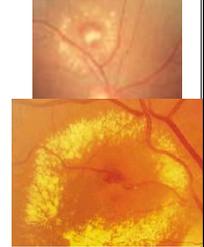


Introduction to Retinal Arteriolar Vascular Disease (including hypertensive retinopathy)

Leo Semes, OD
Professor, UAB Optometry

Hypertensive retinopathy review

- Retinal vessel narrowing triples the risk of CHD in patients with hypertension (HTN) and increased lipid levels!
- Generalized sclerosis (increased ALR) also occurs as does focal constriction.
- Findings may also include
 - flame-shaped nerve-fiber-layer hemorrhages,
 - cotton-wool spots,
 - exudative edema,
 - vessel sheathing,
 - **Macroaneurysm** →
 - vessel tortuosity [may be seen in normals, too]



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Hypertensive retinopathy review

- Crossing changes are common (Gunn's sign).
- Papilledema in advanced cases (significantly associated with vein occlusions).
- Choroidal damage
 - Elschnig spots
 - Seigrest streaks, coalesced areas of chorioretinal atrophy.
- Asymmetric presentation is indicative of carotid obstruction.

28

Management/Treatment

- There is no ocular treatment for hypertensive retinopathy, *per se*; control the systemic disease.
- Management of the consequences of Hypertensive retinopathy would include treatment of the cystoid macular edema resulting from vein obstruction (occlusion).

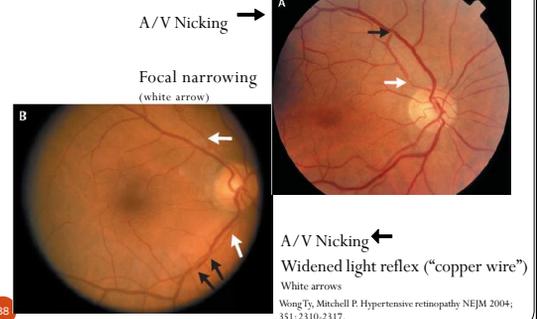
29

Differential Diagnoses

- Diabetic retinopathy
- Retinal venous obstruction
- Hyperviscosity syndromes
- Congenital hereditary retinal arterial tortuosity
- Ocular ischemic syndrome
- Radiation retinopathy

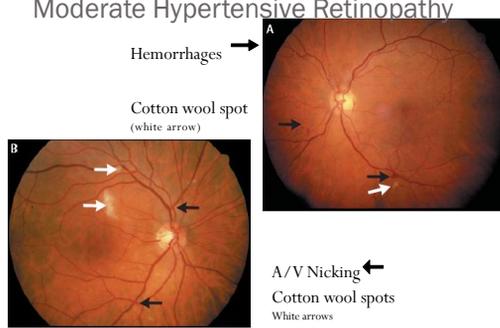
30

Mild Hypertensive Retinopathy



38

Moderate Hypertensive Retinopathy



Hemorrhages →

Cotton wool spot (white arrow)

A/V Nicking ←

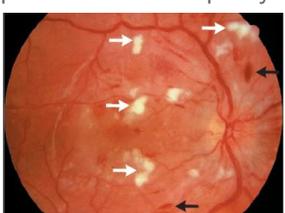
Cotton wool spots

White arrows

Wong Ty, Mitchell P. Hypertensive retinopathy NEJM 2004; 351: 2310-2317.

39

Malignant Hypertensive Retinopathy



Hemorrhages →

Cotton wool spots (white arrows)

Disc swelling

Wong Ty, Mitchell P. Hypertensive retinopathy NEJM 2004; 351: 2310-2317.

40

What does all of this mean?

I. Pathophysiology

Reflective of retinal circulatory changes in response to elevated BP

Vascular response to elevated BP is increased regulatory tone (autoregulation) seen clinically as generalized narrowing of the arterioles

Persistently elevated BP leads to thickening of the intimal walls of the arterioles with hyaline degeneration (sclerotic changes) leading to:

- focal arteriolar narrowing
- changes in the A/V crossings
- alterations of the light reflex

41

What does all of this mean?

