Title:

Eye Pain: An ophthalmic perspective

Learning Objectives:

1. The learner will recognize 3 historical findings that would suggest an ophthalmic cause to eye pain

2. The learner will be able to discuss why ophthalmic pathologies can present with eye pain

3. The learner will describe at least 5 different ophthalmic causes of eye pain and know how to make the diagnosis by clinical examination.

CME Questions:

1. Which of the following is true regarding ischemic ocular pain?

a) Is frequently encountered with acute central retinal vein occlusion
b) Is a common cause of chronic eye pain in patients with microvascular mononeuropathy
c) Can be associated with ophthalmic surgeries such as scleral buckling
d) Carotid dissection is the leading cause when ischemic eye pain is secondary to a carotid artery pathology

2. What headache type would lead you to look for an ocular source?

a) Thunderclap
b) Asthenopic
c) Orthostatic
d) Pulsatile

3. Pain on eye movement can be seen with optic neuritis, perioptic neuritis, scleritis, trochleitis, and orbital myositis. Which of the following statement is true?

a) Trochleitis can be associated with systemic autoimmune diseases
b) Similar to optic neuritis, perioptic neuritis spontaneously improves in the majority of patients
c) A short course of ibuprofen is often curative in cases of orbital myositis
d) The role of neuroimaging is very limited in patients with posterior scleritis

Keywords (Max 5):

1. Scleritis

2. Trochleitis

3. Myositis

4. Perioptic neuritis

5. Optic neuritis

Introduction/Abstract:

"Doctor, my eye hurts …"

Eye pain may have an ophthalmic or orbital source even in the absence of ocular redness or eyelid edema or erythema (Fiore, et al, 2010). Yet, on the other hand, ocular redness, and/or lid edema or proptosis may be secondary to non-ocular or non-orbital disease processes (Brazis PW, 2002 and Friedman DI, 2008).

Body:

1. PERTINENCE OF PAST MEDICAL HISTORY

A past medical history should be inclusive of family history (especially regarding ocular disorders or headache syndromes; Dr. Frishberg will cover migraine) and should cover injuries, illnesses, treatments and surgeries from prenatal to current time. Review all medications and supplements in use, and check for any temporal relationship between changes in medication regimen and onset of symptoms. Consider whether any medications in use may be contributing to ocular dryness. The patient should specifically be questioned regarding past circumstances of eye, face, head or neck pain and should be queried regarding any history of injury or surgery of the eyes, face, head or neck. The patient should be specifically question regarding periocular, facial and/or scalp or neck injections of botulinum toxin, steroids, fillers or other agents. The patient should be queried as to whiplash injury or any "therapeutic" manipulation of the neck. A specific inquiry regarding history of any type of cancer anywhere in the body should be made, and the patient should be queried regarding any "removal, burning off or freezing off" of any facial or scalp lesions. Anyone with a cancer history deserves a lower threshold for obtaining neuroimaging, in the event of persistent, recurrent, extended or metastatic cancer as etiologic of their eye pain. A specific inquiry should be made regarding history of known auto-immune disease or of present or prior episodes of inflammation or pain in any region of the body.

2. REVIEW OF SYSTEMS

Any known abnormalities of smell or taste? Any visual symptoms? Any facial, head or neck pain, swelling or numbness? Have there been any recent periocular or facial rashes or vesicles? Any epiphora? Any nasal congestion, post-nasal drip, coughing or alterations in voice? Change in sensorium or general well-being? Recent unintended weight gain or loss? Loss of appetite? Malaise? Fevers or night sweats? Any aches, pains, areas of tenderness or swelling in any part of the body? (Dr. Digre will cover GCA).

3. HISTORY OF THIS EYE PAIN

Location and distribution of the pain; does it follow a sensory dermatome? When the pain precedes the rash and eruption, an astute examiner may have an opportunity for early diagnosis and treatment of herpes zoster ophthalmicus, thereby significant reducing the risk of years of painful neuralgia or keratouveitis (Sanjay S, et al, 2011 and Liesegang TJ, et al, 2008). Although pain typically precedes the rash, sometimes the presenting dermatomal symptom is itching or paresthesia, rather than pain (Goh CL, et al, 1997). Sometimes, a patient may present for consultation with a history of chronic pain, which if dermatomal, should prompt consideration of prior herpes zoster, sometimes with no history of rash or vesicles.

