Stroke From Other Etiologies
Masquerading as Migraine-Stroke

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There has been a recent increase in the number of studies dealing with migraine-stroke. I describe five patients in whom migraine-stroke was the clinical diagnosis but in whom the subsequent clinical events or autopsy showed a different mechanism for the cerebral infarction. Three patients had arterial dissection (one proven at autopsy), one had marantic endocarditis that had been missed on two echocardiograms (proven at autopsy), and one had generalized atherosclerosis and diabetes. These patients demonstrate that important and different etiologies may produce what seems to be the migraine-stroke syndrome. The result may be failure to recognize specific therapeutic measures that could have vitally important benefit to the patient. (Stroke 1991;22:1068–1074)

Until recently, cerebral infarction related to migraine was considered rare, with only 64 cases reported before 1983. Several recent publications suggest that "migraine-stroke" is more common than was previously suspected, but the mechanism leading to the stroke is still not well understood. In cases for which autopsy data are available, a single cause for the stroke has not been consistently observed. While vascular hyperplasia, vascular dissection, cerebral edema, and endarteritis have all been reported with migraine-stroke, the presence of migraine at stroke onset does not mean that migraine initiated these vascular factors producing the stroke. In fact, it is not unusual to find no cause for the stroke, even at autopsy. With little supportive evidence, carotid or vertebral vasospasm resulting in a critical degree of cerebral hypoperfusion is frequently believed to be the underlying mechanism for stroke.

I describe five patients with a history of migraine headache who developed cerebral infarction. Migraine-stroke was the initial diagnosis, but the diagnosis was changed subsequently.

Case Reports

Patient 1

A 42-year-old woman was seen in the emergency department with a 2-day history of severe migraine headache. She had a long history of migraine without aura, and her headaches had recently been increasing in intensity and frequency. Precipitating factors included a lack of sleep, alcoholic beverages, and stress. Associated features included photophobia, phonophobia, nausea, and occasional vomiting. Her headaches responded well to nonnarcotic analgesics.

While the patient was being examined, she developed the sudden onset of right-sided weakness and aphasia. An emergency two-dimensional echocardiogram (2D-echo) was suggestive of mitral valve thickening, and the patient received heparin. The next day the same 2D-echo was reassessed and believed to be normal, and the anticoagulant treatment was discontinued. During the next 2 weeks the patient's hospital course was complicated by a second cerebral infarction, this time to the right hemisphere, a progressive decrease in the level of consciousness, and disseminated intravascular coagulation (DIC) of unknown cause. There had been no evidence of DIC during admission investigations. Additionally, respiratory distress led to her intubation and transfer to the intensive care unit.

Cranial computed tomography (CT) after the first stroke showed a left cerebral infarct, and a second CT scan showed the second right-sided infarct (Figure 1). Cerebral angiography after the initial stroke showed branch occlusion in the left middle cerebral artery (MCA) territory. The remainder of the angiogram was normal. The results of a collagen disease workup and hematological investigations were normal, as were three sets of blood cultures. A second 2D-echo after the second infarction was again reported as normal. After completion of the initial investigation, migraine-stroke was considered to be the most likely diagnosis. The diagnosis remained unchanged until the patient died since cardiac, hematological, and collagen disease workup failed to support an alternate diagnosis.
Two weeks after admission, the patient died of complications of DIC and respiratory failure. At autopsy, the two cerebral infarcts were clearly evident. There was no evidence of atherosclerotic vascular disease. Unexpected findings on general autopsy included a grade IV carcinoma of the cervix and marantic endocarditis affecting the mitral valves. Additionally, there was evidence of extensive systemic embolization in the spleen, pancreas, kidneys, and mesentery. Systemic and cerebral emboli were most likely secondary to dislodgement of thrombi from the mitral valves, which unfortunately could not be diagnosed during life.

**Patient 2**

This 29-year-old man had a long history of migraine with and without aura. His headaches were unilateral and associated with nausea, vomiting, and photophobia. Occasional headaches were preceded by visual symptoms of fortification spectra that lasted for 10–15 minutes. Headaches after the visual auras were commonly very severe. No definite precipitating factors were evident, and the severe headaches required narcotic analgesics for relief.

On the day of admission the patient developed a severe migraine headache without aura and had to leave work. There was no history of trauma. By the evening, his headache had abated somewhat and the patient attended a church service. At approximately midnight, the headache suddenly became very severe and while awake the patient developed involuntary spasms affecting his left arm and leg. Except for the unusual severity, the headache had characteristics typical of previous migraines. During the initial emergency evaluation, the patient was awake and alert but showed intermittent left-sided decerebrate posturing. The results of right-sided motor and sensory examination appeared normal. An initial emergency CT scan was normal. Overnight the patient became comatose and continued to show intermittent decerebrate posturing. A cerebral four-vessel angiogram was interpreted as normal although a small irregularity of unknown significance was noted in the basilar artery. The results of hematological, collagen disease, and cardiac investigations were normal. A repeat CT scan showed bilateral superior cerebellar infarcts. The patient remained in a chronic vegetative state for 6 weeks and subsequently died of complications of sepsis.

