Don’t Let Swollen Optic Nerves Make You Nervous

Brad Sutton, OD, FAAO
Clinical Professor
IU School of Optometry
brsutton@indiana.edu

Financial disclosures

- No financial disclosures

Examination Techniques

- Stereoscopic viewing essential
- VA and VF: SVP
- Pupil testing and color vision
- Brightness comparison and red cap test

Papilledema

- Bilateral* optic nerve head swelling secondary to increased ICP
- Swollen, blurred margins with splinter hemorrhages and exudates as well as nerve fiber layer edema. Patton’s folds may be seen

Papilledema

- May be asymmetric or very rarely unilateral (sequential swelling)
- VA varies but typically mild reduction only or no loss at all
- May get diplopia secondary to abducens nerve compression
- With increased ICP, can get choroidal folds only (before papilledema) at lower pressure levels

Papilledema

- VF usually shows enlarged blind spot
- No pupillary defect. Normal color vision
- SVP absent with obliterated cup
Papilledema (IIH)

Papilledema IIH age 15

OCT

Papilledema (HTN)

Papilledema (tumor)

Subtle papilledema (IIH)
Patton's folds: RNFL thickness 231 in OD, 295 in OS

Patton's folds: now you see them......

Back then in 2007 you did not...

Patton's folds
Longstanding papilledema with optic atrophy (IIH)

Papilledema OCT NFL

NFL edema

Papilledema OCT

Papilledema OCT
**Increased ICP**

- Variations are due to anatomical considerations
- If the channels connecting the central cavity and optic nerve sheath allow equal flow on both sides and in both directions, papilledema will occur and will improve with decreased ICP

**Increased ICP**

- If there is a difference in the communications then the edema will be asymmetric. Usually the result of a smaller bony canal opening on one side limiting the swelling.
- If the valves are one-way then the swelling will not improve rapidly with Tx

**Increased ICP**

- An acute rise in ICP that resolves rapidly is not typically associated with papilledema. Elevation must be chronic
- Increased pressure is transmitted from the sub-arachnoid space to the optic nerve head via the nerve sheath. Venous pressure in CRV increases
- Disruption in axoplasmic flow at lamina cribosa leads to swelling

**Increased ICP**

- Studies show that ONH swelling as measured by OCT can decrease (but not instantly resolve) immediately after lumbar puncture
- Measured in lateral decubitus position with OCT sideways!
- Shows that reduction of ONH compression is very rapid
- Shows that pressure in spinal column is associated with pressure at ONH

**Etiologies of Increased ICP**

- Space occupying lesion; must always be ruled out!
- Infection or anatomical abnormality
- Malignant hypertension
- IIH
- Certain medications
- ? Sleep apnea (obesity): ICP may be elevated only at night! Men especially
- Must order MRI in all cases

**Idiopathic Intracranial Hypertension (IIH)**

- Older term is "pseudotumor cerebri"
- Young overweight females (F 8X M)
- 1/100,000 in population as a whole; 20/100,000 in 20-44 year old women 10% over ideal weight
- May be related to medications including TGN, HRT, lithium, high dose Vitamin A supplementation, steroid withdrawal
- Sleep apnea link
IIH

- Symptoms of transient blur, diplopia, tinnitus (intracranial noises, not just ringing), headaches, etc.
- ICP usually severely elevated; normal is 50 – 200 mmH20. Over 25 cm (250 mm) considered definitively abnormal. Single measurement can be misleading: levels can vary over 24 hours.
- Very rare variant of normal pressure IIH. S/S, but repeatedly normal ICP.

ICP: diagnosis requires normal MRI / MRV and CSF studies with elevated ICP.
- Watch for spinal chord tumors.
- Differential: Cerebral Venous Sinus Thrombosis.
- MRV.

CVST

- Mostly young women.
- Often not overweight.
- Can be life-threatening.
- Treat with blood thinners, Diamox.

Can be seen with MRI, but potentially missed if MRV not performed.

IIH Management

- Refer to a neurologist.
- Medical management includes Diamox, Lasix.
- Weight loss.

