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Clinical Crossroads: Diabetic Retinopathy

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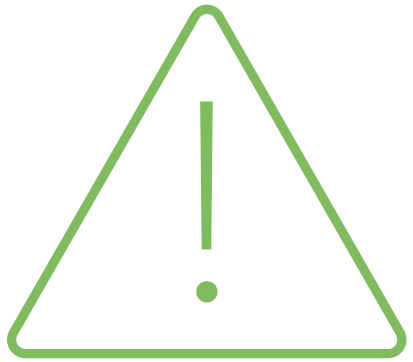
Financial Disclosures

Ashleigh Levison, MD has the following financial relationships to disclose



Name of Commercial Interest(s)	Nature of Relationship	What was Received
Abbvie, an Allergan Company	*Advisory Board*	Compensation

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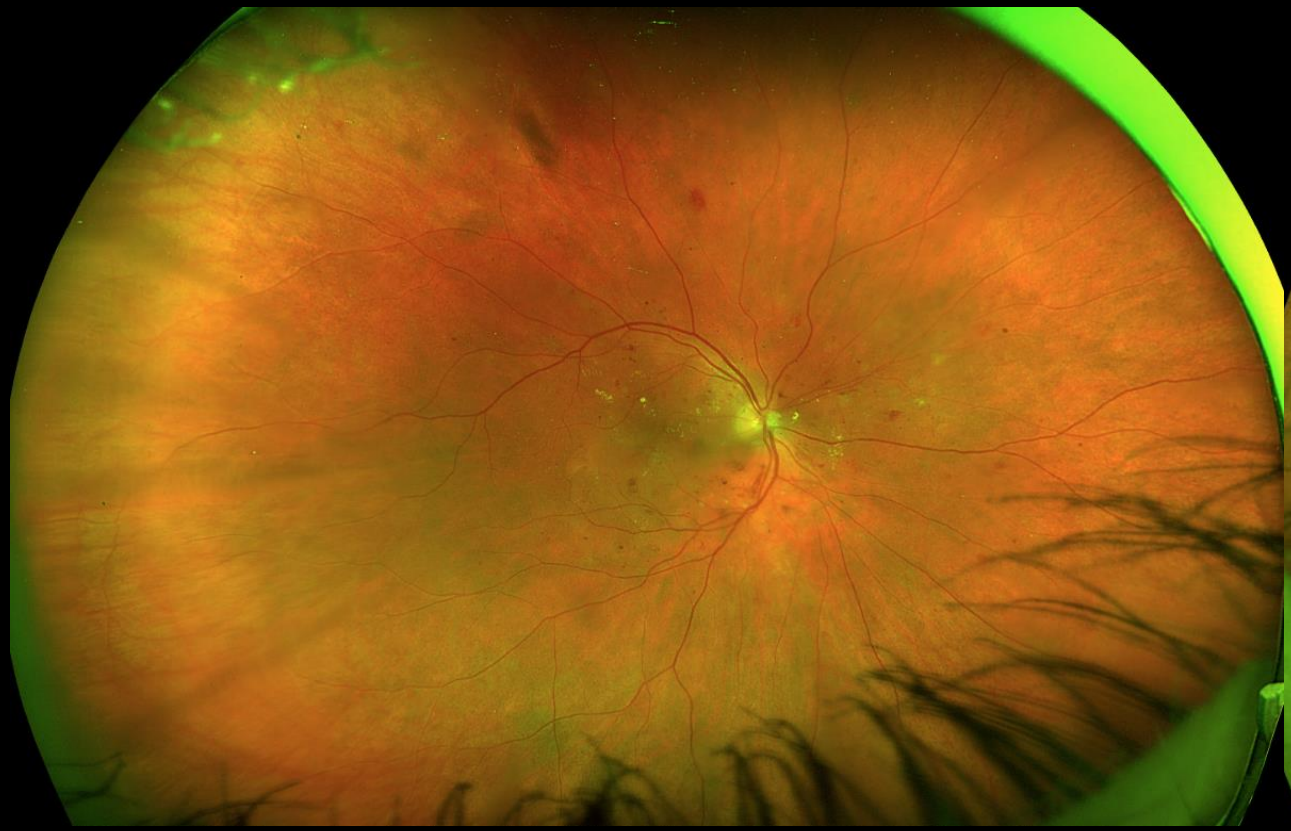
Introduction and epidemiology

