Neuro-ophthalmic Grand Rounds

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Financial Disclosures

• With respect to this lecture, I have no relevant financial relationships to declare.

Course Goal

• To provide useful clinical information in the diagnosis and treatment of neuro-ophthalmic disorders.
  ▪ Functional anatomy
  ▪ Case examples
  ▪ Common conditions
  ▪ Interactive

Cranial N. Testing

12 Cranial Nerves:
  - CN 1 – Frontal lobe
  - CN 2 – Thalamus
  - CN 3-4 Midbrain
  - CN 5-7 Pons
  - CN 8-12 Medulla

Bob Marley get up, stand up
The Visual Pathway

- Retina has 10 layers

- Optic Nerve Head
  - Optic Nerve - Intracocular, Intraorbital, Intracanalicular, Intracranial
  - Optic Chiasm - Nasal fibers cross, Temporal fibers do not
  - Optic Tract - Contains retinal fibers from both eyes
  - Optic Radiations - Travel to Temporal, Parietal and Occipital lobes

- Visual Cortex - Termination of all nerve fibers in Occipital Lobe

* Visual field loss secondary to retina and optic nerve disease usually occurs monocularly.*
  - Examples: ARMD, Glaucoma, Optic Neuritis, Intraocular/orbital Tumors

Visual Fields

- Visual Field defects obey anatomy

Pre-chiasm
Chiasm
Post-chiasm

LGN of Thalamus

Pre-chiasm
Chiasm
Post-chiasm

Humphrey Visual Fields – Bitemporal VF defect

Interpretation of Visual Field Defects

Field loss secondary to optic chiasm lesion = bitemporal defect

- Pituitary adenoma
- Craniopharyngioma
- Glioma
- Meningioma

VF loss secondary to optic tract or radiation disease will occur as a homonymous hemianopic defect.

Examples: Brain tumor, Stroke, Anuerysm
Anisocoria

- Is the abnormal pupil the larger or smaller one?
  - Pupil Aniso = in bright and dark illumination → physiologic
  - Pupil Aniso > in bright illumination → parasympathetic problem
  - Pupil Aniso > in dark illumination → sympathetic problem

- What is the position of the lids?
  - Always check eyelid position (ptosis, retraction)
  - Always check the direct, consensual and near responses (LND)

Pupillary Control: Basics

- The physiology behind “normal” pupillary activity is a balance between the sympathetic and parasympathetic nervous systems.
- Parasympathetic innervation leads to pupillary constriction.
- The pathway of pupillary constriction begins at the Edinger-Westphal nucleus near the Oculomotor N nucleus.
- The fibers enter the orbit with CNIII fibers and ultimately synapse at the ciliary ganglion.

Parasympathetic Pathway: Constriction
**Pupil Basics: Dilation**

- Sympathetic innervation leads to pupillary dilation and lid elevation.
- Sympathetic innervation begins at the cortex with the first synapse at the Cilio-spinal Center of Budge.
- Post synaptic neurons travel all the way through the brain stem and finally exit through the cervical sympathetic chain and the superior cervical ganglion (SCG).
- They synapse at the SCG where third-order neurons travel through the carotid plexus and enter the orbit through the first division of the trigeminal N.

**Sympathetic Pathway:**

- Dilation, Lid elevation

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**Pupils**

**Cranial Nerve 3 Palsy**

- May present as pupil involved/spared ophthalmoplegia

Ophthalmoplegia caused by:

- Microvascular disease (infarction)
- Aneurysm
- Tumor
- Trauma
- Infection (syphilis)
- Idiopathic

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**Cranial Nerve 3 Palsy – Pupil involved ophthalmoplegia**

**Medical emergency if pupil is dilated !!!**

- Complete pupil involvement – Send to ER ... 20% die within 48 hrs
- Relative pupil involvement (poor light reflex, slightly larger size)
- Pupil spared

**Presentation**

- Posis – Levator muscle is affected
- “Down and Out”
- Limited ocular motility
- Complete or relative sparing of the pupil—in general a good sign
- May be painful
Cranial Nerve 3 palsy – Pupil involved ophthalmoplegia

All 3rd nerve palsies with a blown pupil are an aneurysm until proven otherwise !!!!

