

# A Case of Benign Reactive Uveal Lymphoid Hyperplasia treated with Intravitreal Aflibercept

Victoria Ly<sup>1</sup>, Kinza Ahmad MD<sup>1</sup>, Eugenia White MD<sup>1</sup>, Frank LoRusso MD<sup>2</sup>, Matthew Wilson MD<sup>3</sup>, Velimir Petrovic MD<sup>2</sup>

<sup>1</sup>Harvey and Bernice Jones Eye Institute, University of Arkansas for Medical Sciences, Little Rock, AR

<sup>2</sup>Department of Ophthalmology, Central Arkansas Veterans Health System, Little Rock, AR

<sup>3</sup>Hamilton Eye Institute, University of Tennessee Health Science Center, Memphis, TN

## Introduction

- Benign reactive lymphoid hyperplasia (BRLH) of the uvea is a rare disease and is considered an ocular inflammatory pseudotumor.
- It is a reversible enlargement of lymphoid tissue thought to be the result of a chronic inflammatory response to hyperstimulating antigens<sup>1</sup>.
- There is no definitive treatment for BRLH of the uvea, but reported treatments include steroids, biologics, cryotherapy, radiotherapy, and surgical excision.
- This is the first case of uveal BRLH treated with intravitreal Aflibercept injection.

## Case Report

- Chief complaint:** 83-year-old man with presented with 2 weeks of photopsia and decreased VA OD
- Past medical history:** hypertension, hyperlipidemia, hypothyroidism, sleep apnea, sensorineural hearing loss, and a remote smoking history
- Past ocular history:** pseudophakia OU, YAG laser capsulotomy OS

## Ocular Examination

- Visual acuity:** 20/150 OD and 20/20 OS, with normal IOP and no RAPD
- Slit-lamp exam:** well-positioned IOL OU, open posterior capsule OS
- Dilated fundus exam:** discrete pinpoint black pigmentation in the periphery OD with multiple shallow choroidal elevations in the macula and peripapillary area and an inferotemporal pigmented lesion (Figure 1); unremarkable OS



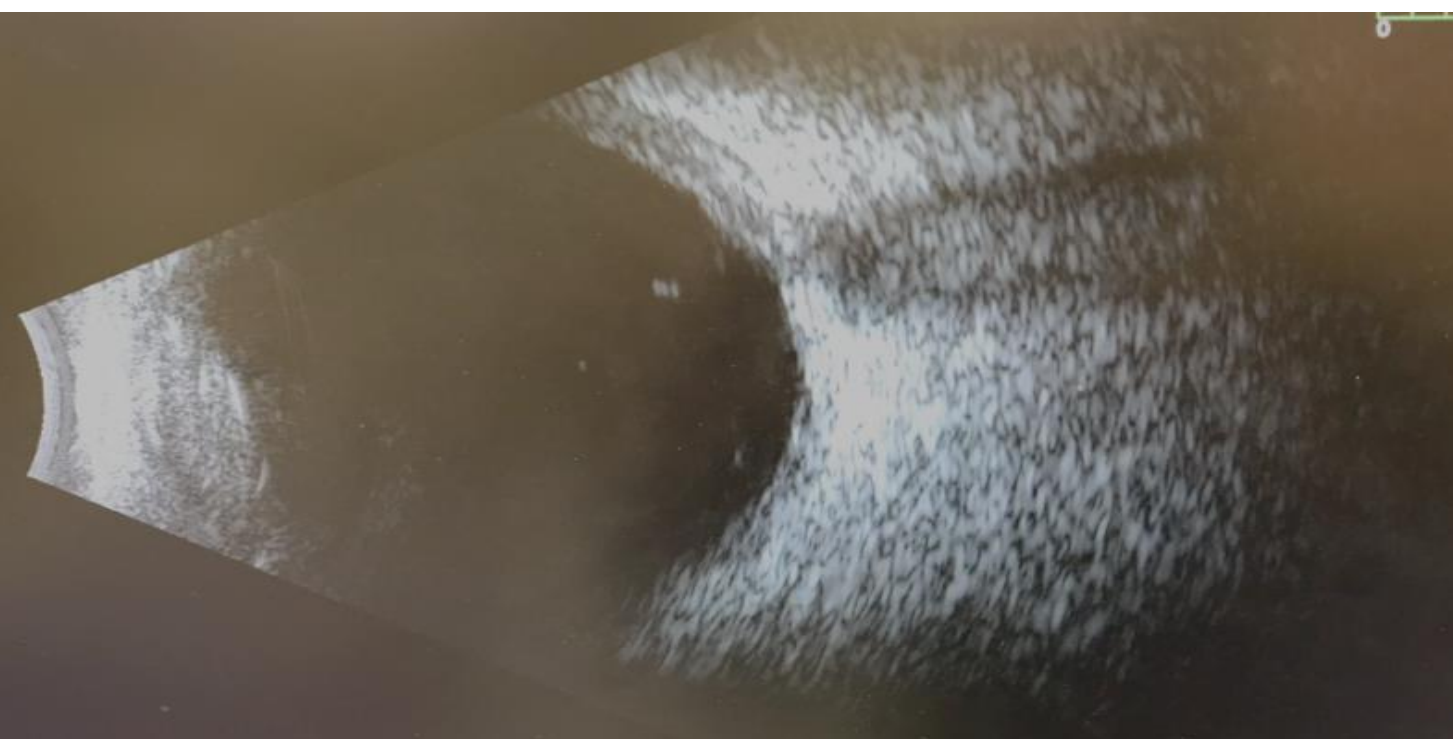
**Figure 1.** Autofluorescence of the right eye showing pinpoint areas of alternating hyper and hypo-autofluorescence in the right eye. Faint circular demarcation around the macula is visible which corresponds with the shallow choroidal elevations seen on clinical fundus exam.

