PEDIATRIC OPTIC NEURITIS

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I HAVE NO RELEVANT FINANCIAL DISCLOSURES

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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

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- 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 neurologic episodes.

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EXAM

- VA:
  - OD 20/100
  - OS 20/800
- Pupils
  - 6 -> 5 OU
  - 2+ RAPD OS
- Tpalp
  - Soft OU
- Ocular motility
  - full OU
- VF to confrontation
  - full OU

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EXAM

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

DFE

- Normal macula, vessels and periphery OU

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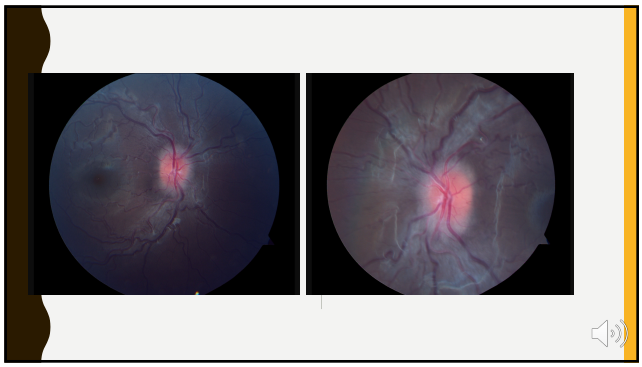

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QUESTIONS FOR THE AUDIENCE

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

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QUESTIONS FOR THE AUDIENCE

- **Diagnostics?**
  - MRI
  - Lumbar puncture
  - Labs

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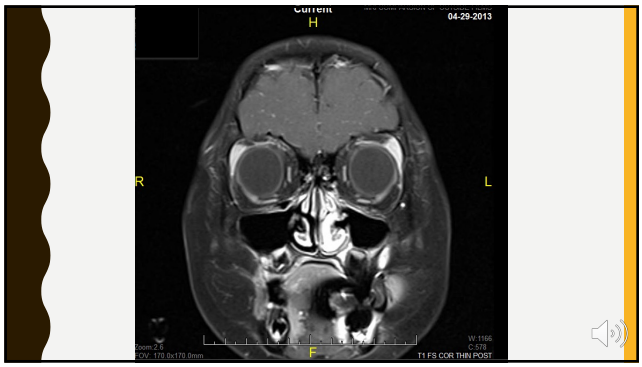
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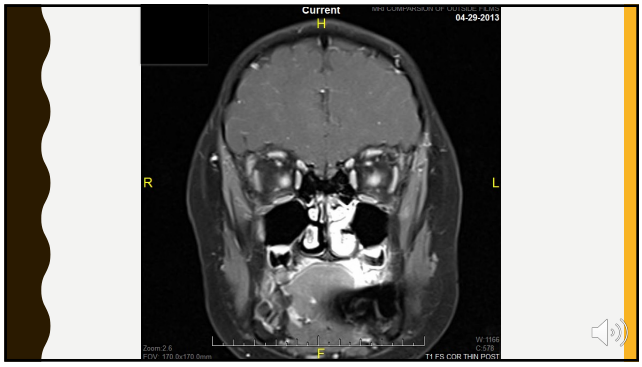
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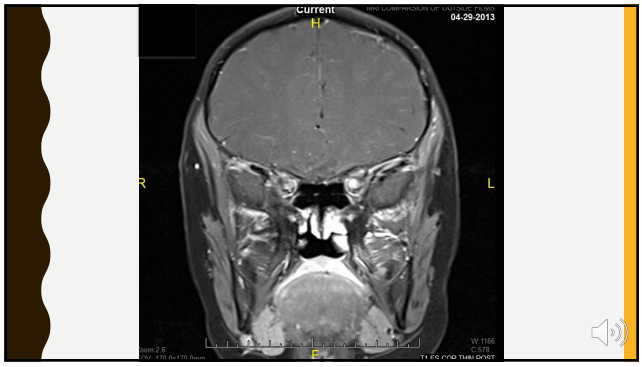
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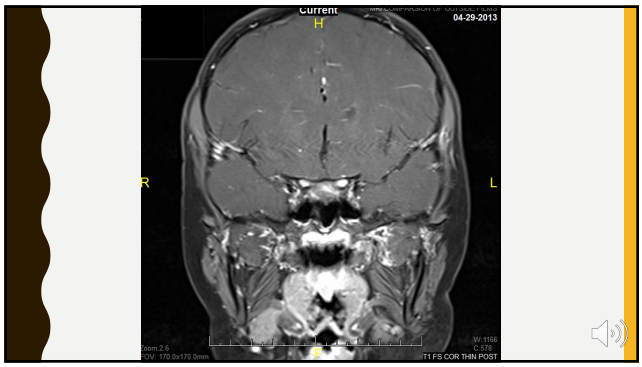
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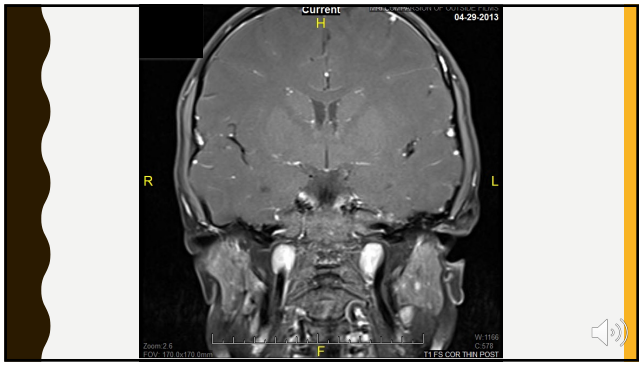
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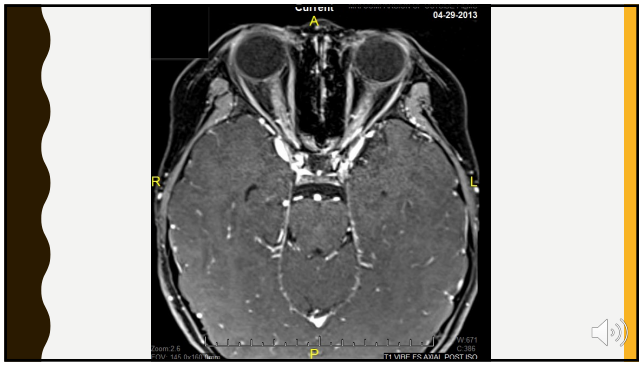
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BLOOD TESTS