Levator

Superior
Division

Superior Rectus

Medial Rectus

Inferior Rectus

Inferior Oblique

CN 3

Cranial Nerve 3 palsy

– Pupil involved ophthalmoplegia

Terson’s Syndrome

Symptoms:

• Vertical and horizontal diplopia
• Ptosis
• Pain may be severe (aneurysm) ....variable with diabetes
• Acute = aneurysm or ischemic vascular cause
• Progressive = infiltrative or compressive cause

Management:

• Referral to Neurologist/Neuro-Oph immediately
• MRI / MRA / CT
• Catheter Cerebral Angiography – if aneurysm suspected ****
• ESR, CRP if Giant Cell Arteritis is suspected

• 90% of aneurysmal third-nerve palsies have pupil involvement.
• Half of patients diagnosed with aneurysmal third-nerve palsies have a subarachnoid hemorrhage within 2 weeks.
• Half of those patients who hemorrhage will die soon after.
• Catheter Cerebral Angiography is the best imaging tool, however, it may cause stroke or myocardial infarction in 1% - 2% of patients.
• A lack of anisocoria in an isolated third-nerve palsy does not rule out aneurysm or a compressive lesion. **
Horner Syndrome:

- Miotic pupil, ptosis, anhydrosis
- Anisocoria will be greater in dim illumination
- Therefore, a sympathetic problem

Sympathetic Pathway:

- Dilation, Lid elevation

Pupils

- 10% cocaine test - indirect acting sympathomimetic
- Blocks the reuptake of norepinephrine
- No pupil dilation with cocaine = Horner
- Hydroxyamphetamine 1% (Paredrine) -> Location

Paredrine 1% --> pupil doesn’t dilate = post-ganglionic lesion
Paradrine 1% --> pupil does dilate = pre-ganglionic

* Must wait 48 hours after Cocaine testing to instill Paredrine

Pupils

- Newer pham diagnostic test
  - 0.5% or 1.0% Apraclonidine (Iopia
  - Alpha agonist (mainly alpha 2, some 1)
  - Works by denervation hypersensitivity of \( \alpha_1 \)-receptors in the pupil dilator muscle.
  - Dilates a Horner pupil (supersensitivity)
  - Paredrine still needed for localization

Questions?
Post-Apraclonidine

Digital infra-red photos under scotopic illumination. Note reversal of anisocoria after Apraclonidine, indicative of a Right Horner Syndrome.

Acknowledgement: Kelly Malloy, OD

Horner Syndrome

Causes:
- Idiopathic
- Tumor – Pancoast tumor
- Neuroblastoma – children
- Cluster headache – young men
- Trauma – carotid artery dissection
- Iatrogenic

Work-up:
- Look at old photographs “FAT Scan”
- Cocaine / Iopidine testing
- Neurological examination
- CT of the head and neck
- Child = rule out neuroblastoma

Congenital Horner Syndrome

- Heterochromia iridis
- Straighter hair
- Lower brachial plexus palsy
- Possible legal implications (birth and delivery injury)

Argyll-Robertson Pupil

- Resting Miosis (≤ 2.5 mm) in darkness
- No direct pupil response
- Brisk near response (LND)
- Preserved vision?
- Dilates poorly

Causes:
- Syphilis, Multiple Sclerosis, Lyme, Sarcoidosis
Resting Miosis

No light response, brisk near

Acknowledgement: Kelly Malloy, OD

Retinal findings in syphilis
Stages of Syphilis: Systemic
- Primary – Chancre
- Secondary – Sore throat, fever, skin rashes, mucous membranes affected, etc.
- Latent stage
- Tertiary – (benign and severe stages)
  - Cardiovascular and Central Nervous Systems

