Optic Neuropathy Part 1:
Inflammation, Demyelination & Infection

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Objectives

1. Describe how to diagnose an optic neuropathy

2. List the differential diagnosis of inflammatory optic neuropathy
Pre-Lecture TEST!

The following three individuals each present with unilateral visual loss noted over the preceding few days.

Is the evaluation the same for each patient?
#3.
Most optic neuropathies in young adults are:

1. Inflammatory
2. Infectious
3. Ischemic
4. Compressive
History

Onset: acute vs. chronic

Inflammation
  Demyelinating, Non-Demyelinating
Infection
  Syphilis, Lyme, Bartonella, TB
Ischemic
Compression
  Tumor, Graves, Disc Drusen
Hereditary
  Leber
Miscellaneous
  Lymphoma, Leukemia
History

Pain vs. Painless

Inflammation
- Demyelinating,
- Non-Demyelinating

Infection
- Syphilis, Lyme,
- Bartonella, TB

Ischemic

Compression
- Tumor, Graves,
- Disc Drusen

Hereditary
- Leber

Miscellaneous
- Lymphoma,
- Leukemia
History

Systemic vs. Eye

Inflammation
- Demyelinating,
- Non-Demyelinating

Infection
- Syphilis, Lyme,
- Bartonella, TB

Ischemic
Compression
- Tumor, Graves,
- Disc Drusen

Hereditary
- Leber

Miscellaneous
- Lymphoma,
- Leukemia
History

PMH: thyroid, cancer

- Inflammation
  - Demyelinating, Non-Demyelinating
- Infection
  - Syphilis, Lyme, Bartonella, TB
- Ischemic
- Compression
  - Tumor, Graves, Disc Drusen
- Hereditary
  - Leber
- Miscellaneous
  - Lymphoma, Leukemia
History

Family Hx: vision loss

- Inflammation
  - Demyelinating,
  - Non-Demyelinating
- Infection
  - Syphilis, Lyme,
  - Bartonella, TB
- Ischemic
- Compression
  - Tumor, Graves,
  - Disc Drusen
- Hereditary
  - Leber
- Miscellaneous
  - Lymphoma,
  - Leukemia
History

Social Hx: travel, cat scratch

Inflammation
  Demyelinating,
  Non-Demyelinating
Infection
  Syphilis, Lyme,
  Bartonella, TB

Ischemic
Compression
  Tumor, Graves,
  Disc Drusen
Hereditary
Leber
Miscellaneous
  Lymphoma,
  Leukemia
Examination

Acuity & Color Vision

Acuity spared

Acuity decreased

Inflammation
- Demyelinating,
- Non-Demyelinating

Infection
- Syphilis, Lyme,
- Bartonella, TB

Ischemic

Compression
- Tumor, Graves,
- Disc Drusen

Hereditary
- Leber

Miscellaneous
- Lymphoma,
- Leukemia
Examination

Visual fields

Inflammation
Demyelinating, Non-Demyelinating
Infection
Syphilis, Lyme, Bartonella, TB
Ischemic Compression
Tumor, Graves, Disc Drusen
Hereditary
Leber
Miscellaneous
Lymphoma, Leukemia
Examination

Relative Afferent Pupillary Defect

Inflammation
- Demyelinating, Non-Demyelinating
- Infection
  - Syphilis, Lyme, Bartonella, TB

Ischemic Compression
- Tumor, Graves, Disc Drusen

Hereditary
- Leber

Miscellaneous
- Lymphoma, Leukemia
<table>
<thead>
<tr>
<th>Examination</th>
<th>Inflammation</th>
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<tr>
<td>Motility</td>
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<td>Miscellaneous</td>
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<td>Lymphoma, Leukemia</td>
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</table>
Examination

External
Examination

Slit Lamp

Courtesy of Dr. Adam Kaufman

Inflammation
  Demyelinating, Non-Demyelinating

Infection
  Syphilis, Lyme, Bartonella, TB

Ischemic
  Compression
  Tumor, Graves, Disc Drusen

Hereditary
  Leber

Miscellaneous
  Lymphoma, Leukemia
Examination

Fundus

Inflammation
- Demyelinating, Non-Demyelinating
- Infection
  - Syphilis, Lyme, Bartonella, TB

Ischemic Compression
- Tumor, Graves, Disc Drusen

Hereditary
- Leber

Miscellaneous
- Lymphoma, Leukemia
Examination

Fundus

Inflammation
  Demyelinating,
  Non-Demyelinating
Infection
  Syphilis, Lyme,
  Bartonella, TB

Ischemic
Compression
  Tumor, Graves,
  Disc Drusen
Hereditary
  Leber
Miscellaneous
  Lymphoma,
  Leukemia
Optic Neuritis

