Case Studies 3

Chapter 44

The Woman with Migraine and Recurrent Stroke

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Case History

A 31-year-old female physician reported an 11-year history of episodic migraine with and without visual aura. On four occasions in the past, she had experienced left hemiparesis with one of her typical headaches, and on one other occasion, a headache was accompanied by expressive aphasia, right hemiparesis, and complete loss of vision in the left eye; her aphasia and hemiparesis subjectively resolved, but her vision, although improved, remained impaired.

Her initial examination was notable for a partial left afferent pupillary defect, 20/400 acuity in the left eye, mild left hemiparesis, extensor plantar responses bilaterally, and cortical sensory signs in the left hand.

Brain computed tomography scan demonstrated evidence of old bilateral infarcts at the vertex and within the centrum semiovale. Elective arteriography was notable only for nonvisualization of the left ophthalmic artery.

Four days following the elective arteriogram, she developed global aphasia, right hemiparesis, and increased left eye visual loss, all in conjunction with a severe, pulsatile, lateralized headache.

Emergent cerebral arteriography demonstrated tapering stenosis and occlusion of the left internal carotid artery (ICA) several centimeters distal to the extracranial bifurcation (Figure 44-1). Follow-up arteriography 2 days later was normal.

Questions on the Case

Please read the questions, try to answer them, and reflect on your answers before reading the author's discussion.

- Aside from migraine, what causes of ischemic stroke should be considered in this case?
- How did migraine contribute to the stroke process in this case?
- How might one intervene acutely to treat this patient and prevent recurrent stroke?

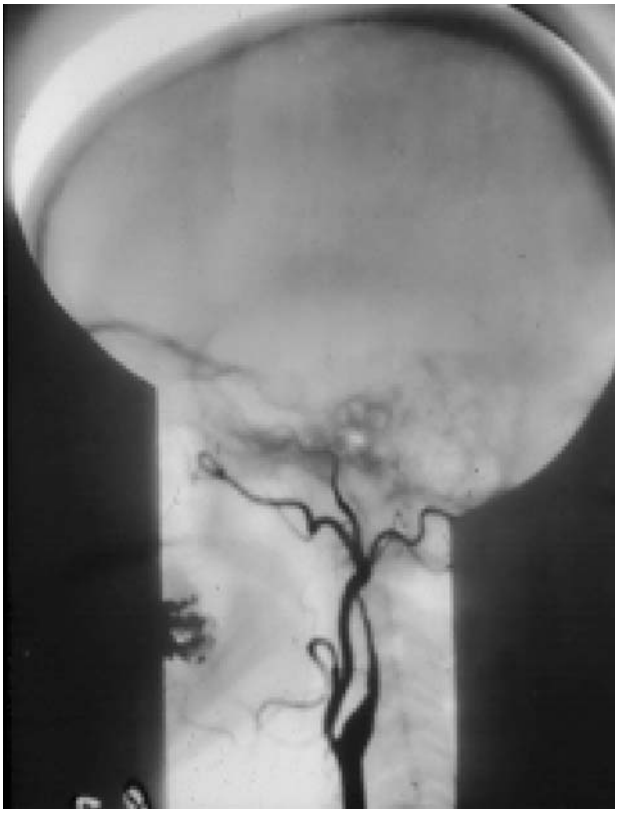

Figure 44-1. Selective left common carotid arteriogram demonstrates tapering stenosis and occlusion of the distal cervical component of the left internal carotid artery.

Case Discussion

The causes of stroke in the young are legion, but to the experienced clinician, one fact stands out starkly: if the cause of the patient's stroke is not apparent at the conclusion of the initial bedside evaluation, then the odds are low that one will identify with confidence a specific etiology for the stroke. If, on examination, abnormalities are found, their clinical relevance is not always apparent. For example, to make a definitive diagnosis in a young stroke patient who has a mechanical prosthetic cardiac valve, and whose international normalized ratio is subtherapeutic, verges on the axiomatic; but what does detection of a patent foramen ovale (PFO) imply in the young patient who has no other obvious cause for stroke?

