Secondary Open Angle Glaucoma

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Glaucoma refers to the group of diseases that have in common a characteristic optic neuropathy with associated visual field loss for which elevated intraocular pressure (IOP) is one of the primary risk factors.
Glaucoma - Epidemiology

- Glaucoma is a major worldwide health concern, because of its usually silent, progressive nature, and because it is one of the leading preventable causes of blindness in the world.
- Over 3 million individual over age 45 in the US are estimated to have POAG.
- 84,000-116,000 are bilaterally blind from POAG. (VA 20/200 or worse or visual field less than 20 degrees)
- Glaucoma is the second leading cause of blindness in the world (surpassed only by cataracts, a reversible condition).
- More than 3 million people are bilaterally blind from POAG worldwide, and more than 2 million people will develop POAG each year.
- Primary Angle closure glaucoma is responsible for half of glaucoma blindness worldwide.
- Number cases worldwide 64.3 million (2013), increasing to 76 million in 2020 and 111.8 million by 2040
Glaucoma Risk Factors

- Risk factors
  - Advancing age - single most important but is untreatable.
  - Family history (1st degree relative)
  - African heritage. Prevalence POAG in whites >40 yrs old is 1.1-2.1%. It is 3-4 times higher in blacks than whites.
  - Elevated IOP - only treatable factor
  - Optic nerve cup size
  - Refractive error - myopia for POAG, hyperopia for ACG
  - Prevalence of ACG is highest in inuits (2-40x whites), prevalence 0.1% in whites of US/Europe. Asians somewhere in between.
  - Women develop ACG 3-4 times more often than men.
Glaucoma

- Many types of glaucoma and ways to classify them.
  - Open angle glaucoma
    - Primary open angle
    - Secondary open angle
      - Pseudoexfoliation, pigment dispersion
      - Phacolytic, steroid induced
    - Normal tension
    - Juvenile open angle
    - Glaucoma suspect/Ocular Hypertension
  - Closed angle glaucoma
    - Acute angle closure
    - Chronic angle closure
    - Secondary angle closure
      - Neovascular, uveitic, iridocorneal endothelial syndrome
      - Posterior segment tumor, uveal effusion
      - Aqueous misdirect, suprachoroidal hemorrhage
  - Childhood glaucoma
    - Primary congenital/infantile
    - Associated with congenital anomalies (aniridia, rubella)
    - Secondary glaucoma (trauma, retinoblastoma)
Secondary Open Angle Glaucoma

- Secondary open angle glaucoma can be subdivided based on site of aqueous outflow obstruction

  - **Pre-trabecular** - outflow obstructed by a membrane covering the TM
    - Neovascular glaucoma, Iridocorneal endothelial syndrome, epithelial ingrowth

  - **Trabecular** - the meshwork gets clogged up and undergoes secondary degeneration
    - Pigmentary, Red blood cells, ghost cell glaucoma, phacolytic, uveitic, PXG, trabeculitis, scarring

  - **Post-trabecular** - TM normal but outflow obstructed by elevated episcleral venous pressure
    - Carotid-cavernous fistula, Sturge-Weber syndrome, Obstruction of Sup vena cava
Glaucoma Drops First Line

- **Prostaglandin Derivatives (Latanoprost, Travoprost, Bimatoprost, Tafluprost)**
  - Decreases IOP 25-35%, Peak effect 10-14 hrs, onset of action within hours, Dosed 1 drop QHS, better response when taken at bedtime, this may help avoid hyperemia, BID dosing decreases effect

- **Side effects**
  - Local - Conjunctival hyperemia, darkening of the iris and periorcular skin (inc melanosomes), hypertrichosis, cystoid macular edema, reactivation of herpetic keratitis, uveitis
    - Light irides 10-20% experience darkening while brown or two tones may have 60% with darkening. May be permanent.
  - Systemic - headache, myalgias, malaise, flu-like symptoms

- **Contraindications**
  - Caution in inflammatory glaucoma, cme, history of herpes keratitis, pregnancy
Beta Blockers (Timolol, Levobunolol, Betaxolol, Carteolol, Metipranolol)

- Decreases IOP 20-30%, peak effect 2-3 hrs, given qam-BID
- Side effects
  - Local - allergy, punctate keratitis
  - Systemic - Bradycardia, Heart block, Bronchospasm, CNS depression, syncopy
- Contraindicated in heart failure, bradycardia, 2nd and 3rd degree heart block, asthma, COPD
  - May see less effect at night and if on systemic beta blocker
  - May avoid pm dosing in NTG patients, less effect at night and could lower BP
  - Use with caution in children because of high systemic levels
  - Caution in pregnancy and nursing mothers - fetal bradycardia, cardiac arrhythmias have been reported. High concentration found in breast milk.
Glaucoma Drops Adjunctive