## Additional Testing

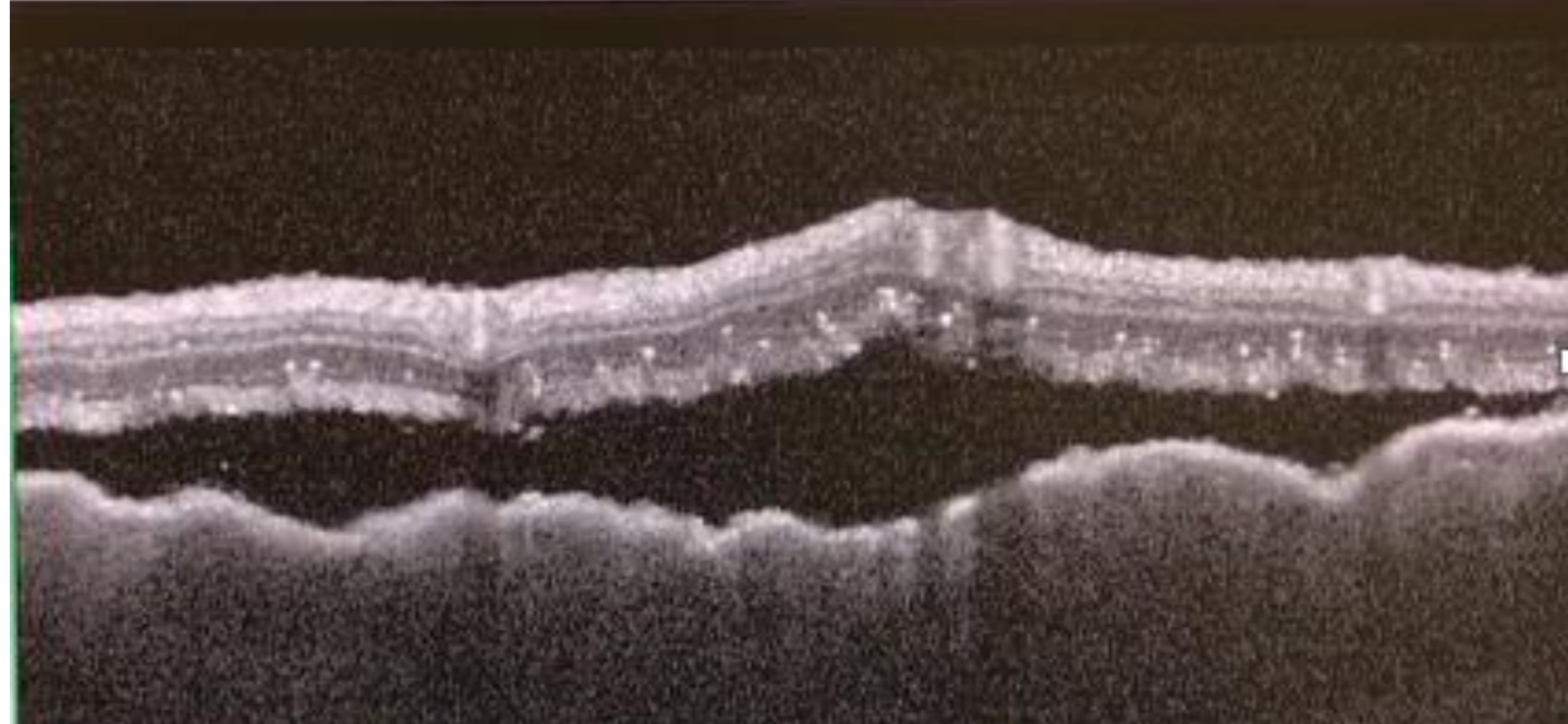
- B scan:** choroidal thickening and serous subretinal fluid OD (Figure 2)
- OCT:** choroidal thickening with exudative RD over the macula OD (Figure 3)
- Fluorescein angiogram:** pinpoint areas of hyperfluorescence and areas of hypofluorescence consistent with subretinal serous fluid OD (Figure 4)
- Diagnostic workup for infectious/inflammatory conditions:** negative
  - CBC, BMP, LFT, CRP, ACE, ESR, lysozyme, Lyme antibodies, syphilis IgG, T-spot, Bartonella antibody

## Differential Diagnoses

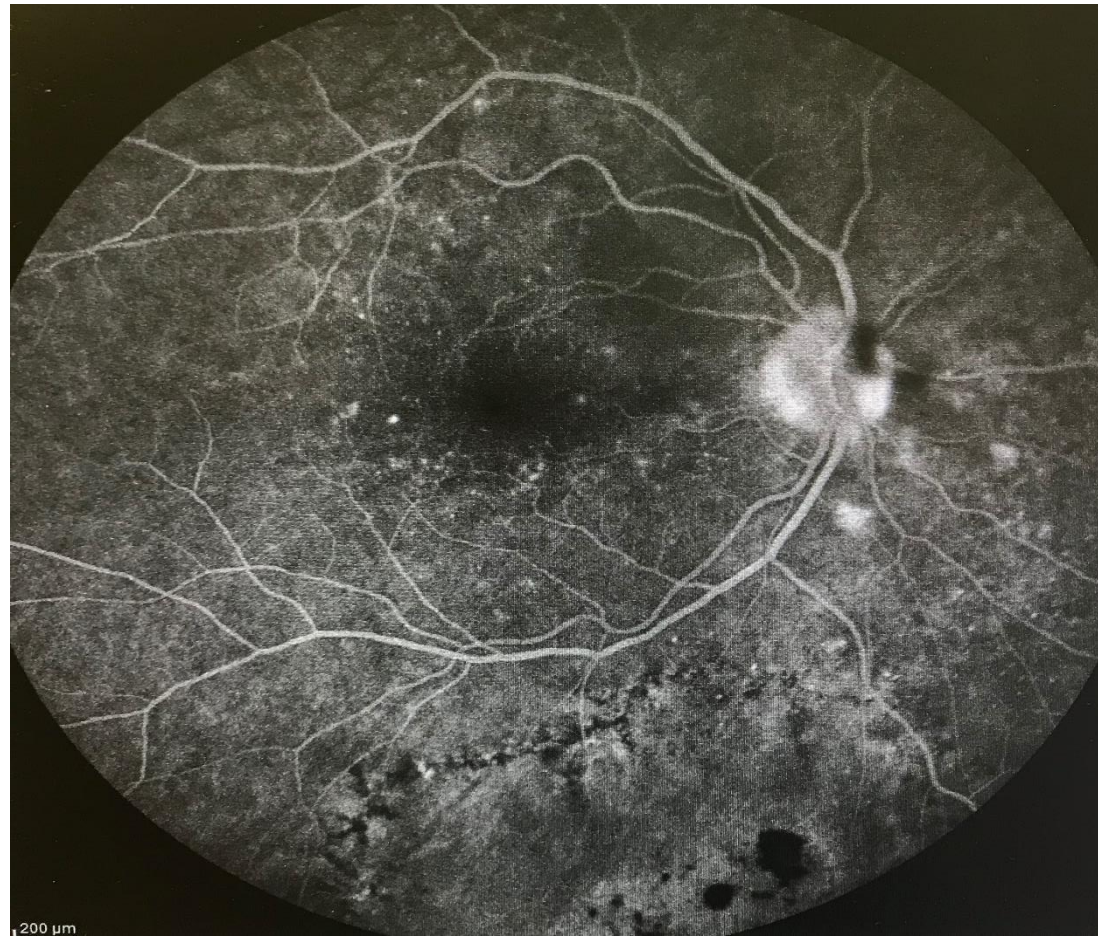
- Scleritis**
- Coat's disease**
- Vogt-Koyanagi-Harada**
- Primary Intraocular Lymphoma**
- Polypoidal choroidal vasculopathy**
- CNS lymphoma**
- Benign Reactive Uveal Lymphoid Hyperplasia**



**Figure 2.** B scan of the right eye showing choroidal thickening and serous fluid.



**Figure 3.** OCT macula of the right eye on initial presentation, demonstrating subretinal fluid with choroidal thickening and hyperreflective pinpoint areas in the outer retinal layers.