I. Pathophysiology (con't)

In the exudative stage, disruption of the BB barrier occurs secondary to

- Smooth-muscle & endothelial cell necrosis
- Blood and exudate visible
- Retinal ischemia*

The retinal manifestations include

Hemorrhage

Exudate

Cotton-wool spots & ONH swelling (rarely)

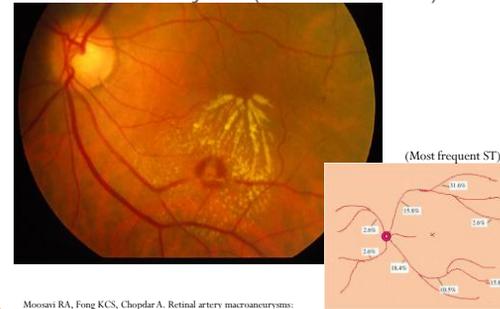
Macroaneurysms (in chronic HT) →

BRVO (in chronic HT)



42

Macroaneurysm (in chronic HT)



(Most frequent ST)

Moosavi RA, Fong KCS, Chopdar A. Retinal artery macroaneurysms: clinical and fluorescein angiographic features in 34 patients Eye (2006) 20, 1011-1020.

43

What does all of this mean?

II. Relationship to systemic blood pressure

- Arteriolar narrowing and A/V nicking are present after 6-8 years of elevated BP (suggesting a response to chronically elevated BP)
- Other signs such as narrowing, hemorrhages, macroaneurysms and CWSs are related to current but not previous hypertension and may represent a marker for the future development of HT

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What does all of this mean?

III. Risk of Stroke

- Patients with hypertensive retinopathy (esp. narrowing, hemorrhages, macroaneurysms and CWSs) were 2X – 3X more likely to have stroke (fatal and non-fatal) than those without HR

IV. Risk of Coronary Heart Disease (CHD)

- Arteriolar narrowing significantly increases risk of having CHD (2X – 6X)

45

Recommended clinical management

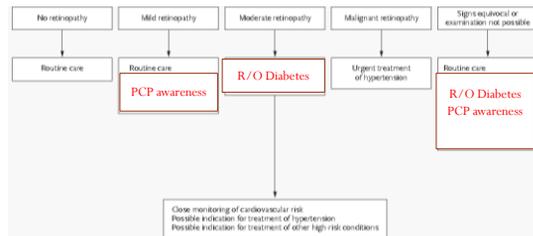
Table 1. Classification of Hypertensive Retinopathy on the Basis of Recent Population-Based Data.

Grade of Retinopathy	Retinal Signs	Systemic Associations ^a
None	No detectable signs	None
Mild	Generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, opacity ("copper wiring") of arteriolar wall, or a combination of these signs	Modest association with risk of clinical stroke, ^{41,42} subclinical stroke, ⁴³ coronary heart disease, ^{44,45} and death ⁴⁶
Moderate	Hemorrhage (blot, dot, or flame-shaped), microaneurysms, cotton-wool spot, hard exudate, or a combination of these signs	Strong association with risk of clinical stroke, ^{41,42} subclinical stroke, ⁴³ cognitive decline, ⁴⁴ and death from cardiovascular causes ⁴⁵
Malignant	Signs of moderate retinopathy plus swelling of the optic disk [†]	Strong association with death

^a A modest association is defined as an odds ratio of greater than 1 but less than 2. A strong association is defined as an odds ratio of 2 or greater.
[†] Anterior ischemic optic neuropathy, characterized by unilateral swelling of the optic disk, visual loss, and sectorial visual-field loss, should be ruled out.

46

Recommended clinical management



47

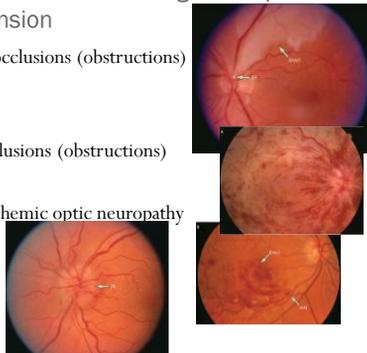
Consequences of hypertension in the eye

- Hypertensive retinopathy, choroidopathy and optic neuropathy
- Anterior ischemic optic neuropathy
- Venular occlusions (obstructions)

48

Sight- and vision-threatening consequences of hypertension

- Arteriolar occlusions (obstructions)
- Venular occlusions (obstructions)
- Anterior ischemic optic neuropathy



49

(?)Retinal Artery Obstructions (Occlusion)