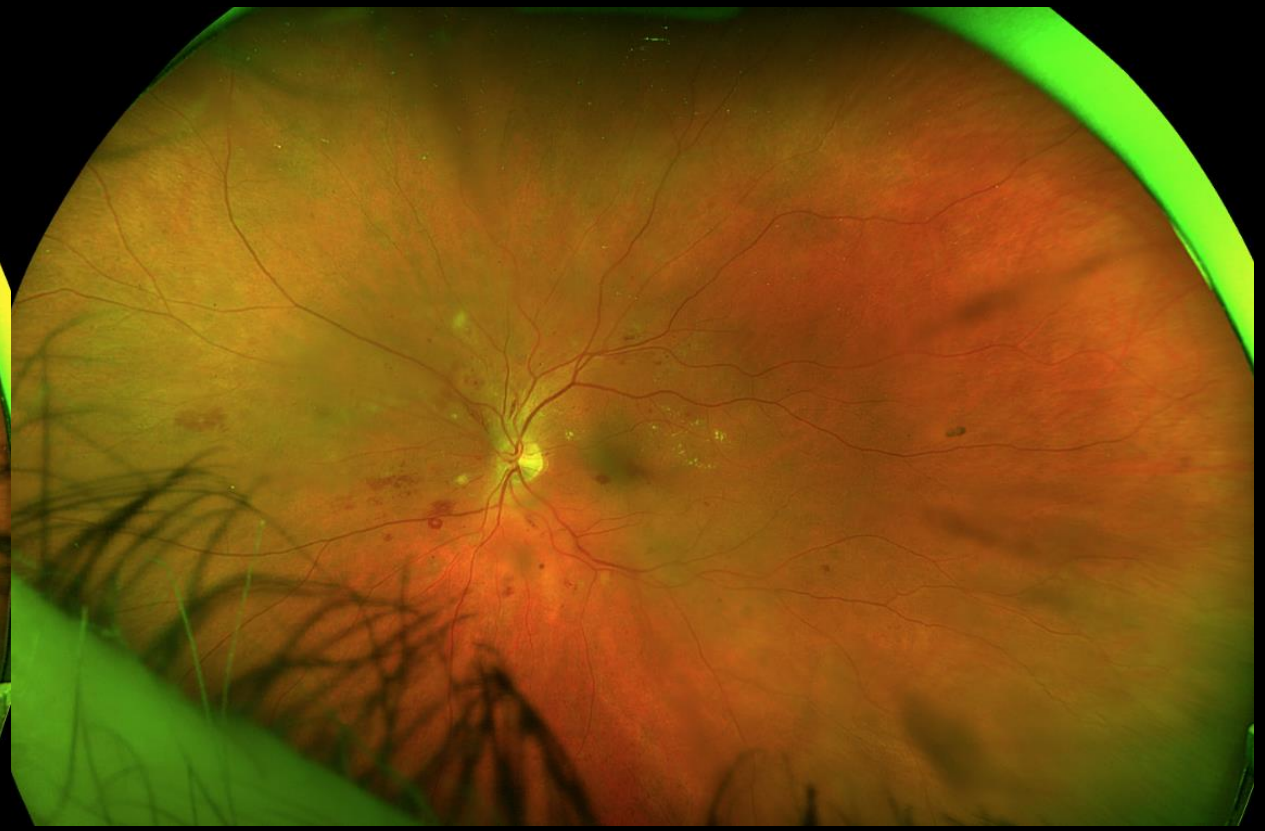
- Diabetic retinopathy (DR) accounts for ~5% of all cases of blindness worldwide
- However, in developed/industrialized nations, DR is the leading cause of blindness
- Duration of diabetes and level of glycemic control have the largest impacts on the risk and severity of developing retinopathy
  - After 20+ years of disease, 99% of T1DM and 60% of T2DM will have DR
  - About half of those with DR will have proliferative disease

Clinical Case- Part I

- 55yo man with type 2 diabetes mellitus is referred to retina clinic for evaluation and management of diabetic eye disease. T2DM was diagnosed 20 years ago, and he has poor glucose control, with recent A1c measurements > 9.0 (normal range < 5.7). He has no vision symptoms or complaints. On exam, his VA is 20/20 OU, IOP within normal limits, and the anterior segment shows trace nuclear sclerosis OU but is otherwise unremarkable. Posterior segment and imaging are as follows.

Imaging





What would be your next step in the evaluation and management of this patient?

Decision point

What would be your next step in the evaluation and management of this patient?

1. Observe for now, counsel the patient on the importance of better glucose control, and have them return to clinic in 6 mo
2. Obtain a fluorescein angiogram in clinic
3. Initiate a trial of intravitreal anti-VEGF injections in one eye

Click here to learn more about NPDR

Non-proliferative diabetic retinopathy (NPDR)

- DR first manifests as **intraretinal** **vascular** changes
  - Microaneurysms (MA)
  - Intra-retinal or dot-blot hemorrhages (IRH or DBH)
  - Venous beading
  - Intraretinal microvascular abnormalities (IRMA)
- These changes in turn cause vision loss through 2 mechanisms
  - Poor blood flow → capillary non-perfusion and macular ischemia
  - Diabetic macular edema (DME)

