46 year-old woman

- Decreased vision x 3-4 months OS > OD
- Transient visual obscurations
- Diplopia a few months ago, not now
- + nausea, vomiting, pulsatile tinnitus
- Recent vertigo, balance issues, dx with seizures
- Significant headaches, since decompression of Chiari malformation 13 years ago
- Scheduled for surgery for herniated disc in neck
- Last eye exam – 2 years prior: normal

Examination Results

- VA: OD 20/70 OS 20/100
- Color (Ishihara): OD 0/14 OS 0/14
- Pupils: PERRL (+ 0.3 log) APD OS
- Normal motility (-) abduction deficit
- Normal anterior segment exam
- IOP: OD 21 mm Hg OS 22 mm Hg
- BP: 140/90
Day of Initial Presentation

10 days after initial presentation

Bilateral optic nerve sheath fenestration
V-P shunt

Progressive vision loss OU over the next 1-2 months
– ultimately to the level of NLP OU
IIH or PTC can have devastating vision loss!!
Idiopathic Intracranial Hypertension Treatment Trial (IIHTT)

- ClinicalTrials.gov identifier: NCT01003639
- Information obtained from: ClinicalTrials.gov on March 26, 2010
- NORDIC (Neuro-Ophthalmology Research Disease Investigator Consortium)
- A Multicenter, Double-blind, Randomized, Placebo-controlled Study in Subjects With Idiopathic Intracranial Hypertension With Mild Visual Loss

Weight-Reduction and/or Low Sodium Diet Plus Acetazolamide vs Weight-Reduction and/or Low Sodium Diet Plus Placebo

**CASE 1**

42 year old woman

- Noticed right eye has been pointing upward x 1 month
  - Getting progressively worse
- Denies diplopia
- History of poor vision OD due to macular scar
• Recently saw PCP due to not feeling well
• Right arm weakness
• Slurring words
• Difficulty swallowing
• Some breathing difficulties

• PCP ordered an MRI to r/o MS
  – Reported to be normal
• Pt also went to local ER – another MRI
  – Normal - no etiology determined
  – Pt scheduled for neurology consult in 2 months
• Neurologic Exam
  – Weakness of neck flexor muscles
  – Weakness of right upper extremity

Myasthenia Gravis

• Acetylcholine receptor antibodies
• Binding **** 1500 (normal < 0.30)
• Blocking *** positive 75 (normal <15)
• Modulating *** positive
• All thyroid tests negative
• Chest CT

• Admitted to hospital for evaluation / treatment for fear of myasthenic crisis
  • Plasmapheresis (ICU), IVIG, Mestinon, Prednisone
CASE 2

66 year-old woman with droopy lids

- Hx of Grave’s disease and thyroid eye disease
- S/p lid surgery because of lid retraction (1996)
- Was told then that as she aged, her lids would get more droopy
- Wants to get lids surgically lifted
- Lids are interfering with vision
- Occasional diplopia, mainly when tired or when reading, seems stable since thyroid problems

Systemic Hx:
- HTN x 20 yrs
- Hypercholesterolemia
- S/p TIA in 2002
- Grave's disease
- Seizures
- Anemia
- Osteoarthritis
- S/p knee replacement complicated by blood clots
- S/p TMJ surgery in 1987
- Sleep apnea
- BPPV

- Followed by: cardiologist, gastroenterologist, endocrinologist, otolaryngologist, hematologist and PCP
• VA: OD 20/20 and OS 20/20
• Color: OD 14/14 and OS 14/14
• PERRLA (-) RAPD
• CF: Full OU when lids held
• Exophthalmometry: OD 25 mm and OS 25 mm
• SLE: EBMD OU
• TA: OD 13 mm Hg and OS 13 mm Hg
• DFE: large cupping OU (-)edema, (-) pallor
• Normal neurologic exam: no weakness
• Labs:
  – TSH
  – T3\T4
  – Acetylcholine Receptor Antibodies
    • Binding **H 0.34 (normal <0.3)
      – Binding repeated **H 0.47
    • Blocking
    • Modulating

• Chest CT
  – No thymoma

• Treatment
  • Mestinon 60 mg tid
    – Significant improvement in ptosis
    – Lid is up most of the day
Mestinon (pyridostigmine)

- Cholinesterase inhibitor
- Inhibits destruction of acetylcholine by cholinesterase
- Allows greater transmission of nerve impulse across neuromuscular junction
- Longer duration of action and fewer GI side effects as compared with neostigmine

Mestinon

- Side effects
  - Muscarinic
    - Nausea, vomiting, diarrhea, abdominal cramps, increased peristalsis, salivation, and bronchial secretions, miosis, diaphoresis
  - Nicotinic
    - Muscle cramps, weakness
    - Take with meals to decrease muscarinic symptoms
    - Sometimes other medications given to decrease side effects