Nonspecific term describing optic nerve involvement by inflammation or demyelination (sometimes infection?).
### Differential Diagnosis of Optic Neuropathy

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<tr>
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<th>Compression</th>
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<tr>
<td>• Typical optic neuritis (idiopathic, demyelinating)</td>
<td>• NAION</td>
<td>• Lymphoma, Leukemia, other</td>
<td>• Tumor, Graves, ↑ICP, drusen</td>
<td>hypotony, trauma, vit-pap traction, pseudo, papillophlebitis, CRVO</td>
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<tr>
<td>• Atypical Optic Neuritis (perineuritis, neuromyelitis optica, sarcoid, autoimmune (AON), chronic relapsing inflammatory (CRION), other systemic (SLE, Wegeners)</td>
<td>• AAION</td>
<td>• Hypoperfusion (anemia, blood loss, hypotension, DM)</td>
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<td>Infection</td>
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<td>• Syphilis, Lyme, Bartonella, TB, HZV, CMV, sinusitis</td>
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<td>Hereditary – Leber?</td>
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Optic Neuritis

When you hear the word “typical” optic neuritis what do you think of?

1. Demyelination
2. Idiopathic
3. Infection
4. Neuromyelitis optic
5. Other
Differential Diagnosis of Optic Neuritis

- “Typical”: idiopathic, demyelinating

- “Atypical”: neuromyelitis optica, sarcoid, autoimmune (AON), chronic relapsing inflammatory (CRION), other systemic (SLE, Wegener)

- Infectious: Syphilis, Lyme, Bartonella, TB, HZV, CMV,
Why do we call it “Typical?”

Optic neuritis and MS
Typical Optic Neuritis

- Demyelinating, Idiopathic
  - Mild disc swelling (no exudate/hemorrhage)
  - Not steroid dependent

Atypical Optic Neuritis

- Disc swelling may be severe (with exudate/hemorrhage)
- May be steroid dependent
Atypical Optic Neuritis

- Important to diagnose because they are usually **responsive to steroids and/or antibiotics** and need treatment to improve vision.

- May also be **steroid dependent, relapsing** as the steroid dose is reduced sometimes requiring immunosuppression for many years.
Optic Neuritis Treatment Trial (ONTT)

Entry Criteria

• age 18-45
• unilateral optic neuropathy, symptoms < 9 days
• no systemic disease except MS
• 459 enrolled

2 thrown out (aneurysm, pit tumor)
Typical Optic Neuritis (Demyelinating/Idiopathic)

- Retrobulbar neuritis: 65%
- Papillitis: 35%
spectrum of VF defects in the ONTT
Do corticosteroids improve the ultimate visual recovery in demyelinating optic neuritis?

1. Yes
2. No
3. Not sure
Optic Neuritis Treatment Trial - Visual Outcome

Visual acuity 20/40 or better:

- placebo: 94.3%
- IV steroids: 93.7%
- oral steroids: 92.6%

IV only affects rate of recovery - not final vision!
ONTT: Development of MS at 15 years

- 50% regardless of MRI
- 25% if MRI normal at onset
- 72% if ≥1 plaque at onset
Atypical symptoms for demyelinating optic neuritis

- Older
- Painless
- Bilateral
- Progressive
- Non-resolving
Atypical signs

- Hemorrhage
- Marked disc edema
- Cotton wool patches
- Exudate
- Sector edema (NAION)
- Pallid edema (A-AION)
Differential Diagnosis of Optic Neuritis

• **“Typical”**: idiopathic, demyelinating

• **“Atypical”**: neuromyelitis optica, sarcoid, autoimmune (AON), chronic relapsing inflammatory (CRION), other systemic (SLE, Wegener)

• **Infectious**: Syphilis, Lyme, Bartonella, TB, HZV, CMV,
Neuromyelitis Optica (Devic)

- Idiopathic inflammatory demyelinating CNS disease
  - Unilateral or Bilateral optic neuritis
  - Transverse myelitis
  - Monophasic or polyphasic course
Neuromyelitis Optica - Diagnosis

- Serum Biomarkers – NMO-IgG
  - Targets aquaporin-4, dominant water channel protein
  - Specificity reported 95-100%

- Diagnostic Criteria:
  - Optic neuritis and acute myelitis + 2/3 of the following:
    - Spinal cord lesion extending >3 vertebral segments
    - Brain MRI findings not satisfying MS criteria
    - NMO-IgG seropositive

Wingerchuk et al. Neurology 2006; 66(1), 1485-1489
Neuromyelitis Optica (NMO)

**Treatment**

- Multicenter Retrospective Study (Mayo & Johns Hopkins)
- Relapse & treatment failure rates of azathioprine, mycophenylate and/or rituximab

- Relapse rate reduced by:
  - 88% Rituximab
  - 87% Mycophenylate
  - 72% Azathioprine

- Remission rate:
  - 66%*
  - 64%*
  - 47%

- If fail one drug, high response to second.

