Ophthalmic findings in patients with headache

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Introduction

Headaches are a common complaint in the eye clinic. Patients may localize pain around the eyes, behind the eyes, or between the eyes. Patients may have associated ocular complaints including:
- Redness
- Diplopia
- Ptosis
- Tearing
- Photopsias
- Photophobia
- Visual loss and others

As an eye care provider, one must recognize diseases that present with visual signs and symptoms.

Introduction

The most common types of headaches are tension type headaches which have a prevalence of 40%.
The prevalence of migraine in the U.S. is about 12%.
Both are more common in women.
These are likely under estimations since headaches are under reported and not everyone seeks medical attention.
Headaches impact school and work function.
Headache evaluation and treatment can be costly.

How do we experience pain?

Pain is detected by nociceptors which are found on the skin and cornea.
There are different nociceptors for temperature (thermal), mechanical and chemical stimuli.

Main stromal nerve bundles enter the peripheral cornea near the corneoscleral limbus uniformly from all direction.

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How do we experience pain?

Corneal innervation is via the long ciliary nerves, a branch from the nasociliary branch of the ophthalmic nerve.
How do we experience pain?

- The ocular and retrobulbar structures are innervated by the ophthalmic branch of the trigeminal nerve.

How do we experience pain?

- The trigeminal nerve carries pain sensation to the brainstem which carries the input to the contralateral cerebral cortex where pain is processed.

Intracranial pain sensitive structures

- Meningeal and portions
- Dura at the base of the
- Venous sinuses
- Cranial nerves (5,7,9,1)
- Upper cervical nerves

Mechanism of pain

- Traction on pain sensitive areas
- High or low cranial pressure
- Inflammation
  - Meninges/CSF
  - Meningitis
  - Subarachnoid hemorrhage
- Arteries
- Migraine
- Referred pain
  - Irritation to specific nerve will radiate to the area of innervation

Evaluating headache patients

- Thorough history:
  - New-onset or worsening symptoms have a more urgent need for evaluation than patients who have had stable symptoms for many years
- Complete eye exam:
  - Do not skip confrontation fields or pupil checks
  - Look at the optic nerve, retinal vessels and periphery

Evaluating headache patients

- Office testing:
  - Visual fields most important
  - FA
  - OCT
- Imaging:
  - Ordered based on the clinical exam
  - MRI/MRA/MRV/CT scan, etc.
  - MRI more detailed than CT scan
- Referrals:
  - Based on history and clinical exam
Headache types

- Headaches are classified as primary or secondary, then further subdivided.
- Primary headaches are headaches without an underlying pathology.
- Primary headaches include:
  - Migraine headache
  - Tension-type
  - Cluster headache
- Secondary headaches are due to infection, inflammation, neoplasm, and other idiopathic causes.

Migraine types

- 1.1 G43.0 Migraine without aura
- 1.2 G43.1 Migraine with aura
  - 1.2.1 G43.10 Typical aura with migraine headache
  - 1.2.2 G43.10 Typical aura with non-migraine headache
- 1.2.3 G43.104 Typical aura without headache
- 1.2.4 G43.105 Familial hemiplegic migraine
- 1.2.5 G43.105 Sporadic hemiplegic migraine
- 1.2.6 G43.103 Basilar-type migraine
- 1.3 G43.82 Childhood periodic syndromes
  - that are commonly precursors of migraine
  - 1.3.1 G43.82 Cyclical vomiting
  - 1.3.2 G43.820 Abdominal migraine
- 1.3.3 G43.821 Benign paroxysmal vertigo of childhood
- 1.4 G43.81 Retinal migraine
- 1.5 G43.3 Complications of migraine
  - 1.5.1 G43.3 Chronic migraine
  - 1.5.2 G43.2 Status migrainosus
  - 1.5.3 G43.3 Persistent aura without infarction
  - 1.5.4 G43.3 Migrainous infarction
  - 1.5.5 G43.3 Migraine-triggered
  - [...] G40.x or G41.x to specify the type of seizure
- 1.6 G43.33 Probable migraine
  - 1.6.1 G43.33 Probable migraine without aura
  - 1.6.2 G43.33 Probable migraine with aura
  - 1.6.3 G43.33 Probable chronic migraine

