BACKGROUND
The patient is a 34-year-old Caucasian female who presents with a chief complaint of being unable to tolerate daily medications for migraine prevention. She reports that her headaches began at age 14, but were infrequent at that time. She sought medical help 6 years ago, when she had headaches triggered by increased stress, but now reports increasing pain and frequency of attacks prompting her to seek medical attention once again. The patient’s headaches now occur twice/week with an average of 1 day of lost work/week.

She describes her headaches as unilateral and localized to the orbital area of her skull. They are associated with light, sound, smell, and touch sensitivity. In addition, the patient reports that mild nausea accompanies most of her headaches, but that she experiences intense vomiting with menstrually associated headaches. Before her headaches, the patient has an aura with blind spots or scintillating scotomata.

MEDICAL HISTORY
The patient is in generally good health with a medical history significant only for mitral valve prolapse. There is no history of head trauma.

SOCIAL HISTORY
The patient is in a high-pressure career, serving as Chief Executive Officer of a software start-up company. She is engaged to be married in 4 months. The patient denies any history of alcohol or drug abuse; she also states there has been no history of physical, emotional, or sexual abuse.

FAMILY HISTORY
There is a positive family history of migraines (mother and sister).

PHYSICAL EXAMINATION AND DIAGNOSTIC WORKUP
On physical examination, the patient is a well-developed, slender, Caucasian female with an unremarkable medical and neurologic examination that is negative for focal abnormalities. Routine complete blood count, chemistry profile, and magnetic resonance imaging (MRI) are within normal limits. A transcranial Doppler ultrasonography (TCD) was performed because the patient intended to go scuba diving on her honeymoon. This test was positive for the presence of a large patent foramen ovale (PFO).

DIAGNOSIS AND TREATMENT
The patient received a diagnosis of migraine 6 years ago and was started on sumatriptan by her primary care physician. However, she had intense chest pain with the injection and did not respond to the oral tablet. Currently, she takes zolmitriptan for abortive treatment, which works marginally well. A variety of prophylactic therapies have been initiated without success. These include tricyclic antidepressants, β-adrenergic blockers, and neuromodulators. The patient could not tolerate amitriptyline or nortriptyline because of impaired cognition. She reported difficulty in concentrating and feelings of grogginess. With the neuromodulating drugs, the patient experienced similar adverse effects: dizziness (gabapentin), drowsiness (valproate), and difficulty driving (topiramate). β-adrenergic blockers were discontinued because of exercise intolerance.

CONTINUING TREATMENT PLAN AND FOLLOW-UP
The patient initiated botulinum toxin type A therapy; the starting dose was 50 U injected into the suboccipitalis muscle, which has been gradually increased to a total dose of 200 U. At her 4-week follow-up visit, the patient’s headaches were mild, occurring approximately once/week, and responding to zolmitriptan for acute attacks.

*This case study is based on a roundtable symposium held in Los Angeles, California, on February 18, 2006.
CASE STUDY

The patient has been under my care since 2001, and currently, she is seen approximately twice yearly for botulinum toxin type A injections (which last 6 months). Her headache attack frequency is stable at 1 to 2 attacks/month. Because of her PFO, the patient was approached about being a candidate for the Migraine Intervention with STARFlex (NMT Medical Inc, Boston, Mass) Technology Trial, but has elected not to participate.

BACKGROUND INFORMATION

There appears to be a relationship between PFO and migraine headache, in that PFO is more common in patients who have migraine with aura, and migraine with aura is more prevalent in patients with PFO. Specifically, patients who suffer from migraines with aura are twice as likely to have a PFO (41%–48%) than the general population (16%–20%). Right-to-left cardiac shunt at rest through a PFO also is more common in patients who have migraine with aura (15%) than in control patients with PFO who do not experience migraines (0%), suggesting that interatrial communication may play a role in the pathogenesis of migraines. According to some reports in the medical literature, closure of the PFO in patients who are divers with decompression illness may reduce migraine symptoms; however, there have been no prospective, randomized, sham-controlled studies to confirm this finding from retrospective analyses.

DISCUSSION

Dr Schim: What did you tell the patient about scuba diving?

Dr Aurora: I advised her not to scuba dive and shared the literature available on the subject with her. The patient reviewed the information and decided not to scuba dive; she went snorkeling instead.