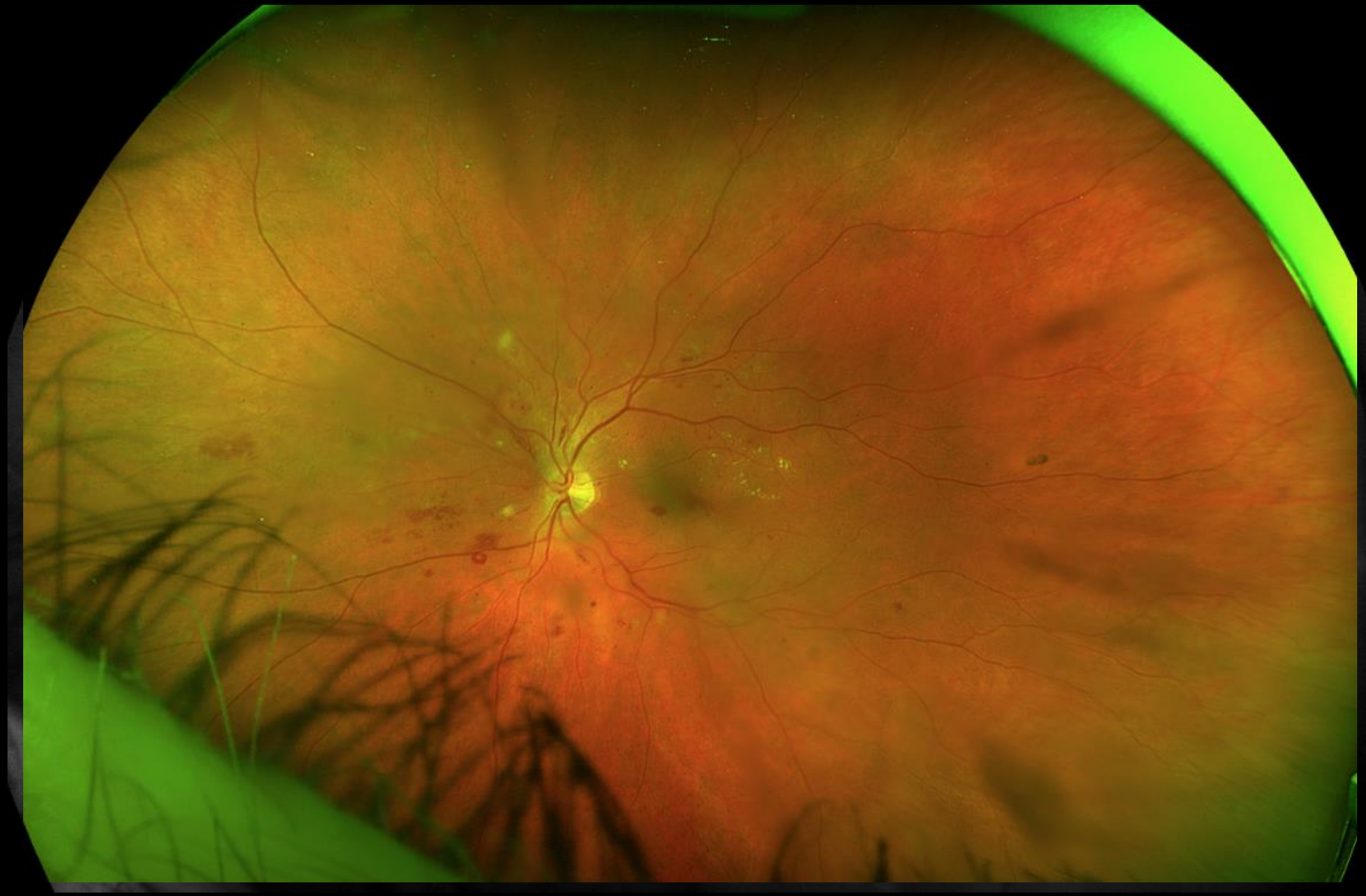
Categorizing NPDR

- Mild NPDR = only scattered MAs in the retina, no other anomalies
- Moderate NPDR = more abnormalities than mild NPDR but not reaching the level of severe NPDR
- Severe NPDR = “4-2-1” rule, meaning any of the following criteria…
  - 4 quadrants of MAs
  - 2 quadrants of venous beading
  - 1 quadrant with IRMA

- Degree of retinopathy and presence of DME determines how closely to follow the patient

