Course Goal

• To provide useful clinical information in the diagnosis and treatment of optic nerve disorders.
  • Functional anatomy
  • Common conditions
  • Case examples
  • Interactive

Functional Anatomy

• The Optic N. links the eye with the Central Nervous System (CNS).
• Composed of retinal ganglion cell axons that synapse in the lateral geniculate nuclei (LGN).

Intraocular Optic Nerve

• AKA “Optic N Head”
  • Nerve Fiber Layer
    • Unmyelinated axons
      • allow max light transmission to photoreceptors
    • Coalesce into bundles as they enter ONH
  • Lamina Choroidalis
    • Glial cells with intertwining cell processes
    • Nerve fibers enter ONH and turn to exit the globe at level of choroid
**Optic Nerve Head**

- Lamina Cribosa
  - 6-10 perforated connective tissue plates
  - Allow passage of NFL bundles
  - Support for nerve fibers
  - Axons become myelinated at LC posterior border

**Intraocular Optic Nerve**

- Optic Disc
  - Visible tip of intraocular ON
  - Vertical ellipse
    - 1.5mm x 1.8mm
    - No photoreceptors

**Intraocular Optic Nerve**

- 90% of fibers arise from macula
- Therefore, early signs of ON Dx reflect macular function
  - Reduced acuity, contrast sensitivity
  - Impaired color vision
  - Central scotoma

**Nerve Fibres**

- Fiber in red circle
- Posterior ciliary vessels
- Nerve root fibers
- Photoreceptors (not shown)
- Outer plexiform layer
- Optic disc (not shown)
Intraorbital Optic Nerve

- 25 mm long
- Shaped like elongated S
- Allows limited motion
- Surrounded by fat, EOMs (and nerves)
- Also close proximity to Ophthalmic A., Ciliary Ganglion and nerves

Case

- 12 yo BF
- S/P fever 2 wks prior
- Patient has a cat
- Note disc edema and macular star

Objective Findings

- BCVA 20/20 OD
  20/80 OS
- Full extraocular movements
- +RAPD OS
- Dyschromatopsia OS
- Confrontation VF deficits OS
- BP 121/69 mmHg

Neuroretinitis

Note disc edema and macular star

Optic Nerve Quiz

- The most likely etiology is:
  a. Herpes simplex
  b. Streptococcus
  c. Diabetes
  d. Bartonella henselae

Outcome

- Visual prognosis for CSD NR is good.
- Most patients experience significant recovery, regardless of treatment.
- Some clinicians treat with ciprofloxacin, doxycycline, other AB.
Intraorbital Optic Nerve

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

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

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.

MRI Findings with MS

Left ON: no disc edema

Bright signal lesions (seen best with T2 scan) representing areas of demyelination
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 steroids: 250 mg methylprednisolone qid x 3 days, oral prednisone (1mg/kg) x 11 days
  2. Oral steroids: prednisone 1mg/kg/day x 14 days
  3. Oral placebo: 14 days

The ONTT

- Steroids

ONTT: Results

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

Prognosis

- Natural history: worsening over days to weeks followed by spontaneous recovery
  - 79% of patients begin to recover by 3/52
  - 93% of patients show improvement by 5/52
- Ongoing clinical improvement to 1 year
- VEP latency improves to 2 years

Optic Neuritis

- Retrobulbar ON trace temp pallor from prior optic neuritis
  - Improving VF
### Prognosis
- Severity of initial visual loss is related to final visual outcome
- Most recover well
  - 74% ≥ 20/20
  - 92% ≥ 20/40

### Visual Sequelae
- Optic nerve head pallor will develop
- VF deficits may persist
- Uhtoff’s phenomenon
- Pulfrich phenomenon

### Managing Optic Neuritis and MS
- Positive MRI
  - Consider immunomodulatory therapy ie. interferon or glatiramer acetate
- Patients should be seen by neurology

### Optic Neuritis and MS
- Clinical diagnosis
  - 2 demyelinating attacks separated in time and space
  - Sequential optic neuritis in one eye then the other meets criteria
  - Discrete attacks in the same eye meets the criteria
- Radiologic: Mac Donald Criteria

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

### Conclusions
- Patients must be investigated for demyelination
- Remember the atypical optic neuritis
Intracanalicular Optic N.