**Figure 4.** Left panel showing early phase fluorescein angiogram (FA) of the right eye at 25 seconds and right panel showing late phase FA of the right eye at 5 minutes. Multiple pinpoint areas of hyperfluorescence/staining with areas of leakage, some areas of hypofluorescence consistent with serous fluid and RPE changes. FA of the left eye was normal, not pictured here.

## Clinical Course

1-week follow-up

1<sup>st</sup> Eylea injection

2<sup>nd</sup> Eylea Injection

1-year follow-up

- VA OD: CF
- MRI brain/orbits: wnl
- Referral to ocular oncology
- Treatment: prednisolone acetate was initiated
- Initial drops changed to Durezol
- A therapeutic trial of Intravitreal Eylea (Aflibercept) 2mg/ 0.05mL- **first injection**
- 2 weeks post-injection, vision improved to 20/100 OD and serous RD over the macula decreased in size (Figure 5)
- 6 weeks post-injection, vision improved to 20/40 OD
- 8 weeks post-injection, vision decreased to 20/60 OD and patient elected for a **second injection**
- 1 month after the second injection, his vision improved to 20/40 OD and the sub-retinal fluid had resolved significantly (Figure 6)
- 2 months after the second injection, there was complete resolution of the serous retinal fluid and his vision improved to 20/20 OD with correction
- Resolution of the serous retinal fluid and improved vision has been maintained at his follow-up 1-year out from his initial presentation at 20/25- OD (Figure 7)

## Diagnosis and Discussion

### Diagnosis

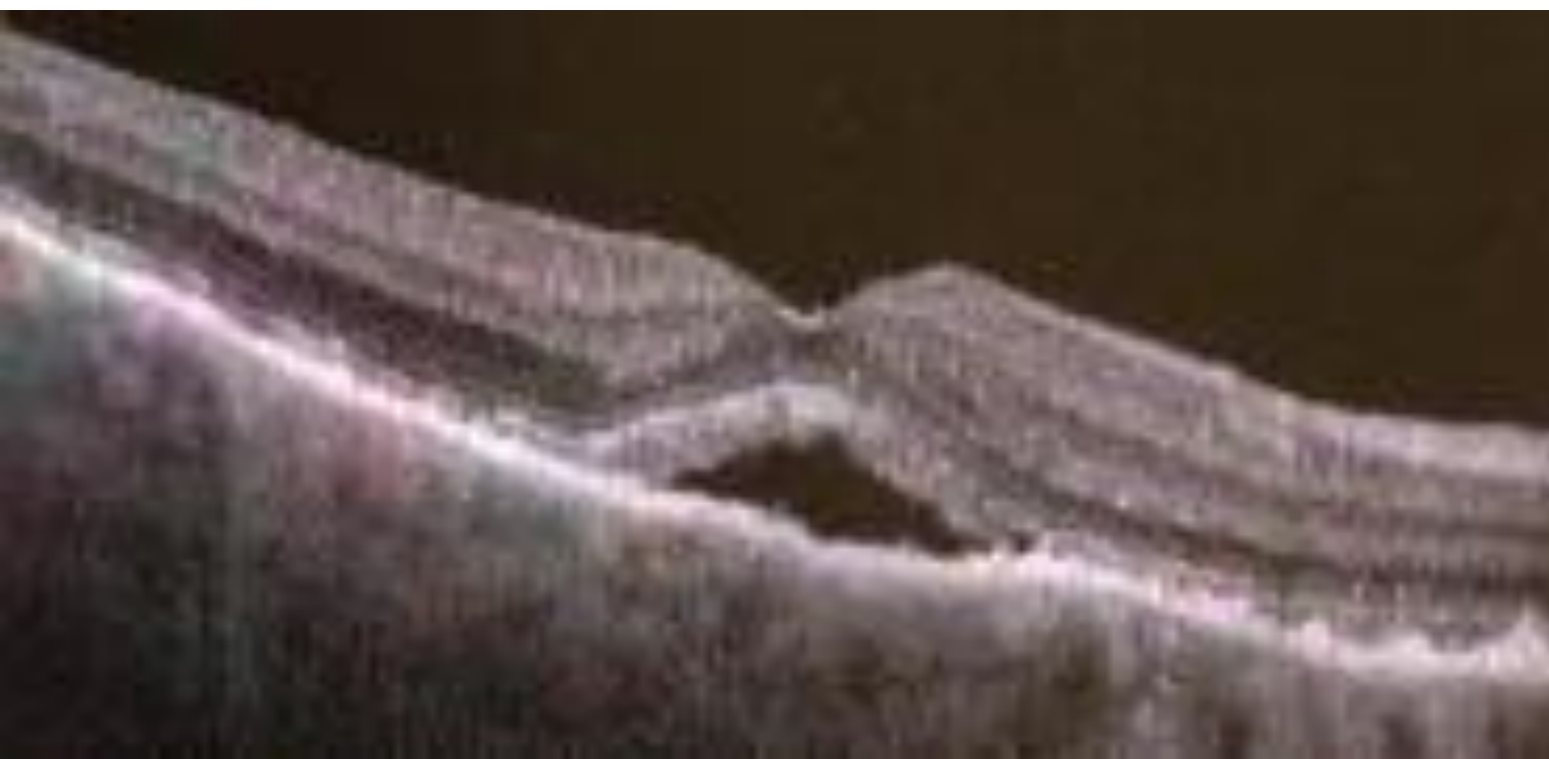
- Ocular oncologist (MW) concluded that the B scan, clinical findings, and negative workup were all consistent with B cell proliferation of the choroid.