Back to our patient…

Imaging



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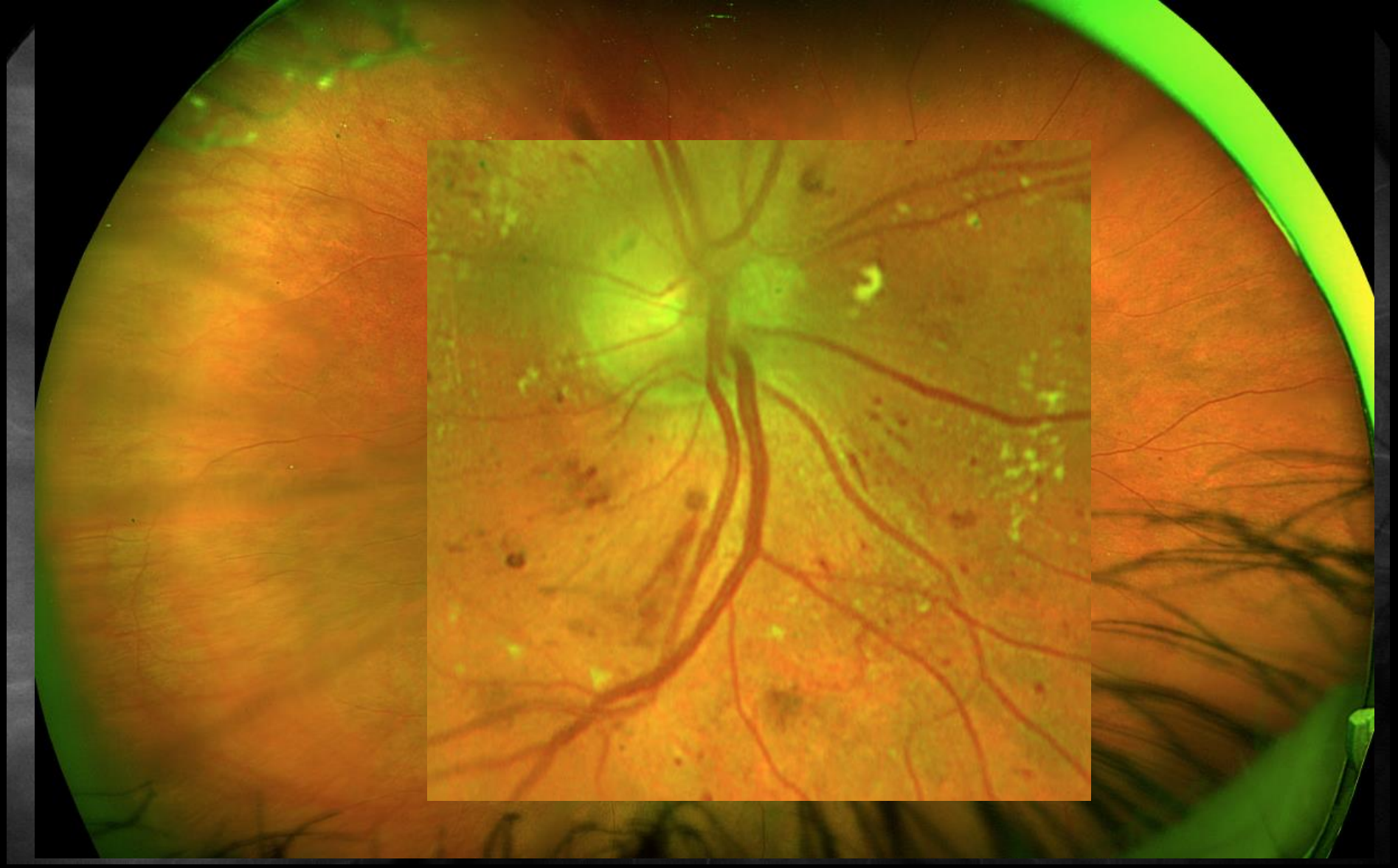
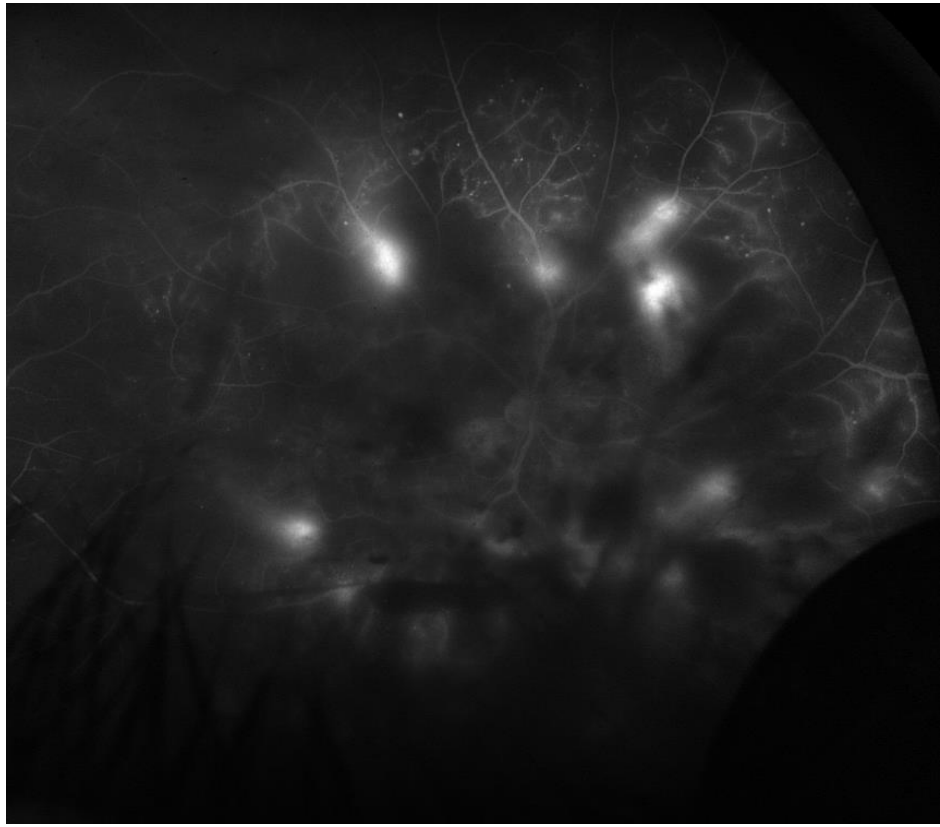


Click here to learn more about fluorescein angiography

Recognizing the beginning of more advanced proliferative diabetic retinopathy, you decide to follow more closely and have the patient return in 4 months

Fluorescein angiography

- Light-sensitive, light-emitting dye that illuminates the path of blood flow through the retina
- Dark hypofluorescent findings
  - Blockage from vitreous hemorrhage
  - Areas of ischemia and capillary non-perfusion
- Bright hyperfluorescent findings
  - Staining of microvascular anomalies (MAs)
  - Leakage from vascular incompetence → highlights areas of edema
  - Leakage from neovascularization



Click here to return to our case

Intravitreal injections in DR

- **V**ascular **E**ndothelial **G**rowth **F**actor (VEGF) → neovascularization
- **Anti-VEGF** compounds reverse the pathogenic effects of VEGF in diabetic retinopathy and other retinal conditions
- 2 main uses of anti-VEGF injections in DR
  - To treat visually significant DME (reduces leakiness of blood vessels)
    - If there is significant fovea-involving DME and/or decrease in VA 20/30 or worse
  - To induce regression of neovascularization and treat proliferative DR
- Complications: endophthalmitis, retinal detachment (including "crunch" phenomenon), hemorrhage, inflammation
- Requires consistent treatment; can regress if patient misses appts

Click here if the use of anti-VEGF was premature

Click here if anti-VEGF was used appropriately

Clinical Case- Part II

- The patient returns 6 months later as instructed and reports increasing floaters and decreased vision in the right eye beginning approximately 3 months ago; he did not call in to the office at the time because he knew he had this scheduled follow-up coming up. VA is now 20/40 OD, 20/20 OS with normal IOP OU. The anterior segment remains unchanged from previous exam but the posterior segment of the affected right eye appears as follows.

