Retinal Vascular Occlusive Disease

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Financial Disclosures

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Consultant/Advisory Board/Lecturere

- Visionix (Optovue)
- iCare
- Apellis
- Iveric Bio
- LKC Technologies

- There are no financial relationships that affect the content of this program

Retinal Vascular Occlusive Disease: IMPORTANT TOPIC!!!

- Retinal vein occlusion is the second most prevalent retinal vascular disease (DR #1)
- Strong association with systemic disease
  - Morbidity and mortality highly associated

Main Risk Factors: AGE and SYSTEMIC VASCULAR DISEASE

Retinal Vein Occlusions

GUIDELINES AND SCREENING RECOMMENDATIONS

Definition of Retinal Vein Occlusion

Partial or complete obstruction of a retinal vein

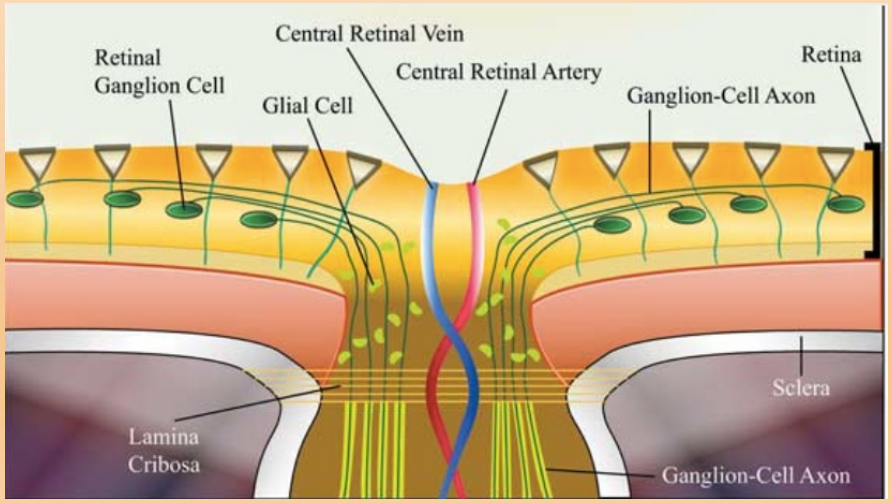
- Classified by **location** of occlusion

CRVO: Central Retinal Vein Occlusion
BRVO: Branch Retinal Vein Occlusion
HRVO: Hemi-Retinal Vein Occlusion

- Classified by **extent** of retinal ischemia
  - Ischemic vs. Non-Ischemic

Retinal Vein Occlusion: Etiology

- **Atherosclerosis** of the adjacent Central Retinal Artery
- The CRA compresses the CRV in the region of the lamina cribrosa
- This induces thrombosis (blood clot) in the lumen of the vein



Systemic Etiology: CRVO

- **Hypertension (most common systemic)**
- Diabetes
- Hyperlipidemia
- Cardiovascular Disease
- Hyperviscosity Syndromes
- Vasculitis: Sarcoid, Syphilis, SLE
- ??COVID

- Miscellaneous:
  - Drugs (Oral Contraceptives, diuretics)
  - Migraine

More detailed evaluations for bilateral cases or in patients who are <50 years.

Ocular Etiology: CRVO

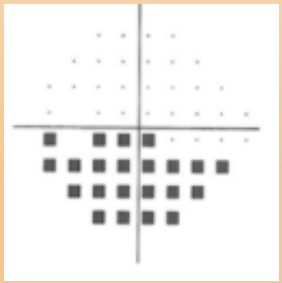
- **Ocular Hypertension/Glaucoma (most common ocular)**
  - (Causes increased pressure in the ONH sheath causing further compression and contributes to occlusion)

- Optic Disc Edema
- Optic Disc Drusen
- Orbital Tumor and abscess
- Cavernous Sinus Thrombosis
- Thyroid Eye Disease

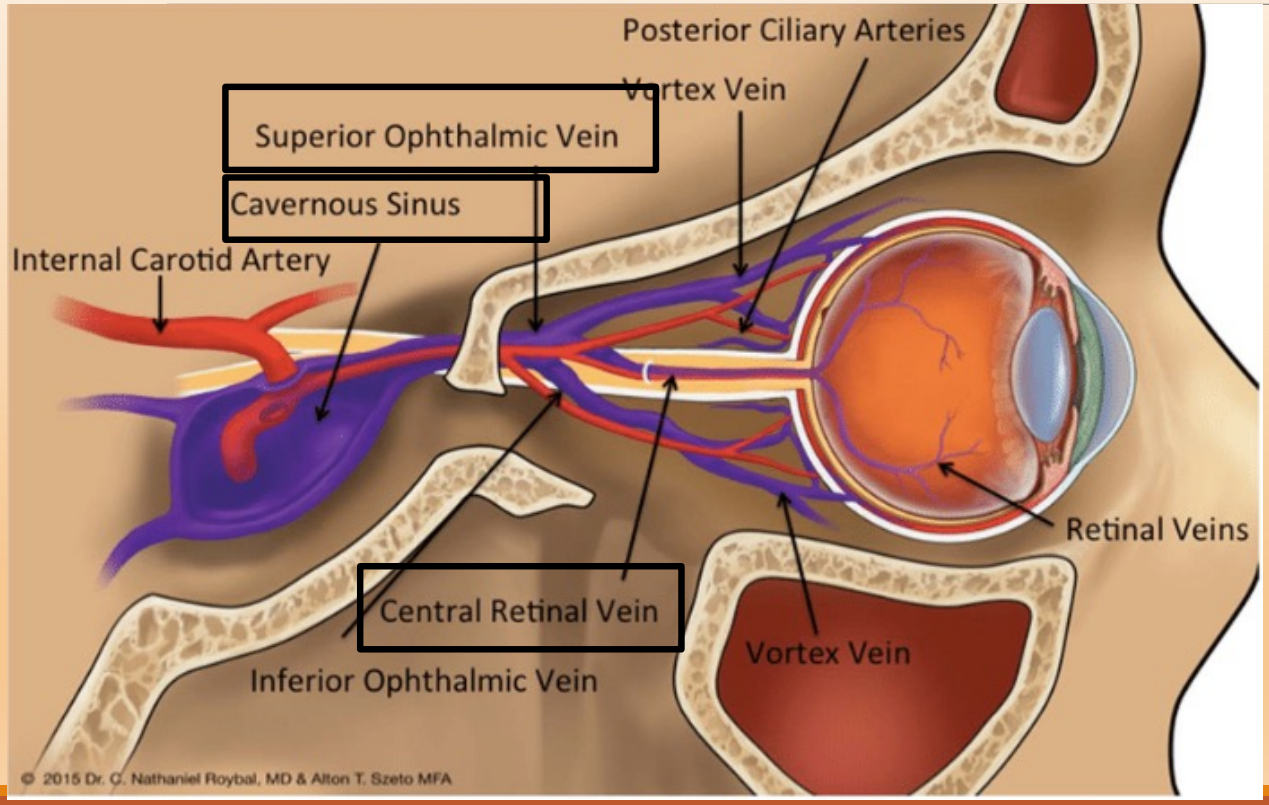
← Other factors that result in compression

What are patient's going to report?

- Progressive, **painless** decrease in vision and field of vision
  - *Extent varies on type of occlusion*
  - Unilateral
  - Loss of VA; varies with degree of ischemia



Let's Review the Anatomy; CRVO

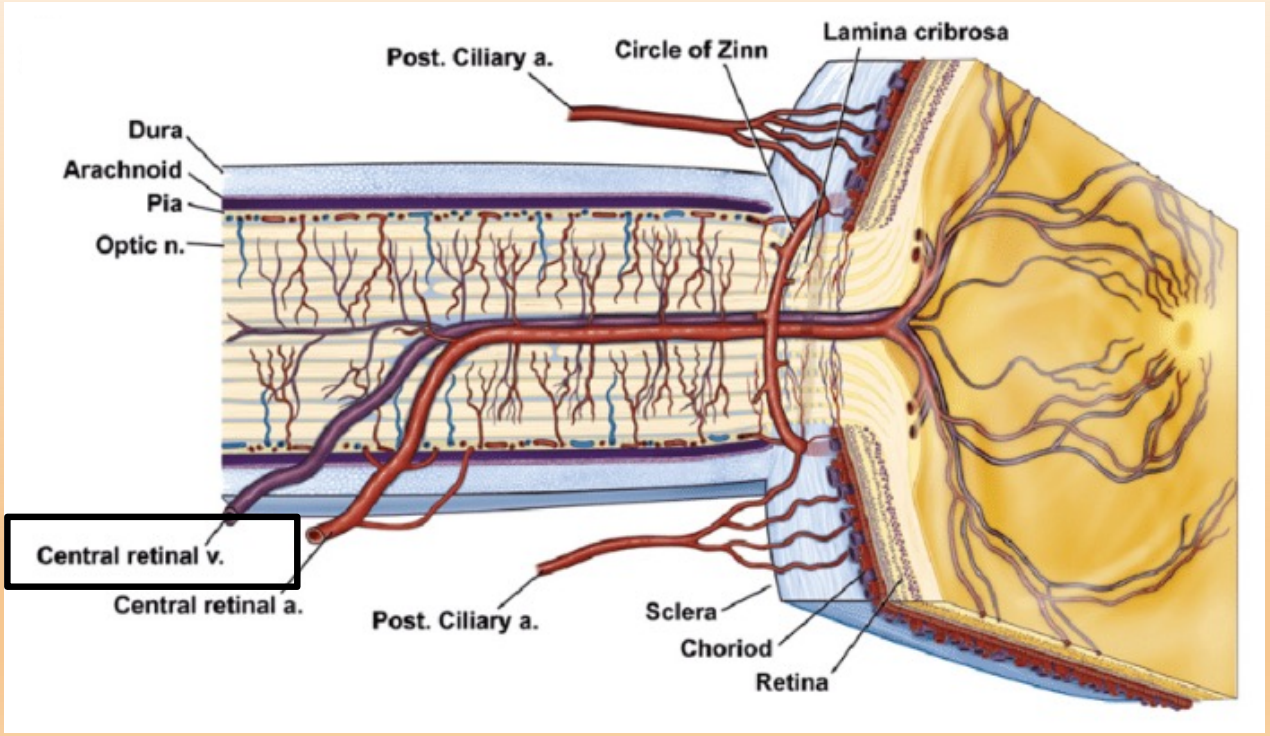


Central Retinal Vein:

