Chiefs' Rounds

WillsEye Hospital

Oct 8, 2021

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Disclosures

I have no financial relationships to disclose.

I will not discuss off label use and/or investigational use in my presentation.

64 yo female presents with “corner of left eye turning pink,” worsening over 2 weeks

Past Ocular History

- None

Past Medical History

- Migraines
- HLD
- Graves
- Anxiety
- Depression

Past Surgical History

- Radioactive iodine and thyroidectomy
- Hernia repair
- Knee surgery

Medications

- Almotriptan
- Bupropion
- Methimazole
- Lansoprazole
- Nortryptyline
- Topiramate

Social and Family History

- Never smoker. No recreational drug use
- FMHx:
  - Multiple myeloma, high blood pressure (mother)
  - Stroke (father)
  - Unknown cancer (maternal grandfather, grandmother)

Review of Systems

- Somewhat blurred vision OU
- No double vision
- No eye pain
- No floaters
- No weight loss

Exam

V_{sc} < 20/70 ph 20/40
20/40 ph 20/20

P < Pharm dil
Pharm dil

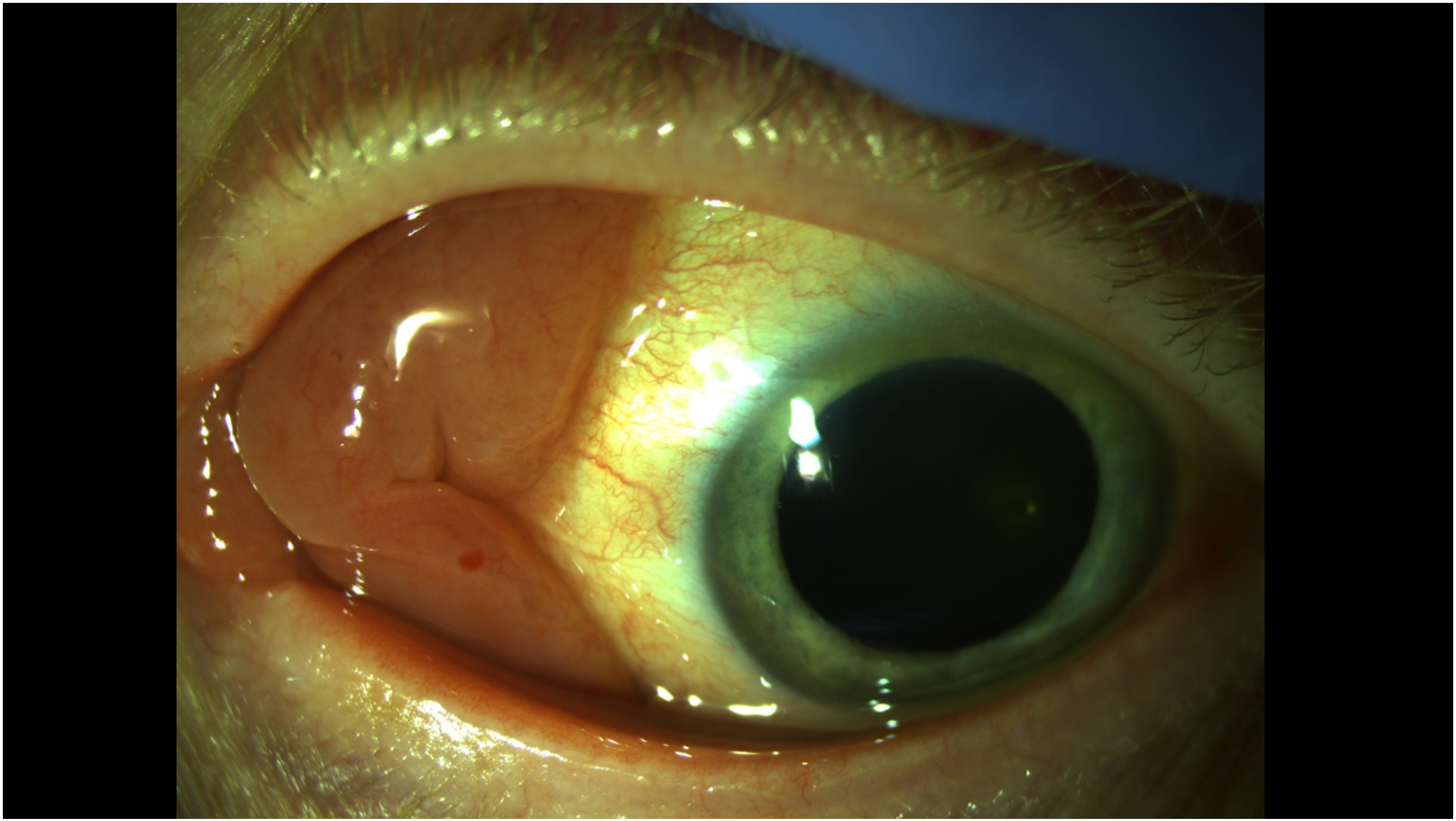
T < 16
13

CVF < Full
Full

EOM < Full

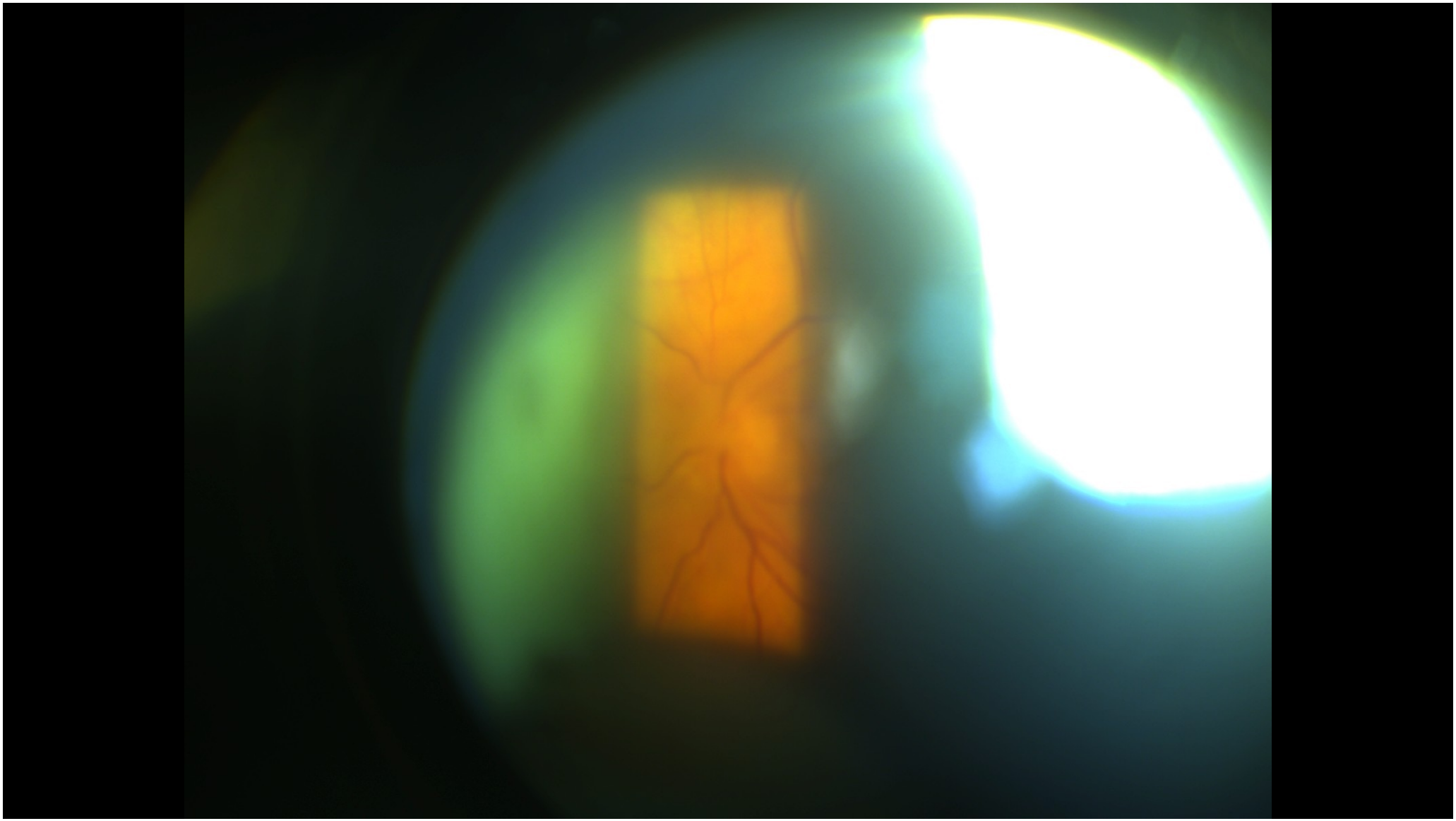
80 100 95
80 95
80 100 95

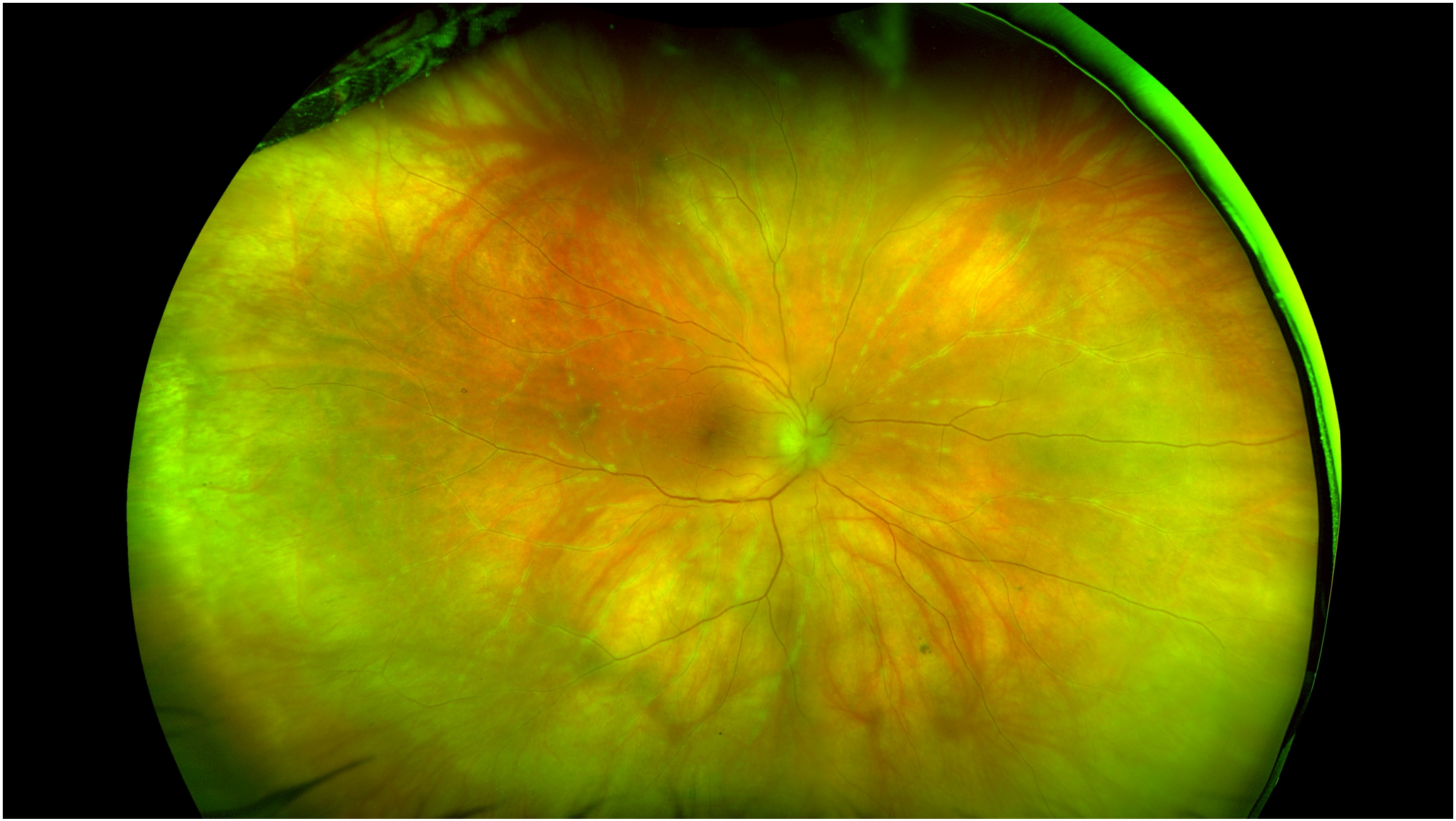
CP < 8/8
8/8



Anterior Exam

OD		OS
Normal	**Lids**	Normal
Nasal salmon-colored subjconjunctival lesion along inferior fornix	**Conjunctiva**	**Large nasal salmon-colored subconjunctival lesion extending from inferior fornix and involving caruncle**
SPK	**Cornea**	SPK
Deep and Quiet	**Anterior Chamber**	Deep and Quiet
Flat	**Iris**	Flat
2+ NS	**Lens**	2+ NS



