Retinal Manifestations of Systemic Disease

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## Retinal Plaques

- Several different types of plaques can often be visualized in the retinal vasculature
- Pt is typically elderly, has HTN, CAD, hypercholesterolemia/hyperlipidemia, and/ or atherosclerotic disease
- Often totally asymptomatic and found on routine exam

## RISK FACTORS

- Age
- HTN
- Vascular disease
- Past vascular surgery
- SMOKING
- High TOTAL cholesterol
- Men> women

## Prevalence

- Beaver Dam Eye Study: 1.3%
  - smoking, HTN and DM
  - 9x more likely after age 75 vs. 43-54
    - after 75, 3.1% prevalence
    - Equates to 1.2 million people with emboli 43-86
      - » 450,000 are 75-86
    - Fatal stroke 3x as likely over 8 years in pts with emboli, adjusting for other factors
  - OD>OS
  - Bilateral very infrequently

## Prevalence

- Blue Mountain Eye Study1.4%
  - HTN, smoking, Vascular disease
- LA Latino Eye Study: 0.4%
  - Smoking, CAD, h/o MI, HTN
- Singapore Eye Study: 0.6%
  - Smoking, high cholesterol, h/o angina

## Retinal Plaques

- May present with amarosis fugax, transient episodes of monocular blindness
- Rarely, may report transient ischemic attack (TIA) , which is above with hemiparesis, parasthesia or aphasia

## Retinal plaques

- Three different types of plaques, but all share strong association to significant cardiovascular disease
  - HH 80% > fibrino-platelet 14% > calcific 6%

## Retinal Plaques

- Cholesterol (Hollenhorst) plaque
  - Most common
  - shiny yellow-orange in appearance
  - from plaque in the ipsilateral carotid artery
  - Rarely causes occlusion, unless multiple
  - Typically occurs at bifurcations
  - Mobile in nature

## Retinal Plaques

- Fibrino-platelet
  - Appear as dull white to gray, long plugs
  - Typically within arterioles, not at bifurcations
  - May break-up and dissolve with time
  - May lead to BRAO or CRAO
  - Often associated with carotid disease or mitral valve insufficiency

## Retinal Plaques

- Calcific
  - Appears more whitish than HH
  - Dull, non-reflective, white
  - Classically within arteriole, not at bifurcation
  - Typically immobile
  - Most dnagerous, asoOften cause BRAO
  - Often from cardiac arethromas of heart valves

## Retinal plaques

- Talc retinopathy
  - Represents an exogenous plaques as opposed to others
  - Appears typically as multiple shiny yellow plaques within capillaries in posterior pole
  - Typically smaller than other plaques
  - Typically seen in IV drug users
  - Rarely cause complications, but reported cases of associated NV and occlusions

## Retinal plaques

- No direct management of plaques is needed
- Management is aimed at discovering source of embolus to decrease risk of other emboli, occlusion, or stroke
- Pts need referral to internist for complete physical

## Retinal Plaques

- Assess risk factors with PCP
  - DN, HTN, lipid panels
- Carotid ultrasound
- MRA: non-invasive image with 2D/3D
- TEE: invasive, probe into esophagus to image heat valves
  - Helpful with calcific
- CTA: CT scan of arteries construct 3D images

## Carotid Ultrasound

- First line screening test
- ORDER WITHIN TWO WEEKS!!
- Identifies flow rate and % stenosis
- Common, internal, and external
- Only ≈20% of asymptomatic emboli will have significant carotid stenosis

## Retinal Plaques

**<50-60% occlusion**

- ORAL TREATMENT
  - Anti-Platelet
    - ASA
  - Anti-coagulation
    - Comadin, platelet
  - Cholesterol meds

**>70-99%**

- SURGICAL TREATMNET
  - Carotid edarterectomy
  - Angioplasty
  - Reduces risk of future stroke!

