I HAVE NO RELEVANT FINANCIAL DISCLOSURES

CASE

- CC: vision loss and eye pain
  - HPI: 8 yo F who presents with 1 week of eye pain with movement and 4 days of increasing blurry vision OS > OD. Mother denies any preceding illness.
  - PMH: none
  - POHX: no surgeries, glaucoma, trauma
  - FHX: no h/o blindness nor autoimmune disease
• SHx: No EtOH or tobacco. Dog at home but no other animals. No tick nor cat bites recently.
• ROS: No history of lung disease, joint pain or rashes.
• No previous episodes of focal weakness, numbness, loss of bowel/bladder function, vertigo or other focal neurological episodes.

EXAM

• VA:
  – OD 20/100
  – OS 20/300
• Pupils
  – 6–>5 OU
  – 2+ RAPD OS
• Tpalp
  – Soft OU

• Ocular motility
  – Full OU
• VF to confrontation
  – Full OU

Slit lamp:

• Lids and lashes: within normal limits OU
• Conjunctiva and sclera: white and quiet OU
• Cornea: clear OU
• Anterior chamber: deep and quiet OU
• Iris: round and reactive, no neovascularization of the iris
• Lens: clear OU

Dye:

• Normal retina, vessels and periphery OU
QUESTIONS FOR THE AUDIENCE

Differential:

- Optic neuritis
- Idiopathic intracranial hypertension
- Neuromyelitis optica
- Intracranial mass
- Optic nerve glioma

QUESTIONS FOR THE AUDIENCE

Diagnostics:

- MRI
- Lumbar puncture
- Labs
**BLOOD TESTS**
- CBC: wnl
- ESR 31 (mild elevation) CRP <.3 (wnl)
- RF: Negative
- NMO Ab: negative
- ACE: 70 (mild elevation)
- ANA: neg
- ANCA: negative
- MOG Ab: negative
- Slightly elevated B12 and folate

**LP RESULTS**
- Opening pressure: 25
- Cell counts RBC <1, WBC 2-3
- IgG index 0.5 (wnl)
- Protein: 18
- Glucose: 53
- ACE <6 (wnl)
- oligoclonal bands: none
- myelin basic protein < 2.0 (wnl)
- HSV, EBV, Toxo, Mycoplasma negative

**TREATMENT**
- IV steroids 29g, 30mg/kg/day -> 90 mg/day for 3 Days followed by 2 week taper starting at 1 mg/kg
FOLLOW-UP

• VA HOD1
  - OD 20/100
  - OS 20/800
• VA HOD2
  - OD 20/70
  - OS 20/200
• VA HOD3
  - OD 20/20
  - OS 20/10
• Year 2 VA
  - OD 20/10
  - OS 20/10
• Year 2 HVF
  - Reliable and fail OUt

PEDIATRIC OPTIC NEURITIS
WHAT IS THE NEW EVIDENCE THAT YOU NEED TO KNOW?

• Pediatric Optic Neuritis Study (PON1)
• New information about biomarkers
  – Neuromyelitis Optica (NMO)
  – Myelin oligodendrocyte glycoprotein (MOG)
• Evidence based work-up of child with optic neuritis
• Evidence based management of child with optic neuritis

PON1
Multicenter prospective data collection study run by PEDIG as a collaboration with NORDIC
44 children enrolled over 22 months
- Followed for 2 years
- Visual acuity primary outcome
- Also analyzed lab results, MRIs

<table>
<thead>
<tr>
<th>N=30 Eyes</th>
<th>Neurologic Diagnosis at 2 Years</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated Unilateral</td>
<td>9 (35%)</td>
<td></td>
</tr>
<tr>
<td>Isolated Bilateral</td>
<td>3 (12%)</td>
<td></td>
</tr>
<tr>
<td>Acute disseminated encephalomyelitis (ADEM)</td>
<td>2 (8%)</td>
<td></td>
</tr>
<tr>
<td>Myelin Oligodendrocyte Glycoprotein (MOG)</td>
<td>6 (23%)</td>
<td></td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>3 (12%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median (25%, 75% percentile)</th>
<th>Neuromyelitis Optica Spectrum Disorder (NMOED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%) eyes with &lt;20/200 VA</td>
<td>13 (49%)</td>
</tr>
<tr>
<td>N (%) eyes with &lt;20/800 VA</td>
<td>7 (23%)</td>
</tr>
</tbody>
</table>
SUMMARY / CONCLUSIONS FROM PON1

• First prospective study of VA outcomes in pediatric optic neuritis
• Commonly associated with neurologic syndromes
• MOG+ ON very common in this cohort (54%)
• Marked improvement in distance VA observed in large majority of patients without much change between 6 months and 2 years
  - 24 of 30 (80%) and 22 of 30 (73%) were in the normal range for high contrast VA at 6 months and 2 years respectively
• Loss to follow-up too large to comment on MRI predictability
• Enrollment did not meet goal – a randomized trial with these inclusion criteria unlikely to be feasible

CASE 2

• 2 y.o. female with no PMH, presenting with unsteady gait 1 week, R ptosis 1.5 weeks and decreased vision (parents think she is seeing less - holding toys close to face)
• PMHx/Meds/FmHx/SocHx noncontributory
• Vos F&F OU
• Tpalp soft OU
• Pupil 4–2, 4.5–2.5 OU, no rAPD
• Ext Exam 1.5 mm ptosis OD
• Portable SLE normal
PERTINENT LAB WORKUP

