Themes for conferences – No 42

Systemic Arterial Hypertension
Venous Occlusive Disease
Arterial Occlusive Disease
Ocular Ischemic Syndrome

Med. pract. Anton R. Xavier
Dr. med. Claudia Zawinka
Dr. med. Stephan Estermann

August 2016

Vista Diagnostics Zürich
Retinal Vascular Diseases – Some Aspects

• **Systemic Arterial Hypertension**
  • Hypertensive Retinopathy
  • Hypertensive Choroidopathy
  • Hypertensive Optic Neuropathy

• **Venous Occlusive Disease**
  • Branch Retinal Vein Occlusion
  • Central Retinal Vein Occlusion
  • Retinopathy of Carotid Occlusive Disease

• **Arterial Occlusive Disease**
  • Precapillary Retinal Arteriole Obstruction
  • Branch Retinal Artery Occlusion
  • Central Retinal Artery Occlusion
  • Ocular Ischemic Syndrome
Systemic Arterial Hypertension

- Systemic arterial hypertension is defined as systolic pressure of > 130 mmHg or diastolic pressure of > 85 mmHg.

- Target organs of systemic hypertension are the heart, kidneys, brain and the eye.

- Ocular effects of hypertension can be observed in the retina, choroid and optic nerve. Recognition of posterior segment vascular changes may lead to the diagnosis of hypertension.
Systemic Arterial Hypertension

- Hypertensive Retinopathy
- Hypertensive Choroidopathy
- Hypertensive Optic Neuropathy
Hypertensive Retinopathy

- Systemic arterial hypertension affects precapillary arterioles and capillaries, anatomical loci of autoregulation and nonperfusion.

- An acute hypertensive episode may produce focal intraretinal periarteriolar transudates (FIPTs).

- FIPTs are at the precapillary level (deeper, smaller, less white than cotton-wool spots).

- Uncontrolled systemic hypertension leads to
  - nonperfusion at various retinal levels (direct effect)
  - neuronal loss and related scotomata (indirect secondary effect)
Hypertensive Retinopathy

- Retinal lesions of chronic systemic hypertension: Microaneurysms, intraretinal microvascular abnormalities (IRMAs), hemorrhages, hard exsudates, venous beading and new retinal vessels; whereas the latter two are signs of an ischemic retinopathy.

- The relationship between hypertensive vascular changes and the changes of arteriosclerotic vascular disease is complex, with great variation related to duration of hypertension, dyslipidemia, age, and a history of smoking.

- Focal arteriolar narrowing and arterial venous nicking are related to vascular sclerosis.
Hypertensive Retinopathy

- Modified Scheie Classification of „Hypertensive Retinopathy“
  - Grade 0  No changes
  - Grade 1  Barely detectable arterial narrowing
  - Grade 2  Obvious arterial narrowing with focal irregularities
  - Grade 3  Grade 2 + retinal hemorrhages and/or exudates
  - Grade 4  Grade 3 + disc swelling

- Hypertension may be complicated by branch retinal artery occlusion (BRAO), branch and central vein occlusion (BRVO, CRVO) and retinal arterial macroaneurysms.
Hypertensive Retinopathy

- Ischemia secondary to BRVO may result in
  - neovascularization of the retina
  - preretinal and vitreous hemorrhage
  - macular edema
  - epiretinal membrane formation
  - tractional retinal detachment
Hypertensive Retinopathy

Figure 1: Grade 1
Hypertensive Retinopathy

Figure 2: Grade 2

© Vistaklinik
Hypertensive Retinopathy

Figure 3: Grade 3

© Vistaklinik
Hypertensive Retinopathy

Figure 4: Grade 4
Hypertensive Choroidopathy

- Typically occurs in young patients with acute hypertension associated with preeclampsia, eclampsia, pheochromocytoma or renal hypertension.

Findings:
- Lobular nonperfusion of the choriocapillaris may occur and result in Elschnig spots (tan, lobule-sized patch, hyperpigmented and surrounded by a margin of hypopigmentation).

