TEACHING CASE: OPHTHALMOPLEGGIC MIGRAINE

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Case Presentation: A 35-year-old right-handed man presented with a history of episodic, stereotyped headaches since the age of 6. He stated that the episodes are infrequent, occurring no more than once per year and often separated by several years. The headaches are exclusively right-sided, located frontotemporally and behind the right eye, and described as a sensation of constant, steady pressure. They last between 4 and 24 hours and occur with the presence of nausea, vomiting, photophobia, phonophobia, and osmophobia.

The morning after an attack, he will awaken with profound unilateral ptosis, mydriasis, and outward deviation of the right eye with binocular vertical diplopia (worse when looking up and to the left) despite full resolution of the headache. These symptoms will typically last from several days to 8 weeks but have progressed to the point where, interictally, he has developed a mild but persistent defect of right eye movement. Additionally, his right pupil has been steadily increasing in size and is no longer reactive to light.

He denies the presence of an aura or any neurologic symptoms preceding his headache and states that the headache pain itself is of progressive onset. He identifies no triggers. Of note, at age 6 (prior to the onset of his headaches), he states that he fell out of a tree and hit his head with a loss of consciousness for “a few minutes.”

Although the pain is usually responsive to acetaminophen or ibuprofen, refractory headaches are unresponsive to sumatriptan, naratriptan, and eletriptan and have necessitated admission to the emergency department on 4 occasions for pain control with meperidine or hydrocodone. Prior workup included several MRIs of the brain with and without contrast, intracranial MR angiography, and a recent CT angiogram, all of which were normal; however, none of these studies were obtained during an acute exacerbation of his symptoms. Ophthalmologic evaluation revealed only the persistent deficits noted above without any other abnormalities on examination.

He had no other significant medical history and does not take any medications other than a daily multi-vitamin. He reported that he has never used tobacco or illicit drugs, does not drink caffeinated beverages, and has an average of one alcoholic drink per week. He is employed as an engineering manager. He has a family history of hypothyroidism and breast cancer in his mother and coronary artery disease in his father, but states that there is no family history of headache. A thorough review of systems was negative except for the persistent right eye complaints noted in the history.

At this visit, he provided several photos showing the profound ptosis, pupil dilation, and ophthalmoplegia experienced shortly after one of his typical headaches (Fig. 1). Additionally, he produced a series of 3 photos from his neuro-ophthalmologist documenting a mild to moderate baseline defect on right eye adduction with a near-complete inability to adduct the eye one month after one of his typical attacks and then a return to baseline in the last photo dated 3 months after the attack (Fig. 2).

Prophylactic treatments, including calcium channel blockers, had been previously recommended, but the patient was reluctant to take a daily medication for something that only happens once every 1-2 years. Moreover, his primary motive for seeking consultation was not for treatment of the headache pain, but to prevent the ensuing ophthalmoplegia, which is far more disabling.

Vital signs and general examination were normal. Neurologic examination was remarkable for a widely dilated, unreactive right pupil at 8 mm in contrast to the left pupil, which was 4 mm and constricted briskly to 2 mm. Consensual constriction of the left pupil was observed with light
shined in the right eye. There was impaired movement of the right eye in all directions of gaze except for abduction. This was most noticeable on supraduction of the right eye both medially and laterally. Of note, the patient was unable to sustain his baseline-impaired superior gaze for greater than 30 seconds with the right eye.

Routine laboratory studies were normal and investigation for acetylcholine receptor antibodies was negative. Lumbar puncture has never been performed.

At this time, the infrequent nature of his attacks did not suggest the need for prophylactic therapy, but acute treatment of his attacks with a dexamethasone taper (8 mg daily for 3 days, followed by 4 mg daily for 3 days, followed by 2 mg daily for 3 days, then discontinue) was suggested in hopes of aborting his headache pain and preventing exacerbations of his persistent third nerve palsy.

**EXPERT COMMENTARY**

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In this case we are presented the story of a patient who has had infrequent recurrent attacks of painful ophthalmoplegia since childhood. The attacks are always right-sided and consist of head pain with features consistent with migraine followed hours later by what was a transient right 3rd nerve palsy which is now persisting and worsening.

The differential diagnostic possibilities for painful ophthalmoplegia include Tolosa-Hunt syndrome (see Box 1), diabetic oculomotor palsy, posterior communicating artery aneurysm, giant cell arteritis, and various other lesions in or near the cavernous sinus and orbit. These include mass lesions - infectious, inflammatory, or neoplastic, thrombosis, cavernous-carotid fistula, narrow angle glaucoma, high or low intracranial pressure, thyroid ophthalmopathy, sarcoid, Lyme disease, syphilis, brain stem lesions, schwannoma of an ocular motor nerve, Wegener's granulomatosis, carcinomatous and other forms of meningitis, and demyelinating lesions as in Miller-Fisher syndrome. The distinction between Tolosa-Hunt syndrome (and orbital pseudotumor) and ophthalmoplegic migraine (see Box 2) is difficult as both may relapse and remit. The absence of chemosis and proptosis argues against orbital pseudotumor in this case.

**Box 1.—ICHD-II Criteria for Tolosa-Hunt Syndrome**

| A. | One or more episodes of unilateral orbital pain persisting for weeks if untreated. |
| B. | Paresis of one or more of the third, fourth, and/or sixth cranial nerves and/or demonstration of granuloma by MRI or biopsy. |
| C. | Paresis coincides with the onset of pain or follows it within 2 weeks. |
| D. | Pain and paresis resolve within 72 hours when treated adequately with corticosteroids. |
| E. | Other causes have been ruled excluded by appropriate investigations. |

rule out so many others. In ophthalmoplegic migraine the 3rd nerve is involved much more often than the 6th nerve, and involvement of the 4th nerve is quite rare. There are now many reports of enhancement of the 3rd nerve during an acute attack of this disorder and I would recommend that a gadolinium-enhanced brain MRI be performed during the patient’s next attack with attention to the course of the 3rd nerve.3

The ICHD-II no longer classifies ophthalmoplegic “migraine” as migraine but with “Cranial neuralgias and central causes of facial pain.”1 Because the condition is rare there are mostly anecdotal reports to inform us. The pathophysiology is unclear but it may be a “recurrent demyelinating neuropathy.”4 There may be more than one potential etiology including compression by blood vessels. 5 Features inconsistent with migraine include its more frequent occurrence in males and the fact that the headache may last >72 hours. There is no good evidence base to guide treatment. With little evidence some authors advocate preventative treatment with drugs effective in migraine prophylaxis and others have recommended intermittent use of steroids for acute attacks.1,6 In this particular case, given the infrequent attacks, I would favor a course of prednisone with full disclosure of the potential complications, including osteonecrosis, if used repeatedly.

REFERENCES


QUESTIONS FOR DISCUSSION

1. Which neural structures can be affected by lesions in the region of the cavernous sinus?
2. What is the usual age of onset in ophthalmoplegic migraine?
3. What are the features of Retinal Migraine? What is meant by “ophthalmic migraine”?

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.