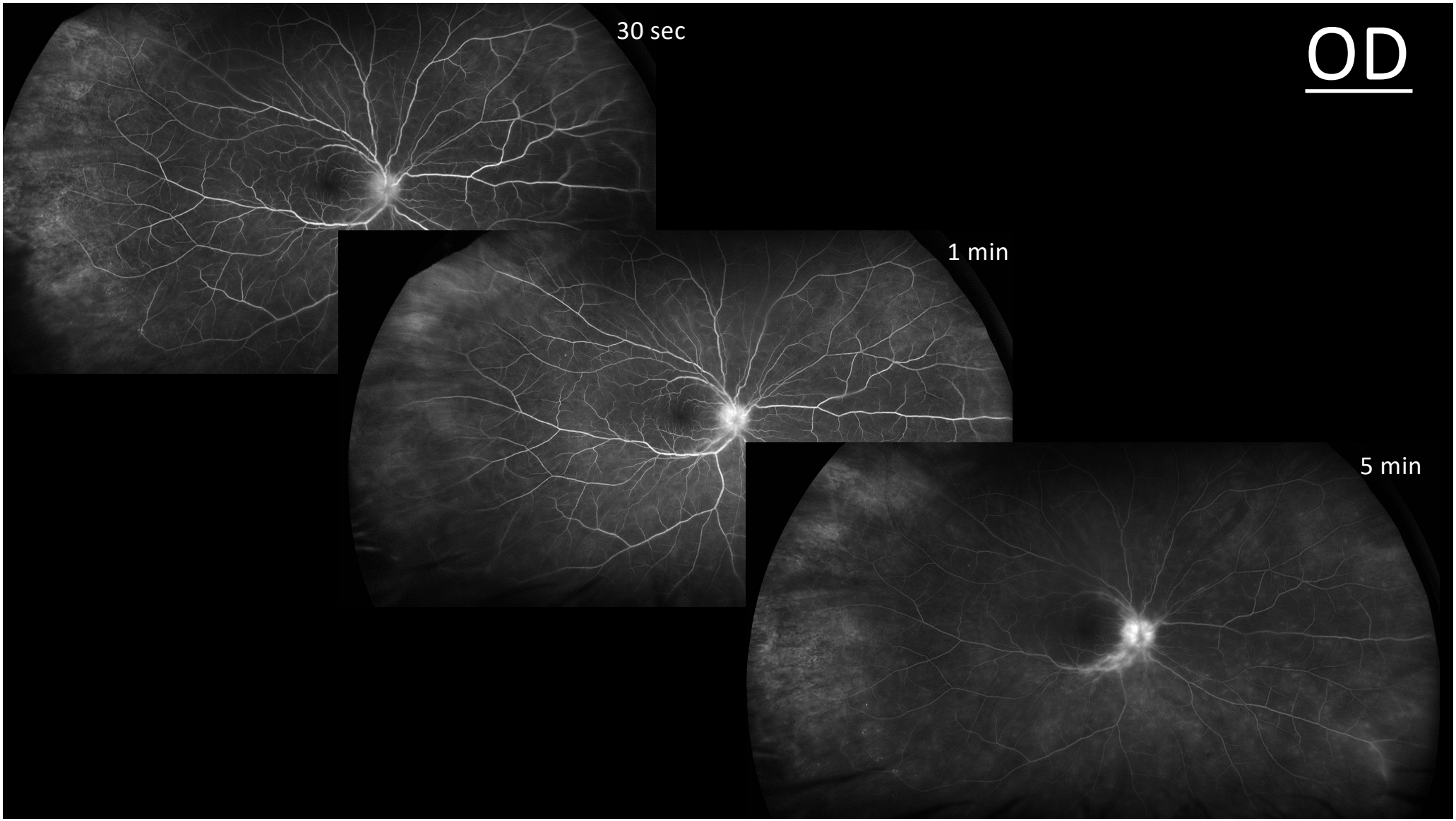


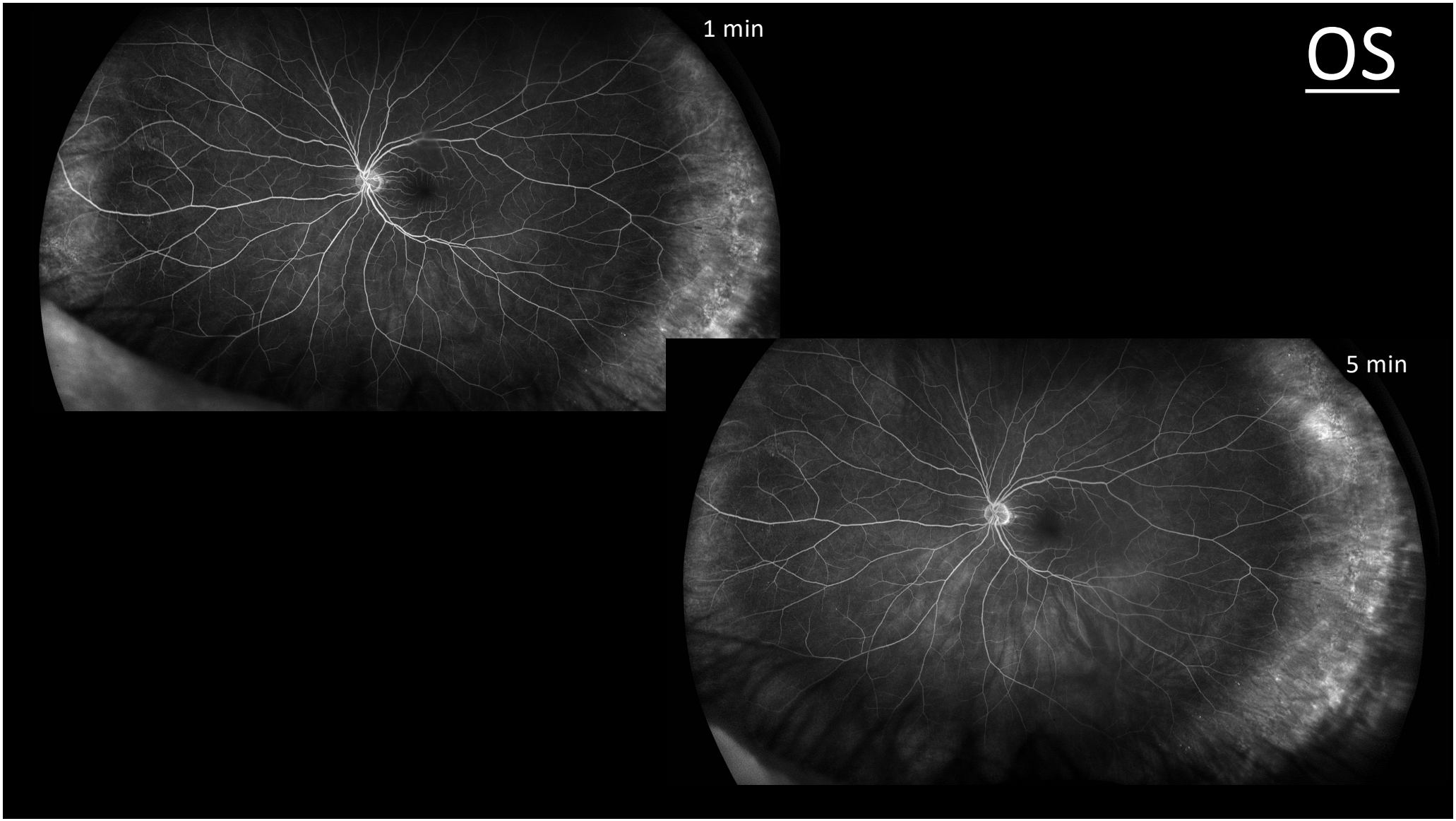
Dilated fundus exam

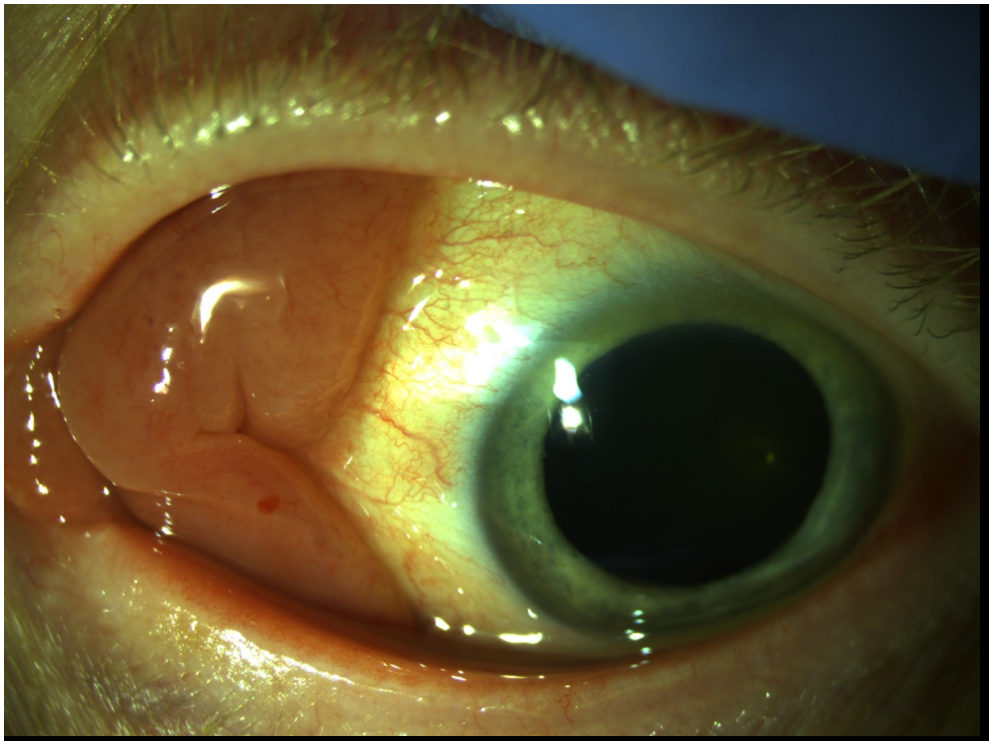
OD		OS
2+ vitreous cell	**Vitreous**	Clear, no vitreous cell
2+ disc edema with blurred margins	**Disc**	Normal, C/D 0.1
Foveal pigmentary changes	**Macula**	No edema, thickening, or hemorrhage.
Attenuated, vasculitis	**Vessels**	Arteriolar attenuation
Normal	**Periphery**	Normal

