

Chronic Migraine: An Interactive Case History, Part 3

A step-by-step guide through the continued diagnosis and treatment of a complex refractory headache patient.

By Lawrence Robbins, MD, Megan Schwarz, and Delia Snediker

This is the third part of our series titled “Chronic Migraine: An Interactive Case History.” Our previous articles^{1,2} followed the diagnosis of a complex patient with the pseudonym “Heather” from age 24 to 30. To recap, Heather has been suffering from migraine and chronic daily headaches (CDH) with neck pain. She has medical diagnoses of irritable bowel syndrome (IBS) and fibromyalgia (FM).

Heather’s case is further complicated by chronic, mild bipolar depression and anxiety. She has been prescribed topiramate to prevent the migraines, which has helped but causes some side effects, including memory problems and paresthesias. Heather has also been taking a small dose, 25 mg, of quetiapine with the following abortive agents: 100 mg oral sumatriptan, zolmitriptan nasal spray, naproxen, ondansetron (for nausea), and hydrocodone in limited amounts. Botox injections were helpful but too expensive.

In addition to medications, Heather exercises, does yoga and biofeedback, and has seen a psychotherapist. Acupuncture and massage have not been useful.

History

Heather is a 30-year-old hairdresser in a salon. Her work can be very physical, and her life has not been easy. She has an ex-boyfriend, Eric, who was abusive; she also was abused by her mom, Sandy, an alcoholic.

A few months ago, Heather ended her relationship with Eric. Now she is trying to turn her life around and is taking college classes at night. She has a new boyfriend, Steve, who is 15 years older and has 2 kids of his own. Heather is currently on 50 mg of topiramate and 25 mg of quetiapine to prevent headaches but cannot tolerate higher doses of either medication. Her irritability and anxiety have complicated her relationships with Steve and her co-workers at the hair salon. Heather is asking us: “Can you give me something else for my moods?”

What Treatment Options Should Be Considered?

As noted, Heather’s mood has been diagnosed on the mild end of the bipolar spectrum. When you suspect a patient may have a mood disorder, it is important to look for signs of a persistently agitated personality, with frequent cyclical depression or excessive energy, and a strong family history of either bipolar disorder or major depressive disorder. A family history

of drug and/or alcohol abuse is also common. A clear hypomanic or manic episode may, however, not be evident. It is crucial to speak with a family member—at least 40% of the time, hypomania is not mentioned or recognized when we simply speak with the patient.

Other mild bipolar signs include early onset of depression (teen years), quick onset of depression, severe depression “for no reason,” opposite reactions to certain medications (such as being up all night with sedatives, mind racing from antidepressants, etc), very high anxiety, insomnia, persistent agitation, a moody personality, and a poor response to antidepressants. Hypomania may manifest itself as a cycle of irritable, brooding pessimism. Depression is the primary problem, much more than the hypomania. Left untreated, self-medication is common.

Whereas a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) may be the treatment of choice for Heather’s mood disorder, these may trigger hypomania. In the past, lamotrigine increased her headaches but did help her mood significantly, whereas oxcarbazepine and sodium valproate gave her side effects.

We decide to add a small amount of an atypical antipsychotic, aripiprazole, to Heather’s regimen. Aripiprazole contains the same class warnings as the other atypical antipsychotics (primarily the risk for diabetes) but is much less apt to cause significant weight gain. With patients with headache who have psychiatric comorbidities, it is best to begin with low doses of medications. We usually begin with tiny doses (1/2 of a 2-mg tablet, slowly increasing to 5 or 10 mg). The common side effects associated with aripiprazole include akathisia, fatigue, headache, nausea, constipation, dizziness, insomnia, and visual disturbances.

Heather is begun on 1 mg of aripiprazole, increasing to 2 mg after 6 days. She is continued on her preventive regimen of 50 mg of topiramate and 25 of quetiapine. Oral sumatriptan has become ineffective for her migraines. Although the zolmitriptan nasal spray does help, it is no longer covered under her medical insurance. Financial considerations often dictate which medications we prescribe. The other generic triptan, naratriptan, is prescribed for Heather; she may use naratriptan with naproxen at the same time.

Six weeks later, Heather calls and states that she is pregnant.

How Does Pregnancy Affect Treatment?

Prior to her pregnancy, we had discussed the risks of taking headache medications with Heather. She and Steve had not planned on having a child right away. So, we now quickly taper her off the headache medications; whether to continue psychiatric medications during pregnancy is a difficult, case-by-case decision.

Our medication choices during pregnancy are limited. For headache treatment acetaminophen is useful. The addition of caffeine may be beneficial. The triptans are pregnancy category C agents and therefore not recommended during pregnancy. Although the ongoing sumatriptan pregnancy registry indicates that incidental use of sumatriptan during pregnancy may be relatively safe, we attempt to avoid its use during pregnancy, as the risk of sumatriptan, like most of our medications, is not definitively known.

