Optic Neuritis

Neuroimaging to guide Diagnosis, Prognosis and Treatment

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Agenda

- Differential diagnosis for focal lesions of the optic nerve.
- Diagnosis: Imaging the intra-orbital optic nerve.
- Prognosis: Predicting outcome for optic neuritis patients.
- Therapy: Neuroimaging to guide Rx with immunomodulatory agents.
- Emerging modalities: DT-MRI and OCT.
Patient J.K.: 24 y.o. woman w/acute vision loss OS

- A 24 year old woman p/w acute vision loss and pain in her left eye.
- Vision “blurry” upon awakening the previous day; deteriorated since.
- No systemic symptoms. Denies accidental trauma to the eye.
- No past medical or surgical history. On no medications except OCPs.
- Ophthalmologic examination: visual acuity OD 20/20, OS 20/200. Fundus exam shows mild optic nerve head swelling OS. Ishahara color plate testing 10/10 OD, 0/10 OS. Left RAPD, and a central field defect on visual field testing.
- Further neurological and general physical exam is unremarkable.
Focal optic nerve lesions

- Tumor (meningioma, glioma, lymphoma, leukemia, mets)
- Trauma (foreign body, retinal detachment, traumatic hemorrhage)
- Infection (viral, Lyme, Toxoplasmosis, Bartonella, syphilis).
- Infarction/Vascular (GCA and NAION, CRAO/CRVO, aneurysms).
- Others: ***Inflammation/Idiopathic demyelinating optic neuritis; genetic: LHON; optic nerve head drusen, drug-induced.
Menu of tests: Imaging the optic nerve

- **CT** = 1° imaging modality if trauma history is unclear (e.g. kids).
  1. orbital fractures
  2. metallic foreign body
  3. intraocular air/blood/hemorrhage
  4. nerve sheath hematoma
  5. calcifications

CT head w/o Contrast

Courtesy of Dr. Jeffrey Velez
Menu of tests: Imaging the optic nerve

- **U/S** = useful if limited fundoscopic exam or if one cannot dilate the pupil. Can help clarify diagnosis of:

1. globe rupture
2. lens dislocation
3. retinal detachment
4. suprachoroidal hemorrhage
5. optic nerve head drusen
Menu of tests: Imaging the optic nerve

- **MRI** = best modality for evaluating orbital soft tissues.
  1. vascular injury
  2. aneurysms
  3. inflammatory lesions
  4. demyelinating lesions
  5. tumors

  *NB:* Contrast (Gd)-enhancement especially helpful in the acute phase of inflammation or demyelination, when the BBB is compromised.

Challenges:

1. Orbit: small area, packed with intraconal fat – must ↓ fat signal!
2. Optic nerve surrounded by CSF within dural sheath – must ↓ CSF signal!
3. Motion artifact common.
4. Anatomic variation in optic nerve length, diameter and tortuosity.
Advantages of different MRI modalities

**T1** – great for imaging orbital anatomy:

- **STIR (Short Tau Inversion Recovery)**
  - Allows better characterization of fat-filled structures.

**T2** – images inflammation and demyelination better:

- **FLAIR (Fluid Attenuated Inversion Recovery)**
  - Edema and gliosis are hyperintense.
  - Heavily T2 weighted, CSF signal is nulled by sampling the MR image at an appropriate time after magnetization inversion, when longitudinal magnetization of CSF is zero.
  - Similar to STIR, except used for CSF instead of fat.
Companion Patient #1: Optic nerve tumors (Axial T2WI FSE)

optic nerve glioma axial T2WI FSE

normal optic nerve anatomy axial T2WI FSE

Courtesy of Dr. Andrew Hines-Peralta and Dr. Moritz Kircher
Companion Patient #1 (cont.)
Optic nerve glioma: Sagittal T2WI

Courtesy of Dr. Andrew Hines-Peralta and Dr. Moritz Kircher
Companion Patient #1 (cont.)
Optic nerve glioma: Coronal T2WI FLAIR
Companion Patients 2 and 3: More Compressive optic nerve lesions

**Rhabdomyosarcoma**
in upper retrobulbar muscle space abutting the optic nerve

**Aneurysmal Bone Cyst**
a well-circumscribed, L-sided multi-cystic orbital lesion. Cavities are filled with hyper-intense hemorrhagic fluid (methemoglobin).

Companion Patient #4: Optic Nerve Meningioma (Coronal T1WI)

Meningioma: selectively enhances the CN II nerve sheath (T1WI post-Gd FS)
Companion Patient #5: Infiltrative process (Coronal STIR)

Orbital lymphoma infiltrating the optic nerve and the surrounding muscles (superior and medial rectus involvement observed)
Back to our Patient: Axial T1WI findings

Axial T1WI: enhancement of L. optic nerve, post-Gd views necessary to confirm finding.
Three sequential coronal STIR images show L optic nerve sheath enhancement.

These findings, in conjunction with the typical clinical presentation and the absence of other symptoms, lead to the diagnosis of acute optic neuritis.
Optic neuritis: recap of J.K.’s presentation

- Typical presentation: optic neuritis (ON) usually affects young patients: ages 20-40, but can also present in infancy and later adulthood.