- Siegrist streaks: linear configuration of similar-appearing hyperpigmentations following the meridional course of choroidal arteries.
Hypertensive Choroidopathy

Figure 5: Elschnig spots

Figure 6: Siegrist streaks

© Kanski – Clinical Ophthalmology, 6th edition
Hypertensive Choroidopathy

- Fluorescein angiography:
  - Focal choroidal hypoperfusion in early phases
  - Multiple subretinal areas of leakage in late phases

Complications:
- Retinal detachments may occur:
  - Focal retinal pigment epithelium (RPE) detachment
  - Extensive bilateral exudative retinal detachment (rare)
Hypertensive Optic Neuropathy

• Hypertensive optic neuropathy has a variable presentation depending less on the degree than the chronicity of the hypertension.

• Findings:
  • Linear peripapillary, flame-shaped hemorrhages
  • Blurring of the disc margin
  • Florid disc edema with retinal venous stasis and macular exudates
Hypertensive Optic Neuropathy

- Differential diagnosis:
  - Diabetic papillopathy
  - Radiation retinopathy
  - CRVO
  - AION
  - Neuroretinitis
Figure 7: Diabetic papillopathy, hyperemic disc swelling
Hypertensive Optic Neuropathy

Figure 8: Radiation retinopathy (microvascular anomalies, hard exsudates)

Figure 9: Focal retinal capillary perfusion missing, microvascular anomalies

© Kanski – Clinical Ophthalmology, 6th edition
Hypertensive Optic Neuropathy

Figure 10: Papillitis, exudates in the macula («macular star»)
Venous Occlusive Disease

- Branch Retinal Vein Occlusion
- Central Retinal Vein Occlusion
- Retinopathy of Carotid Occlusive Disease
Branch Retinal Vein Occlusion

- Ophthalmoscopic findings in the affected retinal area:
  - Superotemporal quadrant (63%) most commonly, nasal vascular occlusions are rare
  - Retinal hemorrhages
  - Retinal edema
  - Cotton-wool spots (NFL infarcts)
  - Dilated and tortuous vein

- BRVO occurs most frequently at an arteriovenous crossing.
Branch Retinal Vein Occlusion

- Findings in eyes with permanent visual loss from BRVO:
  - Macular ischemia
  - Cystoid macular edema
  - Macular edema with hard lipid exudates
  - Pigmentary macular disturbance
  - Subretinal fibrosis
  - Epiretinal membrane formation

- Less commonly:
  - Vitreous hemorrhage
  - Tractional and/or rhegmatogenous retinal detachment
Branch Retinal Vein Occlusion

Figure 11: Retinal hemorrhages

© Vistaklinik
Branch Retinal Vein Occlusion

Figure 12: Cystoid macular edema

© Vistaklinik
Figure 13: Epiretinal membrane
Branch Retinal Vein Occlusion

- Macular involvement determines level of visual impairment.
  - Risk factors for the development of BRVO:
    - Age (mean 60-70 years)
    - Systemic arterial hypertension
    - Cardiovascular disease
    - Increased BMI
    - History of glaucoma
    - Diabetes mellitus is not a major risk factor.
Branch Retinal Vein Occlusion

- Histopathology:
  - Common adventitia binds artery and vein at arteriovenous crossing. →
    Thickening of the arterial wall compresses the vein. →
    Turbulence of flow, endothelial cell damage and finally thrombotic occlusion.
  - Secondary arterial narrowing often develops in the area of occlusion.
Branch Retinal Vein Occlusion

- **Visual Prognosis:**
  - Depends on the extent of capillary damage and retinal ischemia, mainly in macular area.
  - Integrity of parafoveal capillaries is key for visual recovery.
  - Extensive retinal ischemia (>5 disc diameters) can result in retinal or papillary neovascularization in up to 40% of affected eyes; with high risk of preretinal bleeding.
  - 50-60% of patients will maintain visual acuity of 20/40 or better after 1 year.
Branch Retinal Vein Occlusion

