Case 40

History of Present Illness

A 36-year-old woman with no previous headache history developed a painful right eye 5 weeks ago. The pain is a deep, boring ache (2/10) behind the right eye with sharp, brief pains (5/10) intermittently. There was no tenderness or painful eye movements. She denied photophobia, redness, discharge, vision loss, or double vision. She went to an optometrist who diagnosed her with uveitis and gave her steroid eye drops. One week later she developed diplopia and the records showed she had a right abduction deficit and the uveitis was gone. No further testing was performed. Two weeks after that, the optometrist recorded an exotropia. She states that the diplopia is constant and does not fluctuate over the day. She thinks her vision is blurry RE. She is not a native English speaker, and she is a poor historian.

Past medical and ocular history Endometriosis Ovarian cyst	*Past surgical history* Laparascopic salpingo-oophorectomy
Medications Loratadine Ibuprofen Artificial tears	*Family history* Mother—some kind of eye degeneration, not blind
Social history A nun from Africa visiting for one year No alcohol No tobacco	*Review of systems* Seasonal allergies Trouble sleeping Poor appetite Feels sadness and anxiety

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Examination
Acuity with correction Right eye: 20/20 Left eye: 20/15
Color vision Misses half a plate RE Identifies all plates LE
Pupils In bright light RE 4 mm, LE 3 mm In dim light RE 5 mm, LE 4.5 mm RE is sluggish, LE is brisk, no RAPD
Intraocular pressure Right eye: 20 mmHg Left eye: 18 mmHg
External exam 1.5 mm ptosis RUL 2 mm relative proptosis RE Normal facial sensation and strength
Eye motility and alignment RE: 10% abduction, 10% elevation, 10% adduction, and 50% depression (saccades were slowed) LE: Normal
Slit lamp examination Normal
Visual field Normal
Fundus examination Normal
Neurologic examination Normal including facial sensation

Discussion

Ophthalmic Perspective—Dr. Lee

I think it unlikely that she had uveitis. We will never know, but it seems unlikely given the lack of photophobia, red eye, and the resolution in just 1 week. Additionally, the pain did not resolve when the "uveitis" did. Instead, the pain was likely the initial symptom of the process picking off her right sixth nerve then her right third and fourth nerves. She describes blurred vision RE. Her acuity is 20/20 RE and she misses half a color plate with the RE but there is no APD. I do not think she has an optic neuropathy at this point, but it could be the earliest manifestation of one. The third, fourth, and sixth nerves run together in the cavernous sinus, the superior orbital fissure, and the posterior orbit. See also Fig. 18.2 for a diagram of the cavernous sinus, orbital fissure, and cranial nerves. The optic nerve meets them in the posterior orbit. In either case, we need to evaluate the back of the orbit into the cavernous sinus, and I would choose an MRI with gadolinium along with fat suppressed imaging. The pain would make myasthenia unlikely. Although she has

proptosis, this would be a very rapid course for thyroid eye disease (TED), which also does not usually cause ptosis. Finally, the saccades were slowed suggesting a neuropathic cause and not a restrictive process like TED (Case 14). There is an entity discussed in Case 43 called ophthalmoplegic migraine but this almost always occurs first under the age of 10. The pain and subacute progression here would suggest an infectious, inflammatory, or neoplastic cause. We can wait for the MRI to come back or order some basic inflammatory and infectious labs such as CBC, ESR, ACE, ANA, Lyme, RPR (I know she is a nun, but I would still order), Serum IgG4, Quantiferon gold (she is from Africa), C-ANCA.

Neurologic Perspective—Dr. Digre

This woman has painful ophthalmoplegia—pain around one eye associated with partial cranial nerve 3, 4, and 6 dysfunction. She is young (less than 40) and has no known malignancy or known infections. There is a huge differential of painful ophthalmoplegia (see Table 40.1). Imaging is the first step since many findings like aneurysm, sinus disease, and tumors maybe seen. This person deserves evaluation

Table 40.1 Differential diagnosis of painful ophthalmoplegia (in part from Kline, Hoyt)

Trauma
Vascular
Carotid cavernous fistula or thrombosis (Case 37)
Aneurysm: intracavernous or internal carotid/posterior cerebral (Case 42)
Diabetic/ischemic third nerve palsy
Carotid dissection
Vasculitis: granulomatosis with polyangiitis (Wegener's) (Case 15)
Giant cell arteritis (Case 32)
Neoplastic
Primary tumors: Pituitary, Meningioma, Neurofibroma, craniopharyngioma, chordoma, and other(Case 41)
Metastases: nasopharyngeal, squamous cell, lymphoma, myeloma, carcinoma (breast, prostate, lung), melanoma
Infections and Inflammation
Bacterial: sinus (Case 25)
Viral: Zoster (Case 38)
Fungal:Mucormycosis, aspergillosis
Spirochete: syphilis, Lyme
Mycobacterial: TB
IgG 4 disease
Orbital pseudotumor (Case 11)
Other
Sarcoid
Ophthalmoplegic Migraine (Case 43)
Tolosa Hunt Syndrome

