Abstract
This course presents an evidence-based literature review for the primary care practitioner regarding the diagnosis and management of old and new retinal artery occlusions. Cases of central, branch, and cilioretinal artery occlusion will be presented. Clinical clues for identification of past artery occlusions as well as management of future stroke risk will also be discussed with emphasis on key points for patient education.

Learning Objectives
1. Review ocular signs, symptoms, and pathophysiology of artery occlusion.
2. Review clinical clues to detect previous retinal artery occlusion
3. Discuss management and auxiliary testing indicated in RAO
5. Review role of optometrist in patient education regarding stroke sign/symptoms
I. Retinal Artery Occlusions (RAO)
   1. Embolism
      a. Cholesterol most common, originate in carotid artery, plaque presence more important than degree of stenosis, migrate frequently, cause TMVL
      b. Fibrino-Platelet: smooth, migrate frequently
      c. Calcific, originate in heart, usually stationary, high risk cause RAO
      d. Singapore Malay Eye Study: Cigarette smoking and Elevated Cholesterol high risk for retinal emboli
      e. Los Angeles Latino Eye Study: Cigarette smoking strongest association
      f. Not always visible in RAO
   2. “Stroke of the Eye”
      a. Sudden interruption blood flow
      b. Damage to corresponding tissue
      c. Thrombo-embolus
      d. Overlapping systemic risk factors

II. Central Retinal Artery Occlusion (CRAO)
   1. Pathophysiology
      a. Blockage of major artery supplying retina
      b. Retina suffers no detectable damage for 100 minutes
      c. After 240 minutes, massive and irreversible damage \( \rightarrow \) dead retina
   2. Clinical signs/symptoms
      a. Painless, sudden, severe vision loss: \( \sim \) 75% CF or worse (Hayreh Am J Oph 2005)
      b. Cherry Red Spot – choroidal perfusion still present
      c. Diffuse ischemia, retinal whitening, swollen NFL
      d. Retinal artery attenuation
      e. Box-Carring of vessels – sluggish/disrupted blood flow
      f. Optic nerve Pallor
      g. OCT shadowing due to swollen NFL (Ahn et al. Am J Oph 2015)
         i. Presentation: Extent macular edema, retinal layer structure/organization loss determines visual prognosis
         ii. Final: outer retinal layer thinning, photoreceptor defects from choroidal ischemia
h. Non-Arteritic CRAO -66.9% of all CRAO (Hayreh et al. CRAO Visual Outcome. Am J Oph 2005)
   i. 93.2% CF or worse, none better than 20/40
   ii. Non-Arteritic CRAO w/ cilioretinal sparing -14.3% of all CRAO
      i. 60% CF or worse, 20% better than 20/40
      ii. Patent cilioretinal artery improve visual prognosis
j. Transient Non-Arteritic CRAO -4.5% of all RAO
   i. CRA temporarily occluded
   ii. Fall in perfusion pressure, drop arterial BP or rise IOP, vasospasm
k. Arteritic CRAO -16% of all CRAO
   i. Secondary to Giant Cell Arteritis (GCA)
   ii. Posterior ciliary artery and central retinal artery occlusion
   iii. Occult GCA – no systemic symptoms, always order labs to r/o

   a. Ipsilateral carotid artery stenosis
   b. Ischemic Heart Disease
   c. Type 2 Diabetes
   d. Hypertension
   e. Stroke/TIA
   f. Smoking

