Optic Neuritis: Current Diagnosis and Management

Acute Optic Neuritis: Typical History
- Age 20 to 50 years
- Unilateral
- Visual loss does not progress beyond 14 days
- Pain is present, particularly on eye movements
- Visual recovery begins by one month

Acute Optic Neuritis: Typical Findings
- Reduced acuity in one eye
- Vision better than no light perception
- Impaired color vision
- Afferent pupil defect
- Field loss - diffuse, central, arcuate, altitudinal
- Mild or no disc swelling
- No hemorrhages or retinal exudates

Optic Disc Appearance
Optic Neuritis - Clinical Course

- 95% recover to 20/40 or better over several weeks
- 50% have some permanent vision loss (contrast sensitivity, color vision, or visual field), particularly with baseline acuity of 20/50 or less

Optic Neuritis: Treatment

- Current treatment is IV steroids
  - Vision recovers faster (stops inflammation)
  - BUT, final vision no better than without steroids
  - Reduces short term risk of developing MS
- No known treatment prevents permanent vision loss, unmet therapeutic need
- Most high risk patients are placed on immunomodulatory therapy
Optic Neuritis: Risk of Multiple Sclerosis (MS) With Normal MRI

- No pain 0%
- Severe disk edema 0%
- Disc hemorrhage 0%
- Macular exudate 0%
- NLP vision 0%

NLP = no light perception  Arch Neurol, 2008.

Differential Diagnosis (Step 2)

- Ischemic optic neuropathy
- Systemic disease
- Neuro-retinitis
- Hereditary disorders
- NMO

NEURITIS vs ISCHEMIA

<table>
<thead>
<tr>
<th></th>
<th>NEURITIS</th>
<th>ISCHEMIA</th>
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<tbody>
<tr>
<td>Age</td>
<td>30’s</td>
<td>60’s</td>
</tr>
<tr>
<td>Pain</td>
<td>90%</td>
<td>10%</td>
</tr>
<tr>
<td>Field</td>
<td>central</td>
<td>altitudinal</td>
</tr>
<tr>
<td>Fundus</td>
<td>retrobulbar – 2/3</td>
<td>swollen</td>
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Ischemic Optic Neuropathy
DIFFERENTIAL DIAGNOSIS (Step 2)
INFLAMMATORY
(Bilateral, vitreous cells, hemorrhages)

Syphilis
Sarcoid
Lyme
Viral

Neuroretinitis

DIFFERENTIAL DIAGNOSIS (Step 2)
HEREDITARY - Nutritional
(Bilateral central-rectal scotomas)

Leber’s
B₁, B₁₂
Toxic
Optic Discs, VF and OCT

NMO Prognosis: (5 to 10 yrs) Reasons to Distinguish It

• 62% have legal blindness in one eye
• 50% will need an assistive device

NMO: The Chances

♦ Bilateral- 50% present of NMO present with ON, 20% are bilateral vs 0.4% in ON with MS
♦ Severe acuity loss- < 20/200, about 33%
♦ Recurrent ON- about 20%

NMO Tidbits

• Average RNFL thickness
  NMO- 63 microns, typical- 88 microns
  Controls- 102 microns
• About 5% of optic neuritis patients are NMO positive
• Chronic relapsing idiopathic optic neuropathy (CRION). Tend to have progression between episodes
Copper Deficiency Optic Neuropathy

Step 3- Tests

- MRI head with gad (typical or atypical ON)
- LP: IgG index, OCB, cells, protein (atypical ON)
- NMO IgG (recurrent, bilateral or severe ON)
- Leber’s mutations (severe or bilateral ON)
- Serological studies-Atypical ON or systemic symptoms-ESR, ANA, ACE, RPR, Lyme, SSA, SSB, ANCA
- Retinal Tests-ERG, **Fluorescein angiogram**, CAR antibodies, OCT
- VER: Subclinical ON, can use low contrast

Vision and ON as Ideal Models

- Axonal and neuronal loss common
- Sensitive visual function tests
- Structure-function correlation can be captured by OCT
- Unique opportunity to investigate non-myelinated axons

Comparison of Vision Tests

Odds ratio in favor of MS vs. control status (95% CI) for worse vision scores

- High Contrast Acuity ~100% (1.3, 1.9) *P<0.001
- Low Contrast Acuity 1.25% (1.5, 2.2) *P<0.001
- Contrast Sensitivity Pelli-Robson (1.2, 1.8) *P<0.001
- Color Vision D15-D50 (1.0, 1.9)

* Low contrast acuity charts best distinguish MS patients vs. controls, accounting for age