- 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

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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

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TREATMENT

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

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FOLLOW-UP

- VA HOD1
  - OD 20/100
  - OS 20/800
- VA HOD2
  - OD 20/70
  - OS 20/200
- VA HOD3
  - OD: 20/20
  - OS: 20/50
- Year 2 VA
  - OD: 20/20
  - OS: 20/20
- Year 2 HVF
  - Reliable and full OU

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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

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PON1

JAMA Ophthalmology | Original Investigation

Assessment of Pediatric Optic Neuritis Visual Acuity Outcomes at 6 Months

Writing Committee for the Pediatric Eye Disease Investigator Group (PEDIG)

JAMA Ophthalmol. 2020;138(12):1253-12

The Pediatric Optic Neuritis Prospective Outcomes Study

Two-Year Results

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

Neurologic Diagnosis at 2 Years	N
Isolated Unilateral	9 (35%)
Isolated Bilateral	3 (12%)
Acute disseminated encephalomyelitis (ADEM)	2 (8%)
Myelin Oligodendrocyte Glycoprotein (MOG)	6 (23%)
Multiple Sclerosis	3 (12%)
Neuromyelitis Optica Spectrum Disorder (NMOSD)	3 (12%)

N=30 Eyes			
N (%) eyes within age-normal VA range	(20/32 to 20/800)	(20/16 to 20/32)	(20/16 to 20/32)
Median (25th, 75th percentile)	13 (43%)	2 (7%)	2 (7%)
N (%) eyes with <20/200 VA	7 (23%)	1 (3%)	1 (3%)
N (%) eyes with <20/800 VA			

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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

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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

- Vsc F&F OU
- Tpalp soft OU
  Pupils 4->2, 4.5->2.5 OU, no rAPD
- Ext Exam 1.5 mm ptosis OD
- Portable SLE normal

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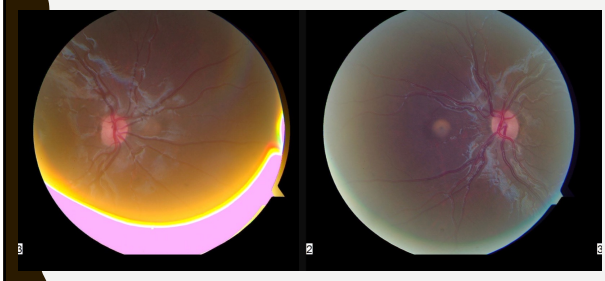

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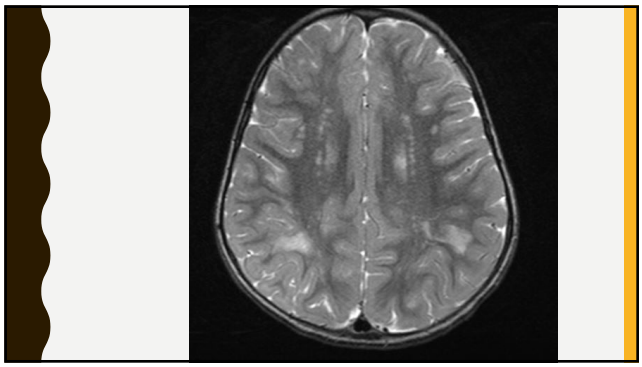

