

Five Retinal Findings Not to Miss 2019
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I. UGH Plus Syndrome associated with PCIOL

A. Definition

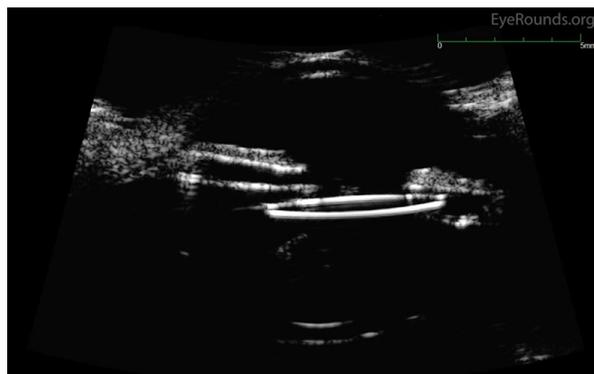
1. Uveitis-glaucoma-hyphema (UGH) syndrome was first described by Ellingson in 1978 and classically included uveitis, glaucoma, and hyphema in the setting of an anterior chamber IOL.
2. UGH syndrome is often used when one, two, or all three of these entities are present in the setting of any IOL causing irritation of the iris or angle structures.
3. UGH Plus: with VH

B. Etiology

1. IOL chafing the iris, iridocorneal angle, or ciliary body, which leads to recurrent trauma to these structures.
2. Uveitis results from mechanical breakdown of the blood aqueous barrier and resultant inflammation.
3. Hyphema results from recurrent damage by the IOL to vascular tissue of the iris, ciliary body, or angle.
4. Intraocular pressure elevation can be caused by pigment dispersion, uveitis, hyphema, direct injury to the aqueous drainage system, or a steroid response to corticosteroids used to treat UGH-related inflammation.

C. Diagnosis

1. Blurred vision, transient vision loss, ocular pain or ache, erythropsia (i.e., objects take on a reddish hue), or photophobia.
2. Slit lamp examination
 - a) Poorly positioned IOL optic or haptic contacting uveal tissue may be directly observe
 - b) Hyphema, cell and/or flare, transillumination iris defects, synechiae, pseudophacodonesis, or corneal pigment
 - c) Gonioscopy may demonstrate blood within the inferior angle, signs of mechanical erosion, poorly positioned haptics, or increased pigmentation of the trabecular meshwork
 - d) Ocular hypertension is often present
(I) optic disc cupping and glaucomatous vision loss may be present in advanced cases
 - e) Ultrasound biomicroscopy and OCT of the anterior segment may be useful to identify IOL position and contact with the iris or angle structures



- f) Posterior segment ultrasound (B-scan) may be useful when vitreous hemorrhage is present, (**UGH Plus Syndrome**).

D. Treatment/Prevention

1. Given that IOL irritation underlies the etiology of UGH syndrome, selection of the appropriate lens type, design, and size is crucial to minimize the risk of developing UGH syndrome.
2. Treatment
 - a) Milder cases can be managed medically with steroids and ocular hypotensive
 - b) Serial intracameral anti-VEGF injections have been used to successfully manage UGH syndrome
 - c) Definitive treatment is to exchange the IOL
 - (1) One of the more common indications for IOL exchange surgery (11.9% of IOL exchanges) Is it a small melanoma or a nevus??

II. **Plaquenil Toxicity**

A. What is Plaquenil?

1. Group of medicines called quinolines.
2. Treat or prevent malaria.
3. Treat rheumatoid arthritis and discoid/systemic lupus erythematosus.

B. 2016: Recommendations on screening for chloroquine (CQ) and hydroxychloroquine (HCQ, Plaquenil) retinopathy were revised in light of new information about the prevalence of toxicity, risk factors, fundus distribution, and effectiveness of screening tools (Ophthalmology 2016;123:1386-1394^a 2016 by the American Academy of Ophthalmology).