- Although systemic diseases are found commonly in patients who suffer from retinal artery obstruction, the true cause and effect may not be clear.
- About 60% of patients have concurrent systemic arterial hypertension, and diabetes is present in 25%.
- Systemic evaluation reveals no **definite cause** for the obstruction in over 50% of affected patients.
- Potential embolic sources are found in less than 40% of cases

50

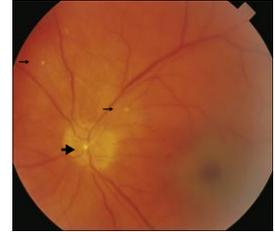
(?)Retinal Artery Obstructions (Occlusion)

- The most common hemodynamically significant association is ipsilateral carotid artery disease, which is present in about 30% of affected patients.
- Carotid noninvasive testing should be considered for all patients who have central retinal artery obstruction, although this is rare <50 years of age.
- An embolic source from the heart is present in less than 10% of patients with central retinal artery obstruction; however, echocardiography and Holter monitoring should be performed, especially in younger (<50) patients.

51

(?)Retinal Artery Obstructions (Occlusion)

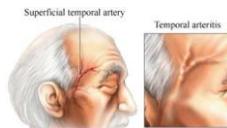
- Acute central retinal artery obstruction. Secondary to an embolus at the lamina cribrosa →.
- Note two other emboli in the superior retinal vessels →.
- Ipsilateral carotid artery disease was present.



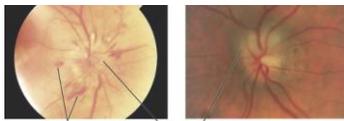
52

Temporal arteritis, Giant-cell arteritis (TA, GCA)

- Clinical picture which accompanies HA, vision decrease)



<http://google.com/images>



retinal hemorrhages disc edema
Giant cell arteritis. (from Kaiser PK, Friedman NJ, Pineda R, II. The Massachusetts Eye and Ear Infirmary illustrated manual of ophthalmology. 2nd edition. China: Saunders; 2004

<http://www.herbalcureindia.com/beauty-tips/images/temporal-arteritis.jpg>

53

Temporal arteritis (GCA) – clinical features

- (1990 American College of Rheumatology criteria)
- 3 of the following 5 items must be present (sensitivity 93.5%, specificity 91.2%):
 - Age > 50 years
 - New-onset headache or localized head pain
 - Temporal artery tenderness to palpation or reduced pulsation
 - Erythrocyte sedimentation rate (ESR) > than 50 mm/h (ELEVATED)
 - Abnormal arterial biopsy (necrotizing vasculitis with granulomatous proliferation and infiltration)

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ESR Normal ranges

Adults (Westergren method):

- Men under 50 years old: less than 15 mm/hr
- Men over 50 years old: less than 20 mm/hr
- Women under 50 years old: less than 20 mm/hr
- Women over 50 years old: less than 30 mm/hr

55

Temporal arteritis (GCA) – clinical features

- Present in < 5% of cases
- Rule OUT temporal arteritis all patients who have a central retinal artery obstruction.
- STAT erythrocyte sedimentation rate (ESR) and if it is elevated OR if clinical suspicion exists, corticosteroid therapy and a temporal artery biopsy are considered.
- Oral steroid therapy may be instituted “prophylactically.”

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Guidelines for oral steroid dosing in GCA (TA)

- Starting dose is usually 60-80 mg/d (prednisone)
- Methylprednisolone @ 250-1,000 mg IV daily X 3 days when acute visual changes secondary to giant cell arteritis are present [requires hospitalization]
- Precautions
 - Polymyalgia rheumatica in the presence of equivocal GCA
 - BUT, in the presence of **STRONGLY SUGGESTIVE** symptoms and signs, **DO NOT DELAY** treatment. Obtain TA biopsy ≤ 10 days

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Clinical course

- Symptoms improve rapidly
 - (headache, lethargy) disappear in 36-72 hours
 - ESR elevation and ischemic manifestations (eg, temporal headache, jaw claudication, localized temporal artery inflammation) diminish in several days.
 - The temporal artery pulse may not return, and visual loss may be permanent.
 - And there is a 50% risk in the fellow eye.
- If the patient shows no significant improvement in a week, consider an alternative diagnosis (typically polymyalgia rheumatica; for which there may be ongoing low-dose steroid treatment)

58

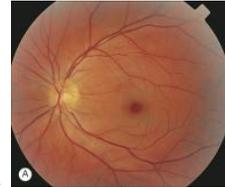
Vision loss and GCA

- ~ 20% of patients have no systemic symptoms
- Conversely, ~ 25% of patients with TA continue to have visual acuities of 20/40 or better.

