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**Disclosures:**

- Paid consultant/speaker for:
  - Carl Zeiss Meditec
  - Regeneron Pharmaceuticals
  - Iveric Bio (Astellas)
  - Optomed
  - Apellis Pharmaceuticals
- Paid advisory board member for LENZ Therapeutics, Notal Vision, Ocuteira, Topcon, Tarsus, Genentech

All relevant relationships have been mitigated

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**OPTIC NEUROPATHY**

Can break down neuropathies into 4 diff diagnostic grps based on disc appearance:

Anomalous	Pale/Optic Atrophy	Normal	Swollen
<ul style="list-style-type: none"> <li>• ON hypoplasia</li> <li>• ON coloboma</li> <li>• Morning Glory</li> <li>• Optic disc pit</li> <li>• Tilted discs</li> <li>• Myelinated NFL</li> <li>• Megalopapilla</li> <li>• Posterior staphyloma</li> </ul>	<ul style="list-style-type: none"> <li>• Compressive optic neuropathy (may also be swollen or normal)</li> <li>• Nutritional/toxic optic neuropathy (may also be swollen)</li> <li>• Dominant/recessive optic atrophy</li> <li>• Assoc with neurodegenerative disease</li> <li>• Assoc with retinal dystrophies</li> </ul>	<ul style="list-style-type: none"> <li>• Optic neuritis (1/3<sup>rd</sup> swollen)</li> <li>• Posterior ischemic optic neuropathy</li> <li>• Traumatic optic neuropathy (acute mild swelling possible)</li> </ul>	<ul style="list-style-type: none"> <li>• Anterior ischemic optic neuropathy</li> <li>• Papilledema</li> <li>• Malignant HTN</li> <li>• Diabetic papillopathy</li> <li>• Inflammatory/infectious optic neuropathies (may also be pale)</li> <li>• Radiation optic neuropathy (may also be normal)</li> <li>• Disc drusen (pseudoedema)</li> <li>• Leber's Hereditary Optic Neuropathy (pseudoedema)</li> </ul>

\* DISCLAIMER: there is considerable overlap among these 4 groups

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**NEURO-OPHTHALMIC EXAM**

- **History:** Used as a guide along with age, gender, underlying illnesses, and disease risk factors shape the rest of the exam to confirm or eliminate each differential
- 3 most crucial qualifiers in determining etiology of VL
  - 1) Laterality
  - 2) Time course
  - 3) Associated symptoms

**Pattern/ Time Course of Vision Loss**

**CHECK VITALS (ESP BP)!!**

- Trauma/head injury?
- Previous surgeries/blood loss?
- Alcohol/drug use?
- Nutrition?
- Family history?
- Previous neuroimaging?
- Occupation?

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**NEURO-OPHTHALMIC EXAM**

**Abnormal Tests in Neuropathy (Afferent Visual Function)**

- BCVA (PHNI if neuropathy)
- RAPD
- Red desaturation & brightness comparison
- Color vision
- Contrast sensitivity
- Visual field
- Optic nerve head examination

**Diagnostic dilemma:** Is VL due to refractive error, amblyopia, media opacity, retinal lesion, ON or chiasmal disease???

**"Subjective APD"**

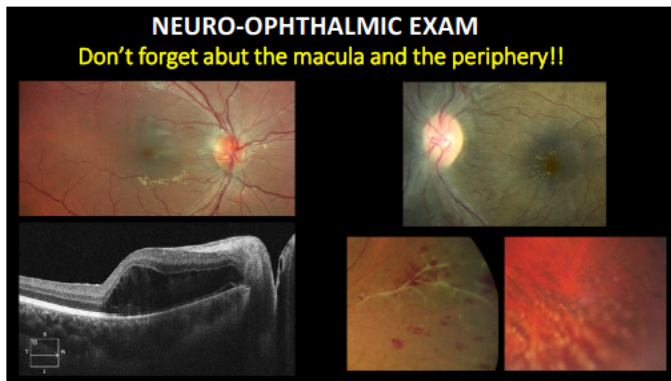
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**Clinical Distinction Between Optic Neuropathy vs Maculopathy**

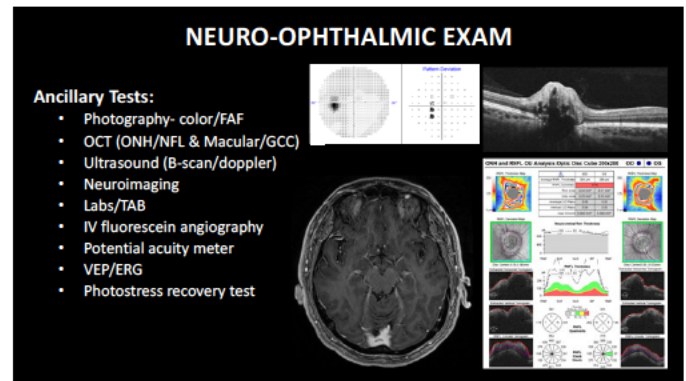
Symptom, Sign, or Test	Optic Neuropathy	Maculopathy
Metamorphopsia	Rare	<b>Common</b>
Darkening of vision	<b>Common</b>	Rare
Photopsia	Rare	<b>Common</b>
Pain	<b>Common in optic neuritis</b> , rare in other neuropathies	Rare
Dyschromatopsia	<b>Severe</b>	Mild
RAPD	<b>Common</b>	Rare (unless severe & asymmetric)
ERG (esp mfERG)	Normal	<b>Abnormal usually</b>
VEP	<b>Large latency delay</b>	Small latency delay

**Diagnostic dilemma:** Is VL due to refractive error, amblyopia, media opacity, retinal lesion, ON or chiasmal disease???

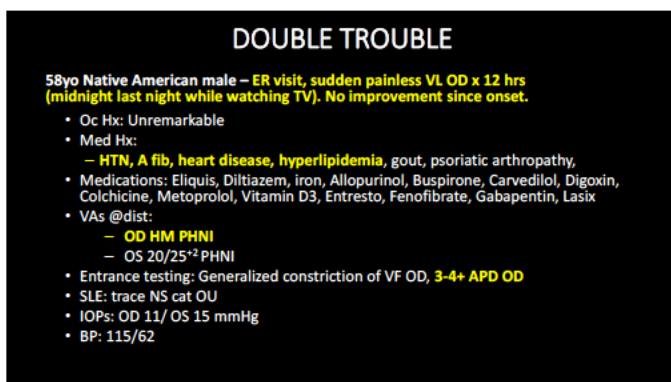
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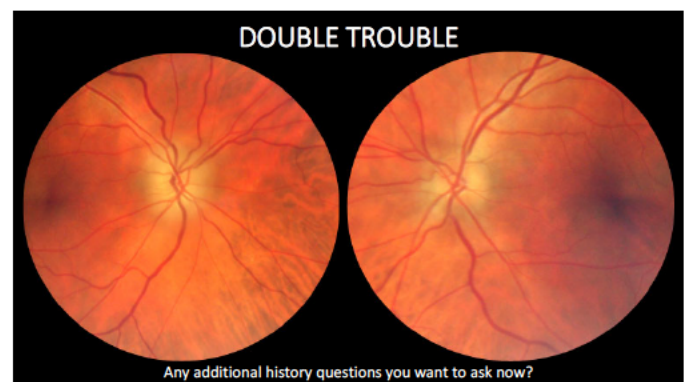
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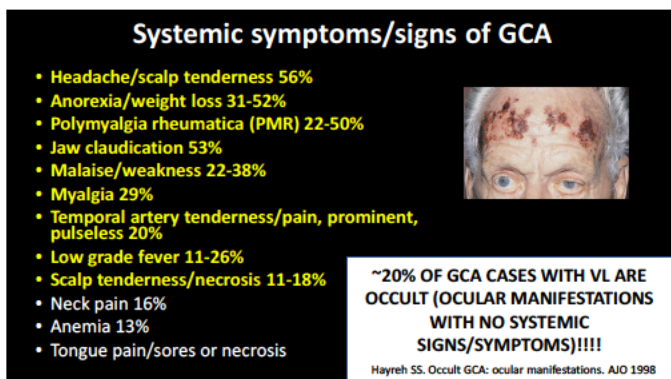
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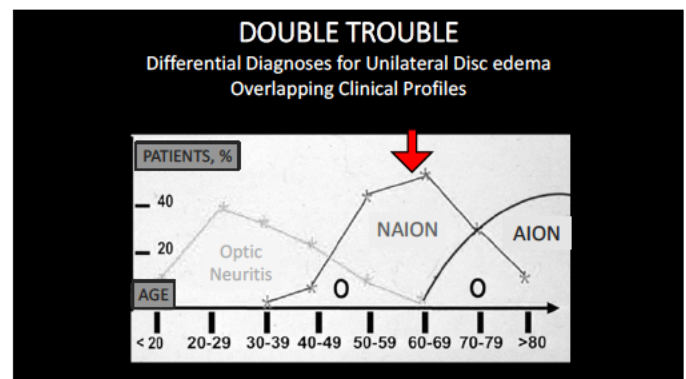
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### OPTIC DISC SWELLING DIFF DX

- Diagnostic dilemma:** Papilledema, anterior ischemic optic neuropathy, optic neuritis, pseudopapilledema, etc.?

Papilledema	NA-AION	Optic Neuritis

**DISC APPEARANCE AND PATTERNS OF VF LOSS MAY BE SIMILAR!!**

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### DOUBLE TROUBLE

Differential Diagnoses for Unilateral Disc edema

Optic Neuritis	NA-AION	A-AION
<ul style="list-style-type: none"> <li>Pain on eye movt 92%</li> <li>Presenting VA variable</li> <li>Central/diffuse VF</li> <li>2/3<sup>rd</sup> Retrobulbar</li> <li>Disc hemorrhages rare</li> <li>77% female, 85% white</li> <li>MRI ON sheath enhancement, WMLs</li> </ul>	<ul style="list-style-type: none"> <li>Painless 90%</li> <li>20/60 or better</li> <li>VL loss can progress for days</li> <li>Altitudinal VF loss</li> <li>Disc edema often sectoral</li> <li>Disc is hyperemic "luxury perfusion"</li> <li>Fellow eye disc at risk</li> <li>Associated with vasculopathic risk factors (HTN etc), sleep apnea, Viagra &amp; Amiodarone</li> </ul>	<ul style="list-style-type: none"> <li>Painful VL 79%</li> <li>CF or worse</li> <li>Nadir in minutes</li> <li>Preceding TMVL possible</li> <li>Disc edema is diffuse &amp; PALLID</li> <li>30% simultaneous bilat involvement</li> <li>80% have systemic GCA symptoms</li> </ul>

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### DOUBLE TROUBLE

Differential Diagnoses for Unilateral Disc edema

**CONCURRENT POST SEG ISCHEMIA (CWS, CILIORETINAL ARTERY OCCLUSION, CHOROIDAL OR INNER RETINAL INFARCTION) = A-AION UNTIL PROVEN OTHERWISE!!**

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### DOUBLE TROUBLE

Differential Diagnoses for Unilateral Disc Edema

Optic Neuritis	NA-AION	A-AION

What systemic testing is needed to differentiate between these diagnoses?

