Zoster Doesn't Take Vacations

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Abstract

Herpes Zoster (HZV) is the reactivation of the latent varicella zoster virus, often induced by stress or a compromised immune system.[1] When the virus reactivates along the trigeminal dermatome, it is likely for ocular involvement to occur, which is then called zoster ophthalmicus (HZO). It is widely understood that zoster can cause inflammation of all parts of the eye including adnexa, conjunctiva, cornea, uvea, and even the retina. This case highlights the relapsing and remitting nature of the course of herpes zoster and the importance proper follow-up care through the various stages of infiltration of the virus throughout the eye.

Case Report

A 75-year-old white male presented to the eye clinic as an urgent referral from primary care to check for ocular involvement of Herpes Zoster. The patient explained that he had woken up 2 weeks ago with blisters on the right side of his face. At that time, he presented to the emergency department, who initiated at 2-week course of valacyclovir. A few hours prior this visit in the eye clinic, the patient was seen by his primary care who determined that he no longer needed to take the valacyclovir. The patient explained that his vision was blurred, and he experienced frequent tearing, he did not have any pain at this time.

POHx: unknown, first ever eye exam
PMHx: hypertension, hyperlipidemia, GERD, right BKA, PTSD
Current Medications: amlodipine, atorvastatin, chlorthalidone, cyclobenzaprine, diclofenac, omeprazole, Medrol dosepak (completed)

Per chart review, the patient presented to the emergency department a few days prior to the onset of the blisters for right hip pain that started one month ago after falling. Of note, at this visit the patient was given injection of ketorolac 30mg IM, and methylprednisone 40mg IM, then prescribed a Medrol dosepak. Five days later he returned to the emergency department for facial swelling, of which he believed was a reaction to the medication. At this time, the patient was diagnosed with herpes zoster and was started on the 2-week course of valacyclovir.

At the initial eye clinic visit, the patient had SPK staining and a possible faint, resolving pseudodendrite. Therefore, preservative free artificial tears (PFATs) were prescribed for lubrication and comfort. The eyecare provider intended to follow-up with the patient in one week, however the patient noted he was going on vacation, so instead he returned sooner, prior to going out of town. At this time, there was early and mild stromal haze, so valacyclovir 1000mg tid was re-initiated. The patient returned after 10 days of vacation with decreased vision. Slit lamp findings revealed extensive stromal edema and possible bullae (Figure 1-3.)

Treatment and Management

Visit	BCVA	Findings	Treatment	
1	20/25	SPK, faint resolving pseudodendrite		
2	20/50-2	mild stromal haze	Valacyclovir 1000mg tid	
3 + 4	20/60	stromal edema, DM folds, possible bullae	Valacyclovir 1000mg tid	Moxifloxacin qid, pred qid
5	20/60+2	stromal edema, DM folds, possible bullae	Valacyclovir 1000mg tid	Moxifloxacin qid, pred qid
6	20/40	stromal edema, DM folds, possible KPs	Valacyclovir 1000mg tid	Pred 6x/day
7	20/25-1	mild K haze	Valacyclovir 1000mg tid	Pred 6x/day for 3 days then qid
8	20/25-1	no active inflammation	Valacyclovir 1000mg tid for 1 month then qday for 6-12 months	Pred taper

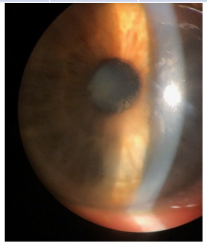

Figure 1. Corneal cross section focused on endothelial folds at visits 3 + 4

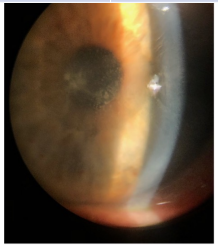

Figure 2. Corneal cross section focused on epithelium at visits 3 + 4

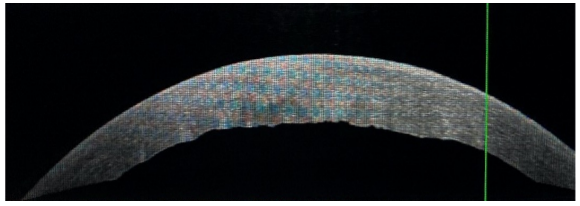

Figure 3. Anterior segment OCT demonstrating scalloped appearance of the endothelium with mild focal endothelial edema. Epithelium and stroma grossly intact.

Discussion

HZO often takes a relapsing and remitting course, as outlined here. If the patient was able to follow-up as suggested by the eyecare provider, topical steroids could have been initiated sooner and perhaps the patient may have healed faster. Instead, after 10 days without follow-up care the patient came back with sight-threatening complications. Anterior segment OCT was used to rule out the presence of epithelial bullae, which provided additional confidence in increasing the dosing of prednisolone.

HZV can manifest almost anywhere in the eye, it is important to understand the pathophysiology and subsequent management for each part of the eye in order to save vision and prevent post-herpetic neuralgia.

- **Eyelids/Adnexa:** preseptal cellulitis
- **Conjunctiva/Sclera:** conjunctivitis (follicles), scleritis[1]
- **Uvea:** anterior and posterior (vitritis, retinitis, optic neuritis) , strongest risk factor for vision loss[2]
- **Cornea:**
  - **Epithelium:** invasion of live virus, SPK, may coalesce to pseudodendrite between day 4-6[3]
  - **Stroma:** immune-mediated response to virus, can cause neovascularization and permanent scarring
  - **Endothelium:** occurs in 1-7% of HZO cases, presents between day 4-7 following rash, can cause corneal decompensation[3]
  - **Neurotrophic Keratopathy:** damage to corneal nerves

It is well understood that HZV can be re-activated by immunosuppression and stress, both of which applied to this patient who had been dealing with the stress of severe pain after a fall and had taken systemic steroids. Further research may be useful to determine the role of steroids in activation of zoster due to immunosuppression as this is somewhat paradoxical in that systemic steroids may then later be used to treat the effects of zoster.[4]

Conclusion

This case demonstrates the use of technology, including anterior segment OCT, to localize and best manage herpes zoster endotheliitis. Understanding the anatomy and pathophysiology of disease allows eye care providers to treat and manage more efficiently. Finally, this case serves as a reminder of the importance of patient education on the course of diseases, including the importance of proper follow-up care. Patient adherence is critical for conditions like herpes zoster than can have lasting, and potentially blinding long-term effects.

Additionally, this reinforces the importance of recommending vaccination for zoster as a public health effort. One study suggested that the vaccinated individuals who still ended up having shingles were 3x less likely to have ocular involvement[5]. It is imperative that eyecare providers promote vaccination in the effort to reduce blindness and post-herpetic neuralgia.

Contact

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Financial Disclosures

None to report

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Starving for Oxygen

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Background

- Ocular ischemic syndrome (OIS) is a unilateral vision-threatening condition associated with severe carotid artery occlusive disease leading to decreased blood flow to the globe. [1,4]
- Central Retinal Artery Occlusion (CRAO) is an ophthalmic emergency presenting as an acute, unilateral, painless loss of vision associated with obstruction of blood flow to the central retinal artery.[3,4]
- A systemic stroke workup is indicated with a diagnosis of OIS or CRAO due to increased concern for impending ischemic strokes.[4]

Case History

- A 72-year-old Caucasian male presented with sudden painless vision loss in his right eye for 2 months.
- Medical history was remarkable for diabetes, hypertension, hyperlipidemia, obstructive sleep apnea, atrial fibrillation, and obesity.

Clinical Findings

Exam	Findings
BCVA	**OD: 20/HM** OS: 20/20
Pupils	Equal, Round, Reactive, **+APD OD**
Anterior Segment	**Whorl Keratopathy OU** **NVI OD**, no NVI OS 2+ NS OU
IOP with Goldmann	**OD: 20 mmHg** OS: 15 mmHg
Undilated Gonioscopy	OD: **NVA nasal/temporal** OS: open CB, no neo

Table 1: Initial anterior segment exam findings OD and OS.

Labs/Tests Ordered	Results
Bilateral Carotid Duplex	**RICA: 16-49% stenosis** LICA: <15% stenosis
CTA of Head and Neck	**RICA: 50% stenosis** LICA: no significant stenosis
Lab Work	ESR: 16 mm/hr CRP: <0.5mg/dL

Table 2: Result of stroke workup including imaging and lab work.

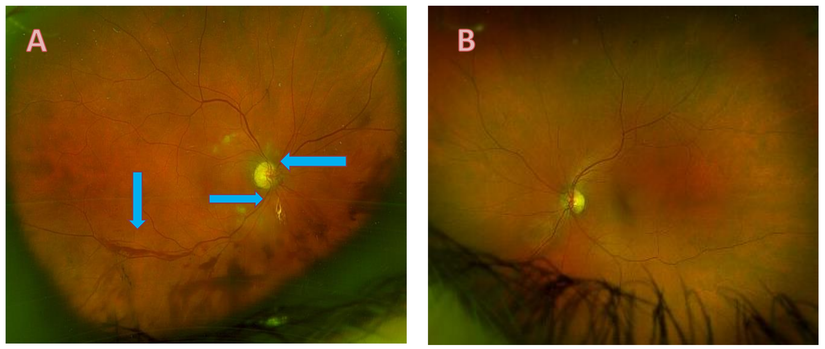

Figure 1: Initial Optos fundus photos:
A) OD: Pre/intraretinal hemorrhages, exudates, and optic nerve pallor with neovascularization of disc (blue arrows).
B) OS: Normal fundus exam.

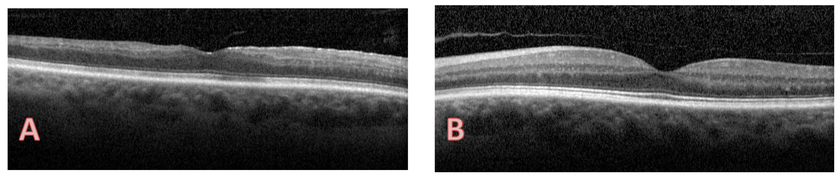

Figure 2: Macular OCT:
A) OD: Note the disorganized and thin retinal layers.
B) OS: Normal retinal layers.

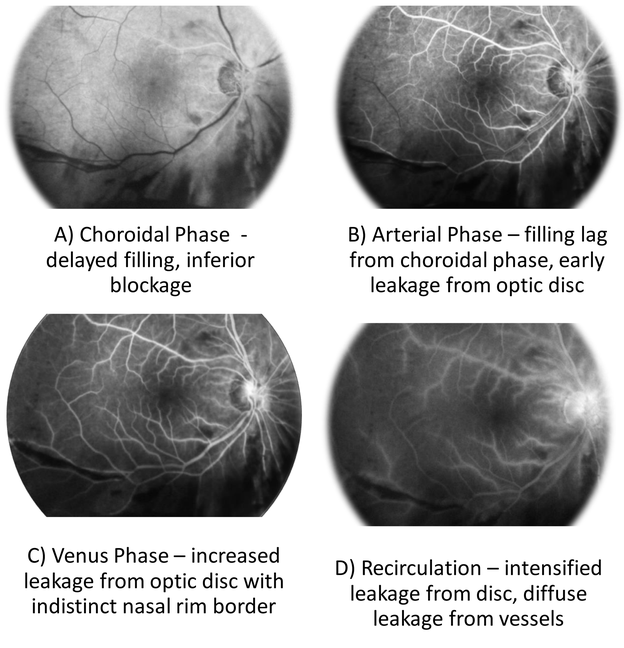

Figure 3: OD: Fluorescence Angiography.

Acknowledgement: The authors would like to thank the James A. Haley Veterans' Hospital and Pennsylvania College of Optometry for support of this presentation.

Diagnosis/Management

- The patient was diagnosed with OIS with a concurrent undiagnosed CRAO right eye.
- Retinal management included 1 anti-VEGF injection followed by 360 PRP OD. Vision prognosis is guarded.
- Discussed medical management with primary care for patient's known systemic conditions as well as stroke preventions.

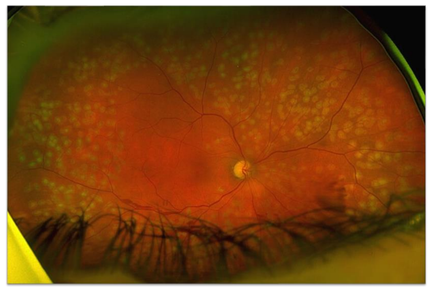

Figure 4: OD: Optos fundus photo after 1 anti-VEGF injection and PRP 360.

Discussion

- Hypoperfusion of the globe in ocular ischemic syndrome (OIS) is rare until >70% stenosis of the internal carotid artery.[1,5]
- However, there is evidence that supports OIS in patients with as little as 50% stenosis when there is poor collateral circulation between the internal and external carotid arteries.[5] This is likely the cause for OIS development in this case report.
- Chronic central artery occlusion typically presents as a perfused retina with a pale optic disc, thin and disorganized retinal layers, and attenuated vessels.[3]
- The concomitant diagnosis of a CRAO was made in this case based on the clinical presentation in a patient with severe sudden/painless loss of vision, +APD OD, and thin and disorganized retinal layers as seen on the macular OCT.

Conclusion

- Ophthalmic vascular occlusive diseases, including CRAO and OIS, can occur concomitantly.
- Systemic comorbidities have a large impact on severity of ophthalmic diseases

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All Tangled Up and Nowhere to Go

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Introduction

An ophthalmic artery aneurysm is a rupture of the ophthalmic artery due to a weakening of the blood vessel wall, usually from prolonged misdirected blood flow causing a ballooning of the weakened vessel wall, ultimately leading to rupture. Typically, these manifestations present at an average age of 52 years. In the event that an aneurysm occurs, the sequelae can be sight, or even life-threatening. Additionally, surgical intervention is quite difficult due to the location and proximity to other critical vascular structures. This case will discuss a patient with no predisposing vascular risk factors that experienced this rare ophthalmic condition at just 37 years old, and his subsequent clinical course over the years following the initial aneurysm.

Clinical Exam

Patient Demographics: A 40 year old white male presenting for routine ocular examination

Chief Complaint: new onset flashes of his left eye only and migraines with no associated triggers. Have been occurring since ophthalmic artery aneurysm in 2018, but have been increasing since last eye exam

Ocular History: 8.5mm x 7mm Left ophthalmic artery aneurysm, onset December of 2018, status-post endovascular coiling

Ocular Medications: none

Medical History: Inflammatory Polyarthropathy, Ulcerative Colitis

Systemic Medications: Leflunomide 10mg, Adalimumab 40mg every 2 weeks, Omeprazole 40mg, Celecoxib 200mg

Clinical Findings

- BCVA: 20/20 OD, OS
- Pupils: ERRL, no APD OU
- EOMS: FROM OU
- CVF: FTFC OD/OS
- IOP: 16/16 mmHg with GAT
- Cornea: 1 small cornea scar OD, clear OS
- Optic Nerve: 0.3 h/v OU, pink/distinct margins
- Macula: flat, intact
- Vitreous: clear OU
- Periphery: No holes/breaks/tears 360
- MRA Interpretation 08/23/22:
- "Metallic artifact medial to the left paraophthalmic ICA, from reported history of endovascular aneurysmal coiling. No MRA evidence of residual aneurysm.
- No large branch artery occlusion, significant arterial stenosis or new saccular aneurysm is demonstrated.
- Anatomic variant includes aplastic right A1. The major intracranial arteries appear of normal caliber. Presumed artifact of the ICA's near the skull base.
- There is an anterior communicating artery.
- The right vertebral artery is dominant intracranially."

VISUAL FIELDS

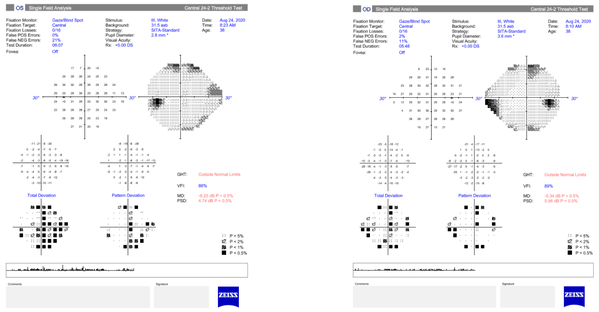

Figure 1. These are the initial 24-2 SITA Standard Humphrey Visual field tests performed when the patient first presented to the Orlando VAMC in 2020. Both fields show scattered, non-specific points.

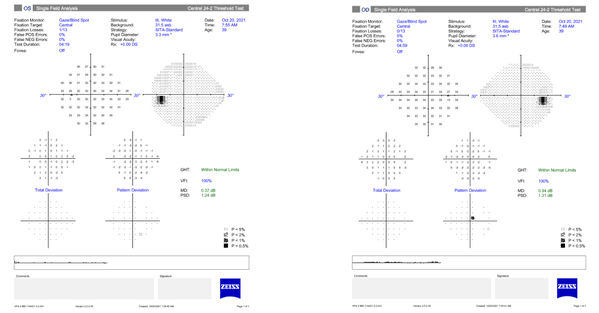

Figure 2. These are the subsequent 24-2 SITA Standard Humphrey Visual Field tests performed. Overall, both visual fields show a relatively clean appearance.

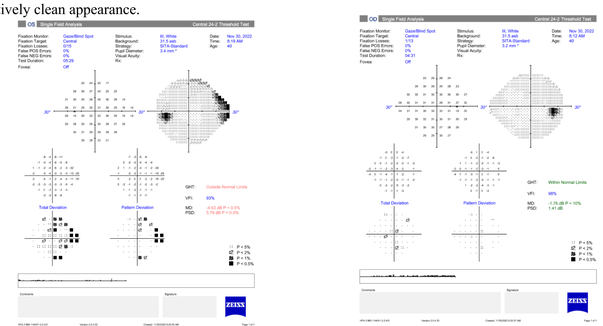

Figure 3. These are the subsequent 24-2 SITA Standard Humphrey FigureVisual fields performed, showing a relatively clean field in the right eye, but a few points in the left eye that respect the vertical midline.

Other Ancillary Testing

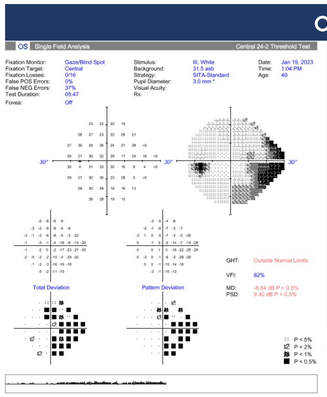

Figure 4. The most recent 24-2 SITA Standard visual field. Showing progression that respects the vertical midline

Figure 5. A still image of the most recent MRA scan taken.

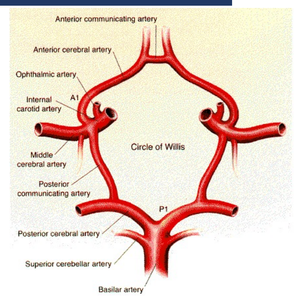

Figure 6. An anatomical reference diagram of the circle of Willis
Source: https://www.nejm.org/doi/full/10.1056/nejm199406023302204

DISCUSSION

The diagnosis of an ophthalmic artery aneurysm is one that cannot be made without neuroimaging. Many times, as is the case with this patient, there are very minimal, if any, presenting ocular signs. Interestingly, in patients who have had surgical intervention for an aneurysm with a flow-diverting stent, ocular findings remain relatively unremarkable.[1] Despite this, there can be changes in the visual function of these patients. While there has been no exact mechanism identified, it would not be unreasonable that the coiling procedure induces a low-grade ischemia originating at the site of the coiling. These ischemic changes may trickle down through the ophthalmic vasculature, and manifest changes in visual field. This is supported as well through findings in the literature stating that, while patients who underwent microvascular surgery did show lower rates of recurrent or new aneurysms, that there was a higher incidence of visual field defects among these patients.[2]

The distinction of patient symptoms is critical in determining the need for diagnostic testing. Some presenting symptoms include new onset headaches that radiate throughout the head, new onset migraines of visual auras, or headaches that cause awakening from sleep.

TREATMENT AND MANAGEMENT

An ophthalmic artery aneurysm is a medical emergency and requires immediate surgical intervention. Typically, these are not discovered until they are large enough to cause diplopia and headaches, or present as a life-threatening emergency upon rupture of the weakened vessel wall.[3] Prior to the advent of modern surgical techniques, the only way to treat this condition was involved microsurgery with a mortality rate of 25%.[3] This is due in part to the location of the ophthalmic artery, as well as the fragility of the aneurism itself. Additionally, the type of surgical intervention may affect surgical outcomes. For example, a coil embolization (as in this patient) is less likely to cause a visual field defect than a more traditional pipeline embolization device; however, is more likely to need a repeat treatment in the future.[4] Vascular surgery of any kind has a high risk of hemorrhage associated with procedure, but the current standard of care consisting of endovascular coiling and/or clipping of the aneurysm before rupture have significantly improved patient prognosis. Currently, mortality rate of this procedure is 9%. While these procedures are now standard of care, the most important risk to be aware of in these patients is a new onset visual field defect due to surgical intervention. Ultimately, in order to maximize chances of survival, surgery must be performed within 48 hours of aneurysm rupture.[5]

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“Real Eyes. Realize. Real Highs.”

A Case on Orbital Apex Syndrome & the Anti-Inflammatory Effects of Cannabis Sativa

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Background

- Orbital apex syndrome (OAS) is a rare ocular disease that can make diagnosis challenging given the proximity of the anatomical structures within the orbital apex.
- OAS involves the dysfunction of the optic nerve (CN II), oculomotor nerve (CN III), trochlear nerve (CN IV), abducens nerve (CN VI), and/or the ophthalmic branch of the trigeminal nerve (CN V1).[1]
- OAS has a wide range of etiologies including inflammatory, infectious, traumatic, neoplastic & other causes.

