TEACHING CASE: INTRACTABLE CYCLICAL HEADACHES IN AN ADOLESCENT

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Case presentation
A 16-year-old male presented to our clinic for the evaluation and treatment of intractable cyclical headaches. He was noted to suffer from infrequent headaches since the age of 6, usually associated with bellyaches and nausea. Such events occurred several times a year, and did not really alter his behavior or school performance. He was not evaluated for these childhood headaches and was not treated accordingly.

The headaches took a downhill course a year prior to presentation, around the age of 15. There were no significant lifestyle changes or clear precipitating factors leading to this deterioration. The headache pattern took a strict cyclic course, occurring every 2 weeks and lasting for about 2 weeks at a time. The headaches were bifrontal, but more predominantly on the right, described as constant throbbing, up to 8/10 in intensity, which could intermittently interfere with sleep. There was associated photophobia and nausea. There was no reported associated tearing, redness of the conjunctivae, or symptoms consistent with Horner's syndrome. There were no associated visual disturbances, no aura, or other neurological symptoms such as speech difficulties or gait problems. Interestingly, the headache-free periods were a time of elation with high energy level, increased social and physical activity.

Past medical history is unremarkable. The patient is an average student in the eleventh grade, with no reported social problems. He and his parents deny smoking, drug or alcohol abuse. He is an athlete playing team sports. He denies any sleep deprivation or other stressors.

Physical exam was completely and consistently unremarkable, even during a headache cycle, with no tenderness upon palpation in the face, head, or neck, no meningeval signs, and no autonomic stigmata such as tearing or injection of the conjunctiva. The neurological exam was unremarkable with normal cognition, perfect vision and visual fields, normal pupillary response, normal funduscopic exam, and no other focal neurological signs.

Extensive investigation included a metabolic workup with normal serum thyroid functions, electrolytes, blood count, liver functions, sedimentation rate, lactate level, and lyme titer. A lumbar puncture demonstrated a normal opening pressure and the cerebrospinal fluid analysis was sterile and noninflammatory. An MRI and MR venogram of the head were unremarkable as well. A sleep deprived EEG was normal.

Over the counter medications such as acetaminophen, ibuprofen, and naproxen had no effect on the course or pattern of his headaches. Oral triptans such as sumatriptan, eletriptan, and rizatriptan, taken as instructed and tried for a substantial period of time provided no abortive relief. Oxygen therapy was ineffective. Prophylactically, the patient was given over the course of the year multiple preventive medications at therapeutic doses including nortriptyline, propranolol, topiramate, verapamil, indomethacin, cyproheptadine, valproic acid, zonisamide, and methergine, with no change in the pattern of the cyclic headaches.

At some point in the midst of another cycle, he was admitted to the pediatric inpatient service for intravenous treatment. Given the Raskin protocol (intravenous dihydroergotamine 0.5–1 mg given every 8 hours), he experienced a complete resolution of his headache within 24 hours, after the fourth dose of intravenous dihydroergotamine. His "usual" cycle of headache was due to spontaneously subside within a week, but the cycle was apparently broken. Due to the success of the ergot treatment, the patient was discharged with nasal dihydroergotamine (Migranal®) for abortive management in his next cycle. However, this provided no relief. Overall, the patient was hospitalized four times during the next 4 cycles of his headache syndrome, and at each time the treatment and effect was interestingly identical—within 24 hours, after the fourth dose of dihydroergotamine, the headaches promptly subsided, and the cycle was broken. Each hospitalization, while aborting the headache, did not prevent the recurrence or timing of the next bout of headaches due to appear a few weeks later (see Figure). Treatment with dihydroergotamine subcutaneously and intramuscularly, subsequently given to the patient as an outpatient treatment, had no effects on the headaches. The patient was given multiple nerve blocks in the neurology headache clinic in Dartmouth Hitchcock Medical Center, including supra-orbital, trochlear, occipital blocks, and even sphenopalatine anesthetic drops, without relief.