If progressive changes in visual acuity or visual field occur, consider an optic nerve sheath decompression.
- Several small fenestrations in the optic nerve sheath are created to allow room for expansion.
- Performed by a neuro-ophthalmologist. Often do worse eye only because 50% get improvement in the fellow eye.

IIH Management

- If recalcitrant….
- Repeated lumbar taps (ugh!).
- Lumbo-peritoneal shunt.
- Ventricular shunt.
Foster Kennedy Syndrome

- Swollen optic nerve on one side, advanced optic atrophy on the other
- Advanced optic atrophy prevents swelling making a bilateral problem appear to be unilateral
- Often seen in chiasmal tumors

Compressive Optic Neuropathy

- Compression leads to axoplasmic stasis and retrograde death of nerve fibers
- Pale, choked, swollen nerve
- Rarely see hemes; + APD

Compressive Optic Neuropathy

- Optic atrophy and severe vision loss with time
- MRI with and without contrast: neurosurgery referral
- Possibly endoscopic optic nerve decompression?

Pituitary tumor post surgery

Sphenoid wing meningioma
Nonarteritic ION

- Swollen, hyperemic nerve with splinter hemes and exudates
- Often sectoral
- Ischemic / hyoperfusion event caused by interruption of micro-vascular circulation, often at night.
- Highly associated with sleep apnea (75-90% in several studies)
- NAION has 5x risk of sleep apnea, 8x risk in women

NAION

- No systemic symptoms; normal ESR / CRP
- Most common cause of ONH swelling over the age of 55 (2-10 cases per 100,000 per year)
- 45-60 year olds (any age possible) with no sex predilection; C > AA

Nonarteritic Etiologies

1) Sleep apnea! Up to 90%
2) Hypertension (med related?)
3) Idiopathic
4) Diabetes
5) Atherosclerosis
6) Migraine
7) Increased Homocysteine / Decreased vitamin B6
8) HIV infection

Nonarteritic ION

- Idiopathic cases (and others) are more common in disc at risk patients.
- Approximately 15% of cases will involve the fellow eye in 5 years (more common with VA < 20/200 in first eye, diabetes, and platelet polymorphisms). Repeat attacks in same eye < 5%

NAION

- VA varies widely from normal to severe loss; 45% 20/40 or better but 33% 20/200 or worse
- VA loss progresses over 2-4 weeks
- VA improves by up to three lines at six months in 40%
- In patients under 50 years of age, there is a higher rate of bilateral involvement and more visual recovery
Nonarteritic ION

- Often APD, color vision usually normal
- Most frequent visual field defect is inferior nasal / partial altitudinal but may get essentially any type. FDT may be more sensitive and often shows spillover of loss in to "non-affected" hemifield
- After swelling resolves the nerve is pale but often not cupped-cupping may occur, however
- Why does area of swelling not always match VF defect?

NAION 2 weeks after onset of symptoms

Nonarteritic ION Treatment

- No treatment other than managing the underlying cause has proven to be consistently effective
- Blood thinners may debatably protect the fellow eye but will not alter the course of recovery.
- Order CBC, ESR and CRP, lipid profile, hemoglobin A1c. Check BP
- Check for sleep apnea!

Steroids?:

- SS Hayreh: 2008 study utilizing oral steroids...
- If VA 20/70 or worse, oral prednisone resulted in VA improvement (3 or more lines) in 70% of treated patients, only 40% of untreated
- Beginning dose of 80mg for 2 weeks with slow taper.
- Small study with IVK was positive
- Small study with IV Rho-Kinase inhibitor (Fasudil) was positive

Clinical trial now recruiting

- Quark pharmaceuticals QPI-1007
- NORDIC
- Sites worldwide
- Intravitreal injection of the drug, sham, or both. (66% chance of treatment)

- QPI-107 is a small interfering ribonucleic acid
- It blocks the production of the protein caspase 2, which is believed to contribute to cell death when there is decreased oxygen
Clinical trial
- NCT02341560 on clinicaltrials.gov
- Must be within 14 days of symptom onset
- No prior attack in same eye, no GCA features
- 50-80 years old
- No attempt at treatment
- No drugs with toxic ON / retinal effects

Incipient ION
- We see it coming, but can we do anything about it?
- Will it always end badly?