Purpose

- Orbital apex syndrome results in ophthalmoplegia & optic neuropathy due to involvement of the ocular structures within the orbital apex.
- Signs & symptoms of OAS include vision loss, diplopia, proptosis, ptosis, pupil abnormalities, absence of corneal sensation/reflex, conjunctival chemosis, choroidal folds, periorbital/facial pain, hypoesthesia of the forehead, optic disc edema, & optic atrophy.[2]
- This is a case report of a patient with an atypical presentation & resolution of OAS

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- Thank you to the Gainesville VAMC Optometry & Ophthalmology Staff

Case Report

68-year-old Caucasian male presents to the urgent ophthalmology clinic

Chief Complaint:

- Decreased vision, binocular diplopia, & restricted eye movement OS ~ 2 weeks

Ocular History & Medications

- Cataracts, dry eye syndrome OU
- PFATs prn OU

Medical History & Systemic Medications

- Type 2 DM, coronary artery disease s/p CABG, myocardial infarction s/p stents, colon cancer s/p colectomy, chemo & radiation
- Glipizide, atorvastatin, metoprolol, aspirin

Pertinent Exam Findings

- BCVA cc: 20/20 OD, 20/50 OS PHNI
- Pupils: ERRL +APD OS
- EOMS: Full OD, Restricted OS (Sup -2, Inf -2, Nasal -2, Temp -3) *diplopia noted on inferior gaze OS*
- Color Vision: 14/14 OD, 5/14 OS
- SLE unremarkable
- DFE elevated blurred optic disc margins 360 without obscuration of vessels and no hemes OS

Imaging

- MAC OCT OD/OS unremarkable

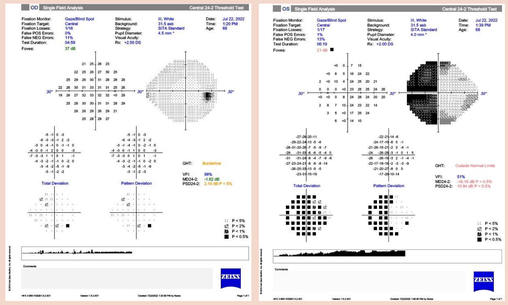


Fig. 1 & 2 Baseline HVF 24-2 SS OD & OS

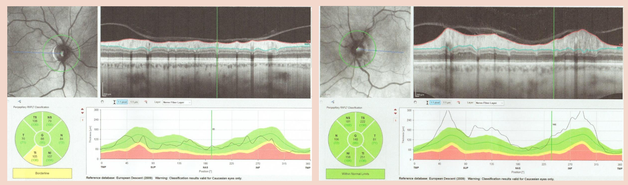


Fig. 3 & 4 Baseline OCT RNFL OD & OS

Discussion

Differential Diagnosis: cavernous sinus syndrome (CSS), superior orbital fissure syndrome (SOFS), & orbital apex syndrome

Anatomy/Pathophysiology:

- Orbital apex = optic canal + SOF
- Optical canal = CN II + ophthalmic artery
- SOF – 3 divisions separated by the common tendinous ring (CTR)
  - Superior: lacrimal & frontal branch of CN V1, CN IV, sup branch of ophthalmic vein, recurrent meningeal artery
  - Middle: nasociliary branch of CN V1, CN VI, sup & inf branch of CN III
  - Inferior: inf branch of ophthalmic vein

Etiology/Management:

- Inflammatory – corticosteroids
- Infectious – anti-microbial therapy
- Iatrogenic/traumatic – corticosteroids & decompressive surgery
- Neoplastic – surgical resection, radiation therapy, and/or chemotherapy
- Vascular – managed conservatively; anticoagulation, endovascular, and/or surgical intervention

Initial Assessment & Treatment

Diagnosis: Suspect Orbital Apex Syndrome OS

- **Pertinent Lab Findings:** significantly elevated IgG4 148.9 (Reference Range: 4-86)
- **MRI:** “soft tissue thickening & enhancement at the left orbital apex extending posteriorly into anterior aspect of the left cavernous sinus”

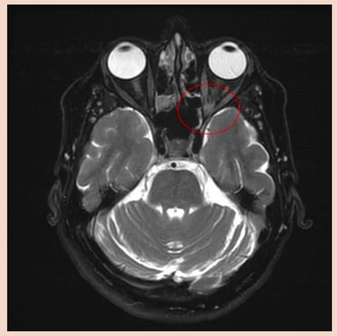


Fig 5. T2 Axial MRI Brain

- Recommended urgent hospitalization & IV steroid treatment, but pt. refused against medical advice
- Pt. smoked ~1 gram of cannabis sativa/daily as only form of treatment option during course of 2-month follow-up period

Outcome

Follow-Up Visit	BCVA OS	Pupils OS	Color Vision OS	EOMs OS	DFE – ONH OS
2-week	20/40	+APD OS	14/14	Restricted OS (Sup -1, Inf -1, Nasal -1, Temp -2)	Mild disc edema
1-month	20/20	–APD OS	14/14	Full OS	No disc edema

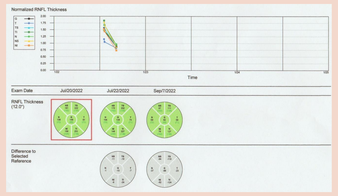
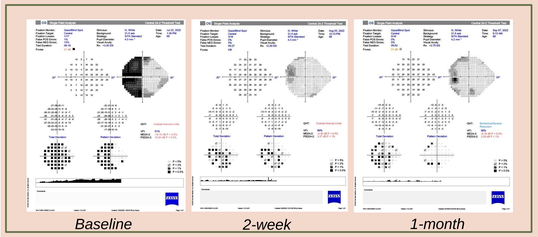


Fig 6. OS OCT RNFL Progression – Resolution of ONH edema



Baseline *2-week* *1-month*

Fig 7. HVF 24-2 SS OS Visual Field Defect Resolution

Future Considerations

- “In multiple experimental models, both in vitro and in vivo, several phyto**cannabinoids**, including Δ9-tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabigerol (CBG), **exhibit activity against inflammation**.” [3]
- An EIU study “compared ocular topical treatment with a **CB2R-selective cannabinoid agonist** to topical NSAID (nepafenac) and corticosteroids (prednisolone and dexamethasone). The CB2R-agonist **resulted in decreased parameters of inflammation** at 6 h, where, interestingly, similar anti-inflammatory actions were not observed with NSAID or corticosteroids.” [4]

Conclusion

- In orbital apex syndrome, it should be the primary goal of the eye care practitioner to localize the lesion and identify its etiology for appropriate treatment.
- There is a future potential for cannabinoids to reduce ocular inflammation across a range of pathophysiological processes.

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2. Goyal P, Lee S, Gupta N, et al. Orbital apex disorders: Imaging findings and management. Neuroradiol J. 2018;31(2):104-125. doi:10.1177/1971400917740361
3. Henshaw FR, Dewsbury LS, Lim CK, Steiner GZ. The Effects of Cannabinoids on Pro- and Anti-Inflammatory Cytokines: A Systematic Review of In Vivo Studies. Cannabis Cannabinoid Res. 2021;6(3):177-195. doi:10.1089/can.2020.0105
4. Lafreniere JD, Kelly MEM. Potential for endocannabinoid system modulation in ocular pain and inflammation: filling the gaps in current pharmacological options. Neuronal Signal. 2018;2(4):NS20170144. Published 2018 Nov 2. doi:10.1042/NS20170144
5. Bagheri, N., Wajda, B., Calvo, C., & Durrani, A. (Eds.). (2016). The Wills Eye Manual (7th ed.). Lippincott Williams and Wilkins.
6. Bowling, B. (2015). Kanski’s clinical ophthalmology (8th ed.). W B Saunders.

STOPPING THE BLEED

A SYSTEMIC APPROACH TO MANAGEMENT OF THROMBOCYTOPENIA RETINOPATHY

Erin Mozingo O.D.

Optometry Resident, Lake City VAMC

Special thanks to Dr. Nirmani Karunathilake

FINANCIAL DISCLOSURES

- None

AUGUST 2022

- History:
  - 69 WM, Vietnam War Veteran
  - POHx: dry eye syndrome, PCIOL OD, cataracts OS, mild/moderate NPDR
  - PMHx: Diabetes, hypertension, steatosis of liver, hematuria, dementia, thrombocytopenia, CAD, hyperlipidemia
  - Last A1c 7.9 on 7/22/22, notes that PCP has been adjusting insulin regimen

AUGUST 2022

Entrance Exam:

BCVA: 20/20 OD, 20/25+3 OS

EOMs: FROM (-)pain (-)diplopia OU

CVFs: FTFC OU

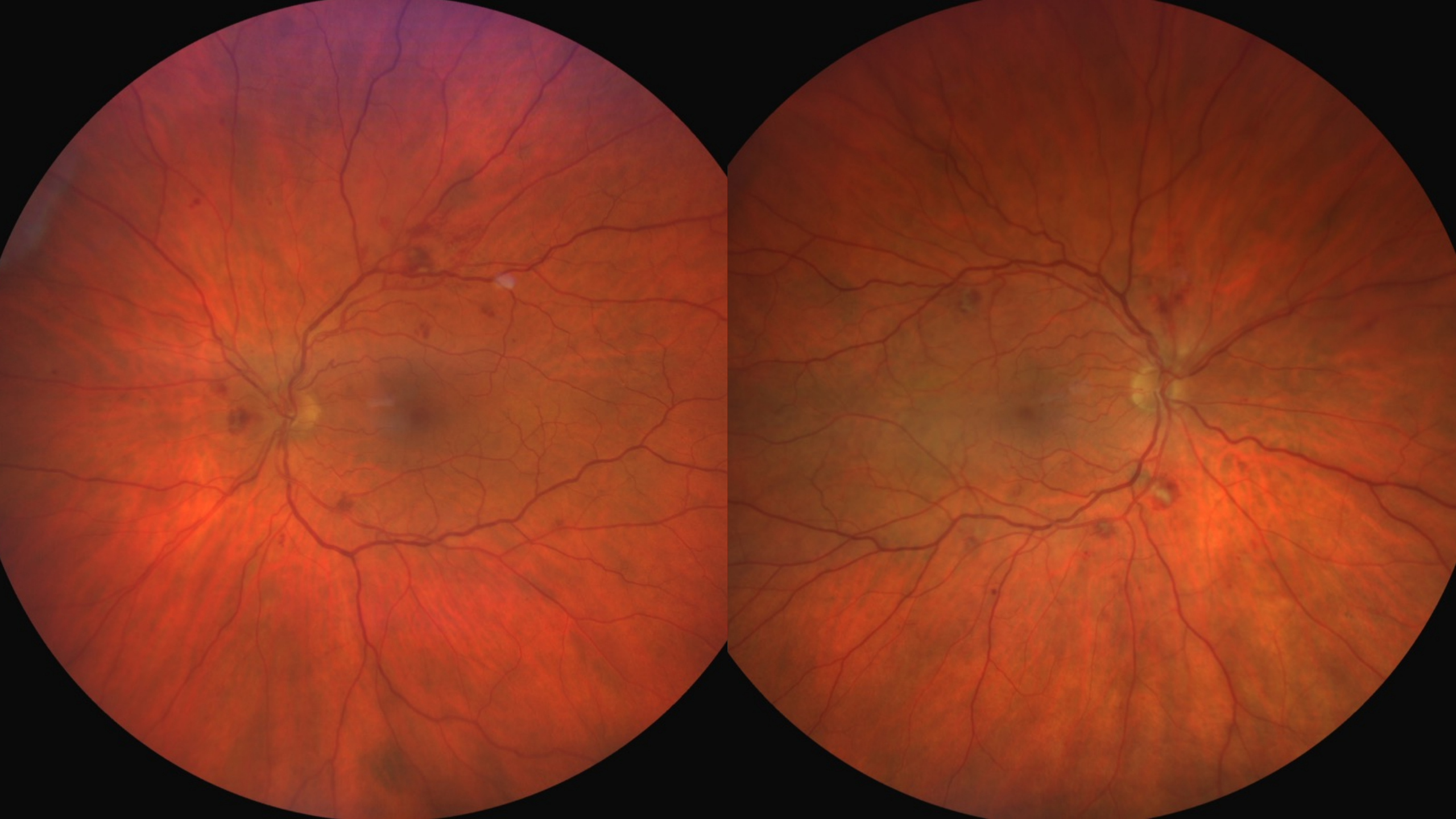
Pupils: errl (-) APD OD, OS

IOP: 16/16mmHg with GAT

AUGUST
2022

Slit Lamp Examination

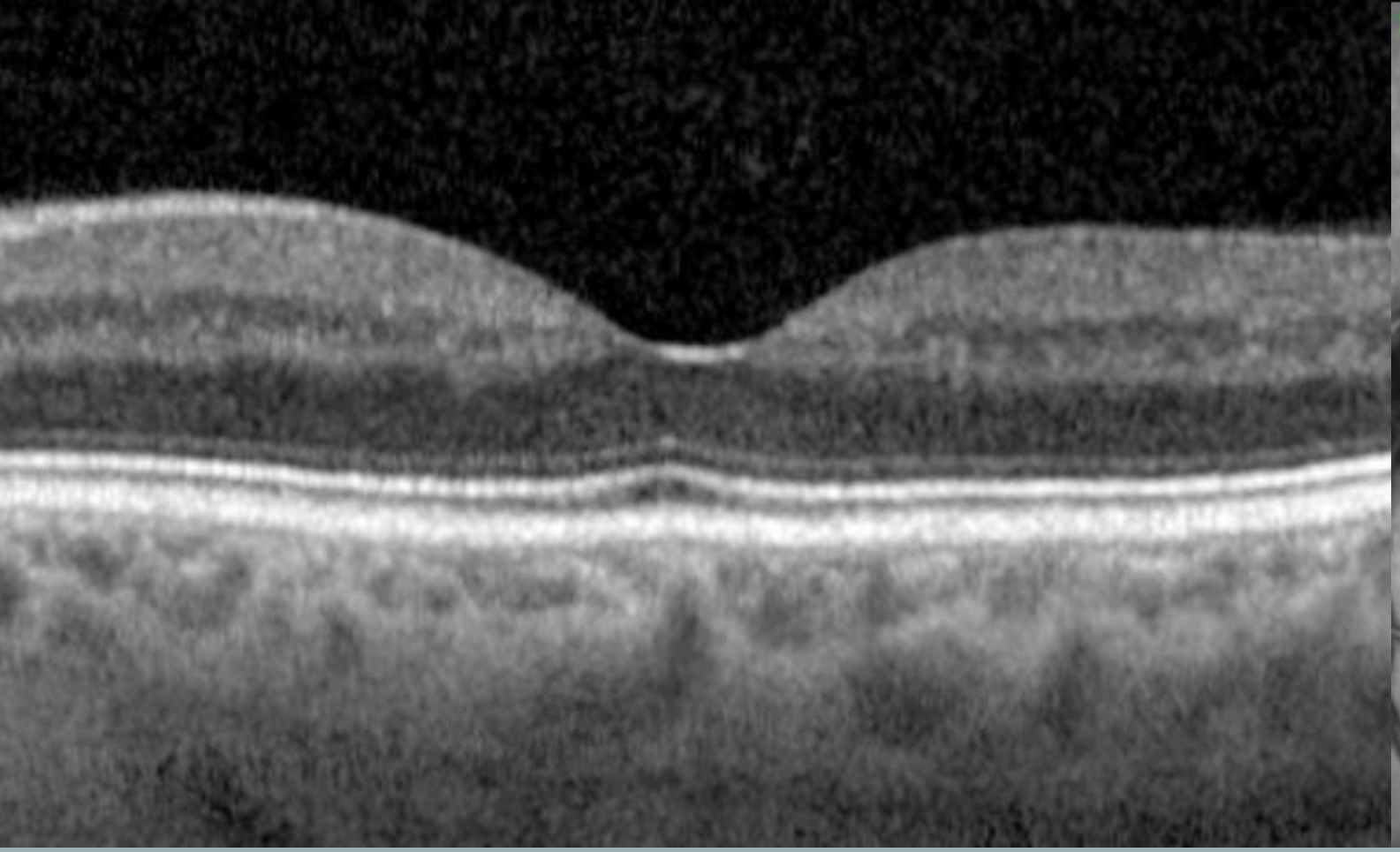
Lids/Lashes	Dermatochalasis, debris OU 1 mm round papilloma RUL
Conj/Sclera	Tr injection 360, pinguecula OU
Cornea	1+ scattered SPK, decreased tear film OU, small round sub-epi scar OD
AC	Deep and quiet, (-)cell/flare OU
Iris	Flat, intact (-)NVI OU
Lens	PCIOL clear and centered OD, 2+ NS and 1+ ACC OS

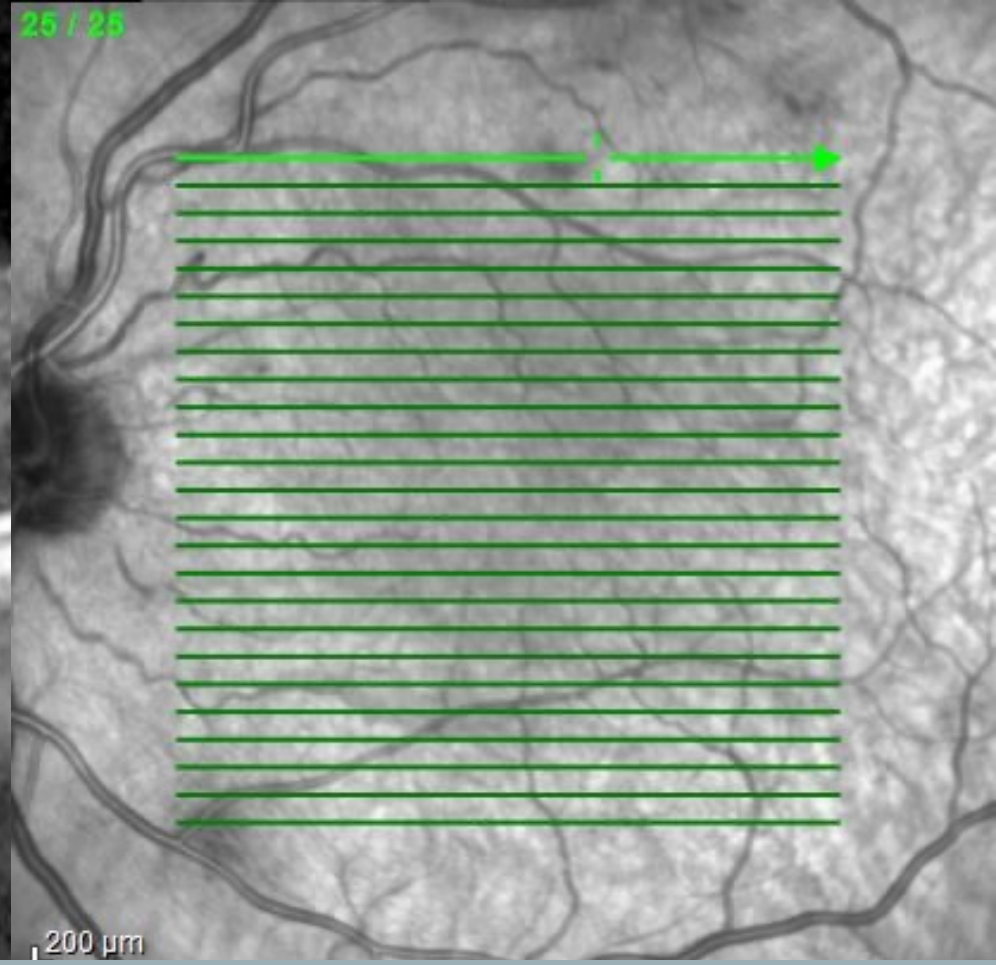


AUGUST
2022

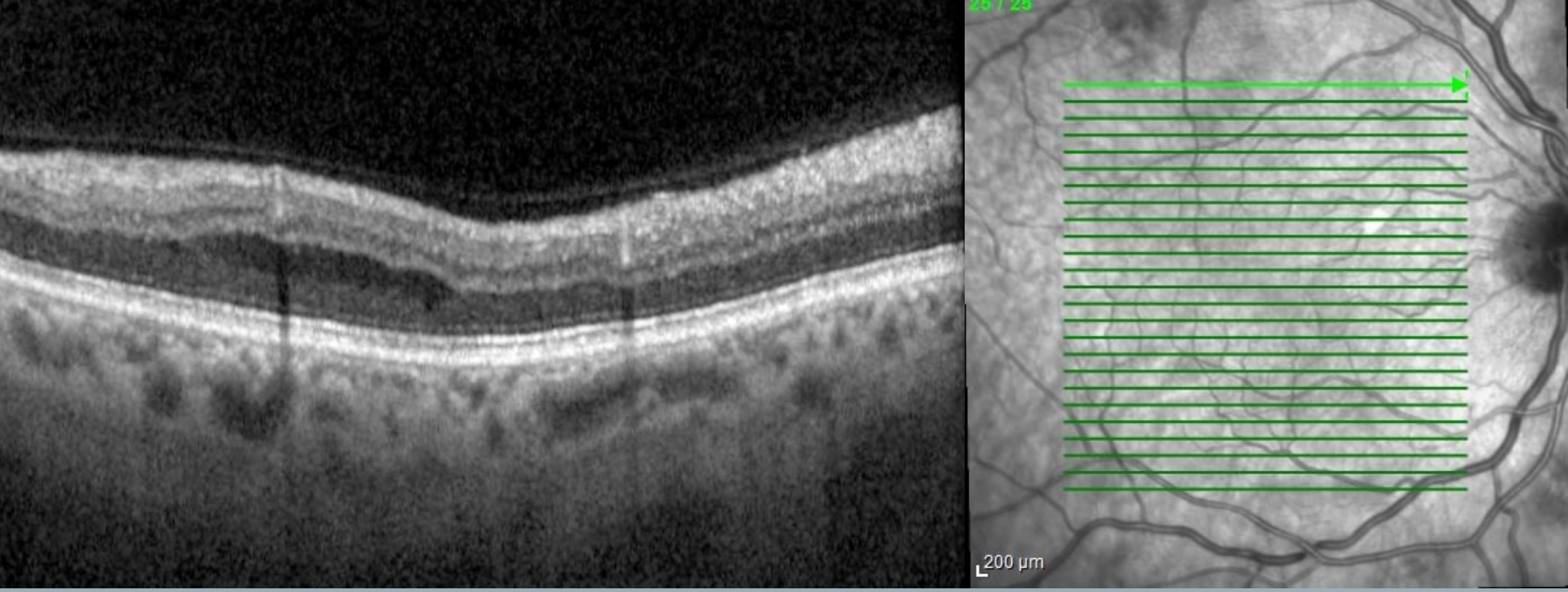
DFE

Vitreous	Syneresis OU
C/D	0.15rnd OU, pink and distinct (-)pallor/hemes/edema/NVD OU
Macula	Flat and intact, few dot hemes parafoveally OU
Post Pole	Scattered blot hemes, few blot hemes with overlying CWS
A/V	0.7, attenuation, few nicking, tortuosity OU
Periphery	(-)holes, breaks, tears 360, reticular degeneration 360, scattered MAs 360, (-)NVE OU