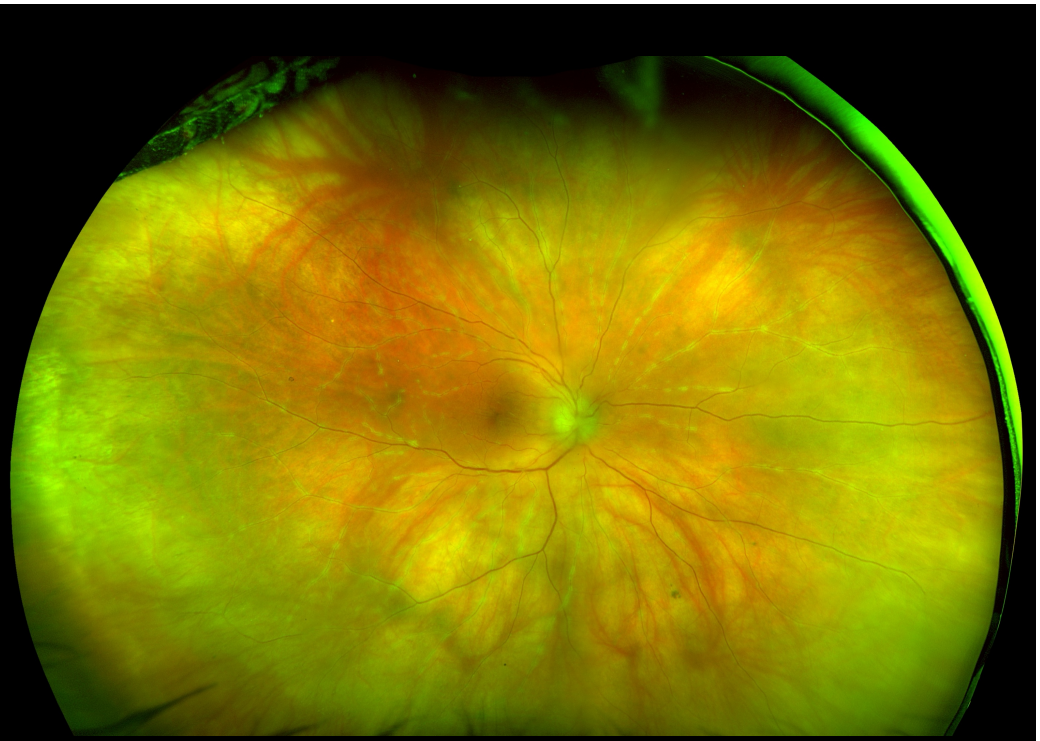
OD

OS

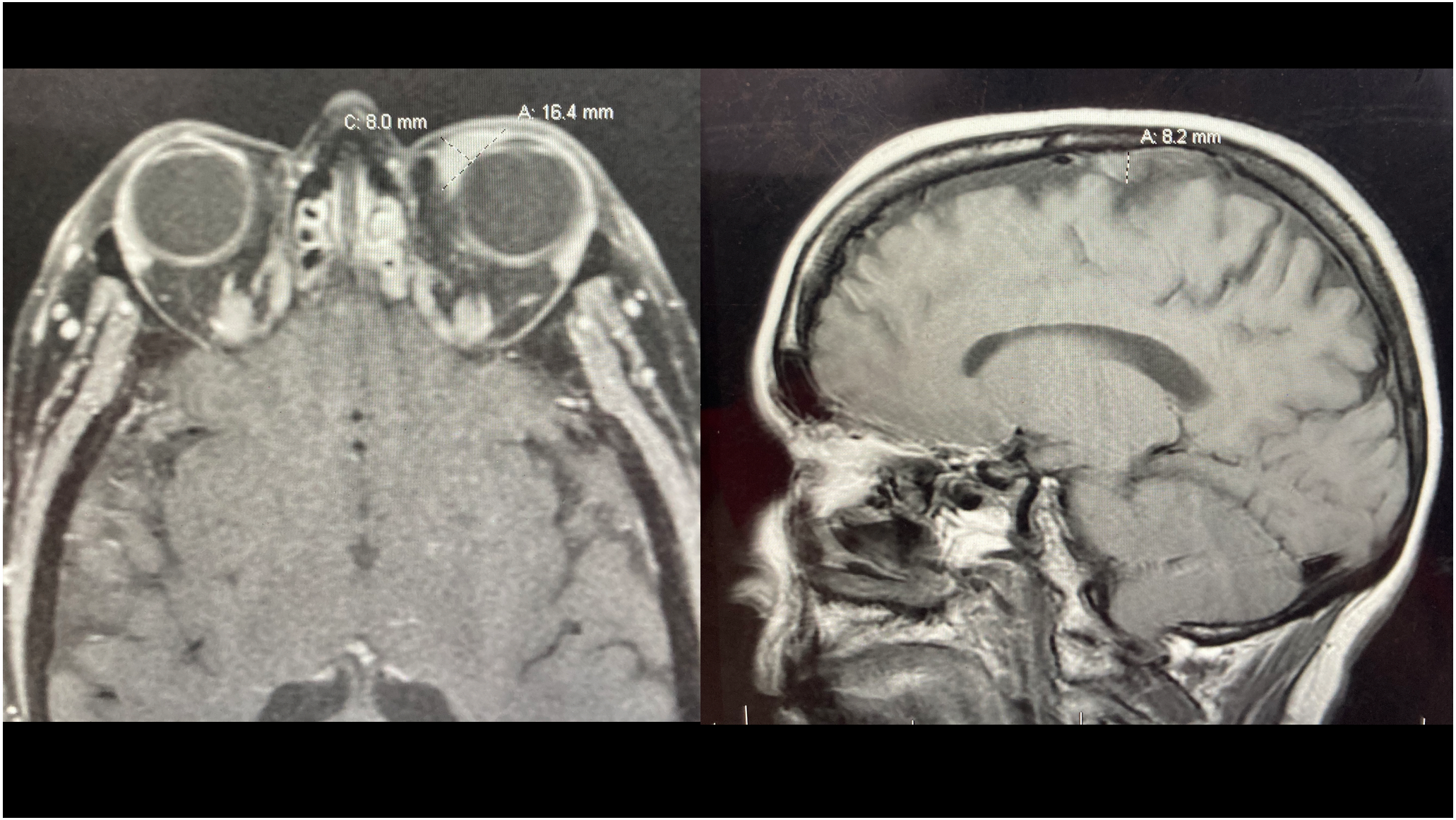

30 sec
1 min
5 min
OD


1 min
OS
5 min





Next steps?


C: 8.0 mm
A: 16.4 mm
A: 8.2 mm

Additional labs and imaging

- MRI brain/orbits w/wo contrast:

