IS IT GLAUCOMA OR A MASQUERADER?

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DISCLOSURES KOETTING

*ALL RELEVANT FINANCIAL CONFLICTS HAVE BEEN MITIGATED

- Ocular Therapeutix
- Glaukos
- Horizon
- Quidel
- Eyevance/Santen
- Ivantis
- Orasis
- Claris Bio
- Aldeyra
- Dompe
- RVL
- Oyster Point
- Allergan/Abbvie
- Alcon
- Visus
- Thea
- Bruder
- Glaukos
- B & L
- Twenty Twenty
- Myze
- Azura
- Scope
- Iveric Bio
- Trukera

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GLAUCOMA DISEASE BURDEN

- approximately 76 million people will suffer from all types of glaucoma
- estimated to reach 111.8 million by 2040
- At least, half of those with glaucoma are unaware that they are affected. In some developing countries, 90% of glaucoma is undetected.
- In many cases, glaucoma may be asymptomatic.
- It is estimated that more than 11 million individuals will be bilaterally blind due to glaucoma in 2020 (around 13% of the cases).

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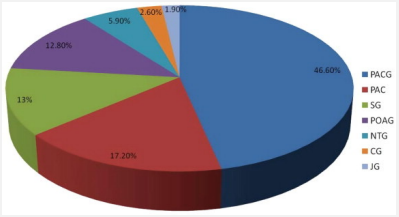

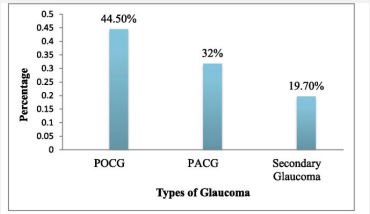

POAG: primary open angle glaucoma, PACG: primary angle-closure glaucoma

SECONDARY GLAUCOMA PREVALENCE

Wubet, G.M., Assefa, A.A. Glaucoma and its predictors among adult patients attending ophthalmic outpatient department: a hospital-based study, North West Ethiopia. *BMC Ophthalmol* **21**, 400 (2021). https://doi.org/10.1186/s12886-021-02168-y

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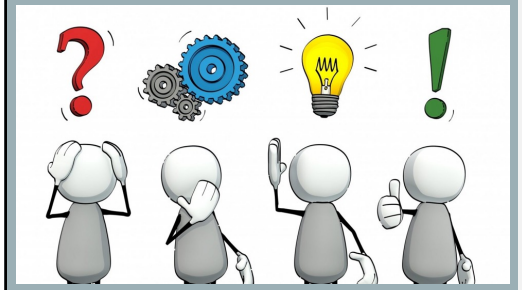
BUT WHEN IS IT SECONDARY GLAUCOMA?



- Optic Nerve cupping
- Medical history
- Visual field analysis
- Angles
- Other clinical clues

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ONH CUPPING

Primary glaucoma vs Secondary glaucoma

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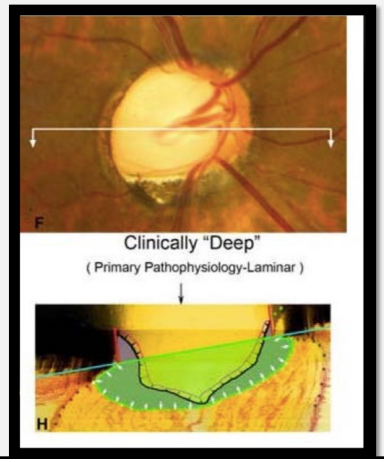
PATHOPHYSIOLOGY OF "CUPPING"

- Glaucomatous
  - Cupping is believed to occur from laminar deformation
  - Deep cupping from laminar insult
  - Deep cups is largely IOP related



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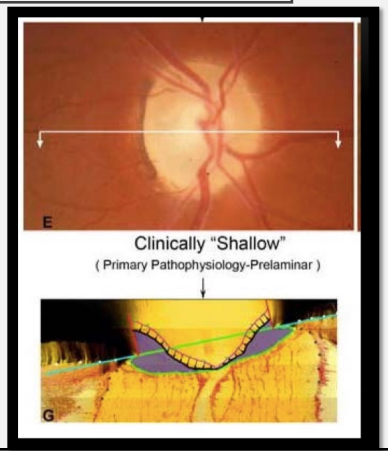
PATHOPHYSIOLOGY OF "CUPPING"