Table 40.2 ICHD 3 beta Diagnostic criteria for Tolosa Hunt syndrome

(A)	Unilateral headache fulfilling criterion C
(B)	Both of the following:
	1. Granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, demonstrated by MRI or biopsy
	2. Paresis of one or more of the ipsilateral IIIrd, IVth, and/or VIth cranial nerves
(C)	Evidence of causation demonstrated by both of the following:
	1. Headache has preceded paresis of the IIIrd, IVth, and/or VIth nerves by _2 weeks, or developed with it
	2. Headache is localized around the ipsilateral brow and eye
(D)	Not better accounted for by another ICHD-3 diagnosis

Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition (beta version). *Cephalalgia*. 2013;33:629–808

as well not only the blood work that Dr. Lee ordered, but also consider a chest X-ray and possibly cerebrospinal fluid evaluation looking for infections. She is from a developing country and tuberculosis is very common. Sometimes, any lesion found needs to be biopsied to rule out secondary causes of painful ophthalmoplegia.

Let us suppose that this work up is largely negative, we are left with the diagnosis of Tolosa Hunt disease. While Tolosa Hunt is usually a diagnosis of exclusion of all of the things listed in Table 40.1, there are criteria to make the diagnosis (see Table 40.2). This condition can present at any age from either gender. Usually pain comes first (like in this case) followed by diplopia. The pain is often really severe—and stabbing, burning, intense boring pain is the usual description. In addition, the pain is around the eye, forehead, or temple. Any of the ocular motor nerves can be involved in addition to the sympathetic and all three divisions of V and rarely the facial nerve or optic nerve is involved. Imaging usually shows enhancement of the cavernous sinus region and this often spreads beyond the sinus into the posterior fossa.

Treatment is usually steroids and one of the real hallmarks of this disease is that steroids really stop the pain. Sometimes as tapering occurs, the pain can recur weeks, months, or years later. The dose for prednisone is variable—in children, it is usually 1 mg/kg/day. In adults, it is usually 60 mg each day and then taper. Other medications considered include methotrexate, infliximab, and rarely radiotherapy.

Non-ophthalmic/Non-neurologic Perspective

Hopefully you can diagnose multiple cranial neuropathies and localize them based on the company they keep. I think a patient like this with diplopia, ptosis, and pain will get an MRI from most physicians. However, I would just comment that you should ask for fat-suppressed images and order contrast when you look

at the orbit. Otherwise, the patient may be getting a second MRI! Given the complexity of the situation, I do not think most primary care providers and neurologists would be comfortable with this patient and this patient should be seen by a neuro-ophthalmologist.

Follow-up

Her MRI showed an enhancing lesion in the right cavernous sinus and right superior orbital fissure (Fig. 40.1). This was not continguous with the paranasal sinuses. Her lab workup was negative, and she was begun on prednisone 1 mg/kg/day for 7 days. She enjoyed complete resolution of her pain and double vision, and repeat MRI was not performed at that time. Two weeks later, she developed recurrent pain. MRI showed no change to the lesion from the first MRI. Another course of prednisone was begun reducing the daily dose by 10 mg every week for 8 weeks with resolution of her pain. A third MRI showed a persistent enhancing lesion with partial interval resolution of the lesion. A neurosurgical biopsy was planned; however the patient

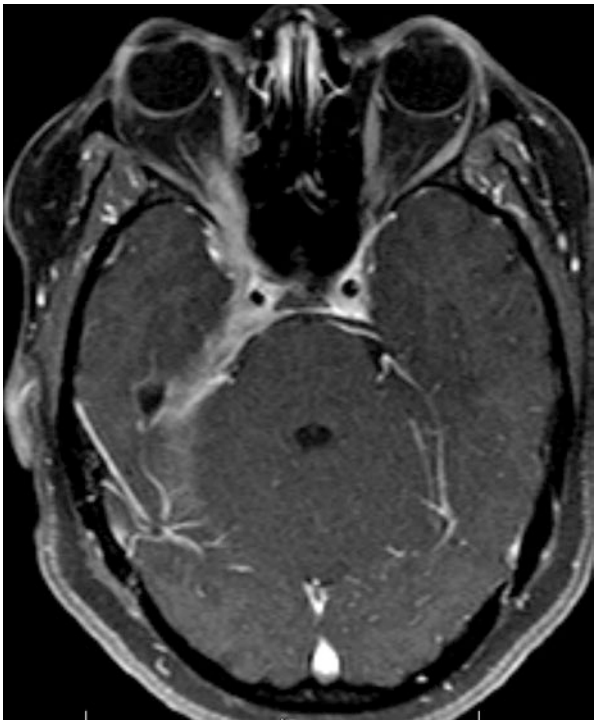

Fig. 40.1 MR (T1, fat desaturated with contrast) Imaging shows enhancement extending from the right superior orbital fissure, through the cavernous sinus along the posterior tentorium of the petrous bone. This is a typical appearance of Tolosa Hunt Syndrome

was found to have an ovarian mass. She remained on 20 mg prednisone for the brain lesion while her ovarian mass underwent biopsy. The mass proved to be benign, and repeat MRI 2 months after the third MRI showed complete resolution of the lesion. She was tapered off steroids and her symptoms did not return. *Final Diagnosis: Tolosa Hunt syndrome*.

For Further Study

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4. Pérez CA, Evangelista M. Evaluation and management of Tolosa-Hunt syndromein children: a clinical update. Pediatr Neurol. 2016;62:18–26.