Case 11

History of Present Illness

The patient is a 49-year-old, right-handed, special education teacher. She presented initially with spells of kaleidoscopic prisms centrally in the right eye 2 days before she was seen. At this point she had no pain, but a dull ache over the right eye. She was treated with aspirin and the spells resolved. About 10 days later she presented to the emergency room with severe right eye pain. The pain was worse with eye movements and she denied any visual loss. She did have some mild swelling around the eyelid and some tearing, but the pain was really severe.

Four years before she presented with diplopia and eye pain. Her examination at that time showed an esotropia (eye crossing) and a mild hypertropia (vertical misalignment). Imaging showed inflammation of the medial rectus muscle. She was diagnosed with orbital myositis, treated with steroids and diplopia and pain resolved.

While she has had migraines in the past, the pain does not feel like migraine.

Past medical and ocular history Wrist fracture Previous orbital myositis Migraine in the past	*Past surgical history* History of uterine ablation for dysfunctional bleeding
Medications Vitamin C	*Family history* Her mother died at age 60 from complications of multiple sclerosis; heart disease in father
Social history Currently single with 3 children Non-smoker No alcohol	*Review of systems* Otherwise feels healthy

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Examination in the Emergency Room
Acuity with correction Right eye: 20/20 with correction Left eye: 20/20
Pupils 6 mm in darkness and 3 mm in light 7 mm in darkness 4 mm in light No RAPD
Intraocular pressure Right eye 20 mmHg Left eye 21 mmHg
External exam Normal—Hertel 14 OU at base of 92 Right eye: She had 1+ erythema and edema of upper and lower eyelid and mild resistance to retropulsion
Eye alignment She had −1 limitation of downgaze in the right eye but was full in other directions. While she was orthophoric in primary gaze she had a small less than 4 diopters of right hypertropia in downgaze
Slit lamp examination Mild chemosis of right eye only. LE was white and quiet. No cell or flare either eye
Visual field Normal
Color vision Ishihara 13/13 OU
Fundus examination Normal
Neurologic examination Normal

Discussion

Neurologic Perspective: Dr. Digre

This patient has visual disturbances and then presents with severe eye pain. Her initial presentation of kaleidoscopic vision was not associated with any eye pain, and it was thought that this could be a migrainous phenomenon so a baby aspirin was started which often improves migrainous aura. At that time she also had a fluorescein angiogram because of the unilateral nature of the visual change, and this was normal.

When she presented to the ER 10 days later with severe pain with eye movements, our first reaction is—this must be optic neuritis. However, she had absolutely no other signs of an optic neuropathy (normal vision, no RAPD, normal fields, and normal color vision).

There are only a few things that could cause eye pain with movement and normal optic nerve function—inflammatory conditions like thyroid eye disease, sinus disease,

cellulitis or infections, vasculitis like granulomatosis with polyangiitis (Wegener's), and sarcoid can all cause pain. Optic perineuritis (inflammation around the optic nerve, without demyelination) can also present like this. Other findings to look for include proptosis, chemosis (inflammation of the conjunctiva), scleral show, lid lag, and swelling around the eye. See Table 11.1.

Thyroid orbitopathy is the most common orbital disorder but it is usually not that painful. The next most likely thought would be idiopathic orbital inflammation, also known as orbital pseudotumor, or orbital myositis. It really is the most common cause of a painful orbital process. While it occurs at any age and sex (women slightly more than men), it often occurs in middle age. When it occurs in children, it is often bilateral, and has evidence of uveitis and even disc edema. The onset can be slowly gradual to acute or subacute. Imaging has been very helpful in defining idiopathic orbital inflammatory disease. Orbital ultrasound is very sensitive to subtle inflammatory disease, but one needs a competent orbital echographer. CT of the orbits with contrast may show enhancing enlarged muscles or a mass in the orbit. MR scan of the orbits with fat saturation and gadolinium enhancement also may be diagnostic—muscle involvement usually does NOT spare the tendon (vs. thyroid ophthalmopathy which does). Further it has several distinct patterns: muscle only involvement where single muscle or multiple muscles are enlarged and enhancing, lacrimal gland enhancement, and sometimes the sclera will also enhance. The optic nerve sheath can also be involved and this is often called peri-neuritis. Sometimes it is very difficult to distinguish optic peri-neuritis from optic neuritis. However, optic neuritis almost always causes visual loss, a relative afferent pupillary defect (RAPD) and change in color vision, while optic peri-neuritis may have NO evidence of optic nerve dysfunction. If the enhancement has intracranial extension and cranial nerves are also involved, this is idiopathic cavernous sinus inflammation and called Tolosa Hunt Syndrome. Occasionally idiopathic orbital disease can be fibrotic and this type does not always respond to steroids.