## Retinal Plaques

- After ruling out underlying etiology, see patient regularly, q 6 -12 mos, to evaluate for additional plaques or other disease associated with vascular disease
  - BRVO/CRVO
  - BRAO/CRAO
  - NTG

## Is it worth working up these patients?

- 18% of pts with retinal emboli had internal or common carotid stenosis>75%
- Higher incidence of stroke
  - 8.5% with emboli vs 0.8% w/o per year
- Pts with cholesterol HH emboli have 15% mortality at 1 yr, 29% by year 3, and 54% by 7 years

## Retinal Vein Occlusions

**BRVO**

- Second most common retinal vascular disorder
- Often associated with systemic HTN
- Peak incidence in 5th to 6th decades, with no sex predilection

**CRVO**

- Very visually destructive disease with strong systemic association
- Typically occurs in men > 50
- Vision is typically compromised, ranging from moderate to total vision loss

## Retinal Vein Occlusions

**BRVO**

- Classic presentation is dilated tortuous veins and dot-blot hemes from site of compression to periphery in sector normally drained by that vein
  - Can also see flame-shaped hemes and cotton wool spots as hypoxia develops
  - Lipid can also develop leading to macula edema

**CRVO**

- Non-ischemic characterized by dot/blot hemes, intra-retinal hemes, and possible macula edema
- Ischemic CRVO presents with dot/blot hemes, flame-shaped hemes, CWS, and gross intra-retinal and macula edema. Also, papillidema commonly present

## Ischemic vs non-ischemic CRVO

- IOP often reduced more with ischemic vs. ischemic CRVO
- APD often present with ischemic
- VA generally reduced more with ischemic
  - Rule of thumb: if VA < 20/200 then ischemic.
- In order to know for certain, FA needed
  - Helps to stratify risks, prognosis

## Traditional Treatment: BRVO

- Branch Vein Occlusion Study Group concluded that grid laser improves visual outcome in eyes with BRVO and vision 20/40 or worse from macular edema
  - BRVO at least 3 months old
  - VA 20/40 or worse
  - FA within 1 month, demonstrating macula edema and absence of foveal ischemia

## Traditional Treatment: BRVO

- Other sequelae of BRVO include neovascularization, either of the retina, disk, or iris (25-30%)
- BRVO study group also concluded that PRP should be administered in eyes with BRVO and Neovascularization
- Results suggest that there may be no advantage to treat to prevent development of NV

## Traditional Treatment: CRVO

- Patients with macular edema from CRVO typically do not respond well to FML at all
- CVOS Study: Improvement on appearance, but no gain in acuity
- Big concern is risk for NVG
  - NVG in 14-20% of all CRVO
  - NVG almost 60% of the time in ischemic CRVO

## BRVO/CRVO

- Management includes diagnosis and management of underlying etiology
- Most often associated with DM and HTN
- However many other possible etiologies
  - Carotid artery disease
  - Hyperlipidemia/hypercholesterolemia
  - Altered platelet function
  - Coats disease
  - Von-Hippel Lindau
  - Eales' disease
  - Trauma

## BRVO/CRVO

- At minimum, should have
  - BP evaluated
  - Fasting Blood sugars (FBS)/A1c
  - CBC
  - Lipid profile
- Additional tests might include
  - Carotid artery evaluation
  - Cardiac evaluation
  - Additional blood tests
    - ANA
    - RF
    - FTA/ABS
    - ESR

## CRVO

**Most common etiologies varied with age at presentation**

- Under age 50
  - Head injury
  - Hyperlipidemia
  - Estrogen, esp oral contraceptives
- Over age 50
  - HTN
  - DM
  - Chronic lung disease

## New Treatments: Steroids

- CRVO SCORE
  - ¼ patients receiving IVT had a 15 letter or better improvement in VA at 12 months
  - Pts 5x as likely to have VA improvement vs. observation alone
- BRVO SCORE
  - Almost equal number of patients in laser or steroid group had > 15 letter improvement
  - More complications in IVT group

## New Treatments: Anti-VEGF

- CRUISE (CRVO) Study:
  - Vision improved > 15 letters in almost 50% of patients vs. 17% with sham at 6 mos
  - mean VA gain of almost 15 letters
- BRAVO (BRVO) Study:
  - Vision improved > 15 letters in over 60% of patients vs. 28% with sham
  - Mean VA gain of approx 18 letters
  - Few side effects in either group