- Non-Glaucomatous: AION
  - Non-glaucomatous cupping believed to occur as pre-laminar tissue thinning
  - Appears as shallow cupping, occurs from pre-laminar insult



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CLINICAL FINDINGS

- OAG is not typically quick onset with visual symptoms
  - AION and ON will occur acutely
  - Compression will be variable
- Non glaucomatous ON will have a dimming or decreased/blurred vision
  - Poor visual acuity
- Non glaucomatous ON will often be asymmetric and may have pain
- Non glaucomatous ON will most often have reduced color vision
- APD more often present in non glaucomatous

9

OTHER FACTORS

- Patients medical history
  - HTN, DM, trauma, MS, ED drugs
- Visual field defects
  - More classic glaucomatous defects
    - Nasal steps
    - Temporal wedges
    - Arcuate defects
    - Paracentral defects

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PATIENT CASES: DO YOU THINK THEY HAVE GLAUCOMA?

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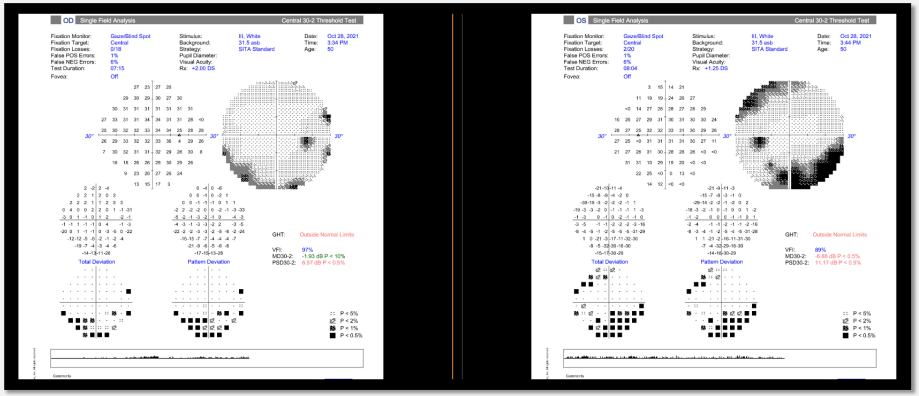
Patient #1

42 year old male



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DOES THIS PATIENT HAVE GLAUCOMA?

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PSEUDOEDEMA

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OPTIC NERVE HEAD BURIED DRUSEN

- ODD are acellular deposits of calcium, amino acids, nucleic acids, and mucopolysaccharides
  - Form in theory from impaired axonal metabolism in genetically predisposed individuals
  - Presence of narrow scleral canals are factors believed to play a role in drusen development
- Located within ONH
  - In front of lamina cribrosa
- Approximately 0.3-2% of the population
- As drusen become larger over time the can cause a progressive visual field defect due to the secondary thinning of the RNFL
  - ODD are accompanied by visual field defects in up to 87% of adult cases

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OPTIC DISC DRUSEN STUDIES CONSORTIUM

- ODD may cause sudden-onset painless vision loss through a variety of mechanisms including
  - non-arteritic anterior ischaemic optic neuropathy (NA-AION),
  - central retinal artery occlusion
  - central retinal vein occlusion,
  - choroidal neovascularization
- In two recent retrospective studies of young individuals (aged 50 years or less) with NA-AION, 51% to 53% of NA-AION eyes had ODD

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PREVIOUS STANDARD OF DIAGNOSTICS

- B- Scan ultrasonography or CT imaging
  - Limitation is that detection requires adequate calcification of the ODD (ergo, less calcified drusen may be missed)
- Fluorescein Angiography and Fundus autofluorescence
  - Intravenous FA and fundus autofluorescence are insensitive to deeper lying ODD

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CURRENT DIAGNOSIS PROTOCOL FROM ODDSC

Prior to Scanning	Optimise scan quality by dilating pupils as needed, measuring corneal curvature and refraction
Acquisition	To visualize deeper structures, use EDI mode, then type in corneal curvature and refraction in the operator system
Dense optic nerve head (ONH) scan	To identify ODD, select EDI mode and high-resolution acquisition, centre a scan area of 15 × 10 degrees covering the entire optic disc area, scan with 97 sections in that area (30 μm between scans), average at least 30 frames, and perform the volume scan in horizontal (axial) direction only
Radial ONH scan	Assess scleral canal size by using EDI mode, select 20-degree 6-line radial scan, and centre scan at optic disc
Peripapillary scan	Evaluate RNFL thickness by deselecting EDI mode, select 12-degree peripapillary scan, and centre scan at optic disc
Macular scan	To exclude macular pathology, deselect EDI mode, centre scan area of 20 × 20 degrees over macula, scan with at least 25 sections (240 μm between scans), and average at least 9 frames
Autofluorescence	To identify autofluorescence, centre scan at optic disc, and average 100 frames