59

Central Retinal Arterial Obstruction

- ≡ An abrupt diminution of blood flow through the central retinal artery severe enough to cause ischemia of the inner retina.
- Classic presentations
 - Abrupt, painless, severe loss of vision. (20/800 or worse)
 - Cherry-red spot.
 - Box-carring of blood flow in the retinal vessels.
 - Ischemic retinal whitening of the posterior pole.



37YO w/ 3-hr Hx of VA loss, VA = 20/60; note subtle whitening of RNFL

61

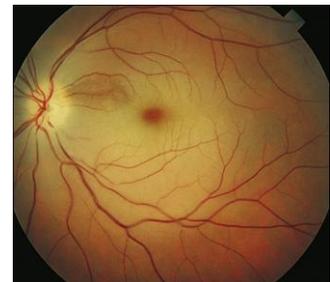
Central Retinal Arterial Obstruction

- 37YO w. 3-hr Hx of VA loss;
At 24 hours S/P: VA = HM

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Ophthalmic presentation with cilioretinal aa sparing

- Note that the papillomacular bundle is perfused.
- The choroidal vasculature is somewhat visible inferiorly but not in the posterior pole



63

Clinical course

- 4–6 weeks after obstruction, retinal whitening resolves
- Optic disc pallor develops
- Arterial collaterals may form on the optic disc.
- No foveolar light reflex is apparent, and fine changes in the retinal pigment epithelium may be visible.
- Vision is not usually restored

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Clinical course

- A 26YO male, diabetic
- CRAO caused by a platelet-fibrin embolus.



65

Clinical course

- Secondary ocular neovascularization is not uncommon after CRAO.
- Neovascularization of the optic disc occurs in 2% of CRAO.
- Vitreous hemorrhage may ensue.
- Iris neovascularization (INV) – 18% (with many of these eyes going on to neovascular glaucoma)
- Anti-VEGF injection appears to reduce the risk of neovascular glaucoma moderately.



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Healthy 37YO M

- 3-hour history of visual loss (VA 20/60).

A: Retinal whitening is very subtle and the retinal vessels appear normal.



(B) FA reveals abnormal arterial filling. (confirming CRAO)

Central Retinal Arterial Obstruction

- Associated features
 - Amaurosis fugax.
 - Visible embolus (25%).
 - Carotid artery disease (33%).
 - Giant cell arteritis (5%).
 - Neovascularization of the iris (18%).
 - Arterial collaterals on the optic disc.

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C) The same eye 24 hours later.

Despite intravenous urokinase, VA = HM

- Intense retinal whitening
- Cherry-red spot
- Note the interruption in the blood column of the retinal arteries.



Central Retinal Arterial Obstruction – Epidemiology

- Rare but potentially devastating visually with strong association to systemic vascular disease.
- 1 in 10,000 outpatient visits
- Men > women (2:1)
- Mean age at onset ~ 60 years (10- 80)
- Bilateral involvement: 1–2% of cases.

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Central Retinal Arterial Obstructions

- Etiology (proposed)
 - Thrombus formation at or just proximal to the lamina cribrosa.
 - Atherosclerosis is implicated as the inciting event in most cases, although congenital anomalies of the central retinal artery, systemic coagulopathies, or low-flow states from more proximal arterial disease may also be present and increase risk.

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Retinal Arterial Obstruction – Pathogenesis

- Thrombotic (solid mass of platelets / fibrin locally formed in the vessel)
- Or embolic (plaque, fat, etc. carried distally or part of a thrombus)

MOST EMBOLI ARISE FROM THROMBI; BUT MAY ORIGINATE IN THE HEART OR CAROTID AND BREAK OFF TO MIGRATE DOWNSTREAM AND LODGE IN THE OPHTHALMIC CIRCULATION

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Retinal Arterial Obstruction – Pathogenesis

- Sources & various types of emboli are similar in CRAO and BRAO (e.g., carotid / cardiac)
- BRAO is far more likely to be embolic than is a CRAO.
 - Over 2/3 of BRAO are caused by emboli
 - Less than one third of CRAO result from emboli.
- Rare but potentially devastating visually with strong association to systemic vascular disease.