DIAGNOSTIC TESTING



DIAGNOSTIC TESTING

DIFFERENTIAL DIAGNOSES

Infectious	Ischemic	Infiltrative	Inflammatory
Endocarditis	Diabetes	Leukemia	Systemic Lupus Erythematosus
HIV/CMV	Hypertension/Vein Occlusion	Lymphoma	Purtscher's
HSV/VZV	Anemia	Radiation	
(Bagheri, 2016)	Ocular Ischemic Syndrome		

DIFFERENTIAL DIAGNOSES

Infectious	Ischemic	Infiltrative	Inflammatory
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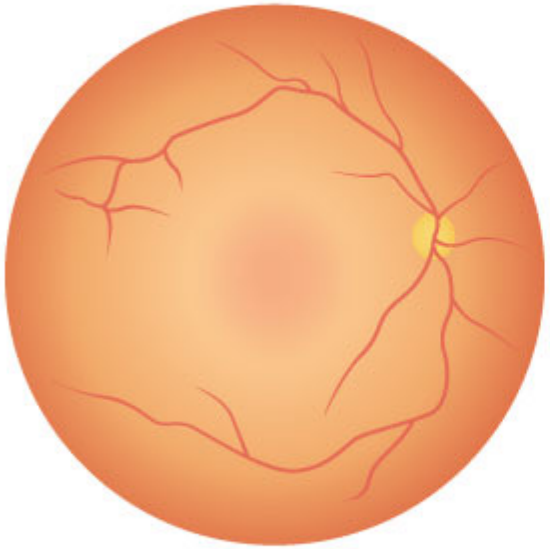
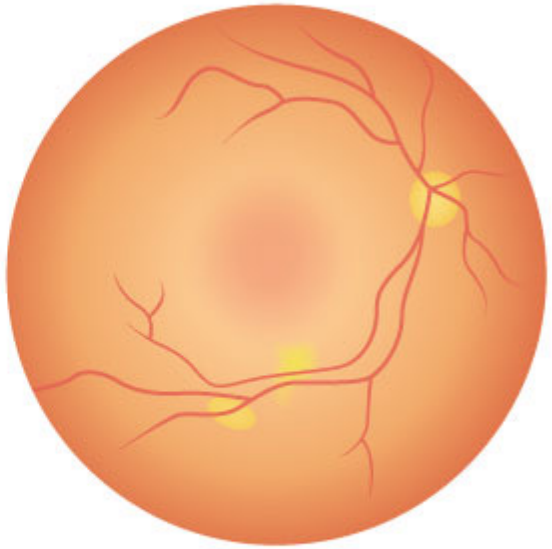
HIV/CMV	Hypertension/Vein Occlusion	Lymphoma	Purtscher's
HSV/VZV	Anemia	Radiation	
	Ocular Ischemic Syndrome		

(Bagheri, 2016)

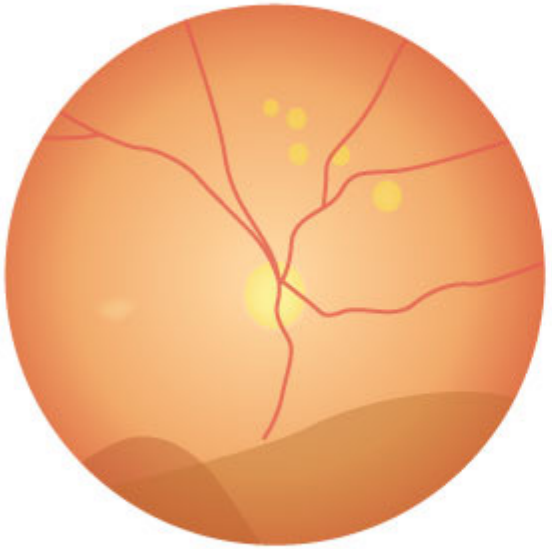
DIABETIC RETINOPATHY



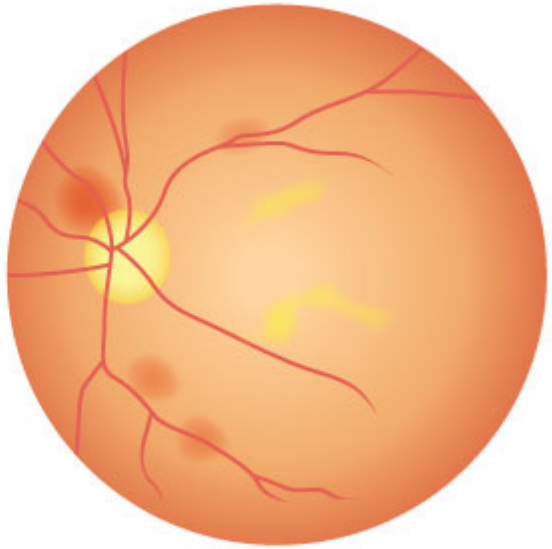
Mild NPDR



Mod. NPDR



PDR

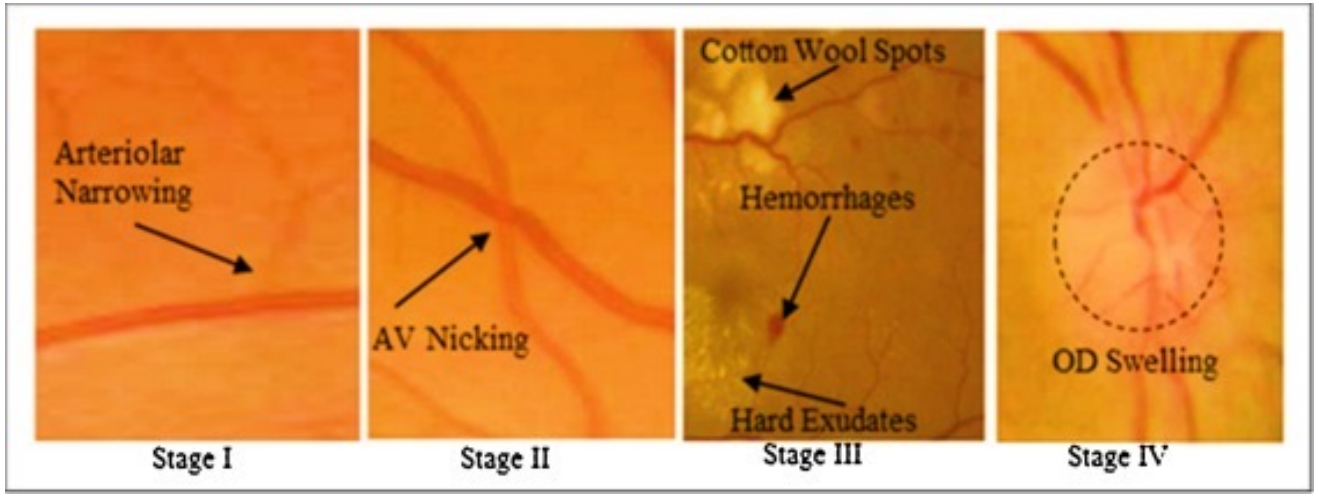


Severe NDPR

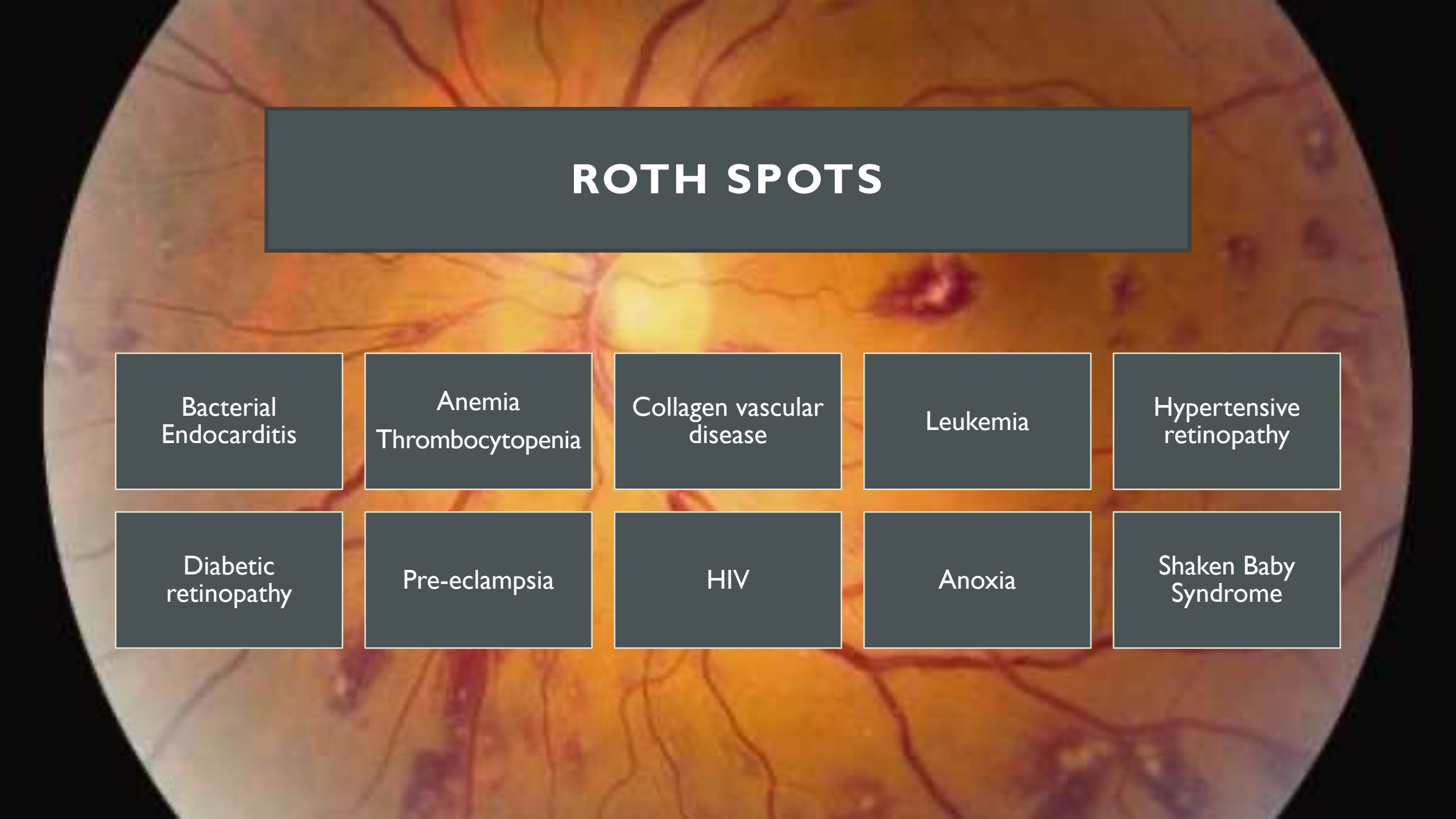
https://www.dolmaneyecare.com/treating-diabetic-retinopathy/the-4-stages-of-diabetic-retinopathy/

HYPERTENSIVE RETINOPATHY

- AV crossing changes (nicking)
- Arteriolar sclerosis (copper wiring)
- Cotton wool spots
- Flame-shaped hemorrhages
- Macroaneurysms
- CRVO/BRVO/CRAO/BRAO
- Malignant: ONH edema and macular star

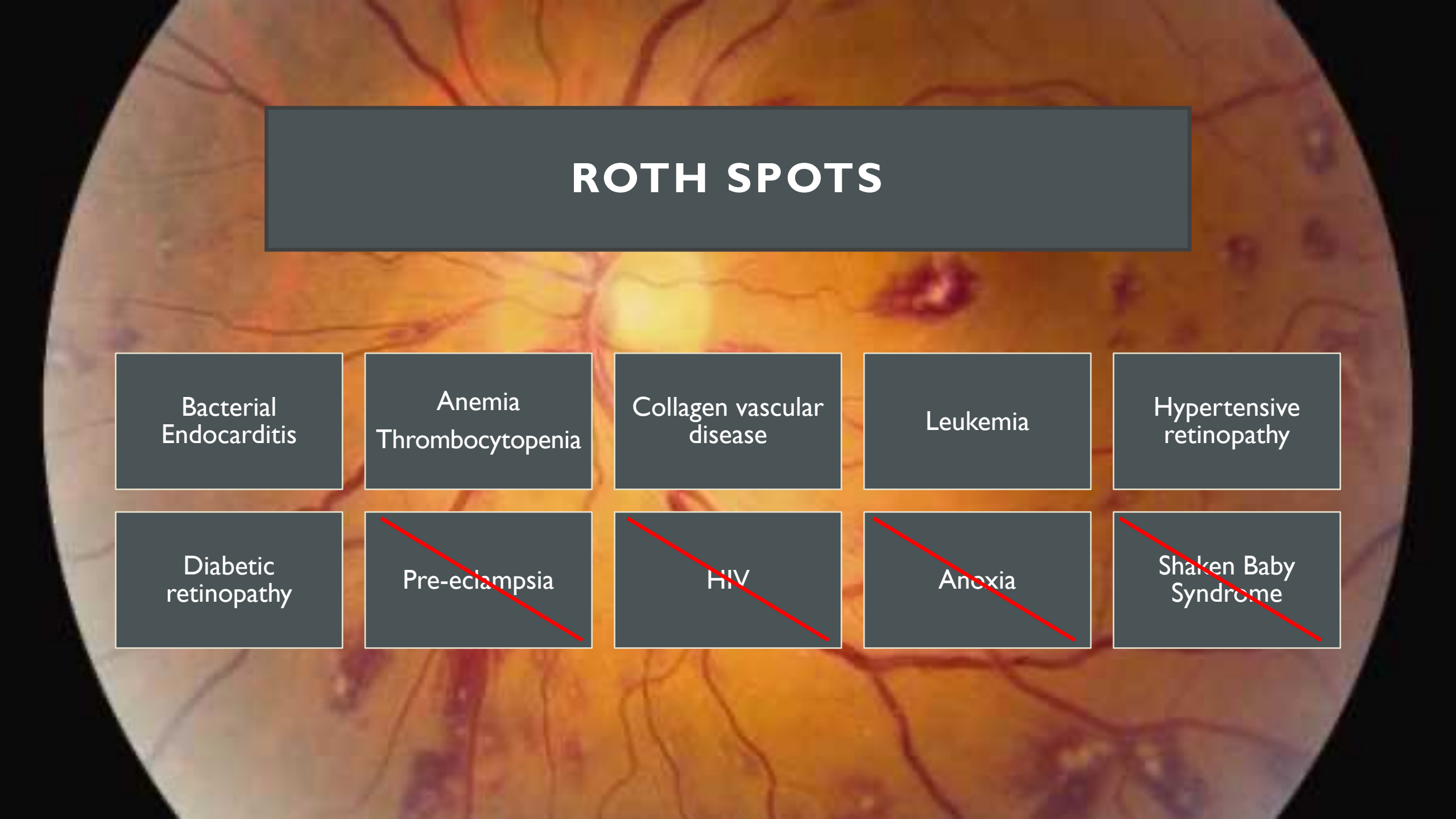


https://www.sciencedirect.com/science/article/pii/S093336571730427X



ROTH SPOTS

Bacterial Endocarditis	Anemia Thrombocytopenia	Collagen vascular disease	Leukemia	Hypertensive retinopathy
Diabetic retinopathy	Pre-eclampsia	HIV	Anoxia	Shaken Baby Syndrome



ROTH SPOTS

Bacterial Endocarditis	Anemia Thrombocytopenia	Collagen vascular disease	Leukemia	Hypertensive retinopathy
Diabetic retinopathy	~~Pre-eclampsia~~	~~HIV~~	~~Anoxia~~	~~Shaken Baby Syndrome~~

Test	Result / Status	Flag	Units	Ref Range
WBC	6.60		k/cmm	4.6 - 10.8
RBC	5.72		M/cmm	4.44 - 6.1
HGB	15.3		g/dL	13.9 - 18
HCT	49.0		%	41 - 52
MCV	85.7		um3	80 - 98
MCH	26.7	L	pg	27 - 33.3
MCHC	31.2	L	g/dL	31.8 - 37.1
PLT	73	L	k/cmm	130 - 440
RDW-SD	46.6		fL	39.0 - 52.2
RDW	14.9	H	%	11.5 - 14.5
MPV	9.3		um3	7.4 - 10.5
IMMATURE PLATELET FRACTION (IPF)	2.0		%	1.2 - 8.6
GRAN #	3.99		k/cmm	1.8 - 7.8
LYMPH #	1.31		k/cmm	1.2 - 3.6
MONO #	1.06	H	k/cmm	0.14 - 0.76
EOSINO #	0.19		k/cmm	0.0 - 0.3
BASO #	0.02		k/cmm	0.0 - 0.2
IMMATURE GRAN.#	0.03		k/cmm	0.00 - 0.2
GRAN %	60.4		%	54 - 65
LYMPH %	19.8	L	%	25 - 33
MONO %	16.1	H	%	3 - 7
EOSINO %	2.9		%	0 - 3
BASO %	0.3		%	0 - 2
IMMATURE GRAN.%	0.50		%	0.00 - 2.00
NRBC #	0.00		k/cmm	0 - 0.2
NUCLEATED RBC/100WBC	0.0		%/WBC	0 - 6

MOST RECENT CBC (07/22/2022)

Test	Result / Status	Flag	Units	Ref Range
WBC	6.60		k/cmm	4.6 - 10.8
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GRAN %	60.4		%	54 - 65
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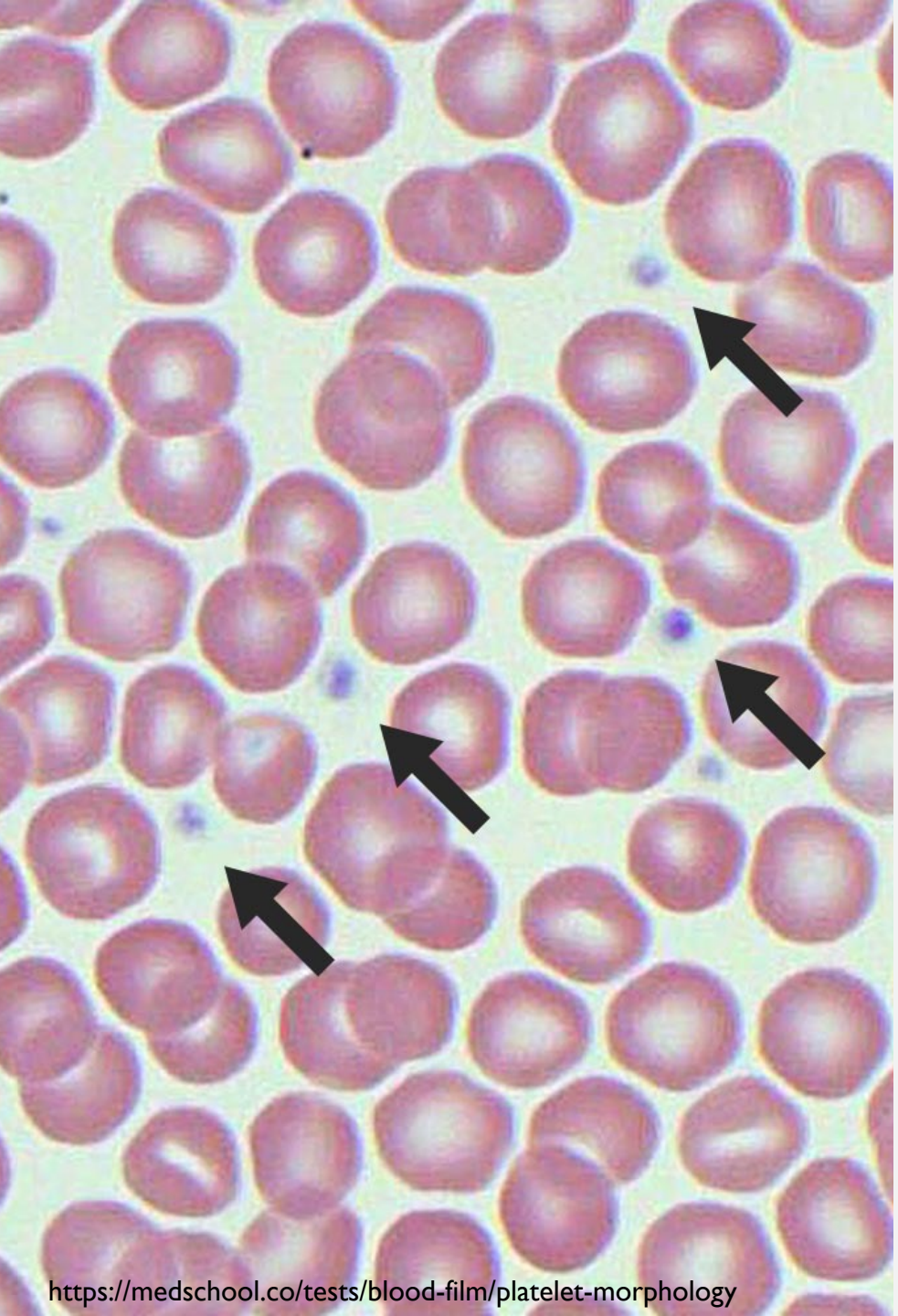