Click for posterior segment exam/images

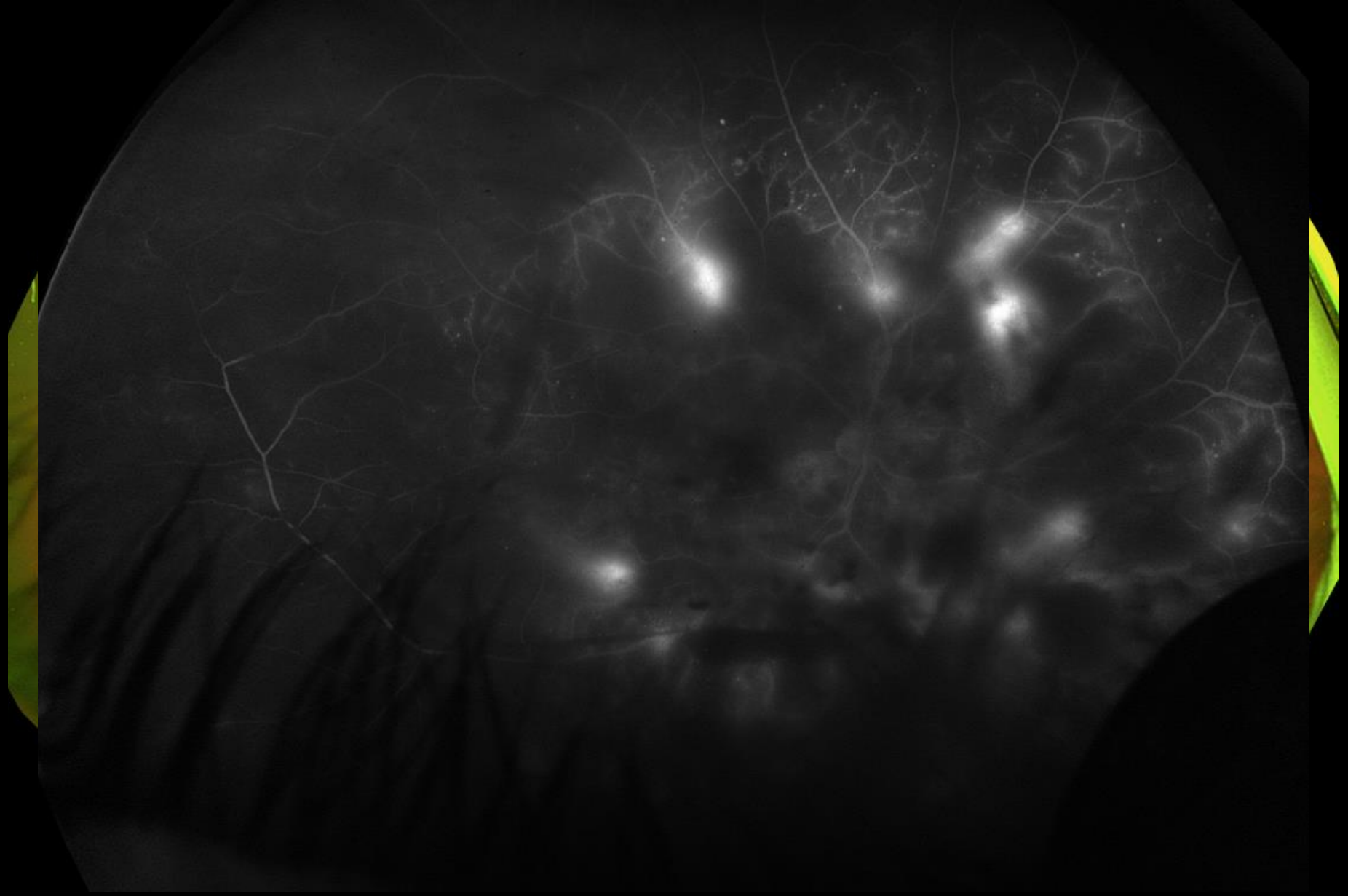
Clinical Case- Part II

- The patient returns 4 months later as instructed and reports recent onset increasing floaters and decreased vision in the right eye. VA is now 20/40 OD, 20/20 OS with normal IOP OU. The anterior segment remains unchanged from previous exam but the posterior segment of the affected right eye appears as follows.

Click for posterior segment exam/images

Clinical Case- Part II

- You start monthly injections in the left eye, which are initially uneventful. The patient notices no improvement or worsening of vision and continues to see well. Several months into this treatment course however, you examine the left eye and notice a small, asymptomatic macula-on rhegmatogenous retinal detachment in the area of your injection site. You laser the detachment but decide to stop further injections for now. You also decide to look more closely and thoroughly at the right eye (which you have not been treating) and find…



Click here to learn more about fluorescein angiography

Decision point

What would be your next step in the evaluation and management of this patient?

1. The patient has high-risk proliferative diabetic retinopathy; start **serial anti-VEGF injections** in the affected eye
2. The patient has high-risk proliferative diabetic retinopathy and there is still a good view of the retina; perform **panretinal photocoagulation** in the affected eye

Click here to learn more about PDR

Proliferative diabetic retinopathy (PDR)

