Evidence Based Management of Secondary Glaucoma
COPE # 45403-GL
Room 243-245
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Abstract:
This course presents an evidence-based literature review for the primary care practitioner regarding the diagnosis, treatment, and management of secondary glaucoma. The most common secondary glaucomas including pseudoexfoliative, pigmentary, uveitic, traumatic, steroid induced, and neovascular glaucoma will be discussed.

Learning Objectives:
1. Identification of ocular signs associated with the most common secondary glaucomas
2. Understanding the pathophysiology and natural history of these risk factors for glaucoma.
3. Review current literature on most effective medical and surgical management in the case of each disease
I. Pseudoexfoliation Syndrome and Glaucoma
   A. Background
      a. Disorder of extracellular matrix where fibrillar basement membrane material is produced by anterior segment structures (endothelium of iris, cornea, trabecular meshwork and epithelium of lens/ciliary body)
      b. Scandinavian (93% of glaucoma in region) and European populations
   B. Pathophysiology and ocular manifestations
      a. Pseudoexfoliative material blocks or restricts aqueous flow at trabecular meshwork and results in an increase in IOP
      b. Pseudoexfoliative deposits on anterior capsule of lens – Bull’s Eye Pattern
      c. Pupillary ruff atrophy
      d. Poor Mydriasis
      e. Corneal endothelial dysfunction
      f. Spontaneous iris hemorrhages
      g. Gonioscopy: patchy pigmentation of TM often greater in eye with more glaucomatous damage.
   C. Natural History and differences compared to Primary Open Angle Glaucoma
      a. Conversion rate from pseudoexfoliation syndrome to glaucoma – approximately 30-40%, ALL initially ocular hypertensive PEX eyes converted to glaucoma
      b. Diurnal fluctuations, higher mean IOP, pressure spikes, higher frequency/severity of ONH damage, worse VF loss, poorer response to medications, more frequent necessity for surgery
      c. Amount of pseudoexfoliative material does not correlate with severity of glaucoma or IOP measurements
      d. Association with angle closure—zonular weakness leads to forward lens movement, pupillary block from posterior synechiae formation
   D. Clinical Management
      a. Suspects vs. Pseudoexfoliative Glaucoma
      b. Only secondary glaucoma found to increase risk for VF progression (EMGT)
      c. IOP lowering medications
      d. Glaucoma surgeries and effectiveness
      e. Increased complication rates for cataract surgery (phacodenesis, poor mydriasis, lens subluxation, harder lens nuclei) – consider surgery sooner
      f. Post cataract surgery management and risks

II. Pigmentary Dispersion Syndrome (PDS) and Glaucoma
   A. Background
      a. Backward bowing of iris causing rubbing of pigmented iris epithelium against lens zonules, leading to the liberation of iris pigment, trabecular meshwork changes and subsequent potential increase in IOP
      b. Young male myopes (78-93% male)
c. Caucasians
d. Accounts for 1-1.5% of glaucoma in the United States

B. Pathophysiology and ocular manifestations
   a. Pigment liberation causing blockage of aqueous outflow at trabecular meshwork
   b. Reverse Pupillary Block- pressure in anterior chamber great than posterior chamber and closes iris-lens flap valve
   c. Triad: Krukenberg spindle on corneal endothelium, transillumination defects or iris, pigment in anterior trabecular meshwork – only 42% show all 3 signs
   d. Anterior chamber: very deep with pigment showers
   e. Iris: heterochromia, anisocoria
   f. Lens: subtle pigment on anterior capsule, pigment at junction of zonules and posterior capsule (Scheie’s line)
   g. Gonioscopy: increased pigmentation, of TM, tends to be homogenous but can be greater inferiorly due to gravity; can also have pigmented Schwalbe’s line
   h. Influence of Exercise – increases pigment dispersion, IOP, decrease aqueous outflow

C. Natural history and differences compared to Primary Open Angle Glaucoma
   a. Conversion rate from PDS to pigmentary glaucoma – approximately 10-15% convert
      i. exercise, blinking, accommodation
   b. Burned out phase
      i. Reduced pigment dispersion and normalized IOP
      ii. Pigment reversal sign
      iii. Zonules rubbed the entire posterior pigment epithelium off iris
      iv. Age related increase in lens axial length, decreased pupil size
   c. Unlike pseudoexfoliation, degree of pigment dispersion tends to correspond to severity of glaucoma
   d. Other cause of pigment dispersion (cataract surgery)

