OCULAR INFLAMMATION AND SECONDARY GLAUCOMA

Eye Learn

All about the Eye

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Ocular Inflammation and Secondary Glaucoma

1. How will you diagnose and classify a case of inflammatory glaucoma? What are the treatment options available? (3+2)+5 D2015

- Inflammatory, or uveitic, glaucoma is a secondary glaucoma that often combines components of open-angle and angle-closure disease.

- In individuals with uveitis, elevated IOP may be caused by a variety of **mechanisms**; appropriate therapy depends on the etiology:
  1. Increased viscosity of aqueous humor;
  2. Fibrin and inflammatory cells blocking outflow through the trabecular meshwork or Schlemm's canal
  3. Swelling (Edema) and dysfunction of the trabecular meshwork;
  4. Endothelial cell dysfunction of the trabecular meshwork
  5. Scarring of the outflow channels;
  6. Development of a cuticular endothelial membrane over the angle;
  7. Liberation of active substances such as prostaglandins; Prostaglandin-mediated breakdown of the blood–aqueous barrier
  8. Neovascularization;
  9. Elevation of episcleral venous pressure;
  10. Forward displacement of the lens–iris diaphragm (uveal effusion);
  11. Pupillary block, and
  12. Formation of peripheral anterior synechiae (PAS) blocking outflow
  13. Corticosteroid-induced reduction in outflow through the trabecular meshwork

- **Pathogenesis**
- Elevated IOP can occur with any type of ocular inflammatory disease but is more common in the chronic forms than in the acute forms.
- Some uveitis patients may have low IOP.
- The etiology is unclear but may be related to a prostaglandin-mediated increase in uveoscleral outflow.
- Hyposecretion of aqueous humor (particularly if ciliary body detachment is present) has often been assumed to be the etiology for low IOP but has not been confirmed, as aqueous flow currently cannot be measured in the presence of uveitis
- In most ocular inflammatory diseases, aqueous humor formation is reduced and IOP is low.
- If outflow facility is reduced as well, however, IOP can be elevated.
- Because of this dual involvement of aqueous humor inflow and outflow, eyes with active inflammatory disease often suffer wide swings of IOP, and glaucoma may be missed if only occasional pressure measurements are made.

- Uveitides commonly associated with **open-angle inflammatory glaucoma include**
  i. Fuchs heterochromic uveitis (Fuchs heterochromic iridocyclitis),
  ii. Herpes zoster iridocyclitis,
  iii. Herpes simplex keratouveitis,
  iv. Toxoplasmosis,
  v. Juvenile idiopathic arthritis,
  vi. And pars planitis

- **Signs**
- The presence of KPs suggests anterior uveitis as the cause of IOP elevation.
- Gonioscopic evaluation may reveal subtle trabecular meshwork precipitates.
- Occasionally, PAS or posterior synechiae with iris bombé may develop, resulting in angle closure.

- **The treatment**
- In most situations, inflammation is suppressed by some combination of topical, systemic, and periocular corticosteroids.
- Rx of inflammatory glaucoma is complicated by the fact that **corticosteroid therapy** may increase IOP, likely by increasing outflow resistance, but possibly by improving aqueous production as well.
- A variety of other medications may be employed to reduce inflammation, including **cycloplegic agents, non-steroidal ant-inflammatory drugs, and immunomodulators such as methotrexate, azathioprine, and chlorambucil**

- **Miotic agents** should be avoided in patients with anterior uveitis, because they may they increase pain and congestion, exacerbate the inflammation and cause formation of posterior synechiae.
- **Prostaglandin analogues** may exacerbate inflammation in some eyes with uveitis and herpetic keratitis that might be confused with the underlying inflammatory condition; however, some patients may benefit from their IOP-lowering effects without increased inflammation.
- These patients can be extremely sensitive to medications (e.g., **acetazolamide**) that decrease aqueous production. In sensitive patients, the pressure can drop from over 50mmHg to under 5mmHg with a single dose. Careful individual titration is needed to arrive at the proper medication regimen.
- **Argon laser trabeculoplasty (ALT)** is not very helpful in eyes with active inflammation. It may cause a mild acute anterior uveitis in some patients and may also lead to peripheral anterior synechiae. For this and other reasons, most surgeons avoid ALT in patients with uveitis.
- Inhibitors of scarring such **as mitomycin-C or 5-fluorouracil (5-FU)** are often useful in this situation, as are tube-shunt devices such as the Ahmed or Molteno valve.
- In a young individual with uveitis and secondary glaucoma, an **Ahmed, Molteno, or Baerveldt implant** may be the preferred first procedure since trabeculectomy, even with antifibrosis agents, is unlikely to work.