Optic perineuritis can be a component of idiopathic orbital inflammation and is very painful—especially with eye movements. While most of the time it is self-limited with good recovery, secondary causes such as granulomatosis with polyangiitis and Behçet's disease can cause severe visual loss.

While there are no official diagnostic criteria, some have suggested: acute orbital pain including pain with eye movements, one or more muscles enlarged in the orbit evident on CT or MR scan, in the face of absent thyroid disease, scleritis or uveitis, normal visual acuity, and a prompt response to steroid therapy.

Aside from imaging, other labs to consider include: CBC, ESR, ANA, ANCA, IgG4, syphilis serology, and lumbar puncture may be helpful to diagnose a secondary cause.

Occasionally a biopsy is needed to make the diagnosis of idiopathic inflammatory disease—for example, when it is not clear if this is a lymphoproliferative (lymphoma), metastatic, or sarcoid orbital disease. The idiopathic form may occur after respiratory or viral illness, may cluster with other immunological disorders (e.g. Crohn's disease).

Recently, IgG4 disease has been recognized to cause idiopathic inflammatory conditions of the orbit and many other organs (e.g. pancreas, salivary glands,

Table 11.1 Causes of orbital inflammation/proptosis and eye pain

Cause	Pain	Symptoms	Signs	Imaging	Laboratory	Comments
Thyroid—most common orbital disorder	Usually mild or absent	Dry eyes, eyes unusually prominent eyes, diplopia	Proptosis, lid retraction, lid lag; muscles usually involved in order include inferior, medial, superior, lateral, obliques	Enlargement of the muscle, but spares tendon	T4, TSH, TRAB, TSI	Most common cause of orbital inflammation; watch for optic nerve compromise; may need orbital decompression or radiation; occasionally steroids helpful
Orbital myositis (idiopathic inflammatory disease)	Can be acute and very painful Pain with eye movement	Usually unilateral eye pain, diplopia, and redness by muscle insertion	Mild proptosis	One muscle, can involve perio-optic nerve, and mass like in the entire orbit; muscle tendon is NOT spared; enlarged lacrimal glands	CBC, ESR, CRP	Steroids are usually helpful
Tolosa Hunt Syndrome	Painful	Diplopia	Cranial nerve palsy—III, IV, VI	Usually shows abnormality into the cavernous sinus	Usually need to rule out malignancy	Look for malignancy, or lymphoproliferative disorder; steroids usually resolve true Tolosa Hunt Syndrome
Sarcoid	Variable but can be painful	Diplopia	Any pattern of muscle involvement; can involve optic nerve	Enhancement of orbital structures; lacrimal glands	ACE, CXR, Chest CT	After diagnosis, treatment with steroids
Vasculitis (e.g. Granulomatosis with polyangiitis (Wegener's disease))	Painful	Diplopia, Red eye	Unilateral or bilateral muscle involvement; episcleritis, scleritis, uveitis	See orbital enhancement and often sinus disease	ANCA, UA	Steroid treatment cyclophosphamide, and rituximab
Infectious (cellulitis)	Painful	Red eye, fever	Proptosis, usually unilateral, chemosis	Can involve whole orbit; image sinuses	Increased WBC; culture and biopsy	Staph, Strep, mucor, aspergillosis; Treat with antibiotic, antifungal, occasionally need surgery
Metastatic disease to orbit	Variable pain	Diplopia	En-ophthalmous, proptosis	Mass in the orbit with bony erosion	Imaging; PET body scan for primary	Breast and lung most frequent

thyroid, etc.). It is often treated with rituximab and steroid treatment can sometimes delay the diagnosis.

Treatment of idiopathic orbital inflammatory disease is usually corticosteroids in doses of prednisone 1 mg/kg for 2–3 weeks with a slow taper. The pain often readily responds and the diplopia improves later. If patients do not respond to this, consider biopsy or another diagnosis or the fibrotic type. Steroid-sparing agents include azathioprine, methotrexate, and infliximab. If the pain recurs or is insufficiently treated with steroids consider other anti-inflammatory medications including naproxen, indomethacin, or gabapentin. Recurrences can occur as well in less than half—but do not be surprised if the inflammation recurs.

