

DOUBLE TROUBLE:
CAN BE HARD TO CHEW

RICHARD YI

GEORGIA RETINA

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NO FINANCIAL RELATIONSHIPS TO DISCLOSE

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Reason for Visit:
Decreased vision OU

History of Presenting Illness:
- 71-year-old male
- Decreased vision OU over 1-2 weeks: "looking through plastic"
- Described as intermittent episodes

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Reason for Visit:
Decreased vision OU

History of Presenting Illness:
- 71-year-old male
- Decreased vision OU over 1-2 weeks: "looking through plastic"
- Described as intermittent episodes

Was evaluated in ED:
- MRI brain, Carotid U/S and EKG all normal

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PAST MEDICAL HISTORY:
HYPERTENSION, ATRIAL TACHYCARDIA

PAST OCULAR HISTORY:
MILD CATARACTS OU

SYSTEMIC MEDICATIONS:
BABY ASPIRIN

OCULAR MEDICATIONS:
NONE

FAMILY HISTORY:
UNREMARKABLE

SURGICAL HISTORY:
NONE

SOCIAL HISTORY:
EMPLOYER OF PRINTING COMPANY
FORMER SMOKER (QUIT 44 YEARS PRIOR)

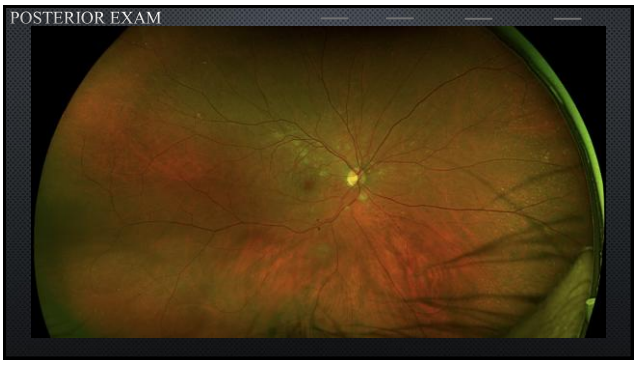
ALLERGIES:
NONE

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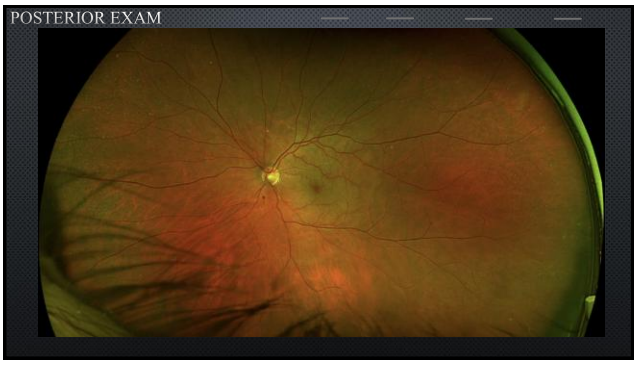
ANTERIOR EXAM

	Right Eye	Left Eye
Visual Acuity:	20/40	20/25
Pinhole:	20/25	NI
Pupils:	5-3 mm, round, no APD	5-3 mm, round, no APD
Extraocular Movement:	Full	Full
Intraocular Pressure:	9	9
Lids and Lashes:	Normal	Normal
Conjunctiva:	Clear, quiet	Clear, quiet
Cornea:	Clear	Clear
Anterior Chamber:	Formed, quiet	Formed, quiet
Iris:	Normal architecture	Normal architecture
Lens:	Trace NS	Trace NS
Vitreous:	PVD	PVD

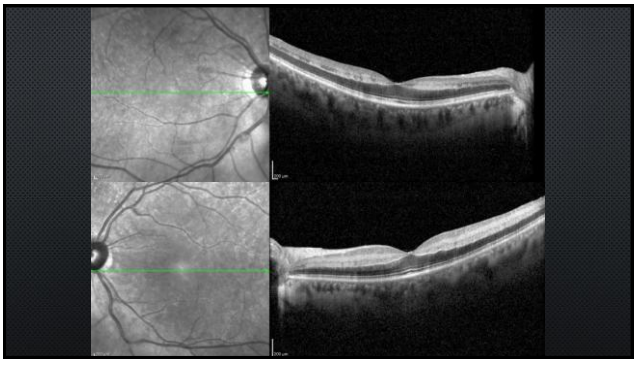
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DIFFERENTIAL DIAGNOSIS

- 71-year-old male with retinal whitening and inner/middle hyperreflectivity OU

Thoughts?