Fuchs' heterochromic iridocyclitis

- **Epidemiology**
- Fuchs' heterochromic iridocyclitis is a chronic but relatively mild form of anterior uveitis associated with cataract and glaucoma.
- Approximately 90% of the cases are unilateral,
- The disease has its onset in the third and fourth decades of life- young to middle adulthood.
- Men and women are affected in equal numbers.
- No racial predilection

- **Etiopathogenesis**
- No specific cause has been identified although toxocariasis and toxoplasmosis have both been implicated by associated antibody findings.
- Rubella virus and antibodies against rubella virus have been found in the aqueous humor of young patients Fuchs'
- Furthermore, the incidence in the United States has significantly declined since the advent of the rubella vaccination program.
- This evidence strongly suggests that rubella infection plays a role in at least some cases of Fuchs'.

- **Symptoms**- Patients are generally asymptomatic until they develop cataract or vitreous opacities.

- **Signs** - It is characterized by **iris heterochromia, low-grade AC inflammation, posterior subcapsular cataracts, & secondary OAG**
- Despite the low-grade inflammation, these patients are classically asymptomatic and present with a non-hyperemic eye.
- **Cornea**- Fine round or stellate pancorneal KPs. Fine filaments on the endothelium
- **AC-** The physical findings in this syndrome include minimal cell and flare.
- **Iris-**
  i. Between the keratic precipitates, a patchy loss of the iris pigment epithelium, hypochromia, grey-white nodules on the anterior iris,
  ii. Heterochromia may be seen in about 70% of Caucasian eyes, if the iris is dark in color, heterochromia may be present in only 25% and the diagnosis may rest on the keratic precipitates and areas of iris atrophy.
  iii. Fluorescein angiography of the iris demonstrates ischemia, leakage, neovascularization, and delayed filling of the vessels.
- **Gonioscopy**
  i. Reveals fine fragile vessels that bridge the angle and can bleed causing an AC hemorrhage, either spontaneously with minimal trauma.
  ii. A classic finding is anterior chamber hemorrhage after a paracentesis during ocular surgery (Amsler sign).
  iii. These vessels are usually not accompanied by a fibrous membrane and typically do not result in PAS formation and secondary angle closure, although in rare cases the neovascularization may be progressive.
- **Posterior segment-** a few opacities in the anterior vitreous, and chorioretinal scars that resemble toxoplasmosis.
- **IOP-**
  i. Increased IOP has been reported in 13–59% of patients with Fuchs' heterochromic iridocyclitis.

ii. Secondary OAG occurs in approximately 15% of patients with this disease
iii. The cause of the glaucoma is not clear, but the angle is open and no peripheral anterior synechiae are seen.
iv. It is postulated that the inflammation eventually produces scarring and dysfunction of the outflow channels.
v. Histologic examination of a few surgical specimens has confirmed the inflammation and scarring of the trabecular meshwork and revealed an inflammatory membrane over the angle.
vi. Glaucoma may also be seen following cataract surgery, neovascularization, or over-zealous treatment with corticosteroids.

- **Treatment**
- IOP control may be difficult, and the IOP does not necessarily correspond with the degree of inflammation.
- The inflammatory component of Fuchs' heterochromic iridocyclitis is generally unresponsive to corticosteroid treatment, part of which may be explained by a possible infectious etiology.
- Elevated IOP is treated with medical therapy, but the results are often disappointing, with only about a quarter of patients achieving satisfactory control
- In the past, the results of conventional filtration surgery were also poor, with less than half of patients achieving control.
- Use of wound-healing retardants such as 5-FU and mitomycin-C has improved surgical outcomes considerably, with
- success rates as high as 72%
- Cataract surgery with in-the-bag intraocular lens implantation is usually successful.