Onset, variability, factors which improve or worsen it? Pain secondary to recurrent corneal erosions is often of diagnostic frustration to patient and physician, as symptoms and findings may be absent when the patient is seen for evaluation, but a history of sharp intense ocular pain, sometimes accompanied by tearing, which may awaken the patient from sleep and/or be present upon arising in the morning is characteristic.

Is the pain altered by visual activity or experience; if so is the character or severity of the pain altered by use of spectacles or contact lenses?

Does the pain vary with blinking, lid closure, eye position or eye movement?

Is the pain altered by instillation of topical lubricants?

Is the eye painful right now?

4. CHARACTER OF PAIN

Does the pain begin in the eye? Does the pain extend beyond the eye? Does the pain ever awaken you from sleep? Is there a diurnal pattern? Burning, itching, pressure, aching, foreign body sensation, ice pick? Tenderness? Photophobia? Phonophobia? Vertigo? Nausea or vomiting?

5. EXAMINATION

Inspection: Is there a head tilt, face turn or chin up or chin down position? Is there facial asymmetry? Is facial muscular strength normal and symmetric? Is there facial swelling or alteration in coloration? Are there any facial scars, lumps, bumps, scaly or crusted lesions, vesicles or scabs; if so, inquire about each.

Complete ophthalmologic examination: sometimes, even a neuro-ophthalmologist should consider the utility of a manifest refraction. Phorias or tropias should be evaluated with and without lens correction. Accommodation may be assessed, and, at times, after pupil evaluation and slit lamp biomicroscopy, even a cycloplegic refraction may be indicated. Richards, et al (Richards AL, et al, 2010) found a high incidence of complaints of eye pain offered by pre-school children with refractive error, amblyopia, blepharospasm or nystagmus. They wondered if children in the 2-6 year old age range may have had "difficulty communicating vague visual symptoms to caregivers," and therefore offered complaints of "eye pain." Nonetheless, it is evident that those who may not see clearly, or who may have phorias or intermittent tropias, will exert more subconscious and conscious effort to maintain clarity of vision, with diminished blink rate, squinting and/or head positioning for optimization of visual clarity. These adaptive mechanisms may reduce blink rate, with resultant dry eye symptoms, and may lead to neck and shoulder muscle spasm, with potential consequent "tension headache," and/or migraine. Additionally, squinting may result in orbicularis fasciculations and/or spasm, along with "pressure" discomfort around the eyes, and sometimes, an "uncomfortable tight band" sensation above the brow, which may extend into the temples. Appropriate correction of refractive errors and/or strabismic disorders not only improves vision, but very often ameliorates ocular discomfort, headaches and/or neck and shoulder discomfort.

Is there any discernible abnormality or tenderness of superficial temporal or scalp arteries?

Sensation of light touch in the distributions of V1, V2 and V3 should be assessed. Following pupil evaluation and slit lamp biomicroscopy, a test of corneal sensation may be indicated.

Inspection of lids: asymmetry? scars or cutaneous lesions? fasciculations? myokymia? edema? discoloration? erythema? altered contours? Is there an S-ptosis? altered eyelash appearance or distribution? entropion? ectropion? MRD-1 and MRD-2. Levator "function" excursion. Dynamic behavior of lid movement: Cogan's lid twitch? Fatigue? Lagophthalmos? Lid lag? Oculo-tarsal gap? Forniceal abnormalities? Are there any areas of tenderness or palpable abnormalities? Is the lacrimal gland symmetrically palpable?

Inspection of orbits: Exophthalmometry. Is there any relative vertical or horizontal displacement of the globe? Is there trochlear tenderness? Any asymmetry or abnormality in resistance to retropulsion?

Sensorimotor evaluation, with assessment of phorias, tropias, ductions and versions, with more detailed evaluation for any abnormality.

Pupil evaluation.