CASE 3
42 year-old woman with diplopia

- Vertical diplopia x 6 weeks
  - Was rubbing eye a lot prior to onset of diplopia
- Progressively worsening, worse in am
- Occasional headaches
- OD feels heavy / strain
- Right eye seems lower than left eye

Systemic Hx:
- S/p 6 full term births
  - Pregnancy related anemia
- No meds
  - Left arm feels numb at times / falls asleep
- Smokes 1 pack of cigarettes/day x 25 yrs
- Fam Hx: HTN, stroke

VA: OD 20/30 and OS 20/20
- Color: OD 7/7 and OS 7/7
- PERRL (‐) RAPD
- HVF: normal field in each eye
- Palpebral apertures: 11 mm OD and 10 mm OS
- Exophthalmometry: 21 mm OD and 19 mm OS
- TA and DFE: normal
- Normal neurologic exam
Need to educate pts to stop smoking. Tobacco use can make thyroid orbitopathy worse.
CASE 4

93 year old woman

- Sudden onset vertical diplopia
  - X 1 week
  - At distance and near
  - Relief with closing either eye
- Associated blur
- Left upper eyelid droopy
  - X 1 week
- Eye pain OU x 1 week
- Generalized weakness x 1 week

- Systemic history
  - Hypertension x 30 years
  - Hypercholesterolemia
  - Arthritis
  - Ovarian cancer 30 years ago
• VA: 20/25- OD 20/20- OS
• Color 13/14 OD 13/14 OS
• (·) RAPD
• CF: full OU
• IOP: 10 mm Hg OU
• DFE: Healthy optic discs, small cupping OU
• (·) edema OU, (·) pallor OU
• Neurologic examination
  – Mild left upper extremity weakness

Palpebral apertures: 11 mm OD and 7 mm OS
Exophthalmometry: 17 mm OD and 18 mm OS
Ocular Motility

Head tilt: 20 right hyper on right head tilt, and 18 right hyper on left head tilt

What is the cause of the supraduction deficit?
What is the cause of the vertical misalignment / supraduction deficit?
• CN III Palsy – superior division
• Myasthenia Gravis
• Thyroid Orbitopathy
• Skew Deviation
• CN IV Palsy

What is the cause of the vertical misalignment / supraduction deficit / ptosis?
• CN III Palsy – partial ? superior division?
  – Forced Duction: negative (no restriction)
• Myasthenia Gravis
  – Forced Duction: negative (no restriction)
• Orbital Mass
  – Forced Duction: positive (restriction)
• Thyroid Orbitopathy
  – Forced Duction: positive (restriction)
• Skew Deviation
  – Torsion: higher eye intorted
• CN IV Palsy
  – Torsion: higher eye extorted
Work-Up

- Could be a partial CN III palsy
  - Get MRI / MRA or CTA to r/o aneurysm
- Get labs to r/o other causes
  - CBC with differential, platelet count, ESR (Westergren), C-reactive protein
  - Lyme titer
  - RPR, FTA-ABS
  - ACE
  - Acetylcholine receptor antibody testing (binding, blocking and modulating),
  - TSH, T4 and anti-Thyroid antibodies (anti-thyroperoxidase and anti-thyroglobulin)

Results

- MRI report
  - mild bilateral proptosis
  - prominent orbital fat
  - mild fatty atrophy of inferior, lateral, and medial rectus muscles OU
- Lab testing
  - elevated TSH at 9.55
  - T3 at 37
  - thyroglobulin antibodies at 1790
  - thyroid peroxidase antibodies at > 1000

Confirms thyroid dysfunction and likely thyroid eye disease / Grave’s disease.

Diagnosis / Treatment

- DX: autoimmune thyroid disease with subclinical hypothyroidism and thyroid orbitopathy
- Endocrine consult
- started on levothyroxine 25mcg daily
6 week follow-up
Pt reports no diplopia x 2 weeks

CASE 5

33 year-old man
• CC: Vertical diplopia x 2 days which resolved 2 days later. Now eye feel strained and having difficulty reading.
• Systemic History
  – Bells Palsy 4 months ago, affected lower left side of face, treated with oral prednisolone
• Medications: None
Exam Findings

BCVA:  
OD 20/20
OS 20/20

Pupils: Isocoric poorly reactive to light but greater response to near stimulus

Color:  
OD 14/14
OS 14/14

Confrontation Fields: Full to finger counting OU
LIGHT/NEAR DISASSOCIATION PUPILS (5 Causes)

- AMAUROTIC (blind eye)
- TONIC
- ARGYLL ROBERTSON
- TECTAL (Dorsal Midbrain Syndrome)
- ABERRANT REGENERATION OF CN III

Exam Findings

SLE: Endothelial deposits OU; mild conjunctiva injection OU; (-) cells or flare

GAT: 10 mmHg OD
9 mmHg OS

DFE: C/D
OD 0.4/0.4
OS 0.4/0.4

optic nerves distinct; (-)pallor
vitreous opacities OU
Assessment:
Suspect Dorsal Midbrain Syndrome