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### DOUBLE TROUBLE

Same day workup:

- Labs:**
  - ESR: 79 mm/hr (lab norm 2-10)
  - CRP: 49 mg/L (lab norm 0-10)
  - Platelets: 423 x 10<sup>3</sup>/mcl (lab norm 150-450)
  - PT/INR: high
  - Glucose 99 mg/dL
  - FTA-abs, RPR, ANA, ACE, RMSF, tick panel, Bartonella – all WNLs
- CT head w/o contrast:** Unremarkable
- Carotid Doppler US:** Bilateral ICA plaque but <50% stenosis (not hemodynamically significant)

**ASSESSMENT:** Very high suspicion for A-AION

**PLAN:**

- IV methyl Pred 250mg q6hrs for 12 doses followed by 80-100mg PO prednisone daily
- Scheduled TAB rt side in 2 days
- Refer to neuro-ophthalmology

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### GCA Work-up

- ESR**
  - A nonspecific marker of inflammation and/or neoplastic disease.
  - High end of normal for men = age/2
  - High end of normal for females = age +10/2
  - Hayreh >46 (mean of 85 in cases of + TAB)
- CRP**
  - An acute phase protein produced by hepatocytes
  - Normal is <2.54 mg/dL
  - Hayreh >2.45 (mean of 6.6 in cases of + TAB)
- CBC with diff and platelet count**
  - Thrombocytosis = ↑ platelet count >400 x10<sup>3</sup>/L
- TAB**
  - Most specific test for GCA (gold standard)
  - Test ipsilateral side of ocular involvement
  - Still perform if ESR/CRP are norm if suspicion is high
- Temporal artery Doppler US**

**Giant Cell Arteritis: Validity and Reliability of Various Diagnostic Criteria**

SOHAN SINGH HETTEL, MD, PhD, DRC, PIERCE A. POORHAUSKY, BS, BAMA ELKANN, MD, AND EDDGET ZIMMERMAN, PhD

The odds of a positive TAB was:  
2.0 times greater with ESR of 47 - 107 mm/hour  
3.2 times greater with CRP > 2.45 mg/dl

**"Elevated ESR and CRP = 97% specific for GCA"**

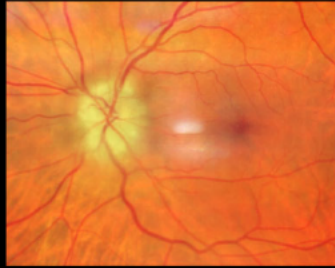
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## DOUBLE TROUBLE

### 3 Day Optometry FU

- Pt on last day of IV methyl pred
- Had TAB yesterday - inadequate sample for evaluation of GCA (repeat TAB left side with neuro-ophthalmologist in 1 week)
- States his vision OS has been decreased since coming out of recovery from TAB
- VAs @dist:
  - OD HM PHNI
  - OS 20/800 PHNI



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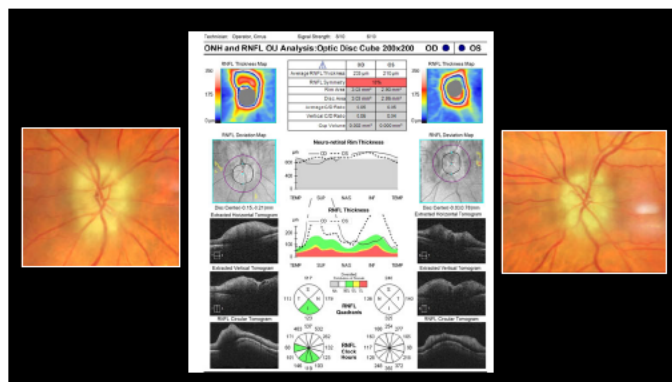
### BASELINE



### 3 DAYS LATER....



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## DOUBLE TROUBLE

### ASSESSMENT:

- Still Highly Suspect A-AION
- Now bilateral involvement despite emergently starting IV steroids



X 3!!

### PLAN:

- Repeat TAB left side with neuro-ophthalmologist in 1 week
- Finish out course of steroids (IV methyl Pred 250mg q6hrs for 12 doses followed by 80-100mg PO prednisone daily)

Left side TAB & another rt side biopsy- both negative for GCA  
Neuro-ophthalmology still highly suspects A-AION but cannot rule out sequential NA-ION due to cardiovascular risk factors esp unstable A-fib

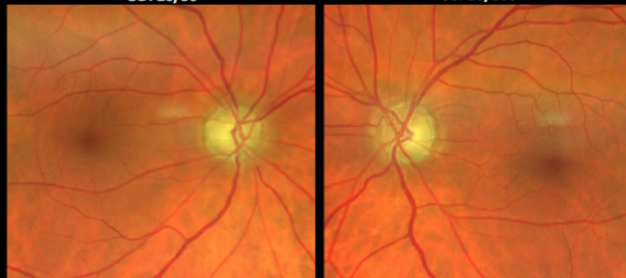
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## DOUBLE TROUBLE

1 year later.....

OD: 20/50

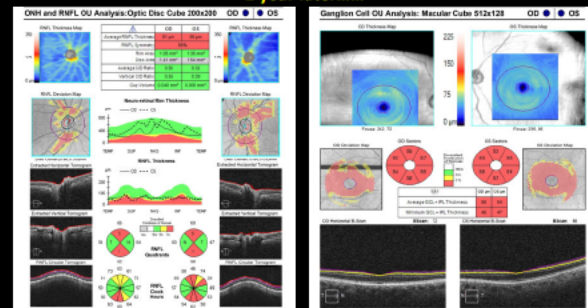
OS: 20/100



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## DOUBLE TROUBLE

1 year later.....



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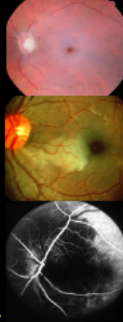
## OCULAR MANIFESTATIONS OF GCA

30-50% OF PTS WITH GCA PRESENT WITH OCULAR INVOLVEMENT!!

- Arteritic anterior ischemic optic neuropathy (A-AION, 80-90%)
  - 30% bilateral at presentation
  - **75% will become bilateral if left untreated**
  - **Can occur within days ~50% within 1 week**
- CRAO 5%
- Cilioretinal artery occlusion 22%
- BRAO 5%??
- CWSs (present in approx 30% with acute vision loss)
- IVFA evidence of SPCA occlusion (choroidal or disc vascular insufficiency/ischemia) ~100%

**SUSPECT GCA IN ANY ACUTE ONSET NEUROLOGIC DEFICIT IN A PT OVER 50 YEARS OF AGE!!!**

Hayreh SS et al. Ocular manifestations of giant cell arteritis. Am J Ophthalmol. 1998 Apr;125(4):509-20.



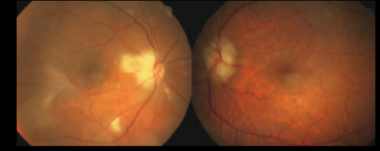
## GCA TREATMENT

**HIT HARD AND HIT FAST TO PREVENT BILATERAL BLINDNESS!**

- When GCA is highly suspected do not wait for TAB results to begin treatment
- IV methyl pred 1g per day x 3 days (250 mg q6h for 12 doses), then switch to prednisone 80 to 100 mg PO qd (or 1 mg/kg per day) day x 1 mo then tapered over 6–12 months while confirming normal ESR and no systemic symptoms
- Vitamin D 2,000 units daily + calcium
- Low dose ASA

Rates of vision improvement:

- **58% improved if steroid administered with 24hr**
- 6% improved if administered after 24hrs



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## The NEW ENGLAND JOURNAL of MEDICINE

introduction to this 10/13/27, 2017 VOL. 377 NO. 4

### Trial of Tocilizumab in Giant-Cell Arteritis

J.H. Stone, K. Tackewitz, S. Dimarzio, M. Khoury, M. Aringer, D. Blochman, E. Braverman, M.C. Cui, B. Dasgupta, J. Bach, C. Salazar, G. Schett, H. Schulz-Knappe, R. Spina, S.H. Teles, and N. Gellman

#### Tocilizumab IL-6 Receptor Antagonist

- Tocilizumab received approval for the treatment of GCA in May 2017<sup>1</sup>
- This is the first medication approved for GCA<sup>1</sup>

Efficacy at Week 52 in the Intention-to-Treat Population in a Randomized Controlled Trial<sup>1</sup>

	Tocilizumab Weekly (n=104)	Placebo (n=104)	Median (IQR) at Week 52	Median (IQR) at Week 52
Patients with sustained prednisone dose at week 52	52	52	54	58
Cumulative median prednisone dose at week 52	1802	1802	8296	3418

**Conclusion:** Tocilizumab (weekly at every other week) + 16-week prednisone taper was superior to placebo + 26-week or 52-week prednisone taper in maintaining glucocorticoid-free remission patients with GCA.