Slit lamp biomicroscopy, followed by assessment with fluorescein and/or vital staining with assessment of tear film and tear flow. Is there any tarso-conjunctival abnormality or asymmetry? Conjunctival injection, chemosis or other abnormalities or asymmetries? episcleral abnormalities or asymmetries? Measurement of intraocular pressure in primary position and in additional positions in the presence of any ductional deficit to check for potential alterations in IOP in different gaze positions to assist in characterizing ductional deficits as restrictive or paretic. If pain was present at the time of the examination, did the anesthetic drop alter the pain? If the pain is clearly diminished by topical anesthetic, reassess the tear film, ocular surface, entire conjunctival sac and seek evidence of past or present keratitis. Check for superficial punctate corneal epithelial abnormalities, subepithelial scars or infiltrates and basement membrane dystrophies. Infectious keratitides of varied etiology (herpes simplex or varicella, Epstein Barr virus, fungal, bacterial or acanthamoeba) may sometimes present with severe pain and yet only mild abnormalities in biomicroscopy. Be sure to lift the lid and look for superior limbic keratoconjunctivitis.

Cycloplegic refraction if indicated and dilated ophthalmoscopy.

Chairside dynamic ultrasonograpy for screening for posterior scleritis, myositis, lacrimal gland enlargement, orbital vascular abnormality, orbital mass or infiltrative process.

6. DIFFERENTIAL DIAGNOSIS OF EYE PAIN, NOT RELIEVED BY TOPICAL ANESTHETIC

Pain from a conjunctival or episcleral source may not be relieved by topical anesthetic.

Pain from deep stromal keratitis and/or endotheliitis may not be relieved by topical anesthetic.

Glaucoma: Persons with very high intraocular pressure (generally greater than 40 mm Hg) may present with headache or eye pain, vision changes, or nausea and vomiting. Although the eye is usually inflamed, inflammation may be absent. Headache pain may be far more severe than eye pain, and is characteristically ipsilateral forehead pain. The mechanisms of glaucoma are many, including angle closure, pupillary block, uveitic, rubeotic, post-traumatic, steroid-induced or even primary open angle.

Uveitis

Ciliary spasm: just as a drop of pilocarpine in a normal eye produces intense headache and eye discomfort with brow and forehead pain, so may ciliary spasm, such as that which may accompany low-grade uveitis in a "quiet eye." In such a case, cycloplegia is both diagnostic in evaluation of pain, and therapeutic.

Meibomitis, chalazia.

Orbicularis, and/or corrugator or procerus spasm (primary or secondary).

Canaliculitis with or without dacryocystitis.

Ischemic pain:

1. Carotid artery stenosis is noted by Dr Digre; ophthalmic artery stenosis may similarly be responsible.
2. May be a consequence of vasculitis.
3. May be a consequence of embolization or thrombosis.
4. May be secondary to a CC fistula or dural cavernous sinus fistula
5. Anterior segment ischemia may present as achy pain following strabismus surgery or scleral buckling surgery.
6. May evolve and worsen in association with ischemic tissue damage.
7. Pain may be a prodrome of a microvascular mononeuropathy or cranial nerve III, IV or VI.

Pre-phthisis

Orbital inflammatory disease:

Severe, life-threatening **fungal infections** may first present with severe ocular or periorbital pain, with little evident external abnormality. In appropriate clinical settings, early endoscopic sinonasal evaluation with biopsy and early diagnosis and treatment may be eye, vision and life-saving interventions.

Thyroid Eye Disease (TED) in its early manifestations, or in mild cases, may present with ocular or orbital or peri-orbital discomfort in the absence of evident ocular redness or eyelid or periorbital edema or erythema. The discomfort may be a manifestation of mild or intermittent lid lag, incomplete blink, stare or night-time exposure, with or without associated reduction in basal tear secretion. The discomfort may be a pressure sensation or sense of "fullness" or ocular awareness, in association with mild-to-moderate myopathy, with or without limited ductions. The discomfort may be a pressure sensation in reaction to reflex orbicularis, corrugator and procerus spasm.

Orbital **Wegener's granulomatosis** may present with eye or periocular pain prior to diagnosis, which is generally established following imaging studies and biopsy. Imaging, in most cases, will reveal paranasal sinus disease, with bony erosion and extension into the orbit (Provenzale JM, et al, 1996).

Dacryoadenitis, infectious or inflammatory (sarcoid, non-specific orbital inflammatory disease)

Scleritis, especially posterior scleritis, may present with severe pain, but in early stages without redness,

chemosis, periorbital edema or proptosis. There may be an associated anterior perioptic neuritis with reduced vision, or there may be choroidal folds, choroidal effusion, serous retinal detachment and/or macular edema. Even in the absence of externally visible signs of inflammation, there is generally tenderness and pain on eye movement. Chairside ultrasonography is very sensitive in detecting the associated posterior sub-tenon's fluid accumulation, but CT with and without contrast or MRI with and without contrast is recommended as an initial diagnostic study. Thin-section pre- and post-contrast axial studies are indicated, but are not always routinely done, and therefore should be specifically requested in cases of suspected posterior scleritis; MRI, of course, would be done with fat saturation.