## Elyea® (afilbercept)

- FDA approved Sept, 2012 for treatment of macula edema secondary to CRVO
- COPERNICUS and GALILEO studies:
  - % of pts gaining 15 letters or more of BCVA
  - Injection q 2 mos for 24 weeks
- COPERNICUS:
  - 56% vs. 12% with sham
  - 17.3 letters gained vs. 4.o lost with sham
- GALILEO:
  - 60% vs. 22% with sham
  - 18.0 letters gained vs. 3.3 lost with sham

## Ozurdex®

- 0.7 mg biodegradable intravitreal dexamethasone insert
- FDA approved for macula edema from BRVO/ CRVO
- 853 patients
  - 20-30% gained ≥ 3 lines vs. 7-12% with sham at 6 mos
  - 7.4 mean letter gaion vs. 4.9 with sham at 6 mos

## BRVO/CRVO Treatment

**Traditional**

- Wait and see
  - 3 mos
  - 20/40 or worse
- Laser for BRVO
- No Tx CRVO
- Evaluate underlying disease

**Now**

- No advantage to wait
  - 1 week
  - VA limit?
- Anti-VEGF for BRVO
- Anti-VEGF for CRVO
- Evaluate underlying disease

## BRAO

- Result of emboli dislodged from elsewhere which travels through the system until a vessel too small for passage is reached
- Arterial occlusion causes anoxia due to lack of oxygenated blood
  - Anoxia causes loss of retinal layers, including NFL through inner nuclear layer

## BRAO

- Occurs most frequently in superior temporal region of the retina
- Visual acuity and field loss dependent on location and extent of blockage
  - VF loss is classically
    a sharp edged defect
    stopping abruptly
    at the horizontal raphe

## BRAO

- Appearance varies as time progresses
  - Initially, affected arteries narrow and retina becomes hazy
  - Over a few hours, the retinal tissues whitens and appears edematous
  - Segmental optic atrophy may also develop in the affected area

## BRAO

- Prognosis depends upon area affected as well as extent of blockage
- Also depends upon prompt therapy, to lesser extent
  - Some studies indicate that if emboli can be dislodged within 1-2 hours, recovery can be complete
  - After this period, initial acuity is not likely to improve

## CRAO

- Mechanism similar to BRAO, but larger embolus causes obstruction prior to laminar cribosa, so entire central retinal artery is obstructed
- Pts typically present with sudden painless loss of vision in an eye that was previously thought to be healthy
- Typically pts from 50-80 years of age

## CRAO

- Vision typically in the hand motion to counting fingers range
- Most often present with an APD as well
- If a cilioretinal artery is present, there may be a small island of vision that correlates to the area of vascular supply
  - Present in about 10% of eyes
- Can see an embolus in 20-40% of cases

## CRAO

- Early appearance is that of retinal narrowing and haziness of retinal tissue
- After 1-2 hours, retina appears white and edematous, with a "cherry red" macula, representing the choroidal blood supply to the macula
- With time, the arteries may assume a more normal appearance, with irregular narrowing often the only clue
- Optic atrophy may occur , but NVG is very rare

## CRAO

- Management often includes attempts to dislodge embolus if pt presents within first 1-2 hours
  - Digital massage, paracentesis to lower IOP, carbogen, anti-thrombolitic agents, etc have little to no value
- Management lies in diagnosis and management of underlying systemic disease

## BRAO/CRAO

- Immediate ESR needed to r/o GCA if pt over 55
  - Only 2%-5% secondary to GCA in one study
- Most often associated with DM, HTN, and carotid artery disease
  - Many other etiologies including: sickle cell, oral contraceptives, Lupus, Bechets disease, Lyme disease, etc

## BRAO/CRAO

- Blood pressure
- Lab tests
  - FBS
  - CBC
  - ESR
  - Lipid profile
  - PT/PTT
  - ANA/RF
- Carotid Artery Evaluation
- Cardiac Evaluation
  - Echocardiogram and possible Holter monitor

## BRAO/CRAO

- Follow-up
  - BRAO: 3-6 mos after ruling out underlying etiology
  - CRAO: follow closely for first 1-3 mos for NVI, then periodically after
    - If NV, then PRP indicated to prevent NVG