D. Clinical Management
   a. IOP lowering medication
   b. Surgery: Peripheral Laser Iridotomy
      i. When is it most appropriate to recommend surgery? Most useful during active stage of disease
      ii. Equalizes pressure between AC and PC, relieves posteriorly bowed iris
      iii. Relieves reverse papillary block
      iv. Most beneficial prior to development of glaucoma
   c. Glaucoma surgeries and effectiveness
      i. ALT vs SLT – proposed mechanisms
      ii. Research on monocyte modulation of aqueous outflow and recruitment to the trabecular meshwork following SLT
III. Uveitic Glaucoma

A. Background
   a. Intraocular inflammation causes rise in IOP
   b. Inflammation treated with corticosteroids \(\rightarrow\) Steroid Responders can also experience a rise in IOP
   c. Trabecular meshwork blocked by inflammatory cells

B. Pathophysiology and ocular manifestations
   a. Peripheral Anterior Synechiae (PAS) can develop and block TM \(\rightarrow\) secondary angle closure glaucoma
   b. Cells
   c. Flare
   d. Keratic Precipitates (stellate vs mutton fat)
   e. Hypopyon
   f. Iris Nodules (Koepppe, Busacca)
   g. Iris Posterior Synechiae
   h. Iris Atrophy
   i. Iris Heterochromia
   j. Band Keratopathy

C. Natural History
   a. Rate of glaucoma development in children versus adults
   b. Risk factors for elevated IOP
      i. Types of uveitis (Posner Schlossman, Fuch’s, HSV highest risk)
      ii. Chronic/recurrent vs. Acute Uveitis – Chronic more likely to have increase in IOP
      iii. Steroid usage – More likely to have raised IOP
      iv. Active vs Inactive Uveitis – active inflammation more likely to have higher IOP

D. Clinical Management
   a. Treat systemic condition
   b. Treat ocular inflammation
      i. Mydriatic
      ii. Corticosteroids (steroid responders) - 18 to 30%, occurs 2-6 weeks after starting (oral, IV, inhaled, topical, periocular, intravitreal)
   c. Treat glaucoma
      i. Role of prostaglandin analogs – reports that Xalatan greater efficacy and lower rates of recurrence of uveitis compared to Cosopt
      ii. LPI

IV. Angle Recession (AR) and Traumatic Glaucoma

A. Background
   a. Recession of anterior chamber following non-penetrating ocular trauma, cleft forms between circular and longitudinal muscles of ciliary body
b. Patient history: common causes of injury inducing angle recession
   i. Sports, recreational activities, assault

B. Pathophysiology and ocular manifestations
   a. Blunt trauma forces aqueous laterally and posteriorly against iris, hydrodynamic force exerts traction on iris root → tear between longitudinal and circular muscles of ciliary body
      i. Obliteration of intertrabecular spaces and Schlemm’s canal
      ii. Direct damage to trabecular meshwork can cause early rise in IOP
      iii. Scarring/fibrosis/atrophy of TM over time leads to gradual decrease in outflow facility with increasing age
   b. Correlation between hyphema and angle recession
      i. 56 to 100% patients with hyphema have some degree of angle recession
   c. Signs of Trauma
      i. Corneal scars, pigment deposits, pupillary sphincter tear (dilated pupil), Vossius ring, hyphema, iridodialysis, torn iris processes, phacodenesis, retinal/choroidal atrophy or hyperpigmentation, tears
      ii. With orbital fracture, watch for orbital emphysema
   d. Gonioscopy appearance
      i. Broad ciliary body band
      ii. Disruption of regular pattern of insertion of iris fibers into the ciliary body or scleral spur
      iii. Localized deepening, change in color/texture of angle
   e. Gonioscopy technique
      i. Compare appearance between angles within eye to detect differences in appearance
      ii. Compare same angle between 2 eyes- important especially for 360 degree angle recession
      iii. May need to switch lens from eye to eye several times