Primary Headache Syndromes

Migraine

Migraine without aura

- A primary headache disorder characterized by unilateral, throbbing pain with nausea or vomiting and light or sound sensitivity.
- May be seen in clinic due to retro-orbital component of pain as well as the photophobia associated with the headache.
- Pain typically lasts a few hours but can last days (status migrainosus).
- Pain is usually moderate to severe and impedes daily activity.
- More commonly seen in women about 3:1

Migraine with aura

- Visual symptoms of migraine aura include:
  - Fortification/scintillating scotomas
  - Flashes of lights
  - Seeing things as if through a wave of heat
  - Broken up pieces in the vision
  - Like looking through broken glass or a kaleidoscope
  - Depixelation

Illustration by Dr. Hubert Aary
Migraine aura

The aura occurs for 15-20 minutes and may or may not be followed by a headache.

Migraine aura without headache

Why does the aura occur?

Mechanism first postulated in 1944 by a Neuroscientist Dr. Leao who described "cortical spreading depression".

It is a wave of depressed cortical activity that follows cortical stimulation usually in the occipital lobe

The wave progresses at 3-5mm/min and begins at the occipital pole.

Migraine aura mechanism

Cortical spreading depression has been supported by functional MRI technology as described by Hadjikhani et al in 2001.

Hadjikhani et al Mechanisms of migraine aura revealed by functional MRI in human visual cortex. PNAS. 2001

Migraine

Genetic predisposition:
- CACNA1A, located on chromosome 19 encodes a calcium channel
- Other chromosomes include 1, 4 and X without any known function

Environmental triggers include:
- Foods
  - Chocolate
  - Spicy foods
  - Sulfites
  - MSG
  - Dehydration
  - Aged cheese
- Stress
- Lack of sleep
- Sunlight

Other migraine types
Retinal migraine

- Monocular visual complaints followed by typical migrainous symptoms.
- Visual phenomena include, loss of vision, peripheral scotoma, flashes of light, zigzags, and colored areas.
- The episodes tend to be stereotypic and are fully reversible.
- To document monocular event, patient needs to have covered each eye.
- The ophthalmic exam needs to be normal as does the evaluation.

If the symptom is loss of vision, one should consider a vascular evaluation.
- Vitals signs
- Neuroimaging (MRA) or ultrasound
- Blood tests for hypercoaguability

If normal, and repetitive events have occurred, then etiology is felt to be vasospastic.

Other theory includes spreading depression of the RGC’s, seen in chick retinas (Van Harreveld, J Neurobiology, 1978).

Vascular occlusions:
- Rare complication of migraine
- Mechanism also felt to be vasospastic
- Can lead to retinal or optic nerve ischemia
- Goal would be to prevent episodes
Basilar migraine

- Consists of transient posterior fossa symptoms followed by headache.
- Ophthalmic symptoms include diplopia and loss of vision.
- Other symptoms include vertigo, nausea, ataxia, weakness, numbness, altered consciousness.
- La Spina et. al (Headache, 1997) have shown decreased cerebral blood flow during the aura phase using transcranial dopplers, EEG and CT perfusion in one case.
- Reversible cranial nerve palsies can be seen on exam as well as transient VF defects.

Ophthalmoplegic “migraine”

- Ophthalmoplegic “migraine” is described as a classic migraine i.e., pounding headache with nausea and/or vomiting followed by a course of ophthalmoplegia due to dysfunction of one or more cranial nerves.
- Some reports show cranial nerve enhancement thus the migraine diagnosis comes to question.
- 3rd nerve most common
- Incidence is around 0.7/million
- Typically seen in childhood
- Diplopia can last up to 3 months
- Most likely inflammatory disorder
- Occasional response to steroids

Ophthalmoplegic migraine

- Treatment depends on the frequency
  - Abortive
    - NSAIDS
    - Triptans
    - Ergotamines
  - Prophylactic
    - Magnesium
    - Butterbur
    - Tricyclic antidepressants
    - Anti epileptic drugs
    - Beta blockers
    - Calcium channel blockers

Prophylaxis of Migraine with Oral Magnesium: Results from a Prospective, Multi-Center, Placebo-Controlled and Double-Blind Randomized Study