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DIFFERENTIAL DIAGNOSIS

- 71-year-old male with retinal whitening and inner/middle hyperreflectivity OU

OD: PAMM OS: CRAO

Bilateral thromboembolic disease
Retinal vasculitis
Hypotension
Trauma
Infectious necrotizing retinitis?
Retinal infiltrative disease?

Next steps?

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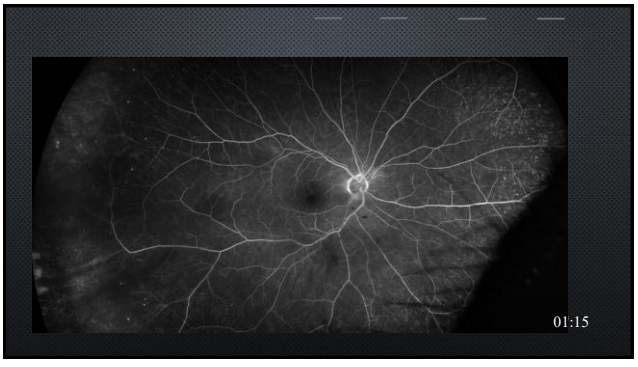
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RETINAL ARTERY OCCLUSION



https://eyewiki.aao.org/File:Cilioretinal_artery_sparing.jpg

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RETINAL ARTERY OCCLUSION

OBJECTIVES:
- Review of Retinal Artery Occlusion Spectrum
- Work up of unusual RAOs
- Management of RAOs

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INTRODUCTION

Cherry-red spot?

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INTRODUCTION

1987: Term "cherry-red spot" was introduced by Bernard Sachs (neurologist) of a child's fundus with lipid storage disorder

Description was also used to describe the retina by Herman Knapp (ophthalmologist)

Leavitt, J. A., & Kerkari, S. (2007). The "Cherry-Red" Spot. *Pediatric Neurology*, *37*(1), 74–77.doi:10.1016/j.pediatrneurol.2007.04.011

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INTRODUCTION

What causes a "cherry-red spot"?

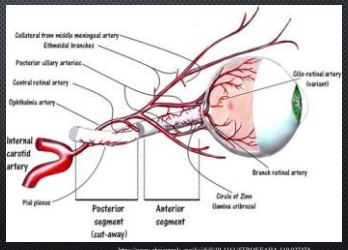
First some anatomy…

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INTRODUCTION

- Central retinal artery = 1st branch of ophthalmic artery
- Cilio-retinal artery = branch short posterior artery (separate branch of ophthalmic artery)

NOTE: fovea is devoid of ganglion cells and receives blood from the choroid



https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.119.027478

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INTRODUCTION

Causes of "cherry-red spot" can vary…

- **Vascular**
- Metabolic storage diseases
  - ❖ Tay-Sachs
- Inflammatory
- Drug toxicity
  - ❖ Quinine, carbon monoxide
- Trauma

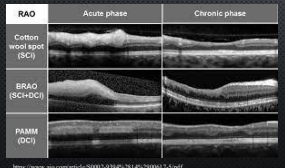
https://eyewiki.aao.org/Cherry-red_spot

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PATHOPHYSIOLOGY

Occlusion results in ischemic environment of the inner retina

Irreversible damage thought to occur after ~105 minutes of occlusion



https://www.ajo.com/article/S0002-9394%2814%2900861-5/pdf

Acutely – appears edematous with retinal whitening

Chronically – becomes atrophic

https://eyewiki.aao.org/Retinal_Artery_Occlusion
https://eyewiki.aao.org/Cherry-red_spot
Hayreh SS, Zimmerman MB, Kimura A, Sanon A. Central retinal artery occlusion. Retinal survival time. *Exp Eye Res*. 2004 Mar;78(3):723-36.
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SYMPTOMS AND SIGNS