Enhanced depth imaging (EDI) optical coherence tomography and autofluorescence protocol specifications for identifying optic disc drusen (ODD)

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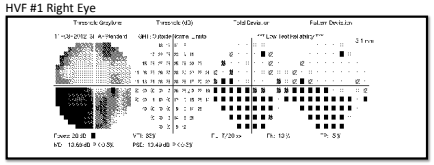
VISUAL FIELDS AND PROGNOSIS

- Up to 87% of ONHD have a visual field defect
- ODDSC study
  - Larger ODD volume was associated with worse visual field defects, not location within ONH
- Most common visual field defect
  - Inferior nasal step
  - Sectoral arcuate scotoma
  - Enlarged blind spot
  - Concentric peripheral constriction

HVF #1 Right Eye



HVF #1 Left Eye

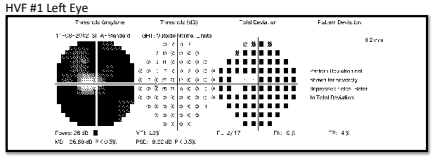


Figure 3

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TREATMENT

- Monitor with visual fields and OCTG
- If vision becomes compromised can treat with topical IOP lowering medications
  - Secondary glaucoma
  - There are no controlled clinical studies to support this approach
- 2018 study
  - Higher IOP was not associated with greater VF loss or thinner RNFL at the time of presentation
  - This suggests that lowering IOP may not be beneficial in preventing visual loss in normotensive eyes with ONHD.

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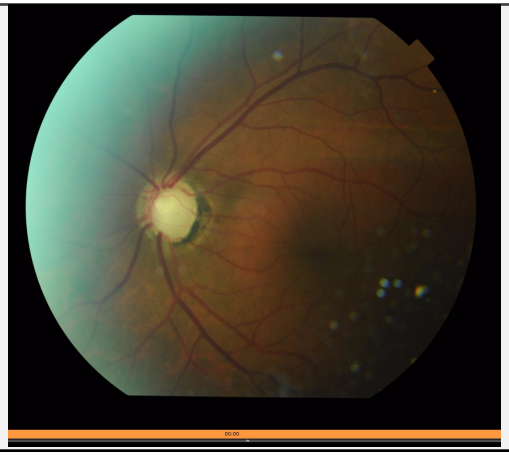
PATIENT # 2



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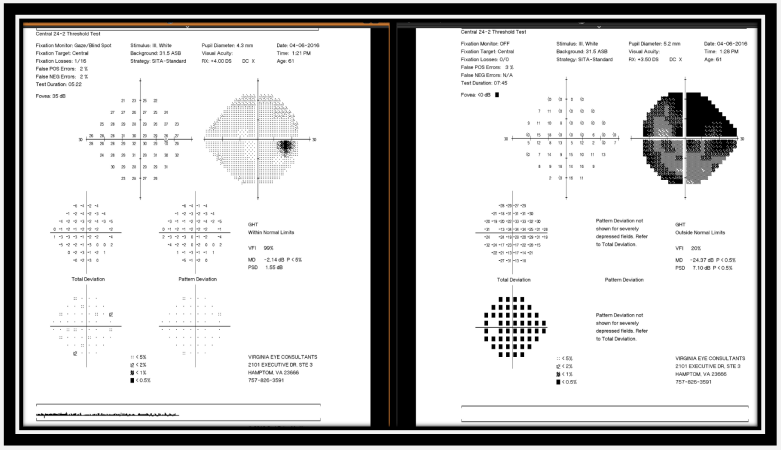

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MORE QUESTIONING

- No history of diabetes
- HTN controlled with oral medication
  - BP normal in office that day
- **Does currently use sildenafil and has used for the last several years**
- No Hx of major surgeries with complications or blood loss/significant BP drop
- Does not report excessive alcohol use

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NOW WHAT?