At autopsy, the two cerebellar infarcts were clearly evident. The basilar artery appeared poorly developed, and the posterior communicating artery was atrophic. At the junction of its upper third and lower two thirds, the basilar artery showed a 5-mm region of hemorrhagic discoloration (Figure 2). Other cerebral blood vessels were grossly normal. Cross-sections of the pons showed bilateral cystic infarcts, and similar infarcts were evident bilaterally in the cerebellum. Cross-sections of the basilar artery at the hemorrhagic region showed a small dissection in the arterial wall, in the middle two-thirds of the media, which reduced the vessel lumen to approximately 10% of its original size. Findings of the remainder of the autopsy were normal.

**Patient 3**

This 56-year-old man had a 40-year history of migraine with and without aura. Most migraine episodes began with unilateral frontal headaches associated with nausea, vomiting, and photophobia. Occasional headaches were preceded by visual symptoms of scintillating scotomas and fortification patterns. These visual auras usually lasted 10–15 minutes.

Other medical problems included a 7-year history of non–insulin-dependent diabetes, controlled hypertension, and symptomatic ischemic cardiovascular disease for which the patient had undergone coronary artery bypass surgery 2 years earlier. There was also a strong family history of cerebrovascular and cardiovascular disease.

On the day of admission, the patient developed a typical migraine headache with aura. The visual symptoms were followed by a unilateral headache, and approximately 20 minutes after the onset of the headache the patient noted the sudden onset of weakness of the right side of his body with speech difficulties. The weakness resolved shortly, but his speech difficulties persisted for several weeks before eventual recovery.

Initial evaluation showed a small infarct in the left caudate on a cranial CT scan. Cardiac and hema-
FIGURE 2. Photograph taken at time of autopsy of brain from patient 2 shows small area of discoloration in basilar artery (arrowheads). Cross-sectional analysis and microscopy showed this to be arterial dissection in media of basilar artery. Distally, right posterior communicating artery is well developed while left posterior communicating artery appears severely atrophic.

tological investigations showed no other abnormalities except hyperglycemia. Migraine-stroke was clinically diagnosed. Angiography was not done because the patient was diabetic. Because of the risk factors for atherosclerotic arterial disease, a cerebral angiogram was later requested by the neurology consultant. Angiography revealed moderate generalized atherosclerosis of the common and internal carotid arteries. In addition, an ulcer with a small thrombus was evident in the proximal left internal carotid artery and there was a complete occlusion of the same artery more distally at the origin of the MCA (Figure 3).

The patient was treated with aspirin and discharged from the hospital. He has remained symptom-free for 20 months.

Patient 4

This 28-year-old woman had a long history of migraine without aura. Her headaches were pounding, bifrontal, and occurred 3–4 times/mo. Associated symptoms included nausea, occasional vomiting, photophobia, and decreased appetite. She presented to the emergency department with a severe headache and right-sided numbness that had developed in the morning. The headache was bifrontal, throbbing, and associated with photophobia. Except for being more severe, the symptoms were typical of her usual migraines. The patient was evaluated and discharged with a diagnosis of "complicated migraine" (migraine with prolonged aura). Recurrence of her symptoms 3 days later led to admission to the hospital, when a cranial CT scan showed a small infarct in the left MCA territory.
Two days later the patient developed speech difficulty, and a repeat CT showed a new infarct in the same MCA territory. Cerebral angiography was subsequently done and showed a left internal carotid artery dissection (Figure 4). The patient received anticoagulant therapy and showed excellent recovery. Anticoagulants were discontinued 6 months later, and the patient has developed no new problems.

Patient 5

This 33-year-old man had a 12-year history of migraine without aura. His headaches occurred 2–3 times/mo and lasted for <24 hours. Associated symptoms included photophobia, sonophobia, irritability, and nausea. Most headaches responded to nonnarcotic analgesics and bed rest.

Twelve days prior to evaluation in the stroke clinic, the patient was involved in a bicycle accident that left him with neck and facial bruising. He did not notice any neurological problems. Four days later, after a strenuous bicycle ride, he developed blurred vision in his left eye (covering the left eye resulted in complete resolution of the symptoms) that was soon followed by a severe left-sided pounding headache and numbness in his right arm. Visual and arm symptoms were severe for an hour and then gradually decreased in severity but did not completely disappear. However, the headache remained intermittently severe for the next 12 days.
FIGURE 4. Left cerebral angiogram of patient 4 shows gradual narrowing of internal carotid artery secondary to arterial dissection. There were no other abnormalities noted on angiography.