- Acute, painless, vision loss
- Blurry vision
- Visual disturbance

"Cherry-red spot" with retinal whitening

- May take hours to develop
- Source of occlusion? (e.g., emboli)

NOTE: with time (~weeks) → edema resolves and retina becomes more atrophic in appearance

- Pale nerve, attenuate vessels, pigmented mottling, shunt vessels, sequelae (NV)

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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SPECTRUM

Extent of artery occlusion
- CRAO
- BRAO
- OAO
- OIS
- PAMM

Even when artery occlusion is confirmed… need to figure what caused the blockage (emboli vs thrombus vs vasculitis process vs spasm vs toxicity vs other)

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DIAGNOSTIC APPROACH

- OCT
  - ❖ Hyper-reflectivity in acute; atrophy is chronic
- FA
  - ❖ Delayed filling in affected areas
  - ❖ NOTE: may not see COMPLETE lack of filling
- ERG
  - ❖ Diminished B wave



https://www.aao.org/patients/retinal-diseases/32/retinal-artery-occlusion

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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DIAGNOSTIC APPROACH

Labs:
- CBC
- Inflammatory markers (ESR, CRP)
  - ❖ **Giant cell work up?**

In younger patients need to be broad…
- Hypercoagulable work up
- Infectious
- Autoimmune
- Lipid panel
- A1c

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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DIAGNOSTIC APPROACH

Images:
- Neuroimaging (MRI brain +/- orbits)
- Carotid artery evaluation
- Echocardiogram

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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MANAGEMENT

Stroke management – modify risk factors
- ❖ May vary depending on secondary causes…

- Ocular massage
- Anterior paracentesis
- Carbogen therapy (carbon dioxide + oxygen)

Overall limited efficacy

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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MANAGEMENT

Role for tPA? EAGLE study

Central retinal artery occlusion: local intra-arterial fibrinolysis versus conservative treatment, a multicenter randomized trial

Martin Schumacher [1], Dieter Schmidt, Bernhard Jurklies, Christine Gall, Isabel Wanke, Claudia Schmoor, Herbert Maier-Lenz, Laszlo Solymosi, Hartmut Brueckmann, Aljoscha S Neubauer, Armin Wolf, Nicolas Feltgen, EAGLE-Study Group

Collaborators, Affiliations + expand

PMID: 20609991 DOI: 10.1016/j.ophtha.2010.03.061

Do not recommend local intra-arterial tPA

Schumacher M, Schmidt D, Jurklies B, Gall C, Wanke I, Schmoor C, Moser-Lenz H, Kolymosi L, Bienzeisler M, Neubauer AS, Wolf A, Feltgen N; EAGLE Study Group. Central retinal artery occlusion: local intra-arterial fibrinolysis versus conservative treatment, a multicenter randomized trial. Ophthalmology. 2010 Jul;117(9):1367-75.e1. doi: 10.1016/j.ophtha.2010.03.061. PMID: 20609991.

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MANAGEMENT

Role for hyperbaric oxygen therapy?


Oxygen therapy in patients with retinal artery occlusion: A meta-analysis

Xiaodong Wu, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Validation, Visualization, Writing – original draft, Writing – review & editing,[1] Shuangshuang Chen, Conceptualization, Data curation, Investigation, Project administration, Resources, Visualization,[1] Shizun Li, Formal analysis, Investigation, Software, Supervision,[1] Ji Zhang, Methodology, Resources, Supervision,[1] Di Luan, Data curation, Validation, Visualization,[1] Shoucai Zhao, Supervision, Writing – review & editing,[1] Zhaohu Chu, Formal analysis, Validation, Writing – review & editing,[1] Yang Xu, Funding acquisition, Resources, Supervision, Writing – review & editing[2,3]

Asaf Achiron, Editor

Possibly a promising option


Case Series | Open Access

Volume 2019 | Article ID 9765938 | https://doi.org/10.1155/2019/9765938

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Hyperbaric Oxygen Therapy in Retinal Arterial Occlusion: Epidemiology, Clinical Approach, and Visual Outcomes

Ana Sofia Lopes, Rita Basto, Susana Henriques, Luísa Colaço, Filomena Costa e Silva, Isabel Prieto, and Francisco Guerreiro

Department of Ophthalmology of Professor Doutor Fernando Fonseca E.P.E. Hospital (Amadora-Sintra), Lisbon, Portugal

Underwater and Hyperbaric Medicine Center, Armed Forces Hospital—Lisbon Pole, Lisbon, Portugal

Wu X, Chen S, Li S, Zhang J, Luan D, Zhao S, Chu Z, Xu Y. Oxygen therapy in patients with retinal artery occlusion: A meta-analysis. PLoS One. 2018 Aug 29;13(8):e0203154. doi: 10.1371/journal.pone.0203154. PMID: 30157266; PMCID: PMC6115716.