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TESTING

- Blood work CRP/ESR
  - NORMAL
- MRI Orbit and head w/ and w/o contrast
  - MRI head NORMAL
  - MRI ABNORMAL
    - Asymmetric hyperintense signal in left optic nerve without enhancement with associated volume loss of optic nerve
      - indicating possible etiology of optic neuropathy

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NON-ARTERITIC ISCHEMIC OPTIC NEUROPATHY

- Localized ischemic event at junction of optic nerve
- May be younger in age than AION (40-60 YOA)
- Signs and symptoms
  - Sudden painless vision loss
    - 30-2 severe defect
    - VA decreased
      - Less severe than AION
  - APD
  - Pale disc swelling
  - Flame shaped heme

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NAION

- Diagnosis of exclusion
  - Normal MRI
    - May find chronic microvascular changes on MRV
  - Normal ESR/CRP
- 40% show some improvement in vision over the next 6 months
  - Monitor with visual fields
- Optic nerve edema will resolve within 8 weeks
  - Can monitor with OCTG
- Risk of contralateral eye involvement

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NAION AND SILDENAFIL

- 2006 study monitoring 13000 men showed no increase risk of NAION in patients on sildenafil when compared with similar population not on the medication.
  - Incidence of 2.8 patients per 100,000 men >50YOA

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NAION AND SILDENAFIL

- 2015 study of 1109 cases of NAION also showed no increased correlation with use of sildenafil or a PDE-5inhibitor within 30 days of onset
- Cases were more likely to have hyperlipidemia, diabetes, hypertension, myocardial infarction and cerebrovascular accident

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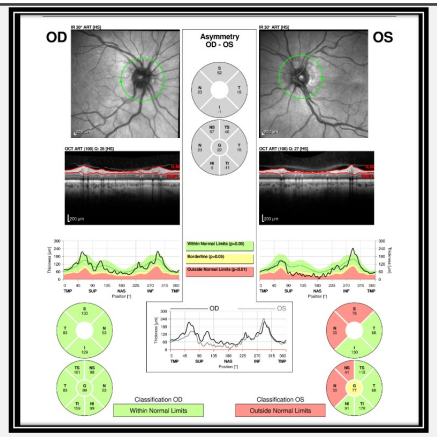
PATIENT #3 3/19/19



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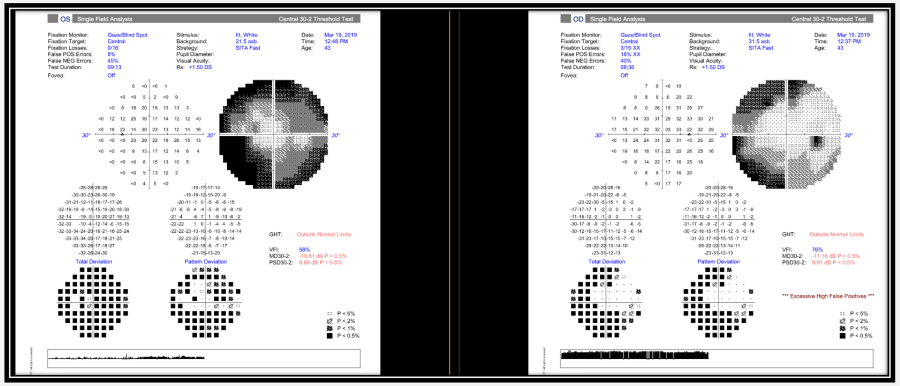
CURRENT VISUAL FIELD



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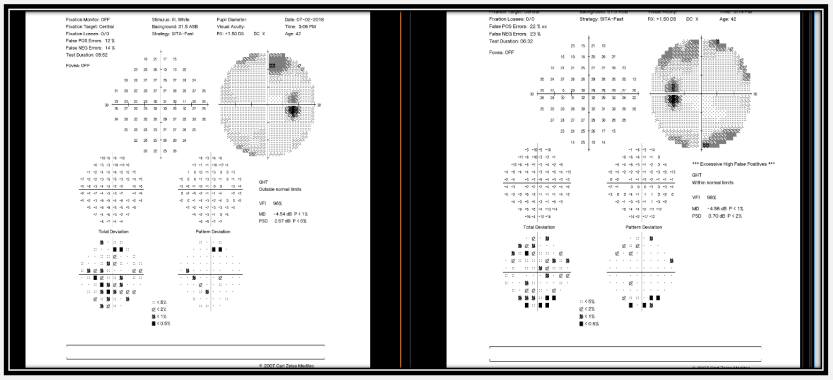
HOW IT STARTED (7/2/18)