4. Management
      i. No treatment acute CRAO, long term prevention stroke/MI
   b. Non Arteritic (NA) vs Arteritic
      i. Patients > 50 years old, r/o Giant Cell Arteritis: ESR, CRP, Platelets
   c. Need complete medical evaluation, previously undiagnosed vascular factors uncovered in 78% CRAO after work-up (Callizo et al. Ophthalmology 2015)
   d. Carotid U/S: Ipsilateral carotid stenosis > 50%, 31% non-arteritic CRAO; Plaque present 74% NA-CRAO
   e. Echocardiography, Electrocardiography
i. 61% NA-CRAO abnormal, mitral/aortic valve source calcific embolus
f. Pulse rate, body mass index, urine analysis
g. Blood pressure, labs
h. Stroke Triage - IMMEDIATE neuro evaluation, preventative stroke Tx
   ii. Co-occurrence ischemic stroke 24.2% RAO patients, ipsilateral brain lesion, 37.5% suffered silent stroke, recommend MRI all RAO (Lee et al. Am J Ophthalmol 2014).
   iii. TIA/Stroke after CRAO only 1% over 3 months, 74% plaque present carotid doppler, 61% embolic abnormality on echocardiography (Hayreh et al. Ocular Arterial Occlusive Disorder and Carotid Artery Disease. Ophthalmology 2017)
i. American Academy of Ophthalmology Preferred Practice Pattern
   i. > 50 years old, rule out GCA: ESR, CRP, Platelets
   ii. Younger patients: systemic evaluation vasculitis, hypercoagulable state
   iii. Embolic work-up (carotid artery, heart)
   iv. Embolism RAO = IMMEDIATE referral nearest stroke center
j. Ocular neovascularization
   i. Follow regular intervals for 4 months
   ii. 18.2% develop NV, 15.2% Neovascular Glaucoma, ave onset 8.5 weeks, range 2-16 weeks (Rudikin et al. Euro J Oph 2010)
   iii. 10.9% NVI, 6.4% NVG, ave onset 3 months, range 1 week to 15 months (Jung et al. Korean J Oph 2016)
   iv. 14.5%, ave 30 days, range presentation – 4 months (Mason et al. Clin Oph 2015)
   v. 2.5% incidence NVG, mechanism of NV development is carotid artery disease. VEGF released 2/2 chronic retinal hypoxia (CRVO, PDR, OIS), CRAO is acute event, dead retina cannot release VEGF (Hayreh et al. Arch Oph 1982.)
k. Long Term
   i. Increased stroke risk up to 10 years (Rim et al. Stroke 2016)
   ii. Stroke risk 10 times higher over 3.5 years vs healthy (Bruno et al. Ann Intern Med 1995)
   iii. Lifetime reduced 10 years vs healthy (Lorentzen SE, Acta Oph 1969)
   iv. 30% died after average 4.2 years (Hankey et al. BMJ 1991)

III. Branch Retinal Artery Occlusion (BRAO)
1. Pathophysiology
   a. Marked stasis of absence of circulation in involved branch arteriole
   b. Arterioles: diameter 100 um, no internal elastic lamina no muscular coat
c. Sudden onset of vision loss

2. Clinical Signs/Symptoms
   a. Retinal opacity, infarction by acute ischemia of inner retinal layers supplied by retinal arteriole, in distribution of occluded branch retinal arteriole, 89% at initial visit vs 13% at 3 months (Hayreh et al. Fundus changes in BRAO. Retina 2015).
   b. Embolus seen 65% of initial visits, migration/disappearance common
   c. FA: no filling of occluded retinal arterioles
   d. OCT: increased thickness of retinal layers, retinal swelling, edema and shadowing

3. Management
   a. Initial acuity 20/40 or better 74%; Eyes worse than 20/40, 79% improved 3 lines or more (Hayreh et al. BRAO Natural History. Ophthalmol 2009)
   b. Papillomacular Bundle involvement predictor of poor vision; OCT shows inner retinal thickening, inner retinal hyperreflectivity, loss of layer by layer integrity
   c. OCT shows destruction inner retinal layers, retinal thinning (Cho et al. Ischemic Injury of PPM is Predictive Marker of Poor Vision in Eyes w/BRAO. Am J Oph 2016)

Good vision = minimal PPM change

Poor vision group = increased retinal thickness, focal hyperreflectivity, but visual improvement was seen at f/u
Poor vision group = increased retinal thickness, focal hyperreflectivity, and loss layer-by-layer integrity in PPM, NO improvement visual acuity at f/u
d. Median time to resolution was 4-5 weeks

e. Visual field, 47% improvement within 7 days

f. Cannot be caused by Giant Cell Arteritis, GCA only affects medium/large arteries and retinal arteries are actually arterioles

g. Embolic work-up: Carotid U/S - Plaque present 64%; EKG: Abnormal 53%

h. Low rate absolute incidence TIA/Stroke, only 2 of 127 over 5 years (Hayreh et al. Ocular Arterial Occlusive Disease and Carotid Artery Disease, Ophthal 2017).