Short vein that runs through the ONH

Retinal circulation drains into the CRV, which drains into the superior ophthalmic vein and then the cavernous sinus

Let's Review the Anatomy; CRVO

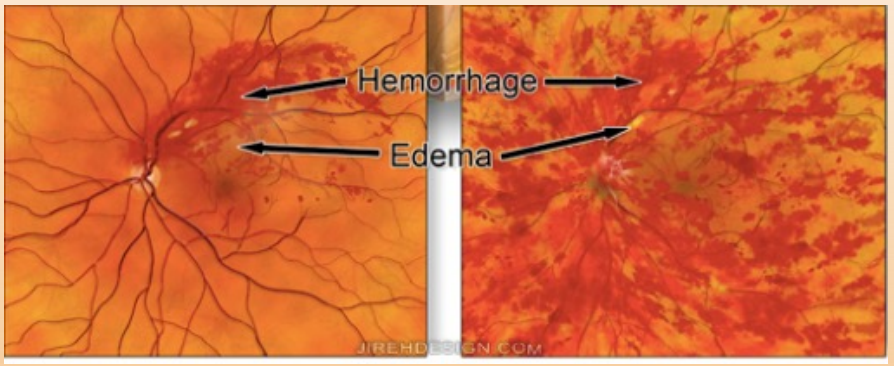


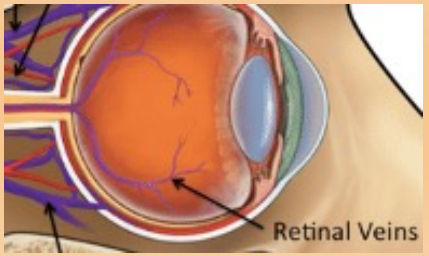
- Obstruction at/or posterior to the ONH

https://www.researchgate.net/figure/Anatomy-of-ocular-circulation-a-artery-b-vein-n-nerve-A-Cut-away-drawing-along-the_fig17_224949360

General Sequelae….RVO

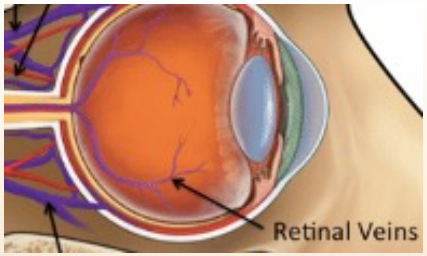
- ❖Complete or partial decrease in venous outflow within the retinal circulation
- ❖Retinal vascular leakage
- ❖Sequalae…..Varies depending on type of occlusion



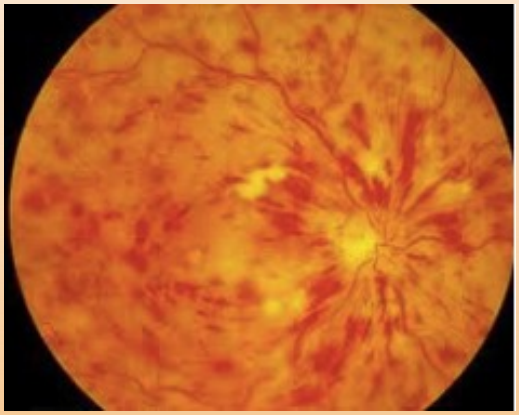


https://retinaeyedoctor.com/central-retinal-vein-occlusions/

Evaluation of CRVO

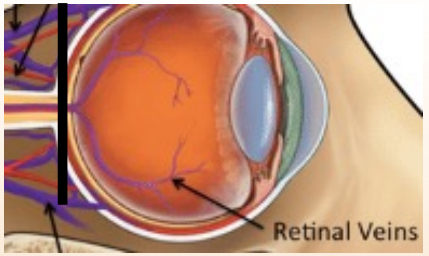


- Clinical findings:
  - Retinal hemorrhages (4 Quadrants)
  - Dilated, tortuous retinal veins

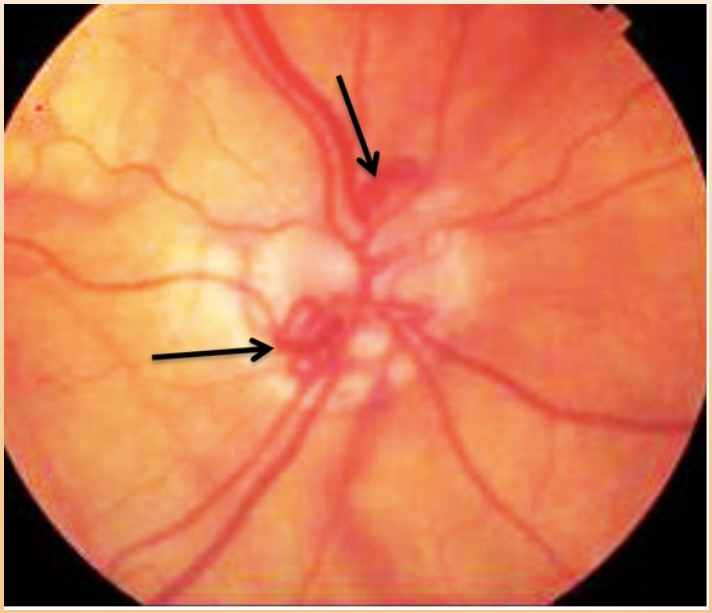


  - Superficial hemorrhages
  - CWS
  - Macular edema

Evaluation of CRVO



- **Later clinical findings:**
  - Collaterals
    - **CRVO**: Between retinal venules and choroidal circulation at the disc
  - Optic Disc Edema



Black arrows: The identified veins are dilated, pre-existing channels connecting retinal venous return to choroidal veins.

http://www.retinareference.com/diseases/28f9641cc2c160e4/images/0a84f11b51

Evaluation of CRVO

- Later clinical findings:
  - Neovascularization
    - iris and retina
  - Vitreous hemorrhage
  - Neovascular glaucoma