73

Differential diagnoses for CRAO

- Single or multiple branch retinal artery obstruction
- Cilioretinal artery obstruction
- Severe *commotio retinae* (history of blunt trauma)
- Necrotizing herpetic retinitis

74

Systemic associations –CRAO

- About 60% of patients have concurrent systemic arterial hypertension
- Diabetes is present in 25%
- Potential embolic sources are found in less than 40% of cases.*
- The most common association (33%) = hemodynamically significant ipsilateral carotid artery disease.
- Temporal (giant-cell) arteritis in 5% of affected patients.
- Systemic evaluation reveals no definite cause for the obstruction in over 50% of affected patients.

75

Management of CRAO

- R/O GCA (TA) – ESR!
- Consider carotid Doppler studies
- Monitor for NV (closely)
 - If iris NV, or ONH NV, consult with retina specialist
- R/O, investigate for systemic associations listed above
- Immediate treatment for acute cases is often futile (retinal damage begins < 20 min w/o O₂)

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Acute CRAO measures

- Increase retinal oxygenation
- Increase retinal arterial blood flow
- Reverse arterial obstruction
- Prevent hypoxic retinal damage
- Temporal arteritis
 - treated emergently with high-dose oral prednisone.
 - Without therapy, the risk to the second eye is great.

77

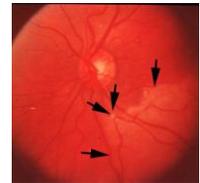
Ophthalmic manifestations (BRAO)

- Abrupt, painless loss of vision in the visual field corresponding to the territory of the obstructed artery is the typical history of presentation.
- Amaurosis fugax (25%) consistent with carotid disease.
- Bilateral presentation is rare. (but may mimic homonymous VF defects)
- Central VA not affected in 50%
- RAPD is common (depending on retinal involvement).

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BRAO (cont.)

- 2/3 are embolic in origin (generally visible)
- Emboli can originate anywhere proximal to the ophthalmic artery.

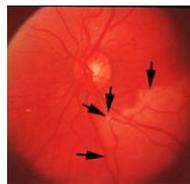


Photography by Dr. H. D. Riley
Indiana University

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BRAO (cont.)

- Risk factors reflect the vasculopathic mechanisms of cardiovascular disease.
 - predisposing family history
 - hypertension
 - elevated lipid levels,
 - cigarette smoking,
 - diabetes mellitus.
- There are 3 main types of retinal emboli
 - Cholesterol (Hollenhorst plaque)
 - Platelet-fibrin
 - Calcific

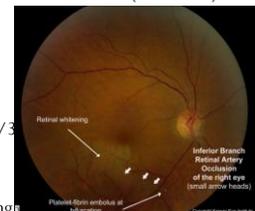


Photography by Dr. H. D. Riley
Indiana University

80

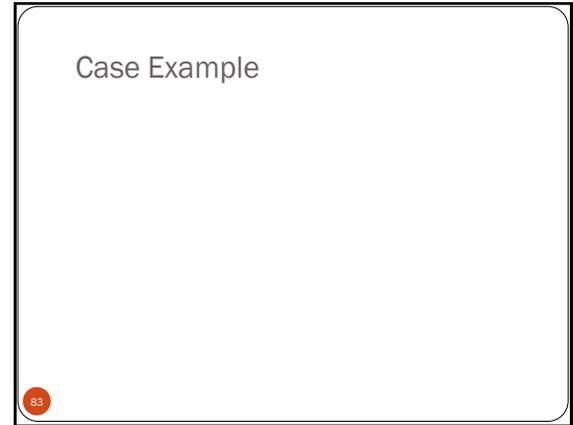
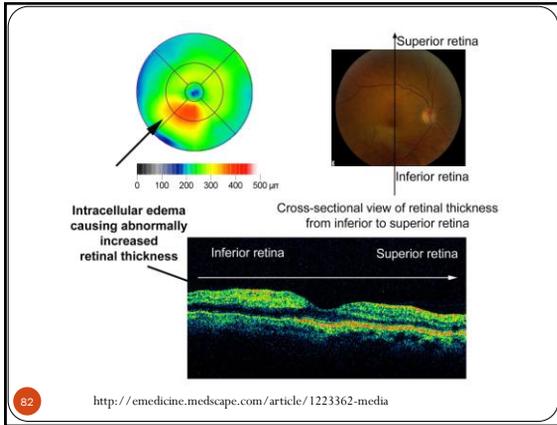
Ophthalmic manifestations (BRAO)

- Retinal whitening that corresponds to the areas of ischemia is the most notable finding.
- Retinal embolus visible (in 2/3 of cases).
- Flame hemorrhages and local areas of inner retinal whitening may at resemble scattered cotton-wool spots.