Defining Visual Change

- 2 lines (10 letters) = clinically meaningful change? 
- 5-letter change more sensitive for high-contrast visual acuity 
- Change by \( \geq 7 \) letters is beyond test-retest variability for low-contrast acuity, correlates w/ QOL 

Worsening Vision by EDSS Progression Status

<table>
<thead>
<tr>
<th>EDSS Progressed (n=188)</th>
<th>EDSS Not Progressed (n=754)</th>
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<tbody>
<tr>
<td>HCA</td>
<td>9.0</td>
</tr>
<tr>
<td>LCA (2.5%) VFT Score</td>
<td>26.6</td>
</tr>
<tr>
<td>LCA (1.25%)</td>
<td>28.2</td>
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</table>

P=0.002  P=0.171  P=0.573

Importance of OCT in Optic Neuritis

- Allows structure-function correlations
- Significant RNFL loss, acute, 99% by 6 months
- Optic neuritis as a model for testing new therapies

Retinal Nerve Fiber Layer Imaging by Optical Coherence Tomography (OCT)

Henderson et al. Brain, 2010

Quantifying Axonal Loss After Optic Neuritis with OCT

- Patients with acute ON (n=54)
- Followed for a mean of 13 months
- 74% developed significant RNFL thinning (20%) in the affected eye
- RNFL values significantly thinner in affected eyes (78 µm) vs. fellow eyes (100 µm, \( P < 0.0001 \))


OCT in Optic Neuritis

- Patients (n=54) with ON, 74% had 20% RNFL loss
- Thickness at \( \geq 3 \) months = 78 ±30 µm in affected eyes
- RNFL <75 µm vs. \( \geq 75 \) µm predicted visual outcome


Relation to Low-Contrast Acuity, Optic Neuritis History

2 lines low-contrast letter acuity = 7.6 µm RNFL, \( P < 0.001 \)


Longitudinal Data: RNFL Thinning for All MS Eyes (n=593)

\* Degree of RNFL thinning significantly greater compared to 0 – 1-year interval

Talman et al., Ann Neurol 2010.
Low-Contrast Acuity Reflects Axonal Loss Over Time


Retinal Neuronal Atrophy in MS Eyes


Spectral-Domain OCT


MS vs. Controls

P values are from GEE models accounting for age and inter-eye correlations.
24 Y.O. WOMAN

- Decreased vision over 7 days
- No pain upon eye movement

Implications

- Subclinical injury is common in MS
- OCT and LCA are important outcome measures for clinical trials in MS
- In practice, used to detect subtle atrophy, longitudinal changes and macular changes
- Correlates with QOL and MRI measures
- Unmet therapeutic need for neuroprotective therapy in MS

EXAMINATION

Acuity: NLP O.D
20/20 O.S.

Pupil: Right amaurotic

Motility: Full
EXAMINATION -MW

♦ Slit lamp exam showed 1+ vitreous cells OD
♦ Tension applanations were 16 OU
♦ Fundus exam revealed the following:

LABORATORY

♦ nl lytes, CBC, LFTs
♦ RPR (-), ESR 40, PPD (-), anergy (+)
♦ ANA 1:320, nl complements
♦ (-) anti- dsDNA, -smith, -RNA, -Ro, -La
♦ ACE 53.18 (10-50)
♦ LP:2W 0R protein:29 glucose:59
♦ nl CXR
Conjunctival and lacrimal biopsies showed non-specific chronic inflammation without granulomas.

Gallium scan was normal.

She was started on steroids and had no improvement.

She underwent biopsy of right optic nerve.
OPTIC NERVE IN SARCOID

- Occurs in 1-5% of pts with systemic disease
- Five categories
  - Primary granuloma of the optic nerve
  - Papillitis
  - Retrobulbar optic neuritis
  - Papilledema secondary to increased ICP
  - Optic atrophy

20 Y.O. MAN

- Decreased vision O.U.
- Visual acuity 20/200 O.U.
- Fields: centrocecal scotomas
30 Y.O. MAN

- Sudden visual loss O.D.
- No pain on eye movement

Central Serous Choroidoretinopathy
72 Y.O. WOMAN
(August 1996)
♦ Progressive visual loss right eye
♦ Right periorbital ache
♦ No neurologic or constitutional symptoms

EXAMINATION
(August 1996)
♦ Acuities: 20/100+ OD, 20/50+ OS
♦ Pupils: sluggish, no APD
♦ Color: no control OU
Summary

- There are typical history and examination features of idiopathic optic neuritis.
- The decision to use corticosteroids for visual impairment in optic neuritis should be individualized.
- Natural history suggests that CIS patients with positive MRIs will progress to CD-MS.
- Corticosteroids followed by immunomodulatory therapy should be strongly considered for such patients.
- Functional and structural visual correlates permit the testing of novel neuro-repair therapies.