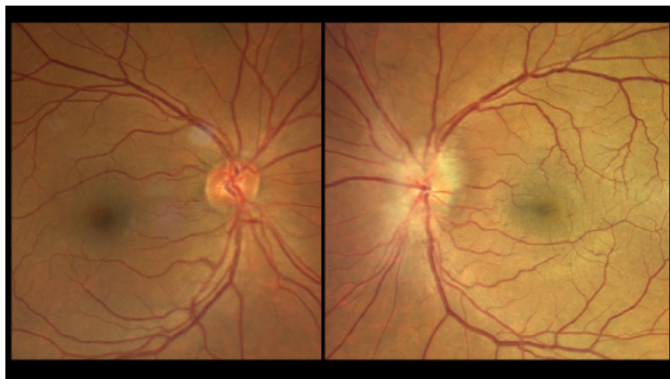
## THE CASE OF THE CURIOUSLY SWOLLEN DISCS

**45yo male – Walk-in NP complaining of missing vision inf right field OS x 1 week, first noticed upon waking, (-) pain**

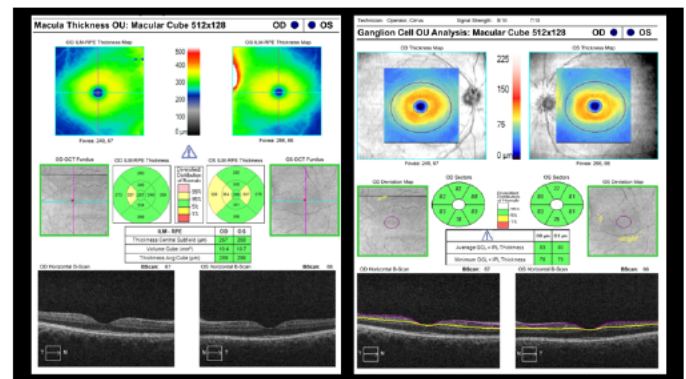
- Oc Hx: approx. -1D to 2D myope, LEE 7mo ago
- Med Hx: **DM type 2 (last a1c 9.6%), HTN, hypercholesterolemia, hx of alcoholism**
- Meds: ASA 81mg, simvastatin, **sildenafil**, lisinopril, insulin, metformin
- VAs @dist:
  - OD 20/20
  - OS 20/20
- Entrance testing: **Inf nasal constriction of VF OS, trace APD OS**
- SLE: WNLs OU
- IOPs: 17 mmHg OD/OS
- BP: 144/92

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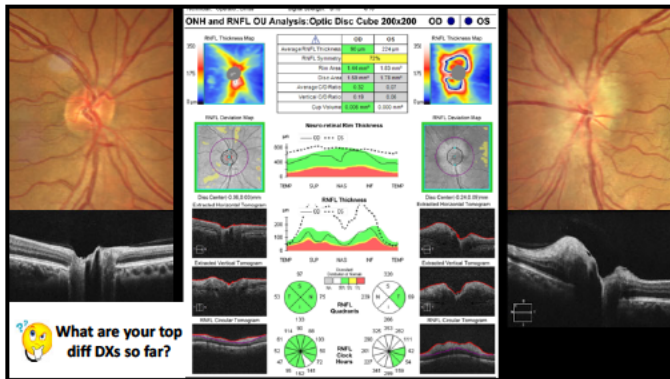
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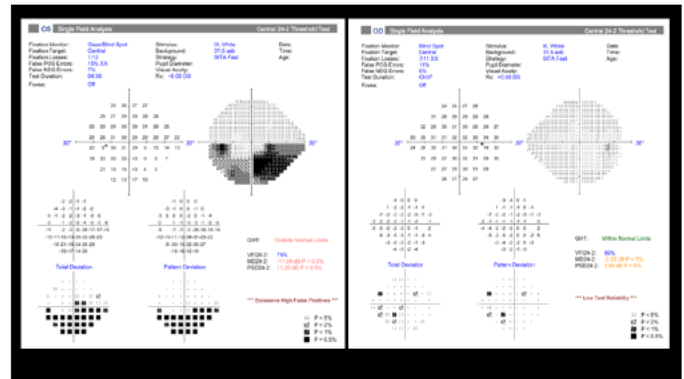
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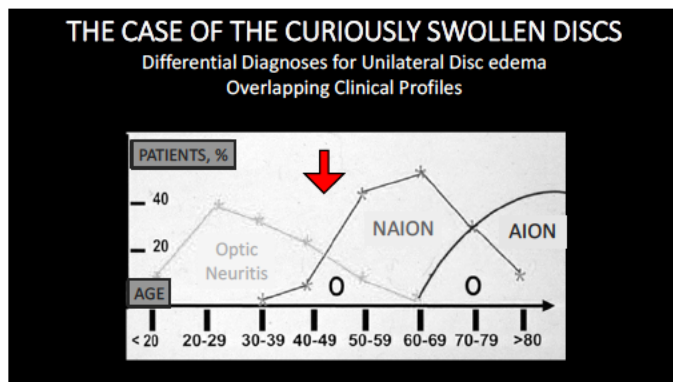
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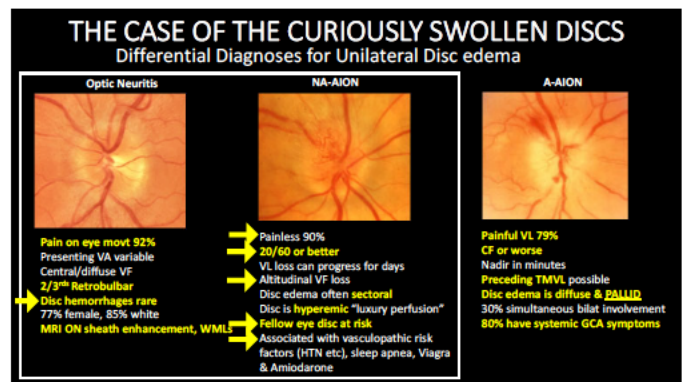
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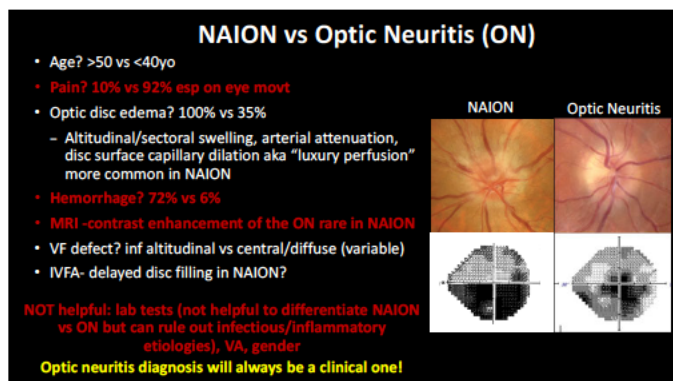
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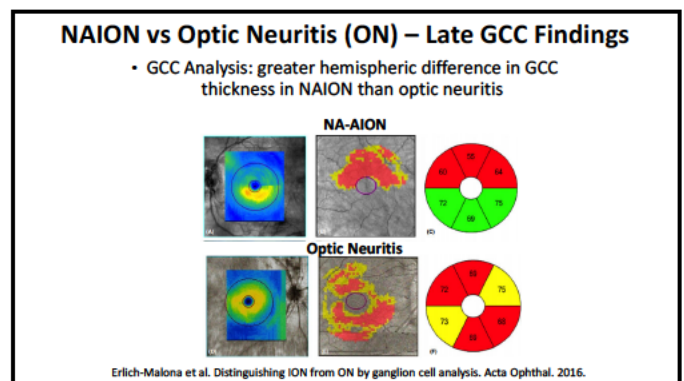
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### Work-up

- Communicate with PCP regarding control of vasculopathic risk factors
- Sleep study
- Cautioned against the continued use of Viagra to decrease risk of NAION in the fellow eye given "disc at risk" appearance
- Could consider (not done in this case)
  - MRI
  - Labs for hypercoagulability/inflammatory or infectious neuropathies
  - Anti-aquaporin 4 (anti-NMO) & anti-MOG antibodies

 What is the patient was over the age of 50yo?

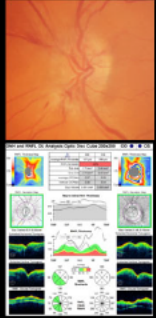
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### NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

- **Most common cause of unilateral disc edema/optic neuropathy in adults > 50yo**
- **Accounts for 90-95% of ant ION cases**

#### Pathology/Mechanism

- Not well understood, but likely some combo of:
  - **ON infarction from SPCA insufficiency** (exacerbated by microvascular arteriosclerotic disease or dysfunctional ONH vasc autoregulation?)
  - **"Compartment syndrome"** phenomenon, axonal crowding at the level of the LC (more vulnerable to ischemia)
  - **Embolitic etiology is thought to be RARE** (unless concurrent retinal/choroidal infarction is present)




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### NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

Fairly well-established risk factors/associated conditions

- **HTN (47%, may also be assoc with acute HTN crisis)**
- **DM (24-34%)**
- **Hypercholesterolemia (70%)**
- **Disc at risk (small crowded ONH or disc drusen)**
- **Sleep apnea**
- Ischemic heart disease (21%, 11% previous MI)
- Major blood loss
- Perioperative spine and cardiac surgery (incidence ~0.1% in high-risk surgeries)
- Hypercoagulable states (antiphospholipid antibodies, ↑homocysteine)
- Anemia
- Migraine (esp pts <50yo)



NAION + acute HTN crisis



Small, crowded disc

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### NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

Questionable risk factors/associated conditions

Nocturnal hypotension????

- Perhaps a contributor in eyes with progressive VL
- Sig association btw progressive VF loss and nocturnal hypotension in pts with HTN taking PO hypotensives (Hyreh 1994 AJO)

New evidence against nocturnal hypotension hypothesis:

24-Hour Blood Pressure Monitoring in Patients With Anterior Ischemic Optic Neuropathy

ESC Clinical Research of Cardiology

Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial


- **No difference in nighttime diastolic nadir** compared to controls
- Pts with NAION consistently had a lower mean daytime BP than controls and a **lag in the usual rise in BP in the morning** to meet increasing daytime demands for perfusion
- 19,084 pts followed for 6yrs
- Half took BP meds in AM, half at bedtime
- **Sig lower risk of CVD, MI, cardiac failure, or stroke with bedtime dosing**

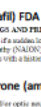
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
### Non-Arteritic Ischemic Optic Neuropathy (NAION)

Questionable risk factors/associated conditions

- **Smoking (49%)?**
- **Certain meds: phosphodiesterase-5 (PDE-5) inhibitors, amiodarone, oxymetazoline, phenylephrine?**
- **Cataract surgery?**
- Hyperopia?
- Papillary vitreous detachment?
- **\*\*NAION eyes do NOT have increased incidence of ipsilateral carotid disease\*\***

 Viagra (Sildenafil) FDA Package Insert

 Cordarone (amiodarone) FDA Package Insert

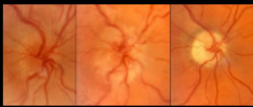
 What is the patient was over the age of 50yo?