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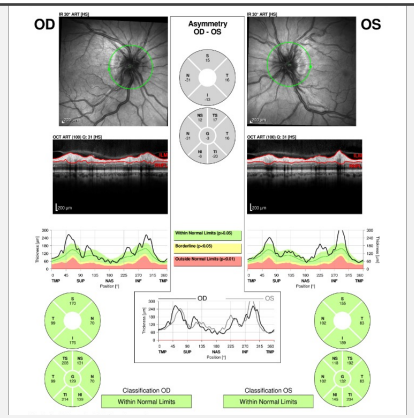
HOW IT STARTED (7/2/18)



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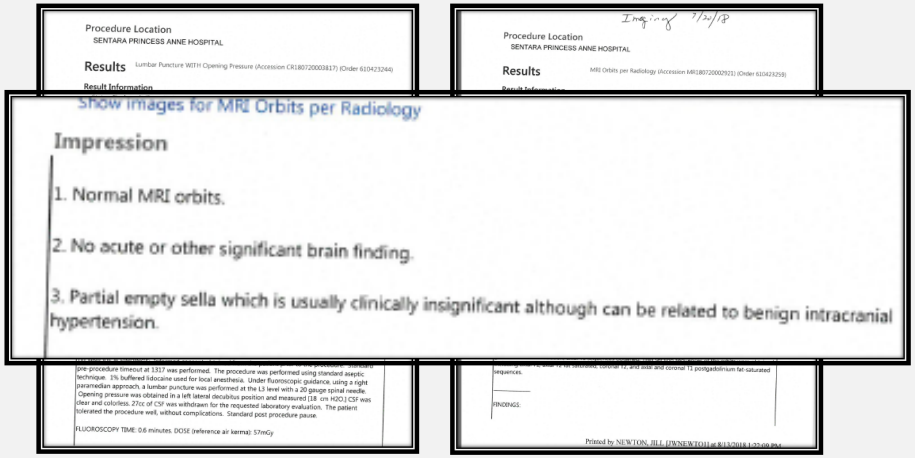
Imaging Obtained 7/20/18



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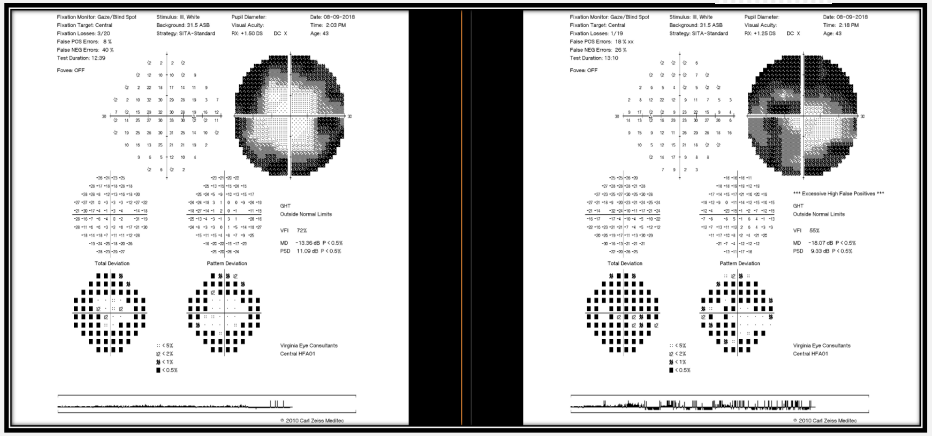
I WEEK AFTER MRI…..
OK THAT ESCALATED!