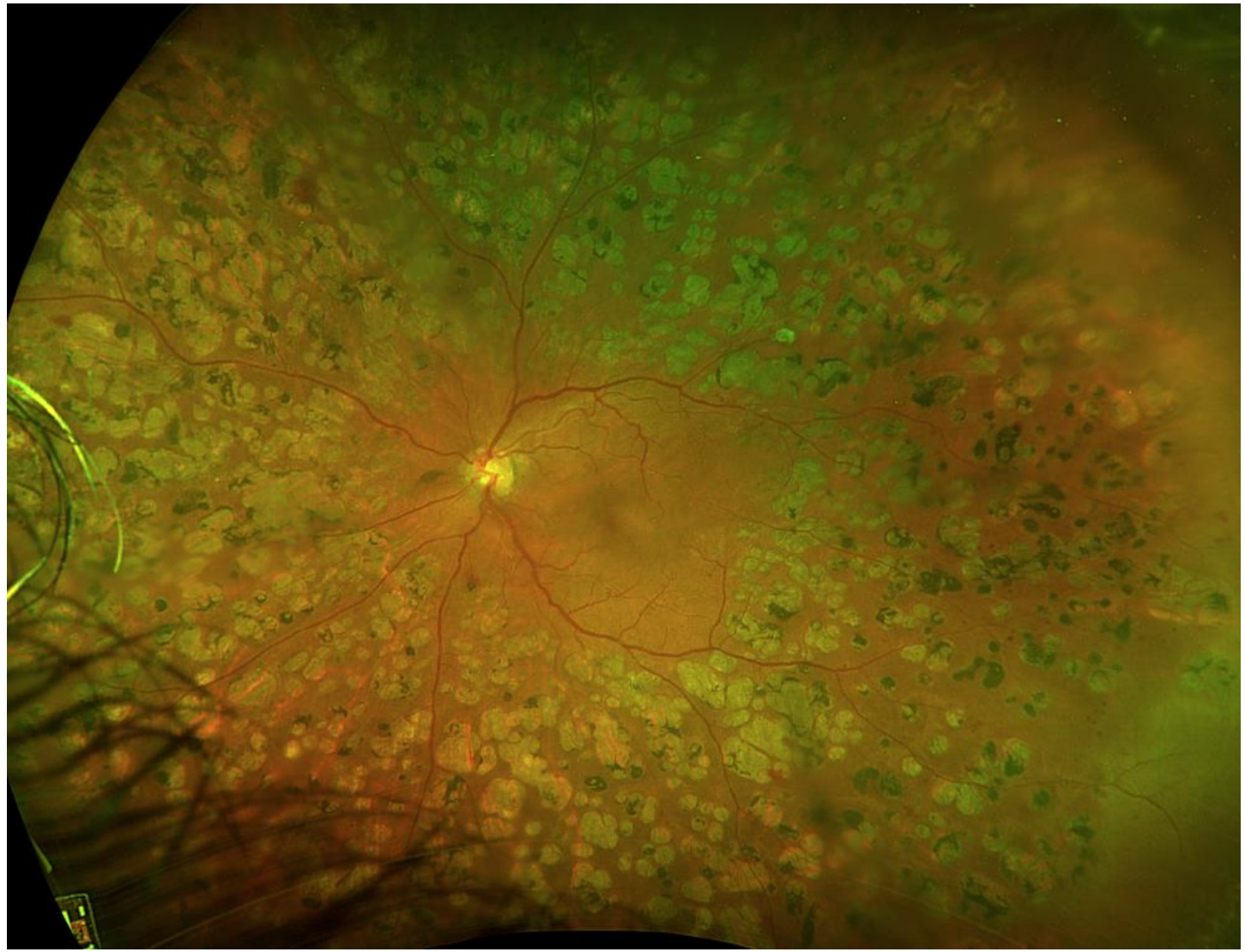
- Retinal ischemia → VEGF and new vessels → membranes, fibrosis
- Divided into “non-high risk” and “high-risk” categories
  - Based on amount of neovascularization and presence of vitreous hemorrhage
- Goal of treatment to control ischemia, reduce bleeding, treat fibrosis and traction
  - Anti-VEGF intravitreal injections
  - Panretinal photocoagulation
  - Surgery (vitrectomy)

Back to our patient

Panretinal photocoagulation (PRP)

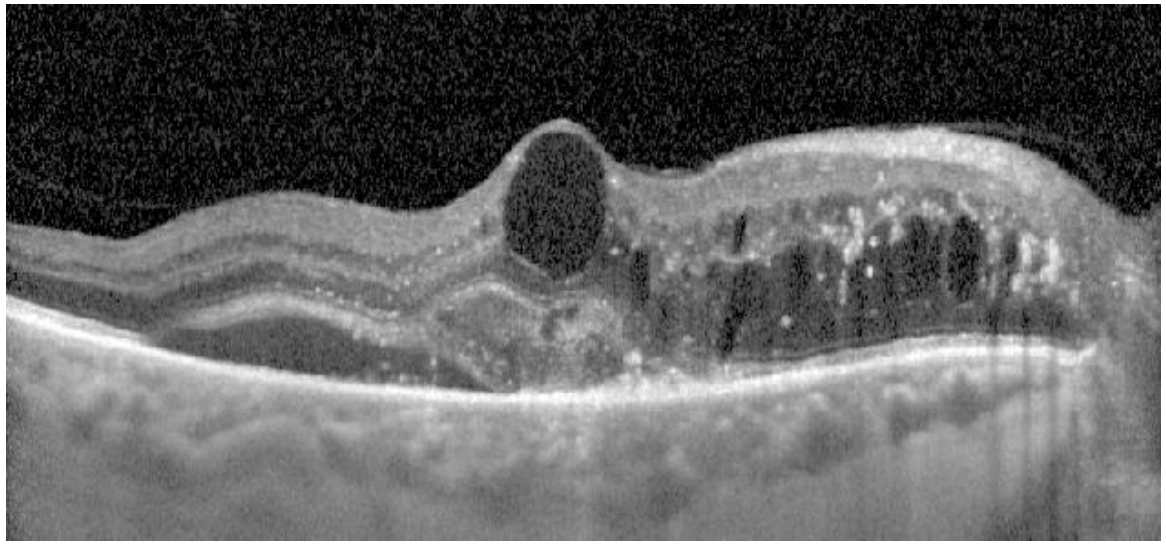
- Laser → thermal damage → destroys peripheral ischemic retina
- Reduces VEGF and increases oxygenation within the retina
- Benefits
  - Significantly reduces rates of severe vision loss
  - Very durable protective/treatment effect
- Downsides
  - Does not treat DME and may worsen DME afterwards
  - Can be painful/uncomfortable for patients
  - Decreased peripheral vision, night vision, contrast, persistent pupil dilation

Return to previous



Clinical Case- Part III

- The patient somewhat tolerates PRP and you are able to perform a partial treatment. However, at the next follow-up 6 weeks later, VA has decreased from 20/40 to 20/80 OD and exam/OCT show significant worsening of DME. What is the next best step in management?