Plan:
Order MRI of brain with and without contrast
Order bloodwork to rule out infectious etiology

Follow-Up 3 days Later
Patient reports no new visual symptoms since last visit.
No change in vision or afferent system testing
MRI completed and read as normal
Lab testing results remarkable for elevated IgG Epstein Barr virus antibody

EOMs at follow-up
No restriction in eye movements, no eyelid retraction
Patient saw neurologist for a lumbar puncture to rule out any infectious or inflammatory etiology

CSF: elevated WBC, IgG, and >5 oligoclonal bands

MRI spine: Multiple enhancing lesions in the cervical spinal cord

DX: Demyelinating Disease
Start Copaxone treatment

CASE 6

63 year-old woman

- Sudden onset diplopia x 5 days
  - At distance and near
  - Horizontal and diagonal
  - Worse in right gaze
  - Resolves with covering either eye
- Headache 2 days ago
  - Above right eye, frontal
• SYSTEMIC HEALTH
  – Diabetes x 15 years
  – Hypertension x 15 years
  – Hypercholesterolemia
  – Arthritis
  – s/p stroke x 3 (last 5 years ago)
    • Residual weakness
  – Medications
    • Naprosen, Detrol, Minocycline, Enalapril, Nefedipine,
      Aggrenox, Alendronate, Metformin, and Pravastatin.

• OCULAR HISTORY
  – Cataracts
  – Glaucoma (longstanding)
    • s/p PI OU
    • Supposed to be on Cosopt and latanaprost
      – Ran out of meds yesterday

• SOCIAL HISTORY
  – Smokes 3-4 cigarettes / weekend x years
  – Few beers per weekend
• VA: 20/25 OD  20/30 OS
• Color 14/14 OD  14/14 OS
• (-) RAPD, anisocoric
• Bright: 3 OD 2.75 OS  dim: 4 OD, 3.75 OS
• CF: full OU
• Palpebral apertures: 7 mm OD  7 mm OS
• IOP: 20 mm Hg OD,  21 mm Hg OS
• DFE: Large cupping OU
• (-) edema OU, (-) pallor OU
• Neurologic examination
• BP: 178/94, pulse 50bpm

Head tilt testing demonstrated 16 right hyper on right
head tilt, and 12 right hyper and 14 eso on left head tilt
What is the cause of the adduction deficit and infraduction deficit?

- CN III Palsy
- Thyroid Orbitopathy
- Myasthenia Gravis
- INO and Skew Deviation
Double Maddox rod testing:
- 15-20 degrees of incyclotorsion OD
- 15-20 degrees of excyclotorsion OS

Management

• INO / Skew
  – Likely secondary to stroke
    • In setting of elevated BP and low pulse
• Admit to hospital for work-up
  – MRI
    • Acute brainstem lesion noted

CASE 7
56 year old woman

Double vision x 1 week with associated dizziness
Hx of HTN x 20 yrs
Dx with MS 10 yrs ago after leg weakness – no treatment
Hasn’t seen a neurologist in 6 years
1 week later

MRI consistent with MS
No other abnormalities found
Pt now under care of neurologist and being treated with Betaseron

CASE 8
54 year-old woman

• Pain in OD x 5 days
• Gray area in OD x 2-3 days
• Colors don’t seem as bright OD
• No other neurologic symptoms

VA OD: 20/200  OS: 20/20
• Color: 0/14 OD  14/14 OS
• PERRL (+) RAPD OD (1.8 log NDF)

• Neurologic Exam is normal
Suspect Optic Neuritis

- Get MRI to confirm enhancement of left optic nerve and r/o periventricular (or other) white matter changes
- Lab tests ordered to R/O infectious/inflammatory causes:
  - ANA
  - ACE
  - RPR
  - FTA-ABS
  - Lyme
  - ESR, etc
- ALL LABS WERE NORMAL
Pt is now NLP OD!

- Tx: IV Methylprednisolone x 3 days
- Followed by oral taper
- Labs all normal
- Lumbar Puncture: (+) oligoclonal bands, elevated IgG
- Not yet clinically definite MS
- Suggest tx with interferon-beta

2 months later
Optic Neuritis – Clinical History

- Young adult
  - More likely a woman
- Unilateral visual loss
- Progresses over hours to days
- 90% with pain, particularly with eye movement

Visual Prognosis

- Spontaneous visual recovery begins within 3 weeks in 80% of patients
- Improvement continues for up to 1 year
- If some improvement does not occur in 5 weeks, reconsider the diagnosis

Treatment Effect on Vision

- No difference between steroid and placebo groups at 6 months
- IV Steroids (not oral) may accelerate recovery by 2 to 3 weeks

(NEJM 326:581, 1992)
Probability of Recurrent Optic Neuritis in Either Eye by Treatment Group

- 41% Prednisone
- 25% Intravenous
- 25% Placebo

P=0.004 Prednisone vs Placebo
P=0.003 Prednisone vs Intravenous

Oral prednisone in standard doses is likely contraindicated in optic neuritis!