The same holds for migraine and stroke. *Many* young people have migraine, and a few of them will suffer stroke; in how many of these cases was migraine actually causative, and in how many did it act merely as an innocent bystander? In a surprisingly high proportion of young patients with stroke, and despite diagnostic evaluations notable for their exhaustively inclusive nature (and expense), the discouraging final diagnosis is often "stroke of unknown cause."

All types of ischemic stroke, even lacunar, may generate acute headache in addition to focal neurologic deficit, but certain conditions are particularly prone to do so. In considering migraine in the differential diagnosis of stroke in a young patient, one obviously should focus on those etiologies: carotid or vertebral artery dissection, embolic infarcts involving cortex (eg, cardioembolism related to atrial fibrillation), eclampsia, use of sympathomimetic drugs, and primary central nervous system angiitis. With the exception of arterial dissection, none of these etiologies appear pertinent to the case presented here. The cerebral arteriogram performed emergently did demonstrate findings consistent with internal carotid dissection, but the rapid resolution of the arterial occlusion is inconsistent with that diagnosis and far more suggestive of vasospasm; others have reported similar clinical presentations and arteriographic findings with migrainous infarction. Extensive blood testing, extended cardiac monitoring, and echocardiography led to no plausible alternative diagnosis in this case.

Migrainous Infarction

The majority of strokes occurring in migraineurs do not take place during an acute migraine attack, and migrainous infarction per se is rare. Current International Headache Society (IHS) criteria for the diagnosis of migrainous infarction require that the afflicted individual possess an antecedent history of migraine with aura and experience acute stroke symptoms "typical of previous attacks." Although this patient's clinical presentation does conform to these diagnostic criteria, such is not the case for many patients with migraine and temporally associated stroke. If migrainous stroke does occur in individuals who lack an aura history, or at times produces deficits that do not match up with previous aura symptoms, then the IHS criteria may be overly restrictive and thus diagnostically insensitive.

The mechanism by which migraine conveys an increased risk of stroke is unclear. Is migraine simply a coincidental marker for another process that is itself solely responsible for generating stroke? Or does migraine interact with coexisting conditions to produce stroke? Or can migraine independently serve to cause stroke? Mitral valve prolapse (MVP) appears to be more prevalent in migraineurs than in control populations, and this has led some investigators to postulate that migraine-associated stroke may result from valvular emboli. Hospital-based studies of migrainous stroke patients, however, have demonstrated a low prevalence of MVP. Anzola and colleagues found an increased prevalence of PFO in individuals reporting migraine with aura and proposed that paradoxic emboli may trigger cortical dysfunction, migraine, and, possibly, cardioembolic stroke. Recently, Milhaud and colleagues reported that young migraineurs who suffer stroke are more likely to have a PFO than nonmigraineurs with stroke. Others have attempted to link migraine to the antiphospholipid antibodies, factor V and prothrombin gene mutations, or other intrinsic or acquired disorders of coagulation, attributing migrainous infarction to arterial thrombosis. Migraine-induced arterial dissection, chronic arteriopathy from repeated migraine attacks, and oligemia related to the migraine process itself all have been proposed as potential sources of migrainous infarction. Finally, the association of migraine with mitochondrial encephalomyopathy, lactic acidosis, and stroke-like symptoms (MELAS) and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), and the occurrence of non-atherosclerotic angiopathies in both disorders, may offer clues to the molecular underpinnings of a more atypical migraine-associated stroke.

While some investigators have reported a paucity of vascular abnormalities on the arteriograms of patients with migrainous infarction who were studied subacutely, others have found that early arteriography may yield a high incidence of findings consistent with arterial vasospasm. Given this patient's prior history, the absence of a more plausible proximate etiology, and most compelling, the findings demonstrated by serial arteriography, it seems quite likely that her migrainous infarctions were a consequence of arterial vasospasm.

