The eye, a window to the brain

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Nothing to disclose
Objectives

1. Understand the importance of the eye and its signs in neurological disease
2. Become acquainted with common eye signs present in common neurological disease
3. Become able to recognize common “neuro-eye” signs needing referral to neurology
Why is the eye important in neurological disease

• 60% of our brain is linked to vision
• 2 million axons in both optic nerves
• Afferent: Optic nerve, retina, chiasm, visual pathways, cortex.
• Efferent: Cranial nerve III, IV, VI, ocular muscles, brain stem control centers.
Common symptoms

• Visual loss (temporal profile; one vs both eyes)
• Diplopia
• Ptosis
• Visual disturbances
• Pupil irregularities
• Eyelid or Facial spasms.
Clinical Approach

- History is the most important part or the assessment.
- Localization ("Where" is the lesion ?)
- Temporal profile
- "What" can be the lesion ?
- Is this an emergency ?
- Can it be treated?
Case 1

- A 68 year old patient with sudden loss of vision in the right eye.
- History of episodes transient loss of vision.
- Diabetes for 30 years.
- Feeling unwell lately with, and loss of appetite, malaise and myalgias.
- Visual acuity: Count finger right, 20/30 left.
- Right RAPD.
Clinical test for the optic nerve

- Visual acuity
- Color Plates
- Visual fields
- Swinging flash light test
- Fundoscopy
Swinging flash light
Case 1

Diagnosis?
Differential diagnosis

- Infection? (no pain, proptosis, injection, normal CT sinuses)
- Bilateral retrobulbar optic neuritis? (too old)
- Anterior ischemic optic neuropathy/AION? (no disc swelling or heme)
- Functional visual loss? (no secondary gain)
- Chiasmal lesion? (no bitemporal hemianopsia)
- Retrogeniculate lesion? (no homonymous hemianopsia)
- Toxic optic neuropathy? (not symmetrical, no atrophy)
- Leber’s Hereditary Optic Neuropathy? (too old, wrong sex, normal appearing nerves)
- Posterior ischemic optic neuropathy/PION? (no blood loss, no recent surgery or severe trauma)
Case Investigations

• ESR = 86
• CRP positive.
• Platelets elevated (560).
• Mildly anemic.
GCA diagnosis

Symptoms

• headache,
• scalp tenderness,
• jaw claudication,
• swollen and pulseless superficial temporal arteries,
• PMR, fatigue,
• weight loss,
• fever, malaise,
• transient monocular blindness,
• diplopia
Diagnosis

- **Stat** ESR, CRP and CBC (platelets).
- ESR can be normal in 15-20% of cases.
- CRP is more sensitive and specific.
- CRP and CBC have 97% sensitivity and specificity.
- Arrange for temporal artery biopsy within 2 weeks, while patient is on steroids.
GCA treatment

• High dose steroids must be initiated as soon as the diagnosis is considered, don’t wait for TABx results

• Return of vision after steroid initiation is <15%

• high dose IV steroids (methylprednisolone IV 1 g x 5 days) vs high dose oral steroids (ex. 100mg prednisone)

• Prednisone for several weeks

• Tocilizumab (Anti IL6)

• Delayed diagnosis of GCA is an important cause of medical malpractice in ophthalmology (and I assume optometry)
Inhibitor of interleukin-6 receptor alpha
Used to treat rheumatoid arthritis (IV or SC)
Recently approved by FDA to treat GCA
  - Subcutaneous (162mg once a week)
Temporal Artery Biopsy
Temporal artery biopsy

- Thickening of the intima, necrosis of the internal elastic lamina and media and lymphocytic infiltration of the vessel wall with giant cells are seen acutely.
- Biopsies of patients on steroids >2 weeks show disruption of the internal elastic lamina but few or no lymphocytes or giant cells, termed “healed arteritis”.
- A temporal artery biopsy specimen ≥ 2 cm confirms the diagnosis in 95% of cases. If negative, a contralateral biopsy has a yield of only 3% (Boyev 1999).
Arteritic ischemic optic neuropathy

• Vision loss is due to ischemic optic neuropathy (ION), either Anterior (disc swelling and blood) or Posterior (without disc edema)

• GCA can also cause CRAO or choroidal infarctions

• GCA patients tend to be older (mean age=75 years) than non-arteritic ION patients (mean age=57 years)

• A true neuro-ophthalmic emergency (54-95% second eye involvement if untreated)
Case 2
Ischemic Cherry Red Spot
Central Retinal Artery Occlusion