https://retinagallery.com/displayimage.php?album=953&pid=7716#top_display_media

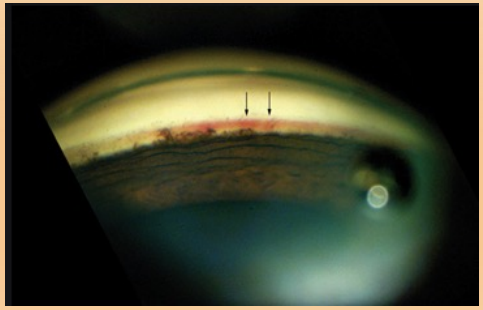
Evaluation of RVO

- **Later clinical findings:**

  Neovascular glaucoma

  60% of patients with ischemic CRVO will develop neovascular glaucoma

  90 Day Glaucoma!



https://retinagallery.com/displayimage.php?album=953&pid=7716#top_display_media

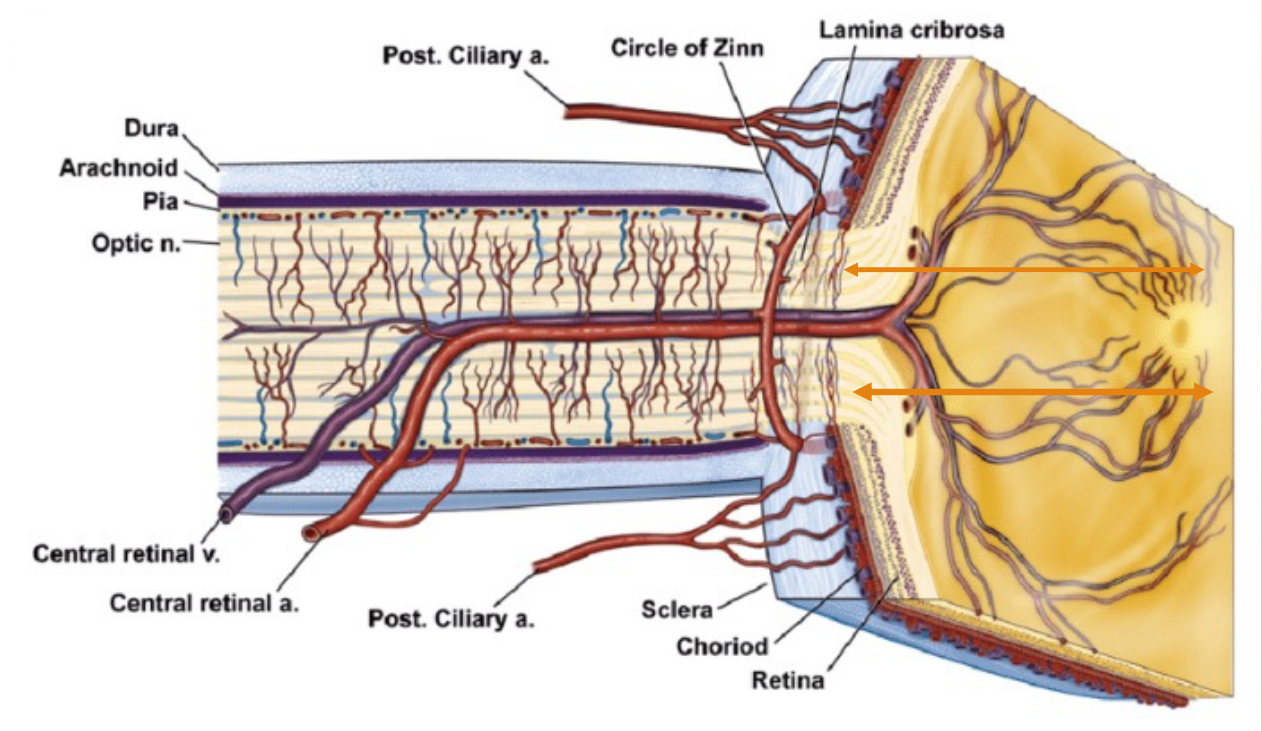
Ischemic vs. Non-Ischemic RVO

- **Visual Acuity**
  - <20/200 associated with non-perfusion
- **Pupillary** assessment for RAPD
  - Corresponds to level of ischemia; (+)APD if ischemic
  - Predictive of eyes at risk for neovascularization
- **FA** is used to evaluate the degree of ischemia
  - Defined by CVOS as eyes with 10-disc areas of capillary non-perfusion
  - CWS, extensive retinal hemorrhages

Retinal Imaging: Ischemic vs. Non-Ischemic

- *Optical Coherence Tomography*
  - Macular edema
- *Optical Coherence Tomography Angiography*
  - Accurately evaluates change in microvasculature (vessel density, size of FAZ)
- *Visual Field Testing*

Let's Review the Anatomy; HRVO



- Occlusion occurring at the disc involving **half** of neurosensory retinal drainage (S or I hemifield)

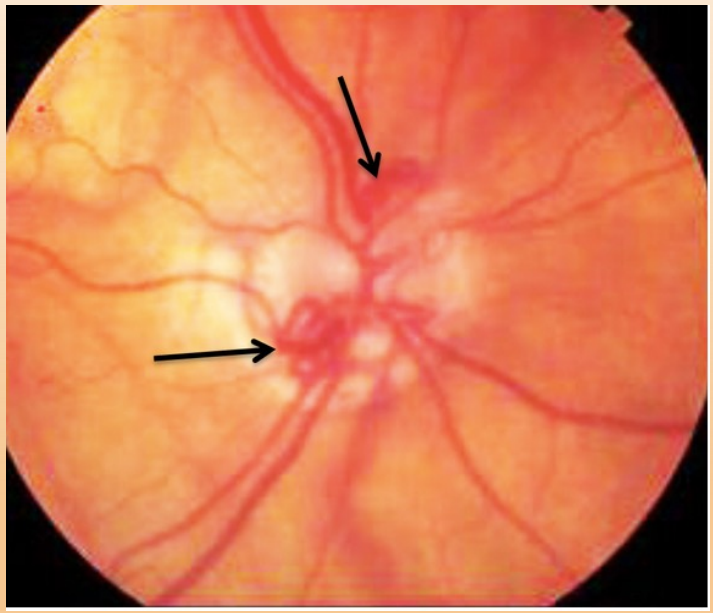
https://www.researchgate.net/figure/Anatomy-of-ocular-circulation-a-artery-b-vein-n-nerve-A-Cut-away-drawing-along-the_fig17_224949360

Evaluation of HRVO

- **Early clinical findings:**
  - Vascular tortuosity and dilation
  - Retinal and macular edema
  - Retinal hemorrhages (2 Quadrants)
    - N and T
  - CWS

Evaluation of HRVO

- Later clinical findings:
  - Collaterals
    - CRVO/HRVO:
      Between retinal venules and choroidal circulation at the disc
  - Optic Disc Edema



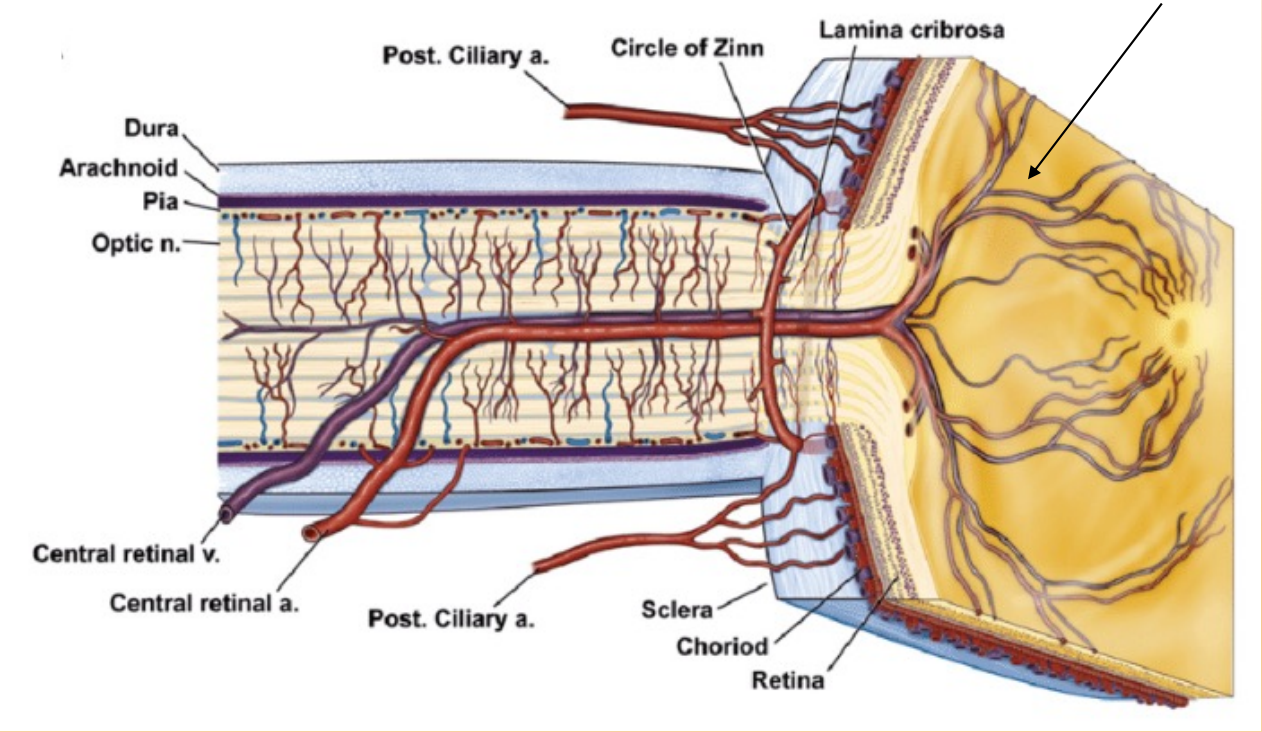
http://www.retinareference.com/diseases/28f9641cc2c160e4/images/0a84f11b51

Evaluation of HRVO

- Later clinical findings:
  - Neovascularization
    - Retinal>iris
  - Vitreous hemorrhage
  - Neovascular glaucoma

https://retinagallery.com/displayimage.php?album=953&pid=7716#top_display_media

Let's Review the Anatomy; BRVO



- Complete or partial obstruction at a branch of the central retinal vein

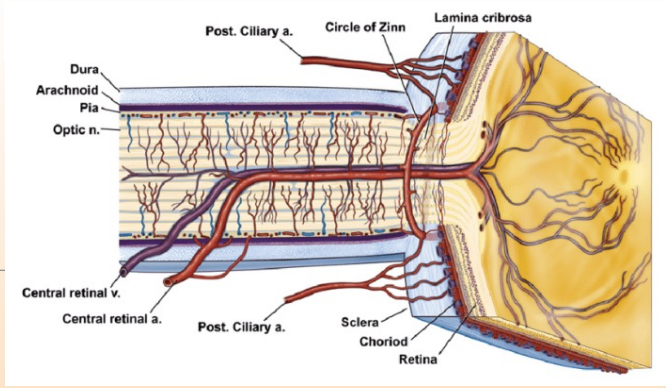
https://www.researchgate.net/figure/Anatomy-of-ocular-circulation-a-artery-b-vein-n-nerve-A-Cut-away-drawing-along-the_fig17_224949360

Evaluation of BRVO

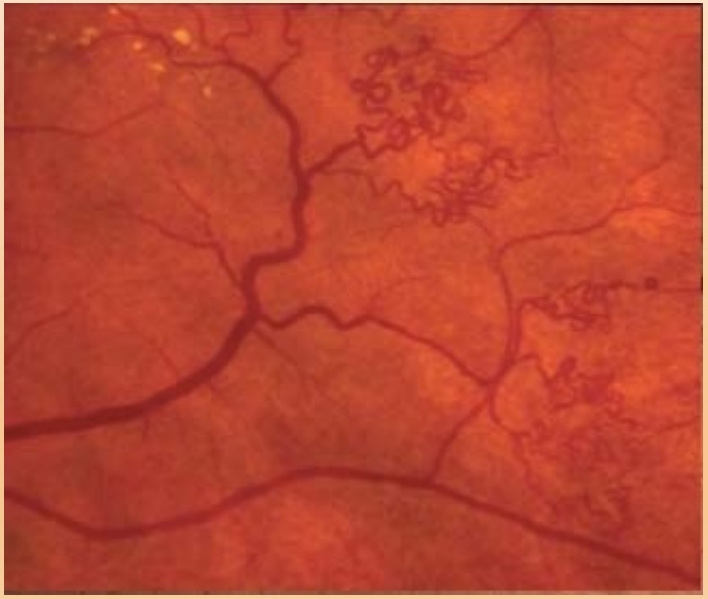
- Clinical findings:
  - Superficial hemorrhages in a sector of the retina along a retinal vein (do not cross the midline)
  - CWS
  - Retinal Edema
  - A dilated and tortuous retinal vein
  - Narrowing and sheathing of adjacent artery

https://www.reviewofophthalmology.com/article/evaluation-and-management-of-retinal-vein-occlusion