Trochleitis (Tychsen L, et al,1984) presents with bilateral or unilateral severe ocular and periocular ache, which may be variable in intensity and episodic. Often, pain is worsened by eye movement. The etiology is usually idiopathic but trochleitis can be associated with systemic autoimmune diseases. In some cases there is a history of migraine, and sometimes one phenomenon seems to trigger the other (Yangüela J, et al, 2002). Often, upon asking a patient if there is a region of greatest discomfort, they will point to the superomedial orbital rim. Clinical examination most often reveals significant tenderness at the trochlea. Paratrochlear corticosteroid injections are most often therapeutic. Relief can also be obtained with high dose NSAIDs. Some patients benefit from botulinum injections of the ipsilateral corrugator and procerus muscles.

Orbital myositis (Costa RM, et al, 2009) presents with pain which worsens with eye movement and is generally most painful in attempted movement in the direction of the inflamed muscle, sometimes with limitation of duction due both to pain, as well as thickening of the involved tendon. While in most cases there is chemosis and injection, which is most severe in the region of the tendon of the involved muscle, as well as periorbital edema and erythema, the early presentation of the disease may be pain, worsened on eye movement, as noted above, with little-to-no external evidence of inflammation. Pain on eye movement is a clinical indication of orbital disease. Myositis is usually evident with chairside ultrasonography, and should be confirmed, at least once by initial study via CT or MRI with and without contrast, with appropriate tailoring of the imaging study to emphasize viewing and analysis of the suspicious muscle. Some patients are found concurrently to have evidence of other auto-immune disease, or may demonstrate other autoimmunity later in life. Treatment is generally with high-dose corticosteroid, with appropriate taper, but tapering too rapidly often leads to recrudescence, prolongation of the course of disease and prolongation of use of corticosteroids. Some patients may benefit from steroid-sparing therapy and some benefit from radiotherapy.

Perioptic neuritis (Dutton JJ, et al, 1985) most often will present with optic neuropathy with pain on eye movement, but unlike optic neuritis, neuroimaging reveals thickening and enhancement of the optic nerve sheath, rather than inflammation within the optic nerve. Most often there is optic nerve head edema. Both the pain and vision are steroid responsive.

Optic neuritis / retrobulbar neuritis

In association with MS
In association with NMO
Vasculitic
Idiopathic

Diffuse orbititis: Rosai-Dorfman, Erdheim-Chester, amyloidosis, etc.

IgG4 disease - Orbital IgG4-related disease is characterized by IgG4-positive lymphoplasmacytic infiltrations in ocular adnexal tissues. Common presenting features include chronic noninflammatory lid swelling and proptosis. Patients often have a history of allergic disease and elevated serum levels of IgG4. Associated systemic IgG4-related lesions may be present. Systemic steroid therapy decreases the size of the lesions, but relapse often occurs when systemic steroid therapy is discontinued.

Orbital Apex – Superior Orbital Fissure – Cavernous Sinus inflammation:

Tolosa-Hunt Syndrome (the differential diagnosis, based on clinical presentation, examination and neuro-imaging often includes infection, neoplasm and sarcoidosis).

Tumors

- **Ocular tumors**: while intraocular tumors may present primarily with pain in a "quiet eye," more often they are

detected during evaluation of painless visual disturbance.

1) Primary
2) Secondary
    a. direct extension from contiguous structures;
    b. metastatic. The most common primary cancers leading to intraocular metastases are breast, lung, and gastrointestinal cancers (De Potter P, et al, 1998 and Mejia-Novelo A, et al, 2004).
    c.

- **Orbital tumors**:

1) Primary

    Eyelid tumors.
    Lacrimal gland tumors (MALT or other lymphoma, pleomorphic adenoma, adenocarcinoma or adenoidcystic carcinoma)
    Schwannoma
    Cavernous hemangioma
    Lymphangioma
    Orbital varix
    Optic Nerve Sheath Meningioma
    Tumorous processes of orbital bone: fibrous dysplasia, aneurysmal bone cyst, chondrosarcoma, meningioma

2) Secondary
    a. direct extension from contiguous structures;
    b. metastatic: lymphoma, bladder (Krauss HR, et al, 1982), breast, lung, GI or prostate cancer. Metastases to the eye and orbit most often take hold and grow from within highly vascular tissues; most have a predilection for choroid, extraocular muscle or the marrow space of the greater wing of the sphenoid.

