Case 43

History of Present Illness

A 6-year-old girl developed a severe unilateral, throbbing headache upon awakening 3 weeks ago. She experienced nausea, vomiting, photophobia and lay in bed. The headache resolved after several hours, but she experienced persistent left eye pain, which she described as sharp. One week later, her left upper eyelid drooped. It was constant and unassociated with vision loss, ptosis, or worsening pain. One week later, she developed diplopia and went to the emergency department (ED). Brain MRI at that time was read as normal. The father notes that her left pupil has been larger "as different as a dime and a quarter."

Past medical and ocular history Born at 39 weeks with normal pregnancy and delivery Achieved normal milestones No ocular or medical history	*Past surgical history* None
Medications None	*Family history* Mother—sick headaches starting in college
Social history Kindergartener, both parents at home, one older sibling. No pets Denies alcohol, tobacco, and street drugs	*Review of systems* No fever, chills, or night sweats Some moderate malaise No neck stiffness No weight loss Feels well

M.S. Lee, K.B. Digre, *A Case-Based Guide to Eye Pain*,
https://doi.org/10.1007/978-3-319-65121-7_43

Examination
Acuity with correction Right eye: 20/20 Left eye: 20/20
Color vision Normal BE
Pupils Pharmacologically dilated by referring ophthalmologist Notes reflect left pupil was larger
Intraocular pressure Right eye: Globe soft to palpation Left eye: Globe soft to palpation
External exam RE appears normal 2.5 mm ptosis LUL No proptosis or enophthalmos
Eye motility and alignment RE was normal LE showed normal abduction and intorsion on downgaze LE 50% adduction, 50% elevation, and 75% depression
Slit lamp examination Normal
Visual field Normal
Fundus examination Normal
Neurologic examination Normal facial sensation and strength Normal neurologic exam besides left CN 3

Discussion

Ophthalmic Perspective—Dr. Lee

Historically, the patient had what sounds to be her first migraine headache 3 weeks ago and suffered persistent LE pain. While she is on the young side, migraine can happen in that age group. Later, however, she develops a slowly progressive, pupil-involving, left third nerve palsy (3NP). We really do not need to ask about myasthenic symptoms, because myasthenia does not cause pain nor affect the pupil. It appears neurologically isolated with intact cranial nerves 2 (normal acuity and color vision), 4 (intorsion with downgaze), 5 (normal facial sensation), 6 (normal abduction), and 7 (normal facial strength). Thyroid eye disease does not cause ptosis. It usually does not occur in this age group or present this acutely. There are also no obvious orbital signs suggesting thyroid eye disease.

We are always worried about aneurysm in a patient with a pupil-involving 3NP. This patient is young for aneurysm, but we do not want to miss it especially since CTA and MRA are noninvasive and apt to find essentially all aneurysms big enough to cause 3NP.

There is a phenomenon known as ophthalmoplegic migraine (recently renamed recurrent painful ophthalmoplegic neuropathy) that usually presents before age 10. Often the child experiences a migrainous headache followed by a third nerve palsy (it can be a sixth or a fourth nerve palsy too). Although the headache resolves within hours, the nerve palsy resolves spontaneously over several weeks. Brain MRI almost always shows enhancement of the third nerve at the root exit zone (This suggests that this is not really migraine). So, I would like to look at the MRI from the ED. If the MRI were not performed with gadolinium, then I would send her for an MRI/MRA brain with gadolinium letting the radiologist know that she has a left 3NP and please evaluate for posterior communicating artery aneurysm. If the original MRI were done well and did not show enhancement, then I would talk to the radiologist and the parents about CTA vs. MRA. Some institutions have better results with one vs. the other but CTA has radiation (which we worry about giving in children).

Neurologic Perspective—Dr. Digre

This child has a family history of migraine and we do not know if she was a colicky baby, but colic can portend migraine as the child gets older. She has a headache 3 weeks before that really sounds like migraine, and the mother obviously knew she had a migraine and sent her to bed to sleep the migraine off. However, the pain persisted and she had sequential ptosis and diplopia and now her examination looks like a pupil involving third nerve palsy. We have to consider the differential diagnosis of a painful third nerve palsy in childhood (see Table 43.1).

Imaging apparently was negative—or at least no gross abnormality was identified. Recurrent ophthalmoplegic neuropathy is a likely diagnosis here. However, according to the ICHD 3 beta criteria (see Table 43.2), the child should have at least three attacks to be called recurrent ophthalmoplegic neuropathy (formerly known as

Table 43.1 Causes of third nerve palsy in childhood

Congenital
Trauma
Tumor
Vascular (aneurysm)
Meningitis
Idiopathic (including ophthalmoplegic migraine)

Table 43.2 ICHD 3 beta diagnosis of Recurrent painful ophthalmoplegic neuropathy (ophthalmoplegic migraine; ophthalmoplegic neuropathy)

(A)	At least two attacks fulfilling criterion B
(B)	Unilateral headache accompanied by ipsilateral paresis of one, two or all three ocular motor nerves
(C)	Orbital, parasellar, or posterior fossa lesion has been excluded by appropriate investigation
(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