IV pulsed methylprednisolone followed by oral prednisone can postpone the development of MS!

(this effect only lasts for the first 2 years)
Optic Neuritis - Risk of MS Based on MRI

- 15 year follow up data
- 0 lesions 25%
- > or = 1 brain lesion – 72%
  - 1 lesion 60%
  - 2 lesions 68%
  - 3 or more lesions 78%

Factors Predicting Low Risk for MS with Normal MRI

- No patients with the following features developed MS
  - Severe disc edema (21 pts.)
  - Hemorrhages, disc or peripapillary (16 pts.)
  - Macular exudates (8 pts.)
  - Absence of pain (18 pts.)
  - VA – NLP (6 pts.)

Can anything else be done to postpone or prevent progression to MS?
Immune Modulating Therapy

- Interferons (Avonex, Rebif, Betaseron)
- Glatiramer acetate
- Natalizumab

- Established therapy for MS
  - Decreases exacerbations
  - Decreases new MRI lesions
  - Decreases disability

A combination of pulsed IV methylprednisolone (Solu-Medrol) + interferon-beta or glatiramer therapy can postpone (? prevent) the development of clinically definite M.S.!

Current Treatment of Optic Neuritis: Abnormal MRI

- IV methylprednisolone (1 g/d x 3d)
- Oral prednisone taper (1 mg/kg/d x 11d, 4-d taper)
- Immunomodulating therapy
- Avoid oral prednisone alone

With Normal MRI

- Consider IV methylprednisolone
- Avoid oral prednisone alone
- Clinical follow up and repeat MRI periodically

Gilénya
- First FDA approved ORAL immunomodulating agent
- Sequesters lymphocytes where there is an P1P receptor
- Higher dosages are associated with macular edema
- Not used for clinically isolated events
- Newly Approved:
  - Aubagio (teriflunomide)
  - Once daily

Differential Diagnosis
- Hereditary
  - Leber’s hereditary optic neuropathy
- Infectious
  - Syphilis, Cat-Scratch fever, Lyme disease
- Inflammatory
  - Sarcoidosis
- Immune – Neuromyelitis optica
- Vascular
- Compressive/Infiltrative
Additional Tests if Atypical

- RPR/FTA/Lyme/Bartonella titers
- ANA, ESR
- ACE level/CXR
- Mitochondrial DNA testing for Leber’s or other mitochondrial processes
- Neuromyelitis optica (NMO) antibody
- CSF analysis (lumbar puncture)

CASE 9

12 year old girl

- reduced VA OS X 4 days
- not feeling well for 2-3 weeks – nasal congestion, pressure / pain over left eye, sometimes when moves eyes
- PCP Rx’d Biaxin (macrolide antibiotic – interferes w/ protein synthesis) and Prelone oral steroid (Prednisolone syrup)
- Systemic Hx: asthma, many food allergies
- VA OD 20/20 OS CF at 2’ (SOSH 1/10 temporally)
- PERRLA (+) APD OS (>1.8 log)
- Decreased red saturation and brightness sense OS
- Normal efferent system
Suspect Optic Neuritis

- Pt admitted to Children’s Hospital
- Get MRI to confirm enhancement of left optic nerve and r/o other abnormalities
- Lab tests needed, including:
  - ANA
  - ACE
  - RPR
  - FTA-ABS
  - Lyme
  - ESR
  - C-reactive protein, etc
ONTT

- Diseases associated with optic neuritis
- (must be screened for these)
  - Sarcoid
  - Systemic Lupus Erythematosis
  - Syphilis
  - Lyme disease
  - Other connective tissue disorders

MRI

- Enlargement and enhancement of left optic nerve (intraorbital portion)
- No indication of abnormal parenchymal signal intensity or enhancement

Lab Testing

- Remarkable for
  - Positive ANA
  - Titer of 1:1280
Causes of a Positive ANA

- Lupus (SLE)
- Scleroderma
- Lupus Erythematosis
- Polymyositis / Dermatomyositis
- Rheumatoid arthritis
- Sjogren's syndrome
- Normal finding (with aging and being female)
- Some drugs (procainamide, hydralazine, isoniazid, antibiotics)
- Infectious mononucleosis (mono) and other infections
- Chronic liver disease

Positive ANA

- Order additional testing
  - Anti-ds DNA (for Lupus)
  - SS-A / SS-B (for Sjogren's)
  - p-ANCA / c-ANCA (for vasculitis / Wegner’s)
  - RF

Lab Testing

- Remarkable for
  - Positive ANA 1 : 1280
  - Elevated Anti-SS-A Ab (110)  normal range 0-19
  - Elevated Anti-SS-B Ab (87) normal range 0-19

- Suggestive of Sjogren’s Disease
Subsequent lip biopsy (salivary glands) was diagnostic (cluster of inflammatory cells) of Sjogren’s Disease.