- In order to evaluate the prophylactic effect of oral magnesium
- 81 patients aged 18–65 years with migraine
- 600 mg (24 mmol) magnesium (trimagnesium dicitrate) daily for 12 weeks or placebo.
- In weeks 9–12 the attack frequency was reduced by 41.6% in the magnesium group and by 15.8% in the placebo group compared to the baseline (p < 0.05).
- The number of days with migraine and the drug consumption for symptomatic treatment per patient also decreased significantly in the magnesium group.
- Duration and intensity of the attacks and the drug consumption per attack also tended to decrease compared to placebo but failed to be significant.
- Adverse events were diarrhea (18.6%) and gastric irritation (4.7%).
- High-dose oral magnesium appears to be effective in migraine prophylaxis.

Primary Headache Syndromes

- Tension-type headache
Tension Headache
- Most common headache encountered
- Usually a band-like pain around the head but can originate at the neck
- Occasionally pain referred between the eyes
- Not usually associated with other symptoms
- Can last hours to days
- Can become a chronic daily tension headache
- Etiology poorly understood but felt to be muscular in etiology

Treatment depends of frequency
- Abortive:
  - NSAIDS
  - Massage
- Prophylactic:
  - Antidepressants
  - Anti-epileptic drugs
  - Botox

Cluster headache
- A periorbital pain lasting between 30 minutes to 3 hours usually in the morning lasting weeks to months.
- Pain is intense and patients feel like they cannot sit still (opposite of migraine).
- Associated with lacrimation, conjunctival injection, miosis, and ptosis.
- Sympathetic inactivity (parasympathetic hyperactivity)

Primary Headache Syndromes
Trigeminal autonomic cephalgias:
- Cluster headache and SUNCT

Cluster headache
- In the U.S. occurs in about 0.4% of men and 0.08% of women.
- Genetic predisposition
- Etiology felt to be due to activation of the posterior hypothalamus
Cluster headache

- If neck pain is severe, must evaluate for carotid artery dissection, though pain would be more constant than intermittent.
- Make sure no cavernous sinus pathology based on your eye exam.
- Treatment depends on frequency:
  - Abortive:
    - Inhaled oxygen: 100% for 15min
    - Prednisone with tapering course
    - Triptans
  - Prophylactic:
    - Calcium channel blockers
    - Anti-epileptic drugs
    - Lithium
    - Tricyclic anti-depressants

SUNCT

- Short-lasting Unilateral Neuralgiform headaches with Conjunctival injection and Tearing
- Very brief episodes of unilateral pain lasting 5 seconds to 5 minutes
- Orbital, periorbital, and temporal pain associated with ipsilateral conjunctival injection and tearing
- Episodes can be few to many per day
- Rare type of headache
- Seen more commonly in men
- Felt to be over activation of the same hypothalamic area as for cluster headache
- Treatments similar to cluster headaches

Secondary Headache Syndromes

Vascular etiologies

GCA

- GCA (TA) is an autoimmune inflammatory disease of T cell origin of medium and large cranial vessels
- Seen in older people
- More common in women than men
- More frequently seen in Caucasians than African-Americans
- Headache is the most common initial presentation and seen in 80% of GCA patients
- Pain is located in the temporal area with tenderness to touch
- People may experience pain in the neck and back of head
- Jaw pain with chewing is classic; at times difficult to tease out from other causes of jaw pain
- Scalp tenderness i.e. combing or placing head on pillow
- Have a low threshold for new headaches in the elderly
- Many ophthalmic manifestations
  - AION
  - CRAO
  - PION
  - Choroidal ischemia
  - Cranial neuropathies
  - 3rd, 4th, 6th N P's
  - Stroke, especially to the posterior circulation
**GCA**
- Evaluated with:
  - Laboratory tests
    - Sedimentation rate (ESR)
    - C-reactive protein (CRP)
  - Temporal artery biopsy
  - Inflammation in intima
  - Disruption of internal elastic lamina
  - Multinucleated giant cells
- Best treatment is steroids
- High dose if acute onset of visual loss
- Some patients may still go blind