- 9 mm in length
- Travels optic canal
- Accompanied by Ophthalmic A.
- No motion permitted, as ON is tethered within canal
- Vulnerable to ischemia, swelling within fixed-area canal

Intracranial Optic Nerve

- 16 mm long
- Area between optic canal and chiasm
- Intracranial ON lies above Carotid A., roof of sphenoid sinus, sella contents.
- Both Ophthalmic A. and Sup Ophth V. course between SR and intracranial ON
Intracranial Optic Nerve

Topographic Organization

- Fibers in ON follow in an arrangement similar to retina.
  - Sup retinal fibers run sup in ON
  - Inf retinal fibres are below
  - Fibers from temporal/nasal retina run in corresponding parts of ON

Lateral Geniculate Nuclei

- Retinal nerve fibers classified into:
  - _____-cellular (or M-cells)
  - _____-cellular (or P-cells)

Ganglion Cell Projections in the LGN

- “Non-linear” M-cells are usually the first to die in glaucoma.

Blood Supply of Optic N.

- Intraocular Optic Nerve
- Intraorbital Optic Nerve
- Intracanalicular Optic Nerve
- Intracranial Optic Nerve
**Blood Supply**

- Distal ON (near globe) supplied by branches of Ophthalmic A.
- Near chiasm, supply is from thin BVs of Carotid and Anterior Cerebral A. systems
- Thin BVs from Ant Comm A. supply dorsal chiasm.
- Inf chiasm supplied by Carotid, Post Comm, Post Cerebral A.

**Axonal Physiology**

- ON axons must conduct action potentials, maintain their structure, protect retinal ganglion cells.
- “Axonal transport” enables ganglion cell bodies to stay informed about activity along axon, at synapse.
Clinical Testing
- History Taking
- Visual Activity
- Visual Field
- Color Vision
- Brightness Comparison
- Pupillary Testing
- Photostress Recovery Test

Visual Fields
- Visual Field defects obey anatomy

Visual Field Interpretation
Visual field loss secondary to optic chiasm = bitemporal defect
- Pituitary adenoma
- Craniopharyngioma
- Glioma
- Meningioma
VF loss secondary to optic tract or radiation disease will occur as a homonymous hemianopsia defect
Examples: Brain tumor, Stroke, Anuerysm

Clinical Testing
- Contrast Sensitivity
- Ophthalmoscopy
- Electrophysiology
  - VEP, ERG
- Imaging Studies
  - Optical Coherence Tomography
  - Neuroimaging
- Cranial N. Workup

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

Disc Edema
Meningitis
Meningitis

Will cause pleocytosis = increase in white blood cells in the CSF
Acute = Hours to days
Chronic = 4 weeks or more
Aseptic meningitis = No CSF bacteria found (example: enterovirus)

PREVIOUS TREATMENT

- 5 Visits to the emergency room
- Visit #4: 10/1/10
  - Tylenol 1000mg
  - Reglan 10 mg
  - Noncontrast CT: unremarkable, with frothy secretions in the sphenoid sinus
- Visit #5: 10/4/10
  - Warm compresses/hot baths/gentle stretching
  - Motrin 600mg q6-8 hrs
  - Flexeril 5mg q4-6 hrs
  - Follow up with PCP and orthopaedic

PHOTOS

Courtesy Dr. Kelly Malloy
**VISUAL FIELD**

**LYMPHOCYTIC CHORIOMENINGITIS**
- Rodent-born viral infectious disease
- Primary host is a common house mouse
- 5% of mice in the US carry LCMV
- Person to person transmission hasn’t been reported