Glaucomatocyclitic crisis

- **Epidemiology**
- Glaucomatocyclitic crisis, also called the **Posner-Schlossman syndrome**
- It is usually seen in young to middle-aged adults and consists of recurrent episodes of recurrent unilateral, mild, acute nongranulomatous anterior uveitis and marked elevations of IOP.
- The prevalence of this condition is low -0.4% in Finland

- **Etiopathogenesis**
- Decreased outflow facility
- It is postulated that the elevated IOP is caused by inflammation of the trabecular meshwork, perhaps mediated by prostaglandins.
- There is also evidence of an association between herpes simplex virus and glaucomatocyclitic crisis, but the significance of this association is unknown.
- In some cases in which glaucomatocyclitic crisis was initially diagnosed, cytomegalovirus DNA was subsequently detected in the aqueous humor by polymerase chain reaction
- The etiology of glaucomatocyclitic crisis remains unknown, but theories include various infections (eg, herpes simplex virus) and autoimmune disease.

- **Signs and symptoms**
- Patients have relatively few symptoms considering the height of their IOPs, but they may complain of slight discomfort, slight blurring of vision, or halo vision.
- Generally this condition is unilateral, but both eyes can be affected at different times.
- The physical findings during an episode of glaucomatocyclitic crisis include
  i. Mild ciliary flush,
  ii. Dilated or sluggishly reactive pupil,
  iii. Corneal epithelial edema, 1–20 fine keratic precipitates
  iv. IOP in the range of 40–60mmhg,
  v. Open angles,
  vi. Faint flare,
- The keratic precipitates may not appear for 2 or 3 days after the IOP has risen, which may obscure the diagnosis.
- The anterior uveitis is mild, with few KPs, which are small, discrete, and round and which usually resolve spontaneously within a few weeks.
- On gonioscopy, KPs may be seen on the trabecular meshwork, suggesting a "trabeculitis."
- The crises last several hours to a few weeks.

- Some patients experience one or two episodes in their lives, whereas other patients experience recurrent crises for many years.
- As a rule, the frequency of recurrences diminishes with age.
- For many years it was accepted that glaucomatocyclitic crisis never caused optic nerve cupping or visual field loss and that aqueous humor dynamics were normal between episodes.
- It is now clear, however, that some patients with glaucomatocyclitic crisis have abnormal aqueous humor dynamics between episodes and that some have underlying POAG.
- Some patients develop optic nerve cupping and visual field loss because of repeated crises or underlying POAG.
- Indeed, some patients develop glaucomatous damage years after initial symptoms appear; therefore, all patients should be monitored indefinitely.

- **Treatment**
- Glaucomatocyclitic crisis is usually treated with topical corticosteroids and topical and systemic glaucoma medications.
- As with all types of uveitis, miotics are avoided.
- Apraclonidine 1% has been found to be particularly effective.
- Some authorities recommend the administration of systemic or topical/ oral non-steroidal anti-inflammatory agents (eg, indomethacin) because of increased aqueous humor prostaglandin levels.
- There is no evidence that long-term suppressive therapy with topical nonsteroidal anti-inflammatory agents or corticosteroids is effective in preventing attacks.
- Because the episodes are self-limited, moderate elevations of IOP should be well tolerated.
- An occasional patient requires filtering surgery because of progressive cupping and visual field loss.
- Successful filtering surgery prevents IOP elevations but does not prevent recurrent episodes of inflammation.
- Recent studies link infection with herpetic viruses such as cytomegalovirus (CMV) with glaucomatocyclitic crisis, indicating a possible role for antiviral therapy.

Precipitates on the trabecular meshwork

- Inflammatory precipitates on the trabecular meshwork can cause a clinical picture that is easily mistaken for POAG.
- In this condition, the eyes are white and quiet, and the only signs of inflammation are a few gray or slightly yellow precipitates on the trabecular meshwork associated with irregular peripheral anterior synechiae.
- Most of these patients have idiopathic disorders, although some later develop a recognizable inflammatory condition such as sarcoidosis, rheumatoid arthritis, or ankylosing spondylitis.
- The precipitates and the elevated IOP are responsive to topical corticosteroid treatment.
- While waiting for this effect, aqueous humor suppressants may be useful to control IOP.
- This uncommon condition may be recurrent and asymptomatic, and these patients should be examined periodically to monitor IOP.
- Inflammatory precipitates have been reported as a cause of increased IOP following ALT.
- As with idiopathic cases, this condition responded to treatment with topical corticosteroids.

