Chapter 36

The Case of Migraine and a Change of Pattern

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Case History

A 51-year-old woman had a history of migraines since her twenties. She had migraines approximately 2 or 3 times a month, which were accompanied by nausea, and light and sound sensitivity. She had never experienced any focal neurologic deficits, either with her migraines or otherwise. The patient usually responded well to 1 or 2 oral doses of sumatriptan succinate 50 mg. Prior to her visit to the headache center, she had been placed on buproprion 150 mg twice a day to control her migraines and comorbid depression. She was also taking propranolol 160 mg to control hypertension and migraines. Her migraines worsened over the last year, becoming more frequent and severe. The migraine frequency continued to be 2 to 3 times a week despite therapy on buproprion and an increase of propranolol to 240 mg. She used abortive migraine treatment more than the recommended three times a week and also rescued with analgesics occasionally.

Questions on the Case

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

- Why has the frequency of the headaches changed?
- What studies can be performed to determine the etiology?
- Is there a differential diagnosis?
- What advice would you give this patient to manage her headaches?

Case Discussion

Diagnosis

This patient seems to have headaches consistent with the International Headache Society criteria for migraine without aura. Her headaches have changed in frequency and therefore would warrant an imaging study. If there were no abnormalities on the imaging study, then other studies to rule out vasculitis and other systemic illness would be performed.

Investigation

Magnetic resonance imaging (MRI) of the brain demonstrated bilateral periventricular, subcortical white matter lesions consistent with ischemia (Figure 36-1). The differential diagnosis would include multiple sclerosis, but the white matter abnormalities were more consistent with ischemia. A work-up to exclude embolism was then pursued. Her stroke work-up included carotid Dopplers, two-dimensional echocardiography, and hypercoagulopathy blood work, all of which were normal. She had a positive transcranial Doppler contrast study with a large right-to-left shunting at rest and with Valsalva maneuver consistent with a patent foramen ovale (PFO).

What is the significance of white matter abnormalities on MRI?

When a meta-analysis was performed on imaging done routinely for migraine, the most common abnormal findings were white matter changes. These white matter abnor-

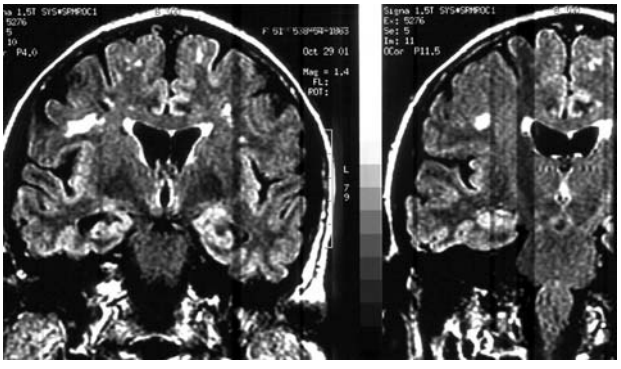

Figure 36-1. Bilateral periventricular, subcortical white matter lesions consistent with ischemia.

malities (WMA) are foci of hyperintensity seen in the deep and periventricular white matter picked up by T2-weighted and proton density imaging on MRI. The WMA are usually not seen on computed tomography scans unless they are confluent, when they may be seen as hypodensities. Several studies have been performed on the prevalence of WMA in migraine. These studies show a variable rate of WMA in the range of 12 to 47% depending on the study, compared to 2 to 14% of controls. Two studies found a higher prevalence of WMA in migraine with aura compared to migraine without aura, whereas four other studies did not demonstrate this. Vascular risk factors, namely, age > 50 years, hypertension, or diabetes mellitus, may increase this prevalence. There may be other associated diseases, such as autoimmune disorders and demyelinating disease, as secondary causes for the WMA. The underlying mechanisms for the genesis of WMA are unclear but have been hypothesized to be as a result of perhaps increased platelet aggregation, repeated attacks of hypoperfusion, or abnormal cerebrovascular regulation. Microemboli have also been suggested as a mechanism; however, cardioembolism has only infrequently been documented. More evidence in the literature on the association of PFO and migraine has emerged in the last few years, and therefore, we may now have one explanation for the findings of WMA in migraine.