Evaluation of BRVO



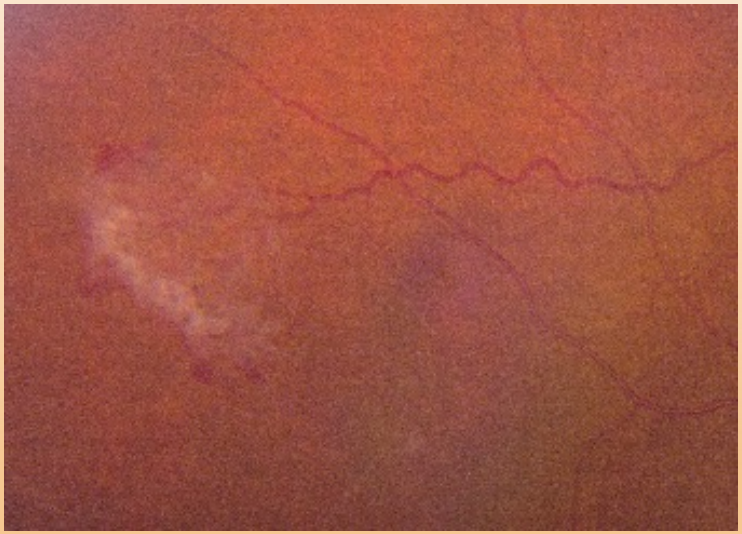
- **Later clinical findings:**
  - Collaterals
    - **BRVO**: Between superior and inferior retinal veins



Venous-venous collateralization. Collaterals bridge the obstructed site or connect to adjacent veins in the periphery

Evaluation of BRVO: SEVERE ischemia….

- Later clinical findings:
  - Neovascularization
    - Due to ischemia
    - Formed as compensatory mechanism



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Evaluation of RVO

STEP-BY-STEP GUIDE

Evaluation of RVO

- ***Three main components:***
  - Medical History
  - Ocular Exam
  - Retinal imaging

Evaluation of RVO: Medical History

- Atherosclerotic risk factors?
  - HTN, hyperlipidemia, diabetes
  - Smoking, obesity
  - Family history of coronary artery disease
- Hypercoagulability risk factors?
- Vasculitis? Prior systemic disease?

https://www.allaboutvision.com/conditions/eye-occlusions.htm

Evaluation of RVO: Ocular History

- Ocular History?
  - Glaucoma, Ocular Hypertension

Evaluation of RVO

- *Three main components:*
  - Medical History
  - **Ocular Exam**
  - Retinal imaging

Evaluation of RVO: Ocular Exam

- **Visual Acuity**
- **Pupil exam**; ?APD
- **Biomicroscopy**; ?iris neovascularization, IOP
- **Gonioscopy**; ?angle neovascularization
- **Dilated fundus examination**; including vitreous and periphery; macular edema; ONH cupping?

Evaluation of RVO

- *Three main components:*
  - Medical History
  - Ocular Exam
  - **Retinal imaging**

Retinal Imaging

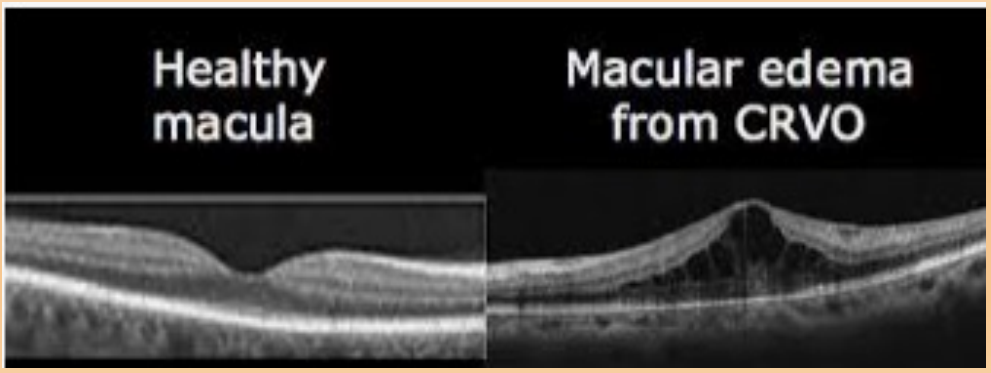
- *Fluorescein Angiography*
  - Essential first step: Detect nonperfused capillary areas and extent of macular ischemia
- *Optical Coherence Tomography*
  - Quantify presence and extent of macular edema
- *Optical Coherence Tomography Angiography*
  - Accurately evaluates change in microvasculature (vessel density, size of FAZ)

Evaluation of RVO: Imaging

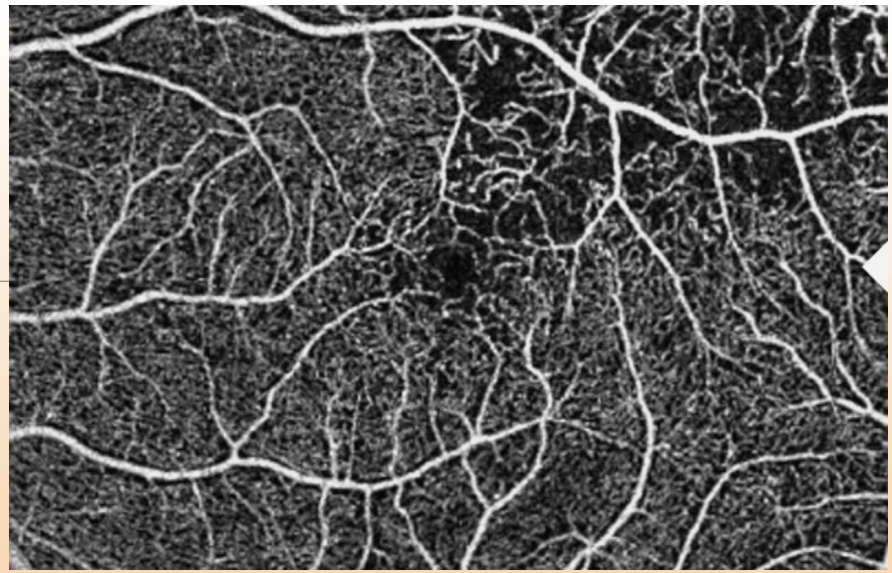
- FA
  - Identify site of damaged A/V crossing
  - Degree of non-perfusion

Evaluation of RVO: Imaging

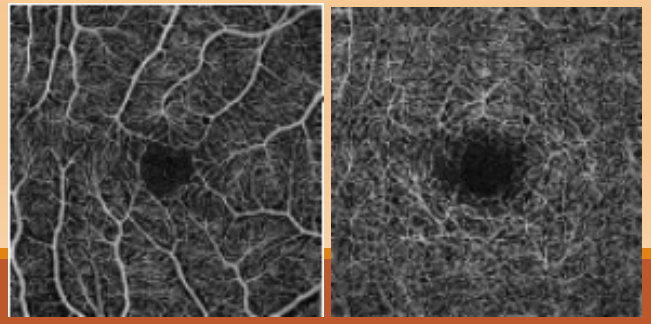
- OCT
  - Detect presence and extent of macular edema; monitor response to therapy

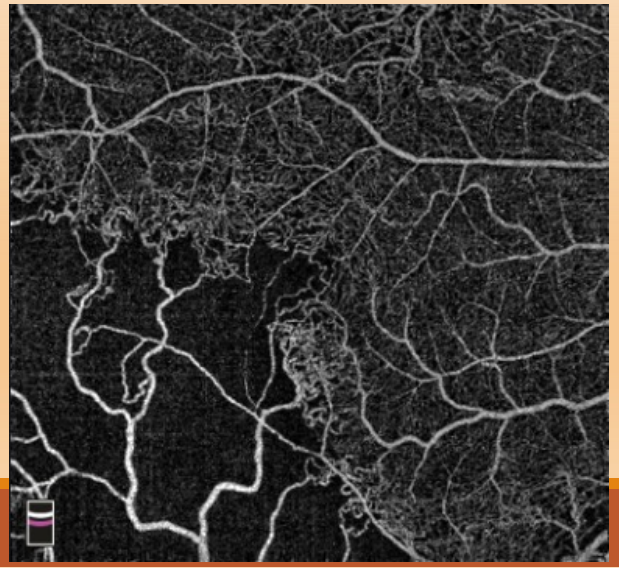


Evaluation of RVO: Imaging



- OCTA
  - Assess degree of capillary non-perfusion
  - Measure size of FAZ





Management: RVO

- Treat and evaluate for underlying medical disorders

Lab work:

Complete blood cell (CBC) count
Glucose tolerance test
Lipid profile
Serum protein electrophoresis
Syphilis serology
Thrombophilic screening, activated protein C resistance, lupus anticoagulant, anticardiolipin antibodies, protein C, protein S, and antithrombin III may be completed.