Herpes simplex

- Elevated IOP is common when herpes simplex causes iridocyclitis, disciform keratitis, or stromal ulcer.
- The increased IOP is caused by inflammation, swelling, and obstruction of the trabecular meshwork.
- Herpetic keratouveitis is usually treated with antiviral agents, cycloplegics, and topical corticosteroids.
- The IOP is controlled with aqueous humor suppressants.
- Glaucoma may be quite severe in these cases and filtration surgery with wound-healing retardants such as 5- FU or mitomycin-C may be necessary to control pressure.
- Argon laser trabeculoplasty has been implicated as a trigger for recurrent herpes simplex keratitis in at least one case and thus is not an attractive treatment option.
- Cyclodestructive procedures have been attempted in many cases, but serious complications have occurred in several eyes and these procedures are best considered as a last resort.

Herpes zoster

- When herpes zoster involves the ophthalmic division of the trigeminal nerve, especially the nasociliary branch, there is often associated keratitis, iridocyclitis, and secondary glaucoma.
- The anterior uveitis can be severe, and secondary open-angle glaucoma occurs in 11–25% of patients.
- The inflammation is treated with systemic antiviral agents and cycloplegic agents; the IOP is controlled by aqueous humor suppressants.
- Topical steroids are used routinely, although there are differences of opinion regarding the optimum timing and intensity of steroid treatment.
- Surgery in actively inflamed eyes is challenging, although some authors have reported excellent results.
- Mitomycin-C- and/or 5-FU-enhanced filtering operations are the procedures of choice, although if the inflammation is severe or active, a tube shunt could be considered.

Sarcoidosis

- Approximately 10% of patients with sarcoidosis develop elevated IOP.
- This occurs through a variety of mechanisms, including
  - Swelling and dysfunction of the trabecular meshwork,
  - Obstruction of the trabecular meshwork by inflammatory cells and debris,
  - Peripheral anterior synechiae,
  - Posterior synechiae with pupillary block,
  - And neovascular glaucoma.
- Patients with ocular sarcoidosis frequently develop thick, broad-based peripheral anterior synechiae that can lead to a scarred and dysfunctional anterior segment well after the inflammatory episode is over.
- Tube-shunt procedures, valved or non-valved (e.g., Ahmed, Molteno, Baerveldt) implantation with adjunctive 5-FU or mitomycin-C may be necessary to control severe cases.
- HLA typing suggests a molecular basis for some of the clinical heterogeneity seen in sarcoid patients.

Juvenile rheumatoid arthritis

- Severe acute and chronic eye disease is an unfortunate but common component of juvenile rheumatoid arthritis.
- Elevated IOP can occur in any of the forms of juvenile rheumatoid arthritis but is most common in young girls with iridocyclitis and monoarticular or pauciarticular involvement.
- Glaucoma can result from posterior synechiae and pupillary block or inflammation of the trabecular meshwork.
- The response to medical treatment and filtering surgery is often disappointing in this condition.
- A few physicians have reported long-term IOP reductions in these children with a modifed goniotomy procedure called **trabeculodialysis.**
- Close ophthalmic follow-up and prompt treatment of ocular pathology are important in maintaining vision.
- Genetic typing may allow more precise and earlier diagnosis, which should facilitate early intervention in select cases.

Syphilis

- Glaucoma often occurs in individuals with congenital or acquired syphilis.
- Secondary open-angle glaucoma can occur in any of the active inflammatory phases of the disease, including acute interstitial keratitis.
- Iridoschisis occurs rarely but may be associated with glaucoma in 50% of cases.
- A late form of secondary open-angle glaucoma occurs in 15–20% of patients.
- In these cases, gonioscopy reveals occasional peripheral anterior synechiae and irregular pigmentation of the trabecular meshwork.
- These patients respond poorly to medical treatment, and it is postulated that there may be an endothelial membrane covering the angle.
- Filtering surgery with wound healing retardants or drainage valve implantation is often required for this condition.
- Syphilis is also associated with **angle-closure glaucoma.**
- Some patients with congenital syphilis have small anterior segments and develop acute or chronic angle closure in later years.

- Elevated IOP has also been reported in association with other inflammatory conditions, including

1. Ankylosing spondylitis, Pars planitis,
2. Behçet's syndrome, Sympathetic ophthalmia,
3. Onchocerciasis, Leprosy,
4. Mumps.