Discuss and initiate anti-VEGF injections

Clinical Case- Part III

- The patient begins anti-VEGF injections and does well. Neovascularization and vitreous hemorrhage regress/resolve, DME resolves, and the patient returns to 20/20 in the right eye. He is very happy with the outcome, but after coming for several more visits, he is eventually lost to follow-up…

- When he returns a year later, VA OD has dropped to CF 3 ft and there is a dense VH in the right eye. Vision and hemorrhage do not improve despite several months of repeat intravitreal injections.

Click to learn more about anti-VEGF intravitreal injections

There is no view for PRP and injections are not working well; therefore you discuss and proceed with surgery for the patient.

Surgical management of PDR

- Vitrectomy is the intervention of choice in certain situations
  - Recurrent or non-clearing hemorrhage
    - Vitreous hemorrhage
    - Premacular/subhyaloid hemorrhage
    - Hyphema/anterior segment hemorrhage leading to glaucoma or corneal staining
  - Tractional retinal detachments (w/ or w/out rhegmatogenous component)
- In cases of early surgical intervention, two main goals are to…
  - Elevate/remove the posterior hyaloid (scaffold for future NV)
  - Apply full PRP intra-op (more comfortable and better visualization)

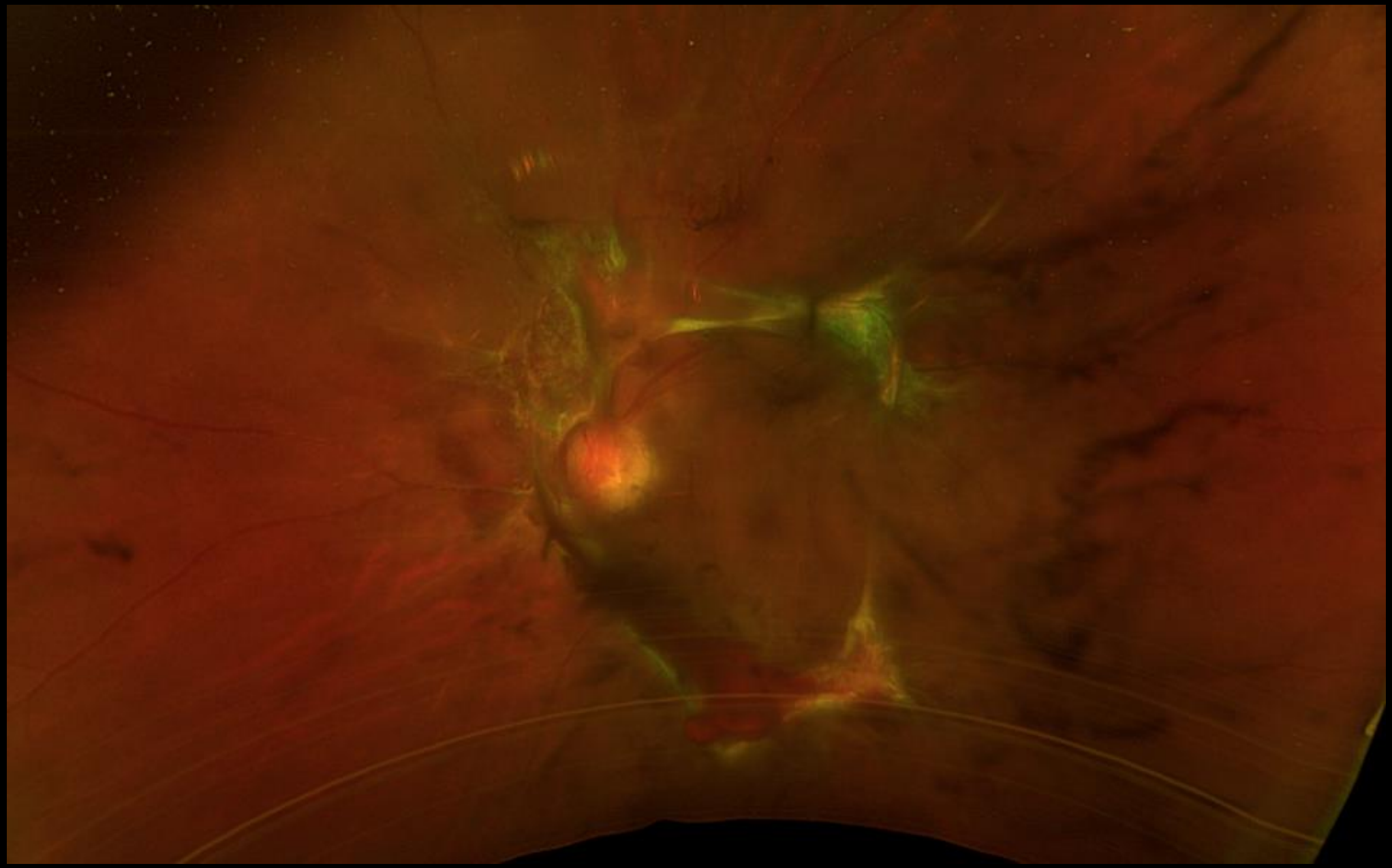
Click to learn more about PRP

- or -

Click to proceed to final part of the case

Clinical Case- Part IV

- The patient undergoes vitrectomy with endolaser in the right eye for non-clearing vitreous hemorrhage. He recovers well and returns to 20/20 OD. DME is resolved. With his newfound good vision, he dives back into work and misses 2 years of follow-up visits…
- When he returns, the right eye is still 20/20 and doing well. However, the patient does not realize that his left eye has decreased to CF VA at 5 feet with the following retina appearance



Decision point

How would you approach the treatment of this patient's macula-involving tractional retinal detachment?