- Reduce IOP

Treatment: Ocular

- Macular Edema
  - Anti-VEGF- 1st line of treatment (Lucentis, Eylea)
  - Intravitreal corticosteroids (s/e) (Ozurdex)
  - Laser photocoagulation

- Iris or Retinal Neovascularization
  - PRP (adjunct use of Anti-VEGF)

BRAVO and CRUISE: Early anti-VEGF treatment leads to better visual outcomes

RVO—Macular Edema: Anti-VEGF Agents

Anti-VEGF agents	Ranibizumab	Aflibercept	Brolucizumab	Faricimab	Bevacizumab
FDA approval for indication	2010	2012	Not approved	Not approved	Not approved
Pivotal studies	CRUISE/ BRAVO	COPERNICUS/ GALILEO			

Treatment group improvements in VA and central macular thickness (CMT) were significant compared to sham

Clinical Pearl

Treatment of systemic conditions, such as unknown diabetes or hypertension, is mandatory to prevent future ***non-ocular*** *life-threatening events. Furthermore, it is the only way to reduce risk for involvement of the contralateral eye.*

Case Examples

RETINAL VEIN OCCLUSION

60-year-old Black female

Reports "curtain over her vision" in the right eye x 2 months… was hoping it would go away.

Evaluation of RVO

- *Three main components:*
  - Medical History: (+)Hypertension, Hypercholesterolemia
    - BP elevated in office, h/o poor cholesterol control
  - Ocular Exam
  - Retinal imaging

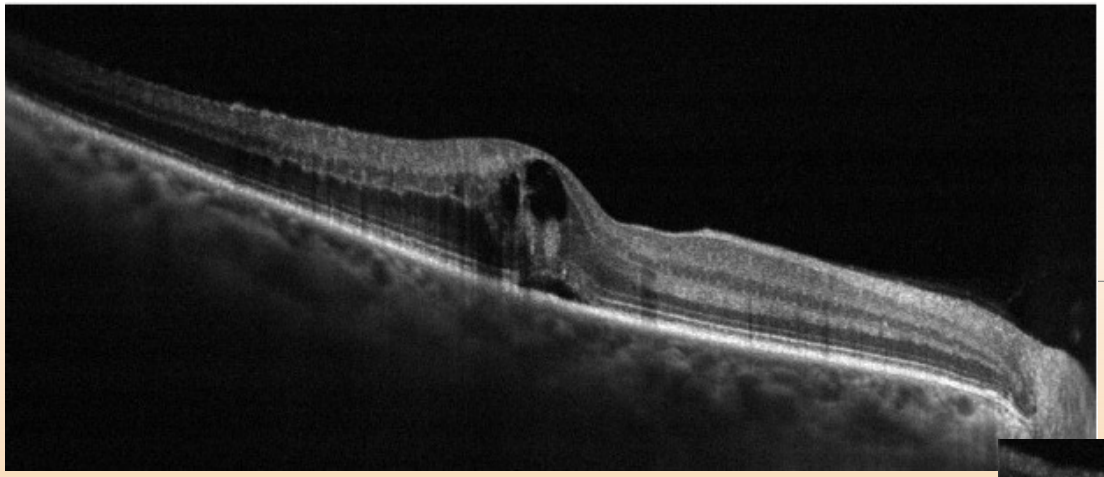
Evaluation of RVO

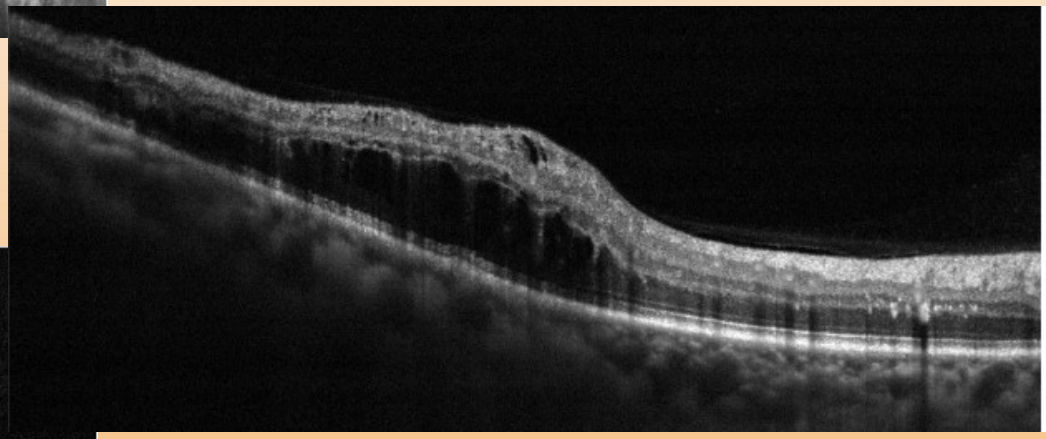
- *Three main components:*
  - Medical History
  - Ocular Exam…VA/?APD, ?Iris/Angle neovascularization,?IOP
  - Retinal imaging

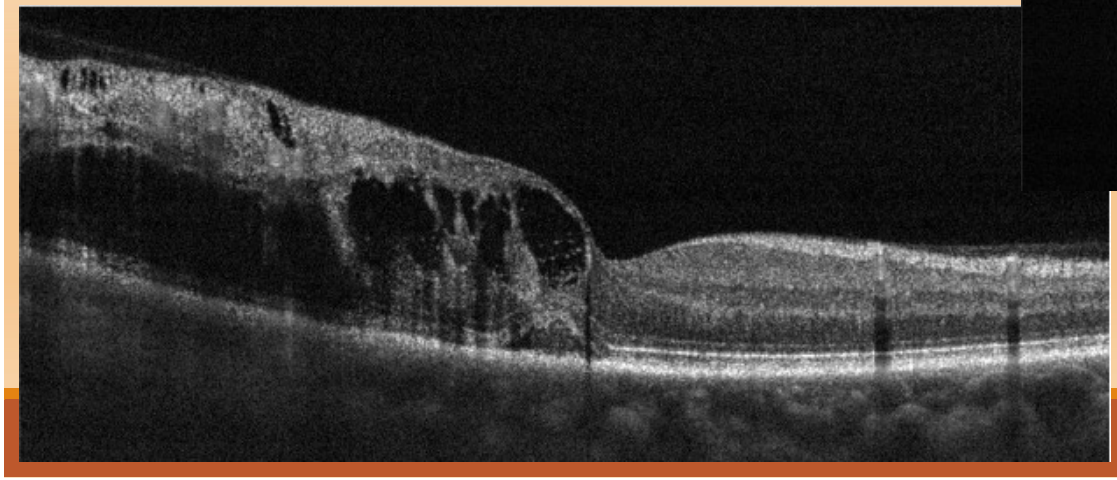
What kind of RVO is this?

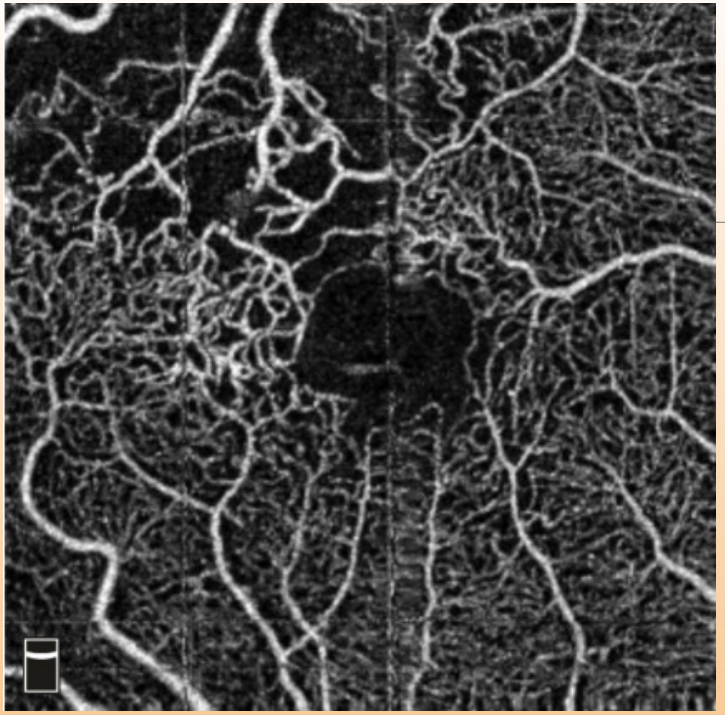
- Vascular tortuosity
  - Crossing changes
- Retinal edema
- Intraretinal hemorrhages
- Superficial hemorrhages
- CWS

- Collaterals!!