- **Alpha-2 agonists (Brimonidine 0.2%, Brimonidine 0.15% and Alphagan P 0.1%)**
  - Decreases IOP by 20-30%, Peak effect 2 hr, trough 12hrs post dose, dosed BID or TID
  - Side effects
    - Local - foreign body sensation, eyelid edema, follicular conjunctivitis (can occur late)
    - Systemic - Fatigue, headache, hypotension, depression, insomnia, syncope
  - Contraindications - Should not be used in infants and young children due to increased risk of somnolence, hypotension, seizures, apnea, and derangement of neurotransmitter due to increased CNS penetration.
  - Caution is recommended in patients on MAOI’s or TCAs, and in patients with severe cardiovascular disease.
Glaucoma Drops Adjunctive

- **Carbonic Anhydrase Inhibitors (Dorzolamide, Brinzolamide)**
  - Decrease IOP by 14-17%, Peak effect 2-3 hrs, dose BID, TID
  - Side effects -
    - Local - burning on instillation, punctate keratitis, local allergy - blepharoconjunctivitis, bitter taste, induced myopia, worsen corneal failure
    - Systemic - mild
  - Contraindications
    - Sulfa allergy
    - Coadministration of topical and oral CAIs is not recommended because no additive effects
**Glaucoma Drops Second Line**

- **Pilocarpine 1-4%**
  - Lowers IOP 15-25%, Peak effect 2hrs, lasts 8 hrs, used qhs - QID
  - Side effect profile and QID dosing make it a second line drug.
    - Systemic side effects - Excessive sweating, salivation, bradycardia, hypotension, bronchospasm, nausea, diarrhea, worsening of Alzheimer’s dementia. Rare with ocular dosing for chronic glaucoma but may occur with frequent dosing in acute glaucoma.
    - Ocular side effects - Miosis, dimming of vision especially in patients with cataracts, induced myopia/ accommodative spasm, brow ache (better after few weeks of use), cataractogenesis, miotic cysts, risk of retinal detachment.
  - Contraindications
    - Uveitic glaucoma - increases inflammation, Glaucoma associated with anterior displacement of lens-iris diaphragm, Aqueous misdirection
    - Avoid in people with breathing problems, heart, kidney, gallbladder dz.
    - Not tested in children, teratogenic at high doses in animals.
Glaucoma Oral Medications

- **Systemic carbonic anhydrase inhibitors (acetazolamide, methazolamide)**
  - Decreases IOP 30%, Peak effect for oral med is 2 hrs, IV onset of action 2 mins, 500mg (5-10mg/kg), Dosed - acetazolamide given BID - QID, Methazolamide given BID
  - Side effects - systemic
    - numbness/tingling of the hands, feet, and lips, malaise, metallic taste with carbonation, anorexia, nausea, somnolence, impotence, loss of libido and depression.
    - Rare effects transient myopia, hypersensitive nephropathy, rash, thrombocytopenia, aplastic anemia.
  - Contraindications include sulfa allergy, renal impairment/kidney stones, cirrhosis
    - Patients on thiazide diuretics and steroids can develop hypokalemia and should have K+ checked.
    - Teratogenic effects demonstrated in rodents - relative contraindication
  - Used for acute high IOP, decrease IOP prior to glaucoma surgery
Glaucoma Medications
Glaucoma Treatment

- **Specific situations**
  - **Pregnancy**
    - Avoid prostaglandins (increase uterine contractility), caution with beta blockers (bradycardia, arrhythmias), CAIs teratogenic in animals.
    - Brimonidine is Class B in pregnancy
  - **Children**
    - Alphagan must not be used in infants and young children (hypotension, bradycardia, somnolence, lethargy), caution with beta blockers
    - Prostaglandins, CAI, and miotics are possible treatments.
  - **Inflamed eye**
    - Avoid Pilocarpine, Prostaglandins
  - **Cystoid macular edema, h/o herpes keratitis**
    - Avoid Prostaglandins
Secondary Open Angle Glaucoma
Pre-Trabecular