Dr Saxton: At some point, it would be interesting to find out the role of PFOs and right-to-left shunts in patients with chronic daily headache (CDH), because I am finding a lot of them in my clinic. We conduct TCD tests in our office, and even patients without auras—patients with CDHs—more than approximately 70% of them have a right-to-left shunt. The problem is that a lot of them are Spencer grade 1.

Dr Rosenberg: I have had several patients who have had migrainous strokes; if they have a PFO, is that a more significant patient? We do not know the answer to that. The American Academy of Neurology guidelines discuss PFO as an indicator of stroke. My real question is, if you have a migrainous stroke, in those cases, will PFO closure eliminate the migraine in that particular instance?

Dr Schim: That is how this was initially discovered. Closure of PFOs eliminated migraines in those patients.

Dr Dodick: How many migrainous infarctions have you seen in the past decade? I have not seen one.

Dr Frishberg: I have seen several of these patients. They typically have an occipital infarct that correlates with the presumed location of their visual aura, leaving them with a homonomous hemianopsia.

Dr Schim: I think some of these cases are people who develop a migraine because of their stroke. The infarct may precipitate symptoms of aura and vascular headache.

Dr Saxton: I have 1 patient who has had migraines with aura for years, and she developed what looked like a reversible ischemic neurologic deficit that went on for a few days, without MRI changes. Her workup determined that she had a PFO. Now she is taking stroke prevention medications. I start my patients on a baby aspirin (acetylsalicylic acid) for prophylaxis whose TCD studies show a right-to-left shunt.

Dr Dodick: I am not disputing this; however, true migrainous infarctions are extremely rare. Why are you performing TCDs in your daily clinical practice if you are not referring patients for closure of their PFOs? How does finding a PFO on TCD affect your management?

Dr Saxton: I look for spontaneous microemboli. These are found before the bubble study is performed. If patients with this condition are placed on a baby aspirin, these disappear on retesting.

Dr Rosenberg: What if you have a patient who comes in with a classic picture of migraine, and the patient has persistent neurologic symptomatology? After performing MRI and diffusion studies, you determine that the patient has an acute lesion, and this is occurring within the context of migraine. To me, that is a migrainous stroke.

Dr Schim: Like Dr Dodick, I also think it is rare, especially if you define migrainous stroke rigorously. In every stroke registry there are approximately 30% of people whose stroke etiology is undetermined, and the percentage is higher in young people. This is when the whole issue of the significance of an observation of a PFO comes about. The one largest study—the PFO in Cryptogenic Stroke Study—reconfirmed a high inci-
dence of PFO (33.8%) in people who otherwise had a stroke of undetermined etiology. However, their risk of second stroke was no higher than people who did not have a PFO. Therefore, it did not translate into a substantial risk.7

**Dr Frishberg:** There are currently 3 different ongoing and as yet unpublished studies looking at whether PFO closure will have an impact on migraine attacks.

**Dr Saxton:** Closure procedures carry a risk for developing thrombus on the device or device embolization. I would not want to have anybody go through a PFO closure just for migraine.

**Dr Schim:** We know that, in general, migraine is not a risk for death. There is a very small risk of the patient having a stroke in relationship to migraine. We can certainly look at and pull out the statistics, and the numbers are exceedingly small. We also know that there is a certain hazard to any of the PFO closure devices, and we do not know what the long-term success or consequence of having one of these is going to be.

**Dr Rosenberg:** We really need a good, randomized clinical study of sham versus true closure of PFOs.

**Dr Dodick:** A study has been done in the United Kingdom of patients with migraine and PFO. None of the patients have had a stroke. Data from this study have been analyzed, and the study failed to meet its primary outcome—it was a negative study. This study has been presented at the American College of Cardiology, American Academy of Neurology, and American Headache Society in 2006, but has not yet appeared in the literature as a full manuscript.

**Dr Schim:** What percentage of this patient’s attacks were associated with aura?

**Dr Aurora:** Her attacks in the beginning were 100% associated with aura. Now she hardly has any aura.

**Dr Mondell:** For therapy, we understand that you chose botulinum toxin type A. Tell us more about your treatment selection process.

**Dr Aurora:** I elected to administer only 50 U of botulinum toxin type A initially, because she has a very slender neck. I was concerned about side effects. I asked myself, “Is she going to have more neck pain?” because, just anecdotally, I think that neck pain occurs in more people who get weak because of botulinum toxin when it’s injected.

**REFERENCES**