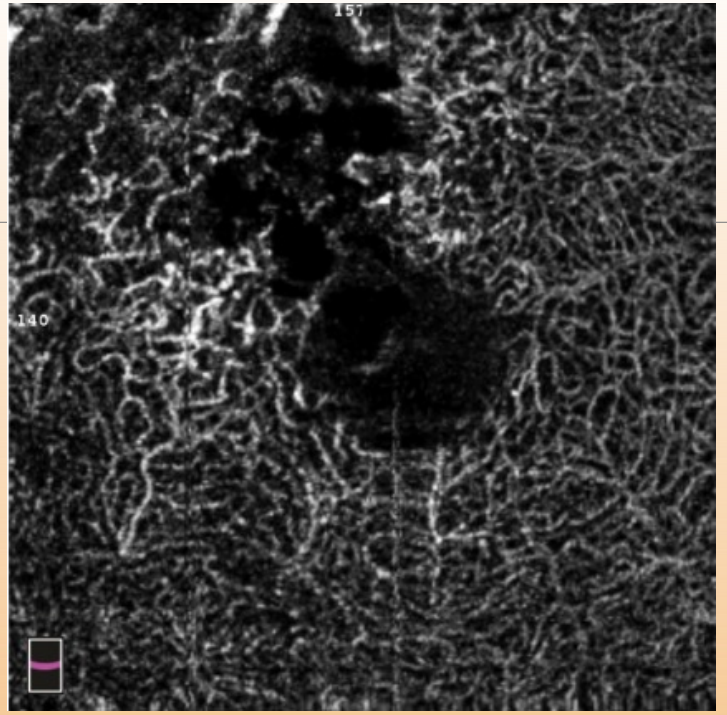




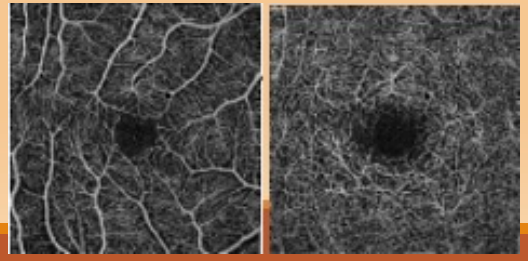


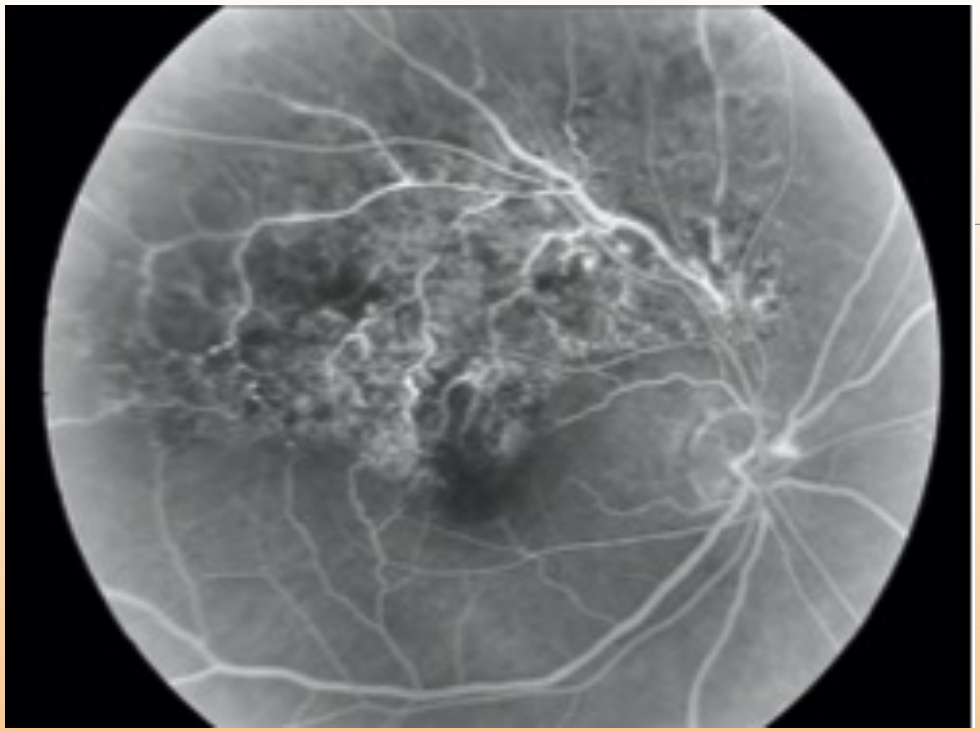


Superficial Capillary Plexus



Deep Capillary Plexus





FA of BRVO:

- Delayed filling of occluded retinal vein
- Varying degrees of capillary nonperfusion

Treatment/Management

- ***Co-Manage with Internist***
  - Optimizing control of systemic arterial HTN and serum lipid levels

- ***Macular Edema***
  - Refer to retinal specialist; Anti-VEGF

57-year-old Diabetic male

- Decreased vision OS
- History of newly diagnosed DM and HTN (1 year)

He candidly reports that he has been having trouble regulating his blood sugar levels….

Evaluation of RVO

- *Three main components:*
  - Medical History: (+)Hypertension, Diabetes
    - A1C 9.0, unknown BS, BP elevated in office
  - Ocular Exam
  - Retinal imaging

Evaluation of RVO

- *Three main components:*
  - Medical History
  - Ocular Exam…VA/?APD, ?Iris/Angle neovascularization, ?IOP
  - Retinal imaging

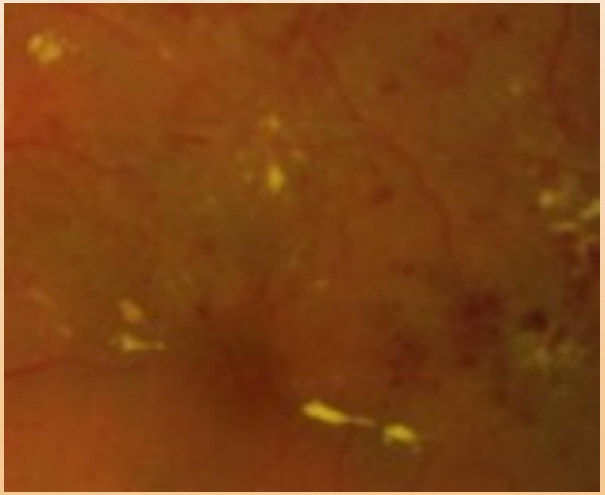
Evaluation of RVO

- *Three main components:*
  - Medical History
  - Ocular Exam
  - **Retinal imaging**

- Vascular tortuosity
  - Crossing changes
- Exudates
- Intraretinal hemorrhages

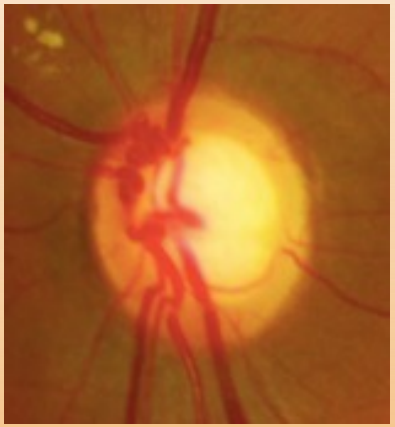
What kind of RVO?

WHAT ELSE??

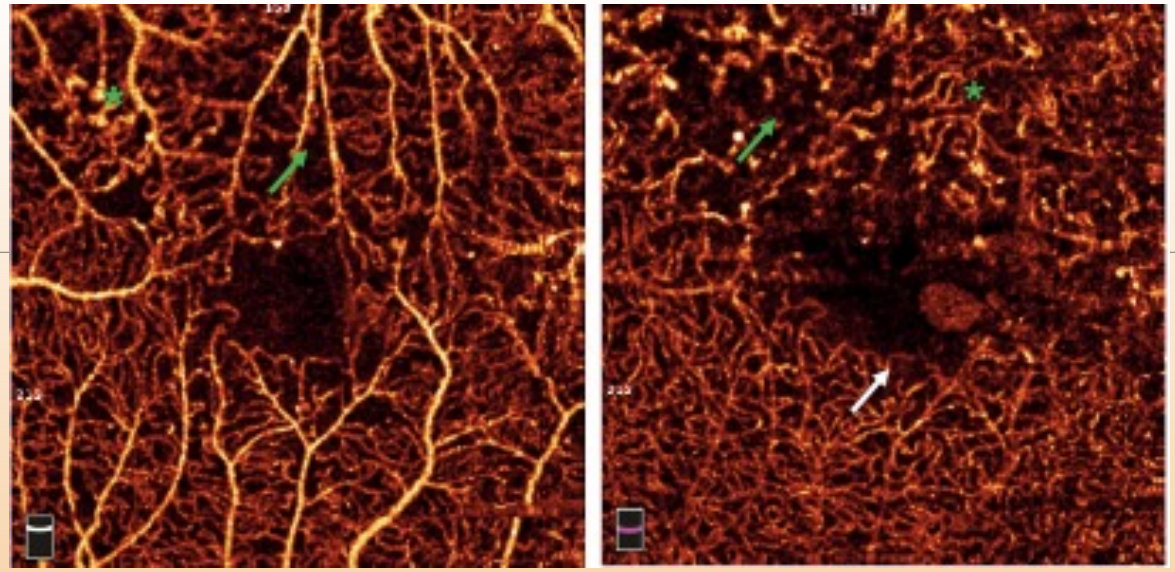


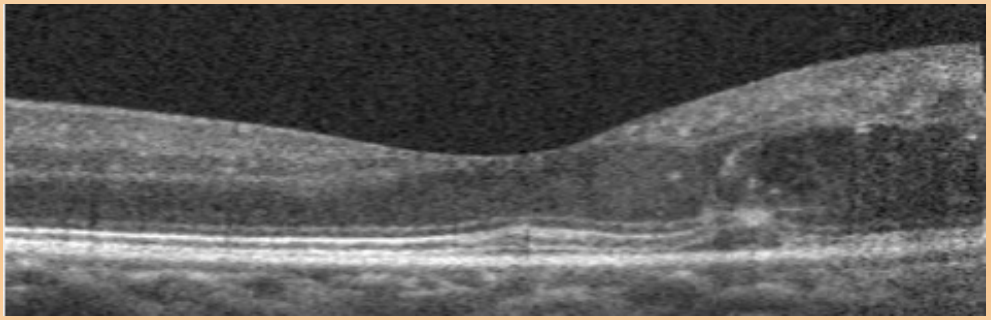
❖Retinal Collaterals

❖ONH Collaterals



❖Between retinal venules and choroidal circulation at the disc





Treatment/Management

- ***Co-Manage with Internist***
  - Optimizing control of systemic arterial HTN, Diabetes
- ***Refer***
  - Macular edema!!

48-year-old Female

”Three months ago the vision in my left eye went bad and I have been seeing strange lights as well.”

