Retinal Vein Occlusion

An Evidence-Based Approach
Corticosteroids, Implants, and Anti VEGF Therapies

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Retinal Vein Occlusion

• Retinal vein occlusion is the second most common cause of visual loss due to retinal vascular disease\textsuperscript{1-3}

• Two major types:
  – Branch retinal vein occlusion (BRVO)
  – Central retinal vein occlusion (CRVO)

• BRVO is the most common\textsuperscript{3}
  – Five-year incidence of 0.6% (21/3558) for BRVO and 0.2% (7/3593) for CRVO\textsuperscript{3}

• Persistent macular edema causes VA loss

Central Retinal Vein Occlusion

- **Pathogenesis**
  - Thrombosis of the central retinal vein
    - At or posterior to the lamina cribrosa
  
  - Atherosclerotic central retinal artery
    - Impinges on central retinal vein
      - Turbulent flow $\rightarrow$ thrombus
Central Retinal Vein Occlusion

• Findings
  – Dilated and tortuous retinal veins
  – Swollen optic disc
  – Intra-retinal hemorrhages
  – Retinal edema
Central Retinal Vein Occlusion

• Risk Factors
  – Eye Disease Case-Control Study
    • Hypertension
    • Diabetes
      – Unlike BRVO
    • Glaucoma
      – Check and treat IOP!

– CRVO in young patients requires more extensive workup for cause
### CRVO In Young Patients – Causes

<table>
<thead>
<tr>
<th>Causes</th>
<th>Sub-Causes</th>
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<tr>
<td><strong>Systemic vascular disease</strong></td>
<td>• Hypertension</td>
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<td>• Diabetes mellitus</td>
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<td>• Cardiovascular disease</td>
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<td><strong>Blood dyscrasias</strong></td>
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<td><strong>Clotting disorders</strong></td>
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<td>• Lupus anticoagulant</td>
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<td>• Anticardiolipin antibodies</td>
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<td>• Antithrombin III</td>
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<td><strong>Paraproteinemia and dysproteinemias</strong></td>
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<td><strong>Vasculitis</strong></td>
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<td>• Sarcoidosis</td>
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<td><strong>Autoimmune disease</strong></td>
<td>• Systemic lupus erythematosus</td>
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<td><strong>Oral contraceptive use in women</strong></td>
<td>• Closed-head trauma</td>
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<td><strong>Other rare associations</strong></td>
<td>• Optic disc drusen</td>
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<td>• Arteriovenous malformations of retina</td>
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Central Retinal Vein Occlusion

- Management
  - Iris neovascularization
  - PRP to eyes prior to NVI
    - NO benefit
      - Even if very ischemic
  - Once neovascularization detected
    - Prompt PRP
Branch Retinal Vein Occlusion

• Findings
  – Superotemporal quadrant most common
    • 63%

  – Occurs at arteriovenous crossing
    • Artery and vein bound together in a common sheath
    • Arterial thickening compresses vein
      – Turbulent flow → thrombus formation
Branch Retinal Vein Occlusion

• **Findings**
  – Within one sector of the retina
    • Superficial hemorrhages
    • Retinal edema
    • Cotton-wool spots
    • Dilated and tortuous vein
    • Corresponding artery narrowed and sheathed
Branch Retinal Vein Occlusion

• Risk factors
  – Identified by the Eye Disease Case-Control Study
    • Hypertension
    • Cardiovascular disease
    • Increased BMI at age 20
    • Glaucoma
  – Note: Diabetes not an independent risk factor
Branch Retinal Vein Occlusion

• Visual Loss
  – Acute
    • Macular hemorrhage
    • Macular edema
    • Capillary occlusion
  – Chronic
    • Macular ischemia
    • CME
    • Macular pigmentary changes
    • Epiretinal membrane formation
    • Subretinal fibrosis
Macular edema- FFA
Branch Retinal Vein Occlusion

- Neovascularization
  - BVOS defined ischemic BRVO
    - Area of non-profusion > 5 disc diameters
  - Large areas of non-profusion increase risk of neovascularization

- Apply scatter PRP to areas of retinal ischemia
  - Only when neovascular complications develop
    - NVI, NVE, NVD
Clinical Trials and Venous Occlusive Diseases

• Laser studies
  – 1980s Branch Vein Occlusion Study (BVOS)
  – 1990s Central Vein Occlusion Study (CVOS)
• 2009 Steroid studies
  – SCORE Study
  – Ozurdex Trials
• 2010 Anti-VEGF Ranibizumab studies
  – BRAVO and CRUISE
• 2012 Aflibercept
  – GENEVA
Branch Retinal Vein Occlusion

- **Branch vein occlusion study**
  - Treated eyes more likely to gain 2 lines of vision
  - Treated 65%, untreated 37%
Central Retinal Vein Occlusion

• Management
  – Macular edema
    • Central Vein Occlusion Study Group
      – Grid laser treatment in the macula
        » DOES reduce angiographic evidence of edema
        » DOES NOT improve vision
Primary Results: The Standard Care versus Corticosteroid for Retinal Vein Occlusion Study (The SCORE Study)
SCORE CRVO Conclusion

• Both triamcinolone groups were superior to the observation group for VA at 12 months
• Visual benefit as early as 4 months
• Visual benefit continued to 24 months
• The 1-mg dose has a safety profile superior to that of the 4-mg dose and similar to observation
OZURDEX™ is preloaded into a sterile, single-use, specially designed applicator to facilitate injection of implant directly into the vitreous.

- Injectable, biodegradable intravitreal implant contains 0.7 mg (700 μg) dexamethasone in the NOVADUR™ solid polymer drug delivery system (preservative-free).
- Poly (D,L-lactide-co-glycolide) PLGA biodegradable polymer matrix, which slowly degrades to lactic acid and glycolic acid as dexamethasone is gradually released.
Ozurdex Trials Conclusions

• DEX groups’ time to gain 15 letters was significantly shorter than sham eyes through day 90

• Mean change in BCVA was statistically:
  – Better for DEX groups for BRVO through day 180
  – Better for DEX groups for CRVO through day 90

• Persistence of efficacy in 21% BRVO; 17% CRVO at month 12 required only 1 Rx
Long-Term Outcomes Using Ranibizumab for Treatment of Branch Retinal Vein Occlusion
Conclusions

• On average, visual and anatomic outcomes following 6 monthly ranibizumab injections were maintained with 6 months of PRN treatment.
  – In the 0.5 mg group, further improvements in BCVA and CFT were observed at Month 7 for patients who continued to receive ranibizumab at Month 6, while improvements obtained in the first 6 months of treatment were reduced at Month 7 for patients who skipped ranibizumab at Month 6.

• With initiation of PRN treatment at Month 6, sham/0.5 mg patients had, on average
  – smaller BCVA gains from baseline at Month 12 compared with the ranibizumab treatment groups.
  – decreases in CFT at Month 7 that were maintained through Month 12.

• Ranibizumab treatment seemed to accelerate resolution of retinal hemorrhages in BRVO.

• Safety outcomes were consistent with previous Phase III ranibizumab trials.
Long-Term Outcomes Using Ranibizumab for Treatment of Central Retinal Vein Occlusion
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Intravitreal Aflibercept Injection for Macular Edema Following Central Retinal Vein Occlusion