The patient was seen in the emergency room by the neurosurgery service. A cranial CT scan was normal, and he was discharged with a diagnosis of complicated migraine. During the next 12 days the patient had intermittent episodes of right facial paralysis with associated speech difficulties. He was seen by physicians on several occasions, and the diagnosis of complicated migraine remained unchanged. His past history was unremarkable, and the patient was on no medications.

Examination showed color desaturation in the left eye and minimal signs of left parietal lobe dysfunction (right arm drift, agraphesthesia, and hyperreflexia). Findings of the remainder of the clinical examination were normal. Specifically, carotid pulsation was normally felt on both sides and there were no audible bruits.

A repeat cranial CT scan was again normal, and an electroencephalogram showed left temporal slowing. Angiography was done to look for carotid artery dissection. The left internal carotid artery was occluded 3 cm beyond the bifurcation, and its appearance was consistent with carotid dissection (Figure 5). The patient received anticoagulant therapy and has remained symptom-free during a follow-up of 12 months.

Discussion

All five patients had migraine headaches. Focal neurological symptoms had developed during episodes of migraine or migraine-like headache in all patients, and in all patients initial investigations failed to show any other etiology for the cerebral infarction. Initial investigations, however, did not include cerebral angiography in all patients. In two patients a definite cause for the stroke could be found only at autopsy, whereas in the remainder, although the initial presentation was suggestive of migraine-stroke, subsequent developments led to the proper diagnosis. Patient 3 is particularly interesting. In this case, a typical migraine headache with aura developed 20 minutes before the onset of stroke and, although initially suspected as the mechanism for the cerebral infarction, this etiology was clearly proven wrong after completion of cerebral angiography.

Migraine is a common neurological disorder occurring in 20–30% of the population. It is therefore not unusual to find patients with cerebral infarction who also have a history of migraine. The development of cerebral infarction during a migraine headache does not always mean that the two are related. In fact, as was seen clearly with our third case, the mechanism of stroke may be very different. In some migraine sufferers, acute migraine headache may result from the stress associated with cerebral infarction. Approximately 30% of patients with acute stroke develop a headache. Thus, the headache at the onset of a cerebral infarction in a migraine sufferer may actually not be a migraine headache. In rare patients with migraine and stroke the two may be related, but the mechanism leading to stroke in such cases is not fully understood.

Autopsy-documented cases of migraine-stroke are rare. Hunt's patient, a 35-year-old woman, had a right hemiplegia, and autopsy showed thrombosis of the left common carotid artery with endarteritis and thickening of the adventitia. The patient of Neligan et al was a 41-year-old woman who had developed bilateral cerebral infarctions in rapid succession. At autopsy, multiple small infarcts were evident in the basal ganglion. Small cerebral arteries, especially those near the infarcts, showed hyperplasia of the intima. Buckle et al reported a 16-year-old patient with complicated migraine in whom a cerebral angiogram, done just prior to death, showed narrowing of the extracranial and intracranial arteries. At autopsy, there was severe swelling of the brain but no vascular pathology was evident. Sinclair reported a 26-year-old man who developed a left hemiparesis during a migraine headache and died soon thereafter. At autopsy, a nontraumatic dissection was evident in the right MCA. In the absence of another etiology, the
dissection was believed to be related to migraine. Finally, the most recent case of fatal migraine was reported by Silby and Fryer in 1984. Their patient, a 58-year-old woman, had suffered from migraine with aura since childhood. On the day of admission, she suffered flexor spasms of her left arm that were soon followed by a severe right frontal headache and left hemiparesis 1 hour later. She died 10 days later of complications of cerebral edema. Autopsy confirmed the right cerebral infarction, and a red thrombus was evident in the right MCA. The findings of a cardiac evaluation were normal, and the cerebral arteries were "patent." The infarction was believed to be secondary to "arterial vasospasm." There are rare reports of stroke from other etiologies presenting together with migraine or migraine-like headaches. This has most frequently been seen in association with the antiphospholipid antibody syndrome. Patients with the mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like events (MELAS) syndrome also commonly present with migraine-like headaches and frequent strokes. In one patient with concurrent MELAS syndrome and Kearns-Sayre syndrome, carotid arterial angiography showed segmental narrowing and branch occlusions. This patient also had a cardiomyopathy. Other conditions presenting with stroke include intracranial arterial vasculitis, occipital lobe arteriovenous malformations, and pregnancy with transverse sinus thrombosis. Recognition of such conditions is important because treatment may need to be changed. There may be genetic implications, and the prognosis may be different with different diseases.

Acknowledgments

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References


Figure 5. *Left cerebral angiogram of patient 5 shows tapering occlusion of internal carotid artery, consistent with arterial dissection. No other abnormalities were found on four-vessel angiography.*

KEY WORDS • cardioembolic stroke • dissection • migraine
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