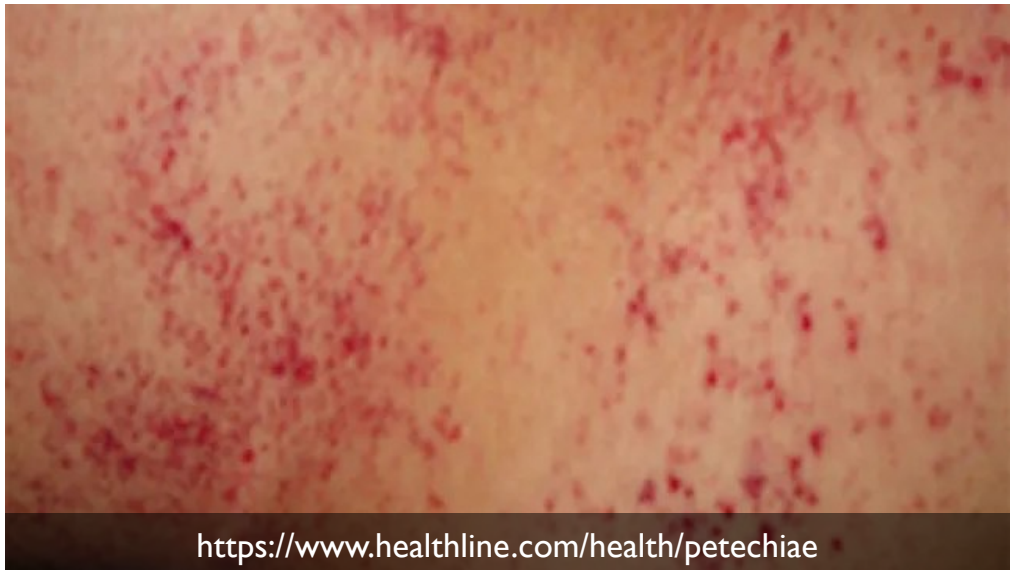
https://medschool.co/tests/blood-film/platelet-morphology

THROMBOCYTOPENIA

- Definition: low platelet count
  - fewer than 150x10^3 plt per microliter
- Causes (Mayo Clinic, 2022)
  - 1. Trapping of platelets in the spleen
  - 2. Decreased platelet production
  - 3. Increased destruction of platelets

THROMBOCYTOPENIA

- Signs/Symptoms(Mayo Clinic, 2022)
  - Excessive bruising (purpura)
  - Superficial bleeding (petechiae)
  - Prolonged bleeding after injury
  - Nose or gum bleeds
  - Blood in urine or stool
  - Fatigue
  - Enlarged spleen


https://www.healthline.com/health/petechiae

TREATMENT AND COMPLICATIONS

Treatment (Mayo Clinic, 2022)

Table 4. Distribution of retinopathy in the case series

Disease (Grading)[a]	Number of patients	Fundus abnormalities	%
Anemia			
Mild	38	2	5.26
Moderate	45	3	6.67
Severe	33	23	69.69
Thrombocytopenia			
Mild	15	0	0.00
Moderate	10	0	0.00
Severe	3	2	66.67
Very severe	6	2	33.33
Anemia + Thrombocytopenia			
Mild a + mild t	8	1	12.50
Moderate a + mild t	10	1	10.00
Severe a + mild t	4	1	25.00
Mild a + moderate t	10	1	10.00
Moderate a + moderate t	8	2	25.00
Severe a + moderate t	8	7	87.50
Mild a + severe t	2	0	0.00
Moderate a + severe t	8	5	62.50
Severe a + severe t	2	2	100.00
Mild a + very severe t	2	0	0.00
Moderate a + very severe t	5	3	60.00
Severe a + very severe t	9	9	100.00
Normal controls	47	1	2.13
Total	**273**	**65**	**23.81**

[a]a, anemia; t, thrombocytopenia.

(Carraro, 2001)

OCULAR COMPLICATIONS

- Up to 90% of patients with hematological disorders have visual disturbances (Carraro, 2001)
  - Prevalence increases with severity of disease

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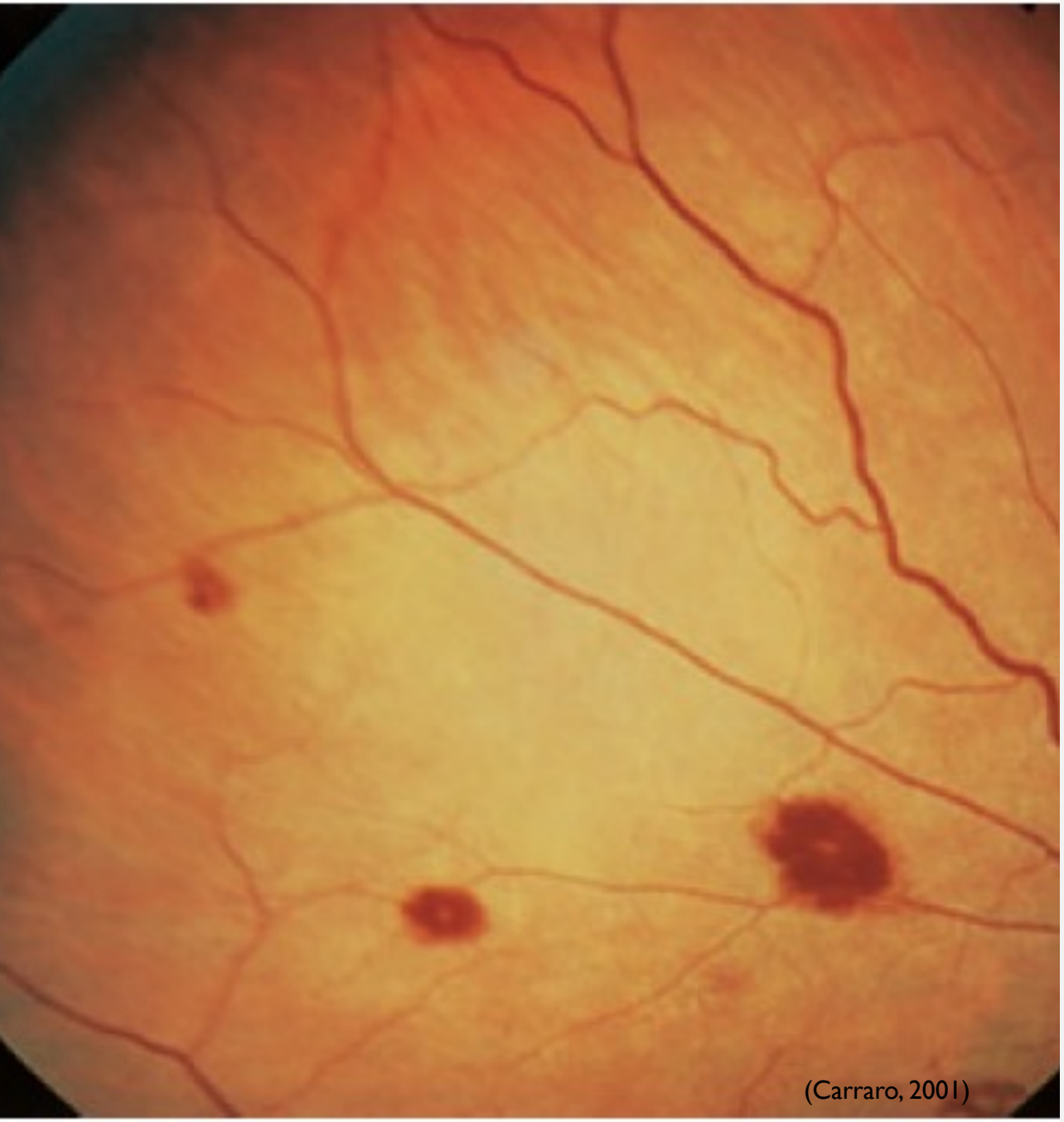

(Carraro, 2001)

OCULAR COMPLICATIONS

- Most frequent signs (Carraro, 2001):
  - Retinal hemorrhages, white centered
  - Venous tortuosity
  - Ischemic retinopathy
  - Soft exudates
  - Macular hemorrhages (Kaspi, 2022)
    - 30% of patients with severe thrombocytopenia
  - Optic nerve edema (rare)
  - Vitreous hemorrhage

OCULAR COMPLICATIONS

Risk Factors

- age, hemoglobin, MCV, platelet levels, acute blood loss

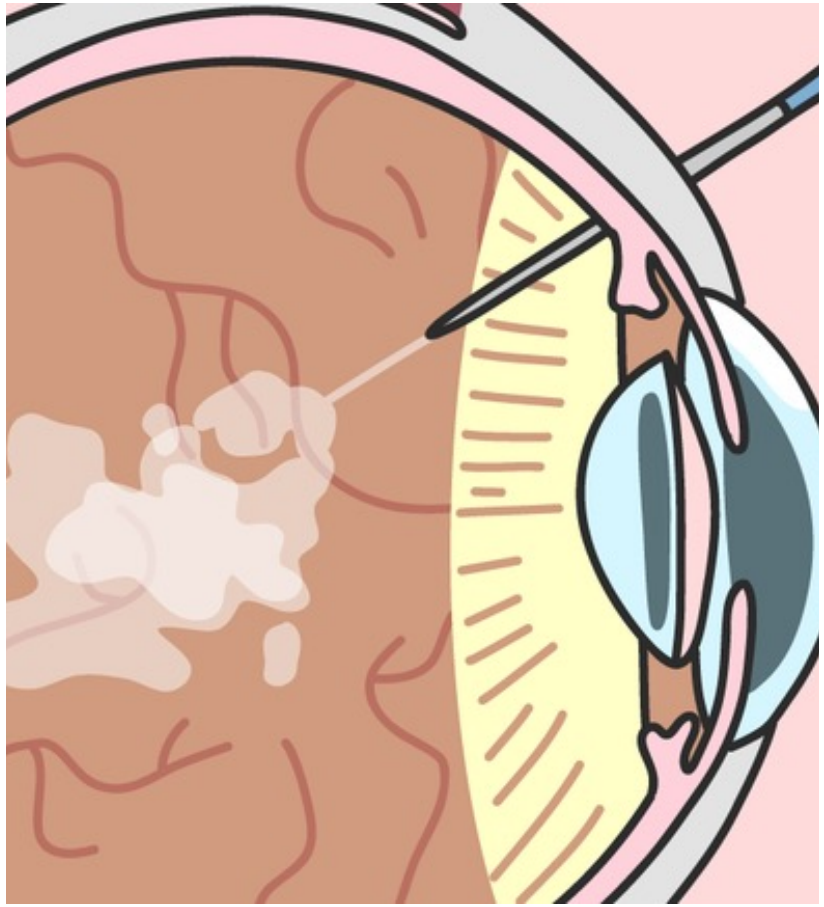
JCI insight

Thrombocytopenia is associated with severe retinopathy of prematurity

Bertan Cakir, … , Lois E.H. Smith, Ann Hellström

JCI Insight. 2018;3(19):e99448. https://doi.org/10.1172/jci.insight.99448.

TREATMENT AND MANAGEMENT



ANTI-VEGF VS. STEROIDS

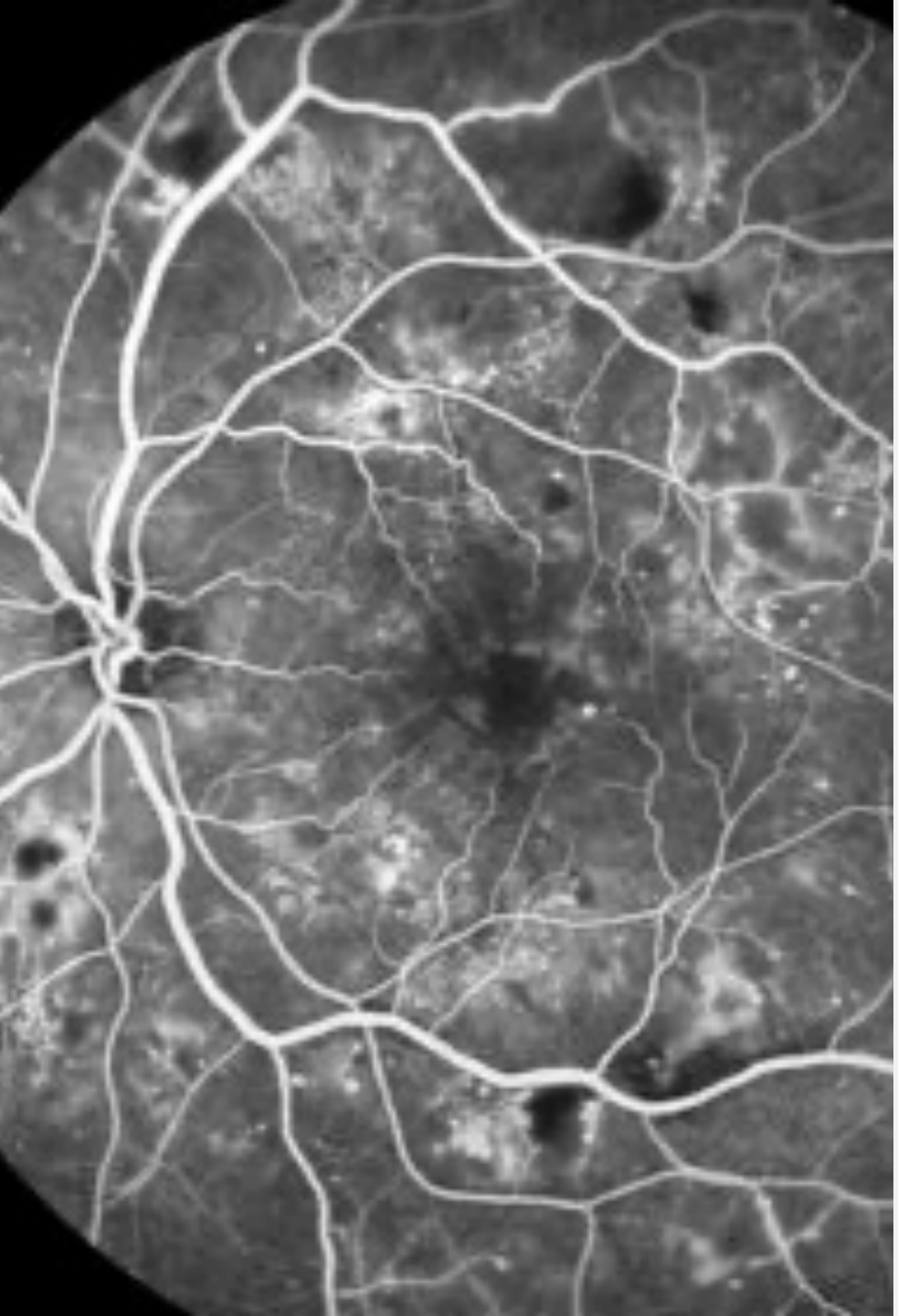
CASE REPORTS

Idiopathic thrombocytopenic purpura and its fundus features in a patient with diabetes mellitus

R, Rajesh; Shanmugam, Mahesh P; Sagar, Pradeep[1]

Author Information

Indian Journal of Ophthalmology: November 2020 - Volume 68 - Issue 11 - p 2587-2589
doi: 10.4103/ijo.IJO_933_20

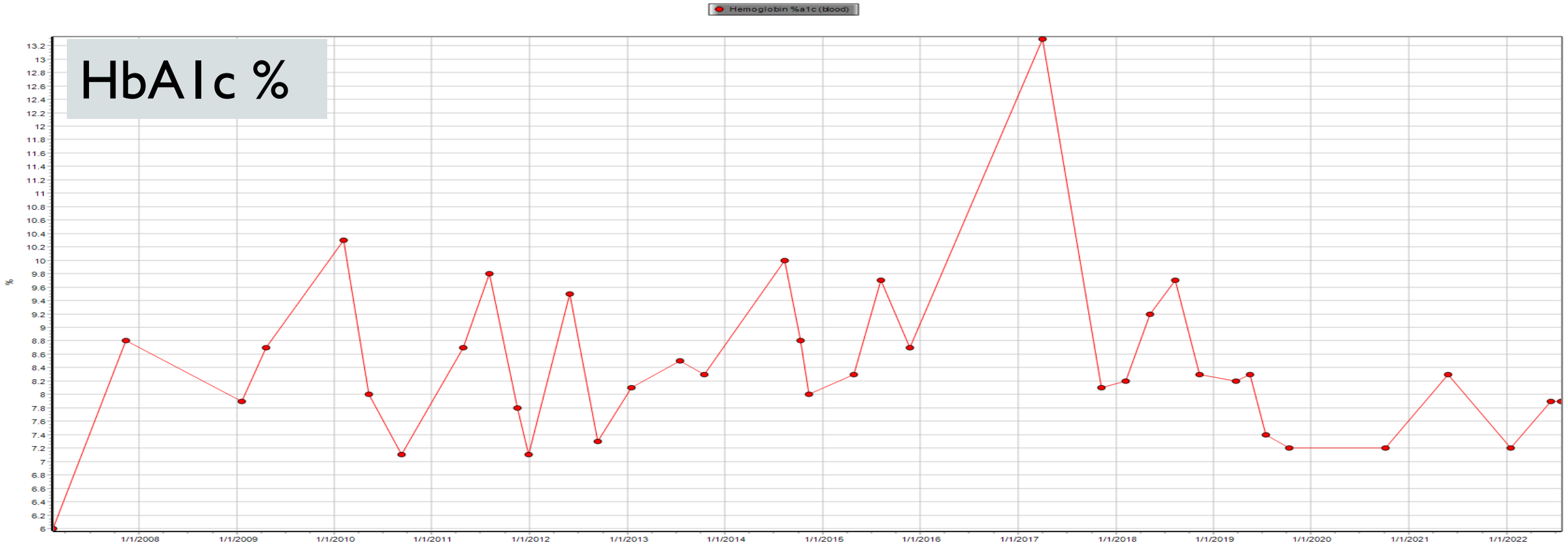


FOLLOW-UP APPOINTMENT: NOV 2022

"Liver tests are normal but ultrasound demonstrated heptomegaly and evidence of fatty infiltration of the liver. He has NASH (non alcoholic steatohepatitis) with his thrombocytopenia and fibrotest consistent with advance fibrosis, likely cirrhosis"

"Ischemia due to platelet imbalance and vasculopathy/clotting. Need IVFA to see if from arterial problem"

SYSTEMIC APPROACH


Hemoglobin %a1c (blood)
HbA1c %
%
13.2
13
12.8
12.6
12.4
12.2
12
11.8
11.6
11.4
11.2
11
10.8
10.6
10.4
10.2
10
9.8
9.6
9.4
9.2
9
8.8
8.6
8.4
8.2
8
7.8
7.6
7.4
7.2
7
6.8
6.6
6.4
6.2
6
1/1/2008
1/1/2009
1/1/2010
1/1/2011
1/1/2012
1/1/2013
1/1/2014
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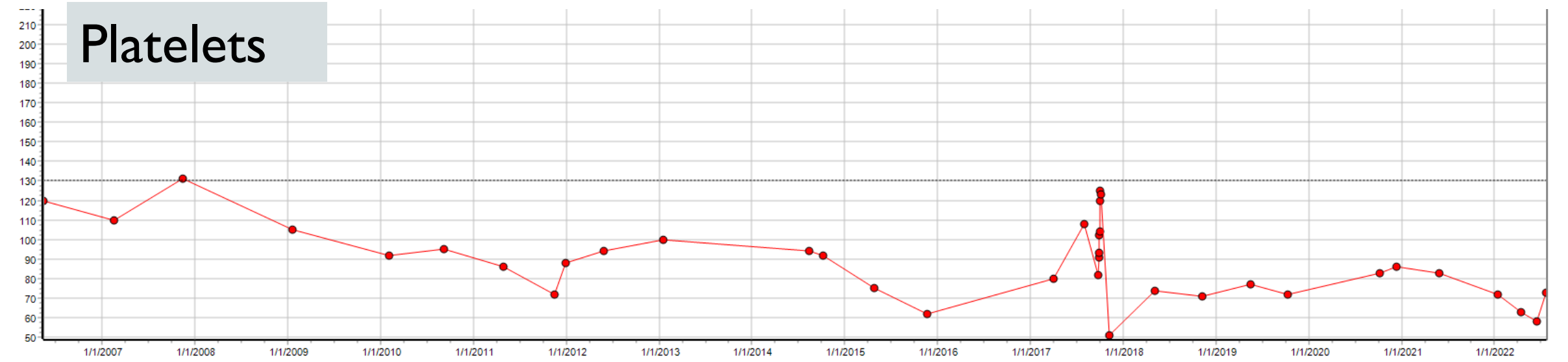
1/1/2019
1/1/2020
1/1/2021
1/1/2022