**Carotid artery dissection**
- Usually presents with acute neck pain radiating to the head and eye.
- Most common ophthalmic finding is Horner’s syndrome.
- Others include amaurosis fugax due to intraluminal clot, CRAO, and ocular ischemia.
- Dissection usually occurs after a neck trauma:
  - MVA
  - Chiropractor
  - Sport injury
- Can be spontaneous:
  - Ehler’s Danlos
  - Collagen vascular diseases
  - Fibromuscular dysplasia

**Horner’s syndrome**
- Ptosis
  - Due to weakness of Müller’s muscle
- Anisocoria noted more in the dark
  - Lack of innervation of the sphincter muscle in the iris
- Conjunctival injection
- Facial anhidrosis of lesion below carotid bifurcation at the neck

**Carotid artery dissection**
- Vertebrobasilar system
  - Symptoms of neck pain with or without neurological symptoms but most have associated stroke.
  - Typically occurs due to trauma.
  - Ocular findings occur due to brain stem ischemia typically involving the PICA branch from vertebrobasilar artery (Wallenberg syndrome).
    - Horner’s syndrome
    - Rotatory nystagmus
    - Skew deviation

**Aneurysms**
- Most common are arterial outpuchings (saccular or berry-type).
- They can be found incidentally, after rupture, or after neurologic compromise.
- Ocular manifestations are based on location of the aneurysm.
- Headaches can be due to aneurysm with the pain typically on the side of the lesion.
Aneurysms

Optic nerve and chiasmal compression can occur due to ophthalmic, internal carotid, anterior communicating artery and a few other smaller vessel aneurysms.

Aneurysms and visual loss

- Typical history is slowly progressive loss of vision but can suddenly worsen if aneurysm expands.
- Headaches may not always be present.
- Exam typically shows reduced visual acuity and abnormal visual fields.
- VF defect in one eye if pre-chiasmal and both if chiasmal or retro-chiasmal.
- The optic nerve may appear pale.

Aneurysms and diplopia

- Typically presents with slowly progressive diplopia but may also experience sudden diplopia with aneurysm expansion.
- Pain can also be present typically on the side of the lesion.
- The most common location for an aneurysm to cause diplopia is in the cavernous sinus.
- The 6th nerve is most commonly affected first in cavernous carotid artery aneurysms.

Aneurysms and diplopia

- All pupil involved third nerve palsy should be evaluated for aneurysm formation.
- Typical location is the posterior communicating artery.
- Aberrant regeneration of the third nerve should always be investigated for aneurysm.
Aneurysms
- Neuro-imaging is necessary to make the diagnosis.
- Treatment is via aneurysm coiling, gluing or clipping.
- Main goal is to prevent aneurysmal rupture and expansion.
- Patient may still have permanent ocular dysfunction even after treatment.
- Diplopia can be managed with prismatic lenses, strabismus surgery, or occlusion as last resort.

Secondary Headache Syndromes
Headache due to high and low intracranial pressure

High intracranial pressure
- High intracranial pressure leads to generalized headache, neck pain, or retro-bulbar pain.
- Pain worsens with laying down.
- High ICP may lead to papilledema.
- Papilledema is most commonly due to pseudotumor cerebri, but one must always exclude a primary etiology first.

Pseudotumor cerebri
- Other symptoms are transient visual loss for few seconds, visual loss, whooshing sounds, and diplopia.
- Idiopathic reason for high ICP
- Seen more commonly in women
- Weight related
- Diagnosed by clinical exam based on papilledema, normal brain imaging, high ICP on spinal tap with normal CSF consistency.
- 6th nerve palsy may also be seen on exam.

Pseudotumor cerebri
- Evaluation includes:
  - Complete eye exam
  - Visual field testing
  - Brain and venous sinus imaging
- Management is either medical or surgical based on visual function.
- Medical treatment includes weight loss and diuretics (acetazolamide, lasix)
- Surgical managements are optic nerve sheath fenestration and ventriculoperitoneal shunting.

Visual fields in pseudotumor cerebri
High intracranial pressure

Other causes of high ICP are intracranial masses/lesions, meningitis, and venous sinus thrombosis.

Low intracranial pressure

Pain is usually worse with sitting up
Pain located in the occiput, but can be diffuse.
Most commonly seen after spinal tap but other causes include CSF leak from trauma or surgery
Can occur spontaneously
Ophthalmic findings include 6th nerve palsy due to tugging on the stretched nerves
loss of vision is rare but can occur due to chiasmal sagging.