- Retinal infarct
- Central retinal artery occlusion
- Acute painless monocular blindness
- Loss of retinal transparency except in the fovea
Acute retinal ischemia

Different visual outcomes
Same systemic implications
Acute Retinal Arterial Ischemia

- Same situation if:
  - Transient visual loss
  - BRAO
  - CRAO
  - OAO

- Same vascular territory as brain (anterior circulation)
- Same mechanisms and causes as cerebral ischemia (add giant cell arteritis)
<table>
<thead>
<tr>
<th>Study</th>
<th>DWI-MRI Results</th>
<th>Correlation with Abnormal DWI-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hellenius (USA) 2012</td>
<td><strong>DWI+ in 31/129 (24%)</strong> [CRAO/BRAO: 33% vs TMVL: 18%] \nSame vascular territory as VL in 28/31 \nSmall, multiple (65%) infarctions</td>
<td>Neuro sx + \nPermanent VL &gt; TMVL \nIdentified cause \nEmbolic cause</td>
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<td>Lee (Korea) 2014</td>
<td><strong>DWI+ in 8/33 (24.2%)</strong> [CRAO: 27% vs BRAO: 20%] \nSame vascular territory as VL in 8/8 \nSmall, multiple (100%) infarctions</td>
<td>Neuro sx + \nIdentified cause \nEmbolic cause</td>
</tr>
<tr>
<td>Tanaka (Japan) 2014</td>
<td><strong>DWI+ in 4/13 (30.8%)</strong> No description</td>
<td>NA</td>
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<td>Lauda (Germany) 2015</td>
<td><strong>DWI+ in 49/213 (23%)</strong>&lt;br&gt;[CRAO: 53%; BRAO: 31% vs TMVL: 16%]&lt;br&gt;Same vascular territory as VL in 55%&lt;br&gt;Small, multiple (35%) infarctions</td>
<td>Neuro sx +&lt;br&gt;CRAO &gt; BRAO &gt; TMVL&lt;br&gt;Identified cause&lt;br&gt;Embolic cause</td>
</tr>
<tr>
<td>Cho (Germany) 2016</td>
<td><strong>DWI+ in 6/46 (13%)</strong>&lt;br&gt;No description</td>
<td>Identified cause&lt;br&gt;Embolic cause</td>
</tr>
<tr>
<td>Golsari (Germany) 2017</td>
<td><strong>DWI+ in 17/112 (15%)</strong>&lt;br&gt;[CRAO: 76%; BRAO: 12% vs TMVL: 12%]&lt;br&gt;Same vascular territory as VL in 71%&lt;br&gt;Small, often multiple infarctions</td>
<td>CRAO &gt; BRAO &gt; TMVL&lt;br&gt;Identified cause&lt;br&gt;Embolic cause</td>
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Acute symptomatic OAO or CRAO should prompt an immediate referral to the nearest stroke referral center for prompt assessment for consideration of an acute intervention.

Specifically, patients with greater ischemia require more frequent follow-up.
Case 3

- 38 y/o woman consulted for blurry vision and decreased vision in the right eye for the past 24 hours. The patient also mentioned that along with the visual impairment she has had pain about the eye when she tries to look to either side by moving her eyes.

- Medical history negative. No medications
Case 3

• VA OD 20/200 OS 20/25
• Normal fundoscopic exam
• + Afferent pupillary defect OD
• Normal exam otherwise
Optic Neuritis

- Sudden loss of vision.
- Pain with eye movements.
- Females > Males.
- RAPD present.
- Optic disc normal.
- MRI is important for MS risk determination.
MRI in optic Neuritis

White matter lesion predicts high risk for development of MS (70% over 15 years)
Typical Isolated Optic Neuritis:
Risk of MS Based on Initial MRI

Typical Isolated Optic Neuritis:
Risk of MS if MRI normal

- Risk = ZERO
- If:
  - No pain
  - No light perception vision
  - Severe disc edema
  - Hemorrhagic disc edema
  - Retinal exudates
Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria

Lancet Neurol 2017
Alan J Thompson, Brenda L Banwell, Frederik Barkhof, William M Carroll, Timothy Coetzee, Giancarlo Comi, Jorge Correale, Francesco Compston, Massimo Filippi, Mark S Freedman, Kazuo Fujihara, Steven L Galetta, Hans Peter Hartung, Ludwig Kappos, Fred D Lublin, Ruth A Miller, Aaron E Miller, David H Miller, Xavier Montalban, Ellen M Mowry, Per Soelberg Sorensen, Mar Tintoré, Anthony L Traboulsee, Marco Uitdehaag, Sandra Vukusic, Emmanuelle Waubant, Brian G Weinshenker, Stephen C Reingold, Jeffrey A Cohen

