headaches persisted and became associated with photophobia. On Day 2 after the onset of his headache he was admitted to the hospital.

On admission, his neck was supple and the general and neurologic examinations were normal. A lumbar puncture on Day 3 was traumatic and had an opening pressure of 130 mm; there were 10,200 erythrocytes and five leukocytes; CSF protein content was 60 mg/100 ml and glucose content was 64 mg/100 ml. There was no xanthochromia. CBC, blood electrolytes, and
FIGURE 4. Case 3. Right vertebral angiogram on Day 5 showing narrowing of proximal superior cerebellar arteries and narrowing and dilatation of their hemispheric branches bilaterally (white arrows).

blood chemistries were all normal. On Days 5 and 6 cranial CT and magnetic resonance imaging brain scans were done; both were normal. On Day 5 a cerebral angiogram showed segmental narrowing of the origins of both superior cerebellar arteries and of their hemispheric branches (Figure 4) as well as segmental narrowing of the sylvian branches of the middle cerebral artery (not illustrated).

His headache persisted, and on Day 9 he developed tingling numbness of his left face, arm, and leg for 1 hour. On Day 16 a repeat angiogram showed changes similar to the original angiogram; his headache temporarily worsened following the procedure. He was discharged the next day with only a mild headache.

On Day 25 after the onset of his illness, 9 days after discharge, a severe headache recurred. Five days later he was admitted again to the hospital; general and neurologic examinations at that time were normal. A repeat lumbar puncture showed an opening pressure of 190 mm; the CSF was clear and colorless with no erythrocytes and three leukocytes. He was discharged 2 days later feeling much improved. He has been free of symptoms for >7 months.

Case 4

A 34-year-old man was admitted to the hospital because of a rash. He had been well until 2 months before admission, when he developed otitis media that required drainage and amoxicillin therapy. After 2 weeks on antibiotics he developed hemorrhagic bullae on the dorsum of his feet associated with pain in his knees and later with pain in his elbows, hips, and shoulders. The amoxicillin was stopped, and the rash cleared only to flare again on his feet, trunk, and elbows. One month before admission he was started on 40 mg/day prednisone, and the rash improved for 2 weeks but worsened when the prednisone was tapered. During his illness he lost 20 pounds, suffered persisting arthralgias of multiple joints, and coughed up a small amount of blood on one occasion.

Physical examination at admission revealed purpuric lesions of his feet, hands, arms, buttocks, trunk, face, and lips; the remainder of the general and neurologic examinations were normal. The following laboratory studies were normal or negative: CBC, electrolytes, liver enzymes, blood urea nitrogen and creatinine, antinuclear antibody, rheumatoid factor, hepatitis B surface antigen, VDRL, chest x-ray, and electrocardiogram. Sedimentation rate was 45 mm/hour. A skin biopsy was consistent with but not diagnostic of leukocytoclastic vasculitis. The prednisone dose was increased to 60 mg/day, after which no new skin
lesions appeared. In the morning of the fifth hospital day he complained of severe generalized headache and complained that his right leg, particularly his foot, was weak. That evening he slumped to his left and experienced several minutes of left arm and leg weakness associated with a left Babinski's sign and brisk reflexes in all limbs. In the afternoon of the sixth hospital day he became severely paretic in his right face, arm, and leg and weak in his left leg so that he was unable to walk. A cranial CT scan was normal. A lumbar puncture yielded clear, colorless CSF with an opening pressure of 200 mm; the fluid contained two erythrocytes and 16 leukocytes, all lymphocytes; protein content was 51 mg/100 ml and glucose content was 64 mg/100 ml. A cerebral angiogram showed bilateral segmental narrowing of the supraclinoid internal carotid arteries, proximal middle and anterior cerebral arteries (Figure 5), and the proximal posterior cerebral arteries (Figure 6). He was started on 150 mg/day cyclophosphamide and heparin; the prednisone was continued.

Over the next 4 days he generally improved, only to develop a recurrent severe right hemiparesis. On the thirteenth hospital day he was temporarily dysarthric. On the nineteenth hospital day, a repeat angiogram showed much, but less, narrowing of the distal internal carotid (Figure 7) and proximal posterior cerebral arteries, but changes were more pronounced in the basilar artery (Figure 8). During the days following angiography he made steady improvement and was discharged on the twenty-sixth hospital day with a normal neurologic examination. First the cyclophosphamide, then the prednisone were tapered and stopped.

An angiogram 4 months later, while the patient remained asymptomatic, was completely normal (Figure 9).
Analysis of Cases

The four patients were healthy young people (aged 47, 37, 19, and 34 years) whose neurologic syndrome began with a severe headache. Unilateral or bilateral hemiparesis, visual field defects, and sensory deficits developed abruptly, and at their worst the symptoms were profound in three patients. The symptoms fluctuated in severity or recurred with intervals of normalcy or steady improvement. Cases 1 and 2 had mild residual hemiparesis; Case 1 also had visual field defects. At the onset of the illness, Case 1 had a seizure and Case 2 temporarily lost consciousness; otherwise mentation remained clear throughout their prolonged clinical courses. Full resolution of the headache and stabilization of the recurring or fluctuating motor and sensory abnormalities took between 2 weeks and 2 months.

Cerebral angiographic patterns were distinctive and characteristic, showing narrowing (often severe) of the arteries contributing to and arising from the circle of Willis. Segments of narrowed vessels alternated with dilatation or vessel segments of normal caliber. Similar but less striking changes were also present in smaller cortical vessels in Cases 1, 2, and 3. In all four patients the narrowing was bilateral and involved both the anterior and posterior circulations, though not necessarily equally.