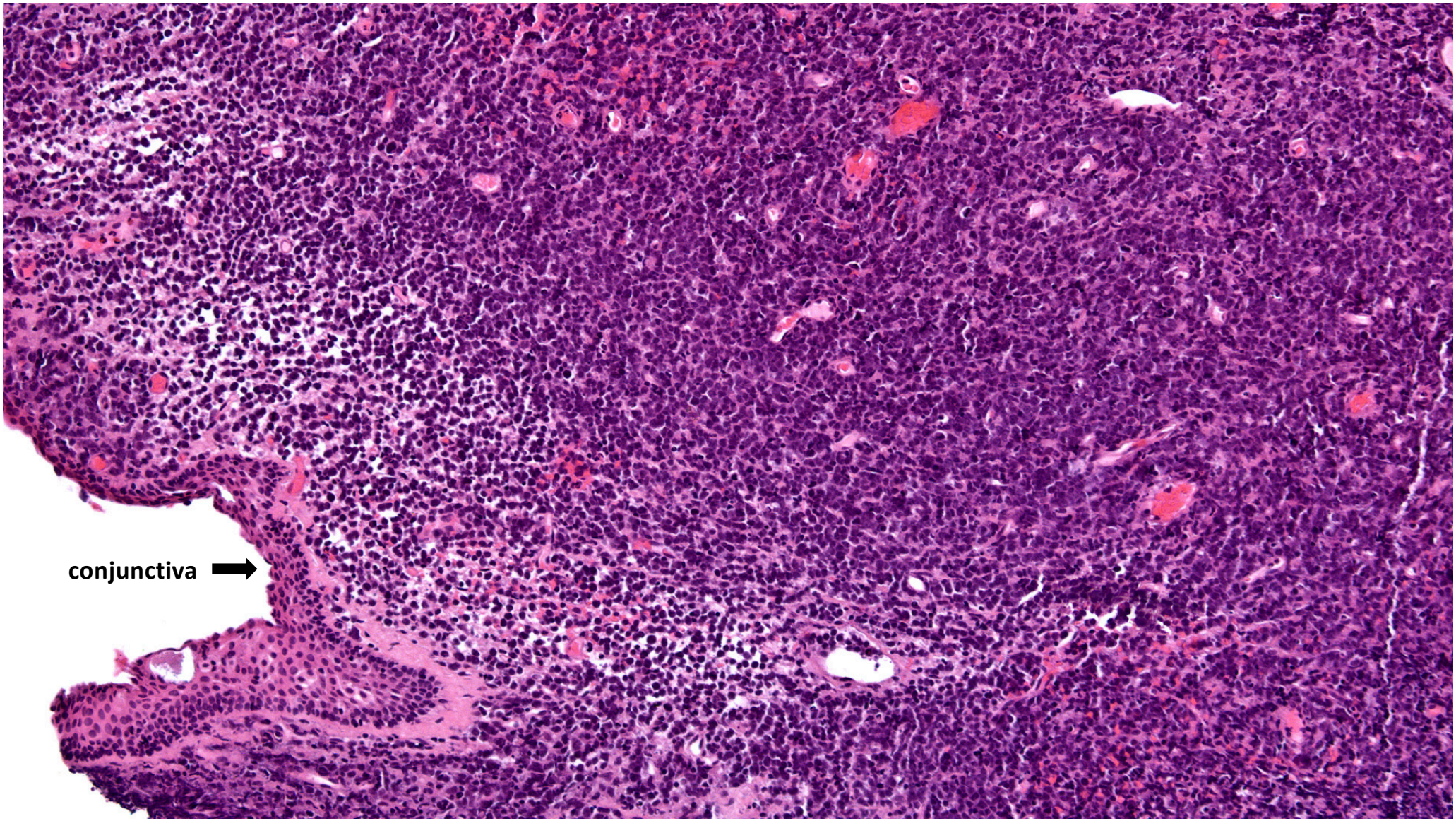
  1) A 2.1 cm left preseptal enhancing mass abutting the left globe with retrobulbar intraconal fat infiltration and ill-defined enhancement of the posterior sclera and distal optic nerve sheath complex