NAION

NAION

NAION

NAION
NAION secondary to OSA

NAION OD secondary to HIV

Old NAION OD

Bilateral NAION secondary to OSA (40% blood oxygen level)

Accompanying VF

NAION OD and fellow eye
NAION OD: The Beginning

Optic atrophy / incipient ION

NAION OS

Optic atrophy OU

ION OS with matching VF / NFL loss

Arteritic ION

- Pale disc swelling with splinter hemorrhages
- Over 60 years old, F>M, Caucasians
- Increased ESR and C-Reactive protein
- ESR normal in about 25%
- VA 20/200 or worse in 60% of cases
Arteritic ION
- Sudden, painless loss of vision with APD
- Altitudinal VF loss most common, others possible
- Symptoms of GCA but about 1/3 are symptom free
- Very high five year mortality rate

Giant Cell Arteritis
- GCA is a disease of unknown etiology (emerging evidence that zoster may be involved?) affecting the large and medium arteries including the temporal, ophthalmic, and posterior ciliary arteries
- Symptoms include HA, scalp tenderness, jaw claudication, malaise, fever, and fatigue

GCA
- May also see CWS, CRAO, and amaurosis fugax
- 20% of cases with ocular involvement are CRAO, 80% ION
- Obtain stat Westergren ESR, CRP, CBC (anemia-false ESR)

Giant Cell Testing
- Normal ESR is age/2 for men and age +10/2 for women
- C-Reactive protein testing is not specific for GCA but it is nearly 100% sensitive so very useful test
- Temporal artery biopsy when indicated

Giant Cell Arteritis
- 25% of untreated patients develop AION
- 2/3 will develop in the second eye within weeks if not treated
- Rheumatology referral

Giant Cell Treatment
- IV hydrocortisone followed by long term oral prednisone.
  Maintenance dose of 10mg daily for years. Follow ESR, other markers
Temporal (Giant Cell) Arteritis

- Newly FDA approved treatment
- Subcutaneous Tocilizumab (Actemra)
- Used with steroids (not in place of): makes steroid dose much lower
- Immunosuppressant
- Risk of infections, no live vaccines
- Delivered IV
- Also used with RA and other forms of arthritis

Amiodarone induced optic neuropathy

- Mimics NAION in nerve appearance but bilateral instead of unilateral
- Afflicts 2% of patients taking it
- Slow, insidious onset of visual loss
- Slow, complete recovery over many months after medication is discontinued (very long half-life)

Viagra / Cialis / Levitra and NAION

- 553 cases officially reported to the FDA by the end of 2014, 443 were Viagra
- ? Under reported
- These medications also occasionally used for pulmonary HTN
- Visual loss most often noted upon awakening the morning after use
- Is the association real or coincidence?
- Likely the "straw that broke the camel's back" in those with risk factors. But.................

ED drugs and NAION

- Very interestingly, has been reported in a 7 month-old infant, 28 year old, and 33 year old, presumably all taking them for pulmonary HTN
- At those young ages, not as likely to have other NAION risk factors
- Also, 2 reported cases of PION with Sildenafil, one in a 39 YO female with pulmonary HTN

Viagra / Cialis

- What is the proposed mechanism? Nitrous oxide release actually dilates vessels.....but drops blood pressure.
- Do ION patients have faulty autoregulation?
- Ask all males with NAION about ED drug use. D/C if using to protect fellow eye.

Optic Neuritis

- Unilateral (usually) swollen nerve. Often retrobulbar (2/3) with no visible abnormality. Hemes uncommon
- Diffuse visual field loss or enlarged blind spot. Subtle defects often present in the fellow eye
- Centro-cecral defect with Goldmann perimetry
- About 5% in US bilateral, but 30% in Asia
Optic Neuritis

- Younger patients (20-40 peak), F > M: more common in Caucasians
- APD, wide range of VA loss, decreased color vision; pain on eye movement

Optic Neuritis

- Often associated with post viral syndromes or demyelinating diseases such as MS (initial symptom in 20% of cases-usually retrobulbar)
- VA recovers over weeks to months to near baseline level but often seems dim or washed out to the patient
- Get MRI in most cases
- May represent form fruste MS
- Several cases reported linked with use of TNF (tumor necrosis factor), Used for RA & JA: etanercept, infliximab, etc.