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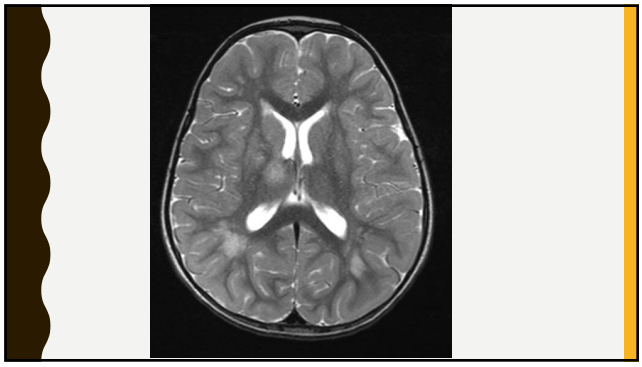

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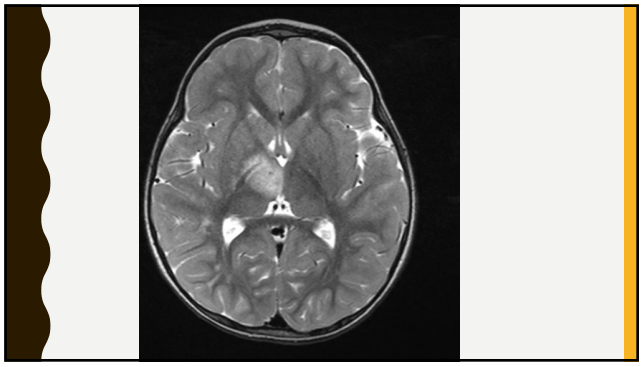

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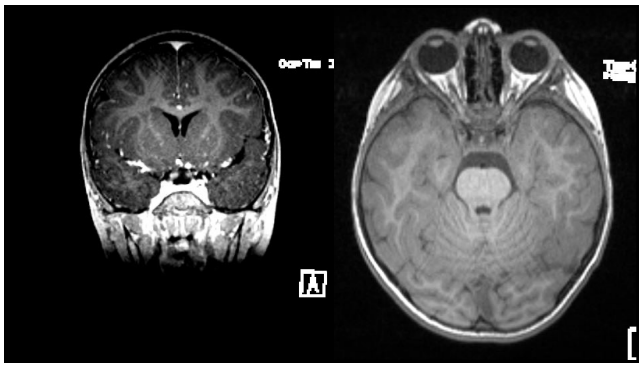

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PERTINENT LAB WORKUP

- Normal CBC
- LP protein 29, Glucose 60
  - RBC 1, WBC 11 (11 PMN, 66 L, 23 M)
  - MBP 8.02 (high)
  - Culture negative
  - IgG synthesis and other CSF studies normal
- Infectious workup negative

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DIAGNOSIS

- Bilateral optic neuritis
- Right horner syndrome
- Multifocal white matter lesions consistent with demyelinating disease/ADEM
  - MOG antibody added to lab work -> Positive

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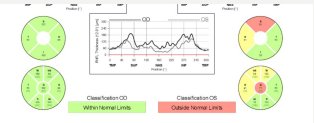
COURSE

- 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 os
  - No further episodes



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MOG IN PON1


Letters JAMA Ophthalmology May 2021 Volume 139, Number 5
RESEARCH LETTER
MOG-IgG Among Participants in the Pediatric Optic Neuritis Prospective Outcomes Study

- 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)

	MOG+	MOG-
Female	6/7 (86%)	3/6 (50%)
Bilateral	4/7 (57%)	2/6 (33%)
Presenting VA (median)	1.7 logMAR(~20/1000)	0.4 logMAR (20/50)
6 month VA (median)	0.1 logMAR (20/25)	0 logMAR (20/20)

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

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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 edema
  - 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

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NMO SPECTRUM DIS

- Inflam
  axonal
- Diseas
- Chara
  weakn
- Rarely
- Suspe
- Visual
- Diagn

Immunotherapy	Acute Treatment	Chronic Treatment
Steroids	X	
Plasmapheresis	X	
IVIG	X (retrospective study, when plex is not available)	
Azathioprine		X
Mycophenolate mofetil		X
Rituximab		X
Emerging treatments	**Mechanism**	
Eculizumab	Anti-CD5 prevents complement cascade, 1st FDA approved treatment specifically for NMOSD	
Satralizumab	IL6 receptor antagonist blocks inflammation and blood brain barrier permeability	
Tocilizumab	IL6 receptor antagonist blocks inflammation and blood brain barrier permeability	
Aquaporumab (preclinical)	Anti-AQP4 monoclonal antibody competes with AQP4	

International consensus diagnostic criteria … spectrum

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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 plex not available)
  - If not suspicious for NMO, most practitioners in PON1 still treated with IV steroids although there is no definite consensus

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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 q3 months after treatment with OCT and visual field
- I repeat the MRI at 2 years (if not before)

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THANK YOU!

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