NMO Optic Neuritis Treatment

- IV Corticosteroids
  - Potentially decreases attack severity and speeds recovery

- Therapeutic Plasmapheresis
  - Effective rescue treatment if steroid unresponsive
NMO Spectrum Disorders

Defined as either recurrent optic neuritis or extensive transverse myelitis.

Myelin Oligodendrocyte Glycoprotein (MOG) vs. Aquaporin 4 (AQP4)

- 215 pts, 7.4% MOG, 64.7% AQP4
- MOG more likely to be male, bilateral optic neuropathy, single attack, better recovery

NMO vs. MS

Differentiating optic neuritis in NMO vs. MS

• Retrospective
• 26 NMO, 26 MS patients with optic neuritis
• NMO longitudinally more MRI enhancement
• Cut-off of 17.6 mm, 77% specific, 80% sensitive for NMO

AQP4 vs. MS vs. MOG

Differentiating optic neuritis with MRI

• Bilateral more common in AQP4 + MOG (80% vs 20%)
• Chiasmal/Optic Tract more common in AQP4
• Longer segment involvement in AQP4 + MOG

Sarcoid can cause optic neuropathy with or without disc swelling. Check angiotensin converting enzyme, CXR if disc swelling is more than mild.
Chronic relapsing inflammatory optic neuropathy (CRION)

- Steroid responsive and steroid dependent inflammatory optic neuropathy but no evidence of sarcoidosis.
- Do not develop any related neurological, systemic or ocular disease.
- A retrospective diagnosis of CRION may then be made if no other cause of the optic neuropathy can be found.

Kidd D, Burton B, Plant GT, Graham EM. Brain 2003;126:276-84.
Autoimmune optic neuropathy

- Recurrent optic neuropathy requiring steroids.
- ANA or anticardiolipin antibodies
- no diagnosed collagen vascular disorder.
- Biopsy of non-sun exposed skin shows evidence of vasculitis.

Which of the following is a way to distinguish demyelinating optic neuropathy from atypical optic neuritis?

1. Presence of pain
2. Severe disc swelling
3. No plaques on MRI
4. Good visual recovery
Atypical Optic Neuritis

Inflammatory
- Neuromyelitis Optica (Devics)
- Sarcoid
- Autoimmune Optic Neuropathy (AON)
- Chronic Relapsing Inflammatory Optic Neuropathy (CRION)
- Other systemic (SLE, Wegeners)

Infectious
- Syphilis, Lyme, Bartonella, TB

Chikungunya virus
Optic Neuritis Associated With Chikungunya Virus
WHEN DO YOU THINK OF INFECTION?

- Systemic illness suggests virus
- Bilateral simultaneous papillitis
- Atypical demographic (age)
- Immune compromise
- Neuroretinitis
- Associated uveitis
Which of the following is the most common infectious optic neuropathy you see?

1. Bartonella henselae
2. Tuberculosis
3. Syphilis
4. Cytomegalovirus
Neuroretinitis - optic disc swelling and macular star of exudate.

cat scratch disease, idiopathic, toxoplasmosis, syphilis

NOT MS!
3 days after symptoms started

10 days after symptoms started
Cat scratch disease
(Bartonella henselae)

painful lymphadenopathy
Parinaud’s oculoglandular syndrome
neuroretinitis
white retinal lesions
peripapillary serous RD

Treatment?
ciprofloxacin, doxycycline, rifampin
CMV may cause an “isolated” papillitis, check the periphery!
Syphilitic Optic Neuropathy

- Papilitis, neuroretinitis, normal disc

Tuberculous Optic Neuropathy

- Papilitis in most
- Uveitis in 79%
Estimated TB incidence rates, by country, 2009

Estimated new TB cases (all forms) per 100 000 population

- 0–24
- 25–49
- 50–99
- 100–299
- ≥300
- No estimate
Herpes Zoster

Optic neuropathy occurs days to several weeks after onset of rash in V1 distribution.

+/- disc swelling

Visual prognosis poor
TEST
Answers
Degree of disc swelling worrisome.

MRI and CXR, ACE, lysozyme, Cat scratch

Final Dx: sarcoidosis
#2.

Neuroretinitis - not MS

Check: Bartonella henselae (Cat scratch), RPR
#3.

retrobulbar optic neuropathy c/w idiopathic demyelinating optic neuritis.

MRI, if plaques then IV solumedrol, neurologist for imuno-modulating therapy.
Summary

1. Most optic neuropathy in young adults is inflammation or infection.

2. The prevalence of many optic neuropathies depends on where you live.

3. Important to make correct diagnosis because vision recovery may depend on it.
Thank-you for your attention.