In addition, we avoid barbiturate-containing drugs, such as butalbital. Prednisone, in very limited amounts, may be considered; opioids, also in limited amounts, are relatively safe but do have possible congenital side effects. Ondansetron, over-the-counter Emetrol, and metoclopramide can be used for nausea during pregnancy.

For treatment of Heather's headaches, we prescribe ice, biofeedback/relaxation, acetaminophen with limited amounts of caffeine, minimal amounts of hydrocodone, and ondansetron for nausea.

As for preventives, propranolol, in limited amounts, has been used during pregnancy. Verapamil has also been used and has relatively few risks during pregnancy. Magnesium and omega-3 fatty acids may be used. Most medications, such as topiramate, are pregnancy category C agents, and the risks are not definitively known. Tricyclic antidepressants (TCAs) are best avoided.

With regard to psychotropics, the atypical antipsychotics (quetiapine, aripiprazole, etc) may turn out to be relatively safe, but definitive answers on these are still pending. There is a "neonatal SSRI syndrome," with the infant showing signs of jitteriness, increased muscle tone, irritability, and respiratory distress. Up to 30% of infants exposed to SSRIs during the third trimester may have this syndrome.

With SSRIs, the issues of low birth weight, premature delivery, and neonatal pulmonary hypertension are possible complications, but studies have been conflicting. Paroxetine is best avoided. Sertraline is the SSRI most often used and may be the safest SSRI during pregnancy. Regarding mood stabilizers, lithium may be used but has some rare associated defects including Ebstein's anomaly, a cardiac valve defect. Valproate must be avoided. Lamotrigine is much safer than valproate but may cause cleft palate, among other problems. We avoid benzodiazepines. As always, risks versus benefits and informed consent are important areas of discussion with the patient. For more information, refer to OTIS (Organization of Teratology Information Services) at otispregnancy.org or call 866-626-6847; also drugs.com (and similar sites).

Stress at Home

Heather's mother, Sandy, has been drinking more alcohol and "borrowing" money from Heather. Sandy is a continued source of stress, and she does not get along well with Steve, Heather's boyfriend. Heather's old therapist retired and she would like to see a new one, but money and time are barriers to seeing a therapist.

Heather calls and is very upset—she has had a miscarriage during week 8 of her pregnancy. Post-miscarriage, Heather plunges into a deep depression. She has a reasonable support system consisting of Steve and her sister Emily. She is able to work at her salon. For the depression, we restart her medications (25 mg of quetiapine, 2 mg aripiprazole). For the headache and fibromyalgia pain, we again add 10 mg of nortriptyline at night. Heather did reasonably well on nortriptyline in the past, without hypomania. For crisis times, with both headache and depression, I often retreat back to medications that have been helpful in the past. Some bipolar patients tolerate antidepressants well, without hypomania, particularly if they are on a mood stabilizer. Others become manic or hypomanic. It is important to begin with low doses of an antidepressant and increase the amount slowly.

At This Point, Would You Consider Botulinum Toxin or Occipital Nerve Blocks?

Heather has insurance coverage again and requests that we administer botulinum toxin type A (BTX-A). BTX-A is FDA approved for the treatment of chronic migraine (defined as 15 days per month, 4+ hours per day of migrainous headache). The FDA-indicated protocol is 31 injections at various sites about the head and neck; 155 total units. I often use lower doses, from 50 to 100 BTX-A units per patient. We give Heather 75 total units (15 injections, 5 units each), injected into the anterior as well as posterior areas.

Because she has been suffering from severe daily migraine with occipital pain and tenderness, we also administer occipital blocks with bupivacaine. Although the addition of corticosteroid in the occipital injection may help, I usually avoid adding steroids. Occipital injections often help until the BTX-A injections are effective, which may take 1 to 4 weeks.

Now aged 32, Heather is seeing a new psychotherapist. She is encouraged to join Al-Anon to deal with her mom's drinking. Heather has dropped out of community college because of her depression. She has been able to continue working but is under-functioning at work. Both headaches and depression are major contributors to this. Heather's boyfriend, Steve, has recently begun using cocaine again, and Heather joins in. The cocaine cycles Heather into hypomania.

What Treatment Should Be Considered?

In the past, Heather has been referred to psychiatrists and psychotherapists. She is willing to see a therapist, but not a psychiatrist, as she says, "It never works out with any psychiatrist. I do not connect and it is too expensive." Steve recently went into rehab, but Heather rejects

the idea of rehab. With the help of a therapist, she is able to quit cocaine on her own, which is unusual.

We increase the aripiprazole to 5 mg and reintroduce lamotrigine. Heather is now on quetiapine (25 mg at night), aripiprazole (5 mg every morning), and lamotrigine (25 mg slowly increasing to 100 mg). We have warned Heather to discontinue lamotrigine with any sign of a rash. The BTX-A has decreased her headaches for 3 months, but she can no longer afford the BTX-A injections.