- Therapy: Pharmacotherapy of BRVO
  - Intravitreal anti-VEGF antibodies (primary therapy option): Reduction of retinal thickness and improving vision
  - For the treatment of macular edema associated with BRVO three anti-VEGF agents (ranibizumab, aflibercept and bevacizumab) are currently used
  - BRAVO study:
    - Monthly ranibizumab (0.3 or 0.5 mg) compared with sham injection in 397 eyes, follow-up 6 months
    - Gain of visual acuity of 16 (0.3 mg) to 18 (0.5 mg) letters in ranibizumab group; 7.3 letters in sham group
Branch Retinal Vein Occlusion

- Therapy: Pharmacotherapy of BRVO
  - VIBRANT study:
    - Efficacy of aflibercept over grid laser for macular edema in BRVO.

- Therapy: Pharmacotherapy of BRVO
  - Intravitreal triamcinolone:
    Temporary reduction of retinal thickness, side effects are elevated IOP and development of posterior subcapsular cataract.
Branch Retinal Vein Occlusion

- Therapy: Grid laser photocoagulation
  - Considered for the following 2 major complications:
    - Chronic macular edema with intact perifoveal retinal capillary perfusion and visual acuity of 20/40 or worse
    - Posterior segment neovascularization
Branch Retinal Vein Occlusion

- Therapy: Photocoagulation
  - Neovascularization of the iris in eyes with BRVO in 1%.
  - Scatter panretinal laser photocoagulation to prevent the development of neovascular glaucoma.

- Effectiveness of photocoagulation (BRAVO-Studies):
  - Gaining at least two lines of visual acuity in laser-treated group (65%) vs. untreated group (37%)
  - Scatter argon laser photocoagulation reduced the risk of neovascularization from 22% to 12% and vitreous hemorrhage from 60% to 30%.
Branch Retinal Vein Occlusion

- Therapy: Pars plana vitrectomy
  - in cases with persistent vitreous hemorrhage or retinal detachment.
Central Retinal Vein Occlusion

• Findings:
  • Dilated and tortuous retinal veins
  • Swollen optic disc
  • Intraretinal hemorrhages
  • Retinal edema

• 2 Forms:
  • Nonischemic
  • Ischemic
Central Retinal Vein Occlusion

• Pathogenesis:
  • Thrombosis of the central retinal vein posterior to the level of the lamina cribrosa.
  • An atherosclerotic central retinal artery may impinge on the central retinal vein → turbulence, endothelial damage, and thrombus formation.

• Nonischemic CRVO:
  • Good visual acuity
  • Mild afferent pupillary defect
  • Mild visual field changes
Central Retinal Vein Occlusion

- **Nonischemic CRVO:**
  - Dilatation and tortuosity of all branches of the central retinal vein.
  - Dot-and-flame retinal hemorrhages in all quadrants.
  - Occasionally macular edema with decreased visual acuity.
  - Mild optic disc swelling.
  - Prominent disc edema is seen in younger patients due to a combined inflammatory and occlusive mechanism.
  - Fluorescein angiography: prolongation of the retinal circulation time, breakdown of capillary permeability, minimal areas of nonperfusion.
  - Anterior segment neovascularization is rare.
Central Retinal Vein Occlusion

Figure 14: CRVO without ischemic areas

© Vistaklinik
Central Retinal Vein Occlusion

- Ischemic CRVO:
  - Poor vision
  - Afferent pupillary defect
  - Marked venous dilatation
  - Extensive 4-quadrant retinal hemorrhages
  - Retinal macular edema
  - Cotton-wool spots
  - Fluorescein angiography: widespread capillary nonperfusion, prolonged intraretinal circulation
  - Visual prognosis poor, only 10% of eyes achieve vision better than 20/400
  - Dense central scotoma
Central Retinal Vein Occlusion

Figure 15: CRVO with ischemic areas

© Vistaklinik
Figure 16: Intraretinal central edema

© Vistaklinik
Central Retinal Vein Occlusion

- **Ischemic CRVO:**
  - Iris neovascularization is up to 60% in ischemic eyes, usually occurring 3-5 months after the onset of symptoms.