The angiograms demonstrating segmental constriction were performed from 4 to 12 days after the onset of the initial headache. In Case 1, in which the initial angiogram was performed on Day 4, the abnormality was slight; another angiogram on Day 16 showed a more fully developed state. In Case 2 the changes in the basilar artery were initially thought to be consistent with standing waves or FMD, but a lesser abnormality in the second and full resolution in the third angiogram excluded these possibilities. Case 4 had a CSF pleocytosis, suggesting an arteritis; however, the similarity of his clinical course and angiographic patterns to those of the other cases, marked improvement in the anterior circulation while the
Figure 7. Case 4. Progress top: left and bottom: right carotid angiogram was improved, but lumen calibers were still reduced.
posterior vessel changes were still prominent, and sudden complete clinical resolution with a fully normal angiogram later excluded the possibility of arteritis and suggested another process. In Cases 1, 2, and 4 the angiographic abnormalities were still present when the patient was recovering or had fully recovered; in these three cases repeat angiograms 1–4 months later showed complete resolution of the vessel constriction. A biopsy of a minimally involved artery in Case 1 during recurrence of the symptoms was normal. A salient and remarkable feature of all four patients was the occurrence during their illness of days of normalcy or improvement.

Discussion

There are reports of 12 cases\textsuperscript{3–10} in the literature that resemble our patients clinically and angiographically, although the nosologies are different and include "migrainous vasospasm" and "arteritis," the latter with negative biopsies. Six\textsuperscript{8,9} occurred in the postpartum period, five\textsuperscript{3–6,10} were idiopathic, and one\textsuperscript{7} occurred in association with an unruptured saccular aneurysm. We have seen three additional cases, two following carotid endarterectomy and one during the third week of Guillain-Barré neuropathy.

Sixteen of the 19 cases that have come to our attention were women. Of the 19, there were two patients aged 10–19 years, four aged 20–29 years, four aged 30–39 years, two aged 40–49 years, and three aged >50 years; the ages of four were not specifically stated, although two were postpartum women. A salient and constant feature of the cases was the occurrence of a sudden, high-intensity headache associated with nausea, vomiting, and sometimes photophobia, much like a ruptured saccular aneurysm. In one case a seizure preceded the headache; in seven cases one or more seizures occurred at or near the time of onset or in the next few days, leaving a variable postictal sequela that slowly resolved. In 12 cases recovery from the motor or sensory deficit was complete or nearly so. Three had a persisting hemiparesis (one also had a field defect and one had aphasia), and one deliv-
FIGURE 9. Case 4. Follow-up bilateral (left: left and right: right) carotid and (bottom) left vertebral angiograms were normal.
oped bilateral hemiparesis and cortical blindness. Three other patients, after developing unilateral or bilateral hemiparesis, sank into a coma and died, one 6 days, one 18 days, and one 4 months after the onset of headache. Of the 12 cases with complete recovery, the illness, from the onset of headache to recovery, lasted 6–30 days. The duration of the illness was specified in three of the four cases in which the deficits persisted and ranged from 16 days to 6 months.

The CSF was perfectly normal in eight cases, and in another three the presence of a small amount of blood was thought to be due to trauma. In those cases the protein content was elevated at 51, 55, and 125 mg %; in three there was a pleocytosis (of six and 16 leukocytes, respectively) and in three the CSF was either not sampled or the results were not recorded. In no case was an infectious agent isolated nor was there evidence of a ruptured saccular aneurysm. The eight cases with abnormal CSF findings are included because in most instances the abnormalities were minor or incidental, and in all cases the abnormalities proved not to be indicative of a specific process. In six cases study of the pathology of vessels involved angiographically was available, in three by biopsy and in three at autopsy. In no case were anatomic abnormalities discovered.

Reversible vasoconstriction of the cerebral vasculature is recognized to occur following subarachnoid hemorrhage due to a ruptured saccular aneurysm,1,11 and following sympathomimetic drug intoxication,12–14 surgical manipulation,15 and closed head injury.16 Alternating segments of constriction and dilatation are sometimes seen in leptomeningitis and various cerebral vasculitides,17 including the acquired immunodeficiency syndrome18 and following herpes zoster ophthalmicus.19 It has not been a feature in cases of pathologically proven primary granulomatous angiitis of the central nervous system,20–22 because this latter process appears restricted to vessels of ≤0.5 mm diameter that are not visualized with angiography. Finally, it has been postulated that the migraine prodrome and headache are due to reversible vasoconstriction followed by dilatation. Radiographic demonstration of these events is limited to two case reports.33,34

The clinical and angiographic characteristics of the cases we considered are most consistent with a physiologic segmental narrowing of arteries without a structural correlate such as a cellular infiltrate. The known occurrence of transient, fully reversible vasoconstriction following subarachnoid hemorrhage, sympathomimetic drug abuse, surgical manipulation, and closed head injury suggests that various forms of chemical and mechanical stimuli can precipitate the process. The migraine syndrome may represent another variation and may also be multifactorial. Regarding migraine, the 19 cases considered here demonstrate that reversible arterial narrowing and dilatation can cause or can at least be closely associated with severe recurrent headache and transient (or permanent) neurologic deficits. Its common occurrence in young women and in the postpartum period suggests a hormonal influence. Our cases may well represent a severe, “clustering” form of migraine. Recognition of the clinical-angiographic syndrome may better define the circumstances of its occurrence.

References


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