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### NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

#### Prognosis/Clinical course

- **Nonprogressive (~75%) and progressive forms exist**
  - If progressive, usually occurs within the first month
- **VA stable or improves in most without tx (IONDT)**
  - 31% gained ≥3 lines at 2 years
- Repeated attacks in the same eye are unusual (6.4%)
- Fellow eye risk/bilateral involvement
  - **5 year risk of 2nd eye involvement ~15%**
  - **Lifetime risk may be as high as 30-40%**
  - Greater risk in **younger pts (<50yo)** those with DM/HTN, and worse VA



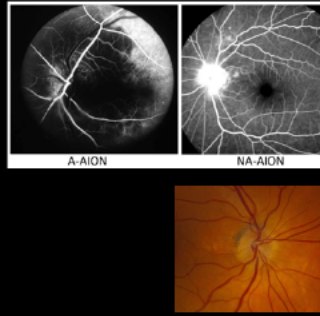
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## NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

### Work up

- Patients  $\geq 50$ yo: ESR/CRP/CBC with diff and platelet count; maybe also IVFA to R/O GCA
- Neuroimaging is usually unnecessary in older pts with classically presenting NA-AION
- Younger pts: Labs for hypercoagulability/inflammatory or infectious neuropathies, MRI to exclude optic neuritis/compressive or infiltrative conditions
- All pts: Investigate for DM, HTN, chol, cardiovascular disease, sleep apnea
- Embolic WU (carotid eval) unnecessary unless concurrent retinal/choroidal ischemia/retinal emboli



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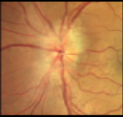
## NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY (NAION)

### Management

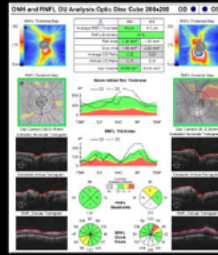
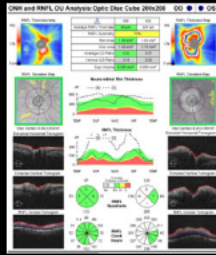
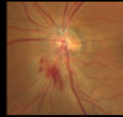
- **No proven therapy**
- **Control systemic predisposing risk factors/cardiovascular risk factor modification**
- **D/C smoking**
- **Caution against use of high-risk meds (erectile dysfunction drugs, amiodarone) in individuals with history of NA-AION and "discs at risk"**
- **81mg ASA?** -does not work as prophylaxis for the fellow eye but may reduce risk of secondary stroke
- Avoid over treating HTN?
- Levodopa and carbidopa? Benefit in one study, non-reproducible

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### Baseline

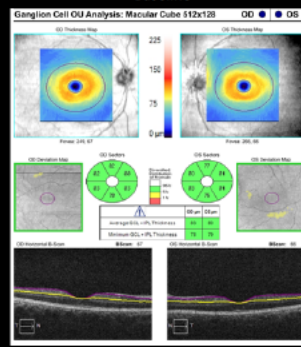


### 1 month FU

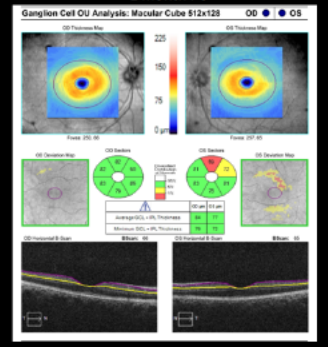


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### Baseline

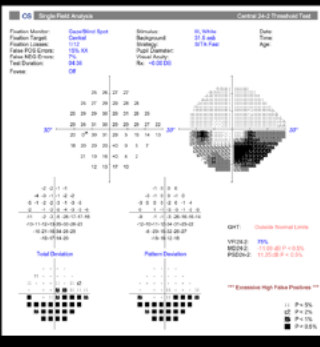


### 1 month FU

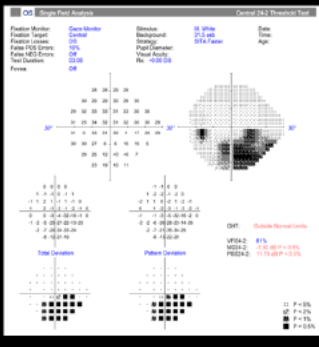


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### Baseline



### 1 month FU



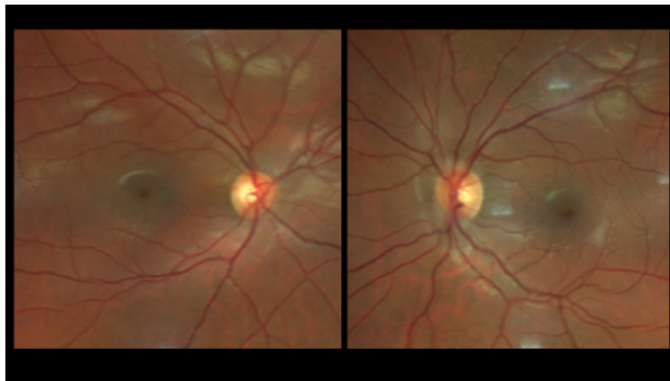
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## WHEN THE LITTLE THINGS MATTER MOST....

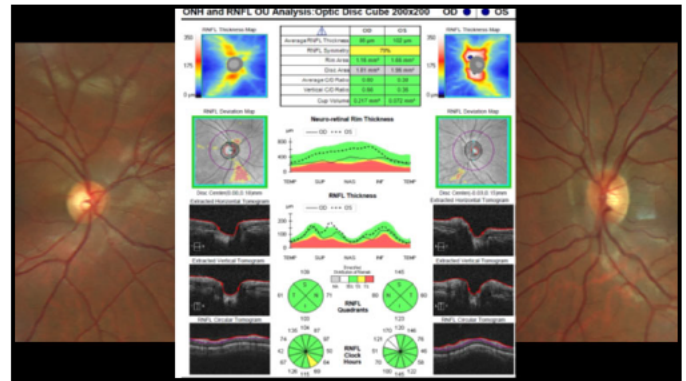
**27yo Native American female – Sent over from urgent care, sudden central vision loss OS 6 days ago that has been worsening, headache and pain (7/10) worse on eye movt**

- Oc Hx: Unremarkable
- Med Hx: depression, anxiety, asthma, eczema, bipolar disorder, smoker
- Meds: Albuterol/Ipratropium inhaler
- VAs @dist:
  - OD 20/25
  - OS LP (PHNI)
- Entrance testing:
  - CVF: Central/inferior constriction of VF OS
  - Pupils: Sluggish direct response OS, 2+ APD OS
  - EOMs: Full but with pain OS
- SLE: WNLs OU
- IOPs: 13 OD/OS mmHg
- BP: 111/76

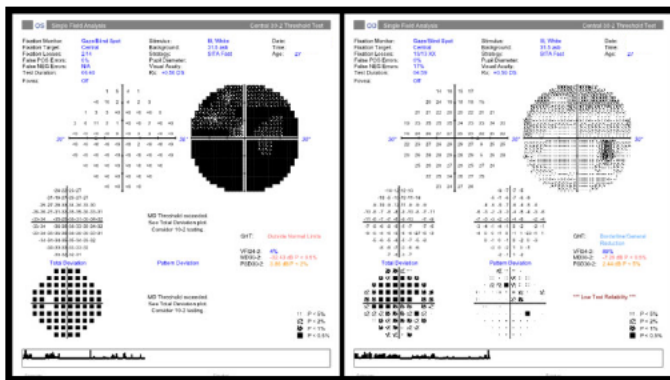
48



49



50



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### Work-up

Optic nerve sheath enhancement from optic neuritis OD

T1 w/ contrast without fat suppression      T1 w/ contrast with fat suppression

Neuroimaging (MRI brain and orbits)

- With & w/o contrast enhancement
- + orbital fat suppression
- T2 with FLAIR

FLAIR (fluid level attenuated inversion recovery)

Labs?

- Inflammatory / infectious / hypercoagulability
- Anti-aquaporin 4 (anti-NMO) & anti-MOG antibody

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### Neuroimaging

What is this patient's risk of CDMS over the next 15 years?

- MRI of brain and orbits w/ & w/out contrast with fat suppression and FLAIR

T1 MRI w/ contrast      Optic nerve sheath enhancement

T2 MRI with FLAIR      Cortical white matter lesions

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### Diagnosis & Plan

#### Retrobulbar optic neuritis OS

- Tx: **IV methylprednisolone 1g/day** x 3 days + 60 mg oral prednisone x 11 days with taper of 20 mg on day 1, followed by 10 mg on days 2 to 4
- Refer to **neurology** for full neurologic exam & consideration of **immunomodulatory tx** (started on diroximel fumarate)
- Vit D level

54

## OPTIC NEURITIS (ON)

### Prognosis/clinical course

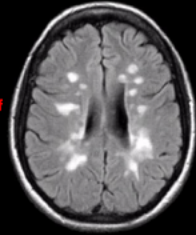
- Recovery should begin within 1 month
- 72% expected to be 20/20 after 15 years
- Similar prognosis at 1 year regardless of treatment

### Development of MS

- One episode of ON does not = MS

★ The most reliable predictor for the future development of MS is the presence of MRI white matter lesions

- ONTT 15 year FU
  - Overall, 50% developed CDMS
  - Positive MRI- 72%
  - Negative MRI- 25%
- Other predictive tests- CSF oligoclonal bands in pts with normal MRI



55

## OPTIC NEURITIS (ON)

- **Atypical ON cases work-up!**- MRI (brain & spinal cord), CBC, FTA-abs, RPR, tick panel, ACE, CXR, ESR/CRP, ANA, anti-AQP4 (NMO), anti-MOG antibodies, CSF analysis, bartonella ab panel, B12 & folate, copper, genetic mitochondrial analysis, ERG prn

### Atypical ON features:

- NLP (NMO)
- Progression of VL after 1-2 weeks
- Simultaneous bilateral VL (NMO, lebers, toxic)
- Disc/retinal hemorrhages (NA-ION, syph)
- Severe disc swelling
- Macular/retinal exudates (neuroretinitis)
- Vitritis/uveitis (sarcoid, syph)
- Retinal vein sheathing (sarcoid, SLE)
- Lack of partial recovery by 1 month
- Absence of pain
- Persistent pain

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## OPTIC NEURITIS (ON)

### Treatment

**Scenario #1:** First episode of typical acute ON, MRI white matter lesions & no prior history of MS

- Consider IV corticosteroids followed by PO pred taper
  - Reduces the risk of CDMS for the first 2 years
  - Hastens visual recovery
  - Do NOT give PO steroids alone!!!
- Refer to neurologist/neuro-ophthalmologist for possible treatment with immunomodulatory med to reduce the risk of developing CDMS
  - CHAPS, ETOMS, BENEFIT, PreCISE
- Vit D supplementation is levels are low

**Scenario #2:** First episode of typical acute ON, MRI negative, and no prior history of MS

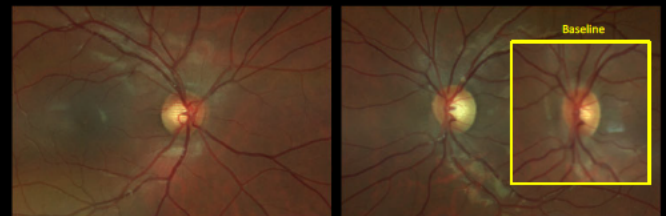
- Observation vs IV corticosteroids followed by PO pred taper
- Repeat MRI at 3, 6, 9, 12 months then yearly