- **Dissemination in space:** MRI ≥1 asymptomatic or symptomatic T2 lesion in at least 2 areas (periventricular, juxtacortical, infratentorial, spinal cord)
  
  => *Can include symptomatic lesion, but NOT the optic nerve*

  and

- **Dissemination in time:**
  - **MRI Dissemination in time:** simultaneous presence of asymptomatic or symptomatic enhancing and nonenhancing lesions (*Does NOT include optic nerve*)
  - OR oligoclonal bands in CSF
Optic neuritis
treatment and natural history

• ONTT. Oral vs IV steroids
• 90% of people with optic neuritis will recover most of their vision within six months of onset.
• 14% will have a recurrence of optic neuritis in the affected eye
• 12% will develop optic neuritis in the other eye within 10 years.
• One or more abnormal lesions on the MRI, the risk of MS within 15 years is 72%.
Inflammatory Optic Neuritis

NMO Antibodies (NMOSD)

- Optic neuritis:
  - Bilateral
  - Severe
  - No recovery
  - Recurrent

- Important: changes management
- Obtain NMO antibodies in all optic neuritis!

*Neurology* 2009; 73:302
*JNO* 2012; 32:154
Inflammatory Optic Neuritis
MOG Antibodies

- Optic neuritis:
  - Bilateral
  - Recurrent
  - More often disc edema
  - More often cells in CSF
  - In patients who have negative NMO antibodies

- Important: changes management
- Obtain MOG antibodies for all optic neuritis?
Case 4
Case 4

- A 53 year old man presents with acute diplopia.
- Previous episodes few years ago, which lasted two months and recovered.
- Diabetes, and hyperlipidemia.
- Visual acuity: 20/20 OU.
- Pupils: Equally reactive, pupils equal in size.
Pupil-Sparing Third Nerve Palsy

• Diabetes, hypertension, hyperlipedemia, smoking, high hematocrit.
• Pupil is spared.
• Pupil involvement reported only in 14%-32% but anisocoria (difference in pupil size) is less than 1 mm (relative-sparing).
• Improve within 4-12 weeks (defer neuro-imaging).
Case 5
Case 5

- 78 year old man with acute diplopia, and headache.
- Diabetes, hypertension, atrial tachycardia.
- Prior history of tight feeling around the eye with 20 seconds of diplopia.
- No history of jaw claudication or transient visual loss.
Pupil-involving Third Nerve Palsy

Urgent MRI/MRA or MRI/CTA
Pupil-involving 3rd Nerve Palsy

- Pupil involvement indicates compression of the pupillary fibers.
- **Posterior communicating artery aneurysm**, or mass.
- Neuro-imaging (MRI/MRA, MRI/CTA, Angiogram is the gold standard for aneurysm detection).
## Risk of Aneurysm and “Rule of Pupil”

<table>
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<tr>
<th>Ophthalmoplegia</th>
<th>Pupil</th>
<th>Aneurysm Risk</th>
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<tbody>
<tr>
<td>Complete/Partial</td>
<td>Complete</td>
<td>86%-100%</td>
</tr>
<tr>
<td>Partial</td>
<td>Spared</td>
<td>30%</td>
</tr>
<tr>
<td>Complete</td>
<td>Spared</td>
<td>very low</td>
</tr>
</tbody>
</table>

If signs of sub-arachnoid hemorrhage present (headache, photophobia, nausea) “rule of pupil” **does not** apply.
III nerve palsy evaluation

- **Pupil-involved III nerve palsy or progressive III nerve palsy**
  - requires immediate attention.
  - MRI + gad and MRA brain or CT angiogram (CTA).
  - Cerebral arteriogram

- **Acute partial III nerve palsy without headache**
  - MRI and MRA.
  - If pupil spared, follow
  - pupil dilates, proceed with CTA or arteriogram

- **Pupil-sparing complete III nerve palsy**
  - >40-year-old check for diabetes and HTN.
    - Do not need to proceed with emergency imaging.
    - Not improved by 2 months, proceed with MRI and MRA.
  - >60, especially with new onset headache
    - check ESR and CRP for giant cell arteritis

- **Aberrant regeneration of III nerve**
  - Eyelid retraction in adduction and/or infraduction, miosis in adduction.
  - Only caused by compression (aneurysm, tumor, prior trauma) and requires imaging study if no trauma history
Case 6