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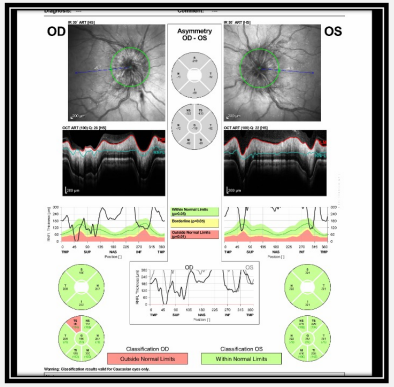
EMERGENT ONH FENESTRATION



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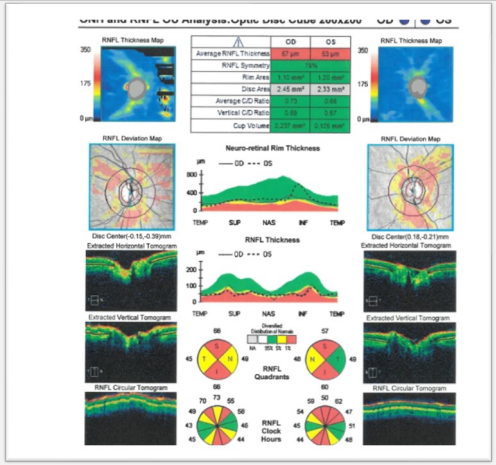
WHAT ABOUT THIS PATIENT?



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MR ORBIT W/WO CONTRAST - 06/01/2022.

Optic Nerves/Chiasm:
Unchanged prominent CSF around optic nerves. Unchanged right greater than left optic nerve atrophy, greatest at the prechiasmatic and chiasmatic area. No suprasellar mass.

Orbits:
No masses, infiltration or enhancement of orbital fat.

Extraocular Muscles:
Normal in size, shape, and enhancement.

Lacrimal:
Normal lacrimal glands. No abnormality at the location of lacrimal sacs.

Extra-Orbital:
Mild sequential mucosal thickening of the paranasal sinus. The imaged mastoids are clear. The pituitary gland is mildly flattened within the sella that is partially filled with CSF, unchanged from prior.

Extra-Orbital:
Mild sequential mucosal thickening of the paranasal sinus. The imaged mastoids are clear. The pituitary gland is mildly flattened within the sella that is partially filled with CSF, unchanged from prior.

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IDIOPATHIC INTRACRANIAL HYPERTENSION

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MODIFIED DANDY CRITERIA

- No other causes of increased intracranial pressure present with CSF opening pressure of 20cm to 25 cm water, required at least one of the following:
- Pulse-synchronous tinnitus (pulsatile tinnitus)
- Cranial nerve VI palsy
- Frisen Grade II papilledema
- Echography for drusen negative and no other disc anomalies mimicking disc edema present
- MRV (Magnetic Resonance Venography) with lateral sinus collapse/stenosis preferably using ATECO technique
- Partially empty sella on coronal or sagittal views and optic nerve sheaths with filled out CSF spaces next to the globe on T2 weighted axial scans

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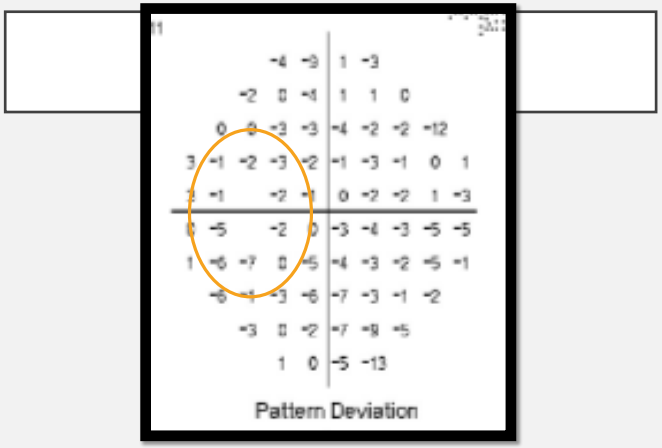

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IIH

- AKA Benign intracranial hypertension and pseudotumor cerebri
- Increased intracranial pressure with unknown cause
  - Diagnosis of exclusion
- Signs and symptoms
  - Headaches, tinitis, tingling in fingers and toes
- Diagnosis
  - EOM, OCT-G, 30-2, color vision, red cap
  - SVP?
  - MRI
    - Within 1-2 weeks
  - Lumbar puncture
    - Increased exiting pressure with normal fluid
  - Pregnant patients
    - Usually not treated

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IIH

- Causes
  - Weight
  - Birth control
  - PCOS
  - Minocycline, doxycycline, etc
- Long term concerns and treatment
  - Diamox (acetazolamide)
  - Topamax
  - Shunt
  - Optic nerve fenestration
  - Weight loss
    - Approx. 10% body weight loss has been show to reverse