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**Disc Edema**

**Viral Meningitis**
- Herpes Virus meningitis is diagnosed more frequently than before because of better techniques … PCR
- HSV meningitis is more common than HZV meningitis
- CSF work up through PCR (polymerase chain reaction)
- Treatment: IV Acyclovir Q 8 hrs x 14 days

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**Disc Edema**

**Bacterial Meningitis**
- ~ 30,000 new cases diagnosed each year in the United States
- Streptococcus pneumoniae (pneumococcus)=most frequent etiology
- Neisseria meningococcus
- Haemophilus influenzae
- Treatment: IV ampicillin, cephalosporin, chloramphenicol

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**Disc Edema**

**Other causes of Meningitis**
- Lyme
- Syphilis
- TB
- Listeria
- Amoeba (swimming)
- West Nile Virus

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**Questions and Comments?**
**Pseudotumor cerebri**

- 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), and the most important neurological manifestation is papilledema, which may lead to progressive optic nerve atrophy.

**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%)

**PTC**

- Endocrine risk factors confirmed in epidemiological studies
  - Female sex
  - Reproductive age group
  - Menstrual irregularity
  - Obesity
  - Recent weight gain

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![Age at diagnosis of PTC](image)

Peak during 4th decade

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![PTC Papilledema](image)

![Optic Atrophy](image)

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![PTC](image)

The cerebrospinal fluid circulation.
The superior sagittal sinus and the site of cerebrospinal fluid absorption, the cauliflower-like arachnoid granulations.

**Disc Edema**

Modified Dandy’s criteria - Pseudo Tumor Cerebri (PTC)

- The patient is awake and alert
- Patient has signs and symptoms of increased intracranial pressure (nausea, vomiting, headache and disc edema)
- Absence of neurological signs except for CN 6 palsy
- Normal neuro-imaging (MRI, MRA, CT must be normal and done before the LP)
- Cerebrospinal pressure must be greater than 200 mm H2O (average opening LP pressure in PTC patient is 300-400)
- CSF must be normal in composition

**Disc Edema**

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

**Lumbar Puncture**

ICP is normally 0–10 mm Hg

**PTC: Treatments**

- Workup must include MRI, MRV and LP (spinal tap)
- Weight loss (10% body weight)/dietician
- Diamox (acetazolamide) 250mg bid is the most commonly used diuretic medication.
- PO Prednisone?
- Surgical treatments currently used are optic nerve sheath fenestration. This allows egress of CSF directly into the orbital fat, where it is absorbed into the venous circulation.
- Lumboperitoneal shunt Sx.

**OPTIC NERVE SHEATH FENESTRATION**
Pseudotumor cerebri and diabetic retinopathy

Disc Edema

Questions and Comments?

Developmental Disorders

- Anomalous Elevation of the Optic Nerve
  - I.e. “Crowded disc”
- Buried Drusen
- Optic N. Hypoplasia
- Superior Segmental Optic N. Hypoplasia
- Hemioptic Hypoplasia
- Tilted Disc
- Morning-Glory Syndrome
- Astrocytic Hamartoma
- Melanocytoma
- Coloboma
- Optic Pit

ONH Drusen

ONH drusen  B-scan of ONH drusen

Note lumpy/humpy margin

Hereditary Optic Neuropathy

- Dominant Optic Atrophy
- Recessive Optic Atrophy
- Leber’s Hereditary Optic Neuropathy
- Neurologic Syndromes
- Metabolic Disease
**Misc. Optic Neuropathies**

- Radiation Optic Neuropathy
- Neuroretinitis
- Carcinomatous Optic Neuropathy
- Diabetic Papillopathy
- Papillophlebitis
- Optic Perineuritis
- Autoimmune-Related Retinopathy and Optic Neuropathy Syndrome (AARON)
- Non-glaucomatous Optic Disc Cupping

**Key Points**

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

**Conclusion**

- Optic N. disease can:
  - Result in significant vision loss
  - Signal the presence of life-threatening disease
  - The primary eye care provider plays a crucial role in the diagnosis and treatment of optic nerve disease.

**Thank you!**

Carlo and Joe