Evaluation of RVO

- *Three main components:*
  - Medical History: (+)H/O 2 miscarriages
  - Ocular Exam
  - Retinal imaging

Evaluation of RVO

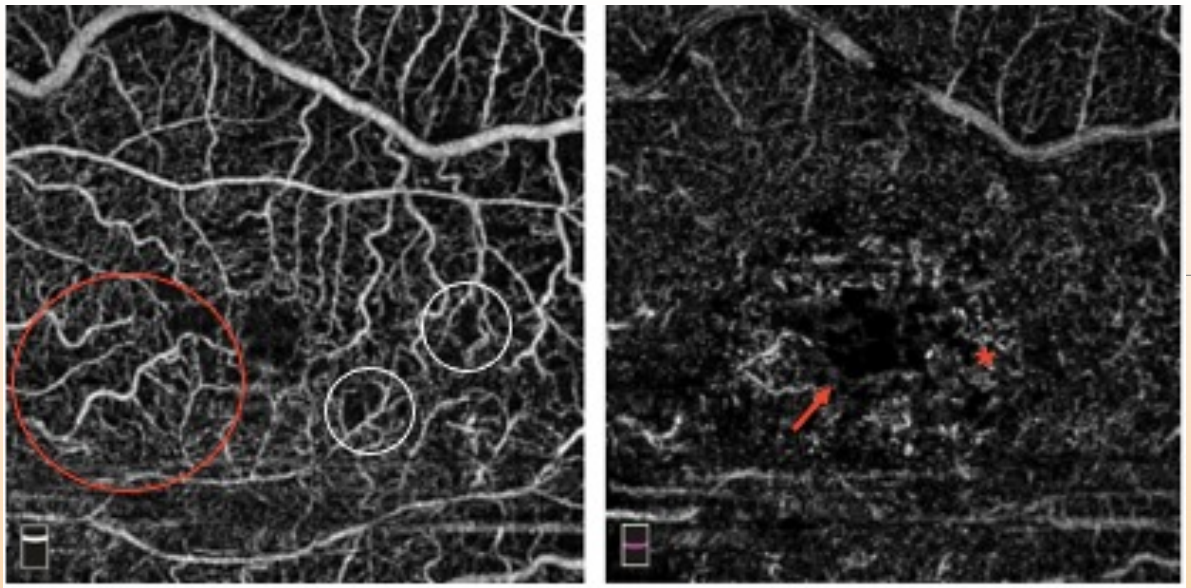
- *Three main components:*
  - Medical History
  - Ocular Exam…VA/?APD, ?Iris/Angle neovascularization, ?IOP
  - Retinal imaging

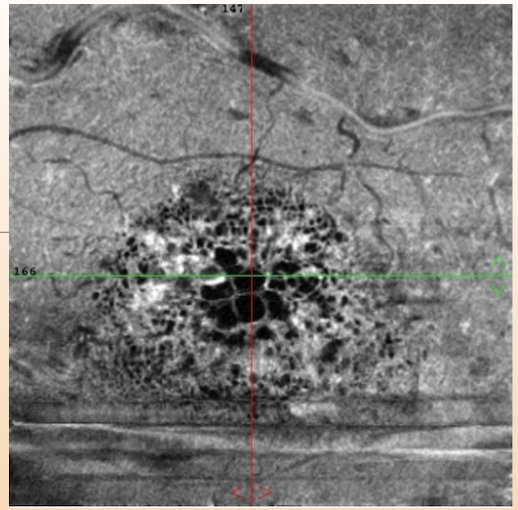
What kind of RVO?

- Flame shaped hemorrhages in all 4 quadrants
- Intraretinal hemorrhages
- Papilloretinal edema
- Engorgement and tortuosity of major retinal veins

Evaluation of RVO

- *Three main components:*
  - Medical History
  - Ocular Exam
  - **Retinal imaging**

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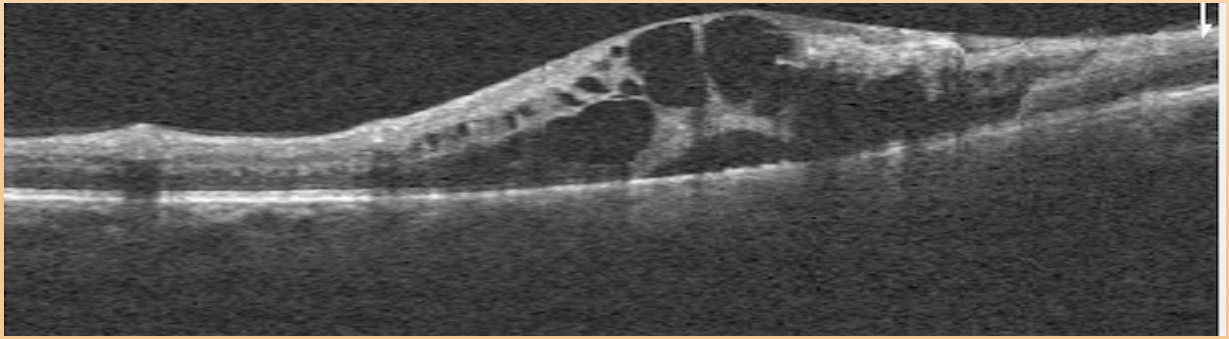
166



What kind of RVO?

- ***Suspected Non-Ischemic CRVO… Why??***
  - VA 20/100… with continued improvement
  - Absence of APD
  - Milder degree of hemorrhages
  - No CWS
  - Normal VF

RECALL:: Systemic Etiology: CRVO

- **Hypertension (most common systemic)**
- Diabetes
- Hyperlipidemia
- Cardiovascular Disease
- Hyperviscosity Syndromes
- Vasculitis: Sarcoid, Syphilis, SLE

- Miscellaneous:
  - Drugs (Oral Contraceptives, diuretics)
  - Migraine

More detailed evaluations for bilateral cases or in patients who are <50 years.

Evaluation of RVO: Medical History

- Atherosclerotic risk factors?
- Hypercoagulability risk factors?
  - **Younger patients**

Lab work:

Complete blood cell (CBC) count
Glucose tolerance test
Lipid profile
Serum protein electrophoresis
Chemistry profile
Hematologic tests
Syphilis serology
Thrombophilic screening, activated protein C resistance, lupus anticoagulant, anticardiolipin antibodies, protein C, protein S, and antithrombin III may be completed.

https://www.allaboutvision.com/conditions/eye-occlusions.htm

Diagnosis: Hyperviscosity Disorder

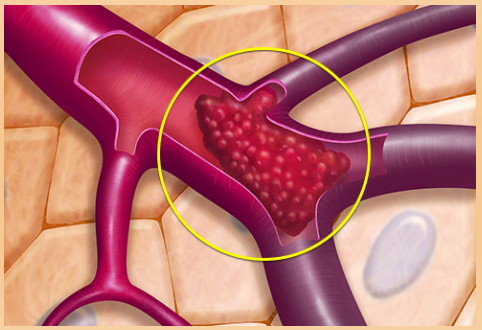
- *Pt history was crucial in diagnosis*
  - *Co-Manage with hematologist; communication is a MUST*
- *Refer!! (macular edema)*
  - Anti-VEGF

Retinal Vein Occlusion Associated With COVID-19

What we know about SARS-CoV-2:

(the virus that causes COVID 19)

- *The virus was initially considered primarily a respiratory illness*
- ***HOWEVER:*** *COVID-19 results in a uniquely profound pro-thrombothic cascade leading to both arterial and venous thrombosis*



Pathophysiology behind hypercoagulable state:

- Severe inflammatory response originates in the alveoli leading to thrombosis of pulmonary vasculature
- Leads to a state of local coagulopathy
- Followed by generalized hypercoagulable state resulting in vascular thrombosis

What we know about SARS-CoV-2:

(the virus that causes COVID-19)

- *The hypercoagulable state induced by COVID-19 may be linked with CRVO which is also associated with hypercoagulation*

RECALL:

- **Hypertension (most common systemic)**
- Diabetes
- Hyperlipidemia
- Cardiovascular Disease
- Hyperviscosity Syndromes
- Vasculitis: Sarcoid, Syphilis, SLE

A review of the literature…..

Coronavirus disease-19–associated retinal vascular occlusions tend to occur in individuals younger than 60 years. Retinal vein occlusion is the most frequent occlusive event, and outcomes are favorable in most cases.