- Normal CBC
- LP protein 29, Glucose 60
  - RBC 11 (11 PMN, 66 L, 23 M)
  - MNP 8.02 (high)
  - Culture negative
  - IgG synthesis and other CSF studies normal
- Infectious workup negative

DIAGNOSIS

- Bilateral optic neuritis
- Right Horner syndrome
- Multifocal white matter lesions consistent with demyelinating disease/ADHM

- MOG antibody added to lab work - Positive
COURSE

- IV steroids x 3 days
- Sent home with oral steroid taper
- 1 month visit:
  - F&F OU, ptosis resolved, all neurologic symptoms resolved
  - MRI improved
- 5 years later:
  - 20/20 OD and 20/25 OS
  - Pallor
  - No further episodes

MOG IN PON1

- MOG is a myelin protein on the outer surface of myelin sheaths
- MOG+ disorder is thought to be a biomarker for CNS demyelinating disease that overlaps but is distinct from MS and NMOSD (more on next slide)
- Patients in the PON1 study were asked to participate in a sub-study evaluating MOG antibodies sent to Mayo Clinic
  - 13 patients consented to have their serum tested
  - 54% positive (7/13)

<table>
<thead>
<tr>
<th></th>
<th>MOG+</th>
<th>MOG-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>6/7</td>
<td>3/6</td>
</tr>
<tr>
<td>Bilateral</td>
<td>4/7</td>
<td>2/6</td>
</tr>
<tr>
<td>Presenting VA (median)</td>
<td>1.7 logMAR (20/1000)</td>
<td>0.4 logMAR (20/50)</td>
</tr>
<tr>
<td>6 month VA (median)</td>
<td>0.1 logMAR (20/25)</td>
<td>0 logMAR (20/20)</td>
</tr>
</tbody>
</table>

Small sample! Lots of room for bias in this sub-study! Large confidence intervals!

MOG+ DISEASE

- Often found in patients diagnosed with ADEM, NMOSD, myelitis, optic neuritis
- Prospective study of 239 children with demyelinating syndrome (Armangue et al. Lancet Neurology 2020)
  - MOG+ in ~50% of the children (only 5% of adult ON)
  - 68% ADEM, 17% optic neuritis, 11% myelitis, 5% NMOSD
- Optic neuritis is a very common presentation (either isolated or as part of ADEM)
  - Bilateral ON rare
  - MRI enhancement of optic nerve sheath and surrounding fat (“perineural enhancement”) is fairly common and specific
- Respond well to steroids generally
- Overall very good prognosis and visual recovery
- Relapsing cases may require immunotherapies (no RCTs yet)
  - IVIG very frequently used, also azathioprine, mycophenolate mofetil, rituximab
NMO SPECTRUM DIS.

Inflammatory CNS disorder characterized by severe immune-mediated demyelination and axonal damage predominately targeting the optic nerve and spinal cord.

- Disease specific antibodies (anti-aquaporin-4, AQP4)
- Characteristic symptoms include acute bilateral optic neuritis, transverse myelitis (limb weakness, bladder dysfunction)
- Rarely can present similarly to MS with brain lesions too
- Suspect in cases of severe, unremitting or relapsing optic neuritis
- Diagnosis matters because treatment is different! And MS treatment can worsen NMO!

**Immunotherapy**

<table>
<thead>
<tr>
<th>Acute Treatment</th>
<th>Chronic Treatment</th>
</tr>
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<tbody>
<tr>
<td>Steroids</td>
<td>X</td>
</tr>
<tr>
<td>Plasmapheresis</td>
<td>X (retrospective study when plasma not available)</td>
</tr>
<tr>
<td>Azathiprine</td>
<td>X</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>X</td>
</tr>
<tr>
<td>Rituximab</td>
<td>X</td>
</tr>
<tr>
<td>Eculizumab</td>
<td>Anti-C5B prevents complement cascade, 1st FDA approved treatment specifically for NMOSD</td>
</tr>
<tr>
<td>Satralizumab</td>
<td>IL6 receptor antagonist blocks inflammation and blood brain barrier permeability</td>
</tr>
<tr>
<td>Aquaporunab</td>
<td>Anti-AQP4 monoclonal antibody competes with AQP4</td>
</tr>
</tbody>
</table>

**SUGGESTED WORK-UP AND MANAGEMENT**

- In a child suspected of having optic neuritis
  - MRI brain and orbits
    - Look for enhancement of the optic nerve(s)
    - Longer lesions more likely with NMO or MOG
    - Perineural enhancement more specific for MOG
  - Look for associated lesions (ADEM, MS, NMO)
  - Lumbar puncture
    - Evaluate for biomarkers of MS
    - Evaluate for evidence of infection
  - If suspicious at all for NMO, admit for steroids and plasmapheresis (or IVIG if plasma not available)
  - If not suspicious for NMO, most practitioners in PON1 still treated with IV steroids although there is no definitive consensus

**MY PERSONAL OPINIONS, NOT UNIVERSALLY DONE**

- I suggest sending MOG antibody in all cases of pediatric optic neuritis
- I also send NMO in all cases given the importance of the diagnosis and ease of testing
- I follow all patients approximately 3 months after treatment with OCT and visual field
- I repeat the MRI at 2 years (if not before)
THANK YOU!