- **Systemic associations:**
  - Age: 90% of patients > 50 years.
  - Systemic arterial hypertension
  - Diabetes mellitus
  - Open-angle glaucoma: increased IOP is a rare cause of central vein occlusion.
Central Retinal Vein Occlusion

Figure 17: Neovascularization, rubeosis iridis
Central Retinal Vein Occlusion

- Systemic associations:
  - Oral contraceptives
  - Diuretics
  - Blood dyscrasias (polycythemia vera)
  - Dysproteinemias, e.g. alpha 1 antitrypsin deficiency
  - Vasculitis, e.g. sarcoidosis, systemic lupus erythematosus
  - Hyperhomocysteinemia
  - Protein S/C deficiency
Central Retinal Vein Occlusion

- Differential diagnosis:
  - Hyperviscosity retinopathy:
    - Bilateral
    - Related to dysproteinemia (e.g. Waldenström macroglobulinemia or multiple myeloma)
    - In many cases hyperviscosity can be reversed by plasmapheresis
  - Diagnostic tests: serum protein electrophoresis and measurements of whole blood viscosity
Central Retinal Vein Occlusion

• Work-up:
  • Measurement of IOP to detect glaucoma.
  • Gonioscopy to determine a predilection for angle-closure glaucoma.

• Management:
  • Treatment of any associated medical conditions (hypertension, diabetes, hypercholesterinemia, hyperhomocysteinemia, history of smoking).
  • Reduction of platelet adhesiveness (e.g. Aspirin)
  • Cave: Conversion nonischemic to ischemic CRVO possible, 15% in the first 4 month, 34% after 3 years.
Central Retinal Vein Occlusion

• Therapy:
  • Intravitreal anti-VEGF agents (Lucentis®, Eylea®, primary therapy option)
    • CRUISE study: Gain of visual acuity of 13.9 (0.3 and 0.5 mg) letters in ranibizumab group; 7.3 letters in sham group
  • Corticosteroids (intravitreal) to reduce macular edema
  • Effectiveness of grid pattern photocoagulation for macular edema, especially in younger patients.

• Surgical therapy of CRVO:
  • Surgical decompression via radial optic neurotomy (sectioning the posterior scleral ring, retinal vein cannulation with tissue plasminogen activator (t-PA)).
Central Retinal Vein Occlusion

- Iris neovascularization:
  - Most important risk factor of iris neovascularization is the extent of retinal ischemia
  - Intraretinal blood

- Therapy:
  - Scatter panretinal photocoagulation
  - Anti-VEGF agents to reduce iris neovascularization in the short term
Retinopathy of Carotid Occlusion Disease

- Chronic ipsilateral carotid occlusion can cause ischemic retinopathy, that is similar in appearance to a partial occlusion of central retinal vein.
- Originally called venous stasis retinopathy.
- Hemorrhages are commonly deep and round, more often located in the midperipheral retina.
- Retinal veins are dilated in both (CRVO and carotid artery occlusion disease, CAOD).
- Veins more tortuous in CRVO than CAOD.
- Measurement of retinal artery pressure by ophthalmodynamometry to differentiate between the 2 entities:
  - CRVO normal artery pressure
  - CAOD low artery pressure
Arterial Occlusive Disease

• **Physiology:**
  • Blood supply to the inner layers of the retina is provided by the central retinal artery or cilioretinal artery (if present, in 15-30% of eyes).

• **Pathophysiology:**
  • Retinal ischemia results from vascular pathologies affecting the entire branch of carotid artery.

