Venous Occlusive Disease

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History

- RVO patients commonly report decreased vision and blurring in one eye, but it’s typically painless with sudden onset. They may also report distortion of images, and their visual disturbances may be limited to one part of the visual field.
Classic features of branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO), include intraretinal hemorrhages and tortuosity and dilation of the retinal blood vessels. Macular edema, exudates and cotton wool spots may be present.
Retinal Vein Occlusion

- Retinal vein occlusion is the second most common cause of visual loss due to retinal vascular disease\(^1\)-\(^3\)
- Two major types:
  - Branch retinal vein occlusion (BRVO)
  - Central retinal vein occlusion (CRVO)
- BRVO is the most common\(^3\)
  - Five-year incidence of 0.6% (21/3558) for BRVO and 0.2% (7/3593) for CRVO\(^3\)
- Persistent macular edema causes VA loss
Central Retinal Vein Occlusion

- Findings
  - Dilated and tortuous retinal veins
  - Swollen optic disc
  - Intra-retinal hemorrhages
  - Retinal edema

All four quadrants
Central Retinal Vein Occlusion

◆ Classification
  ❖ Based on amount of non-profusion on fluorescein angiography
    » Ischemic
      ✦ ≥10 disk areas
    » Non-ischemic
      ✦ < 10 disk areas
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 → thrombus
Central Retinal Vein Occlusion

- Non-ischemic CRVO
  - Less dilation and vascular tortuosity
  - Dot and flame hemorrhages in all quadrants
  - Less or no disk swelling

- Angiogram shows
  - Delayed A-V transit time
  - Leakage
  - Minimal capillary dropout

- Neovascularization is rare
Central Retinal Vein Occlusion

- Ischemic CRVO
  - Extensive hemorrhage
  - Retinal edema
  - Marked venous dilation
  - Cotton-wool spots
  - Angiogram show
    - Widespread capillary nonprofusion
  - Visual prognosis poor
    - Only 10% have >20/400 vision
- NVI
  - As high as 60% of eyes
  - Occurs 3-5 months post occlusion
    - “the three month glaucoma”
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

- Systemic vascular disease
  - Hypertension
  - Diabetes mellitus
  - Cardiovascular disease
- Blood dyscrasias
  - Polycythemia vera
  - Lymphoma
  - Leukemia
- Clotting disorders
  - Activated protein C resistance
  - Lupus anticoagulant
  - Anticardiolipin antibodies
  - Protein C
  - Protein S
  - Antithrombin III
- Paraproteinemia and dysproteinemias
  - Multiple myeloma
  - Cryoglobulinemia
- Vasculitis
  - Syphilis
  - Sarcoidosis
- Autoimmune disease
  - Systemic lupus erythematosus
- Oral contraceptive use in women
- Other rare associations
  - Closed-head trauma
  - Optic disc drusen
  - Arteriovenous malformations of retina
Central Retinal Vein Occlusion

◆ Management
  ❖ Family medical doctor to manage
    » Hypertension
    » Diabetes
    » Elevated cholesterol
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
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

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
Clinically, we see the repercussions of RVO disease stages that follow the initial occlusive event — capillary permeability and leakage, edema, inflammation, vessel remodeling and recanalization, neovascularization if ischemia is present, and fibrosis.
Fluorescein angiography

- Delayed venous filling, hypofluorescence caused by hemorrhage and capillary nonperfusion, dilation and tortuosity of veins, leakage due to neovascularization and macular edema
OCT

- OCT provides us with a more efficient, less invasive and less costly way than repeat FA to evaluate and monitor RVO and associated macular edema over time.
Clinical Trials for RVO

• 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
BVOS and CVOS

- **BVOS**: Argon MGL is preferable to observation for patients with macular edema secondary to branch retinal vein occlusion (BRVO) and vision of 20/40 or worse.

- **CVOS**: Macular grid photocoagulation is not recommended for treating macular edema due to central retinal vein occlusion (CRVO).
Pan Retinal Photocoagulation

- **Management**
  - Iris neovascularization
  
  - PRP to eyes prior to NVI or NVE
    - NO benefit
      - Even if very ischemic
  
  - Once neovascularization detected
    - Prompt PRP
Primary Results: The Standard Care versus Corticosteroid for Retinal Vein Occlusion Study (The SCORE Study)
SCORE BRVO

Mean change from baseline in visual acuity letter score

-5
0
5
10
15

SC
1 mg
4 mg
The SCORE-BRVO trial results support grid laser as the SC treatment for macular edema secondary to BRVO because:

- Similar efficacy in all 3 treatment arms up to month 12
- Improved efficacy for laser beyond month 12
- Superior safety profile of SC over 1-mg and 4-mg TA
SCORE CRVO

% With VA Gain of 15 letters or More
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.
Injectable, biodegradable intravitreal implant contains 0.7 mg (700 μg) dexamethasone in the NOVADUR™ solid polymer drug delivery system (preservative-free).
Ozurdex Mean Change BCVA
BRVO(GENEVA trial)
Ozurdex Mean Change BCVA
CRVO(GENEVA trial)
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
Anti-VEGF Trials

- Ranibizumab (Lucentis)
  - BRAVO and CRUISE

- Afilbercept (VEGF-Trap eye, Regeneron)
  - Galileo and Copernicus
Mean Change from Baseline BCVA (BRVO)
Mean Change from Baseline (CRVO)
Anti-VEGF Trials

- **BRAVO**: Ranibizumab monthly for 6 months better than observation/laser in BRAVO. Improved VA: 61% vs 29% eyes gained 15 or more letters
- **CRUISE**: Ranibizumab monthly for 6 months better than observation. Improved VA: 48% vs 17% eyes gained 15 or more letters
◆ Treat all patients who have edema and a vision complaint, even if their Snellen visual acuity is 20/20.

◆ One reason is that the longer we wait to treat, the less vision we can expect the patient to recover. Another reason is that Snellen acuity is not a true assessment of visual function.
Treatment regimens for RVO now typically start with monthly injections of anti-VEGF agents before patients are switched to as-needed dosing with monthly monitoring.
Gauging Response to Treatment

- First-line therapy for RVO-associated macular edema is an anti-VEGF agent.
- BRAVO and CRUISE studies of ranibizumab analysis showed that in patients with central retinal vein occlusion, 90% of the response to treatment occurred within the first three injections. Therefore, if I see no response after three injections, I’m confident that monotherapy will not be adequate, and I move to the next option.
- Use caution in our patients who are at highest risk for ATEs, particularly patients 85 and older.
- Focal laser therapy often is used adjunctively after 5–6 months of initial therapy.
Despite the advances in pharmacologic therapy, many eyes with RVO continue to lose vision. The common final pathway appears to be photoreceptor cell death.

Future research for RVO treatments may focus on neuroprotective and photoreceptor regeneration therapies to improve sight in patients who have limited vision due to RVO.
Thank you for your attention