C. Natural History
   a. 6-7% of eyes with recession of iridocorneal angle will eventually develop glaucoma
   b. Correlation between extent of angle recession and decrease in outflow
      i. Eyes with less than 180 degrees recession unlikely to develop glaucoma
      ii. 180 to 360 degrees of angle recession greater risk of developing late-occurring glaucoma
   c. Two peak incidences of glaucoma
      i. 1st peak- first few weeks to years after trauma, easier to treat with medications alone
      ii. 2nd peak- 10 or more years after injury, more difficult to treat and may require surgical intervention
d. Other signs of trauma – subconjunctival hemorrhage, corneal scars, hyphema, iris sphincter damage, iritis, vossius ring, rosette cataract, phacodendesis, commotion retinae, choroidal rupture, macular hole, retinal tear
e. Glaucoma in fellow eye – is angle recession a risk factor or merely a trigger for glaucoma development in somebody who is already going to develop the disease?

D. Clinical management
   a. IOP lowering medications
   b. Argon laser trabeculoplasty unsatisfactory
   c. Trabeculectomy (43% in AR vs 74% POAG success rate)
      i. Bleb fibrosis earlier, increased tendency for fibroblast proliferation, change in aqueous humor properties

V. Steroid Induced Glaucoma
   A. Background
      a. Oral, IV, inhaled, topical, perioocular or intravitreal corticosteroid therapy can cause ocular hypertension
      b. If ocular hypertension not recognized and treated, subsequent glaucomatous optic neuropathy can develop.
   B. Pathophysiology
      a. Steroid Response: physical/mechanical changes in microstructure of TM, increased deposition in TM, decreased capacity for phagocytosis by endothelial cells in TM
   C. Natural History
      a. Ocular hypertension can develop within 2-6 weeks following steroid use
      b. Approximately 18-30% exhibit a steroid response or increase in IOP
      c. Armaly study, 90% of POAG patients responded with IOP elevation greater than 6 mm Hg
      d. IOP returned to baseline approximately 1 week after discontinuation of medication
      e. Bimodal distribution of increased risk: Older patients and children
      f. Pre-existing POAG, glaucoma suspect, and first degree relative with POAG are important risk factors for steroid-induced ocular hypertension
      g. Most patients successfully managed with topical glaucoma medications
      h. Surgical techniques required in less than 2% of cases
   D. Clinical Management
      a. Increased popularity of intravitreal triamcinolone for subretinal fluid, macular edema and adjunctive therapy in treatment of CNVM has led to increase in steroid induced ocular hypertension

VI. Neovascular Glaucoma
   A. Background
a. Severely blinding, intractable disease
b. Need to have high index of suspicion for development

B. Pathophysiology
   a. Retina starved for oxygen → VEGF released, moves anteriorly through pupil
      → NVI develops → VEGF travels to angle → NVA develops → fibrovascular membrane → PAS and Angle Zipped Up → Increased IOP
   b. Most common diseases associated with NVG
      i. Ischemic CRVO – 45% develop NVG, highest risk first 7-8 months, primary factor for blindness is NVG not ischemic CRVO
      ii. Ocular Ischemic Syndrome
      iii. Proliferative Diabetic Retinopathy
   c. Other causes: BRVO, BRAO, CRAO, Radiation Retinopathy, Tumor, Chronic Uveitis, Chronic RD, Retinopathy of Prematurity, Sickle Cell Retinopathy, Eales Disease

C. Natural History
   a. Once NVA develops, fibrovascular membrane is sticky and leads to peripheral anterior synechiae, angle becomes “zipped up” and IOP spikes.

D. Clinical Management
   a. Do not let it develop!
   b. Have high index of suspicion for which conditions can lead to neovascular glaucoma and treat underlying condition early
   c. Topical Steroids - evidence that they inhibit angiogenesis and NV, but be aware of steroid responders masking as NVG, perform gonioscopy
   d. Cycloplegics
   e. Cyclodestruction
   f. Alcohol Injection
   g. Evisceration, Enucleation, Exenteration
Bibliography


Akdemir MO, et al. The Effect of PEX and PEX Induced Dry Eye on Central Corneal Thickness. Current Eye Research, Early Online, 1-6, 2015.