### Discussion

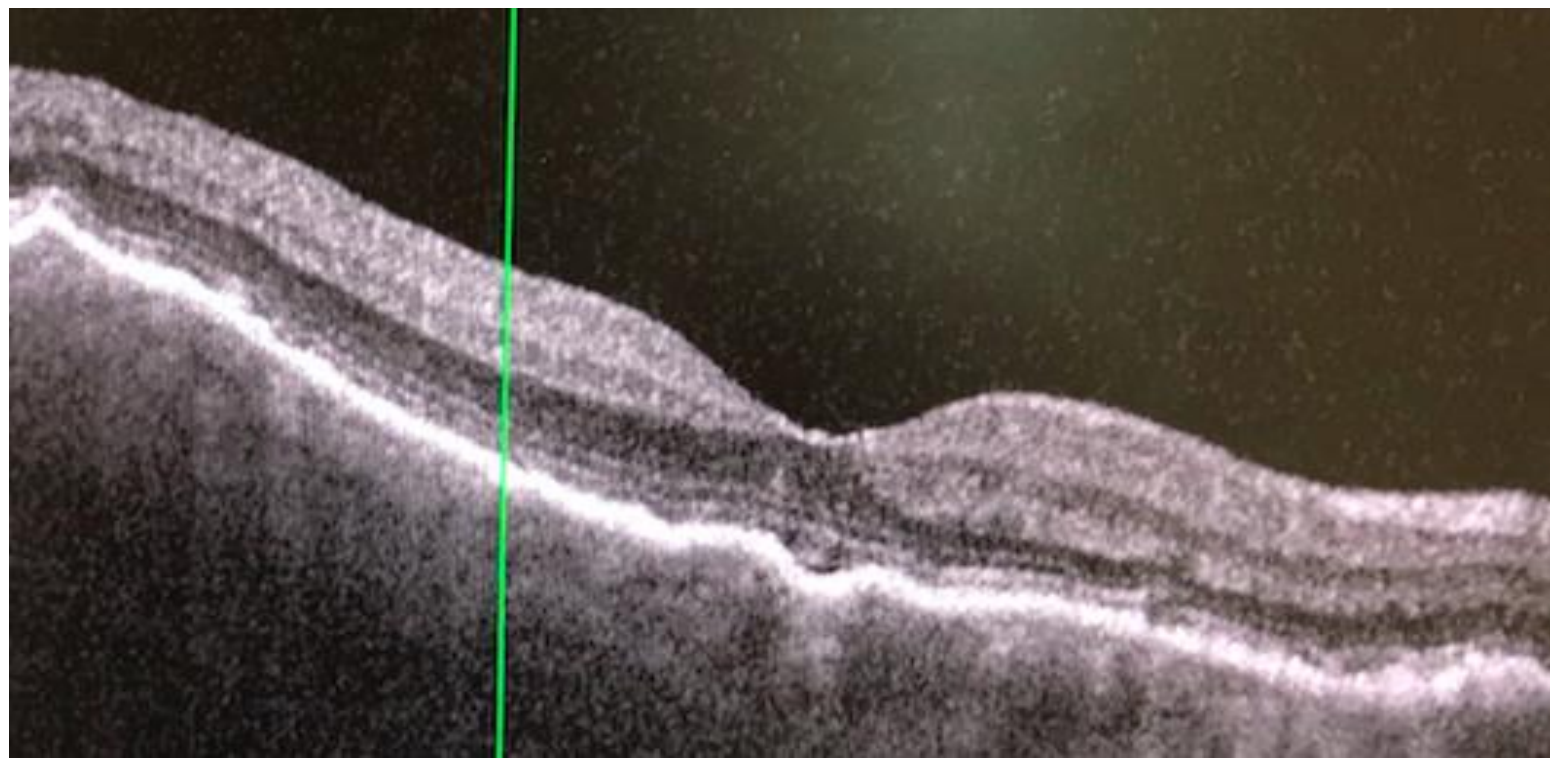
- Diagnosis: Benign reactive uveal lymphoid hyperplasia**
- Aflibercept is a soluble decoy receptor that binds VEGF-A, VEGF-B, and PlGF and prevents the activation of VEGF receptors, which promotes angiogenesis.
- It is an FDA-approved treatment for wet ARMD, macular edema from RVO, DME in patients with DR.<sup>2</sup>
- VEGF has been implicated in pathologic vascular remodeling and is also a tumor growth factor expressed in various tumors, including lymphoma, and correlates with tumor angiogenesis and progressive disease.<sup>3,4,5</sup>
- We hypothesized that Aflibercept would inhibit proliferation of lymphoid tumor cells.
- Prevention of VEGF-driven angiogenesis by Aflibercept would limit the macular edema and reduce the exudative retinopathy and retinal detachment.



**Figure 5.** OCT macula of the right eye 2 weeks after the first Eylea injection showing improvement in subretinal fluid.



**Figure 6.** OCT macula of the right eye 4 weeks after the second Eylea injection showing significant improvement in the subretinal fluid.



**Figure 7.** OCT macula of the right eye at the most recent follow up visit 1 year after initial presentation with maintained resolution of subretinal fluid.

## References

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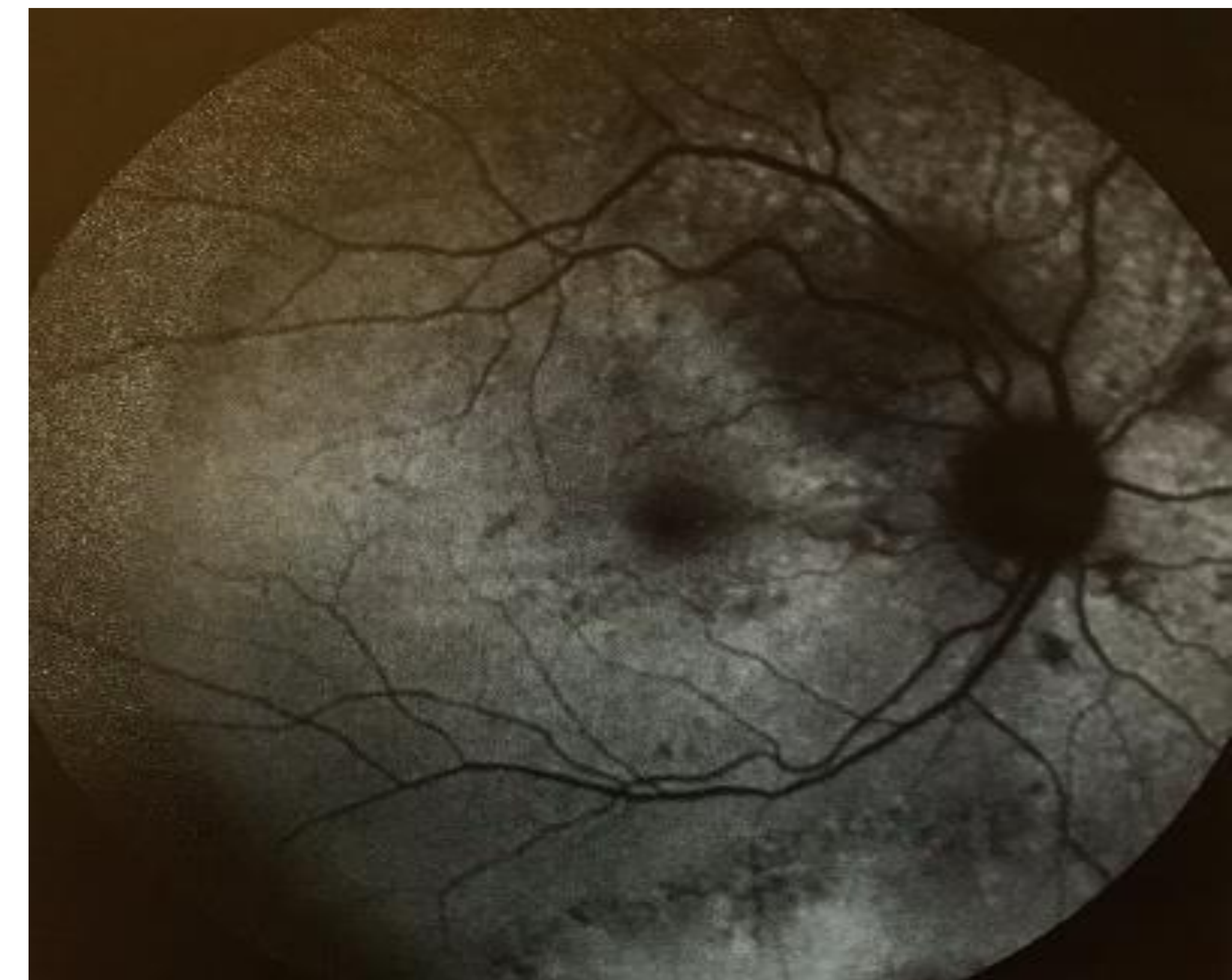