• Ophthalmic arterial occlusive disease can cause total blindness.
Arterial Occlusive Disease

- Types of Arterial Occlusive Disease:
  - Precapillary Retinal Arteriole Obstruction
  - Branch Retinal Artery Occlusion
  - Central Retinal Artery Occlusion
  - Ocular Ischemic Syndrome
Precapillary Retinal Arteriole Obstruction

- Acute obstruction of the radial peripapillary capillary net $\rightarrow$ NFL infarct (cotton-wool spot) $\rightarrow$ inhibiting axoplasmic transport in the NFL.

- Cotton-wool spots:
  - Inner retinal ischemic spots, superficial, white, usually $\frac{1}{4}$ disc area or less in size, perpendicular to the optic disc.
  - Fading in 5-7 weeks
  - Persist longer in association with diabetic retinopathy
Precapillary Retinal Arteriole Obstruction

Figure 18: Cotton-wool spot, hemorrhages, microaneurysms

© Vistaklinik
Precapillary Retinal Arteriole Obstruction

- Area of ischemia $\rightarrow$ inner retinal atrophy $\rightarrow$ subtle retinal depression in OCT.

- Effect on visual function (loss of visual acuity, visual field defects) depends on the size and location of the occluded area.
Precapillary Retinal Arteriole Obstruction

- Several risk factors:
  - Systemic arterial hypertension
  - Cardiac embolic disease
  - Carotid artery obstructive disease
  - Sickle cell retinopathy
  - Radiation retinopathy
  - Vasculitis
  - Collagen-vascular disease
  - Leukemia
  - AIDS
Branch Retinal Artery Occlusion

• Initially an acute BRAO may not be apparent ophthalmoscopically.

• By the time (hours to days) causes an edematous opacification due to infarction of the inner retinal layer.

• With time, the occluded vessel recanalizes, perfusion returns, and the edema resolves.

• A visual field defect results.
Branch Retinal Artery Occlusion

Figure 19: Superotemporal occlusion, multiple embolies

© Vistaklinik
Branch Retinal Artery Occlusion

• Occlusion is due to an embolization or thrombosis of the affected vessel.

• 3 different types of emboli:
  • Cholesterol emboli (Hollenhorst plaques) arising from the carotid arteries
  • Platelet-fibrin emboli associated with large vessel arteriosclerosis
  • Calcific emboli arising from diseased cardiac valves
Figure 20: Hollenhorst plaque
Figure 21: Platelet-fibrin emboli
Figure 22: Calcific embolus
Branch Retinal Artery Occlusion

- Rare causes of emboli:
  - Cardiac myxoma
  - Fat emboli (from long-bone fractures)
  - Septic emboli (from infective endocarditis)
  - Talc emboli (in intravenous drug users)

- Rarely migraine can cause ocular arterial occlusion in patients < 30 years.
Branch Retinal Artery Occlusion

- Other associations:
  - Trauma
  - Coagulation disorders
  - Sickle cell disease
  - Oral contraceptive use / pregnancy
  - Mitral valve prolapse
  - Inflammatory and / or infectious etiologies such as toxoplasmic retinochoroiditis and syphilis
  - Connective tissue disorders, incl. giant cell arteritis

- Management is directed toward determining systemic etiologic factors.
Central Retinal Artery Occlusion

- Sudden, complete and painless loss of vision.

- The retina becomes opaque and edematous, particularly in the posterior pole where the nerve fiber and ganglion cell layers are thickest.

- Superficial macular opacification and a cherry-red spot in the foveola.

- With time, the central retinal artery recanalizes and the retinal edema clears.
Central Retinal Artery Occlusion

• The effect on visual acuity is usually permanent because of the infarction of the inner retina.

• Better vision prognosis if cilioretinal artery is present.