- Diagnostic triad: 1. monocular **vision loss** (hours to days)

  2. **dyschromatopsia**

  3. **pain** with eye movement

*Drawings by a British artist diagnosed with optic neuritis, who attempted to portray his visual deficits.*
Optic neuritis: primer continued…

- Visual prognosis: deficits remit spontaneously over weeks ↔ months.

- Variants: insidious (typical onset is sudden!), chronically progressive, irreversible vision loss (typically resolves!), or unaccompanied by pain (typically painful with eye movements!)

- Bilateral attacks: rare in adults, more frequent in children.

- Recurrences in the affected eye or the fellow eye: 10-34%

- Largest trial is the ONTT, the Optic Neuritis Treatment Trial – available 10 year follow-up data on 455 patients, completed in 2004.
Imaging to inform Prognosis

1. **Visual Prognosis**
   - Visual acuity or extent of CN II lesion on MRI not predictive of speed or extent of recovery.
   - Prognosis excellent: >93% of patients improve by 5 weeks.

2. **Neurologic prognosis: ON as “harbinger of MS”**
   - Baseline brain MRI is a strong predictor of risk of CDMS in patients with monosymptomatic optic neuritis.
   - Do not want to commit our patient to a lifetime on immunomodulatory therapy unless @ high risk.
   - However, these drugs have been shown to reduce risk of disability in MS patients so want to start early if risk is high.

Relationship to MS

- MRI = used to stratify risk of developing MS
  - Baseline brain MRI: estimate # of white matter lesions during first ON attack.
  - Number of white matter lesions correlate with risk of further demyelination.
  - 2 randomized, placebo-controlled studies have found that patients w/clinically isolated demyelinating syndromes, such as optic neuritis, at high risk for MS may benefit from the early institution of disease modifying agents. (Chen L et al. Ocular Manifestations of Multiple Sclerosis. Contemporary Ophthalmology. 4:24. 2005. 1-6)

- Conclusions: Baseline brain MRI has a robust predictive value due to its ability to reveal an underlying vulnerability to axonal damage that predisposes optic neuritis patients to recurrent demyelinating injury.

Patients with one or more lesions on baseline MRI are at increased risk (P<0.001).

Our Patient: Multiple lesions on FLAIR MRI (Baseline scan)
J.K.’s Baseline Brain MRI (Axial T2W FSE)
Follow-up for our patient J.K.

- Detailed questioning revealed that J.K. experienced 1 month of trigeminal neuralgia in the year prior.

- She also noted paresthesias and tingling during trip to Iceland in 2005. Diagnosed with Raynaud’s by PCP but no imaging work-up until later.

- Underwent brain MRI after her episode of optic neuritis.

- As discussed, MRI is sensitive for detecting demyelinating MS lesions.

- However, there is a “window of opportunity” to image: the acute and chronic MS lesions give abnormal MRI signals due to different reasons: edema in the acute flares, gliosis in chronic lesions.

- During the time window between the two, when the edema has mostly resorbed and gliosis has not yet occurred, MRI may not detect these lesions.
Emerging Modalities: DT-MRI

- Axonal loss due to transection, not only demyelination, has been shown in histopathological and immunocytochemical studies of acute MS lesions.

- This leads to retrograde (Wallerian) degeneration over time.

- Recent studies demonstrated that axonal damage, originally thought to occur only late in MS, actually occurs quite early, even at the time of first demyelinating episode such as optic neuritis.

- Unfortunately, MRI-FLAIR cannot discern in fine detail the ongoing damage or subtle improvement in the optic nerve. Therefore, need new imaging modalities!

- **Diffusion Tensor-MRI** may provide *in vivo* information about CNII pathology (it monitors ↑ in mean diffusivity and ↓ fractional anisotropy, which have been found to correlate with axonal disruption).
Emerging Modalities: Optical Coherence Tomography (OCT)

- non-invasive, non-contact, performed in short-time frame.

- perfect for monitoring (with histological accuracy) axonal loss over time and correlating axonal loss with drug therapy.

- initially used in glaucoma to provide images of the macula with histological accuracy and to measure the retinal nerve fiber layer thickness.

- Retinal nerve fiber layer (RNFL) imaging and other methods have confirmed that axon transaction occurs in optic neuritis plaques.

- OCT has a new application in optic neuritis and MS, as patients with optic neuritis have been shown to have decreased thickness of peripapillary RNFL compared to controls.

- as a result, there is enthusiasm about generating specific guidelines for OCT use to assess axonal preservation/protection in clinical trials of ON and MS (Sergott et al. 2006)

Conclusions:

- **Idiopathic optic neuritis** manifests with sudden, reversible loss of vision (TRIAD: decreased visual acuity, color washout, and pain w/eye movement!)

- **MRI of orbit**: rules out compressive and traumatic injuries.

- **Baseline brain MRI**: detects areas of demyelination and informs prognosis.

- **Corticosteroids** accelerate visual recovery, no effect on final visual outcome.

- **Recent research on MRI-DT and OCT/RNFL in ON patients** suggests benefit for earlier therapeutic intervention with immunomodulatory agents.

*** In order to use these emerging imaging techniques in clinical trials of immunomodulatory agents, reliable end-points are needed to ensure uniformity of clinical trials!
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