# Case Presentation

- An 83-year-old man presented to the clinic with two weeks of photopsia and decreased vision in his right eye.
- **Past medical history**
  - hypertension
  - hyperlipidemia
  - hypothyroidism
  - sleep apnea
  - sensorineural hearing loss
  - remote smoking history
- **Past ocular history**
  - bilateral pseudophakia
  - YAG laser capsulotomy in the left eye
- **Initial exam findings**
  - **Visual acuity:** 20/150 OD, no change with pinhole; 20/20 OS
  - **Pupils:** reactive to light, with RAPD
  - **Intraocular pressure:** normal
    - **Anterior segment exam:**
      - well-positioned IOL in each eye
      - open posterior capsule OS

## – Dilated fundus exam:

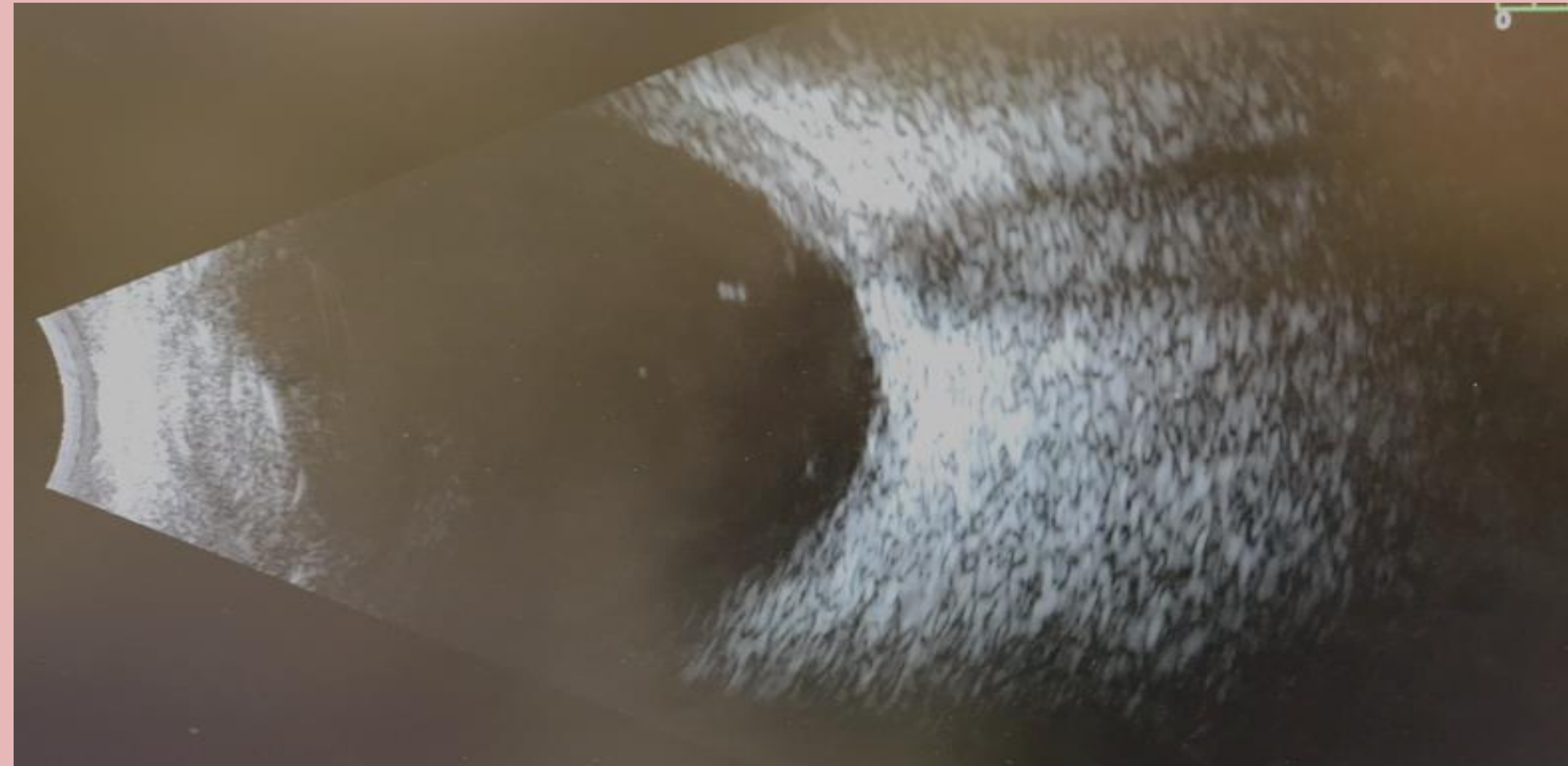
- *Discrete pinpoint black pigmentation in the periphery of the right eye with multiple shallow choroidal elevations in the macula that correspond with circular demarcation around the macula on autofluorescence*
- *Peripapillary and inferotemporal pigmented lesions*