- No definite indication of Lupus, Rheumatoid Arthritis at this point.
- IV Methylprednisolone. Began treatment with CellCept (immunosuppressant), Prednisone taper.

Sjogren’s Syndrome

- Autoimmune disorder
- Typically in 4th-5th decade, but any age possible
- Associated with the sicca complex
  - Dry mouth
  - Dry eye
  - Lymphocytic infiltration of the exocrine glands
    - (10% can get non-Hodgkin lymphoma)
  - Any organ can be affected
  - 2nd most common rheumatologic disorder after SLE

Sjogren’s

- Lab test
  - Elevated ESR in 80%
  - + RF possible
  - Anemia
  - Leukopenia
  - Anti-SS-A
  - Anti-SS-B
  - Antisalivary duct antibodies (in secondary Sjogren’s)

- Biopsy (definitive diagnosis)
  - Salivary gland
  - Lower lip
CASE 10

40 year old asymptomatic woman

- Hx of keratoconus
- Came in for CL eval, and anterior uveitis was noted
- On Pred Forte qid OS and Nevanac (NSAID prodrug) qid OS
- Photosensitivity – stable x years
- Denies other symptoms

Systemic Hx:
- Hypercholesterolemia – no meds
- S/p removal of axillary lymph nodes (infxn?)
- S/p 2 full term uncomplicated pregnancies
- Asthma
- Meds: Advair, Combivent, Zyrtec, Claritin
• VA: OD 20/25 OS 20/60
• Color: 13/14 OD and 0/14 OS
• PERRL (+) >1.8 log RAPD OS
• No ptosis or proptosis
• Normal ocular motility exam
• SLE: only few residual cells
• TA: OD 18 mmHg OS 21 mm Hg
• Normal neurologic exam
Labs for Optic Neuropathy

- CBC
- C-reactive protein
- ESR
- Platelet count
- Lyme titer (if + get Western blot IgG and IgM)
- ANA with reflex titer
- ACE
- RPR & FTA-ABS
- Vitamin B 12
- Folic acid
- Methylmalonic acid
- SPEP

Work-Up

- MRI – brain & orbits w/ w/o gad
  - Arnold Chiari I malformation
  - No other structural abnormalities or abnormal enhancement
- Labs
  - CBC **elevated eosinophils 11.6%**
  - Platelets
  - ESR **H 85 mm/hr**
  - CRP **H 1.22**
  - Folate
  - B12
  - Lyme titer
  - RPR / FTA-ABS
  - ACE **H 254**
  - ANA

Chest CT

- Findings compatible with longstanding sarcoidosis
  - Bulky lymphadenopathy
  - Parenchymal changes
  - Scarring
- Lower lobe infiltrate? Possible superimposed bacterial pneumonic component
- Pt referred to pulmonologist and surgeon
  - Lung biopsy performed (+) for sarcoid
Neurosarcoid

- Occurs in 5-15% of pts with sarcoid
- CN VII is commonly affected
- CN II and VIII also affected
- Can be a mononeuropathy, peripheral nerve involvement, CNS involvement
- Can see leptomeningeal enhancement
- Active inflammation responds very well to steroids
  ([Oral steroids are fine for sarcoid])

CASE 11
20 year-old man

- Pain OD on upgaze x few days
- Today, vision OD is “off”
- Denies diplopia, transient vision loss
- Denies headache
- A few days ago, he felt feverish, but did not check his temperature
- Fam HX: Father dx with Lupus in 20s

BCVA: OD 20/50 and OS 20/20
- Color 14/14 OD and 14/14 OS
- Pupils – pharm dilated
- CF: full OU
- HVF: essentially normal OU
- SLE and IOP normal OU
- BP: 104/70
- Temp: 98.8 degrees

Humphrey Visual Field: At initial presentation. Note only slightly enlarged blind spot in the right eye, and fairly preserved central visual field.
Pt denies any rashes (only when asked)
- He does admit to a scratch by a cat (kitten) several weeks ago (only when asked)
- A few weeks ago, his right eyelid was swollen
- Pt has several scars on his forehead, above right eye, and on his nose

Labs Ordered – told to have done today!
- CBC
- C-reactive protein
- ESR
- Platelet count
- Lyme titer (if + get Western Blot Lyme IgG and IgM)
- ANA with reflex titer
- ACE
- RPR
- FTA-ABS
- Bartonella Quintana titer
- Bartonella Henselae titer
Follow-up 5 days later

- Pt notes a spot in right vision, that is getting larger
- Reduced central vision
- Since last visit, has had chills and fever
- Has also had headache
- Decreased appetite
- Unable to work – doesn’t feel right
- Labs not done until 2 days ago – not complete

Lab results (so far)

- ANA (+) titer and pattern not yet known
- Lyme titer is (+) WB IgG (-), IgM (+)
- ACE slightly elevated at 70
- ESR: 44
- CRP: pending
- Bartonella titers: pending

- BCVA: OD 20/200 and OS 20/20
- Color 1/14 OD and 14/14 OS
- Pupils – trace RAPD OD
- CF: very large blindspot OD
- HVF: large blindspot OD – extending past fixation and superiorly out to 10 degrees
- SLE and IOP normal OU (-) cells
Humphrey Visual Field: 6 days after initial presentation. Note significant increase in blind spot in the right eye. The left field was unreliable due to patient fatigue.