Ana Sofia Lopes, Rita Basto, Susana Henriques, Luísa Colaço, Filomena Costa e Silva, Isabel Prieto, Francisco Guerreiro, "Hyperbaric Oxygen Therapy in Retinal Arterial Occlusion: Epidemiology, Clinical Approach, and Visual Outcomes", Case Reports in Ophthalmological Medicine, vol. 2019, Article ID 9765938, 5 pages, 2019. https://doi.org/10.1155/2019/9765938

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MANAGEMENT

Role for hyperbaric oxygen therapy?

- Hyperoxygenation and reduction of gas bubble size in bloodstream
- Increasing supply via collateral and choroidal circulations to cover the metabolic demands of retinal cells, while the central retinal artery re-cannulates

Contraindications:

- Pneumothorax, pregnancy, epilepsy, severe claustrophobia, acute infection, uncontrollably high fever

Wu X, Chen S, Li S, Zhang J, Luan D, Zhao S, Chu Z, Xu Y. Oxygen therapy in patients with retinal artery occlusion: A meta-analysis. PLoS One. 2018 Aug 29;13(8):e0203154. doi: 10.1371/journal.pone.0203154. PMID: 30157266; PMCID: PMC6115716.

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PROGNOSIS

Visual prognosis guarded

- Usually severe enough to cause long term changes
- Presence of functional cilioretinal artery = better outlook

Sequelae: neovascularization

- 18% prevalence with mean onset of 8.5 weeks

https://eyewiki.aao.org/Retinal_Artery_Occlusion

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DIFFERENTIAL DIAGNOSIS

- 71-year-old male with retinal whitening and inner/middle hyperreflectivity OU

OD: PAMM

Bilateral thromboembolic disease
Retinal vasculitis
Hypotension
Trauma
Infectious necrotizing retinitis?
Retinal infiltrative disease?

OS: CRAO

The patient shared history of jaw claudication, noted while chewing pork rinds. Started around vision changes

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WORK UP

- Sent to ED for high suspicion for GCA
- Recommended workup:
  - ESR, CRP, CBC
  - Complete stroke work up (neuroimaging, EKG, echocardiogram, carotid US)
  - Consult neurology
  - Start high dose methylprednisolone (250 mg q6 hours)
  - Temporal artery biopsy

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WORK UP

- Neuroimaging normal
- Echo normal
- Normal ESR (15 mm/Hr) and CRP (<0.5 mg/dL)
- Cardiolipin and beta-2 glycoprotein negative

CBC – thrombocytosis (platelets: 428, normal is 150-400)

Temporal artery biopsy – granulomatous arteritis

IV methylprednisolone (1000 mg daily) for 5 days → PO prednisone (60 mg daily)

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

1890 – Bayard Hutchinson used term "thrombotic arteritis"
- 80-year-old with notable temple pain

1932 – Horton et al coined the term temporal arteritis (Mayo)
- Two cases with symptoms of fever, weakness, headache, pain, difficulty chewing
- Biopsy revealing inflammation

1941 – Gilmour described presence of giant cells as part of disease

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Hunder GG. The early history of giant cell arteritis and polymyalgia rheumatica: first descriptions to 1970. *Mayo Clin Proc*. 2000;81(8):1071-1083. doi:10.4065/81.8.1071

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

- Generalized granulomatous inflammation of medium/large-sized vessels
- Elderly, median age 75.8 years
- Females (2-6x) > Males
- More common of Caucasian of northern European descent
- Risk factors: smoking, low BMI, early menopause, adrenal hypofunction