Diagnosis?
Evaluation of Horner’s

- Miosis, and partial or mild ptosis (upper and lower lid).
- Dilatation lag, **anisocoria worse in dark.**
- Cocaine test
- Hydroxyamphetamine (not used much).
- MRI/MRA of the head/neck/upper chest CT.
Oculo-sympathetic Pathway
Acute Horner’s Syndrome

- Painful Horner’s syndrome is a neurologic emergency.
- Although can be seen in many types of headaches (Cluster, Migraine etc).
- Rule out **ICA dissection**.
- MRI/MRA of the head/neck/upper mediastinum is indicated.
Horner’s Syndrome (MRI)
Carotid Dissection

A Lateral View at Base of Skull
- Compression of Cranial Nerves
- Jugular Foramen
- MASTOID AIR CELLS
- Cervical Sympathetic Chain
- Carotid Canal
- Sympathetic Nerve Plexus
- Pseudoaneurysmal Dilatation

B Cross Section
- CN IX
- Hematoma
- CN XI, XII, X
- Lumen

C T1-Weighted Axial MRI
- Hematoma
- Lumen of ICA
- Oral Cavity
- Spinal Cord
Carotid Dissection
Carotid Dissection
ICA dissection

• Prevent stroke
• Antithrombotic therapy vs stenting.
• Referral for a neurovascular specialist.
Case 7
Case 7

17 y/o young woman 2 weeks headache and blurry vision
Optic Neuropathy

Papilledema

- Disc swelling from ↑ intracranial pressure
- Any age
- Painless
- Bilateral
- Spares visual acuity
- Constriction of visual field
Papilledema

Causes

- Intracranial mass lesions
- Hydrocephalus
- Meningeal processes
- Cerebral venous thrombosis
- Idiopathic intracranial hypertension (IIH)
IIH: Diagnosis in 2018

- Not just a diagnosis of exclusion
- New diagnostic criteria
  - Isolated increased ICP (headaches, diplopia)
  - Papilledema
  - MRI/MRV: rule-out intracranial disease and venous sinus thrombosis
  - CSF: normal
  - CSF-OP: $\geq 25$ cm H$_2$O (28 cm in kids)
IIH in 2018

- IIH is everywhere there are obese people

Top 10 Most Obese Countries

1. United States of America – 109,342,839
2. China – 97,236,700
3. India – 65,619,826
4. Brazil – 41,857,656
5. Mexico – 36,294,881
6. Russia – 34,701,531
7. Egypt – 28,192,861
8. Turkey – 23,819,781
9. Iran – 21,183,488

(July 1st, 2017)
IIH: Poor Visual Prognosis

- Patient characteristics
  - Black race. *Neurology* 2008; 70: 861-7
  - Severe obesity. *J Neuroophthalmol* 2013; 33: 4-8
  - Anemia / sleep apnea syndrome / HTN
IIH in 2018

- IIH is more than just “headaches and papilledema”
  - Chronic disease
  - Depression
  - Reduced quality of life
  - Disability

IIH is expensive
Idiopathic Intracranial Hypertension (IIH)
Treatment

- Diagnostic lumbar puncture
- Acetazolamide (1-4g/day)/ topiramate
- Weight loss
- Treatment of “risk factors”
- Treatment of headaches (chronic >50%)

**Predict the prognosis**

=>Follow visual fields and fundus
=>LP/Surgery (ONSF, CSF shunting/ Stent/ Obesity)
Idiopathic Intracranial Hypertension (IIH)
Treatment: Weight loss is essential

- 6-10% of body weight reduces ICP
  - Improves headaches and papilledema
- Weight gain triggers IIH recurrence

Obesity and Weight Loss in Idiopathic Intracranial Hypertension: A Narrative Review

Suresh Subramaniam, MD, MSc, FRCPC, William A. Fletcher, MD, FRCPC

Bariatric Surgery or Non-surgical Weight Loss for Idiopathic Intracranial Hypertension? A Systematic Review and Comparison of Meta-analyses

James H. Manfield¹, Kenny K-H. Yu¹, Evangelos Efthimiou², Ara Darzi³, Thanos Athanasiou¹, Hutan Ashrafian²,³

increasing BMI. Weight loss is an effective treatment for IIH. Long-term maintenance of initial weight loss is helped modestly by lifestyle modification programs and possibly by selected commercial weight loss programs. New anti-obesity drugs may provide further options for IIH therapy in the future.

doi: 10.1097/WNO.0000000000000448
Take home

1. The eye is a window to the nervous system
2. Common eye signs include:
   • Blindness
   • Papilledema
   • Ptosis
   • Double vision (binocular)
   • Anisocoria
3. Understanding their meaning will help you expedite care