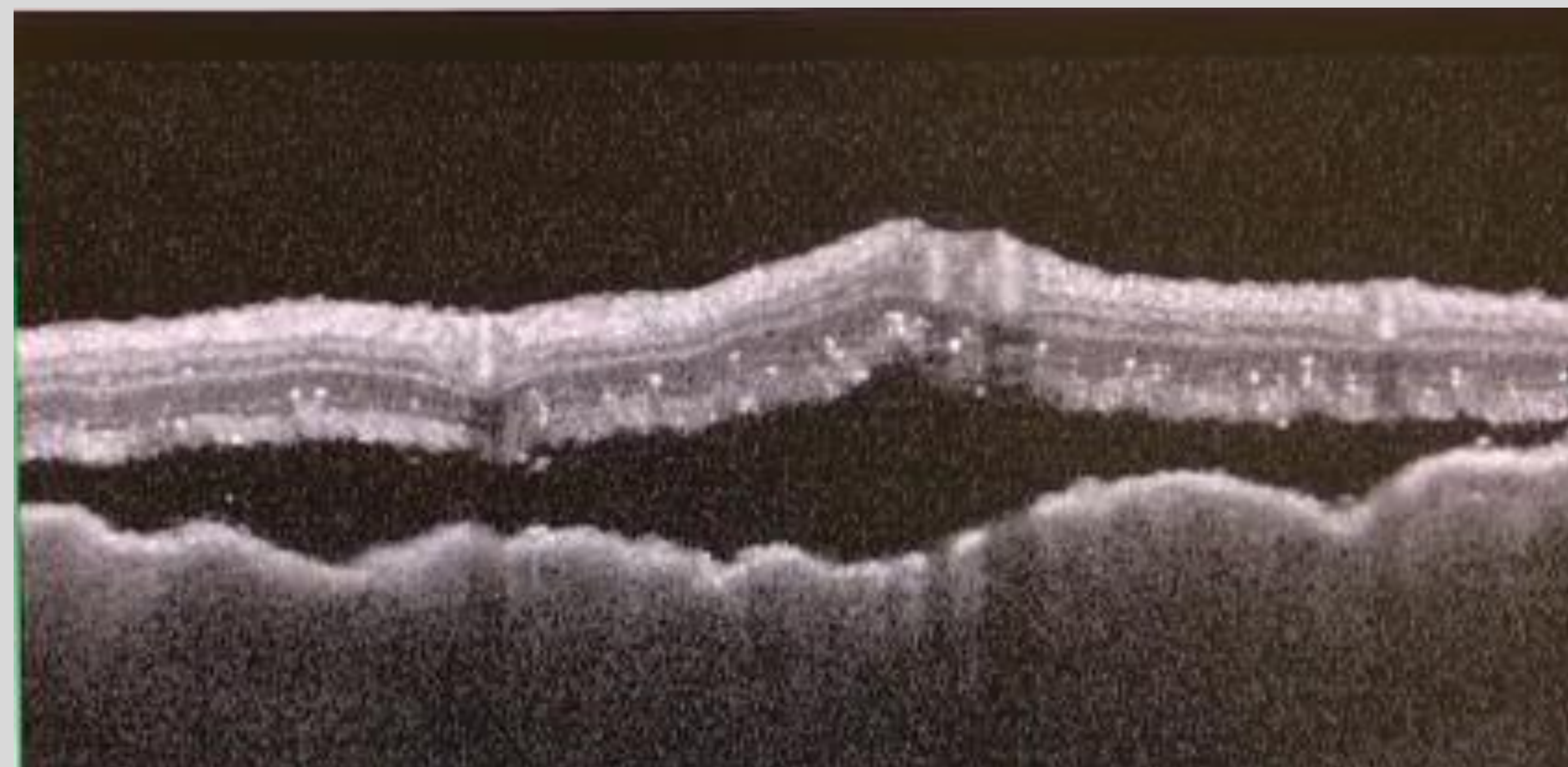


# Diagnostic Testing

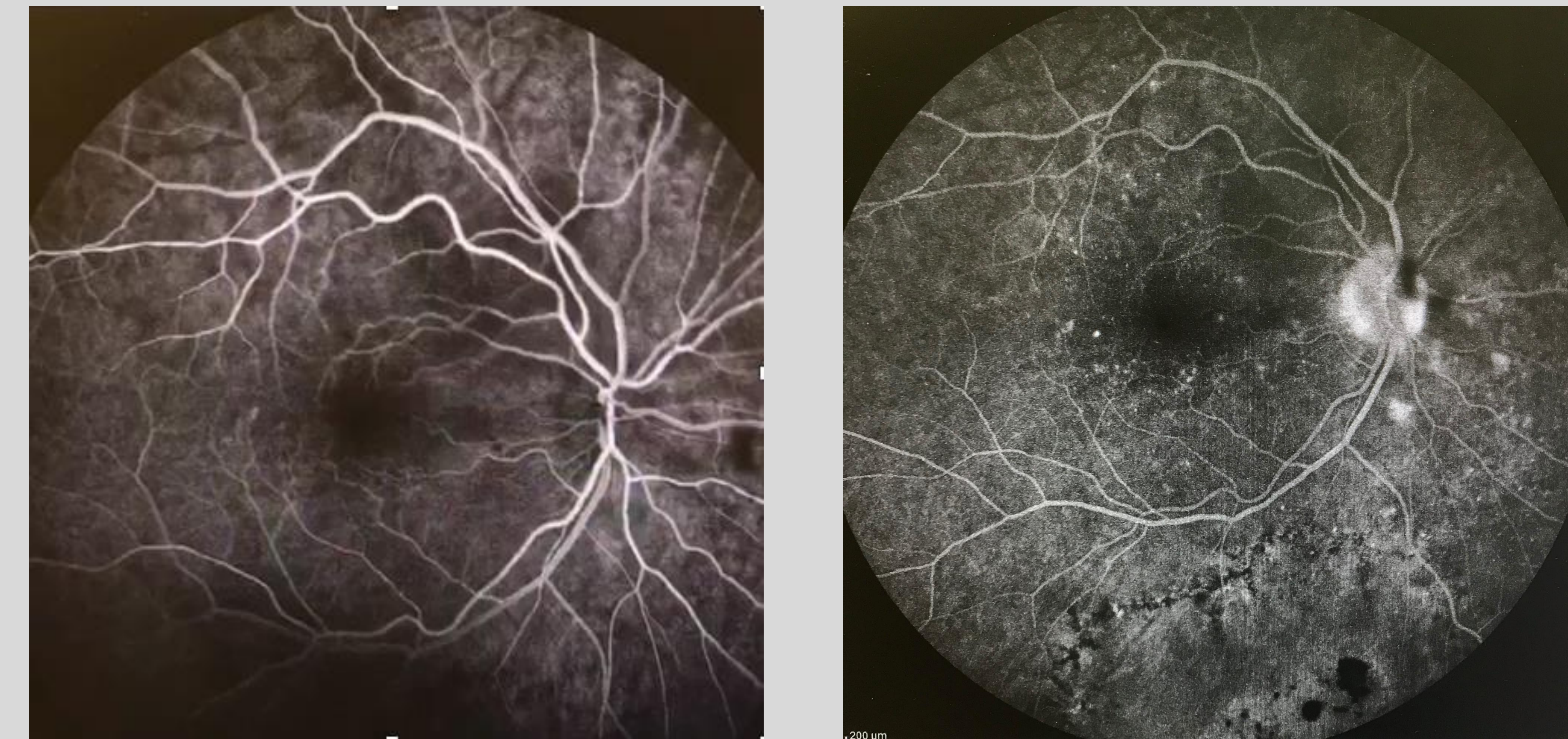
- **B scan of the right eye** revealed choroidal thickening and serous fluid.



- **OCT of the macula of the right eye** demonstrated subretinal fluid with choroidal thickening and hyperreflective pinpoint areas in the outer retinal layers.



- **Fluorescein angiogram of the right eye** at 25 seconds (left) and 5 minutes (right) showed pinpoint areas of hyper-fluorescence with areas of leakage and areas of hypo-fluorescence consistent with serous fluid and RPE changes.



- CBC, BMP, LFT, CRP, ACE, sedimentation rate, lysozyme, Lyme antibodies, syphilis IgG, T-SPOT, and Bartonella testing were all negative.