Platelets
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
1/1/2007
1/1/2008
1/1/2009
1/1/2010
1/1/2011
1/1/2012
1/1/2013
1/1/2014
1/1/2015
1/1/2016
1/1/2017
1/1/2018
1/1/2019
1/1/2020
1/1/2021
1/1/2022

Date	A1c %	Platelet Level	Retinopathy
March 2017	13.1		Mild NPDR
Oct 2017	8.1	125 (personal high)	No DR
Feb 2018	8.2	51 (rapid fall)	No DR
May 2018	9.2	71-86	No DR
Aug 2018	9.7	71-86	No DR
Oct 2018 – May 2019	8.3	71-86	No DR
July 2019 – Oct 2020	7.2	75	Moderate NPDR
May 2021	8.3	70	Moderate NPDR
Jan 2022	7.2		Moderate NPDR
June-July 2022	7.9	55, 73	Moderate NPDR - worsened

DIABETES AND THROMBOCYTOPENIA

No significant difference in platelet count in diabetic patients vs. non-diabetic patients (Chen, 2017)

Metformin and sulfonylureas (glimepiride, glyburide, glipizide) inhibit platelet aggregation (Rodriguez, 2020)

A VA APPROACH

VA has established a presumptive service connection for Veterans, Reservists, and National Guard members exposed to contaminants in the water supply at Camp Lejeune from August 1, 1953 through December 31, 1987 who later developed one of the following eight diseases:

***Adult leukemia**
***Aplastic anemia and other myelodysplastic syndromes**
***Bladder cancer**
***Kidney cancer**
***Liver cancer**
***Multiple myeloma**
***Non-Hodgkin's lymphoma**

In accordance with the 2012 Camp Lejeune health care law, VA provides cost-free health care for certain conditions to Veterans who served at least 30 days of active duty at Camp Lejeune from January 1, 1957 and December 31, 1987. Qualifying health conditions and increased risk factors include:

***Esophageal cancer**
***Breast cancer**
***Kidney cancer**
***Multiple myeloma**
***Renal toxicity**
***Female infertility**
***Scleroderma**
***Non-Hodgkin's lymphoma**
***Lung cancer**
***Bladder cancer**
***Leukemia**
***Myelodysplastic syndromes**
***Hepatic steatosis**
***Miscarriage**

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***Aplastic anemia and other myelodysplastic syndromes**
***Bladder cancer**
***Kidney cancer**
***Liver cancer**
***Multiple myeloma**
***Non-Hodgkin's lymphoma**

In accordance with the 2012 Camp Lejeune health care law, VA provides cost-free health care for certain conditions to Veterans who served at least 30 days of active duty at Camp Lejeune from January 1, 1957 and December 31, 1987. Qualifying health conditions and increased risk factors include:

***Esophageal cancer**
***Breast cancer**
***Kidney cancer**
***Multiple myeloma**
***Renal toxicity**
***Female infertility**
***Scleroderma**
***Non-Hodgkin's lymphoma**
***Lung cancer**
***Bladder cancer**
***Leukemia**
***Myelodysplastic syndromes**
***Hepatic steatosis**
***Miscarriage**

CONCLUSION AND KEY POINTS

- Causes of retinopathy are limitless
- Diabetes is tricky
- Systemic approach

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Multimodal Imaging of Bilateral Diffuse Uveal Melanocytic Proliferation

Joshua Black, OD

Bascom Palmer Ocular Disease Resident

Financial Disclosures

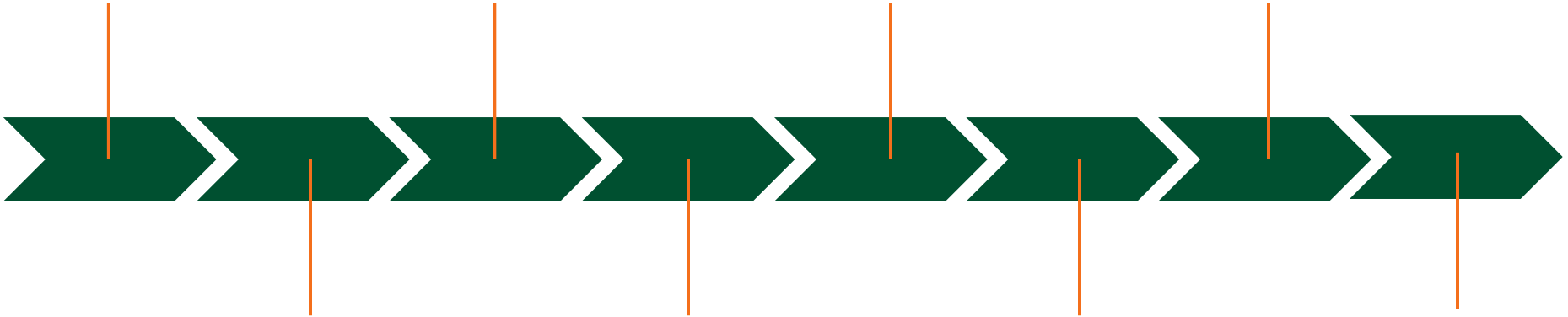
- None

Case Presentation

- Chief Complaint
  - A 78-year-old Caucasian male presented for a retina evaluation and second opinion after a recent episode of blurry vision in both eyes

History of Present Illness: Timeline

Status post resection of lung adenocarcinoma 1 year prior to presentation



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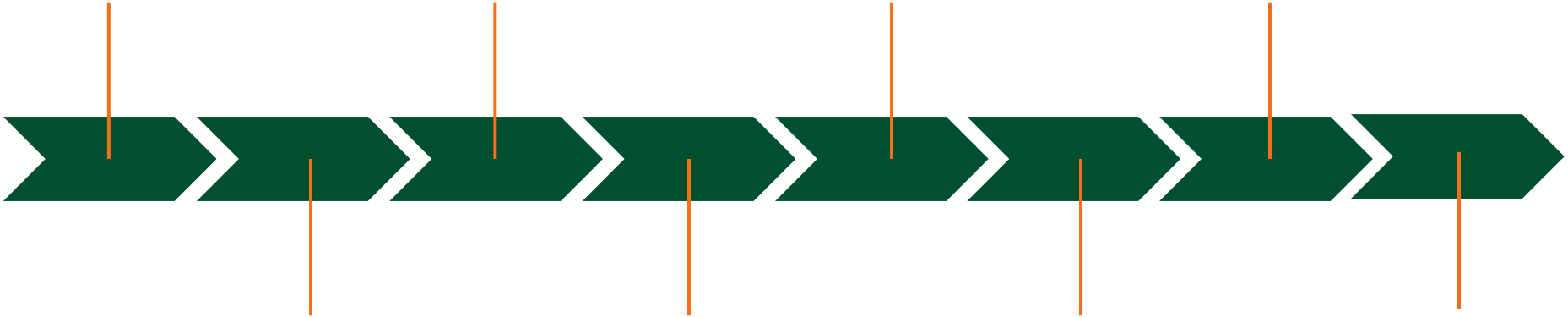

Placed on a 1-year course of chemotherapy treatment of atezolizumab infusions every 21 days

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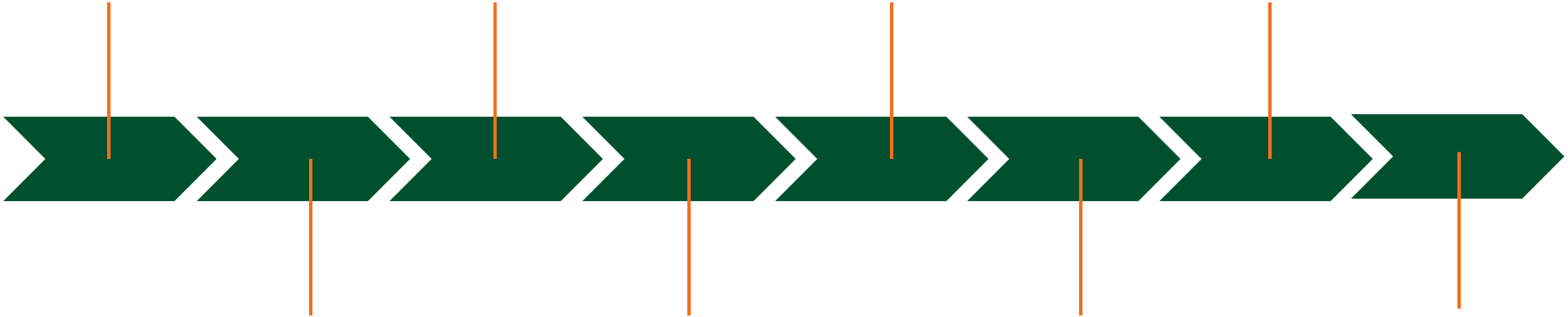

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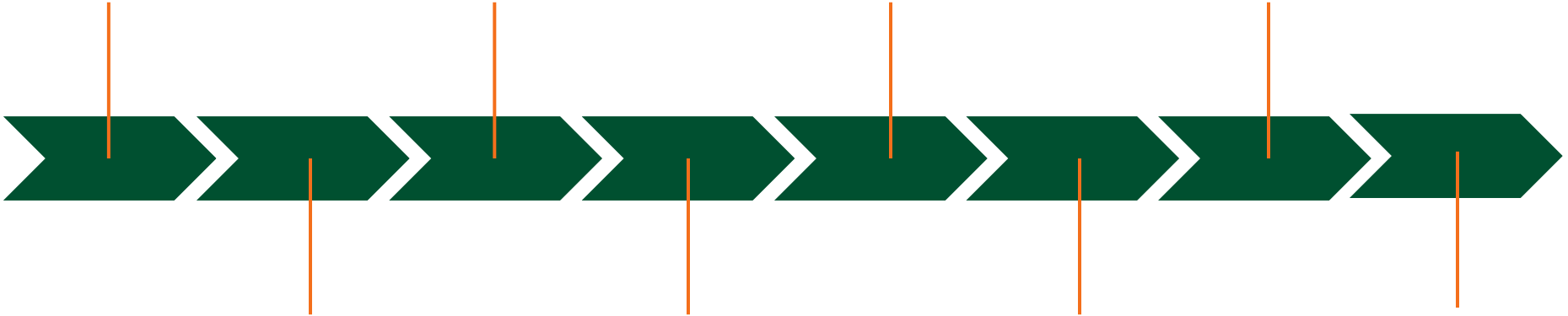

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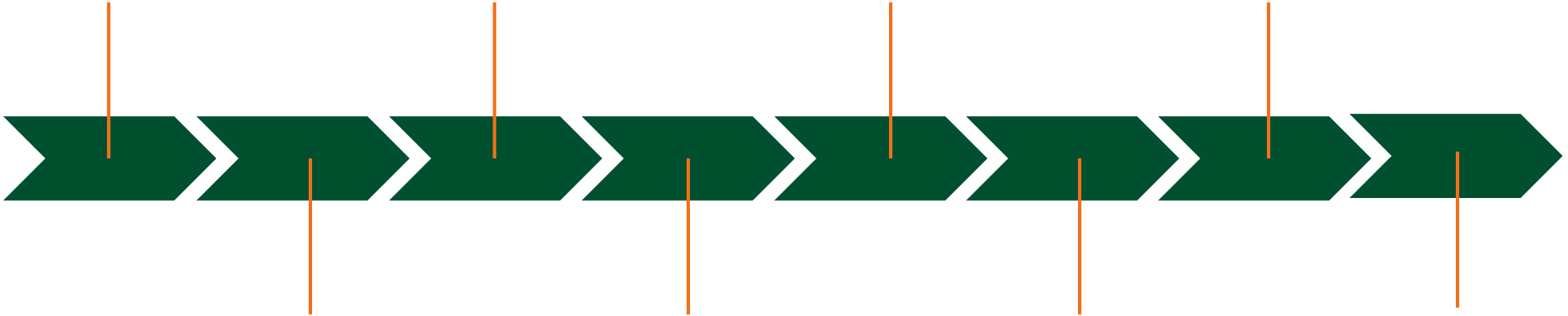

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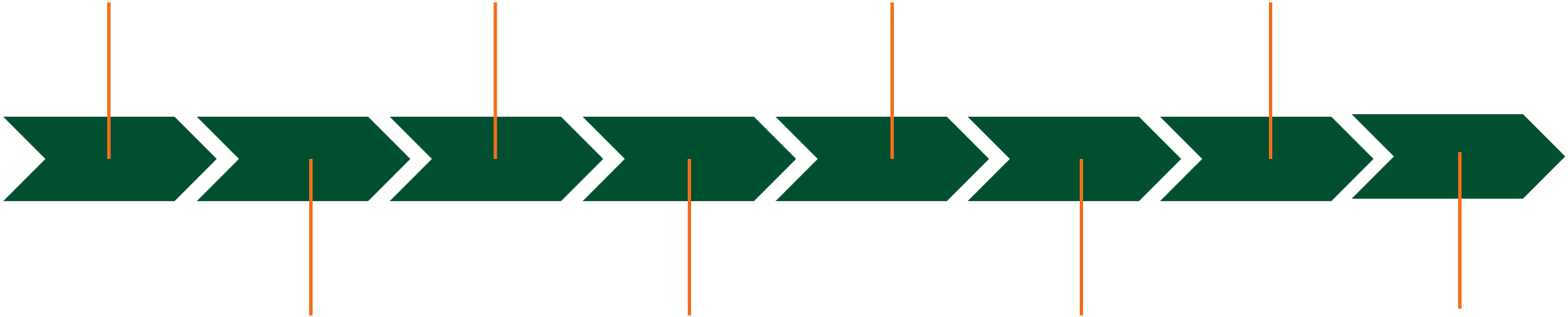
Community retina specialist diagnosed bilateral central serous chorioretinopathy (CSC) while on steroid taper

History of Present Illness: Timeline



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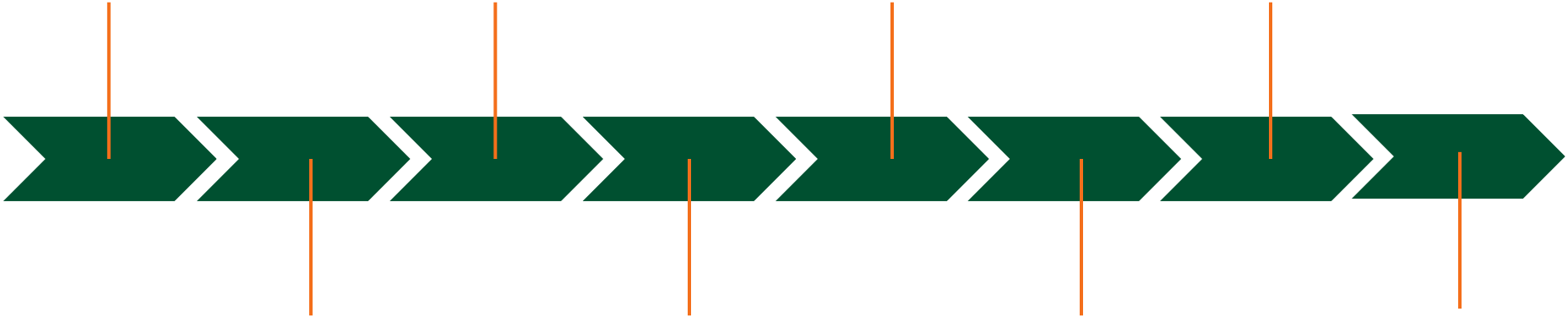

Histories

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- **Medications**
  - Venlafaxine for depression
  - Rosuvastatin for cholesterol

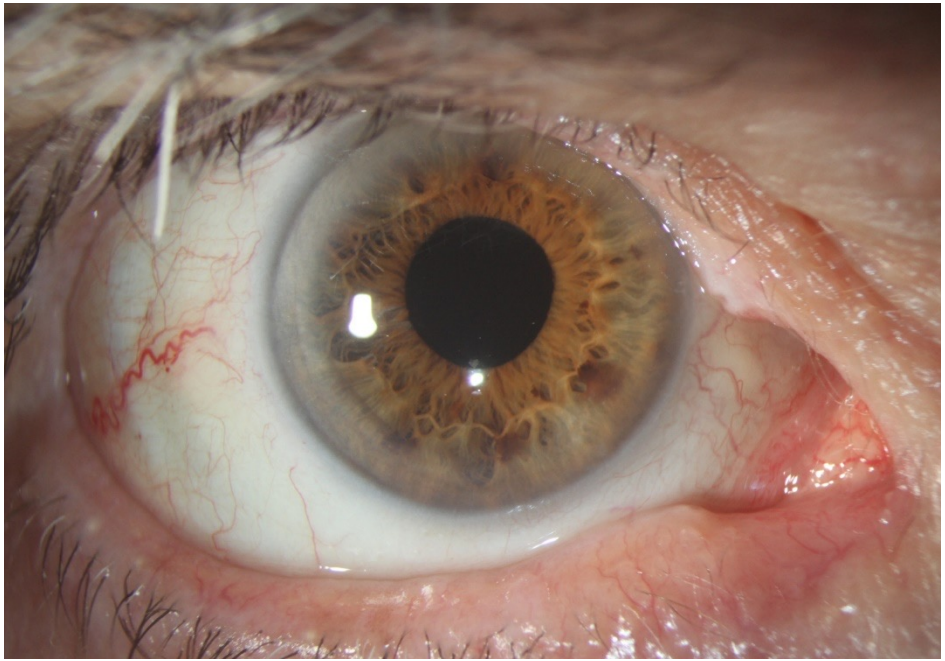
Review of Systems

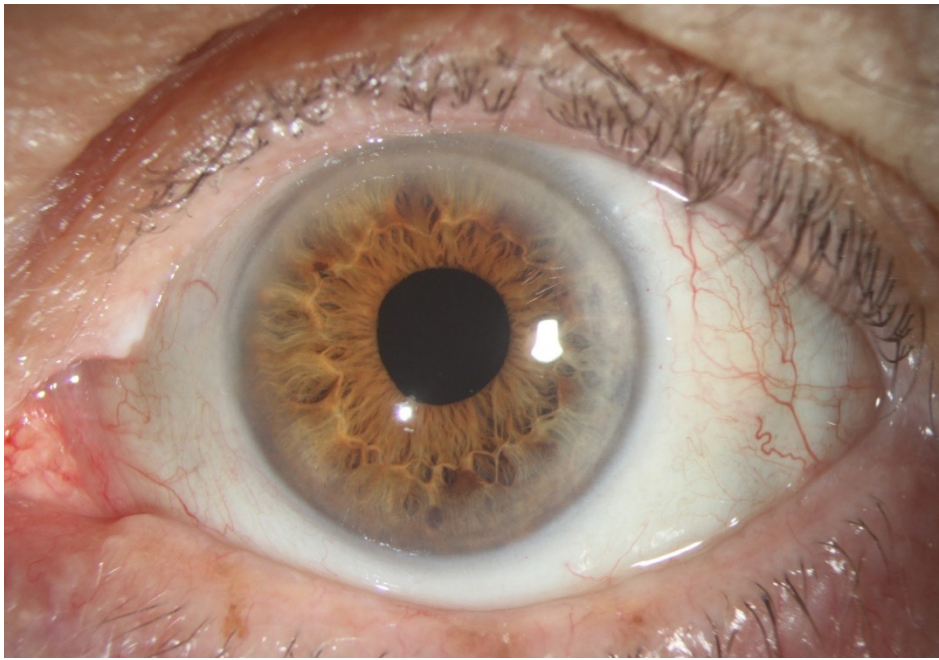
- Gastrointestinal: Negative
- Neurological: Negative
- Skin: Negative
- Genitourinary: Negative
- Psychiatric: Negative
- Musculoskeletal: Negative
- Endocrine: Negative
- Cardiovascular: Negative
- Respiratory: Negative
- Heme/Lymph: Negative

Exam Findings

- **Snellen BCVA**
  - 20/25 OD & OS
- **Confrontation Fields**
  - Full to finger counting OD/OS
- **Extraocular motilities**
  - Full range of motion OD/OS
- **Pupils**
  - Round, reactive, no APD OD/OS
- **Refraction**
  - OD: -0.50 + 3.25 x 180
  - OS: -0.50 + 2.25 x 175
- **Intraocular pressure**
  - OD: 14 mm Hg
  - OS: 13 mm Hg