<http://emedicine.medscape.com/article/1223362-overview>

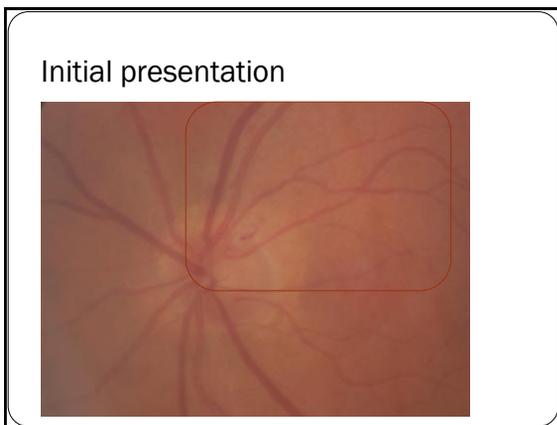
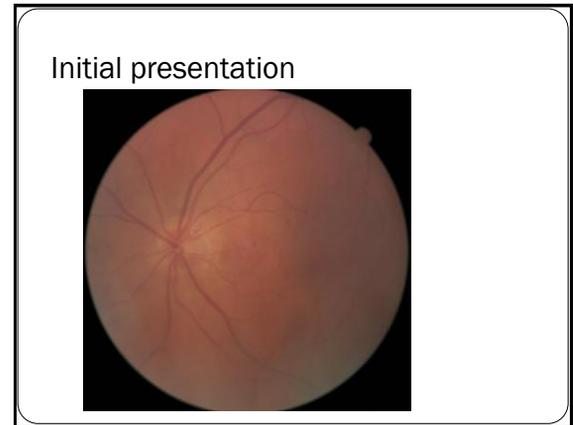
81



63 W/M with sparklers

- VA 20/20 in each eye
- Anterior segment evaluation – unremarkable for age
- DFE . . . (OS)

84

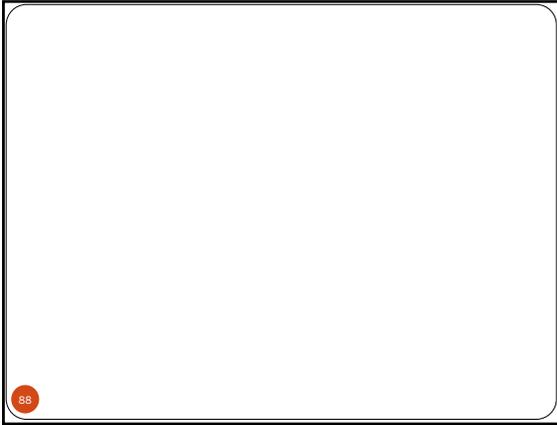


Follow-up at 3 weeks

Outcomes

- Sent to internist for evaluation
- Complained of dizziness, as well
- Carotid Doppler evaluation revealed obstruction of significant magnitude to recommend surgery
- Patient had L carotid endarterectomy < 6 wks following initial presentation

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Branch retinal artery obstruction Epidemiology

- Less common than CRVO
- Men > women (2:1) Ex., < 50 years, men = women)
- Mean age of affected patients is 60 years (range: teens to 70s).
- Most are in their 50s or 60s.
- OD (60%), OS (40%)
 - (greater possibility of cardiac or aortic emboli traveling to the right carotid artery).
- BRAO is more frequent in the temporal retinal circulation
 - (consistent with the greater blood flow to the macular retina).

Branch Retinal Artery Obstruction

- ≡ An abrupt diminution of blood flow through a branch of the central retinal artery severe enough to cause ischemia of the inner retina in the territory of the affected vessel.
- Classic presentations
 - Retinal whitening in the territory of the obstructed vessel.
 - Embolus (66%).
 - Visual field defect that corresponds to the territory of the obstructed vessels.