Table 43.3 Causes of a painful third nerve palsy

Vascular causes
Ischemia
Aneurysm
Pituitary apoplexy
Fistula (cavernous)
Inflammation
Giant cell arteritis
Tolosa Hunt Syndrome
Infection
Meningitis
Tumor
Pituitary tumor
Pituitary apoplexy
Demyelination
Multiple sclerosis
Other
Ophthalmoplegic migraine or recurrent ophthalmoplegic neuropathy
Herniation

ophthalmoplegic migraine). In general, this is seen more frequently in girls at around age 4–10. However, it has been reported in individuals over 50. Pain is often orbital or periorbital and the pain most frequently occurs before the onset of the cranial neuropathy and the headache often goes away before the third nerve palsy resolves. The pain may have some migraine symptoms like nausea, and vomiting, photophobia but about 1/3 do not. The third nerve is most frequently involved—rarely the sixth alone or combined with CN 3. The majority of individuals will have typical migraine in between third nerve attacks. The pupil is most often partially or completely involved. The spinal fluid is usually normal. The cause of the recurrent neuropathy is unknown but some think it is a recurrent demyelinating event. Treatment of the neuropathy is usually waiting, treat the pain with non-steroidal anti-inflammatories, but some have suggested steroid therapy. Third nerve palsies are always tricky especially when they are painful (Table 43.3).

Non-ophthalmic/Non-neurologic Perspective

If you are comfortable diagnosing a 3NP, then you could consider ordering an MRI/MRA with contrast. It is critical that you talk to the radiologist about the diagnosis of a 3NP and get a reading the same day because of the risk of aneurysm. It is also MUCH better to use a radiologist with neuroradiology fellowship training.

Follow-up

I reviewed the MRI personally. It was done with gadolinium and was not read by a neuroradiologist. The scan showed avid enhancement in the area of the left third nerve exit zone consistent with recurrent ophthalmoplegic neuropathy or ophthalmoplegic migraine (Fig. 43.1). Because the migraine headache occurred 1–2 weeks before the 3NP and the patient noted moderate malaise, a lumbar puncture was also performed to evaluate cell count, protein, glucose, cytology, and Lyme. The spinal fluid was normal. The patient's 3NP resolved over the next 4 weeks. The patient's parents were warned that it is not unusual for this to recur over the patient's lifetime. *Final diagnosis: Ophthalmoplegic migraine (Probable recurrent painful ophthalmoplegic neuropathy).*

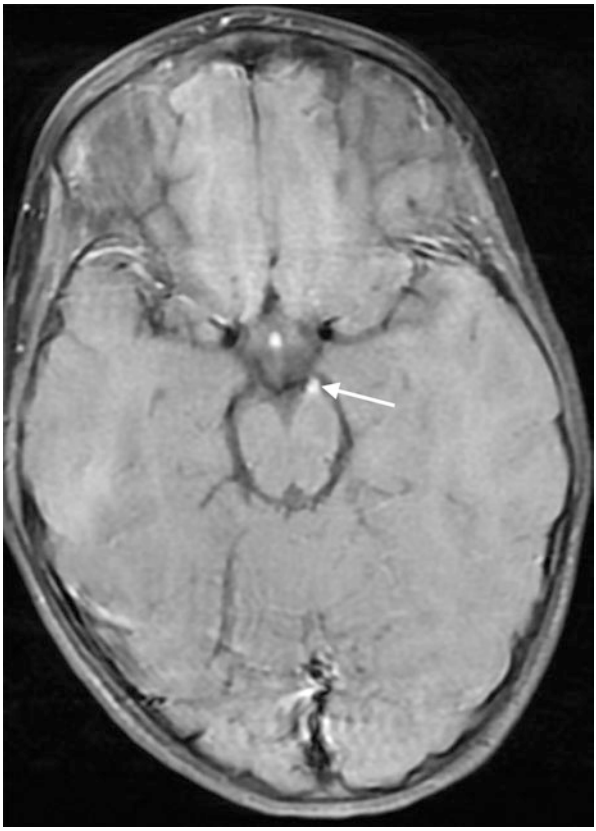

Fig. 43.1 Axial T1 postgadolinium MRI shows the typical bright signal at the left third nerve (*arrow*) exit zone between the cerebral peduncles

For Further Study

1. Elmalem V, Hudgins PA, Bruce BB, Newman NJ, Biousse V. Underdiagnosis of posterior communicating artery aneurysm in noninvasive brain vascular studies. J Neuroophthalmol. 2011;31:103–9.
2. Forderreuther S, Ruscheweyh R. From ophthalmoplegic migraine to cranial neuropathy. Curr Pain Headache Rep. 2015;19:21.
3. Gelfand AA, Gelfand JM, Prabakhar P, Goadsby PJ. Ophthalmoplegic "migraine" or recurrent ophthalmoplegic cranial neuropathy: new cases and a systematic review. J Child Neurol. 2012;27(6):759–66.
4. Schumacher-Feero LA, Yoo KW, Solari FM, Biglan AW. Third cranial nerve palsy in children. Am J Ophthalmol. 1999;128(2):216–21.