1. Urgent surgery within a few days to maximize vision recovery
2. Delayed/planned surgery within 1 month with pre-op anti-VEGF
3. Defer surgery and pursue serial anti-VEGF injections

Click here to learn more about TRDs

Tractional retinal detachment

- Untreated proliferation of neovascular membranes can lead to extensive adhesions between the retinal surface and the posterior vitreous/hyaloid face
- If the patient then develops a PVD, the lifting hyaloid will exert traction and elevate the retina, rather than cleanly separating
- Mechanism is different from that of rhegmatogenous RDs (a break)
- But, can have combined RRD-TRD if the traction pulls a stretch break within the retina
- “Crunch” = rapid regression/contraction of fibrovascular membranes leading to dramatic worsening of the TRD

Return to previous

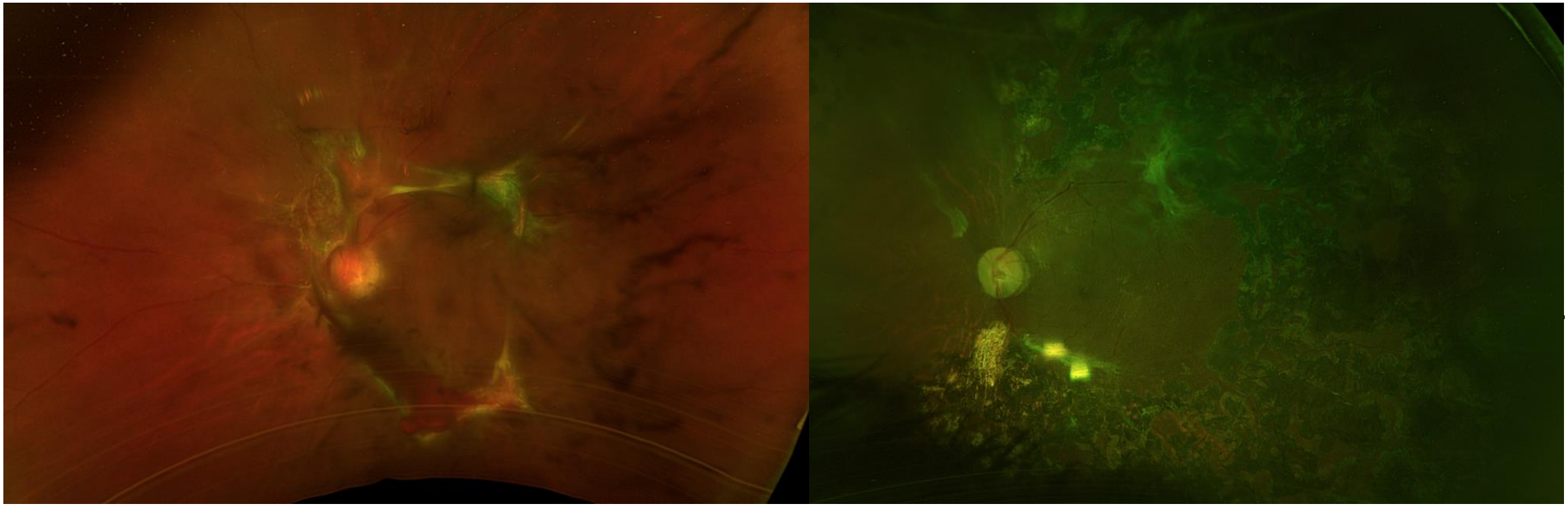
Clinical Case- Part V

- The only availability for emergency surgery is at night, at a hospital that does not perform a high volume of retina surgery. You are not familiar with their equipment, and the nurses and assistants are not experienced with the tools or steps of the surgery. There is excessive intra-operative bleeding (in part because you did not take time to do pre-op anti-VEGF injection or hold anticoagulation), and you are unable to maintain a view to successfully complete the surgery. Post-op VA worsens further to HM, and the eye becomes inoperable.

- Final outcome: 20/20 OD, HM OS

Learn more about TRDs

Clinical Case- Part V



- Final outcome: 20/20 OD, 20/20 OS (optimal outcome)

Learn more about TRDs

Clinical Case- Part V

- You have had past success with treating TRDs medically and so decide to proceed with serial anti-VEGF injections OS for this patient. However in this case, after 3 months of injections you observe dramatic contracture of the fibrotic areas and significant and sudden worsening of the detachment. You discuss surgical treatment options with the patient but counsel that visual prognosis is very guarded even with optimal outcomes. The patient declines to pursue surgery and opts for comfort care OS.

- Final outcome: 20/20 OD, HM OS

Learn more about TRDs

Surgical management of TRDs

- Generally not a surgical emergency, as compared to RRDs
  - May be more urgent if there is an open break/rhegmatogenous component
- Small or peripheral (non-macular) TRDs can be observed or treated medically with injections/laser
- Pre-operative anti-VEGF 1 week prior to surgery can reduce bleeding complications intra-operatively, with minimal crunch risk
- Can be complex surgeries requiring careful peeling and dissection of adherent fibrovascular membranes from the retinal surface

Summary

- DR is divided into non-proliferative and proliferative disease (with further subdivided categories and risk stratification within each)
- Intravitreal injections and laser (PRP) are main treatments for more advanced and/or visually significant disease
- Surgery can be useful for certain advanced DR complications
- Surgery is rarely performed as an emergency procedure in DR (with a few exceptions)