**Scenario #3:** Recurrent bouts of ON with prior dx of MS

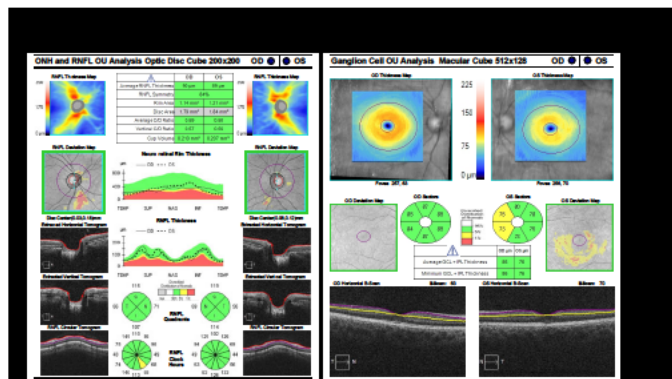
- Discuss with neurologist/neuro-ophthalmologist

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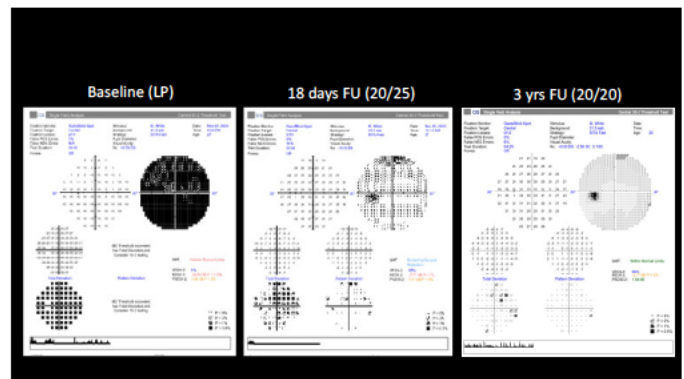
## 18 days FU



58



59



60



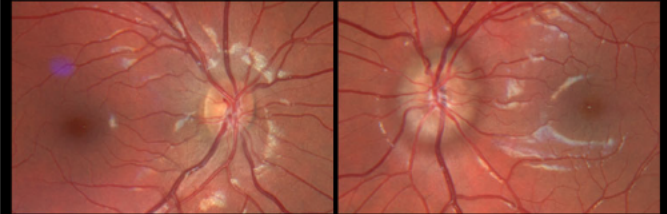
## DIGGING DEEP

17yo female – Routine exam, complains of blur at distance x 1-2yrs

- Oc Hx: Unremarkable
- Med Hx: WNLs, no meds
- BCVAs @dist:
  - OD -1.00 sph 20/20<sup>-2</sup>
  - OS -1.00 -0.25 x 075 20/20<sup>-1</sup>
- Entrance testing: **Nasal constriction of VF OS, 1+ APD OS**
- SLE: WNLs OU
- IOPs: OD 12/ OS 11 mmHg
- BP: 117/82

61

## DIGGING DEEP

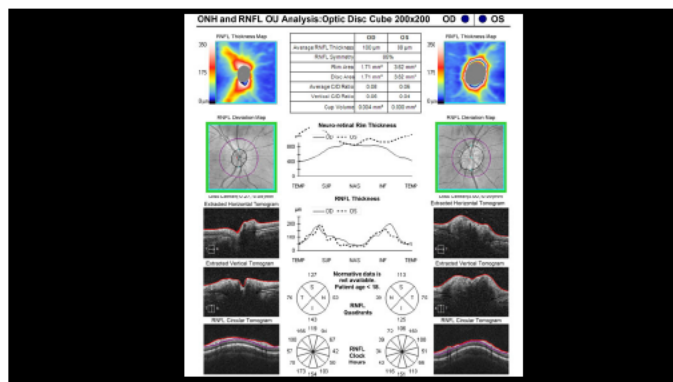


Are there features of TRUE papilledema present?



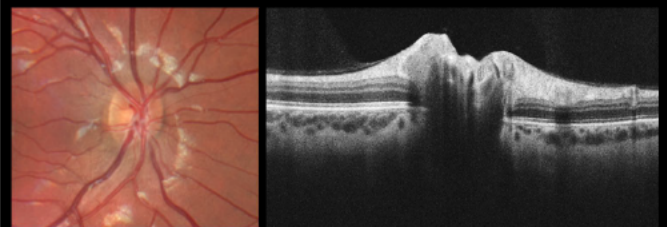
What additional ancillary testing is needed?

62

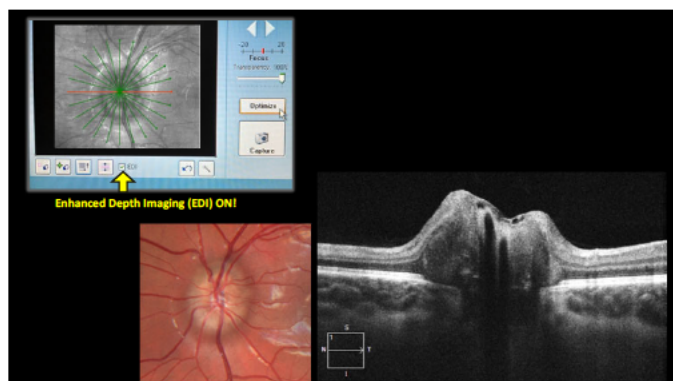


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## DIGGING DEEP

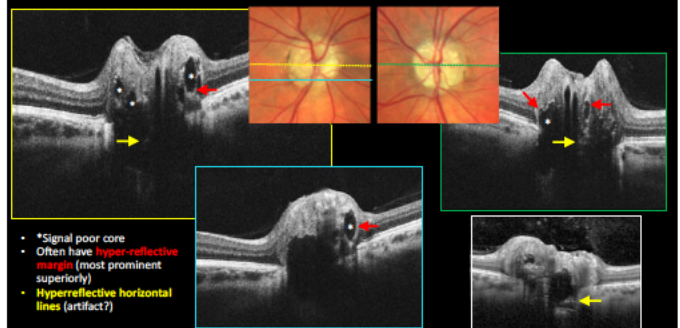


64



65

## OCT APPEARANCE OF DISC DRUSEN



66

## Peripapillary Hyperreflective Ovoid Mass-like Structures (PHOMS)



- A **nonspecific OCT sign** of prelaminar peripapillary axonal distension/herniation and crowding that **can occur in acquired and dysplastic ONH anomalies** (optic disc drusen, papilledema, myopic tilted discs, etc.)

- **PHOMS are NOT optic disc drusen!!!**; & NOT an optic disc drusen precursor

PHOMS



\* Disc drusen hyporeflective core

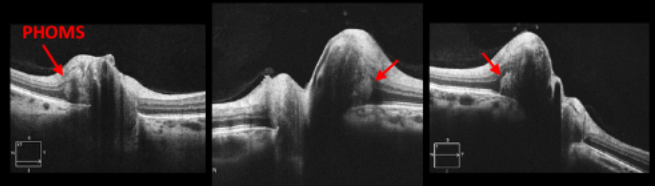
White arrow = Disc drusen hyperreflective margin or "hat"

Fiona Costello, et al. The Role of OCT in Differentiating ODD from Optic Disc Edema. Asia-Pac J Ophthalmology 2018

67

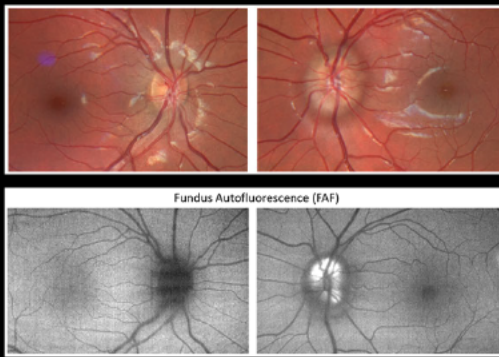
## Peripapillary Hyperreflective Ovoid Mass-like Structures (PHOMS)

- **PHOMS are NOT optic disc drusen!!!**



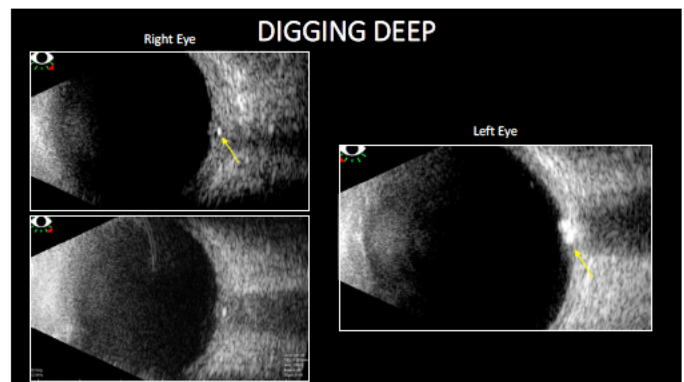
Fiona Costello, et al. The Role of OCT in Differentiating ODD from Optic Disc Edema. Asia-Pac J Ophthalmology 2018

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Fundus Autofluorescence (FAF)

69



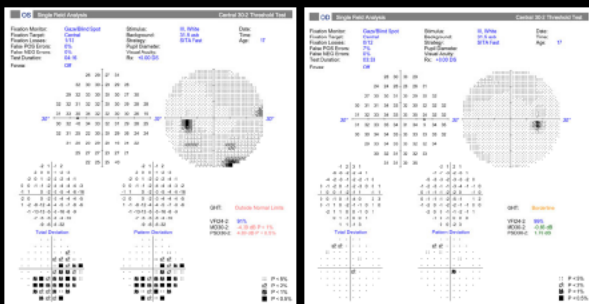
Right Eye

DIGGING DEEP

Left Eye

70

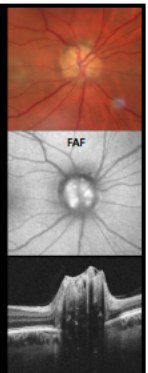
## DIGGING DEEP



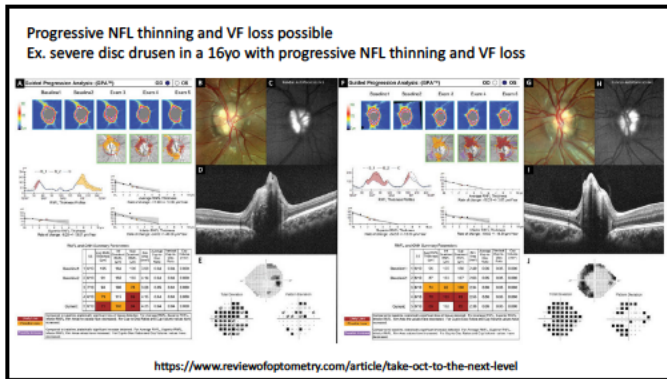
71

## OPTIC DISC DRUSEN

- Colloid bodies within substance of ONH **anterior to the lamina cribrosa**
- Extracellular deposition of axoplasmic material with ultimate calcification (owing to narrow posterior scleral foramen/Bruch membrane opening)
- VL can occur but usually **long-standing, painless, and asymptomatic**
- **Stability demonstrated by serial examination may be key** in confirming a diagnosis of pseudopapilledema
- Signs: irregular (scalloped) disc margin, loss of central cup, anomalous vasculature (trifurcations), variable NFL & VF loss, no IVFA leakage, + SVP in most



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### OPTIC DISC DRUSEN

**Management:**

- Monitor for CNVM, NA-ION, CRVO
- No SOC tx
  - Lower IOP (esp if elevated)?