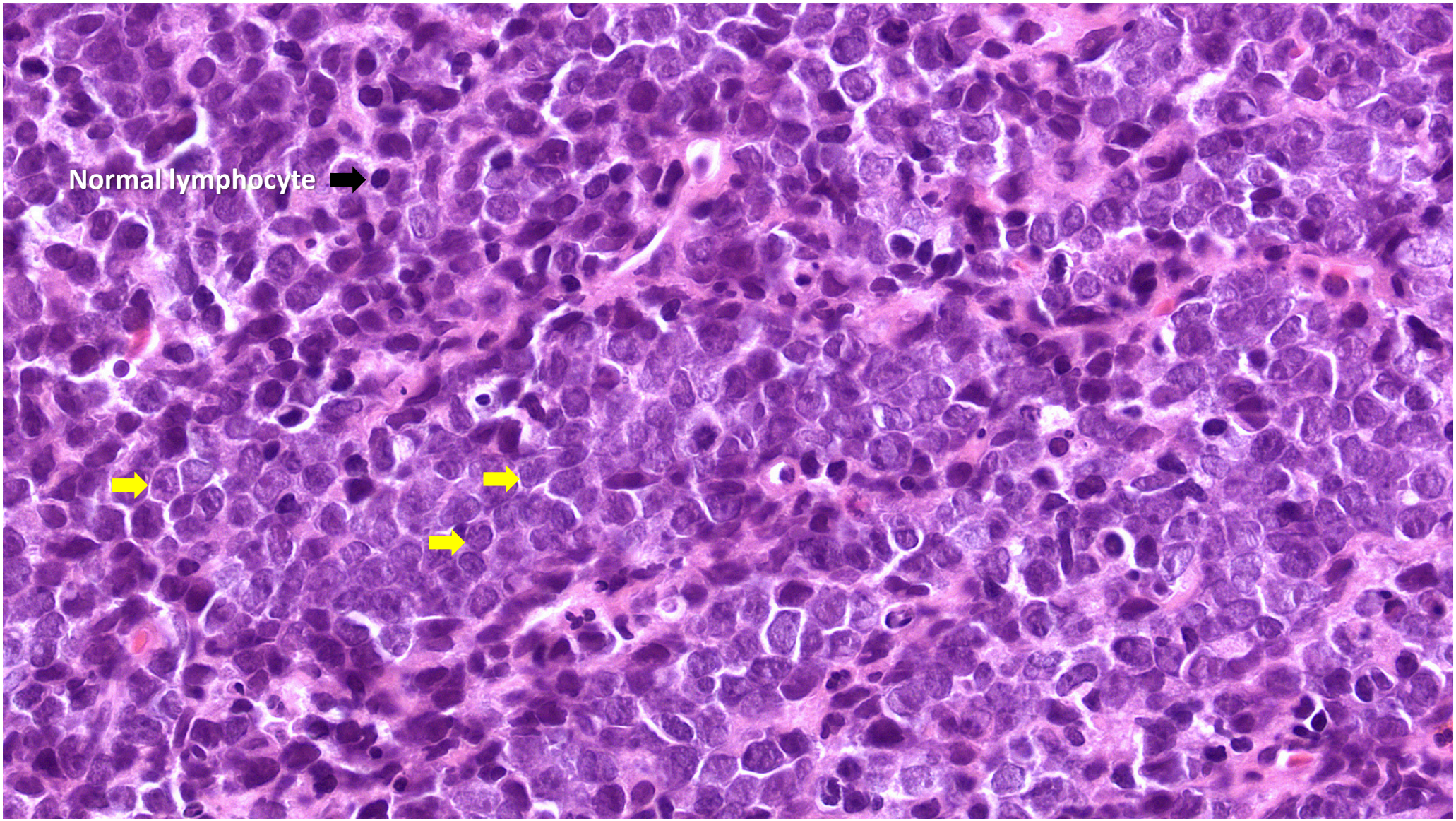
  2) 1.6 cm dural based mass overlying the parietal lobe on the right

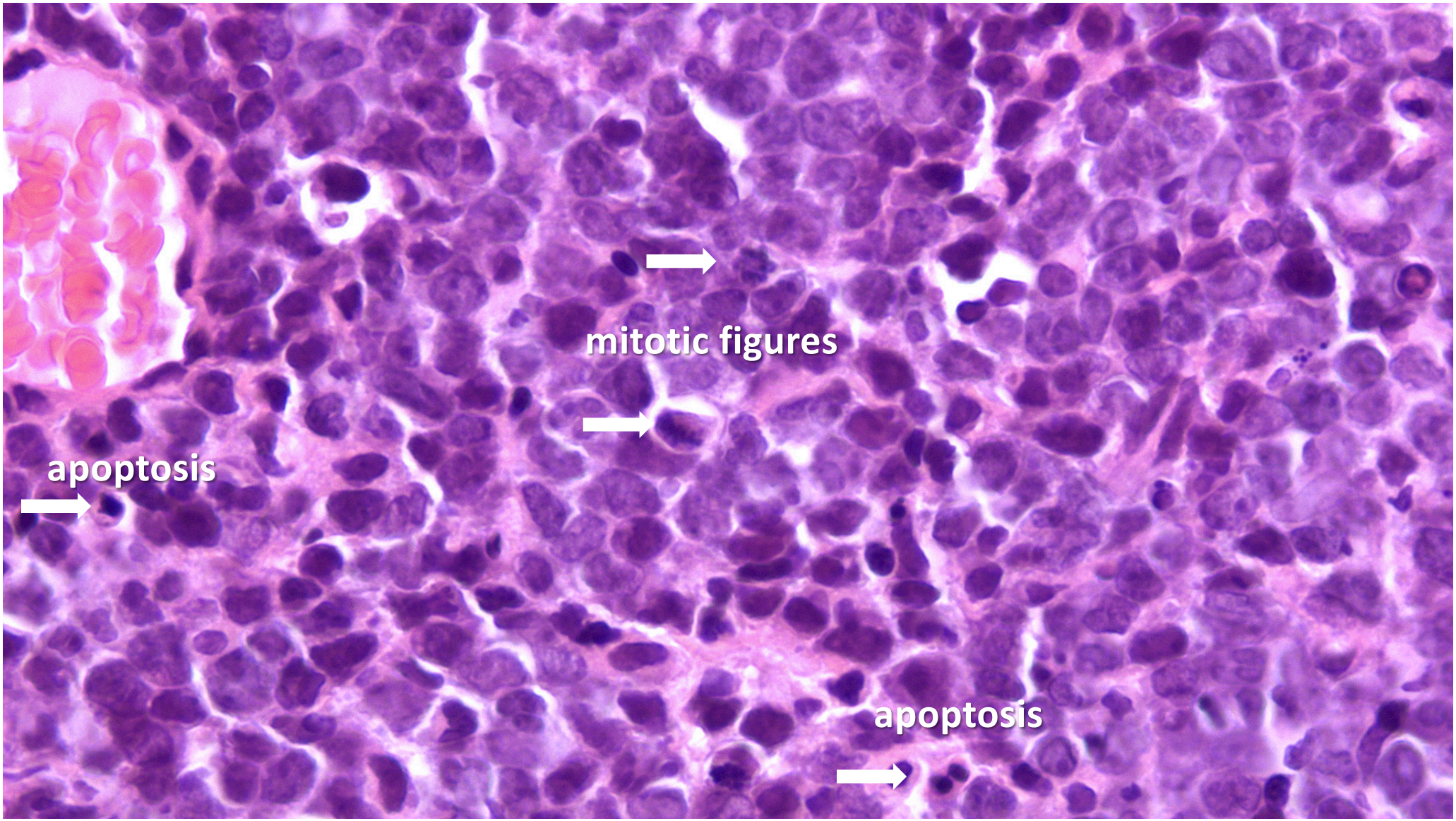
  3) Focal soft tissue lesion within left posterior nares and adjacent nasopharynx on the left side, with associated osseous destruction