Stages: Ocular Syphilis
- Primary – Chancre on eyelid or conjunctiva
- Secondary – Uveitis, optic neuritis, retinitis, episcleritis, scleritis, conjunctivitis, dacryoadenitis, dacryocystitis
  - Ocular findings found in 10% with secondary syph
- Latent stage – may remain so for months or even a lifetime
- Tertiary – Interstitial keratitis, optic atrophy, Argyll Robertson

Syphilis Work-up and Management
- FTA-ABS, RPR
- Lyme titer
- Neuroimaging (r/o MS)
- Rule out Sarcoid: Chest X-ray, ACE, serum lysozyme
- Treatments
  - IV or IM Penicillin G
  - Oral Tetracycline/Doxycycline or Azithromycin

Tonic Pupil:
- Larger pupil – ciliary ganglion is damaged
- Light – near dissociated pupil
- Diminished corneal sensitivity – CN V
- Accommodation may be reduced

Slit Lamp Exam
- Sector paralysis
- Stromal spreading
- Stromal streaming
Causes of Tonic Pupil

Local:
- Varicella – chicken pox
- Ocular surgery (PRP)
- Ocular tumor
- Retrobulbar tumor

Neuropathic:
- Diabetes
- Sarcoidosis
- Syphilis
- Lyme

Tonic Pupil:
- Adie’s tonic pupil = idiopathic
- More prevalent in females (3:1 ratio)
- 90% are unilateral initially
- Fellow eye can become involved later

Tonic Pupil: Diagnosis and Management
- Pilocarpine (1/8 %) instilled into the affected eye = pupil will constrict
  - How to prepare: 7 gt sterile saline + 1 gt 1% Pilo
- Pilocarpine 2% with no reaction = pharmacologic dilation
- Find the underlying cause
- No treatment – leave it alone
- Colored contact lenses
- Near add - may need to be unequal

Tectal Pupils
- Dorsal Midbrain Syndrome
  - Vertical gaze disturbance
  - Convergence retraction nystagmus
  - Light near dissociation of the pupils
  - Lid retraction (Collier’s sign)

Pineal Tumor
### Dorsal Midbrain Syndrome: Causes

- Obstructive hydrocephalus
- Mesencephalic hemorrhage
- Multiple sclerosis
- A/V malformation
- Trauma
- Compression (pineal and other tumors)

### Questions?

### Types of Radiologic Examinations

- X-ray (Plain film)/Conventional Radiography
- Digital Radiography
- Fluoroscopy
- Mammography
- Computed Tomography (CT)
- Magnetic Resonance Imaging (MRI)
- Nuclear Medicine
- Ultrasonography/Echography

### Scanning the Body: Directional Planes

- Three directional planes exist in the brain:
  - medial/lateral = transverse (axial)
  - rostral/caudal = coronal
  - dorsal/ventral = sagittal
Right: Orbital CT shows floor fracture OS and blood in the left maxillary sinus. The medial wall of the left orbit is also fractured.

Left: “Tear drop” sign on plain film X-ray

Computed Tomography (CT) or CAT Scan (Computerized Axial Tomography)

- Images anatomical tissue from a cross-sectional plane of the body.
- A series of sequential “A-scans”
- Each image is generated by computer synthesis of x-ray transmission data obtained in many different directions within a given plane.

CT Scan

- Above, modern CT equipment.
- Below, normal CT of brain w/contrast.

ORBITAL CELLULITIS
**Case History**

- 63-year-old white female presented with recent onset of diplopia and an irritated, proptotic OS.
- PMHx: L Facial N. palsy X 30 years
- FMHx: (+) Breast Cancer (aunt), (+) Ovarian Cancer (sister)

**Ancillary Testing**

- **EOM:** UA of OS in most POG
- **Modified Forced Ductions**
  - OS: (+) resistance in all fields of gaze, retropulsion
- **CN VII**
  - Orbicularis weakness OS
- **Ice-pack Test** (r/o MG)
  - no change in ptosis, EOMs, diplopia
Right gaze
- Note underaction of OS
- No abduction nystagmus OD (no INO)

What is your diagnosis?
Etiology of diplopia?
Etiology of proptosis?