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**6yo white female**

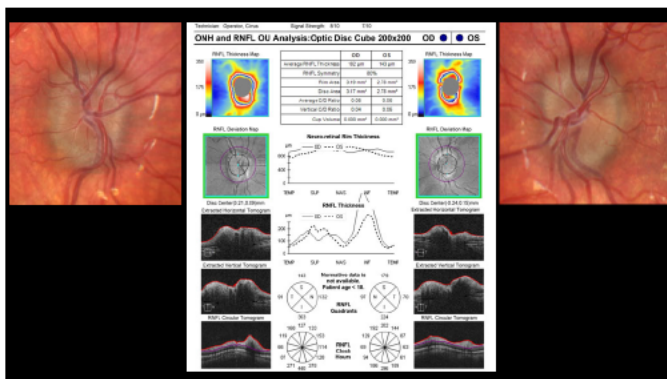
- CC: First eye exam. No ocular or systemic complaints per patient and mother.
- Oc Hx: unremarkable
- Medical Hx: unremarkable
- Meds: none
- Final Refraction
  - OD: +1.00 -1.25x176: 20/20<sup>-3</sup>
  - OS: +1.50 -1.75x002: 20/20<sup>-2</sup>
- Entrance testing and SLE of ant seg: Unremarkable OU
- IOPs 21/20mmHg
- BP: 98/66

75

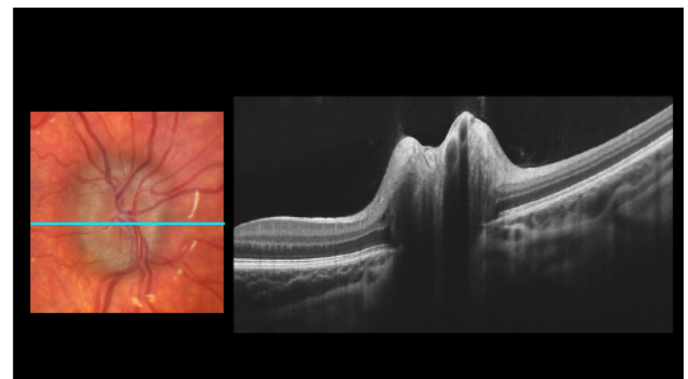
Are there features of TRUE papilledema present?

What extra finding should we specifically look for?

76

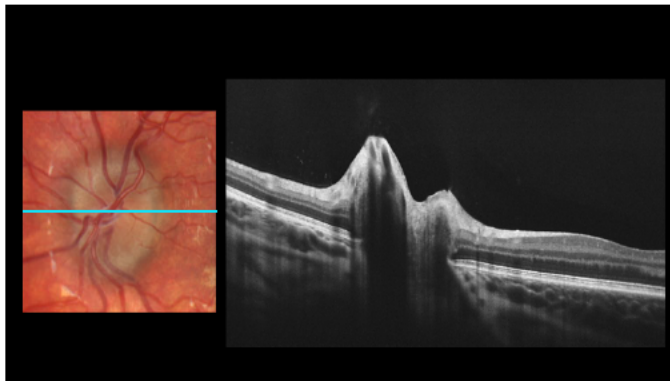


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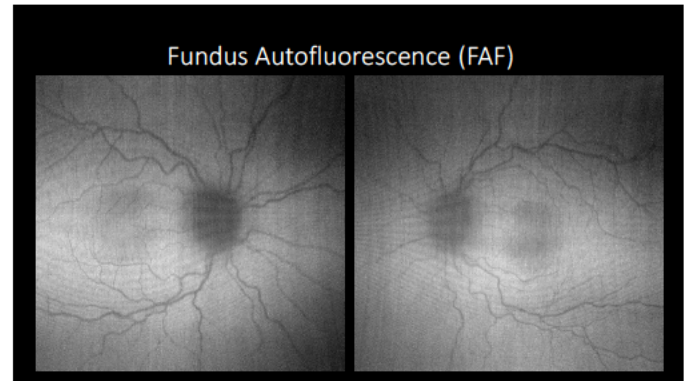


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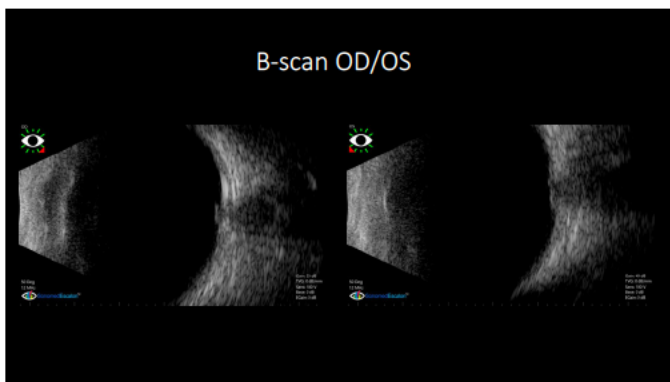




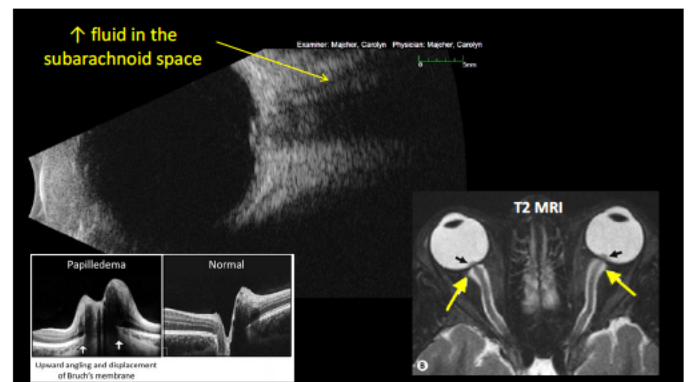
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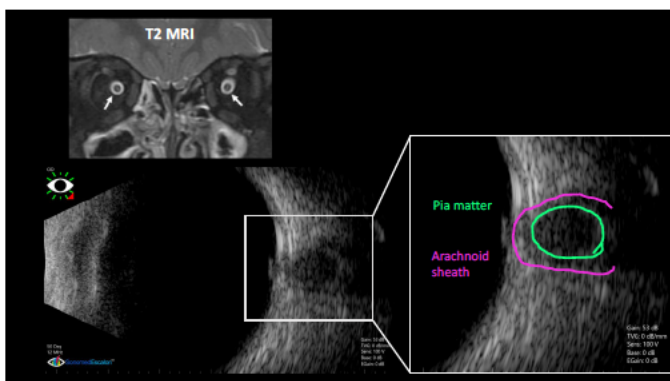
80



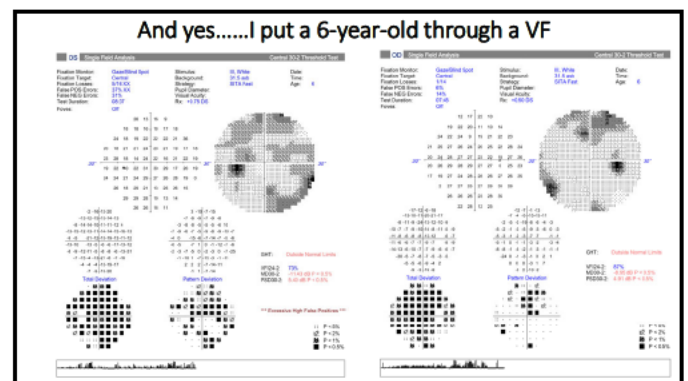
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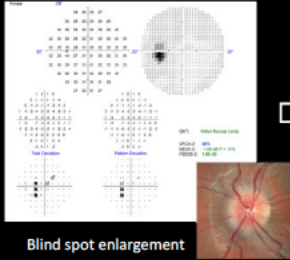


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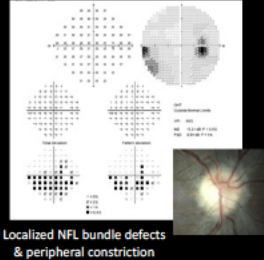
## PAPILLEDEMA – VF LOSS

- Poor correlation between VF loss/acuity and ON appearance/degree of swelling

### Early



### Chronic



85

## MRI/MRV brain and orbits with and without contrast

### MRI Head

- Mild concavity to the superior margin of the pituitary gland (AKA: partially empty sella)...otherwise no intracranial space-occupying lesion and no evidence of acute hydrocephalus.

### MRI Orbits

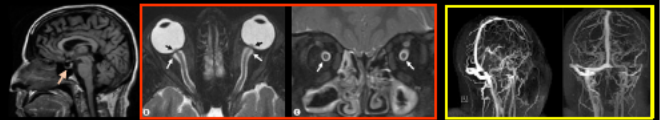
- Bilateral optic disc bulge and increased nerve sheath CSF (distended).

### MRV Head

- The left transverse sinus appears to be significantly hypoplastic. Rt transverse sinus is dominant. No evidence of dural venous sinus thrombosis.

### IMPRESSIONS

- Findings suggestive of raised intracranial pressure



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## Lumbar Puncture

### Opening Pressure

- Elevated at 288 mm of H<sub>2</sub>O

### CSF Analysis/cytology

- Glucose, lymphocytes, monocytes, protein and macrophages all WNL. No atypical or malignant cells identified. VDRL non-reactive and cryptococcus antigen negative.