Follow-Up: 6 days after initial presentation
- Need to r/o Lyme, sarcoid, auto-immune disease
- Ds DNA (-)
- Repeat ACE (-), CXR (-)
- LP (-) for Lyme, sarcoid

- Bartonella titers
- Bartonella Quintana (-)
- Bartonella Hensalea (+)
- (+) IgG > 1:2560
- (+) IgM > 1:800
- DX: Cat-scratch Disease

Follow-Up: 15 days after initial presentation
Neuro-retinitis

- Cat-scratch
- Sarcoid
- Syphilis
- Lyme
- Toxo

- NOT typical in MS

Treatment:

- Antibiotics
  - Doxycycline (pt vomited every time he took this medication)
  - Rifampin
  - Bactrim prescribed in place of Doxycycline
  - Pt then switched to Azithromycin by Infectious Disease
Cat Scratch Disease

Typically transmitted by a kitten (by a scratch or a lick)

Only a minority of the exposures to B. Henselae result in cat-scratch disease. The ability of the cat to transmit the disease is transient

Most cases occur in fall / early summer - related to kitten births and flea infestations

80% of cases occur in patients under age 21

Starts with local infection, then lymphadenopathy, and rarely progresses – e.g. Neuroretinitis, etc.

Cat Scratch Disease

- Treatment / Response:
  - Excellent prognosis - Most cases are self-limiting and fully resolve, even when involving the CNS
  - Drugs of choice – Bactrim, Gentamicin, Ciprofloxacin, Rifampin, Azithromycin

Humphrey Visual Field: 34 days after initial presentation. Note reduction in blindspot size in the right eye corresponding with a reduction in optic disc edema. A central scotoma persists in the right eye, related to the macular star and the reduced visual acuity.
Follow-Up: 34 days after initial presentation

CASE 12
28 year old woman

- 2 weeks prior, noticed blurry vision OS
- Blur persists
- No pain in the left eye
- 3 days prior, noticed pain on eye movements OD
- 1 day prior noticed decreased vision inferior OD
- She is now having difficulty functioning

OTHER SYMPTOMS:
- Weakness and tingling left thigh
  - Several episodes over past few years
  - Thought to be sciatica
  - Thought to be related to being over-weight
    - Lost 30 pounds, but symptom still recurred

SYSTEMIC HEALTH:
- asthma

MEDICATIONS:
- Albuterol, Advair

OCULAR HISTORY:
- Unremarkable

SOCIAL HISTORY:
- unremarkable
• BCVA: OD 20/25 and OS 20/40
• Color 14/14 OD and 10/14 OS
• 25% reduced red saturation OS
• 25% reduced brightness sense OS
• Pupils – pharm dilated
• Normal ocular motility exam

• Slit Lamp Exam: normal OU
• TONOMETRY: OD-16 mm Hg, OS- 16 mm Hg
• BP: 132/92
DDX

- Optic Neuritis OD, Optic Neuropathy OS
- ? Demyelinating Disease

- WORK-UP
  - Lab testing
  - MRI brain and orbits with contrast
  - MRI spine
  - Possible lumbar puncture
TREATMENT:
- IV steroids x 3 days

RESULTS
- MRI brain and orbits – mild enhancement of posterior right optic nerve
- MRI spine: lesion at C3 level
- Pt diagnosed with Multiple Sclerosis at hospital

FOLLOW-UP
- Eye pain returns (was better on steroids)
- Severe headaches
- Leg paresthesias recur (better on steroids)
• BCVA: OD 20/25 and OS 20/20
• Color 14/14 OD and 10/14 OS
• Pupils – equivocal RAPD OS
• Normal ocular motility exam
Because vision did not improve significantly after steroid treatment, and there was spine involvement but no brain involvement, need to consider:

- NMO (neuro-myelitis optica or Devic’s disease)
- Order NMO antibody testing
- Also test for other causes of optic neuritis
- (ANA, Lyme, ACE, FTA-ABS, etc)

NMO antibody was POSITIVE
Positive ANA, positive Sjogren’s antibodies
Pt started on Azathioprine
Then put on Rituximab
— some improvement in filed of right eye
Neuromyelitis optica is, like Multiple Sclerosis an inflammatory, demyelinating syndrome of the central nervous system.

Multiple Sclerosis affects the CNS
- optic nerve
- spinal cord
- brain

Neuromyelitis Optica (NMO) (Devic’s Disease) preferentially affects the optic nerve (optic neuritis) and spinal cord (myelitis).

Within 5 years of disease onset, more than 50% of patients with relapsing neuromyelitis optica are blind in one or both eyes or require ambulatory help.