- **Neovascular Glaucoma**
  - Abnormal blood vessels grow in and obstruct the anterior chamber angle
  - Causes include most commonly Ischemic CRVO and DM, less commonly CRAO and OIS.
  - The above lead to diffuse retinal ischemia which causes production of angiogenic factors (VEGF)
  - Neovascular tissue grows across the angle and later contracts to close the angle.
Secondary Open Angle Glaucoma Pre-Trabecular

- Neovascular Glaucoma
- Presentation - Often presents late with acute increase in pressure. Redness and corneal edema.
- Early diagnosis by examination of iris for vessels can improve prognosis.
Secondary Open Angle Glaucoma
Pre-Trabecular

- **Neovascular Glaucoma**
  - Treatment Drops - give set of all drops (no pilo - inflammatory) and if IOP very high Acetazolamide 500mg IV or PO
  - Intravitreal Avastin and PRP to stop progression of NVI/NVA
  - Often require urgent/emergent tube shunt or if very bad prognosis transscleral cyclophotocoagulation
Secondary Open Angle Glaucoma
Pre-Trabecular

- **ICE - Iridocorneal Endothelial Syndrome**
  - Typically affects one eye, more common in middle aged women.
  - Abnormal corneal endothelial layer with a predilection for proliferation and growth across the angle to the iris.
  - 50% develop glaucoma, many develop corneal decompensation.
  - Association with Herpes simplex virus.
Secondary Open Angle Glaucoma
Pre-Trabecular

- **ICE**
  - Three clinical presentations
    - Chandler syndrome (most common)
      - Hammered silver endothelium and about 40% have some iris atrophy
      - Halos from corneal edema
      - Glaucoma less severe if present
    - Progressive (essential) iris atrophy
      - Severe iris changes and PAS
    - Iris nevus (Cogan-Reese) syndrome
      - Diffuse iris nevus or nodules
      - Some iris atrophy
  - Treatment
    - Medical therapy often fails
    - Trab/Tube
Secondary Open Angle Glaucoma
Pre-Trabecular

- **Epithelial ingrowth**
  - Rare complication of anterior segment surgery/trauma
  - Conjunctival or corneal epithelial cells migrate through a wound and proliferate in the anterior chamber
  - Angle blocked by a membrane, synechial closure, or desquamated epithelial and inflammatory cells
Secondary Open Angle Glaucoma Pre-Trabecular

- **Epithelial ingrowth**
  - **Diagnosis**
    - Persistent postop anterior uveitis
    - Diffuse epithelialization - greyish translucent membrane with scalloped borders on the posterior cornea in the area of a prior wound.
  - **Treatment**
    - Block excision of involved iris and pars plicata of the ciliary body and all layers of cornea and sclera in contact with the lesion. Closed with a tectonic corneoscleral graft.
    - Cryotherapy
    - 5-fluorouracil
    - Trab or tube for elevated IOP. Glaucoma can be intractable/Poor prognosis
Secondary Open Angle Glaucoma
Trabecular

- Pigmentary Glaucoma
- Characterized by liberation of pigment from iris pigment epithelium and deposition on AC structures (PDS)
- Myopia is a risk factor. More common in young myopic males. There is also a cluster of disease in older hyperopic black females.
- Pressure elevated 2/2 pigment stuck in TM and TM degradation and denudation, collapse and sclerosis.
Secondary Open Angle Glaucoma
Trabecular

- Pigmentary Glaucoma
- Presentation
  - PDS/PG often detected at routine exam
- Features
  - Midperipheral TID’s
  - Kruckenberg spindle
  - Heavy TM pigment
- IOP wide fluctuation, increased with exercise
- Lattice degeneration and RD may be higher than in myopes without PDS/PG
Secondary Open Angle Glaucoma Trabecular

- Pigmentary Glaucoma
- Treatment
  - Lifestyle - avoid exercise involving jolting movements - jogging. Pilocarpine may be prophylactic in exercise.
  - Drops - all types
  - ALT/SLT - often effective
  - Laser Iridotomy - may reverse iris concavity and decrease iridozonular contact - benefit not proven
  - Filtration surgery
Secondary Open Angle Glaucoma Trabecular

- **Hyphema**
  - Most traumatic hyphemas resolve without elevated IOP but blood from a hyphema can block the TM and lead to very high IOP.