# Clinical Course and Treatment

1-week  
follow-up

- VA OD: CF
- MRI brain/orbits: wnl
- Referral to ocular oncology
- Treatment: prednisolone acetate was initiated

1<sup>st</sup> Eylea  
injection

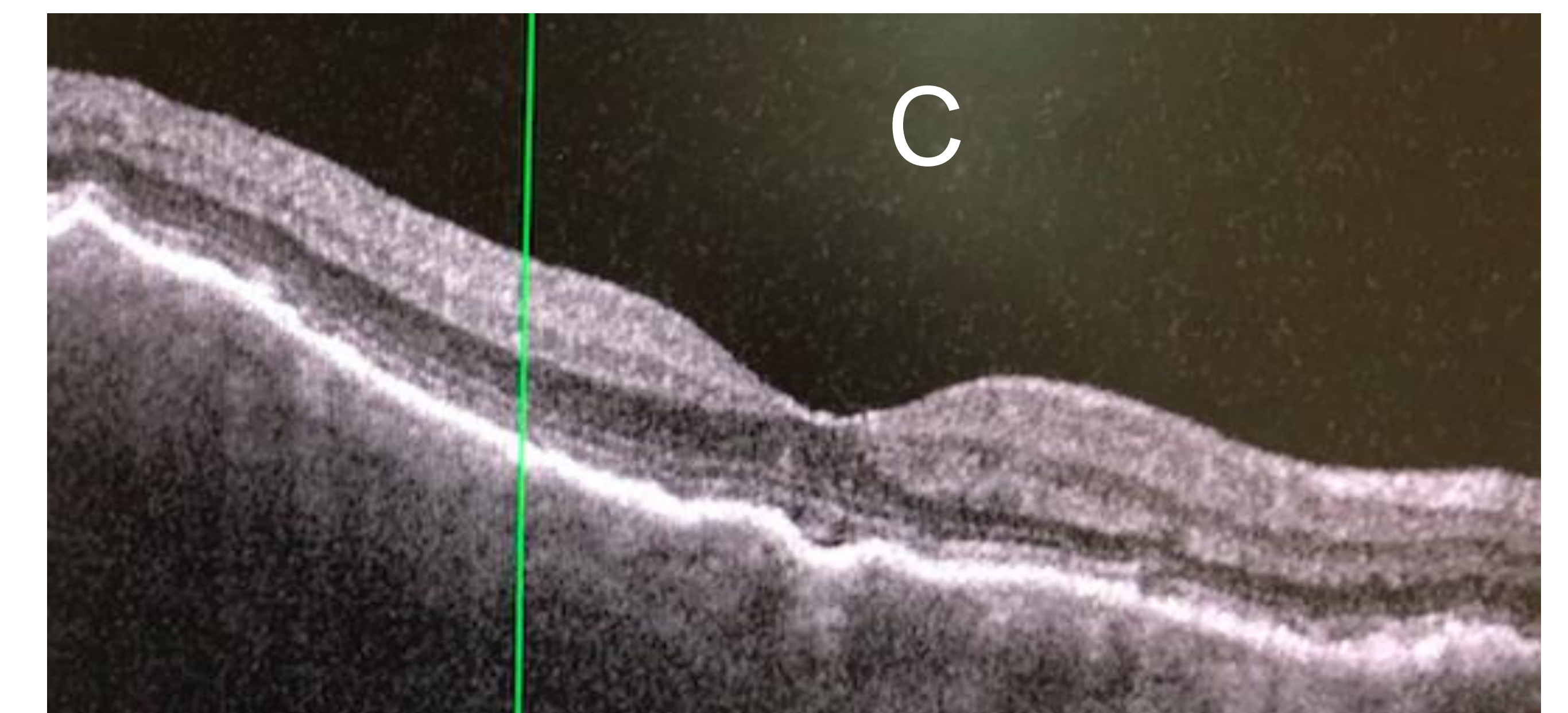
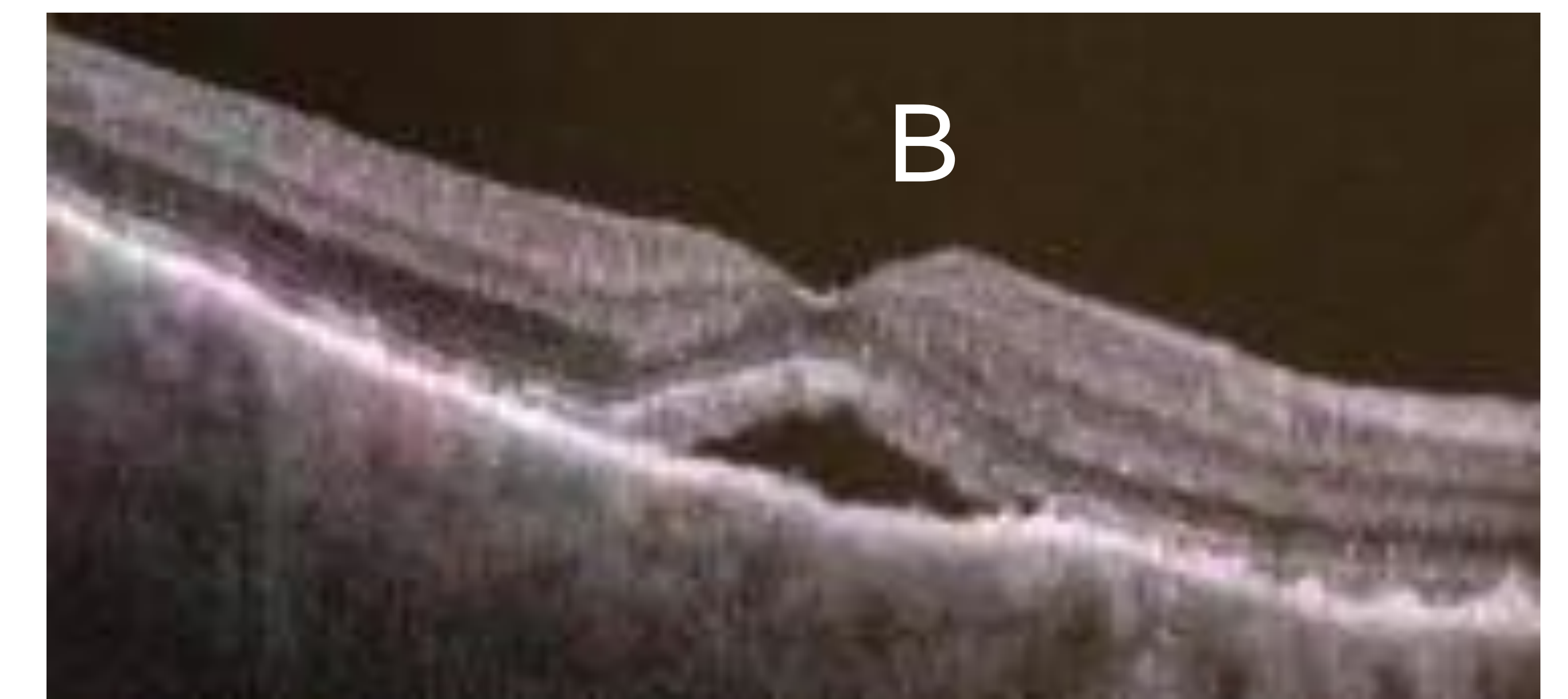
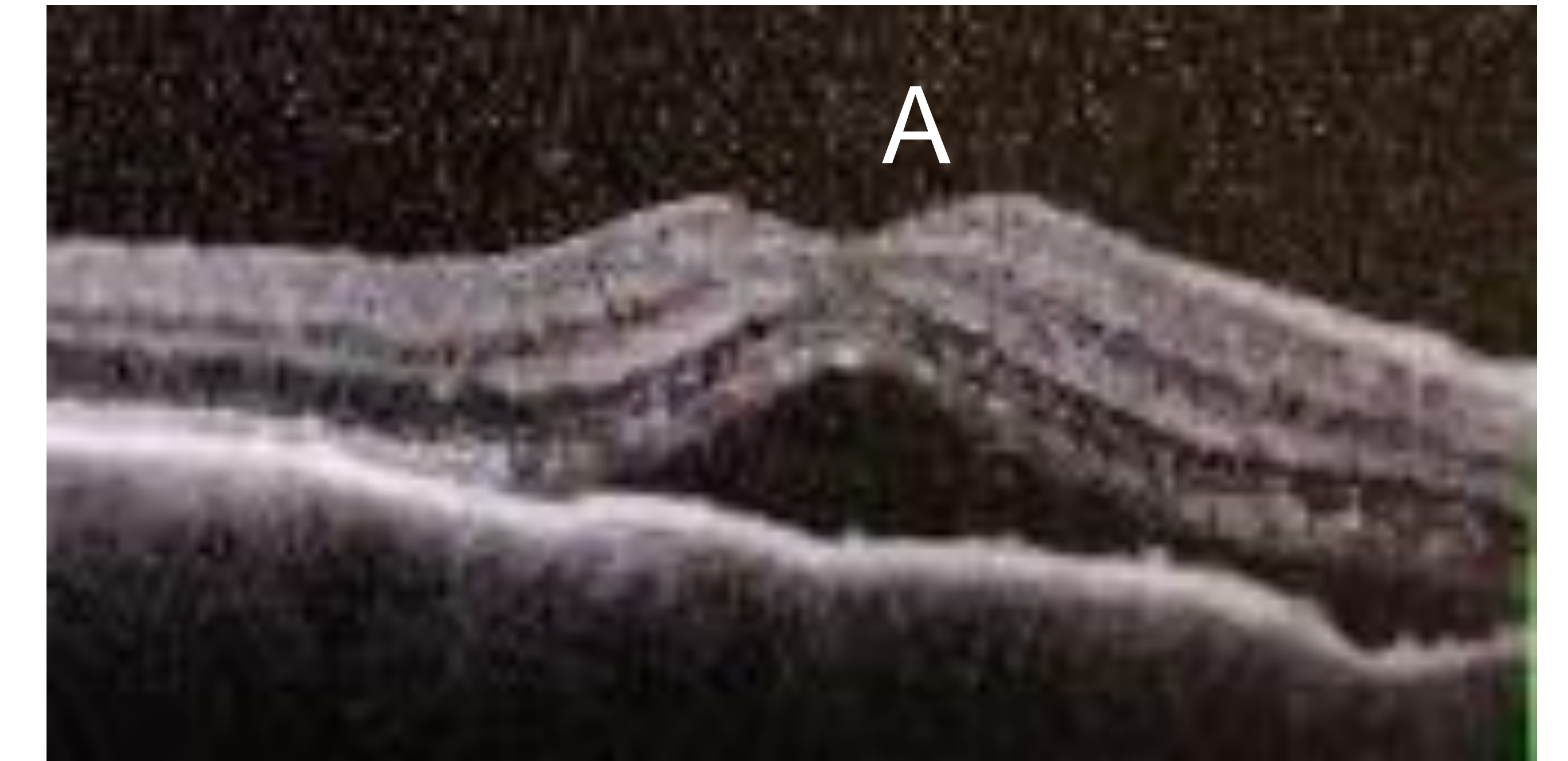
- Initial drops changed to Durezol
- A therapeutic trial of Intravitreal Eylea (Aflibercept) 2mg/ 0.05mL- **first injection**
- 2 weeks post-injection, vision improved to 20/100 OD and serous RD over the macula decreased in size (Figure A)
- 6 weeks post-injection, vision improved to 20/40 OD