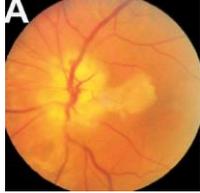
Superior hemi-branch retinal artery obstruction.
Note that the dual trunk of the central retinal artery obstruction has separated proximal to the lamina.

Where is the site of the obstruction?

Not all BRAO are alike!

I. Cilioretinal artery occlusion (CLRAO)

- From where does a CLRA originate?



- 3 distinct subtypes:
 - A. nonarteritic CLRAO alone
 - B. arteritic CLRAO associated with giant cell arteritis →
 - C. CLRAO associated with central retinal vein occlusion (CRVO)/hemi-CRVO

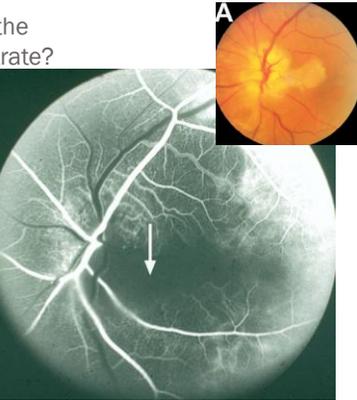
Note the presence of chalky white optic disc edema, which is diagnostic of arteritic anterior ischemic optic neuropathy. A combination of chalky white optic disc edema with CLRAO is diagnostic of giant cell arteritis.

Harshb SS, et al. Branch Retinal Artery Occlusion Natural History of Visual Outcome. Ophthalmology 2009;116:1188-1194.

What does the FA demonstrate?

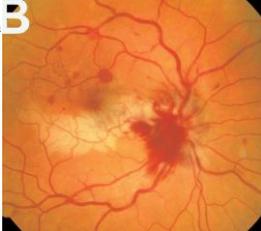
- Normal filling of CRA & lateral (nasal) SPCA
- Impaired filling of choroidal circulation to the ONH, CLRA & medial (temporal) SPCA, (↓)

*If this is an arteriolar obstruction, why is the venous circulation not filled?



Not all BRAO are alike!

- CLRAO associated with central retinal vein occlusion (CRVO)/hemi-CRVO



CLRAO associated with nonischemic central retinal vein occlusion.

Note the junction between the normal (upper) and infarcted retina lies in the foveal region.

Harshb SS, et al. Branch Retinal Artery Occlusion Natural History of Visual Outcome. Ophthalmology 2009;116:1188-1194.

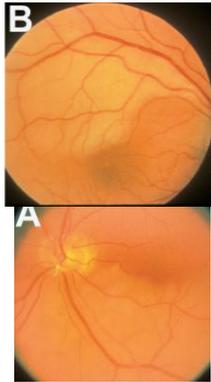
Branch retinal artery occlusion

What do you see as similar between these two presentations and what do you see as distinct?

-
-
-

- 2 subtypes:

- A. Permanent
- B. Transient



Hayreh SS, et al. Branch Retinal Artery Occlusion: Natural History of Visual Outcome. Ophthalmology 2009;116:1188-1194.

94

Branch retinal artery obstruction

- Associated features

- Carotid artery disease - Systemic evaluation indicated
- Cardiac valvular disease – ASAP
- Atherosclerotic disease

- And rarely,

- Cardiac myxoma, long-bone fracture, endocarditis, depot drug injection.
- Systemic clotting disorder or vasculitis.

95

Treatment / Management “B”RAO

- Local ocular massage to dislodge the clot distally; heroic efforts are not as critical as in CRAO, due to the preservation of central vision according to natural history.
- What happens to the outer retina?
- Due to systemic associations (carotid and cardiac disease, the patient will require systemic care).
- **Particular attention is paid to the ophthalmic consequences of CLRAO associated with giant-cell arthritis**

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Outcomes (BRAO)

- VF defect
- Majority (up to 80%) regain 20/40 VS in the affected eye without treatment
- Retinal neovascularization is uncommon; iris neo is very rare

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Combined artery and vein obstructions

- Acute painless severe vision loss
- Foveal vision may be spared (cherry red spot); WHY?
- Hemorrhages in 4 quadrants (consistent with CRVO)
- Associated systemic or local disease rule-outs include:
 - Collagen vascular disorders,
 - Leukemia,
 - Orbital trauma,
 - Retrobulbar injections,
 - Mucormycosis.
- Visual prognosis is generally poor
- Risk of iris neo is about 75%; which means risk of WHAT?