Anterior Segment





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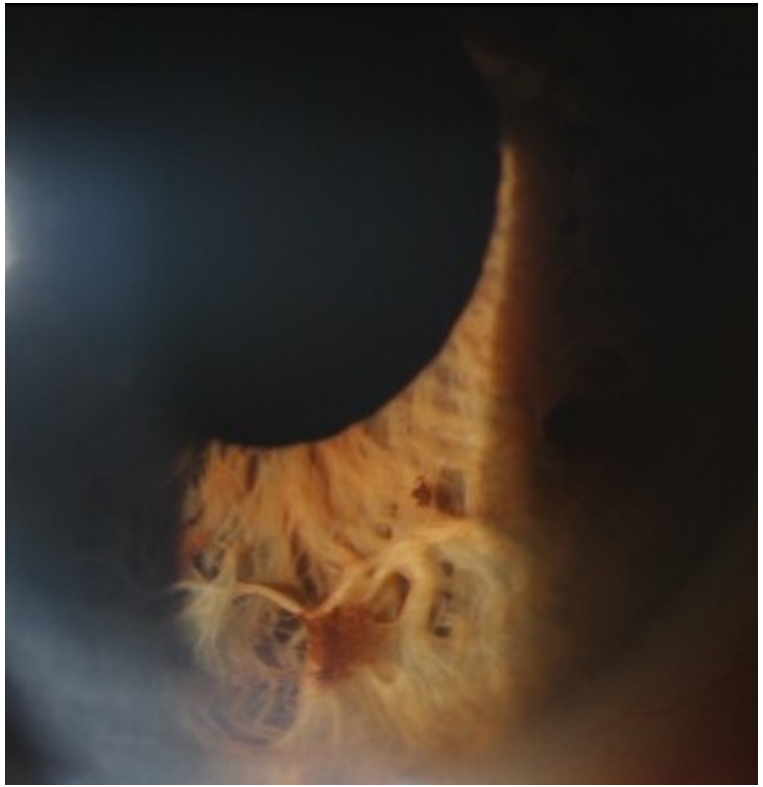
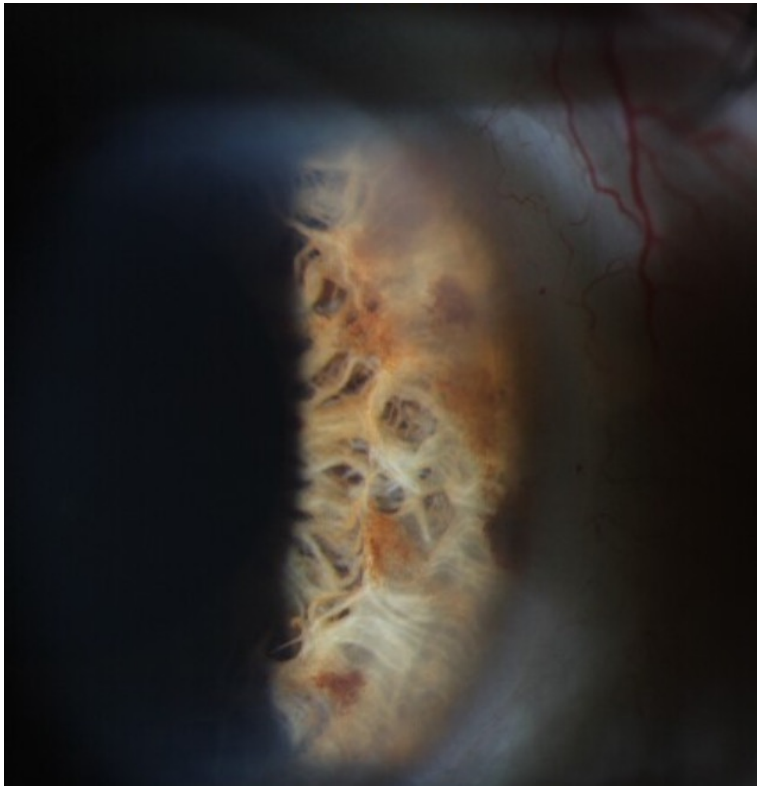
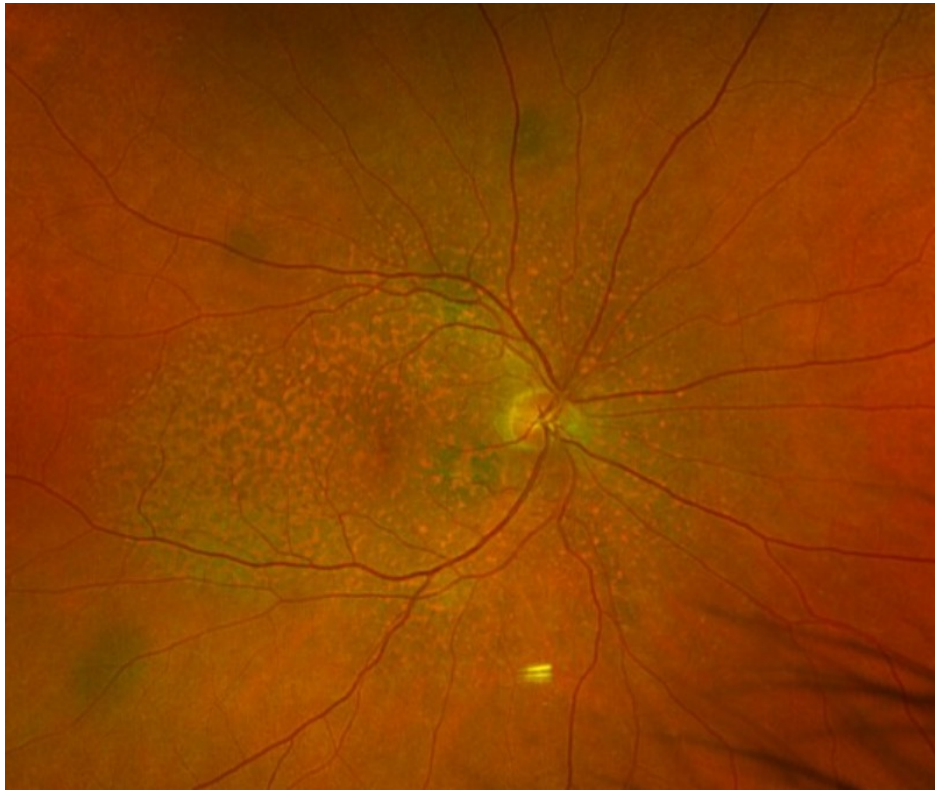
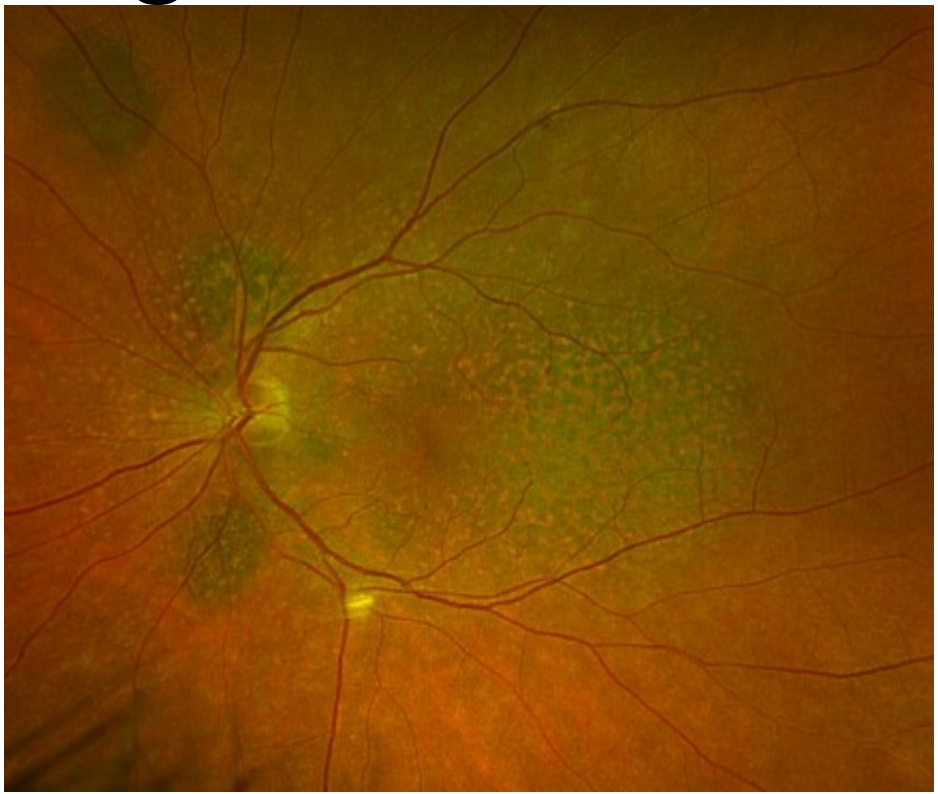