### ASSESSMENT

- Pediatric IIH

### PLAN

- Acetazolamide 9.4mL (235mg total) by mouth every 12 hours

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## Papilledema Causes

Obstructed intracranial venous drainage	Increased intracranial volume	Infectious/inflammatory	Endocrine disorders
<ul style="list-style-type: none"> <li>Venous sinus thrombosis</li> <li>Cerebral or spinal AV malformation/fistula</li> <li>Chiari malformation</li> <li>Hydrocephalus</li> <li>Superior vena cava syndrome</li> </ul>	<ul style="list-style-type: none"> <li>Intracranial or spinal cord mass lesions</li> <li>Intracranial hemorrhage</li> <li>Foster Kennedy syndrome</li> </ul>	<ul style="list-style-type: none"> <li>Syphilis</li> <li>Meningitis</li> <li>Lupus</li> <li>Ear infections</li> </ul>	<ul style="list-style-type: none"> <li>Addison's disease</li> <li>Hypoparathyroidism</li> </ul>
Toxic/pharmacologic	Medical conditions	Others	
<ul style="list-style-type: none"> <li>Tetracycline, minocycline, doxycycline</li> <li>Vitamin A hypervitaminosis</li> <li>Accutane</li> <li>Corticosteroid withdrawal</li> </ul>	<ul style="list-style-type: none"> <li>Malignant hypertension</li> <li>Hypercoagulable states</li> <li>Anemia</li> <li>Obstructive sleep apnea</li> <li>Renal failure/transplantation</li> <li>Pulmonary disease/respiratory insufficiency</li> <li>Gullain-Barre syndrome</li> <li>Craniosynostosis</li> </ul>	<ul style="list-style-type: none"> <li>Trauma</li> <li>Idiopathic intracranial HTN</li> </ul>	

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## Papilledema

### Work up

#### Papilledema is a medical emergency

- Full neurological examination, BP measurement
- MRI/MRV of brain (and orbits) with and w/o contrast
  - Include spinal code if paraparesis or quadriparesis, lumbar pain, a sensory level, hyperreflexia, extensor plantar responses, or bladder dysfunction are present
  - Include MRA if AV malformation suspected
  - CT if hemorrhage suspected
- If other etiologies suspected:
  - ACE, tick antibody panel, ESR, CBC, RPR, FTA-abs, ANA, acid-fast staining, cytology for malignant cells
- If imaging reveals no mass, no chiari, and ventricles not dilated proceed with LP
  - LP with opening pressure measurement & CSF analysis

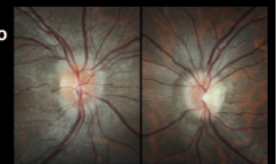


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## IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH)

### IIH Diagnostic criteria

- Awake and alert
- Signs and symptoms of increased ICP (HA, N & V, TVO, papilledema, diplopia)
- Normal neurologic examination (absence of localized findings aside from those expected from increased ICP such as CN 6 palsy)
- Normal MRI/MRV neuroimaging (normal brain parenchyma, ventricular system, and cerebral venous sinuses w/o signs of hydrocephalus, mass or structural defect, and without meningeal enhancement)
- Elevated LP opening pressure (typically  $\geq 250$  mm H<sub>2</sub>O in adults lateral decub position)
- Normal CSF composition
- No other cause of increased ICP present (meds, etc)



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## IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH)

### Management

- Diagnosis and co-management by neurologist or neuro-ophthalmologist
- **Serial ocular exams (color, VFs, OCT, DFE)**
  - weekly or biweekly initially until vision stabilizes or improves
- **Weight loss (10%)**- nonpregnant overweight patients
  - Topiramate, bariatric surgeries, nutrition counseling
- **Acetazolamide**
  - **First line, decreases CSF production**
  - 500mg PO bid to tid initially
- **Topiramate- CAI, HA control, appetite suppression**
- HA management-analgesics
- Severe progressive cases, medical failure:
  - Optic nerve sheath decompression
  - Lumboperitoneal /ventriculoperitoneal shunt

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## Pediatric Idiopathic Intracranial Hypertension (IIH)

### Pediatric IIH

- May be a different underlying mechanism
- **50% males (prepubertal pediatric patients)**
- Affected adolescents tend to be overweight, but obesity and weight gain are not associated risk factors in patients younger than 11 years
- Presentation S/S similar to adults except **CN VI palsy more common (33%)**
- Most cases improve with medical treatment

Liu G, et al. Pediatric IIH. Surv Ophthalmol. Nov-Dec 2007;52(6):597-617.

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## UNDER PRESSURE

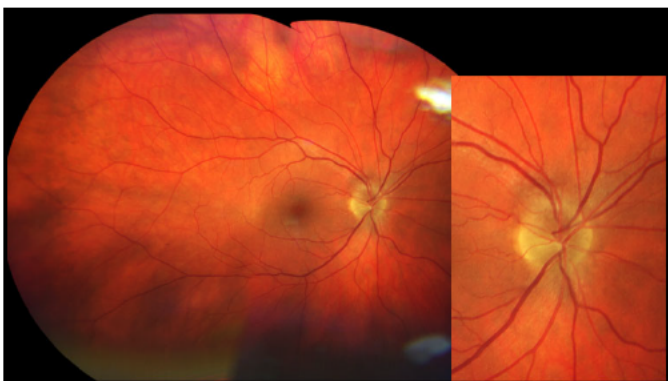
- 58 yo M – sent from PC to optometry for abnormal findings upon DM CFP screening
- CC: occasional **halos around objects** x last few days, **pressure sensation** around eyes OU, slight **HA** 2-3 days ago, new onset; wears hearing aids, new noise/**swishing in ears** worse left ear x 2-3 weeks; denies transient visual obscurations w/w/out postural changes
- Medical history: HTN, DM type 2, hypercholesterolemia, hearing loss
- Medications: alogliptin, amlodipine, aspirin, atorvastatin, canagliflozin, lisinopril, metformin, pioglitazone, tamsulosin

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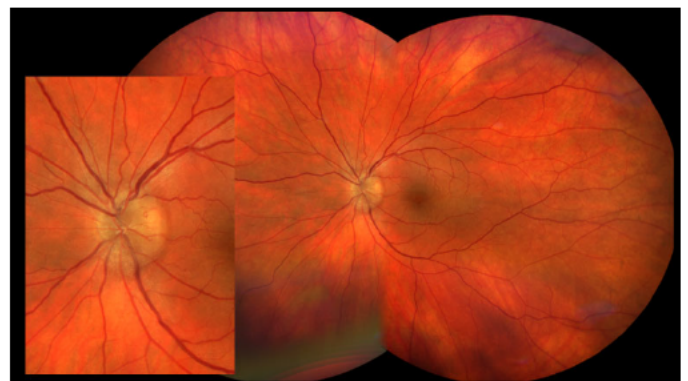
## Examination Findings

Assessment	OD	OS
Unaided VA	20/20	20/20
EOM	Normal	Normal
Pupils	PERRL OU, (-) APD	
IOP (GAT)	21 mmHg	22 mmHg
Anterior segment	Normal	Normal
BP	144/88	
A1c	9.0%	

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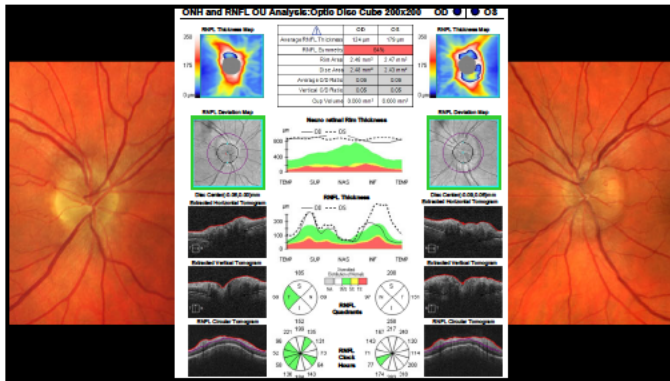


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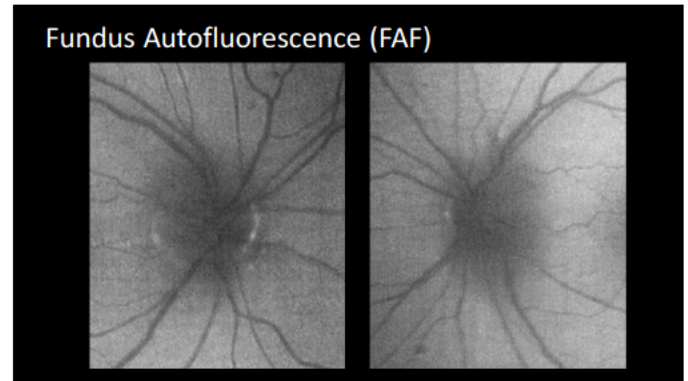


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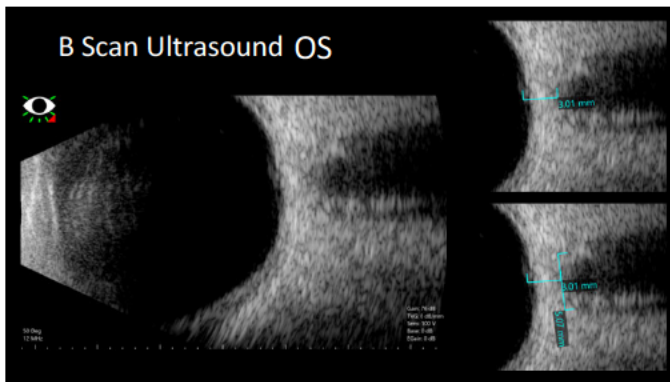




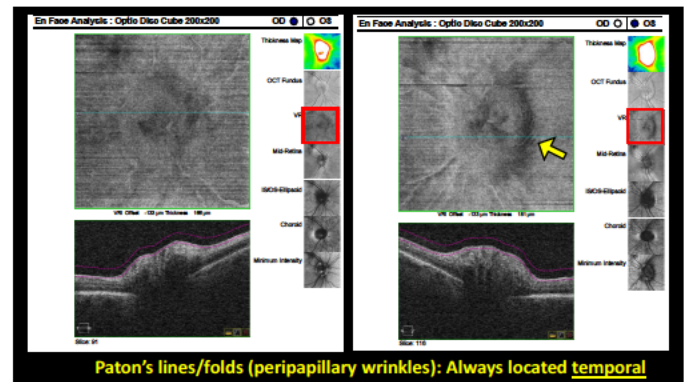
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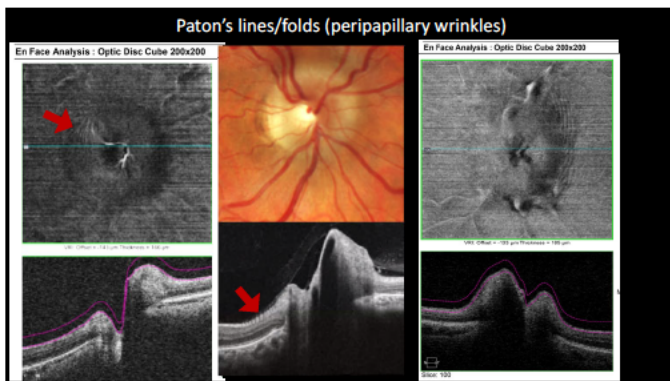
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101