- **Cavernous sinus / skull base tumors**:

1) Primary
    Meningioma
    Schwannoma
    Cavernous Hemangioma
2) Secondary
    a. direct extension from contiguous structures: nasopharyngeal carcinoma, angiofibroma, esthesioneuroblastoma, etc.
    b. metastatic.

Intracavernous carotid artery aneurysm (refer to Dr Digre's manuscript)

Sinonasal disease: allergic, infectious (including fungal), mucocele, inflammatory disease, vasculitis, tumors.

Referred pain, not from eye, orbit or adnexae (refer to Dr Digre's manuscript)

CONCLUSIONS

Eye pain in the "quiet" eye may or may not be a manifestation of disease of the eye or adnexa. The "quiet" eye, upon close inspection, may not be quiet. The neuro-ophthalmologist must be vigilant to consider these when symptoms, signs suggest the diagnosis. Once the diagnosis is made, then treatment can be directed at the underlying pathology. Of great importance, in addition to diagnosis and treatment, is pain management; if your therapeusis does not adequately reduce pain in timely fashion, compassion and standard of care dictate that referrals are made for pain management.

CME Answers:

1. c)

2. b)

3. a)

References:

Brazis PW, Lee AG, Stewart M, Capobianco D. Clinical review: the differential diagnosis of pain in the quiet eye. Neurologist. 2002 Mar;8(2):82-100.

Costa RM, Dumitrascu OM, Gordon LK. Orbital myositis: diagnosis and management. Curr Allergy Asthma Rep. 2009 Jul;9(4):316-23.

De Potter P. Ocular manifestations of cancer. Curr Opin Ophthalmol. 1998;9(6):100–104.

Dutton JJ, Anderson RL. Idiopathic inflammatory perioptic neuritis simulating optic nerve sheath meningioma. Am J Ophthalmol. 1985 Sep 15;100(3):424-30.

Fiore DC, Pasternak AV, Radwan RM. Pain in the quiet (not red) eye. Am Fam Physician. 2010 Jul 1;82(1):69-73.

Goh CL, Khoo L. A retrospective study of the clinical presentation and outcome of herpes zoster in a tertiary dermatology outpatient referral clinic. Int J Dermatol. Sep 1997;36(9):667-72

Friedman DI. Headache and the eye. Curr Pain Headache Rep. 2008 Aug;12(4):296-304.

Krauss HR, Slamovits TL, Sibony PA, Dekker A, Kennerdell JS. Orbital metastasis of bladder carcinoma. Am J Ophthalmol 1982;94:265–7

Krauss HR. Horrible Hyphae – Orbital Infections. http://content.lib.utah.edu/utils/getfile/collection/ehsl-nam/id/998/filename/917.pdf

Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008 Feb;115(2 Suppl):S3-12. doi: 10.1016/j.ophtha.2007.10.009

Mejia-Novelo A, Alvarado-Mirnanda A, Morales-Vazques F, et al. Ocular metastases from breast carcinoma. Med Oncol. 2004;21(3):217–221.

Provenzale JM, Mukherji S, Allen NB, Castillo M, Weber AW. Orbital involvement by Wegener's granulomatosis: imaging findings. AJR Am J Roentgenol. 1996 Apr;166(4):929-34.

Richards AL, Patel VS, Simon JW, Zobal-Ratner J. Eye pain in preschool children: diagnostic and prognostic significance. J AAPOS. 2010 Oct;14(5):383-5. doi: 10.1016/j.jaapos.2010.06.014.

Sanjay S, Huang P, Lavanya R. Herpes zoster ophthalmicus. Curr Treat Options Neurol. 2011 Feb;13(1):79-91. doi: 10.1007/s11940-010-0098-1.

Tychsen L, Tse DT, Ossoinig K, Anderson RL. Trochleitis with superior oblique myositis. Ophthalmology. 1984 Sep;91(9):1075-9.

Yangüela J, Pareja JA, Lopez N, Sánchez Del Río M. Trochleitis and migraine headache. Neurology. 2002 Mar 12;58(5):802-5.