- **History**
  - Mechanism of injury, when it occurred, any vision loss, taking any blood thinners, any h/o sickle cell disease or trait

- **Presentation**
  - Pain, blurring after trauma. On exam gross layering of blood or clot in anterior chamber
  - Size of the hyphema is a useful indicator of visual prognosis, in total hyphema patients only 1 in 3 patients achieve good VA, vision loss mostly secondary to the original trauma.
Secondary Open Angle Glaucoma Trabecular

- **Hyphema**
  - Treatment
    - Check for sickle-cell, stop any aspirin/Nsaids
    - Bedrest, HOB elevated, clear shield at all times, possible hospitalization
    - Avoid scleral depression and gonioscopy unless intractable IOP
    - Close follow-up, daily for first 4 days, check IOP and look for rebleeding. Rebleeding most often occurs day 3-5 and is associated with a worse prognosis
Secondary Open Angle Glaucoma Trabecular

- **Hyphema Treatment**
  - All patients get atropine and prednisolone
- Elevated Pressure - Non-sickle cell disease/trait
  - Beta blocker, carbonic anhydrase inhibitor, alpha agonist (avoid pilo and prostaglandins). Oral CAI if needed.
- Elevated Pressure - Sickle cell disease/trait
  - Start with beta blocker
  - All other agents use with caution
    - Carbonic anhydrase inhibitors may reduce AC pH and induce sickling
    - Brimonidine may affect iris vasculature
    - Pilocarpine and prostaglandins - pro-inflammatory
  - Antifibinolysis with aminocaproic acid can be considered in high risk circumstances
  - Surgical evacuation if persistent elevated IOP or development of corneal blood staining
Secondary Open Angle Glaucoma
Trabecular

- **Ghost Cell**
  - Degenerated RBCs (ghost cells) block the trabecular meshwork.
  - RBC that have lost their hemoglobin, khaki colored
  - Less pliable than normal RBCs, obstruct the TM
  - Can occur 1-3 months after vitreous hemorrhage
  - Ghost cells gain access to the AC through disrupted hyaloid face (which can occur after PPV, CEIO, yag cap)
Secondary Open Angle Glaucoma
Trabecular

- **Ghost Cell**
- Presentation - elevated IOP, many small tan colored cell in AC.
- Treatment
  - Glaucoma drops to control pressure, usually resolves once vitreous hemorrhage resolves.
  - If IOP too high then ac washout, PPV or Trabceulectomy.
Secondary Open Angle Glaucoma

**Trabecular**

- **Phacolytic**
  - Occurs in association with a hypermature cataract.
  - Lens proteins leak though an intact lens capsule and block the meshwork.
  - Macrophages containing lens proteins may contribute to trabecular obstruction.
Secondary Open Angle Glaucoma Trabecular

- **Phacolytic**
- **Presentation**
  - Pain, elevated IOP, decreased vision 2/2 cataract
  - SLE shows corneal edema, hypermature cataract, white particles in the AC - lens material and macrophages, pseudohypopyon
- **Treatment**
  - Pressure control with all glaucoma drops and systemic medication
  - Cataract removal, careful because zonules are often weak
Secondary Open Angle Glaucoma
Trabecular

- **Uveitic**
- Uveitis can lead to open angle and closed angle glaucomas.
  - Secondary open angle glaucoma
  - Angle closure with pupillary block
  - Angle closure without pupillary block
Secondary Open Angle Glaucoma Trabecular

- **Uveitic**
- In acute anterior uveitis initial IOP can be low, ciliary body shut down.
- Later can be elevated from trabecular obstruction by inflammatory debris and cells or from trabeculitis.
  - Trabeculitis is swelling and edema of the meshwork
    - Especially associated with HSV
- Steroid can also cause elevated IOP (steroid responders)
Secondary Open Angle Glaucoma
Trabecular

- **Uveitic**

- **Presentation**
  - Pain, AC cell/flare, injection
  - Corneal edema if IOP very high.

- **Treatment**
  - Steroids - watch for steroid responders, caution with subtenons/intravitreal steroids
  - All drops except Pilocarpine and prostaglandin
  - Systemic carbonic anhydrase inhibitors
  - Surgery - Trab or Tube shunt, CPC
    - Perioperative steroids important, oral steroids may help and slow taper postop
Secondary Open Angle Glaucoma
Trabecular

- **Pseudoexfoliative glaucoma**
  - Caused by deposition of grey white fibrillary amyloid like material in the trabecular meshwork
  - Rare before age 50 y/o.
  - Women>men
  - Prevalence up to 5% in many populations, common in Scandanavia, parts of Africa
  - Thought of as an ocular manifestation of a systemic condition.
Secondary Open Angle Glaucoma
Trabecular

- **Pseudoexfoliative glaucoma**

- **Features**
  - PXF material noted on the corneal endothelium, pupil margin, lens capsule
  - Transillumination defects at pupil margin, flare and AC PXF particles