Management Strategies

Prevention of migraine-associated stroke and acute management of migrainous infarction involve treatment strategies based primarily on common sense and clinical anecdote. Given the association between migraine, heavy smoking, and stroke reported by some investigators, migraineurs, and especially those who report aura and are taking an oral contraceptive, should be strongly advised not to smoke. Recent data from a large meta-analysis of ischemic stroke risk associated with oral contraceptives (OCs) have suggested that migraine may not increase stroke risk in females using a low estrogen preparation. Even so, unusual or prolonged aura, pronounced worsening of migraine symptoms when the patient begins taking an OC, and active smoking should each be considered a relative contraindication to OC use; a prior history of venous or arterial thrombosis represents an absolute contraindication. Triptans and ergotamines should be used cautiously in all patients with prominent aura (especially if the aura is atypical, like aphasia) and not at all in the setting of prolonged aura, or for patients with a prior history of migrainous infarction. Propranolol has been implicated for its alleged role in promoting migrainous stroke, but the evidence supporting this notion is quite thin; suffice it to say that there are probably more effective (if not safer) prophylactic therapies for basilar migraine and for patients with frequent migraine attacks and a prior history of migrainous infarction. Similarly flimsy evidence suggests that cerebral arteriography performed during an acute migraine may induce stroke.

The patient with acute migraine and focal neurologic deficit must be treated with alacrity. Vigorous intravenous hydration with normal saline should be initiated. Pain and nausea should be treated effectively, but with drugs of low or no vasoconstrictive potential (eg, no triptans or ergotamines). In particular, if the patient is typically normotensive, marked elevation of systemic blood pressure should be treated aggressively; migraine may produce a state of cerebral dysautoregulation which resembles that associated with hypertensive encephalopathy or eclampsia, and prolonged elevation of systolic blood pressure theoretically may produce or aggravate cerebral vasospasm. Whether heparin, heparinoids , thrombolytic therapy, or other more stroke-specific acute interventional therapies have any efficacy in treating acute migrainous infarction is unknown.

Patients who have suffered migrainous infarction appear to be at a significantly increased risk for recurrent stroke. Whether that risk can be modified by chronic antithrombotic therapy, effective therapy for migraine prophylaxis, or both is unknown, but a commonsense case can be made for each. Regarding the latter, some investigators have encouraged the use of calcium antagonists, while others specifically have advised against beta-blockers. Probably of more importance than the class of drug chosen is the effectiveness of the agent in preventing prolonged attacks of severe migraine. As for chronic antithrombotic therapy, the existing uncertainty as to what constitutes optimal management mitigates against anticoagulation, the riskier alternative, and in favor of antiplatelet therapy.

Case Summary

This patient was treated acutely with intra-arterial (ICA) infusion of a vasodilating agent and vigorous intravenous infusion of normal saline. She was placed on daily antiplatelet therapy (a combination of aspirin and dipyridamole), along with verapamil 80 mg tid and divalproex sodium (extended release) 1,000 mg per day for migraine prophylaxis. She was given a nonsteroidal anti-inflammatory drug to use for acute treatment of early headache and a hydrocodone/acetaminophen compound for more severe headache. She was instructed to present immediately should she experience a severe headache refractory to self-administered therapy or symptoms suggestive of recurrent transient ischemic attack or stroke.

Selected Readings

Anzola G, Magoni M, Guindani M, et al. Potential source of cerebral embolism in migraine with aura: a transcranial Doppler study. Neurology 1999;52:1622–5.

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Editorial Comments

Migraine and stroke is fortunately an uncommon occurrence, yet anyone taking care of many patients with migraine will eventually see cases. The mechanisms for infarction remain speculative, in large part, so it becomes vital to do a thorough assessment and work-up in patients. Dr. Rothrock's case addresses the usual suspects in such cases, and properly places the clinical problem as one of diagnosis and treatment of stroke in the young. Here, in fact, is the secret—a stroke is a stroke, and it merits a close look for unique and unusual causes in all patients, probably even more so than simply attributing the stroke to migraine. Management on the other hand becomes problematic, since a lot of the most effective therapies for migraine involve the acute use of vasoconstrictors, which obviously must be avoided. Nevertheless, these patients can be managed effectively, as outlined by Dr. Rothrock.

Final diagnosis:

Migraine-associated stroke, migrainous infarction