Typical Features of NMO:

- myelitis with
  - muscle weakness
  - sensory dysfunction
  - bladder dysfunction

- optic nerve (optic neuritis)

Spinal cord

Neurogenic respiratory failure can occur—serious

Exceedingly rare in multiple sclerosis


The detection of neuromyelitis optica immunoglobulin G (NMO-IgG), an autoantibody, in the serum of patients with neuromyelitis optica, distinguishes neuromyelitis optica from other demyelinating disorders

NMO-IgG binds to aquaporin 4, which is the main channel that regulates water homeostasis in the Central nervous system.


NMO-IgG attacks proteins of the AQP4 channels on Astrocytes (toxic to them). The resultant immune reaction, causes Demyelination. This is different than what happens in Multiple Sclerosis.

CASE 13
63 year old woman

- 3-week history of left eye and head pain
- The pain keeps her up at night
- Then, the left eyelid began to droop
- 2 weeks ago, she noticed double vision
- Decreased appetite
- Weakness and fatigue

SYSTEMIC HISTORY:
- Lung cancer 2 years ago
- Surgery, radiation, chemo
- Still undergoing treatment
- Otherwise unremarkable

VA OD 20/40 OS 20/40
- Normal color vision
- (-)APD
- CF: Full OU
- IOP normal
- BP normal
- ONH: (-) pallor OU, (-)edema OU
• Emergent hospitalization to rule out aneurysm
• MRI and MRA negative
• While in hospital CN III palsy progressively worsened
• Cerebral angiogram negative
• Lumbar puncture
• Diagnosed with meningeal carcinomatosis
LEPTOMENINGEAL CARCINOMATOSIS

- Also called neoplastic or carcinomatous meningitis
- Invasion to and subsequent proliferation of neoplastic cells in the subarachnoid space
- Substantial rates of morbidity and mortality
- MRI with contrast can detect leptomeningeal enhancement
- Diagnosis confirmed with CSF cytometry
- Sites of origin
  - Lung
  - Breast
  - Melanoma
  - Medulloblastoma

LEPTOMENINGEAL CARCINOMATOSIS

- Because the leptomeninges cover the cranial nerve roots, tumor seeding of the cranial nerves is not uncommon.
- Can cause symptoms either from encasement of the nerve or by direct invasion with subsequent axonal destruction and demyelination.
  - Can have cranial nerve palsies
- Symptoms include headache (50%), nausea, vomiting, seizures

CASE 14
56 Year old man

• Pain in and behind OD x 3 days
• Pain radiating to back of head
• Pain up to a 7/10 on pain scale
• He used friend’s unknown eye drop and ung in OD
• 2 days ago – felt dizzy and nauseous
• Then diplopia began
• Went to ER – put “drop” in eye, and prescribed ibuprofen for pain

• Hx of elevated BP (not compliant with meds)
• He snores and stops breathing while sleeping, but was never tested for sleep apnea
• Smokes ½ pack of cigarettes per day since age 16
• Hx of cellulitis of right foot a few years ago, for which he was on IV antibiotics

• VA: 20/20 OD 20/20 OS
• Color 14/14 OD 14/14 OS
• Right pupil non-reactive
• CF: full OU
• IOP: 20 mm Hg OD, 17 mm Hg OS
• FE: Healthy optic discs OU
• (-) edema OU, (-) pallor OU
• BP: 147/91
• Neurologic examination – Unremarkable
Ocular Motility

No torsion
What is the cause of an apparent CN III and CN VI palsy?

- CN III Palsy and CN VI palsy
  - Cavernous sinus
  - Orbital apex syndrome
- Thyroid orbitopathy
- Myasthenia Gravis
- Idiopathic Orbital inflammatory Pseudotumor

What is the cause of the diplopia and eyelid asymmetry?

- CN III Palsy and CN VI palsy
  - Eyelid asymmetry from ptosis
  - May or may not be associated pupil involvement
  - Reversing hyper deviation
  - More Eso worse away from affected eye
  - More Eso toward affected eye
    - Cavernous Sinus
    - Orbital apex
- Thyroid orbitopathy
  - Eyelid asymmetry from proptosis
  - No pupil involvement
  - Any motility pattern
- Myasthenia Gravis
  - Eyelid asymmetry from ptosis
  - No pupil involvement
  - Any motility pattern
• Eyelid Measurements
  – Palpebral apertures OD 10 mm, OS 9 mm
  – Lid crease: symmetric
  – Levator function: symmetric

Exophthalmometry
OD 23 mm, OS 18 mm
What is the cause of the apparent CN III and VI palsy with proptosis?