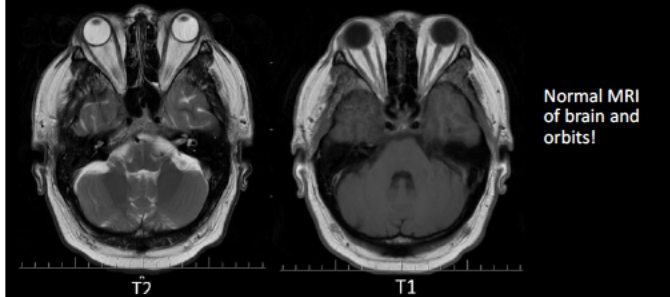
### Management

**Dx: papilledema OU**

1. Referred to ER for emergency **MRI and MRV** of brain/orbits with and without contrast

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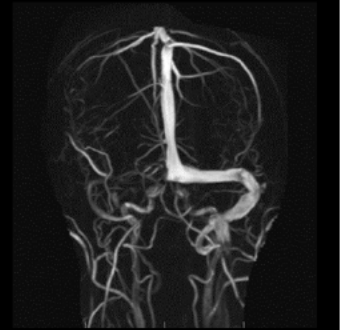
## MRI Results



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## MRV Results

**Thrombosis** of the right transverse sinus, sigmoid sinus, and internal jugular vein



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## Management

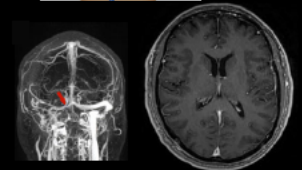
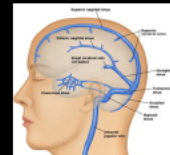
**Dx: papilledema secondary to dural venous sinus thrombosis**

1. US venous doppler of lower extremities
2. Blood work (hypercoagulable panel)
3. Echocardiogram
4. Electrocardiogram
5. Started on Lovenox
6. Rx oral apixaban 5 mg

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## DURAL VENOUS SINUS THROMBOSIS (DVST)

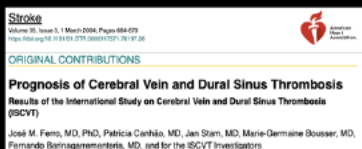
- Thrombosis or obstruction of the cerebral dural venous sinuses
  - Venous hypertension and decreased CSF absorption
- Causes of clot formation- Hypercoagulable states, Contiguous infection (lateral sinus thrombosis secondary to mastoiditis), Contiguous neoplasm (may compress the venous sinuses, impeding venous drainage and leading to clot formation)
- Presentation – Similar to ITH but usually develop more rapidly
- EMERGENCY due to risk of stroke



**RECOMMEND MRV ALONG WITH MRI IN PAPILEDEMA WORK-UP!!**

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## Relevance

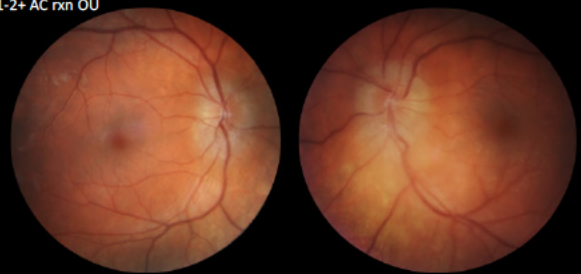


- Cerebral venous thrombosis represents 0.5-1% of all strokes
- Affects ~5 people per 1 million annually
- International Study on Cerebral Venous and Dural Sinus Thrombosis (ISCVT)
  - 78% of cases occurred in patients <50 years of age
  - 8% death rate
  - Risk factors: male, >37 years of age, coma, mental status disorder, intracranial hemorrhage, thrombosis of the deep cerebral venous system, CNS infection, cancer
  - >80% of patients were anticoagulated with heparin

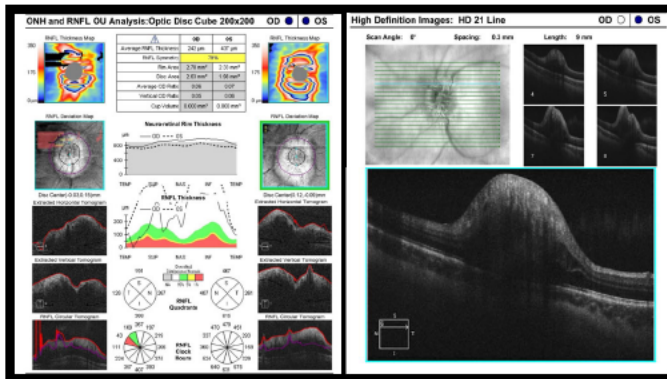
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## THE GREAT MASQUERADER

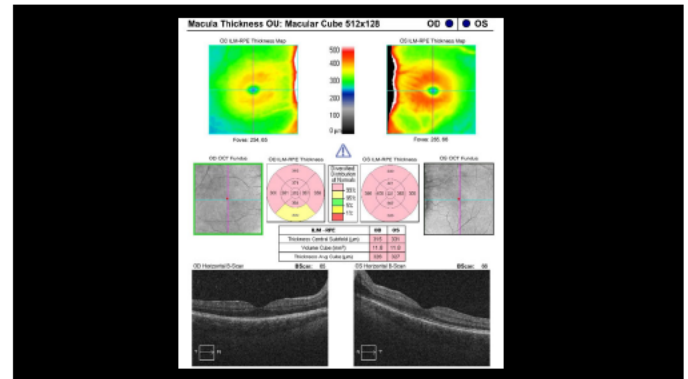
32 male- decreased vision OS > OD, skin rash on arms, headaches and neck stiffness (taking ibuprofen 8-12xs a day). BCVA OD 20/20-2, OS 20/30  
+ 1-2+ AC rxn OU



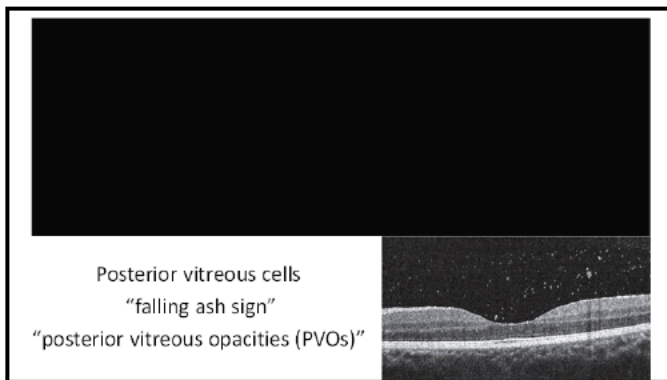
108



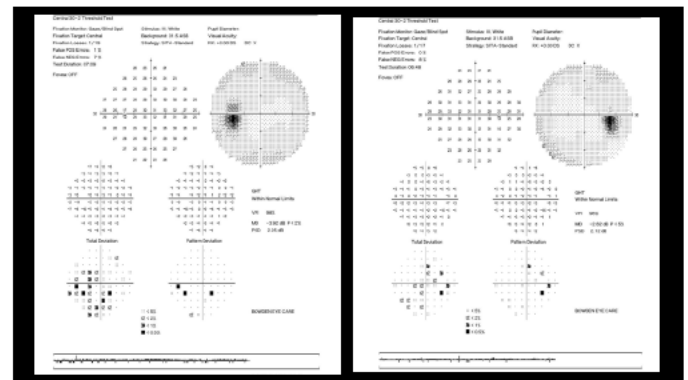
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### Systemic Work-up (panuveitis)

Labs	Systemic disease
Lyme IgG/IgM Ab	Lyme disease
RMSF IgG, IgM	Rocky Mountain Spotted Fever
RPR, FTA-ABS	Syphilis
HIV scr 4 <sup>th</sup> gen	Human Immunodeficiency virus
QuantiferON TB Gold	Tuberculosis
ACE, Serum lysozyme	Sarcoidosis
HLA-B51	Behcet's disease
HLA-DR4, HLA-DR1	Vogt-Koyanagi-Harada (VKH)
Bartonella Ab panel	Cat Scratch
Toxoplasma gondii IgG/IgM Ab	Toxoplasmosis

ESR, CRP, CBC with diff and platelet count

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### THE GREAT MASQUERADER

**Diagnosis:** Panuveitis OS secondary to neurosyphilis

**Treatment:**

- Contact tracing: patient was Ed on contacting all past sexual partners and advising them to get tested
- Referral to Infectious Disease clinic
- Infectious Disease reported to the local Public Health Agency
- Admitted and started on IV infusion penicillin G 24 million units daily x 10 days

**Perform LP in all pts with ocular manifestations**  
**\*\*Ocular syphilis should be managed according to treatment recommendations for neurosyphilis**

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## Syphilis- Ocular Manifestations

- **One of the great masqueraders!**

- Uveitis

- Posterior uveitis, panuveitis most common
- May or may not be granulomatous
- Retinitis, vitritis possible

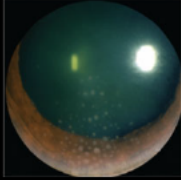
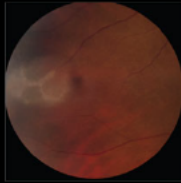
- Chorioretinitis

- Typically multifocal and associated with heavy vitritis

- Vasculitis

- **Papillitis/optic neuropathy**

- Interstitial keratitis
- Conjunctivitis
- Episcleritis or scleritis
- CN palsies
- Argyll Robertson pupils

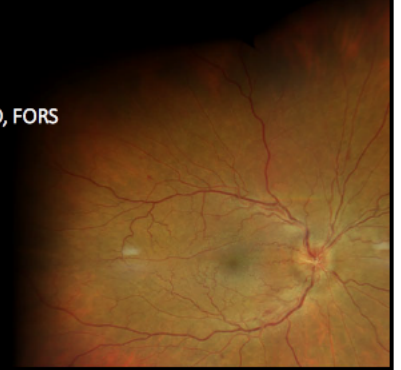


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*Thank you!*

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