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LONG TERM OCULAR CONCERNS

- Secondary glaucoma and ONH RNFL damage
  - Monitor with OCT of ONH
  - HVF 24-2
  - Treat similar to normal tension glaucoma

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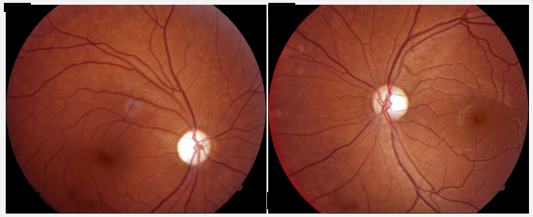
- 46 Year old AA Female
  - Significant vision loss and atrophy OU
  - Multiple occurrences of bilateral optic neuritis x 5 years.



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CC: R eye pain/blurry vision

ASSESSMENT:

#Optic perineuritis, with R eye pain/blurry vision

Onset of R eye pain with lateral movement and blurry vision on 9/15/21 that gradually worsened. Pt presented to ED on 10/12/21. MRI orbits w/wo contrast showed "enhancement involving the perioptic nerve sheath as well as the intraconal optic nerve. Findings may represent orbital lymphoma given nerve and perineural involvement." CSF studies from LP are pending. Pt has completed 3/5 days of IV Solumedrol and reports slight improvement in visual sxs. Pt will need to complete course of steroids and have close f/u with ophthalmology/neurology.

PLAN:

-Pt needs to complete 5 day course of IV Solumedrol, today is day 3/5
-CSF studies pending
-Continued f/u with ophthalmology
-Pt will need close OP neurology f/u, referral placed
-Final recommendations per neurology attending

NMO, IgG, Serum

Status: Final result Visible to patient: Yes (seen) Next appt: 04/08/2022 at 09:00 AM in Neurology

0 Result Notes

	Ref Range & Units	4 d ago
NMO IgG Serum	0.0 - 3.0 U/mL	48.6 ^
Comment:	Negative:	0.0 - 3.0
	Positive:	>3.0

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NEUROLYELITIS OPTICA SPECTRUM DISORDER (NMOSD)

- Previously thought of as variant of MS
- Demyelination of optic nerve and spinal cord
- Associated with aquaporin-4 (a water channel present in glial cells) antibodies.
- Testing for NMO-IgG should be considered in those patients with bilateral ON or ON coupled with longitudinally extensive transverse myelitis (LETM), recurrent ON, or brain MRIs atypical for MS
- No cure, but similar treatment to MS
- Poor prognosis, loss of muscle function, often death occurs 2/2 respiratory complications

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NMOSD VS MS

- Higher likelihood to have ON vs MS
- More likely to present as bilateral ON or to occur in both eyes during separate times
- More likely to have permanent vision loss
  - Minimal to no improvement after resolution of ON
- More likely to exhibit ONH atrophy after ON

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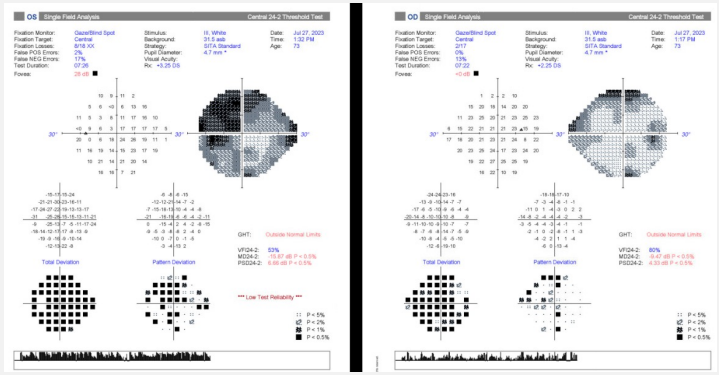
73 YOA MALE



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HISTORY OF BILATERAL OPTIC NEUROPATHY

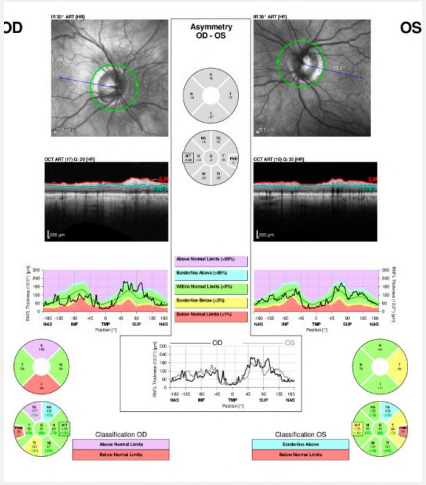
Does not have MS

Does not have NMOSD

No Immune disorders or inflammatory

MRI findings: demyelination versus other (sarcoid)

Neuro Opthalmologist at last appointment: patient being referred to glaucoma today because of the extensive cupping despite the fact that we know he has bilateral optic neuropathy current with potential neurosarcoid v. Other



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WHY THE DECREASED VISION IN OS IF EVERYTHING IS STABLE?