2<sup>nd</sup> Eylea  
Injection

- 8 weeks post-injection, vision decreased to 20/60 OD and patient elected for a **second injection**
- 1 month after the second injection, his vision improved to 20/40 OD and the sub-retinal fluid had resolved significantly (Figure B)
- 2 months after the second injection, there was complete resolution of the serous retinal fluid and his vision improved to 20/20 OD with correction

1- year  
follow-up

- Resolution of the serous retinal fluid and improved vision has been maintained at his follow-up 1-year out from his initial presentation at 20/25- OD (Figure C)





# Discussion- Benign Reactive Lymphoid Hyperplasia of the Uvea

- **Etiology:** ocular inflammatory pseudotumor
- **Epidemiology:** rare; unilateral; affects otherwise healthy persons; mean age = 55 yrs
- **Pathophysiology:** reversible enlargement of lymphoid tissue as a result of a chronic inflammatory response to irritating or hyperstimulating antigens
- **Symptoms:**
  - Most common: decrease in vision with indolent clinical course
  - Proptosis secondary to extrascleral involvement
  - Acute angle closure glaucoma due to ciliary body, iris, or trabecular meshwork involvement
- **Exam findings:**
  - Creamy yellow lesions on the choroid with choroidal thickening and serous retinal detachment
  - Extension into extraocular tissue is also common
- **Differential diagnoses:** primary intraocular lymphoma, diffuse malignant melanoma, metastatic carcinoma, CNS lymphoma, systemic lymphoma, posterior scleritis, sarcoidosis, and infection
- **Diagnostic workup:**
  - Ultrasound scan, computerized tomography, and magnetic resonance imaging can help detect disease and rule out a metastatic lesion
  - Accurate diagnosis often requires a biopsy
    - **Histopathology:** dense uveal infiltrates of mature lymphocytes that form well-defined reactive lymphoid follicles with germinal centers
    - The diagnosis of in this case was made after evaluation by an ocular oncologist



# Discussion- Aflibercept

- There is no definitive treatment for BRLH.
- To our knowledge, we report the first case of BRLH of the uvea treated with Aflibercept.
- Aflibercept is a soluble decoy receptor that binds VEGF-A, VEGF-B, and PlGF to prevent the activation of VEGF receptors.
- VEGF receptors promote angiogenesis. Other possible functions include:
  - upregulate pathologic angiogenesis in cancer and ocular vascular diseases
  - pathological vascular remodeling
  - inhibit proliferation of lymphoid tumor cells
- Kinoshita et al found that blocking VEGF could prevent the onset and tumor growth of ocular adnexal lymphoma.
- Oh et al reported a case of BRLH of the conjunctiva successfully treated with bevacizumab injected subconjunctivally, with an assumption that it would alter the ocular surface blood vessels and lymphatic vessel formation.
- Our hypothesis for the treatment of BRLH of the uvea using intravitreal Aflibercept:
  1. Aflibercept would inhibit proliferation of lymphoid tumor cells
  2. Aflibercept would also limit the macular edema and exudates caused by leaky, fragile pathologic vessels and reduce the exudative retinopathy and retinal detachment.