Due to the strict cyclic component of the headaches, and presence of some migrainous features, the diagnosis of cyclical migraine was made and the patient was put on lithium, up to 300 mg 3 times a day. While tolerating the lithium well (and on adequate levels), with normal thyroid and renal functions followed consistently, the cycle of the headaches did not change after approximately 3 months of treatment. Nighttime melatonin did not alter the course of the headache either. At some point the patient discontinued all forms of...
Figure.—Approximately 6 months’ chronology of patient’s headaches, showing cyclicity (treatment with DHE was given for most of the headache cycles).

pharmacological treatment, and is currently using behavioral techniques for the management of his headaches, with limited success.

DISCUSSION

Cyclical migraine, first described by Medina and Diamond in a series of articles between 1977 and 1982,1-3 is a variant of migraine with an unusual pattern. The migrainous bouts occur in cycles, usually lasting weeks, with a completely asymptomatic period in between the episodes. The location of the headache may be unilateral or bilateral, compared to cluster headache, which is usually unilateral.

This migraine variant does not have a separate definition in the International Classification of Headache Disorders, second edition.4 Applebee and Shapiro argue3 whether such a condition even represents a distinct diagnostic entity. Response to lithium carbonate may be a defining characteristic. Medina5 described a dramatic response to lithium in patients diagnosed with cyclical headaches. His series comprised 27 adult patients with migranous headache attacks occurring in periods of 2 weeks or longer, separated by headache-free periods. All patients had photophobia, nausea, bilateral or unilateral headaches. Nasal congestion, Horner’s syndrome, and tearing occurred in several patients. Only half of the patients responded to abortive ergotamine therapy. Poor response was reported to prophylactic therapy with tricyclics, propranolol, and methysergide. Out of 22 patients treated with lithium carbonate, 19 reported partial or complete resolution of headaches, usually within 1 week. Why patients with cyclical migraines respond so well to lithium is unclear, although some have suggested a link to bipolar disorder, well known for its lithium responsiveness.

Another syndrome that cyclical migraine resembles is cyclic vomiting syndrome, an idiopathic disorder characterized by recurrent, stereotypical bouts of vomiting with intervening periods of normal health. Although it appears to primarily affect children, it is being recognized increasingly in adults. While cyclic vomiting syndrome has also been linked to food allergy, mitochondrial, metabolic, and endocrine disorders, it is also linked to migraine, having a higher prevalence in migraineurs compared to controls (22% vs 5%).6 Cyclic vomiting syndrome, while responsive to antimigraine therapy including amitriptyline, cyproheptadine, and propranolol, is not responsive to lithium.

Despite the lack of response to lithium, our patient’s symptoms seem to fit the diagnosis of cyclic migraine. His symptoms were predominantly that of a migranous headache, with less prominent gastrointestinal-associated complaints. Hence, the diagnosis of cyclic vomiting syndrome is less likely. Moreover, he did not respond to the standard therapy for cyclic vomiting syndrome. The symptoms are not consistent with cluster headache: no response to oxygen and other standard forms of abortive and prophylactic therapy for cluster headache. Furthermore, there were no autonomic stigmata. Perhaps this case, the first report of an adolescent with cyclical migraines, represents a relatively intractable form of cyclical headaches. Or perhaps, on the basis of consistent DHE responsiveness, it occupies a different spot in the migraine-cluster continuum.

REFERENCES


**QUESTIONS FOR DISCUSSION**

1. Other than cluster headache, which other cyclic headache disorders have been described?

2. Which brain structure seems to be implicated in the pathophysiology of cyclic headache disorders?

3. What are the adverse effects associated with short- and long-term use of DHE and other ergot derivatives?

This case presentation and discussion meets the ACGME requirements for residency training in the following core competency areas: Patient Care, Medical Knowledge, Practice Based Learning and Improvement, and Systems Based Practice.