Differential Diagnosis
- Restrictive disease OS, ukn. etiology
  - Thyroid work-up
  - Orbital process
    - Orbital Inflammatory Pseudotumor
    - Mass
  - C_______ s_____ syndrome

What is your plan?
Systemic testing?
Consultation?
Neuroimaging?

Neuroimaging
- Contrast enhanced MRI of the orbit, brain, chiasm, and cavernous sinus
- Results:
  - Enhancing mass involving lacrimal region of the left orbit with enlargement of lateral rectus.
  - Possible involvement of the superior rectus and levator palpebrae superioris.
  - No evidence of cavernous sinus mass.
  - No optic nerve or chiasmal involvement.

Axial section through orbits (low mag)
- Note same area of thickened LLR/lacrimal gland
**MRI Axial section through orbits--T1**
- Note thickening in region of Left LR and lacrimal gland

**Contrast-enhanced axial view through orbits**
- Shows enhancement of soft tissue mass in region of Left lacrimal gland

**Coronal view through orbits**
- Shows thickening of left lacrimal gland region

**Para-sagittal view through Left orbit--T1**
- Shows soft tissue mass superior/anterior to globe

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**Orbital Biopsy Results**
- Malignant neoplasm c/w metastatic carcinoma from the breast with strong staining for the estrogen receptor.
- Diagnostic Mammogram
  - 1 cm spiculated lesion in the upper aspect right breast with associated pleomorphic calcifications
  - 1 cm lesion of upper aspect of the left breast, also suspicious for neoplasm
**Treatment**
- Systemic
  - Hormone therapy: Tamoxifen 10 mg BID
  - Goal is to shrink breast mass b/f surgery
    - After response to hormone therapy, bilateral mastectomy indicated
- Ocular
  - Partial tarsorraphy OS for exposure
  - Consider radiation therapy OS to improve symptoms

**Case Summary**
- Metastatic Disease
  - What to order:
    - MRI/CT scan
    - Mammography
    - Ultrasound

**Questions?**

*This patient was obviously in denial about her cancer.*

*How would you counsel her?*

**Bonus Neuro**

*What is papilledema?*
Pseudotumor Cerebri (PTC)

- PTC or idiopathic intracranial hypertension (IIH) is a disorder of unknown etiology.
- PTC affects predominantly obese women of childbearing age.
- The primary problem is chronically elevated intracranial pressure (ICP).
- Most important neurological manifestation of PTC is true papilledema, which may lead to progressive optic nerve atrophy.

Age at diagnosis of PTC
Peak during 4th decade

PTC: Symptoms

- headache (94%)
- transient visual obscurations or blurring (68%)
- "wooshing noise" in the ear (58%)
- pain behind the eye (44%)
- double vision (38%)
- visual loss (30%)
- pain with eye movement (22%)

The cerebrospinal fluid circulation.

- CSF is produced at a rate of 500 ml/day
- Brain can only contain 150 ml

Outward flow:
- Superior sagittal sinus
- Transverse sinus
- Sigmoid sinus
- Jugular vein
Lumbar Puncture

ICP is normally 0–10 mmH2O

PTC: Treatments

- Workup must include MRI, MRV and LP (spinal tap)
- Weight loss (10% body weight)- dietician/nutritionist
- Diamox (acetazolamide) 250mg bid-qid is the most commonly used diuretic medication.
- PO Prednisone? Topiramate?
- Surgical treatments:
  - Optic N Sheath Fenestration. This allows egress of CSF directly into the orbital fat, where it is absorbed into the venous circulation.
  - Lumboperitoneal Shunt

OPTIC NERVE SHEATH FENESTRATION

Causes of Disc Edema

- Pseudotumor cerebri and diabetic retinopathy

Venous Sinus Thrombosis

ONH Drusen
(Pseudo-papilledema)