Hayreh SS, Podhajsky PA, Raman R, Zimmerman B. Giant cell arteritis: Validity and reliability of various diagnostic criteria. *Am J Ophthalmol*. 1997;123:285-96.
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Salvarani C, Crowson CS, O'Fallon WM, Hunder GG, Gabriel SE. Reappraisal of the epidemiology of giant cell arteritis in Olmsted County, Minnesota, over a fifty-year period. *Arthritis Rheum*. 2004;51(2):264-268. doi:10.1002/art.20237

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Systemic symptoms and signs
- 56% - headache
- 52% - weight loss
- 52% - jaw claudication
- 38% - malaise
- 26% - fever
- 20% - abnormal temporal artery
- 18% - scalp tenderness
- 16% - neck pain
- 13% - anemia

Giant cell arteritis: validity and reliability of various diagnostic criteria

S S Hayreh [1], P A Podhajsky, R Raman, B Zimmerman

Affiliations + expand

PMID: 9063237 DOI: 10.1016/s0002-9394(14)70123-0

NOTE: 21.2% of patients had visual loss with no other systemic symptoms (temporal artery biopsy confirmed)

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Ocular symptoms and signs:
- 98% - vision loss
- 81% - AAION
- 31% - amaurosis fugax
- 14% - CRAO
- 8% - eye pain
- 7% - PION
- 6% - diplopia

Ocular manifestations of giant cell arteritis

S S Hayreh [1], P A Podhajsky, B Zimmerman

Affiliations + expand

PMID: 9559737 DOI: 10.1016/s0002-9394(99)80192-5

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

ESR
- Influenced by age and gender (higher levels with age and female gender)
- Sensitivity (76-92%) and specificity (92%)

CRP
- Can reach abnormal levels within 4-6 hours, more responsive to treatment than ESR
- Not influenced as much to age, sex, other hematologic factors
- Sensitivity (98-100%) and specificity (79-83%)

Platelets (thrombocytosis)
- 60% had thrombocytosis
- Sensitivity (60%) and specificity (98%)

Hayreh SS, Podhajsky PA, Raman R, Zimmerman B. Giant cell arteritis: Validity and reliability of various diagnostic criteria. *Am J Ophthalmol*. 1997;123:285-96.
Parikh M, Miller NR, Lee AG, et al. Prevalence of screened "creutzfeldt-jakob disease" protein within an elevated erythrocyte sedimentation rate in biopsy-proven giant cell arteritis. *Ophthalmology*. 2006;113(10):1842-1845. doi:10.1016/j.ophtha.2006.04.031
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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Temporal artery biopsy – "gold standard" for diagnosis
- Possible for false negatives (5-15%) due to skip lesions
- Sometimes bilateral biopsy is necessary

Ancillary tests:
Color doppler US

MRI/MRA

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González-Gay MA, García-Porrúa C, Llorca J, González-Louzao C, Rodríguez-Ledo P. Biopsy-negative giant cell arteritis: clinical spectrum and predictive factors for positive temporal artery biopsy. *Semin Arthritis Rheum*. 2001;30(4):249-256. doi:10.1053/sarh.2001.20630

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GIANT CELL ARTERITIS (TEMPORAL ARTERITIS)

Management

High dose steroids

Trial of Tocilizumab in Giant-Cell Arteritis

Authors: John H. Stone, M.D., M.P.H., Katie Tuckwell, Ph.D., Sophie Dimonaco, M.Sc., Micki Klearman, M.D., Martin Aringer, M.D., Daniel Blockmans, M.D., Ph.D., Elisabeth Brouwer, M.D., Ph.D., +8 , and Neil Collinson, Ph.D. Author Info & Affiliations

Published July 27, 2017 | N Engl J Med 2017;377:317-328 | DOI: 10.1056/NEJMoa1613849 | VOL. 377 NO. 4

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Tocilizumab

- Inhibition of IL-6
- Sustained remission with steroid taper + toci versus steroid taper + placebo
- Can be associated with infection, gastric perforation, abnormal labs

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SUMMARY

- Retinal artery occlusion can present in spectrum
- Warrants stroke work up (brain, carotids, heart)
- Additional work up warranted in some cases (pediatrics – coagulopathy ; geriatrics – giant cell arteritis)
- TIMING is KEY

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