Optic neuritis and fellow eye

Optic neuritis with atrophy after six weeks

Optic neuritis associated with MS

Optic neuritis
Optic Neuritis Treatment Trial

- 457 patients in three treatment groups: 1) oral steroids (1mg/kg/day x 14 days), 2) IV steroids (250mg Q6h x 3 days) followed by orals (as above for 11 days), 3) placebo
- Hospitalized while on IV methylprednisone
- Traditional treatment of oral steroids proved to be the least effective of the three! Actually increased recurrence rate

ONTT

- IV followed by orals hastens VA recovery by about 2 weeks but does not improve end result
- Delays the onset of MS symptoms up to 2-3 years: no benefit at 5 years

ONTT 15-year F/U

- 294 patients seen 15 years out
- 15-year risk of developing MS was 50% (6% had known MS entering the trial)
- 72% if lesions on original MRI, 25% without
- VA 20/20 or better in 72%
- Factors indicating a lesser chance of developing MS include: 1) male gender, 2) optic disc swelling, 3) peripapillary hemorrhages and exudates, 4) no pain on eye movement, 5) NLP vision

Optic Nerve Head Drusen

- Increased prevalence in small nerves with small cups. Therefore, more common in whites than in AA. Higher incidence in patients with RP (10%)
- Compression of axons leads to stasis of axoplasmic flow and hyaline is excreted then calcifies over time, leading to the formation of drusen
- Nerve appears elevated but no splinter hemes or exudates and the margins are distinct
- Abnormal vessel branching

MS lesions

- Not always visible! Buried early in life but become visible with time. Creation of more drusen push some forward to the surface of the nerve
- Can cause decreased vision and variable visual field defects. More loss with visible drusen
- Common and under diagnosed
Optic Nerve Drusen

- SVP/EVP not affected: APD and color vision loss rare but possible
- Change with time
- Use B-scan or OCT to detect buried drusen
- Also seen with CAT scan, MRI, IVFA, and FAF
ONH drusen

ONH DRUSEN SD-OCT

ONH DRUSEN SD OCT

Color SD-OCT

FAF ONH Drusen

FAF ONH Drusen
Papillophlebitis (optic disc vasculitis)

- An inflammatory variant of CRVO striking otherwise healthy, young adults (f 2x m)
- Disc edema out of proportion with retinal hemorrhaging
- Usually mild VA reduction to around the 20/30 level but can be worse

Papillophlebitis

- Vague prodrome of scintillating, colored lights with visual disturbances
- Enlarged blind spot on the visual field
- Dilated and tortuous veins
- Condition is self-limiting over the course of several months and a complete recovery is the norm
- Separate entity? Systemic work-up? Are we looking for the wrong things? Antiphospholipid antibody syndrome (APA)
Papillophlebitis

Papillophlebitis
**Diabetic Papillitis**
- More common in young, type I diabetics but can also be seen in adults with type II
- Diffuse ONH edema that may be unilateral or bilateral
- Relatively mild vision loss
- No altitudinal defect on VF; various patterns of mild loss seen

**Diabetic Papillitis**
- Slow resolution of ONH edema but complete or nearly complete recovery of vision is the norm
- Like NAION, more prominent in nerves with small cups
- Is it real.............or just a variant of NAION?

**Grave’s disease**
- Remember No SPECS....
- Soft tissue edema
- Proptosis
- EOM involvement
- Corneal involvement from exposure
- Sight threatening complications
- Hyper (most common), hypo, or euthyroid

**Grave’s disease**
- The sight threatening complication is optic neuropathy from compression at the muscle cone
- Requires oral steroids and / or orbital decompression
- Type II Grave’s patients
- 75-80% of Grave’s patients are smokers!

**The end!**