ONH drusen B-scan of ONH drusen
Note lumpy/bumpy margin
Clinical Case

- 32 yo WF
- CC: loss of vision OS over 3 days
- Orbital pain w/eye movement OS
- Reduced color perception OS

Objective Findings

- BCVA 20/20 OD
  20/100 OS
- Full but painful (OS) extraocular movements
- +RAPD OS
- Dyschromatopsia OS
- Decreased contrast sensitivity OS
- VF deficits OS
- BP 130/78 mmHg

Objective Findings

- Left ON: no disc edema

Additional Testing

- The most appropriate course of action is:
  a. No further testing. Follow up in 3 mon
  b. Order MRI of brain and orbits with contrast and fat suppression, f/u 1 wk.
  c. General ophthalmology consult.
  d. Order RPR, FTA-ABS, f/u 1 wk.

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  a. No further testing. Follow up in 3 mon
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  c. General ophthalmology consult.
  d. Order RPR, FTA-ABS, f/u 1 wk.

MRI Findings with MS

Bright signal lesions (seen best with T2 scan) representing areas of demyelination
**Optic Neuritis and MS**

- Clinical diagnosis of MS
  - 2 demyelinating attacks separated in time and space
  - Sequential optic neuritis in one eye then the other meets CDMS criteria
  - 2 discrete attacks in the same eye also meets the criteria
- Radiologic: Mac Donald Criteria

**The Optic Neuritis Treatment Trial (ONTT)**

- Goal: to evaluate the role of corticosteroids in the treatment of unilateral optic neuritis
- Inclusion criteria: unilateral optic neuritis

**The ONTT: Methods**

- Randomization to one of 3 groups
  1. IV + po steroids: 250 mg methylprednisolone qid x 3 days, oral prednisone (1 mg/kg) x 11 days
  2. Oral steroids alone: prednisone 1 mg/kg/day x 14 days
  3. Oral placebo alone: 14 days

**The ONTT**

- Steroids

**ONTT: Results**

- IV steroids
  - More rapid recovery but same endpoint
  - Protective v. placebo at 2 yrs, but not at 3 yrs
- Oral prednisone
  - Higher rate of new ON attacks at 1 year
  - Highest rate of relapse at 5 years

**Optic Neuritis**

- Retrobulbar ON trace temp pallor from prior optic neuritis
- Improving VF
Visual Sequelae

- Optic nerve head pallor will develop
- VF deficits may persist
- Uhtoff’s phenomenon
  - Reduced vision with increased body temp.
- Pulfrich phenomenon
  - Lateral motion perceived as elliptical

Managing Optic Neuritis and MS

- Positive MRI
  - Consider immunomodulatory therapy
  - ie. Interferon (Avonex) or glatiramer acetate (Copaxone)

- Patients w/MS should be seen by neurology

Demyelinating Optic Neuropathy

58 y/o WF w/MS

VA 20/25 OD/OS
APD -

OCT Ganglion Cell Analysis in MS

Questions and Comments?
CHAMPS Study

- Effect of Interferon B 1a treatment in patients with optic neuritis and MRI changes consistent with MS
  - Significantly less CDMS
  - Less progression of MRI lesions

January 23, 2010

- The Food and Drug Administration approved the drug fampridine-SR (referred to as AMPYRA), a selective neuronal potassium channel blocker for the treatment of MS.
- First med shown to enhance some neurological functions in people with the disease.

Optic Neuritis

- Patients with symptoms/signs c/w ON must be investigated for demyelination
- Remember the atypical optic neuritis
  - ON with disc edema (papillitis)

Questions?

Other Important Optic Neuropathies

Lupus Retinopathy and Optic Neuropathy
Key Points

- Understanding the functional anatomy of the nervous system is crucial in identifying causes of neuro-eye disease.
- A targeted history and thorough ophthalmic workup will usually reveal telltale signs.
- Both laboratory testing and neuroimaging are often necessary.
- Co-manage wisely.

Thank you!
Joe