100

Combined artery and vein obstructions



- What clinical features can you identify?

- →
- →
- →
- →

101

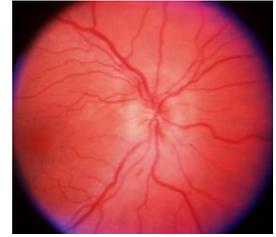
Risks of vascular occlusions

- Central Vein Occlusion
 - (0.1 – 0.4% of general populations > 40)
- Branch Vein Occlusion
 - (0.6 – 1.1% of general populations > 40)
- Risk is 5X greater for BRVO with HT (than w/o)
- Arteriolar occlusions – very low prevalence (< 0.1%) in general population

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AION (non-arteritic anterior ischemic optic neuropathy)

- Painless sudden vision loss
- Note disc swelling and narrowed arteries.
- Prevalence 2-10/100,000 (USA)

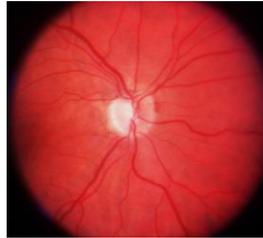


<http://emedicine.medscape.com/article/1216891-overview>

103

AION (non-arteritic anterior ischemic optic neuropathy)

- Note disc pallor with resolution of the acute phase.
- Vision loss is permanent and may be full field or altitudinal.
- Not commonly associated with life-threatening conditions, BUT
- Hypertension, 46.9%;
- Diabetes, 23.9%;
- Myocardial infarction, 11%



<http://emedicine.medscape.com/article/1216891-overview>

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Cilioretinal artery obstruction – review/quiz

- What do YOU think?
- May be isolated, present with CRVO or AION (anterior ischemic optic neuropathy)
- Mild nonischemic CRVO. Note retinal whitening just inferior to the fovea in the distribution of the cilioretinal artery. →



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LS

Systemic Conditions Associated with Retinal Artery Obstructions

- | | |
|--|--|
| <ul style="list-style-type: none"> • ATHEROSCLEROTIC CARDIOVASCULAR DISEASE • Ophthalmic artery plaques, stenosis, or dissection • Carotid artery plaques, stenosis, or dissection • Aortic plaques, stenosis, or dissection | <ul style="list-style-type: none"> • CARDIAC • Valvular disease (including rheumatic fever) • Ventriculoseptal defects • Papillary fibroelastoma • Cardiac myxoma • Mural thrombus • Arrhythmias • Subacute bacterial endocarditis |
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Systemic Conditions Associated with Retinal Artery Obstructions

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| <ul style="list-style-type: none"> • LOCAL OCULAR • Prepapillary arterial loops • Optic nerve drusen • Necrotizing herpetic retinitis • Orbital mucormycosis • Toxoplasmosis | <ul style="list-style-type: none"> • MISCELLANEOUS • Amniotic fluid embolism • Pancreatitis • Migraine • Pregnancy • Oral contraceptives • Cocaine abuse • Intravenous drug use |
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Systemic Conditions Associated with Retinal Artery Obstructions

- SYSTEMIC INFECTIONS
- Syphilis
- Mediterranean spotted fever
- Loiasis
- LOCAL TRAUMA
- Direct ocular compression
- Penetrating injury
- Retrobulbar injection
- Orbital trauma
- Retrobulbar hemorrhage
- Purtscher disease

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Systemic Conditions Associated with Retinal Artery Obstructions

- RADIOLOGIC AND MEDICAL PROCEDURES
- Angiography
- Angioplasty
- Chiropractic neck manipulation
- Depot corticosteroid injection
- SYSTEMIC VASCULITIS
- Susac's disease
- Systemic lupus erythematosus
- Polyarteritis nodosa
- Temporal arteritis
- Sneddon-Wilkinson disease
- Wegener's granulomatosis
- Inflammatory bowel disease
- Kawasaki's syndrome

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Systemic Conditions Associated with Retinal Artery Obstructions

- COAGULOPATHIES
- Antiphospholipid antibodies
- Protein C deficiency
- Protein S deficiency
- Antithrombin III deficiency
- Elevation of platelet factor 4
- ONCOLOGIC
- Metastatic tumors
- Leukemia
- Lymphoma

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