- **Diagnosis usually incidental**

- **Prognosis worse than for POAG**
Secondary Open Angle Glaucoma

- Pseudoexfoliative glaucoma
- Treatment
  - Glaucoma drops - all types
  - Laser trabeculoplasty (SLT/ALT)
  - Cataract extraction
    - May significantly lower pressure
    - Higher complication rate 2/2 poor dilation and zonular weakness
    - Post-op IOP spike
  - Filtration surgery
Secondary Open Angle Glaucoma Trabecular

- **Angle recession**
  - Rupture of the ciliary body from blunt trauma.
  - **Presentation** -
    - Unilateral increased IOP, with history of trauma, can be remote.
    - On exam, signs of prior trauma, Gonioscopy shows widened ciliary body band
  - **Treatment** - all glaucoma drops, ALT/SLT usually not effective
  - Trabeculectomy or Tube shunt
Secondary Open Angle Glaucoma
Post-Trabecular

- **Sturge-Weber (encephalotrigeminal Angiomatosis)**
  - Congenital, sporadic phacomatosis
    - Port-wine stain - facial hemangioma over distribution of one or more branches of the trigeminal nerve
    - Leptomeningial hemangiomas - in the ipsilateral parietal or occipital region may cause contralateral seizures, hemiparesis, or hemianopia
    - Ocular - ipsilateral glaucoma, buphthalmos, dilated episcleral vessels, iris heterochromia, and diffuse choroidal hemangioma
  - Glaucoma ipsilateral to the facial hemangioma occurs in 30%
    - 60% of these occur before age 2, the other 40% occur between 2 y/o and adulthood.
    - Pathogenesis - trabeculodysgenesis and or elevated episcleral venous pressure
Secondary Open Angle Glaucoma
Post-Trabecular

- Sturge-Weber (encephalotrigeminal Angiomatosis)
  - Treatment
    - All glaucoma drops work but must consider age of patient
    - Surgery
      - Goniotomy
      - Combined trabeculotomy-trabeculectomy (high risk of suprachoroidal hemorrhage)
Secondary Open Angle Glaucoma
Post-Trabecular

- **Carotid cavernous (CC) fistula**
- Development of an arteriovenous fistula between the carotid artery and the cavernous sinus.
- Leads to increased venous pressure in the sinus and structures draining into it.
- Ocular manifestations result from
  - Increased episcleral venous pressure
  - Decreased arterial blood flow to the cranial nerves
  - Arterial and venous stasis around the eye
Secondary Open Angle Glaucoma Post-Trabecular

- Carotid cavernous (CC) fistula - Two types
  - Direct type has direct communication of carotid artery to the sinus
    - 75% after trauma
    - Presents days to weeks after the trauma with triad of
      - Pulsatile proptosis
      - Conjunctival chemosis (hemorrhagic)
      - Whooshing sound in the head
  - Other signs and symptoms - vision loss, epibulbar venous dilation, increased pressure, Ant segment ischemia, ptosis, ophthalmoplegia (6th nerve most commonly involved), optic nerve swelling, retinal hemorrhages
    - can be same side, opposite or bilateral
Secondary Open Angle Glaucoma
Post-Trabecular

- Carotid cavernous (CC) fistula - Two types
  - Indirect type arterial blood flows through a meningeal branch of the carotid artery to the sinus.
    - Secondary to spontaneous rupture of an atherosclerotic artery
  - More subtle features
    - Proptosis, dilated corkscrew epibulbar vessels, increase pressure, 6th nerve palsy, fundus exam with moderate venous dilatation
Secondary Open Angle Glaucoma Post-Trabecular

- Carotid cavernous (CC) fistula

- Investigation
  - CT and MRI may demonstrate prominence of the superior ophthalmic vein and enlarged extraocular muscles
  - CT/MRI angiography may be helpful

- Treatment
  - Direct - most are not life threatening. Surgical closure if does not close spontaneously. Trans-arterial approach with coiling, craniotomy may be needed.
  - Indirect - trans-venous occlusion of the involved sinus, spontaneous closure or occluding thrombosis sometimes occurs.
Secondary Open Angle Glaucoma

- Many types of Secondary Open Angle Glaucoma
  - Some very emergent and require quick treatment and likely surgery, NVG and hyphema while others are the very common glaucomas that we treat daily in our clinics, Pigmentary and Pseudoexfoliation syndromes.
  - Be aware of the contraindications and side effects/allergies of the drops we give our patients.
- Questions?