Steve breaks up with Heather after he finishes rehab for cocaine. Heather moves in with her supportive sister, Emily, which stabilizes her situation. Heather does reasonably well, working at her salon, for more than 2 years. At age 33, she continues to work on a number of issues with her therapist, including her difficult mom.

Heather begins to date Eric again. The relationship is stable for 6 months, after which he begins, once again, to abuse her. Heather cannot afford aripiprazole and is on quetiapine and lamotrigine. As needed, she uses naratriptan and ondansetron, but we do not give her hydrocodone because of her bout with cocaine. She is at high risk for addiction because of her bipolar disorder, alcoholic mom, cocaine use, and stressful life. We periodically do occipital blocks and trigger point injections, but she cannot afford BTX-A. Heather now admits that she is ingesting 6 Extra Strength Excedrin daily, along with 8 ibuprofen. She has severe gastrointestinal (GI) pain as a result.

Weaning Off OTC Pain Medications

Medication overuse is common among chronic daily headache patients; it is almost a part of the illness. Some patients, maybe most patients, will have medication overuse headache, whereas other patients who overuse analgesics do not suffer from rebound headache. Treating patients with medication overuse is difficult; the brain becomes “centrally sensitized,” and patients are psychologically and physically dependent on the analgesics. There are a number of protocols for weaning off the various analgesics.

We place Heather on a proton-pump inhibitor (PPI) (omeprazole) to treat her GI issues. She agrees to stop taking the over-the-counter (OTC) Excedrin and ibuprofen and switch to a non-addicting muscle relaxant, tizanidine. Heather is tapered off caffeine over 3 to 5 weeks; overuse of caffeine is a major problem in headache patients. Of course, patients are not always truthful about their OTC and caffeine use. We order blood work; in headache patients, routine blood labs are vital because of the medications prescribed (and overuse). Heather’s liver is mildly irritated, which we would expect to improve over time as long as she is off the analgesics. We restart nortriptyline 10 mg at night and increase lamotrigine to 150 mg, which helps her moods. However, with the increase in the lamotrigine, Heather’s headaches increase. We decrease the dose of the lamotrigine to 100 mg.

Because of her abusive relationship with Eric, Heather moves to a woman's shelter and is temporarily lost to follow-up. When she returns for therapy 8 months later, she is off all medications, unemployed, and very depressed. We place her back on 25 mg of topiramate and 25 mg of quetiapine, with naratriptan and ondansetron as needed.

The new regimen stabilizes Heather's condition, and she is able to live with her sister Emily and go back to working at the salon. She improves psychologically and finds a new therapist. Her mother, Sandy, who is living with Heather and Emily, is a continuing source of stress. The therapist has convinced Heather to enforce boundaries with her mother. Heather is exercising and doing yoga. She tries the herbal preventive Petadolex, the most effective "natural" headache preventive, but it does not help.

Conclusion

Heather is now 35 years old. She reunites with her older boyfriend, Steve, and they become engaged. She wants to become pregnant, and we discuss risks and benefits of the various medications.

Heather decides to continue on the mood stabilizer quetiapine for the time being. She is able to take a small amount (5 mg) of cyclobenzaprine, which helps her fibromyalgia and insomnia. She feels somewhat "drugged" in the morning because of the muscle relaxant. We use flurbiprofen, a non-steroidal anti-inflammatory drug (NSAID), 100 mg once or twice daily. We give Heather Prodrin to use no more than twice per day. Prodrin (acetaminophen, caffeine, and isometheptene) is an improved and non-sedating form of Midrin (Epidrin). Naratriptan helps her, but she tends to overuse the triptans, consuming up to 27 per month. Limiting the analgesics is a continuing battle with Heather, as with many daily headache sufferers. Heather's moods are relatively stable for the moment, and she continues to plan for a baby.

Table. Generic and Brand Names of Drugs Cited in this Article

Generic	Brand
Aripiprazole	Abilify
Botulinum toxin type A	Botox
Cortisone	Prednisone, Decadron, Medrol
Cyclobenzaprine	Flexeril
Flurbiprofen	Ansaïd
Hydrocodone	Vicodin, Norco
Lamotrigine	Lamictal
Metoclopramide	Reglan
Naproxen	Naprosyn

Naratriptan	Amerge
Nortriptyline	Pamelor
Omeprazole	Prilosec
Ondansetron	Zofran
Oxcarbazepine	Trileptal
Quetiapine	Seroquel
Paroxetine	Paxil
Sertraline	Zoloft
Sodium valproate	Depakote
Sumatriptan	Imitrex
Tizanidine	Zanaflex
Topiramate	Topamax
Verapamil	Calan, Isoptin
Zolmitriptan	Zomig

Petadolex is a form of the herb butterbur.

Prodrin is a combination of acetaminophen, caffeine, and isometheptene.

(Author bios)

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