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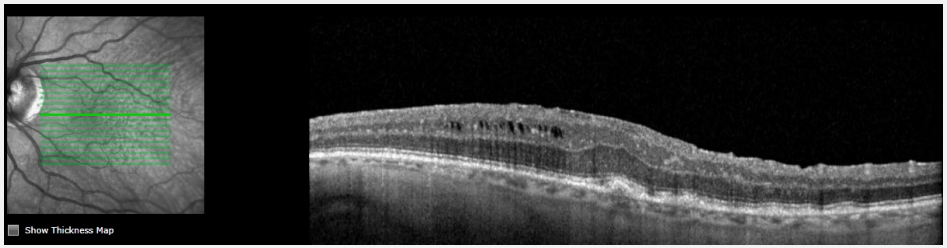
DON'T FORGET THE MACULA



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OTHER FACTORS?

Toxic and Nutritional Optic Neuropathy

- Tobacco
- Methanol
- Ethambutol
- Alcohol
- Vitamin B-12
- Folate
- Copper
- Amiodarone

Neurodegenrative disorders

- Alzheimer's
- Parkinson's

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MIGRAINES

Research Article

The Impact of Migraine on Posterior Ocular Structures

Süleyman Demircan,[1] Mustafa Ataş,[1] Sevgi Arık Yüksel,[2] Melek D. Ulusoy,[1] İsa Yuvacı,[1] Hasan Basri Arifoğlu,[1] Burhan Başkan,[1] and Gökmen Zararsız[3]

[1]*Kayseri Training and Research Hospital Eye Clinic, 38010 Kayseri, Turkey*
[2]*Kayseri Training and Research Hospital Neurology Clinic, 38010 Kayseri, Turkey*

different between the groups. *Conclusions*. This study suggests that migraine leads to a reduction in the peripapillary RNFL thickness and to thinning in choroidal structures. These findings can be explained by a chronic ischemic insult related to migraine pathogenic mechanisms and these findings are considered supportive of the relationship between glaucoma and migraine.

Purpose. To investigate the thickness of the retinal nerve fiber layer (RNFL) and choroid in patients who have migraines in comparison to healthy controls. *Methods*. This study included 76 eyes and patients in the migraine group, 36 with aura (MWA group) and 40 without (MWoA group), and 38 eyes as control subjects. The RNFL and macular thicknesses were analysed with standard OCT protocol while choroidal thickness was analysed with EDI protocol in all subjects. Choroidal thickness was measured at the fovea, 1500 μm nasal and 1500 μm temporal to the fovea in a horizontal section. *Results*. The mean RNFL thickness for nasal and nasal inferior sectors was significantly thinner ($P \leq 0.018$) in the migraineurs' eyes than in those of the controls, as was the mean choroid thickness at the fovea and measured points ($P < 0.0001$). However, the mean macular thickness was not significantly different between the groups. *Conclusions*. This study suggests that migraine leads to a reduction in the peripapillary RNFL thickness and to thinning in choroidal structures. These findings can be explained by a chronic ischemic insult related to migraine pathogenic mechanisms and these findings are considered supportive of the relationship between glaucoma and migraine.

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KEY TAKE HOME POINTS

- If it smells fishy, check it out
- Order testing in house and out of house when appropriate
- Continue to monitor these patients for progression
- Treat when necessary
- Refer or phone a friend when you need help!

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QUESTIONS?

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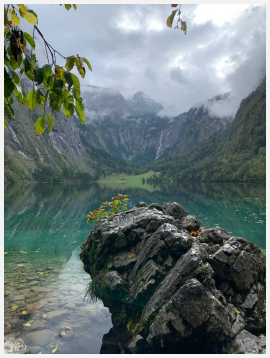
THANK YOU!
DR.CECELIAKOETTING@GMAIL.COM



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