- Orbital Apex / Cavernous Sinus Syndrome
  - Unilateral
  - Can be painful

- Thyroid orbitopathy
  - Unilateral or bilateral
  - Can be painful
  - Eyelid retraction

Work-Up

- Right CN III and CN VI palsy
  - Localizes to right orbital apex or cavernous sinus
- Work-up Needed
  - CT, MRI with and without contrast, MRA, MRV
- DDX
  - Tolosa-Hunt syndrome, Cavernous sinus thrombosis, cavernous sinus fistula, sarcoid, Wegener’s granulomatosis, aneurysm, infectious, other inflammatory
- Urgency
  - Emergent – send to ER
  - Call ahead and let ER know of the findings, localization, and differential diagnosis

Results / Diagnosis

- MRI report
  - Inflammatory process in right cavernous sinus
- Other testing
  - No indication of vascular process, or any other etiology

-Diagnosed with Tolosa-Hunt Syndrome, and started on IV steroids
Tolosa-Hunt Syndrome

- Unilateral
- Intense pain around eye
- Ophthalmoplegia
- Possible involvement of CN III, IV, V, and VI
- Can have proptosis, fatigue, vertigo

Tolosa-Hunt Syndrome

- Exact cause is unknown
- Inflammation of cavernous sinus and/or superior orbital fissure
- Diagnosis of exclusion
- Need to rule out all other causes with labs, imaging, and LP
- Treat with steroids / good prognosis
- Can recur in 30-40% of cases

CASE 15
51 year old woman

- **CHIEF COMPLAINT:**
  - Gradual decrease in vision OD x months / year
  - C/o Pressure sensation behind right eye
  - Denies any other visual, ocular, or neurologic symptoms
  - (-) Headache

- **SYSTEMIC HISTORY:**
  - Has not been medically evaluated in 5 years
    - Due to lack of insurance
  - Thyroid dysfunction as a teenager – not currently treated
  - Osteoarthritis
  - Hit back of head in motor vehicle accident 3 yrs ago
    - No subsequent problems with eyes or vision

- **FAMILY HISTORY:**
  - Remarkable for diabetes, hypertension and stroke

- **CLINICAL EXAMINATION:** Initial Presentation
  - VA: OD 20/40 and OS 20/20
  - Color Vision (Ishihara) OD 0/14, OS 14/14
  - + red desaturation OD
  - + decreased brightness sense OD
  - > 1.8 log RAPD OD
  - CF: inferior temporal defect OD
  - Palpebral Apertures: OD 11 mm, OS 11 mm
  - Exophthalmometry: 21 mm OD, 20 mm OS
  - Ocular Motility: Normal ductions, versions, saccades
  - Cover Test: orthophoric posture - comitant
  - SLE: mild lens changes DU
  - TA: OD 17 OS 17
  - BP: 120/70
5 Months later

- CLINICAL EXAMINATION: Follow-up Presentation
  - VA: OD Light Perception and OS 20/20
  - Color Vision (Ishihara) OD 0/14, OS 14/14
  - + > 1.8 log RAPD OD
  - Palpebral Apertures OD 14 mm, OS 11 mm
  - Exophthalmometry: 5 mm of proptosis OD
  - Ocular Motility: restrictions OD
    - 80% abduction, 90% adduction, 50% infra/abduction

- TA: OD 16 OS 16
• MRI RESULTS:
  - Large, right, anterior-temporal apparent atypical sphenoid wing meningioma, with temporal and frontal intraparenchymal edema, and mass effect on the ventricles

Treatment
  - Pterional craniotomy and resection of apparent atypical meningioma
  - Resection of portion of sphenoid wing with placement of prosthetic orbital roof and lateral wall
  - PATHOLOGY REPORT:
    - Atypical meningioma with chordoid features
    - WHO grade II / III
    - Potential for more aggressive course
    - Radiation treatment recommended
• Meningiomas are benign and slow-growing in about 90% of cases. They arise from the meningeal brain coverings.

• Benign meningiomas fit with the WHO grade I classification, and recur only 7-20% of the time

• Less commonly, meningiomas can be atypical or anaplastic

• 6-8% of meningiomas are atypical, and have the tendency for local recurrence even after complete resection. These atypical meningioma correspond with the WHO grade II classification, and recur at a rate of 29-38%

• 2-3% of meningiomas are anaplastic and show signs of malignancy. They can recur (50-78%) and metastasize to other locations. They are classified as grade III in the WHO scale

• There is a difference in cytogenetic alterations between the benign meningiomas and the atypical and anaplastic meningiomas

• Meningiomas are further classified into 5 types: Meningiothelial, Fibroblastic, Transitional, Psammomatous, and Chordoid (more rare)

• The patient presented here had a relatively rare chordoid meningioma. Chordoid meningiomas get their name because they exhibit features that appear similar to chordomas. (clusters of spindle and epithelial cells in a myxoid matrix)

• Chordoid meningiomas have been associated with hematologic abnormalities (not in this case)
• Not all meningiomas are benign. They can recur, and less likely become malignant.

• Meningiomas mainly cause morbidity due to mass effect and compression.

• Prompt diagnosis and treatment is important to preserve optic nerve function.

THANK YOU.

ANY QUESTIONS?