Low intracranial pressure

Evaluation includes neuroimaging and evaluation for CSF leak.
Treatment is a blood patch, caffeine and abdominal binder.

Secondary Headache Syndromes

Inflammatory conditions

Optic neuritis

Optic neuritis is an inflammatory disease of the optic nerve.
Presenting symptoms are decreased vision and orbital pain with eye movement.
Visual loss can be gradual or sudden.
Pain can precede the visual symptoms.
Symptoms last more than one day to weeks.
More common in women than men
Can occur at any age but late teens to late 30’s more common.

Optic neuritis

Examination reveals
- Decreased VA (20/20 to NLP)
- VF defect/scotoma
- Decrease color VA
- RAPD
- Normal or swollen optic nerve
- Later optic nerve pallor
**Optic neuritis**
- Evaluation is with MRI scan to look for other etiologies such as multiple sclerosis.
- Lab testing can be performed if there are recurrent episodes.
- Treatment usually is with intravenous steroid to allow more prompt visual recovery.
- Treatment may vary depending on etiology and if recurrent.
- Retrobulbar pain dissipates faster with steroid as well.
- Follow up with routine exams, visual fields and OCT can be useful.

**MS MRI**

**Optic neuritis**

**What is wrong?**

**Tolosa-Hunt syndrome**
- A painful ophthalmoplegia due to cavernous sinus inflammation.
- Hunt described:
  - Steady, gnawing, retro-orbital pain
  - Defects in the third, fourth, sixth, or first branch of the fifth cranial nerve, with less common involvement of the optic nerve or sympathetic fibers around the cavernous carotid artery
  - Symptoms lasting days to weeks
  - Occasional spontaneous remission
  - Recurrent attacks
  - Prompt response to steroid therapy
- Can occur at any age
- Any side and can be bilateral.
**Tolosa-Hunt syndrome**
- Evaluated with contrast MRI.
- MRI reveals abnormal enhancement but can mimic that of meningioma or lymphoma.
- LP and lab testing are low yield but done to evaluate for SLE, sarcoid or other vasculitis.
- Biopsy if not steroid responsive or not following typical THS natural history.
- Biopsy may be low yield or reveal lymphocytes, plasma cells of macrophages.
- Treatment is steroids or other immune suppressants if steroid dependent.

**Orbital inflammatory disease/orbital pseudotumor**
- Similar etiologies to Tolosa-Hunt, but the pathology is within the orbit.
- Differences include added proptosis, chemosis, and loss of vision due to optic nerve involvement.
- Same treatment as Tolosa-Hunt syndrome.

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**Orbital inflammatory disease/orbital pseudotumor**

**Secondary Headache Syndromes**
*Headache and the pituitary gland*

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**Pituitary adenoma**
- Pituitary tumors are often found incidentally when evaluating other symptoms (dizziness, trauma).
- Other presenting symptoms are loss of vision, hormonal abnormalities and headaches.
- Diplopia may also occur due to mass effect on the cavernous sinuses.
- Sudden headache and visual symptoms suggest pituitary apoplexy.
- Pituitary apoplexy occurs when there is bleeding into a pituitary tumor.
- Size does matter as chiasmal compression usually requires at least a 1cm mass.

**Pituitary adenoma**
- Exam findings include:
  - Loss of vision
  - Visual field defects especially bitemporal defects
  - They can be subtle superior temporal or dense
  - Vf defects can also be due to tract and anterior chiasmal compression.
  - Diplopia due to 3, 4, or 6 nerve palsies.
Pituitary adenoma

- Diplopia due to hemifield slide (non-paretic diplopia):
  - Bitemporal VF defects with central VF loss do not allow both eyes to foveate thus causing diplopia
- See-saw nystagmus due to large sellar masses:
  - Compression of the Interstitial nucleus of Cajal inferiorly
  - Almost pathognomonic for sellar masses (can be seen in other diseases that cause loss of VA)

http://www.youtube.com/watch?v=iGGvoP1ydtk

Sellar masses

- Other masses to consider:
  - Cranopharyngioma
    - Children and late adulthood
  - Rathke’s cyst
    - Seen in any age
  - Aneurysms
  - Arachnoid cyst
- Treatment is usually surgical
- Visual recovery depends on how long compression was present.

