A Rational Approach to Treating Inflammatory Optic Neuropathies: Which Treatment and Why

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Hot Topics: What’s New in the Optic Nerve
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Objectives

• Enumerate immune and infectious causes of inflammatory optic neuropathy.

• List clinical and diagnostic data impacting treatment of inflammatory optic neuropathy.

• Describe data supporting various treatments of acute inflammatory optic neuropathy.

• List inflammatory optic neuropathies with high risk of poor visual recovery or recurrent disease.
Rational Approach to ON Treatment

• Etiology
• Prognosis
• Therapeutic Options/Data
• Risk of Recurrent Disease
  • Preventative Therapy
ON: Differential Diagnosis

• Infection
• Ischemia
• Toxic
• Genetic
Infectious Optic Neuropathy

- Bilateral
- Optic Disc Heme
- Ocular Inflammation
  - Uveitis
  - Iritis
  - Retinitis
# Treatment of Infectious Causes of ON

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Common Clinical Features</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis (Treponema)</td>
<td>Uveitis, chorioretinitis, vasculitis, papillitis (varied)</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Cat-scratch (Bartonella)</td>
<td>Neuroretinitis (macular star)</td>
<td>Corticosteroids; antibiotics: azithromycin, ciprofloxacin, tetracycline, sulfamethoxazole-trimethoprim</td>
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<tr>
<td>Lyme Disease (Borrelia)</td>
<td>Optic disc edema; reports of intermediate uveitis or papilledema</td>
<td>Ceftriaxone; doxycycline</td>
</tr>
<tr>
<td>Tuberculosis (Mycobacteria)</td>
<td>Papillitis, uveitis, neuroretinitis</td>
<td>Isoniazid, rifampicin, pyrazinamide, ethambutol</td>
</tr>
<tr>
<td>Viral (WNV, HIV, VZV)</td>
<td>Variable: mild optic disc edema, chorioretinitis, vitritis (WNV); normal, mild microangiopathy (HIV); hemorrhagic optic disc edema, cotton wool spots (VZV)</td>
<td>HAART (HIV); acyclovir (VZV)</td>
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# Inflammatory Causes of ON

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<tr>
<th>Etiology</th>
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<tr>
<td>NMOSD</td>
<td>Recurrent, MRI-optic nerve enhancement/extensive lesions; chiasm, NMO-IgG</td>
<td>IVSM; PLEX</td>
</tr>
<tr>
<td>MOG</td>
<td>Recurrent; MRI-optic nerve enhancement/extensive lesions; MOG-IgG</td>
<td>Corticosteroids – may require prolonged treatment</td>
</tr>
<tr>
<td>GFAP</td>
<td>Optic disc papillitis; MRI-perivascular enhancement; GFAP-IgG</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Paraneoplastic</td>
<td>Bilateral; disc edema; vitreal cell; vascular leakage; paraneoplastic antibodies</td>
<td>IVIg; PLEX; corticosteroids; identify and remove inciting neoplasm</td>
</tr>
<tr>
<td>Idiopathic Multiple Sclerosis</td>
<td>Occasional mild disc edema; MRI-optic nerve enhancement/T2 signal</td>
<td>IVSM; PLEX</td>
</tr>
<tr>
<td>Other (CRION, AON)</td>
<td>Recurrent, isolated; MRI-optic nerve enhancement/T2 signal; IgG on skin biopsy</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Optic disc edema; ocular inflammation; multi-system disease</td>
<td>Corticosteroids; TNF-α blocker</td>
</tr>
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Inflammatory Optic Neuritis: Clinical Suspicion

• NMOSD
  • Severe vision loss/field loss (<20/200; MD <11dB)
  • MRI: Posterior optic nerve or chiasm involvement

• MOG-IgG
  • Recurrent optic neuritis; simultaneous TM and ON
  • Steroid sensitive
  • MRI: Significant ON nerve/sheath enhancement

• RION/CRION/AON
  • Recurrent optic neuritis
  • Steroid sensitive

• Paraneoplastic
  • Subacute onset, older age; painless
  • Vitreal cell, retinal vascular leakage

• Sarcoidosis
  • Acute or subacute onset; ocular inflammation
  • MRI: Perineuritis, chiasmitis, enlargement/enhancement optic nerve

• GFAP-IgG
  • Meningoencephalitis; papillitis
ON: MRI and OCT

NMOSD

Jurynczyk et al. Brain 2017: 140; 3128
Laboratory Clues – Serology and CSF

• **Serology**
  • ANA: NMOSD and MOG-IgG (~42%)
  • Anti-neural antibodies: GFAP-IgG
    • NMDA-R-IgG, anti-GAD65, ion channel antibodies
  • Thyroid Abs – 16.7%
  • AchR Abs – 11%; Anti-GAD Abs – 15%

• **CSF**
  • MOG-IgG: Pleocytosis ≥100 cells/ml
  • Oligoclonal bands: MS-related, GFAP-IgG
  • Eosinophils: NMOSD
Optic Neuritis Treatment Trial (ONTT)

No difference in visual acuity between steroid and placebo groups at 6 months*.

*Increase in the rate of normalization of visual field, contrast sensitivity, and visual acuity

(NEJM 326:581, 1992)
Visual Prognosis

• Average recovery after vision loss
  • NMOSD: logMAR 0.4 (~42% worse than 1.0)
  • MOG-IgG: 20/20
  • Sarcoidosis: 20/40
  • CRION/RION/AON & GFAP-IgG: “Good”

• High risk of relapse
  • NMOSD: 63% by 1 year untreated
    • ARR w/treatment: 0.38 (0.04-2.25; N = 83)
  • MOG-IgG

Jurynczyk et al. Brain 2017: 140; 3128
Kidd et al., Brain 2003; 126:276
Staging Acute Therapy

Recovery from attack is often incomplete

Serial treatment generally moves non-responders to partial responders

NMO Pathogenesis

Future Therapies?

- Anti-complement Therapy
- Anti-C5 complement
- C1q esterase inhibition
- Anti-neutrophil elastase
- IVIg
MOG-IgG Disease Pathology

Type II MS Pathology: Lymphocytic infiltrate, IgG, complement

Saadoun et al. (2014), Acta Neuropathol Comm, 2:35
Peschl et al. (2017), J Neuroinflamm, 14:208
Rational Approach to Optic Neuritis Treatment

• Identify the cause
  • Infectious or non-infectious
  • Clinical, imaging, laboratory clues

• Prognosis
  • Generally good
  • Recurrent ON and NMOSD are likely exceptions

• Treatment
  • Intravenous methylprednisolone
  • Early plasma exchange for NMOSD and recurrent ON

• Lingering Questions
  • Combination Therapy
  • Direct treatment of immune effectors (CDC, ADCC)
  • Early use of immunosuppression/immunomodulators