17-year-old female

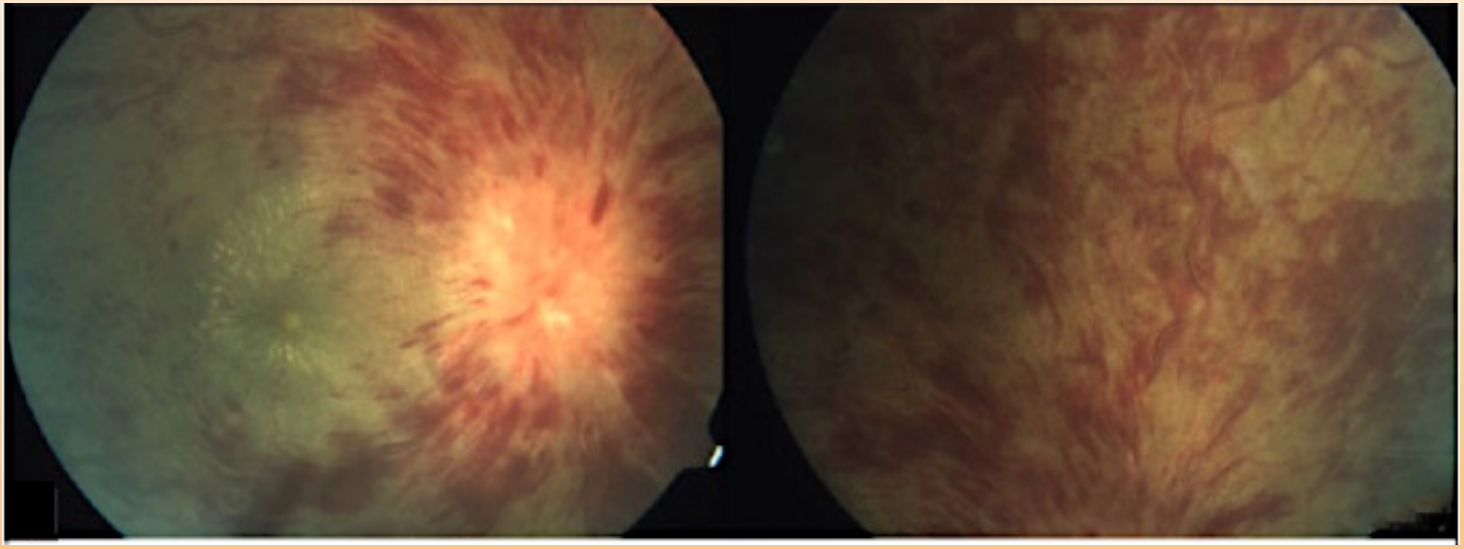
- Presents with diminished vision of 2 days duration

- PMH:
  - (+)Polycystic ovaries
    - Not taking any medication

- BCVA: 20/80 OD, 20/20 OS
- IOP: 16 mmHg OD, 18 mmHg OS
- Anterior segment examination unremarkable

https://journals.lww.com/retinajournal/Fulltext/2022/03000/CHARACTERIZING_COVID_19_RELATED_RETINAL_VASCULAR.8.aspx

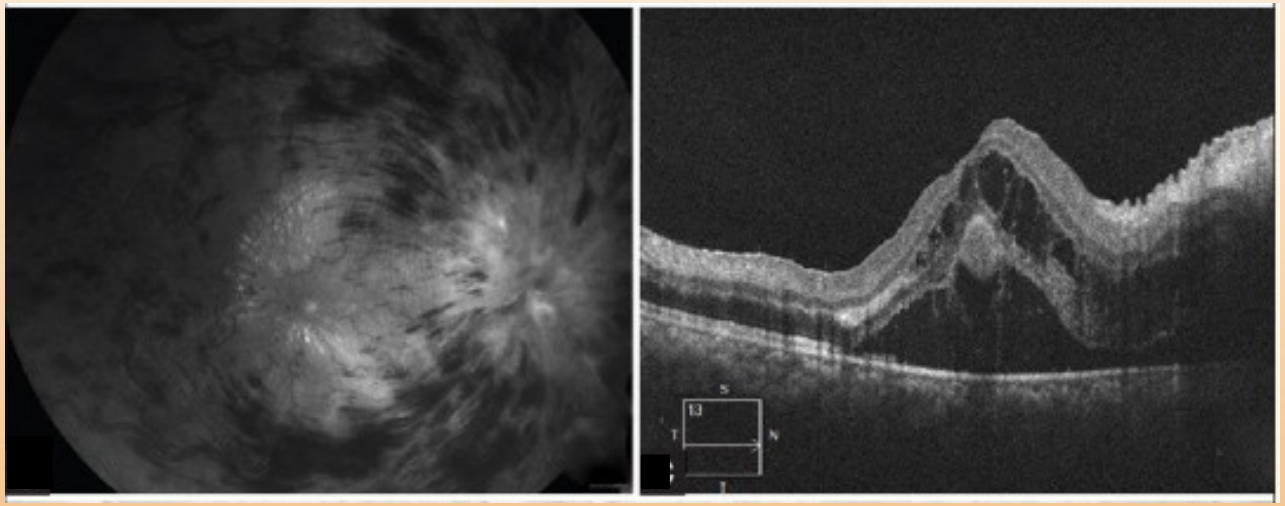
Ocular Examination



Optic disc edema and multiple hemorrhages in all quadrants with a macular star

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7774137/

Ancillary Testing



Optical coherence tomography scan of macula shows neurosensory detachment and cystoid macular edema

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7774137//

Sequelae

- Diagnosis of CRVO was made
- Blood work was ordered:
  - CBC, ESR, RF, peripheral smear, lipid profile, ANA, urine routine micro, blood sugars, ACE, serum homocysteine, blood urea nitrogen, serum osmolality, serum creatinine, D-dimer

Chest x-ray: ground glass appearance consistent with COVID-19

https://journals.lww.com/retinajournal/Fulltext/2022/03000/CHARACTERIZING_COVID_19_RELATED_RETINAL_VASCULAR.8.aspx

Sequelae: D-dimer?

A D-dimer test is a simple blood test that can **help your healthcare provider determine if you may have a blood clotting condition.**

- D-dimer has been observed to be very high in patients with COVID-19 with a 10-fold increase in D-dimer compared to interleukin-6 reflecting true thrombotic disease, possibly induced by cellular activation triggered by the virus.

https://journals.lww.com/retinajournal/Fulltext/2022/03000/CHARACTERIZING_COVID_19_RELATED_RETINAL_VASCULAR.8.aspx

Sequelae

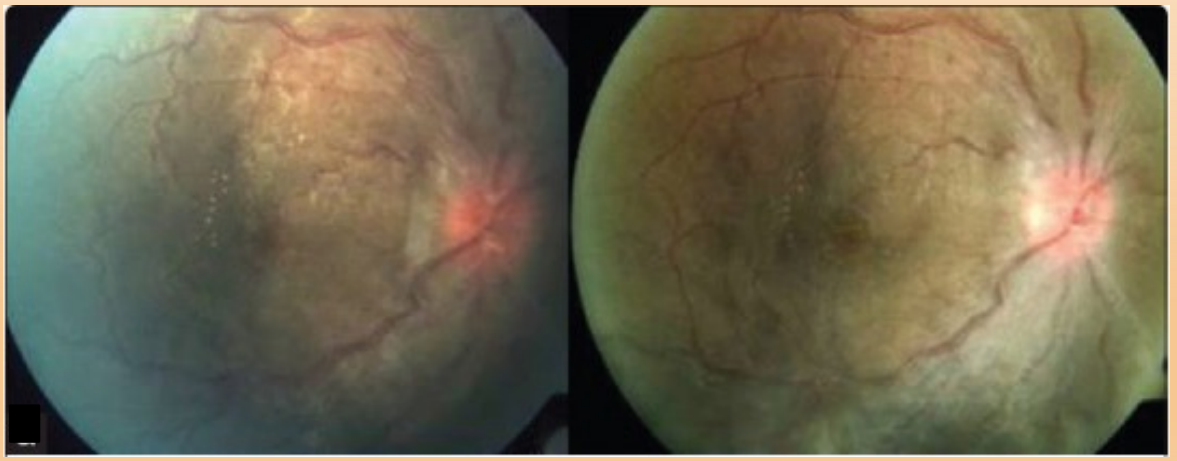
- Subsequent Covid-19 Immunoglobulin test
  - Returned positive for IgG against Novel Coronavirus 2019
    - suggestive of past infection of COVID-19.

    - Based on the above observations, a presumptive diagnosis of CRVO possibly secondary to COVID-19 infection was made

https://journals.lww.com/retinajournal/Fulltext/2022/03000/CHARACTERIZING_COVID_19_RELATED_RETINAL_VASCULAR.8.aspx

Management

- The patient was given Ranibizumab
- On one-month follow up, significant resolution was observed
- BCVA OD 20/60



Resolution of signs after the first injection on the left and further resolution after the second injection in the image on the right.

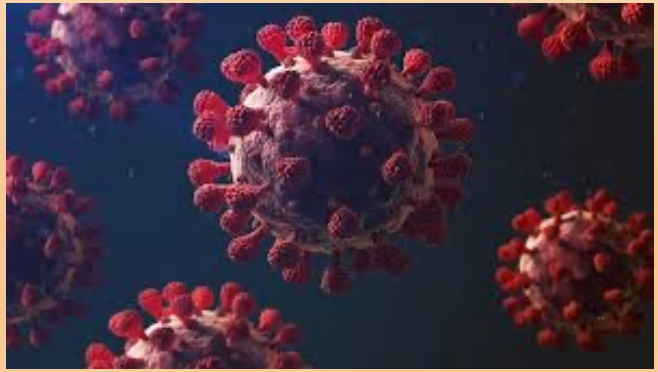
Resolving disc edema after the first injection (L) and resolved peripheral retinal hemorrhages after the second injection (R)

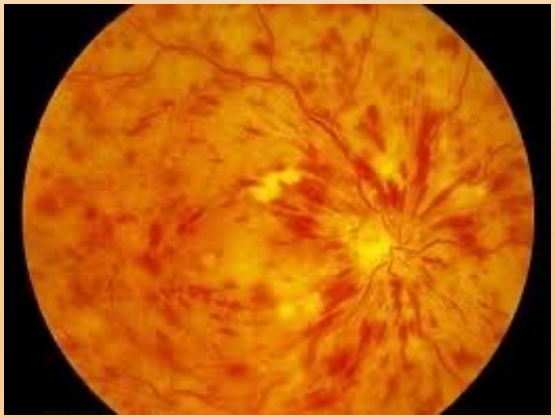
Dramatic resolution of CME after the first injection (L) near total resolution of CME with mild RPE atrophy and ellipsoid layer thinning (R)

Imaging after second injection

Summary:

- Eyes of patients with COVID-19 infection are at risk for vascular occlusive events and that visual symptoms may occur even with milder forms of systemic viral infection.





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