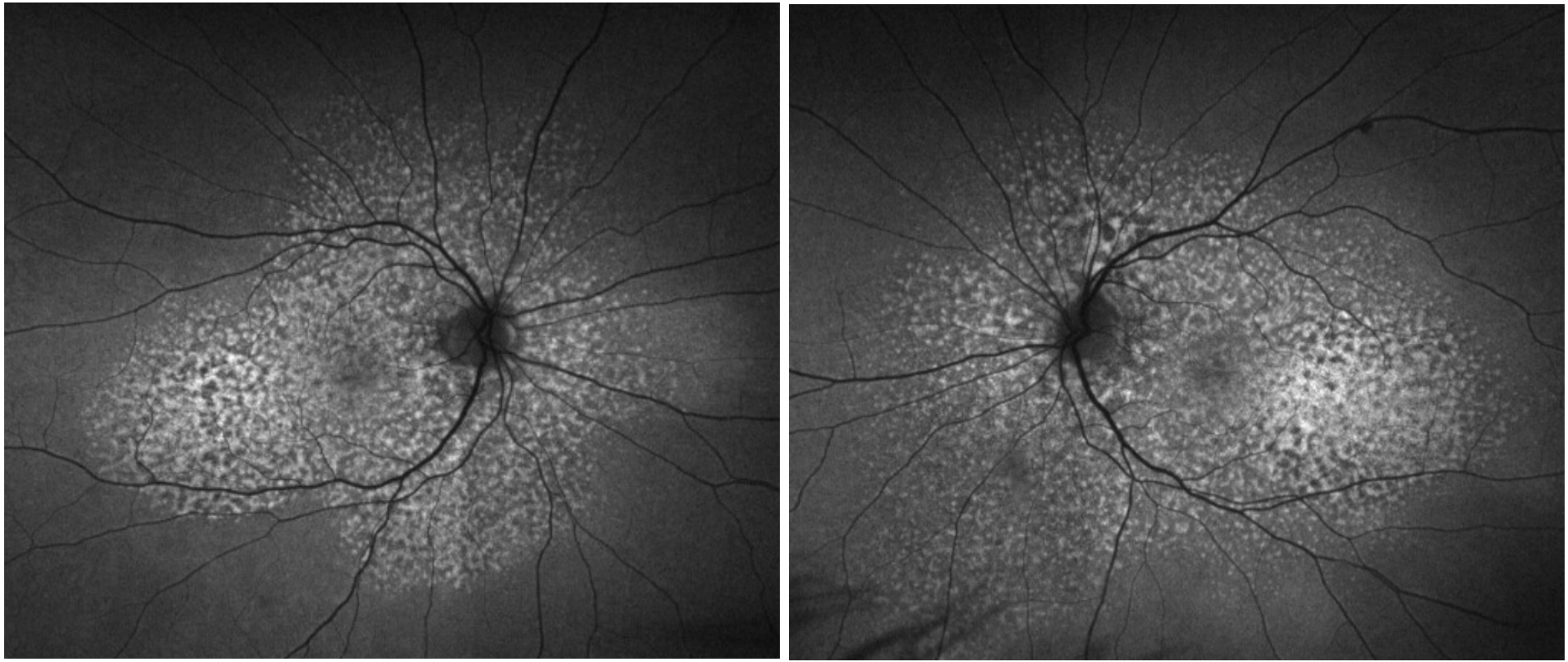


Posterior Segment

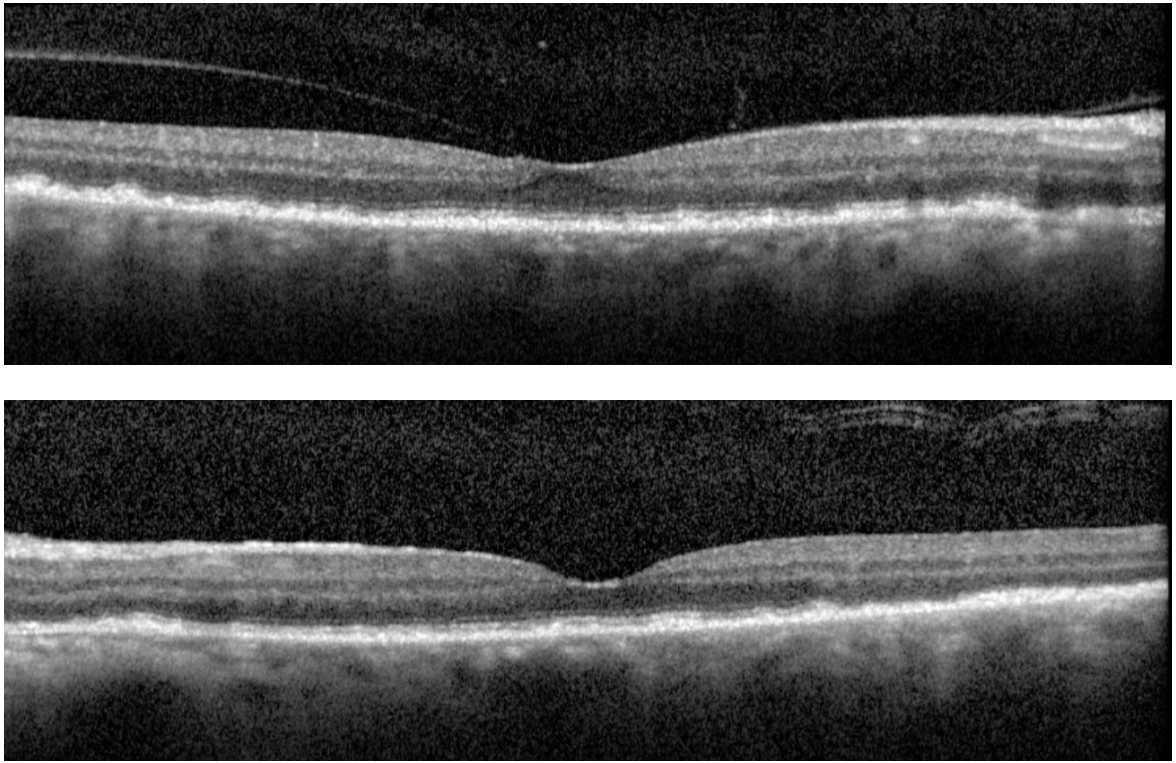




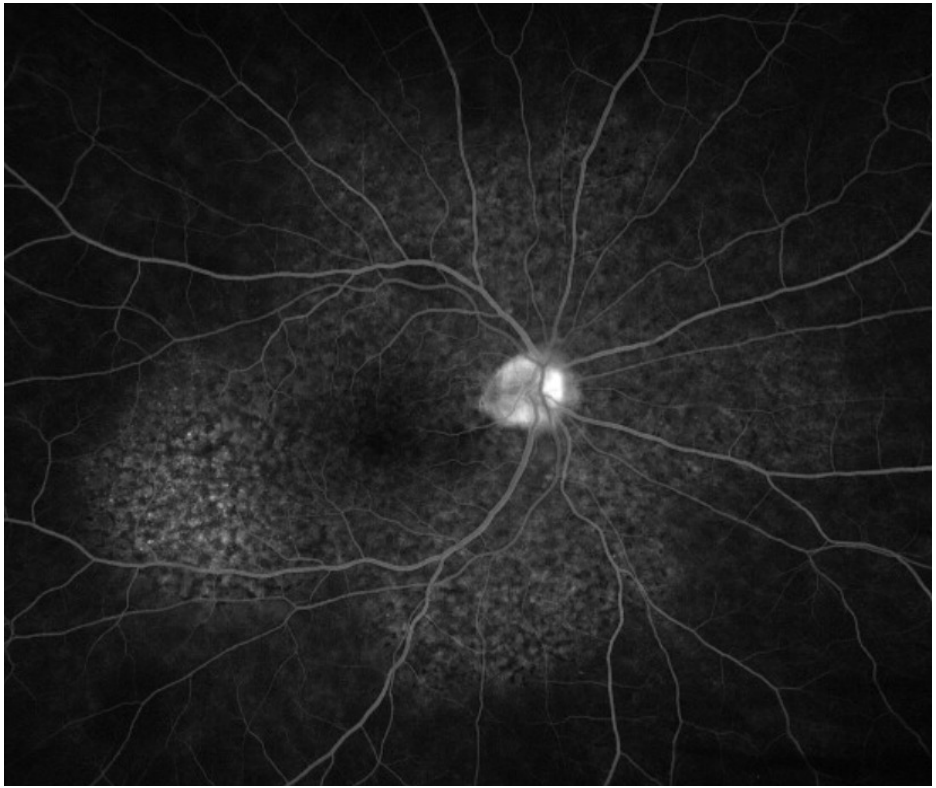
Fundus Autofluorescence

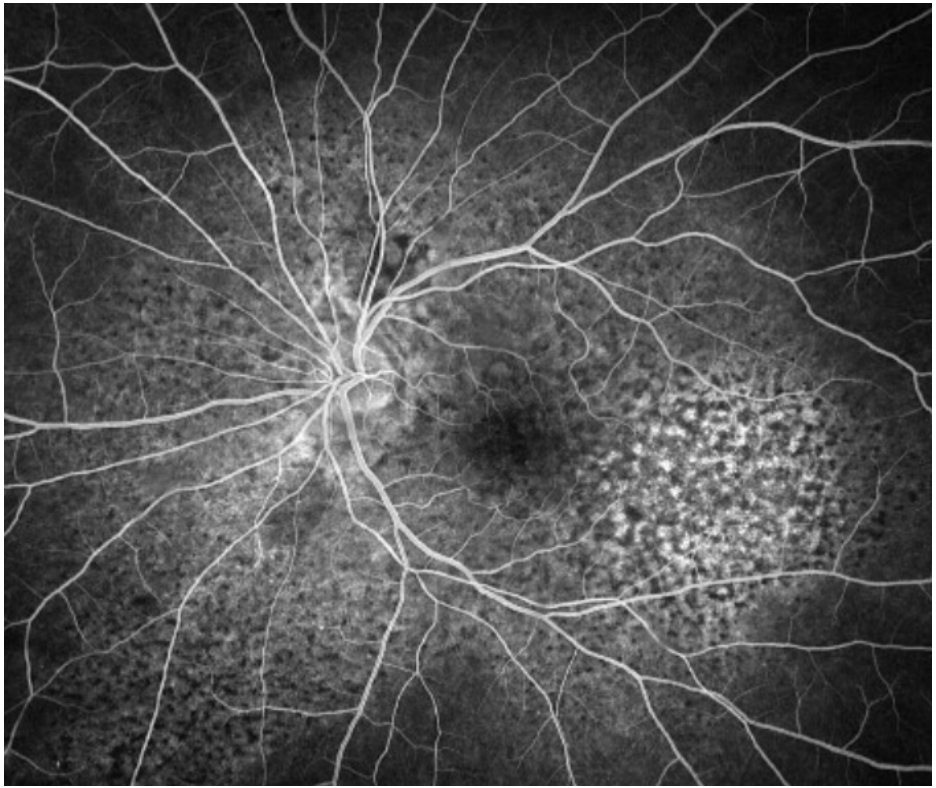


Optical Coherence Tomography

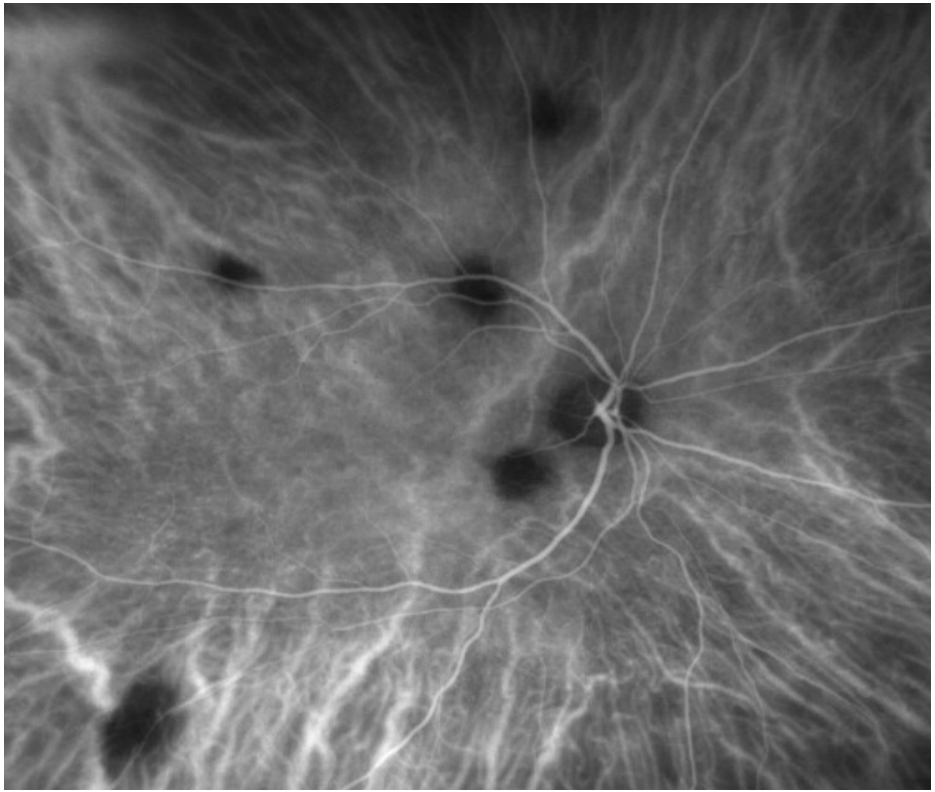


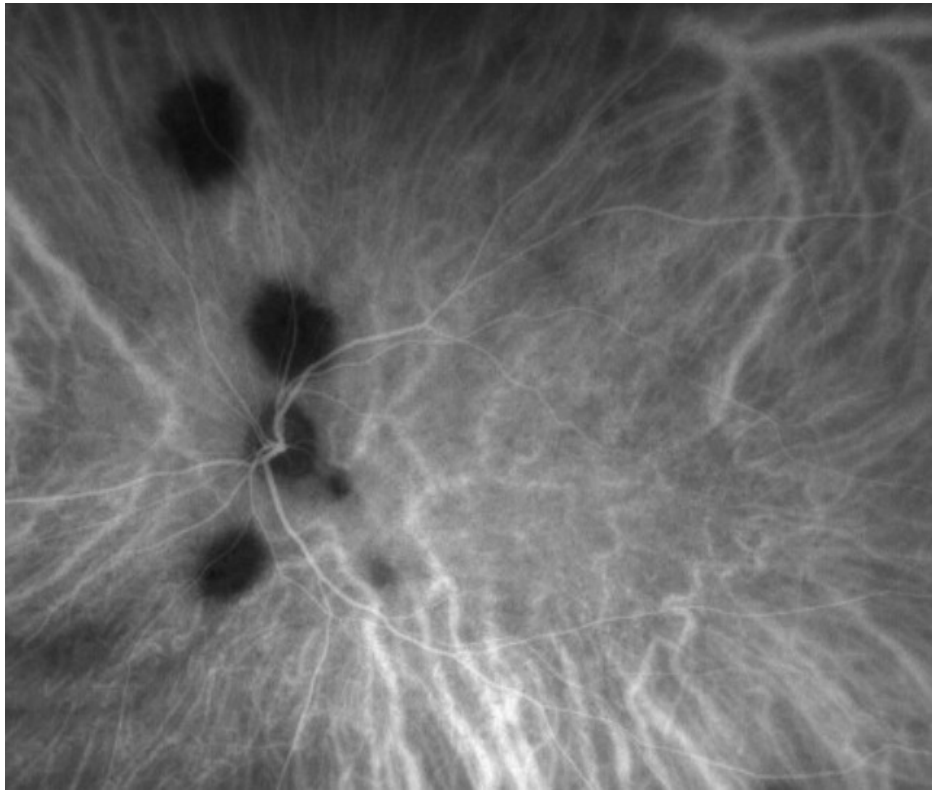
Fluorescein Angiography



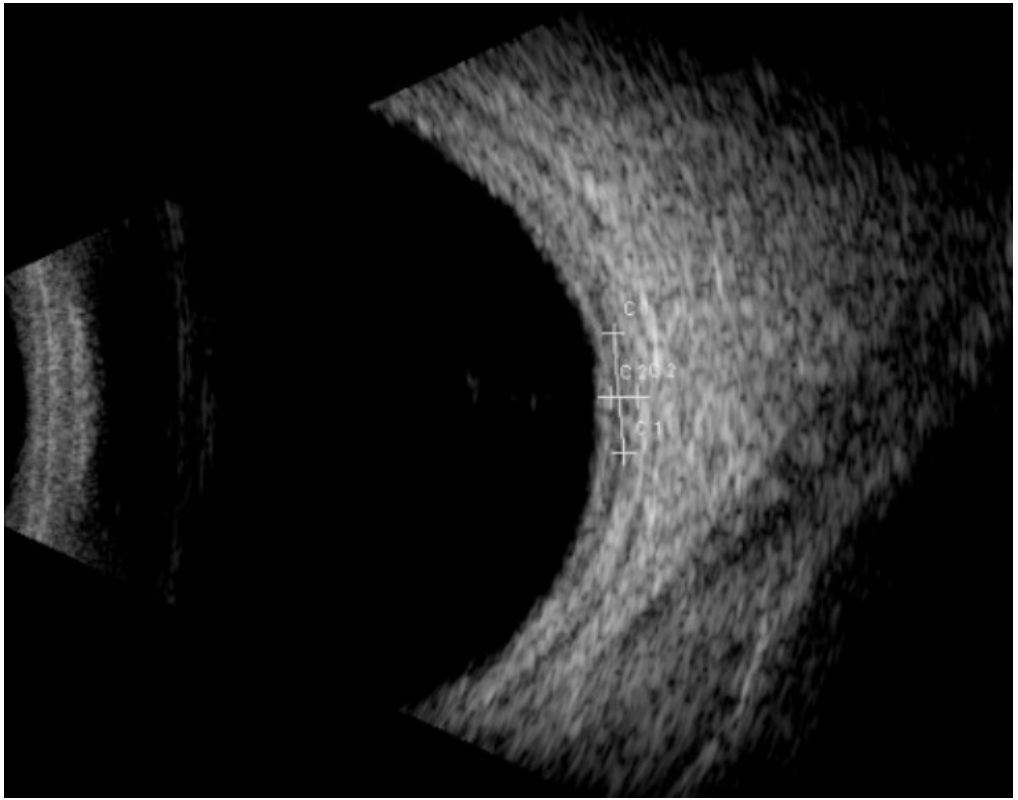


Indocyanine Green Angiography





B-Scan Ultrasound



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BDUMP: Overview

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- Can result in devastating loss of vision
- Associated with poor visual and survival prognosis

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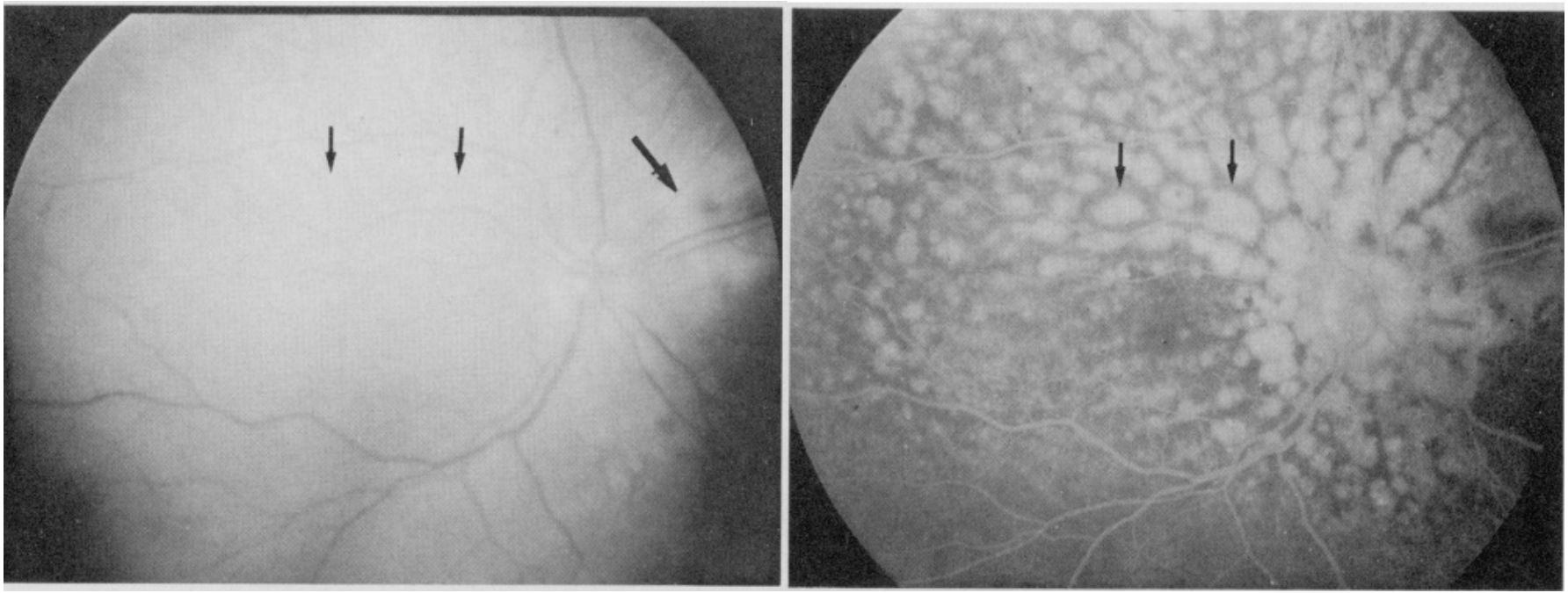

Gass, 1990

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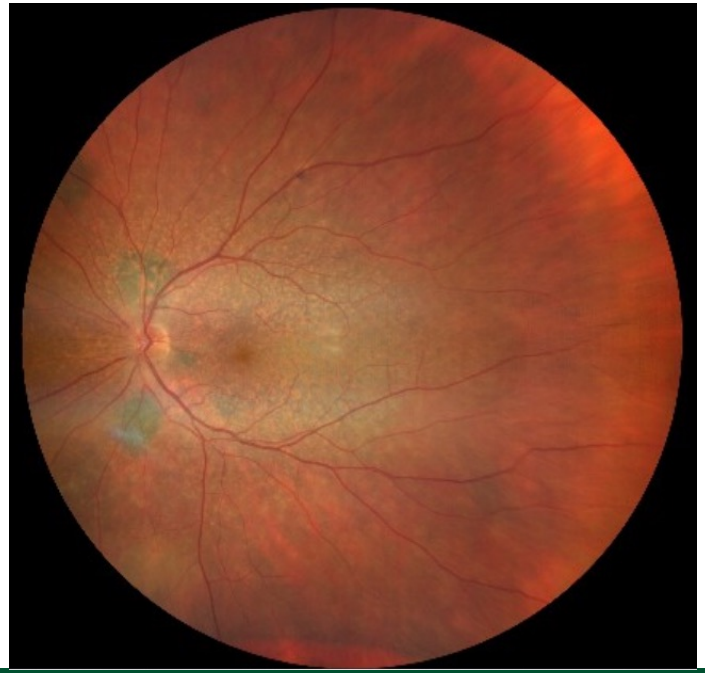

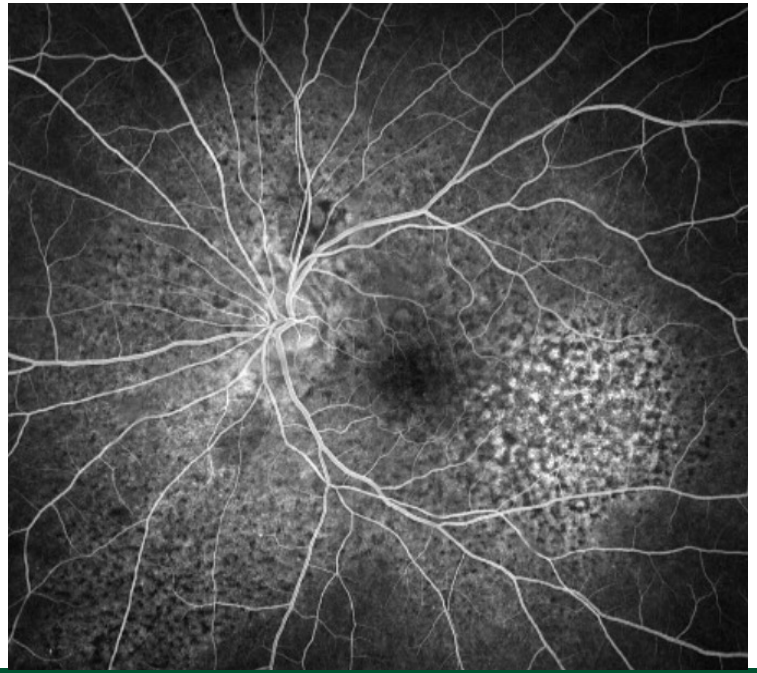

Ocular Cardinal Signs

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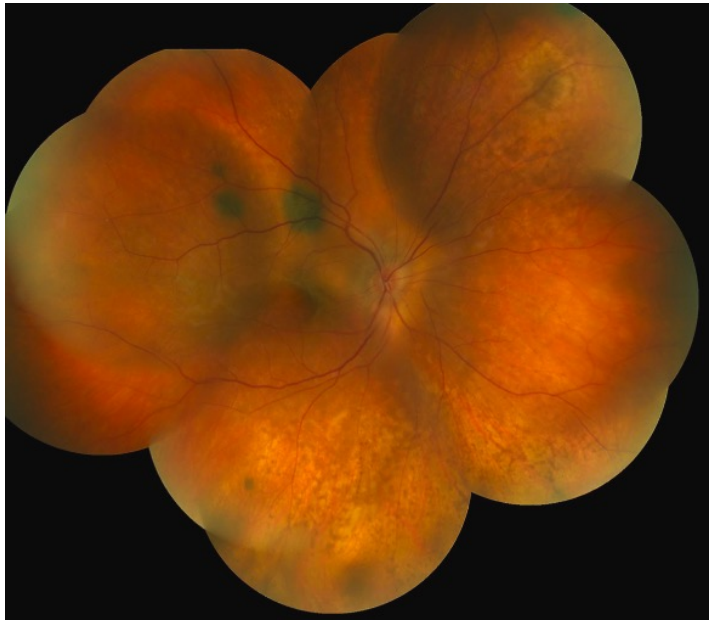

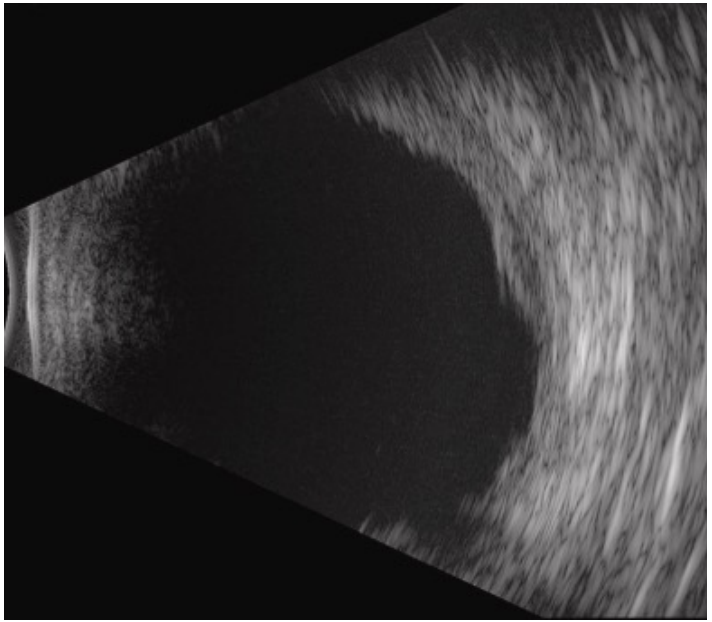

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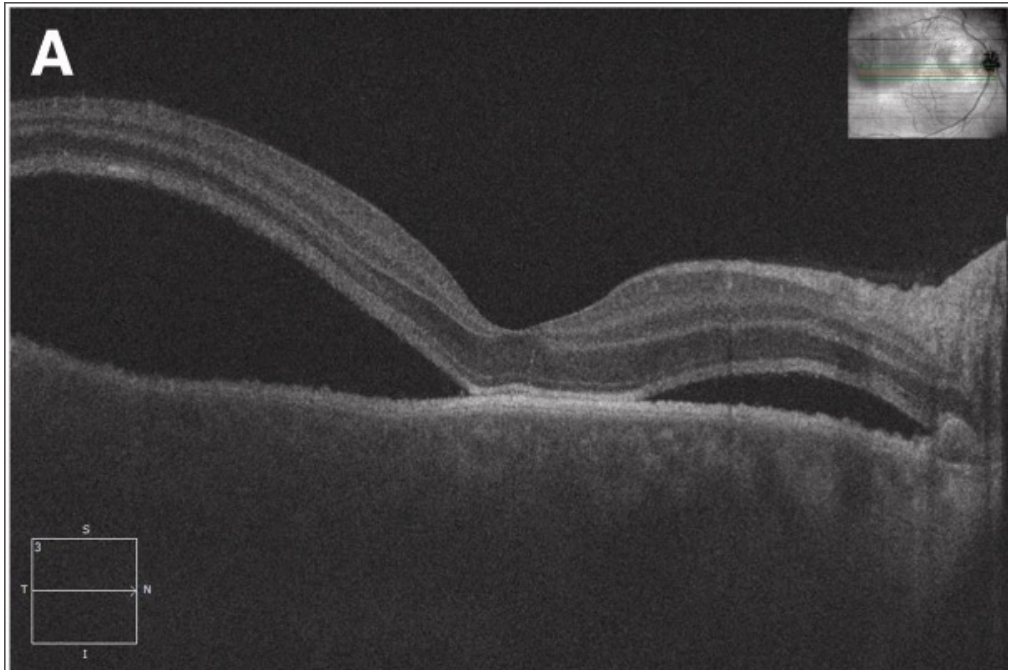
Ocular Cardinal Signs

4. Exudative retinal detachment



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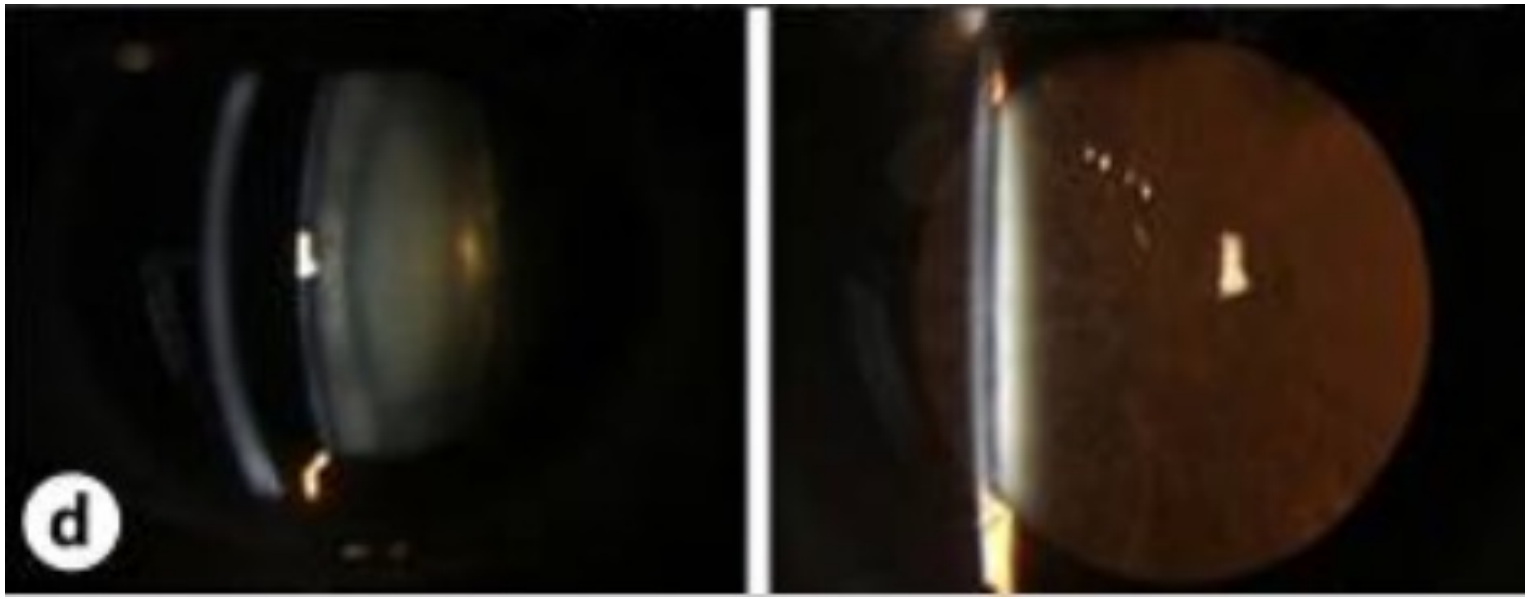

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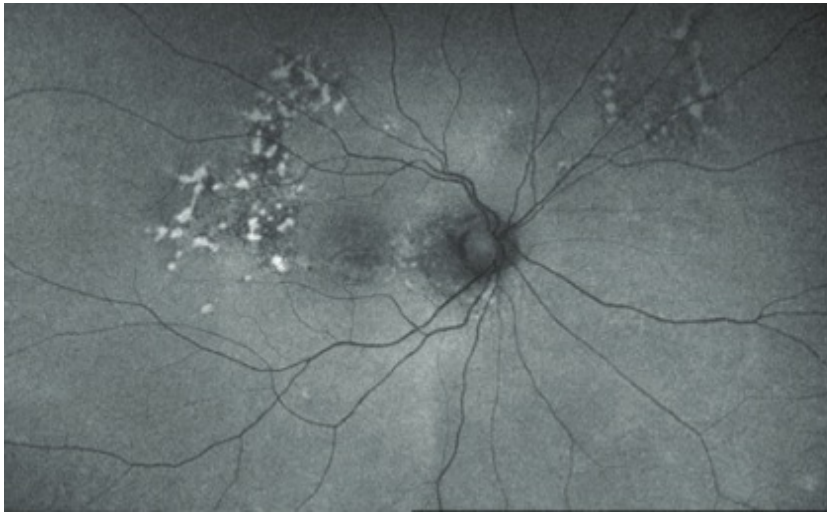
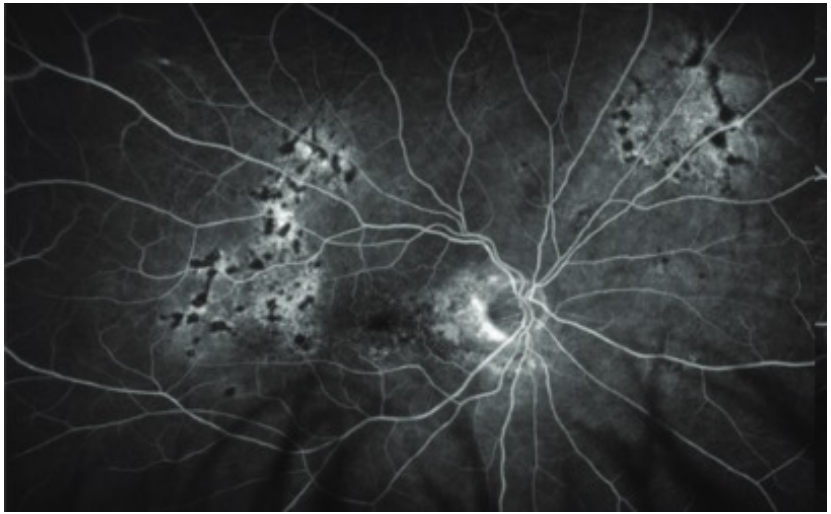
Other Findings