• Return of vision can occasionally happen after obstruction has persisted up to 90 min.
Central Retinal Artery Occlusion

Figure 23:
Cherry-red spot
Central Retinal Artery Occlusion

Figure 24:
CRAO with patent cilioretinal artery

Figure 25:
Regular filling of cilioretinal artery

Central Retinal Artery Occlusion

- Causes of CRAO:
  - Atherosclerosis-related thrombosis occurring at the level of the lamina cribrosa
  - Embolization (20%)
  - Hemorrhage under an atherosclerotic plaque
  - Thrombosis
  - Spasm
  - Dissecting aneurysm within the central retinal artery
  - Giant cell arteritis (1-2%): Laboratory tests (erythrocyte sedimentation rate, C-reactive protein)
Central Retinal Artery Occlusion

• Management:
  • Reduction of IOP
  • Aspirin
  • Local intraarterial fibrinolysis (LIF) not recommended because of no clear trend to benefit from LIF even in patients with young age, no coronary heart disease and early treatment; and higher rate of adverse reactions (Eagle study).

• Complication:
  • Iris neovascularization occurs in 18% of cases in 1-12 weeks after the occlusive event.
Central Retinal Artery Occlusion

- Therapy:
  - Full-scatter PRP is effective in eradicating the new iris vessels (66%).
Ocular Ischemic Syndrome

• Ocular symptoms and signs attributable to chronic, severe carotid artery obstruction.

• Etiology:
  • Atherosclerosis (most common)
  • Eisenmenger syndrome (congenital heart defect → left-to-right cardiac shunt → pulmonary hypertension)
  • Giant cell arteritis
Ocular Ischemic Syndrome

Figure 26: Subacute occlusion of A. carotis interna

Ocular Ischemic Syndrome

Figure 27: Giant cell arteritis

Ocular Ischemic Syndrome

- Epidemiology:
  - Most patients are older than 55 years of age.
  - Typically a relevant (>90%) ipsilateral obstruction of carotid artery is present.
  - Both eyes are involved in 20% of cases.

- Symptoms:
  - Amaurosis fugax
  - Hemispheric TIA
  - Non-disabling stroke
  - Visual loss (usually occurring over a period of weeks to months)
  - Aching pain (localized to the orbital area of the affected eye)
Ocular Ischemic Syndrome

- Clinical findings:
  - Iris neovascularization (66%), increase in IOP (50%)
  - Changes in the anterior chamber (cells, tyndall effect, 20%)
  - Narrow retinal arteries
  - Dilated (but generally not tortuous) retinal veins
  - Retinal hemorrhages
  - Microaneurysms
  - Neovascularization of the optic disc and/or retina
Ocular Ischemic Syndrome

- Fluorescein angiography:
  - Delayed choroidal fillings (60%)
  - Delayed arteriovenous transit time (95%)
  - Prominent vascular staining (85%)
Figure 28: Hemorrhages, narrowed arteries

© Vistaklinik
Ocular Ischemic Syndrome

- Electroretinography:
  - Diminished amplitude of the a- and b-waves as a result of outer and inner layer retinal ischemia.

- Characteristics of patients with ocular ischemic syndrome
  - Ischemic cardiovascular disease in 50%
  - History of cerebrovascular accident in 25%
  - Peripheral atherosclerotic vascular disease in 20%
Ocular Ischemic Syndrome

- **Prognosis:**
  - when rubeosis iridis is present, then in 90% blindness is a result within a year after the disease is discovered.

- **Therapy:**
  - Carotid artery stenting and endarterectomy
  - Ocular therapy:
    - Argon laser photocoagulation for treatment of ischemia, ocular hypertension/glaucoma
Summary

- Anti-VEGF agents are an effective treatment for retinal vein occlusions.

- Minimization and treatment of the cardiovascular risk factors is important in diseases like hypertensive retinopathy, retinal arterial and vein occlusions.

- Iris neovascularization and its following complication (neovascular glaucoma) is a major complication.
Themes for conferences – No 42

References

• Basic and Clinical Science Course
  Section 12 Retina and Vitreous
  2011/2012
  American Academy of Ophthalmology

• Preferred Practice Pattern
  Retinal Vein Occlusions 2016
  American Academy of Ophthalmology
Themes for conferences – No 42

Thank you for your attention.