Ophthalmic Perspective: Dr. lee

The swollen eyelids could suggest a preseptal cellulitis, but the reduced eye movements here indicate an orbital process. With the pain and redness, you should think about orbital infection vs. orbital inflammation. Some clues to an orbital infection would include fever, elevated white count, and sinus disease on neuroimaging. A CT scan might show a subperiosteal abscess, which would definitely push you toward infection. If this is seen, then the patient will need surgical removal of the abscess. In some cases, you just cannot tell if this is infection vs. inflammation. The safer thing to do is to treat with antibiotics first for 1–2 days. If there is no improvement or worsening, then consider prednisone.

There is no clear evidence for how much steroids and how long to treat with steroids for orbital inflammation, so I will give you my management plan, which differs slightly from Dr. Digre. I treat with 60–80 mg prednisone orally for 1 week. If the inflammation resolves and stays away, then I observe and do not do a systemic workup. If it recurs, then I restart the prednisone and taper slowly over 6–8 weeks. If it recurs again, then I pursue a biopsy because I am most worried about lymphoma. We generally think of lymphoma as painless, but it can be painful. If the biopsy is negative, then I might offer the patient an even longer taper of steroids, orbital radiation (2000 cGy over 10 days), or immunosuppression with a steroid-sparing agent. If the patient is very intolerant of steroids, one could consider injection of 40 mg of triamcinolone in the peribulbar region. I also pursue a systemic workup as described above for recurrent orbital inflammation.

Non-ophthalmic/Non-neurologic Perspective

Orbital inflammatory disease is not rare. The most common symptom is diplopia and pain. The signs are usually proptosis, lid retraction, scleral show, and variable extra-ocular movements. Always check visual acuity and look for an RAPD—if there is loss of vision, and an RAPD, then refer the patient for further evaluation for an optic neuritis. The most common orbital disease is thyroid ophthalmopathy

which is usually not that painful. If you see signs of orbital disease and pain, be thinking about other orbital inflammatory disease, of orbital myositis, or orbital pseudotumor is the most common. See Table 11.1.

Follow Up

The history of a previous myositis 5 years before made the suspicion for orbital inflammatory disease. Her evaluation showed an MR scan that showed enhancement of the orbit and perioptic nerve (Fig. 11.1). Extensive laboratory studies showed: Normal CBC, ESR, CRP, RPR, RF, ACE, anti-thrombin elevation, and factor V Leiden and ANCA. Her protein C was mildly elevated. She was treated with prednisone 60 mg which quickly stopped her pain. She was seen back in clinic 10 days later and her examination now was normal—no evidence of a phoria, or chemosis or redness to the eyes. The prednisone was slowly tapered by 10 mg each week. She remained recurrence free for the last 6 months. *Final diagnosis: idiopathic orbital inflammatory syndrome*.

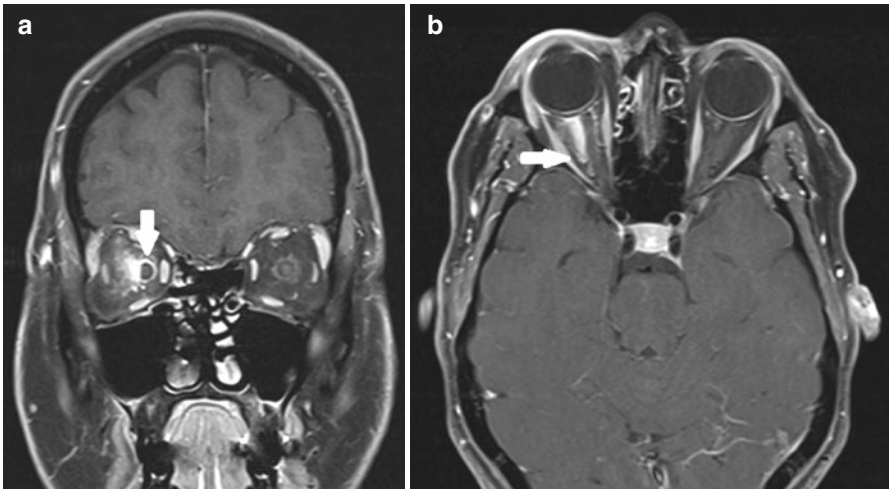

Fig. 11.1 (**a**) Coronal T1 with fat saturation showing the enhancement of the optic nerve sheath (*arrow*) and surrounding orbital tissue. (**b**) Axial T1 with fat saturation showing enhancement of the optic nerve sheath (*arrow*). Note there is mild evidence of proptosis compared to the opposite orbit

For Further Study

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