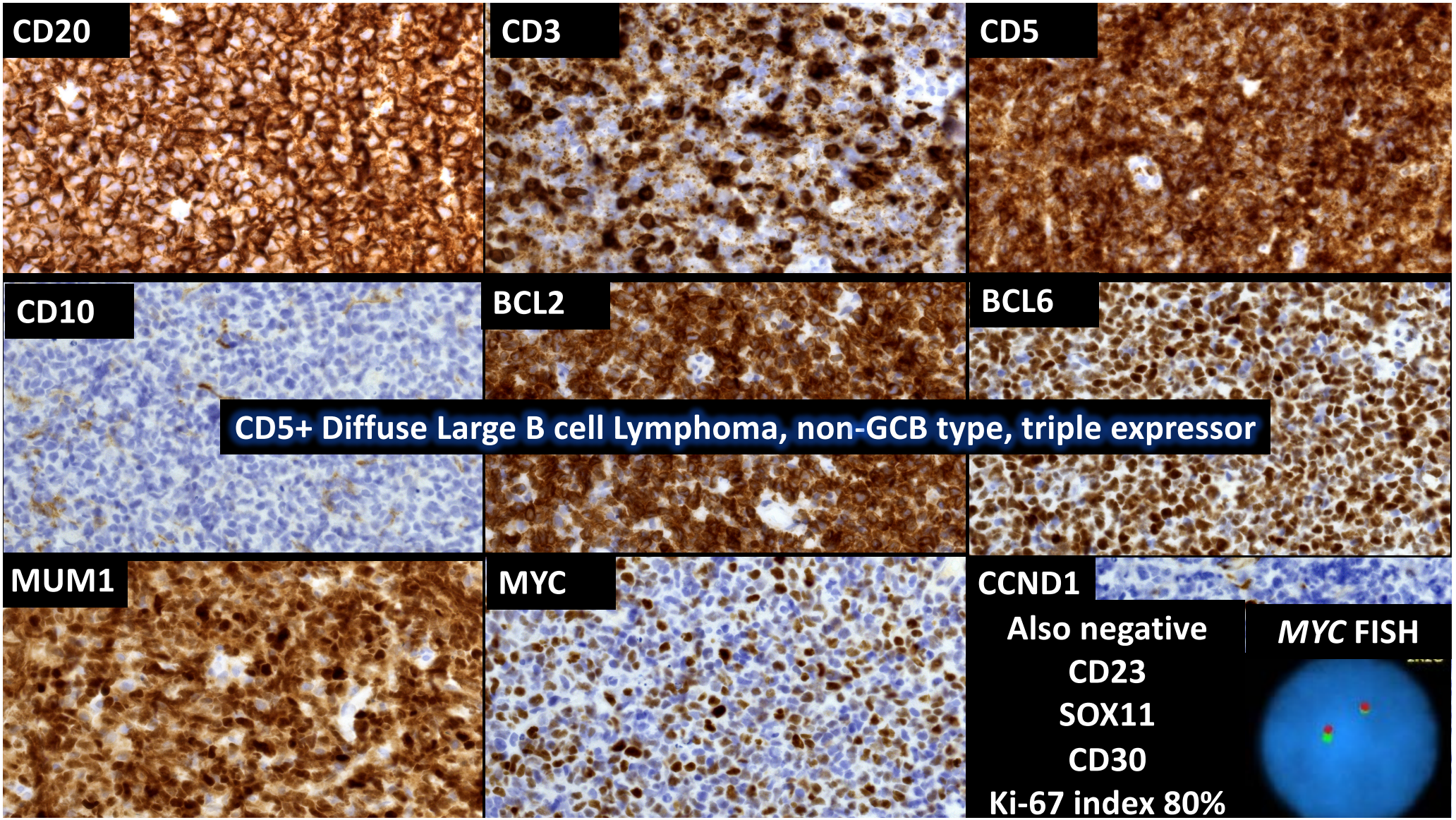
- Lyme, syphilis, quant-gold, CBC, BMP, ESR, CRP wnl

Conjunctival biopsy


conjunctiva


Normal lymphocyte


mitotic figures
apoptosis
apoptosis


CD20
CD3
CD5
CD10
BCL2
BCL6
CD5+ Diffuse Large B cell Lymphoma, non-GCB type, triple expressor
MUM1
MYC
CCND1
Also negative
CD23
SOX11
CD30
Ki-67 index 80%
MYC FISH

Bone Marrow Biopsy

- Atypical CD20+ CD5+ lymphoid aggregate
- IGH gene rearrangement clonality analysis by PCR

RESULT	POSITIVE FOR A CLONAL IGH GENE REARRANGEMENT
DETAILED RESULTS	IGH-FR1: Suspicious for a Clonal Peak: 322 bp IGH-FR2: Negative for a Clonal Peak IGH-FR3: Clonal Peak(s): 94 bp

CSF analysis

- Cytology – atypical (Increased lymphocytes)
- IGH gene rearrangement clonality analysis by PCR

RESULT	POSITIVE FOR A CLONAL IGH GENE REARRANGEMENT
DETAILED RESULTS	IGH-FR1: Clonal Peak(s): 334 bp IGH-FR2: Poor Amplification for Clonal Peak detection IGH-FR3: Poor Amplification for Clonal Peak detection

OCT

Patient Course

- Jan: Developed progressively worsened erythema in the left eye. MRI with orbital and dural based mass in R parietal/frontal region, thought to be benign meningioma.
- Feb: Conj mass biopsy revealed CD5+ DLBCL. BMB and LP done.
- March: PET showed multiple areas of hypermetabolic activity in the L orbit, R cerebellum, spleen, adrenal gland and extensive lymphadenopathy above and below the diaphgram. Started on R-CHOP.
- April: Repeat brain MRI showed enhancement within the frontal lobe and cerebellar hemispheres suspicious for early leptomeningeal and parenchymal metastases. The dural based lesion seen to be stable. Initiated on HD MTX but developed MTX toxicity.
- May: Repeat MRI showed worsening leptomeningeal disease, prompting WBRT. Resumed R-CHOP after. Also discussed options such as **ibrutinib**, HiDAC, intrathecal chemo.
- Sept: Admitted for FTT and depression/suicidal ideation. PET/CT revealed marked clinical improvement with complete resolution of the lymphoma in the neck/chest/abd/pelvis, and significant improvement in brain mets. Fatigued by the many hospital/ER visits, pt elected for home hospice.

	Orbital	Intraocular
Epidemiology	Most common primary malignant orbital tumor	<2% of intraocular tumors
Involvement	Usually a low grade lymphoma (extranodal marginal-zone B-cell and MALT-type lymphomas)	Frequently high grade. Subsets: primary vitreoretinal, primary uveal, and secondary intraocular lymphoma
Symptoms	Chronic red eye, proptosis, double vision	Blurred vision, floaters
Features	Classic "salmon-patch" appearance, restriction in EOMs, periorbital edema, ptosis, hyperemic conjunctiva, and/or a firm palpable mass	Vitreous cells, choroidal thickening, retinal infiltrates, RDs, pseudohypopyon
Differential	Orbital pseudotumor, lymphoid hyperplasia, sarcoidosis, GPA, IgG4, etc	Uveitis, scleritis, reactive lymphoid hyperplasia, infection (CMV, ARN, toxo, etc), metastatic tumor, melanoma
Treatment	Radiotherapy +/- chemo	Radiotherapy +/- chemo +/- intravitreal

Briefly, primary vitreoretinal lymphoma (PVRL)

- Around 60–90% of PVRLs involve the brain subsequently, while 15–20% of patients with primary central nervous system lymphoma will develop PVRL later. The majority of PVRL is of B-cell origin

- Challenging diagnosis
  - Vitreous or retinal biopsy
  - *MYD88* is a gene discovered in the 1990s as a primary differentiation response factor in myeloid precursors. It plays a key role in toll-like receptor signaling and it has been found mutated (L26P) at a high frequency in PVRL samples.