Management Strategies

Recently, percutaneous closure of PFO has become available. With this procedure, using local anesthesia, devices are available to close the PFO with minimally invasive methods. This patient underwent percutaneous closure of her PFO. She has since then reported a marked reduction in her migraines.

Case Discussion

This case exemplifies the comorbidity of risk of stroke and migraine. In both reported studies and epidemiologic surveys (Physicians' Health Study), migraine, especially migraine with aura, has been identified as an independent risk factor for stroke in young adults. Theories regarding causality include presence of platelet hyperaggregability, focal alterations in cerebral blood flow, and a cardiac embolic source (ie, atrial fibrillation, PFO/atrial septal aneurysm, intracardiac thrombus or tumor, mitral or aortic valve pathology, and left ventricular or global hypokinesia or dyskinesia).

In a multifactorial analysis, Milhaud and colleagues showed that PFO is characteristic of young patients (< 45 years of age) with migraine and ischemic stroke (IS). PFO is a well-established risk factor for IS in young adults. Anzola and colleagues reported that the prevalence of PFO in their study population was 48% in migraine with aura patients, 23% in migraine without aura patients, and 20% in control subjects. The risk of stroke in patients with migraine with aura may be due to paradoxical cerebral emboli. Wilmshurst and colleagues reported an effect of cardiac right-to-left shunt closures on migraine symptoms. In their series, 37 patients had transcatheter PFO/atrial septal closures to prevent recurrence of decompression illness or stroke. Twenty-one of the 37 patients had histories of migraine unrelated to diving. Of these 21 migraine patients, 3 had no improvement in their migraine, 8 had improvement in frequency and severity, and 10 had no further migraines. These findings point to a causal relationship between right-to-left shunts and migraine with aura, and closure of the atrial septal defect may reduce or eliminate migraine. This patient exemplifies that removal of right-to-left shunt may help to reduce migraines. The underlying mechanism may require further study. Theoretically, ischemia, albeit at a subcortical level, may predispose to spreading cortical depression. This phenomenon is therefore the putative mechanism of migraine aura. This may be extrapolated into migraine without aura as well, on the basis of positron emission testing data and functional MRI studies.

Selected Readings

Anzola GP, 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

The issue of closure of PFO in patients with stroke was addressed by the American Academy of Neurology (Messé SR, Silverman IE, Kizer JR, et al. Practice parameter: recurrent stroke with patent foramen ovale and atrial septal aneurysm. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2004;62:1042–50). Their conclusions were as follows: "PFO is not associated with increased risk of subsequent stroke or death among medically treated patients with cryptogenic stroke. However, both PFO and atrial septal aneurysm (ASA) possibly increase the risk of subsequent stroke (but not death) in medically treated patients younger than 55 years. In patients with a cryptogenic stroke and an atrial septal abnormality, the evidence is insufficient to determine if warfarin or aspirin is superior in preventing recurrent stroke or death, but minor bleeding is more frequent with warfarin. There is insufficient evidence to evaluate the efficacy of surgical or endovascular closure."

The putative relationship of PFO and ASA to migraine with aura (MA) is being increasingly suggested, as noted by Dr. Aurora. The issue, as summarized in an editorial by Dr. H.P. Adams, is appropriate treatment (Adams HP Jr. Patent foramen ovale: paradoxical embolism and paradoxical data. Mayo Clin Proc 2004;79:15–20). Complicating the picture is the risk for stroke with PFO, and the reported beneficial effect of aspirin in the prophylaxis of migraine (Buring JE, Peto R, Hennekens CH. Low-dose aspirin for migraine prophylaxis. JAMA 1990;264:1711–3). Some clinicians report that the aspirin effect is more likely to be seen in MA. The aspirin could be showing its benefit due to its effect on the undiagnosed and symptomatic PFO subset of MA patients. The story of PFO, migraine, and stroke is still in evolution, and remains controversial, and Dr. Aurora's case helps us to understand this area in the context of an individual patient.

Final diagnosis:

Migraine without aura, with stroke, and with patent foramen ovale