- Not specifically described by Gass, but were later characterized
  - FAF and FA
  - ICG
  - OCT
  - External

FAF and FA Findings

- “Leopard” or “giraffe” spotting on FAF
- Reciprocal pattern on FA





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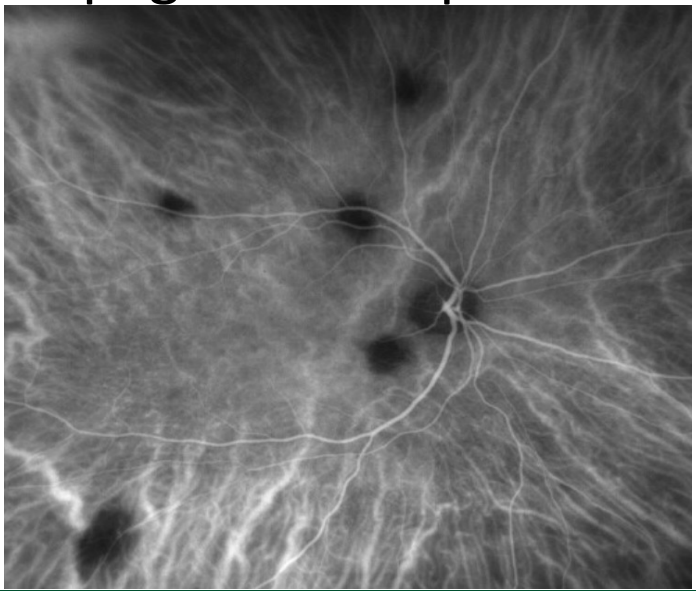
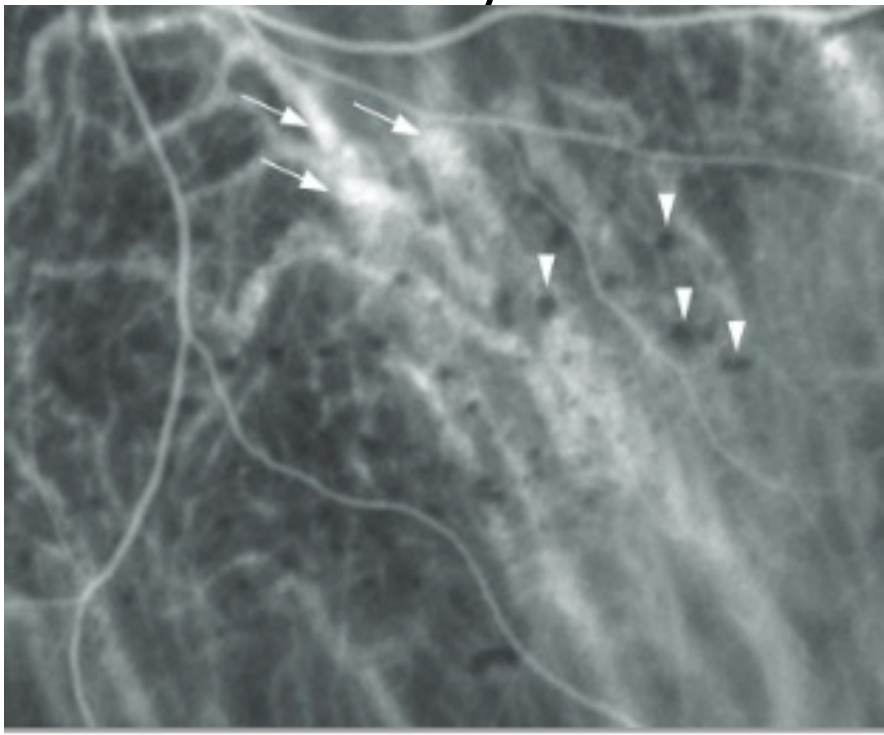
ICG Findings

- Hypocyanescence (blocking) of the uveal melanocytic proliferations
- “Spaghetti and parmesan” sign





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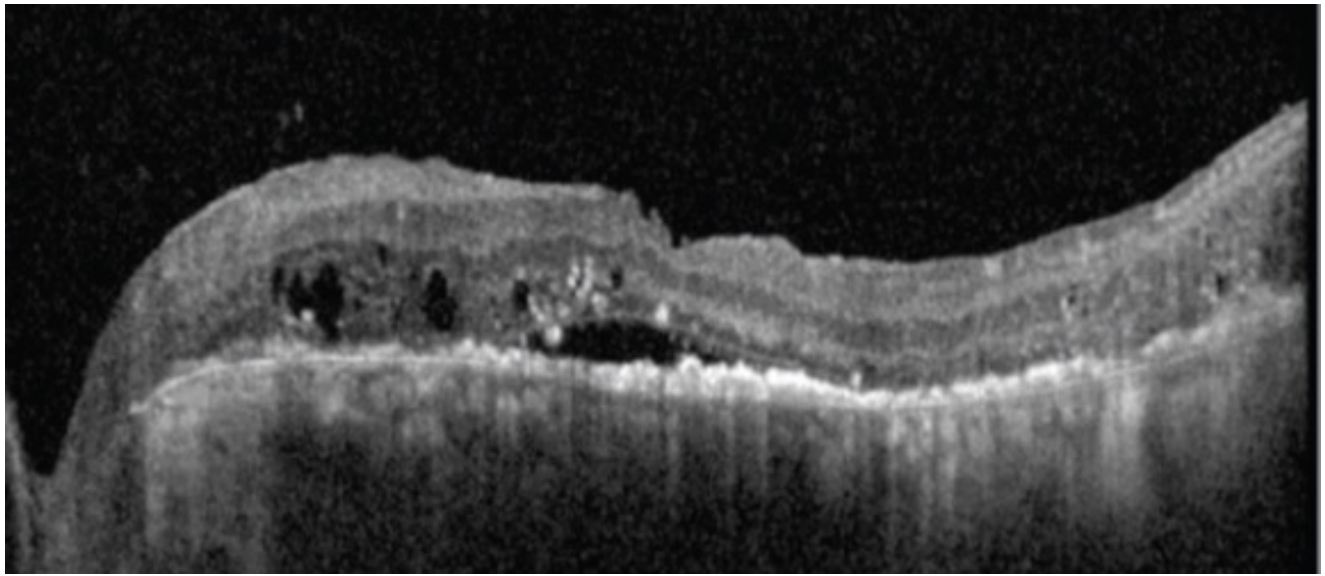
OCT Findings

- Thickened choroid
- RPE hypertrophy/atrophy
- Subretinal and intraretinal fluid
- Bacillary layer detachments have been described



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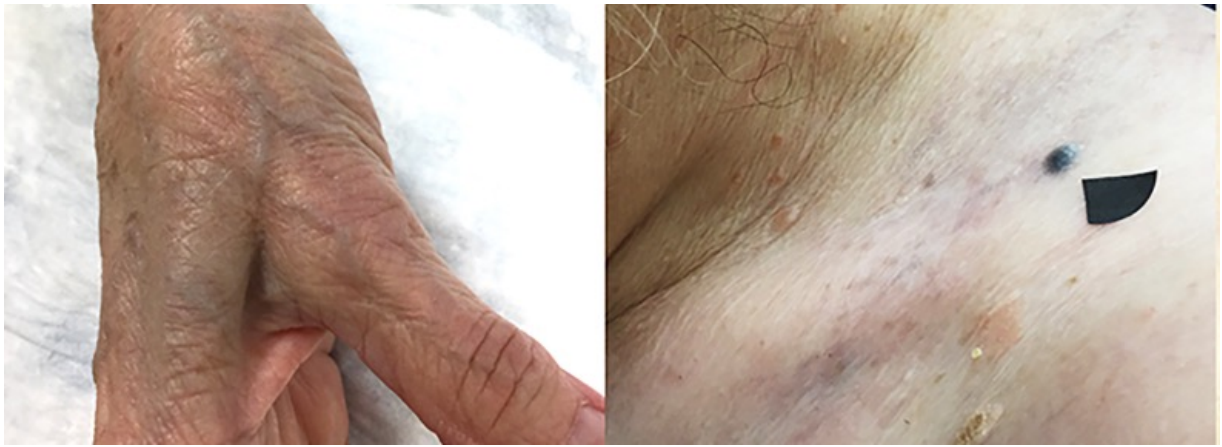
External Findings

- Cutaneous or mucosal hyperpigmentation
- Has been termed “multifocal diffuse integumentary and mucosal melanocytic proliferation” or “DIMP”
- 25% of patients have evidence of non-ocular hyperpigmentation, often involving mucosal membranes[9]



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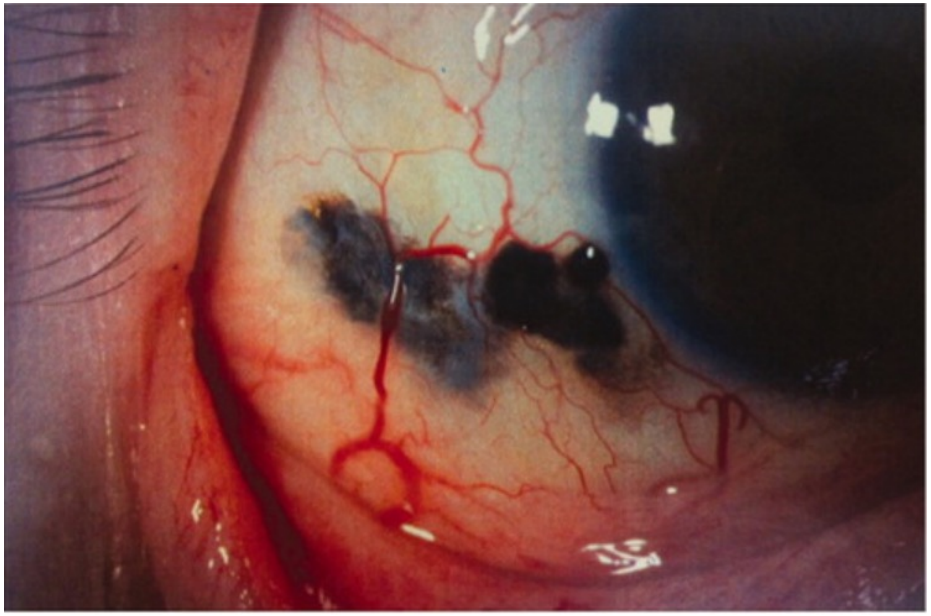
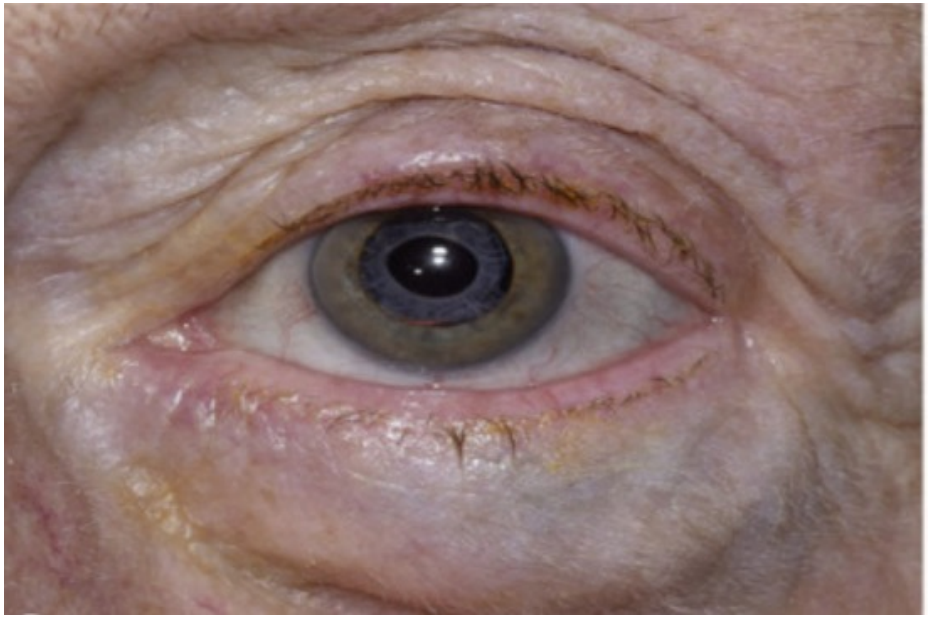
External Ocular Findings





Left: Rahimy E, Coffee RE, McCannel TA. Bilateral diffuse uveal melanocytic proliferation as a precursor to multiple systemic malignancies. Semin Ophthalmol. 2015 May;30(3):206-9.
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Pathophysiology

- Poorly understood

Miles SL, Niles RM, Pittock S, Vile R, Davies J, Winters JL, Abu-Yaghi NE, Grothey A, Siddiqui M, Kaur J, Hartmann L, Kalli KR, Pease L, Kravitz D, Markovic S, Pulido JS. A factor found in the IgG fraction of serum of patients with paraneoplastic bilateral diffuse uveal melanocytic proliferation causes proliferation of cultured human melanocytes. Retina. 2012 Oct;32(9):1959-66.

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- BDUMP patients possess a serum borne factor termed “cultured melanocyte elongation and proliferation factor (CMEP)”

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  - Proposed that the primary malignancy may secrete the serum factor that leads to melanocytic proliferation

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Epidemiology

- Median age at presentation: 65 years
  - Range from 34-89

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Epidemiology

- Median age at presentation: 65 years
  - Range from 34-89
- 61% female, 39% male
- Primary Malignancy
  - Females: Urogenital cancer (69%)
  - Males: Lung carcinoma (52%)

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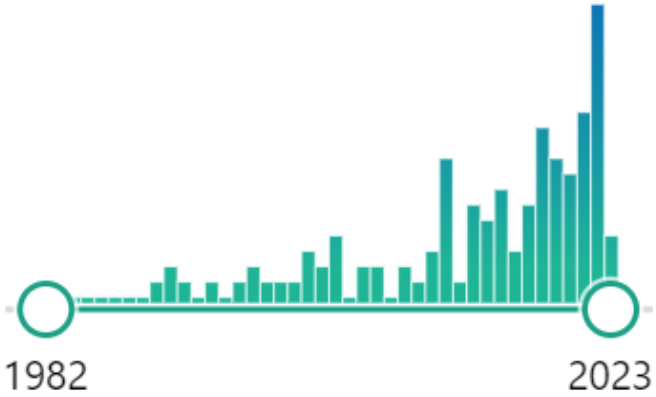
BDUMP on the Rise

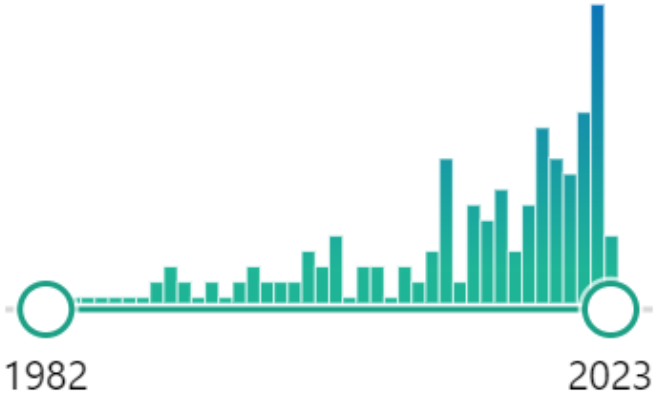
- Rapid increase in cases since Barr in 1982



https://pubmed-ncbi-nlm-nih-gov.access.library.miami.edu/?locale=en-us&action=start&term=bilateral+diffuse+uveal+melanocytic+proliferation

BDUMP on the Rise

- Rapid increase in cases since Barr in 1982
  - Increased cancer survival time?



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- Rapid increase in cases since Barr in 1982
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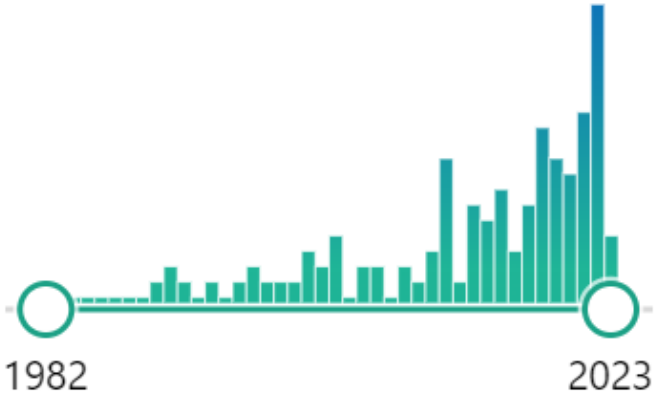
  - Aging population?



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BDUMP on the Rise

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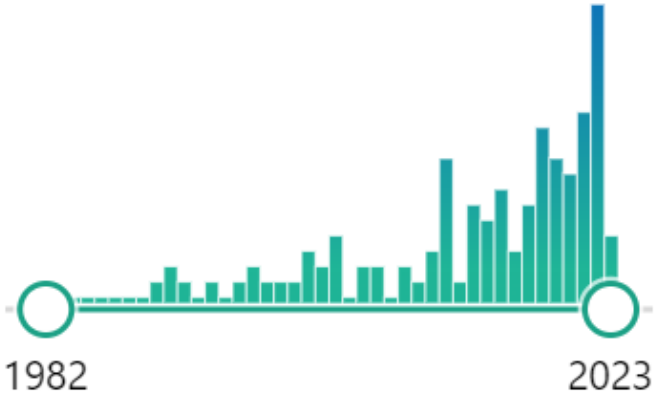
  - Increased cancer survival time?
  - Aging population?
  - Better awareness?



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Prognosis

- Poor
  - Average time from presentation to death is 19 months

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Prognosis

- Poor
  - Average time from presentation to death is 19 months
  - Range of time from presentation to blindness is between 1 and 10 months

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Management

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  - **Plasmapheresis**

Plasmapheresis

- Plasma exchange has been found to temporarily remove CMEP protein

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Plasmapheresis

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Plasmapheresis

- Plasma exchange has been found to temporarily remove CMEP protein
- Has lead to visual improvement in a number of cases
- Reports of plasmapheresis failure also exist
  - Different tumor types may have an affect
  - Underlying malignancy may be replenishing CMEP

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Current Management Goals

- Combined therapy approach:

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Current Management Goals

- Combined therapy approach:
  - Search for systemic malignancy if not known (44%)
  - Treat the primary tumor to stop production of the pathogenic protein
  - Plasmapheresis to reduce serum CMEP

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Back to Our Patient

- Diagnosis
  - Bilateral Diffuse Uveal Melanocytic Proliferation

Back to Our Patient

- Diagnosis
  - Bilateral Diffuse Uveal Melanocytic Proliferation
  - Subretinal fluid noted by outside provider likely reactive central serous chorioretinopathy given the temporal relationship with initiation of corticosteroid use and spontaneous improvement after initiation of eplerenone

Back to Our Patient

- Diagnosis
  - Bilateral Diffuse Uveal Melanocytic Proliferation
  - Subretinal fluid noted by outside provider likely reactive central serous chorioretinopathy given the temporal relationship with initiation of corticosteroid use and spontaneous improvement after initiation of eplerenone
  - It is possible that infiltrative changes to the choroid may incite unusual susceptibility to exudation

Back to Our Patient

- Management

Back to Our Patient

- Management
  - Primary malignancy already treated

Back to Our Patient

- Management
  - Primary malignancy already treated
  - Cataract surgery already performed

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- Management
  - Primary malignancy already treated
  - Cataract surgery already performed
  - Plasmapheresis not indicated

Back to Our Patient

- Management
  - Primary malignancy already treated
  - Cataract surgery already performed
  - Plasmapheresis not indicated
  - **Plan: close observation with serial imaging**

1 Month Follow-up

- Vision stable at 20/25 OU
- Retinas attached
- Patient resumed chemotherapy

Take Home Points

- BDUMP should be considered in cases of bilateral acquired nevi in the setting of known neoplastic disease

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- Multimodal imaging is of incredible value for diagnosis

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- BDUMP should be considered in cases of bilateral acquired nevi in the setting of known neoplastic disease
- Multimodal imaging is of incredible value for diagnosis
- Clinicians should recognize the unique presentation of BDUMP and pursue a thorough work-up for systemic malignancy if not already known

References

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Thank You

- Nicolas Yannuzzi, MD
- Rami Aboumourad, OD
- Imaging department
- My co-residents

Thank You