Secondary Headache Syndromes

Trigeminal nerve diseases

Trigeminal Neuralgia

- Unilateral facial pain described as an “electric shock” along one or more of the divisions of the trigeminal nerve.
- Pain can be elicited with touching, brushing teeth, cold air, or occur spontaneously.

Trigeminal Neuralgia

- The pain is usually brief and can occur many times per day.
- Is it seen in women more than in men.
- The incidence is about 4.5/100,000 and is seen more in older individuals.
- If seen in younger people need to evaluate for primary neurologic disease (demyelinating, tumor...).
- Usually involves the 2nd or 3rd division of the trigeminal.
- Less often 1st (<5%).
Trigeminal Neuralgia
- Evaluation should include MRI and MRA.
- Treatment is based on the MRI/MRA results
- If normal, medications are used and include:
  - carbamazepine
  - Gabapentin
  - Tricyclic anti-depressants
- Surgical treatment includes placing a synthetic sponge between the artery and TN.
- Others include:
  - TN glycerol injections
  - Radiofrequency thermoablation
  - Gamma knife surgery

Trigeminal Neuralgia
- Many interventional treatments damage the nerve thus cause numbness and all the side effects associated such as neurogenic keratitis.

Herpes zoster ophthalmicus
- Activation of varicella virus along ophthalmic branch of the trigeminal nerve.
- Occurs more common in older or in immune suppressed people.
- Initial presentation may be a burning pain along V1.
- Diagnosis may be made more easily once the rash develops.
- The rash is red, with vesicles or pustules, later followed by scabbing.

Herpes zoster ophthalmicus
- Any part of the eye can be involved thus a complete eye exam is important.
  - Cornea
    - Dendritic keratitis
    - SPK
    - Anterior and deep and Stromal Keratitis
    - Neurotrophic keratitis
  - Conjunctivitis
    - Superimposed bacterial conjunctivitis
    - Episcleritis
    - Anterior uveitis
    - PORN/ARN
    - Optic neuitis
    - Diplopia
    - 3,4 or 6 NP

PO RN and ARN
- Treatment of HZO
  - Acyclovir 800 mg five times a day for seven to ten days or
  - Valacyclovir (Valtrex) 1,000 mg three times daily for seven to ten days
  - Famciclovir (Famvir), 500 mg orally three times a day for seven days
  - Often oral prednisone is used to decrease the inflammatory response and facial swelling.
- Bacterial conjunctivitis:
  - Cost compression and topical lubrication
  - Topical broad-spectrum antibiotic indicated for secondary bacterial infection (usually Staphylococcus aureus)
  - Epithelial keratitis
    - Debridement or none
  - Stromal keratitis
    - Topical steroid

Herpes zoster ophthalmicus
- Neurotrophic keratitis
- Topical lubrication
- Topical antibiotics for secondary infections
- Tissue adhesives and protective contact lenses to prevent corneal perforation
- Uveitis
  - Topical steroids
  - Oral steroids
  - Oral acyclovir
  - Scleritis/episcleritis
    - Topical nonsteroidal anti-inflammatory agents and/or steroids
- Acute retinal necrosis/progressive outer retinal necrosis
  - Intravenous acyclovir
  - Laser/surgical intervention
Post herpetic neuralgia

- Post shingles pain
- Worse at onset but can improve with time
- More common in the elderly and in more severe cases
- Pain is burning, tingling and at times sharp/electrical

Medications used include
- Topical capsaicin
- Gabapentin or lyrica
- Carbamazepine
- Tricyclic drugs
- Nortriptyline
- Cymbalta

Summary

- There are numerous types of headaches with ocular symptoms and findings.
- It is important to take a good history noting chronicity of symptoms and whether there is worsening.
- Perform a complete eye exam including confrontation fields, lids, pupils, motility and funduscopy exam.
- Administer visual field testing if the eye exam does not explain the visual complaints especially if there are active symptoms.

New headaches, worsening headaches and headaches in the elderly should always be evaluated.

Recognizing the signs and symptoms can lead to prompt diagnosis and management of potentially vision and life threatening diseases.

References

- Ophthalmoplegic Migraine