Ocul Oncol Pathol. 2015 Dec; 2(2): 66–70.
Published online 2015 Sep 17. doi: 10.1159/000439053
PMCID: PMC4847667
PMID: 27171820

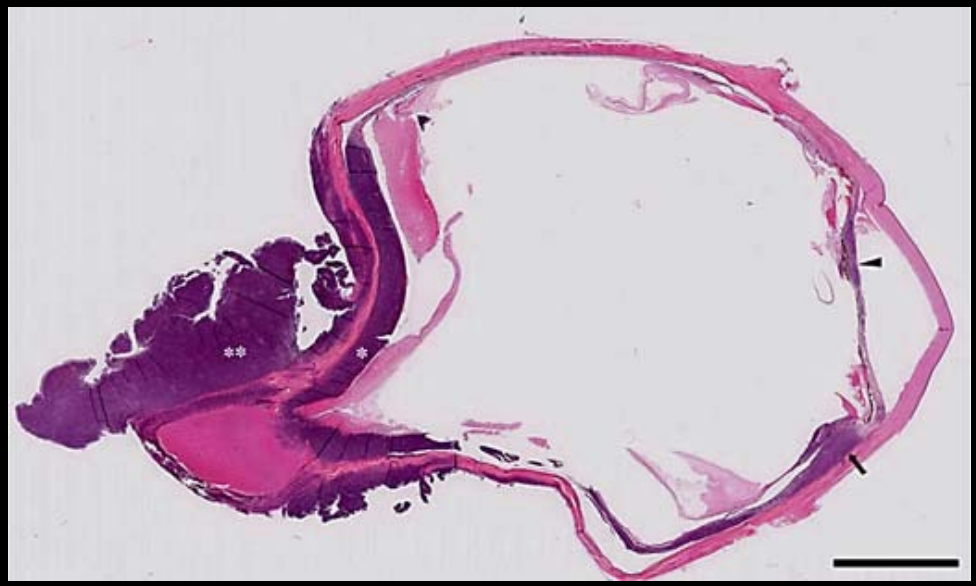
Case of Primary Intraocular Lymphoma with Extraocular Extension

Maki Kuro,[a,*] Kayako Matsuyama,[a] Masato Matsuoka,[a] Ryo Kosaki,[d] Nobuaki Shikata,[b] Tetsuya Nishimura,[a] and Kanji Takahashi[c]

- Case report of a primary intraocular lymphoma with infiltration of the iris, and extension into the sclera and extraocular tissues posteriorly

- Histologically, diagnosed tissue type as DLBCL. Detected tumor cells not only in the scerla itself, but also in the perineural and perviascular areas within the sclera

- There was no evidence of systemic or CNS involvement.



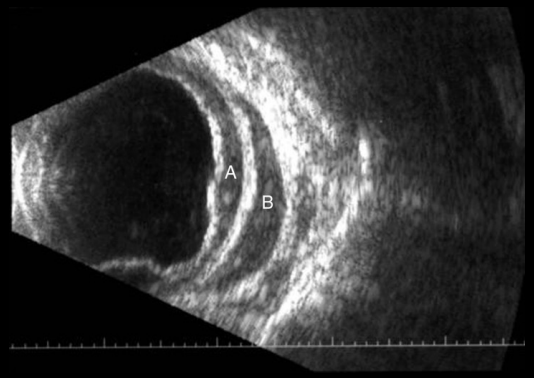
Acta Ophthalmologica Scandinavica

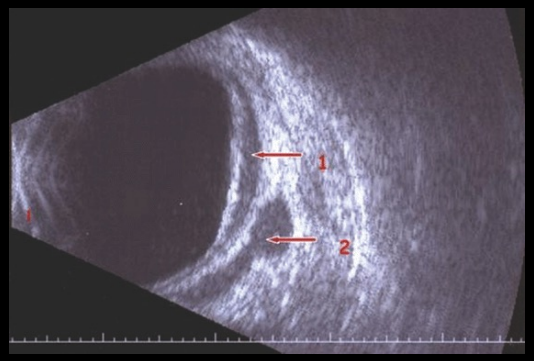
Free Access

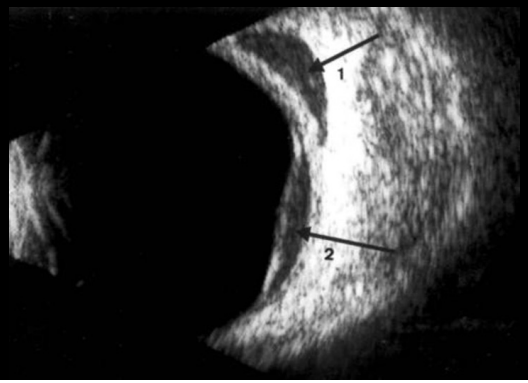
Co-existence of intraocular and orbital lymphoma

Meira Neudorfer, Ada Kessler, Irene Anteby, Dafna Goldenberg, Adiel Barak,

First published: 03 December 2004 | https://doi.org/10.1111/j.1600-0420.2004.00354.x | Citations: 12







- Three cases of concurrent choroidal and periocular involvement
- The clinical ocular presentation, echographic and Doppler characteristics of the patients were similar, although the origin of the lymphoma appeared to be different
- In two pts, the ocular mass was the only manifestation of lymphoma (presumed primary intraocular lymphoma). One pt had known systemic B cell lymphoma and the ocular tumor was considered to be a metastasis.
- The appearance of a choroidal mass was the initial presentation of ocular lymphoma. None had vitreous or systemic involvement (by whole body CT)

Case Reports > Ocul Immunol Inflamm. 1997 Dec;5(4):271-8.

doi: 10.3109/09273949709085068.

AIDS-associated intraocular lymphoma causing primary retinal vasculitis

L D Ormerod [1], J E Puklin

CLINICAL PATHOLOGICAL REVIEW | VOLUME 39, ISSUE 2, P133-140, SEPTEMBER 01, 1994

Intraocular lymphoma presenting as retinal vasculitis

Sandra M. Brown, MD • Lee M. Jampol, MD • Herbert L. Cantrill, MD

DOI: https://doi.org/10.1016/0039-6257(94)90158-9

Case report

Lymphoma masquerading as occlusive retinal vasculitis: A case study

Scott J. Sonne [a], Wen-Shi Shieh [b], Sunil K. Srivastava [c], Bradley T. Smith [b, d]

Summary

- 64 yo female presents to Wills ER with worsening redness in left eye x 2 wks
- Initial exam concerning for conjunctival lymphoma with vitreoretinal and choroidal involvement
- Conjunctival biopsy +DLBCL
- Systemic workup eventually reveals widespread lymphoma with CNS involvement
- Pt received chemotherapy and whole brain radiotherapy with improvement, with significant clinical improvement in mets. However, pt has elected for home hospice at this time.

References

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Thank You

- Dr. Armstrong
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