IV. Cilioretinal Artery Occlusion (CLRAO)

1. Pathophysiology

   a. Normal anatomic variant, part of choroidal supply, hook-like appearance
   b. Present in 32% of eyes
   c. 88% supply portion of macula
   d. Exits nerve separately from central retinal artery
   e. H/O episodes of transient visual blurring before constant blurred vision
   f. 5% all RAO
2. Clinical Appearance
   a. Isolated cilioretinal artery occlusion (40%)
   b. Cilioretinal Artery Occlusion with CRVO (40%)
   c. Cilioretinal Artery Occlusion w/ AION (20%): Arteritic vs Non-Arteritic (Hayreh et al. BRAO Natural History Visual Outcome. Ophthalmology 2009)

3. Management
   a. Supplied by posterior ciliary artery, need to r/o GCA: ESR, CRP, Platelets
   b. Carotid U/S
   c. EKG
   d. Visual Field: centrocecal defect

V. Detection/Management previous RAO
1. Central Retinal Artery Occlusion
   a. Optic Nerve Pallor
      i. Diffuse pallor for CRAO
      ii. CRAO: 63% pale disks within 1 month, 79% pale disks within 2 months, 91% pale disks within 4 months
   b. Cilioretinal collaterals
      i. 4% within 1 month, 18% within 3 months with permanent CRAO
      ii. 32% within 3 months for CRAO with cilioretinal artery sparing
c. APD  

2. Branch Retinal Artery Occlusion  
   a. Optic Nerve Pallor – sectoral, 65% by 3 months  
   b. Sclerosed/attenuated vessels, 28% by 6 months  
   c. Vessel sheathing – 25% by 12 months (vasculitis)  
   d. Collateral vessels  
   e. Corresponding areas of non-perfusion  
   f. Visual field defect  
   g. APD  
   h. Emboli visible  
      i. OCT thinning of retinal: loss inner layers  

3. Embolic work-up, labs, MRI as indicated if not previously performed  

VI. Patient Education  
1. Retinal Emboli and Stroke  
   a. 3 fold greater risk fatal stroke x 8 years (Klein et al. Beaver Dam Eye Study. Arch Oph 1999)  
   b. Mortality rate 56% w/ emboli vs 30% without emboli. 3 fold increase stroke risk (Wang et al. Blue Mountain and Beaver Dam Eye Study. Stroke 2006)  

2. Patient Knowledge regarding Transient Ischemic Attack and Stroke  
   a. Only 8.2% Americans know TIA definition, only 8.6% can identify symptom; elderly who are most at risk at least knowledgeable  
   b. TIA patients surveyed: 44.4% delayed medical attention more than 24 hours; 42.4% recognize TIA symptoms but no change urgency; 87.6% went to family doctor vs only 10% went to emergency room  

2. Triage TIA w/ ABCD²  
   i. A = Age > 60, 1 point  
   ii. B = Blood Pressure > 140/90, 1 point  
   iii. C = Clinical Features, Unilateral Weakness – 2 points, Speech disturbance – 1 point  
   iv. D¹ = Duration, < 10 min is 0, 10 < x < 60 is 1 point, > 60 minutes is 2 points  
   v. D² = Diabetes, Yes then 1 point  
   vi. Predicts high risk of stroke at 7 days, 90 days, (Tsivgoulis et al. Neurology 2010; 74: 1351-1357.
vii. ABCD2 predicts severity of stroke (Chandratheva et al. Stroke 2010)

<table>
<thead>
<tr>
<th>ABCD²-score</th>
<th>7-day stroke risk (95% CI)</th>
<th>90-day stroke risk (95% CI)</th>
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<tbody>
<tr>
<td>0-3</td>
<td>3% (0-7%)</td>
<td>4% (0-9%)</td>
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<tr>
<td>4-5</td>
<td>9% (1-17%)</td>
<td>21% (10-33%)</td>
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<tr>
<td>6-7</td>
<td>24% (6-42%)</td>
<td>43% (22-64%)</td>
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Low risk: ABCD² = 0-3; moderate risk: ABCD² = 4-5; high risk: ABCD² = 6-7.

d. 40% patients admitted for stroke did not know they were having a stroke

e. National administration rate of TpA is 1.6-3% only

f. Patient education regarding stroke signs, urgency of stroke, and potential treatment with clot buster needed.
References


Chandratheva et al. ABCD2 Score Predicts Severity Rather than Risk of Early Recurrent Events after TIA. Stroke 2010; 41: 851-856.


Hayreh et al. Central Retinal Vein Occlusion associated with Cilioretinal Artery Occlusion. Retina 28: 581-
594, 2008.