C. Dose

1. Maximum daily **5.0 mg/kg real weight**
2. Risk of Toxicity: The risk of toxicity is dependent on daily dose and duration of use.
 - a) At recommended doses, the risk of toxicity up to 5 years is under 1% and up to 10 years is under 2%, but it rises to almost 20% after 20 years
 - b) However, even after 20 years, a patient without toxicity has only a 4% risk of converting in the subsequent year.
3. Major Risk Factors
 - a) **High dose**
 - b) **Long duration of use**
 - c) Other major factors are concomitant macular disease, renal disease, or tamoxifen

D. Screening Schedule

1. **baseline fundus examination** to rule out preexisting maculopathy
2. **annual screening after 5 years**, on **acceptable doses**, without major risk factors
3. Screening Tests
 - a) **Automated visual fields**
 - (1) damage is parafoveal in most eyes: **10-2** in **non-Asian** patients
 - (2) damage is extramacular in most Asian eyes: **30-2** in **Asian** patients
 - b) **Spectral-domain optical coherence tomography (SD OCT)**

- c) **multifocal electroretinogram (mfERG)** can provide objective corroboration
 - (1) can get a baseline at KEI
- d) **Fundus autofluorescence (FAF)** can show damage topographically
 - (1) baseline then annually after 5 years
- 4. It is important to check the dosage relative to weight at **every visit** and to ask about changes in systemic status, such as major weight loss/gain, kidney disease, or tamoxifen
- E. Toxicity
 - 1. Retinopathy is not reversible, and there is no present therapy.
 - 2. Recognition at an early stage (before any RPE loss) to prevent central visual loss.
 - 3. Should detect retinopathy before it is visible in the fundus.
 - 4. Questionable test results should be repeated or validated with additional procedures to avoid unnecessary cessation of valuable medication.
- F. Counseling
 - 1. Patients (and prescribing physicians) should be informed about risk of toxicity, proper dose levels, and the importance of regular annual screening after 5 years.
- G. Poor Compliance by Rheumatologists (Braslow, et al May, 2017):
 - 1. Determine adherence of rheumatologists to the hydroxychloroquine (HCQ) dosing guidelines established by the AAO in 2011 and 2016.
 - 2. Reviewed electronic medical records (EMRs) between 2009 and 2016 started on HCQ
 - 3. Weights, height, gender, and HCQ dosage were extracted from the EMR. The recommended maximum starting dose was determined using 2 formulas based on ideal or actual body weight.
 - 4. Main Outcome Measure
 - a) Percentage of patients whose dose exceeded the recommended maximum.
 - 5. Results:
 - a) 554 patients on Plaquenil
 - b) 50% and 47% had been placed on excess initial doses based on the 2011 and 2016 guidelines, respectively
 - c) 297 of 527 (56%) were currently receiving excess maintenance dosing according to 2016 guidelines
 - d) Conclusions:
 - (1) The introduction of the guidelines had no appreciable effect on dosing.
 - (2) Approximately one half of all patients were started on doses in excess of the recommended maximum
 - (3) Slightly more than one-half of all patients currently on treatment continue to receive excess doses.
 - (4) The publication of the consensus guidelines in 2011 had no appreciable effect on HCQ dosing and that transitioning to the 2016 dosing modification is unlikely to change this outcome unless additional steps are taken to improve adherence.
 - (5) Ophthalmology 2017;124:604-608.

III. Is it a small melanoma or a nevus?

A. **TFSOM-(UHHD)**: To Find Small Ocular Melanoma (Using Helpful Hints Daily)

1. **T** = thickness greater than 2 mm
2. **F** = subretinal fluid
3. **S** = symptoms
4. **O** = orange pigment
5. **M** = margin touching or less than 3 mm near the optic disc
6. **U** = ultrasonographic hollowness (versus solid/flat)
7. **H** = absence of halo
8. **D** = absence of druse

B. Five year risk of conversion from nevus to melanoma determined by the **# of risk factors**:

1. none of these factors: 3%
2. 1 risk factor: 38%
3. ≥ 2 risk factors: 50%

4. Most tumors with two or more risk factors probably represent small choroidal melanomas, and early treatment is generally indicated.

IV. Hemorrhagic Occlusive Retinal Vasculitis (HORV) after CE

A. Appearance of retinal vascular occlusion and hemorrhage with subsequent severe vision loss following routine CE with use of Vancomycin

1. Extremely rare: 36 eyes of 23 patients as of May, 2017

B. Common Characteristics of HORV

1. Occurrence after otherwise uncomplicated cataract surgery.
2. Use of **prophylactic intraocular vancomycin** during surgery is the common factor
- 3. Suspect HORV if a patient describes delayed onset visual loss after eye surgery.**
4. Clinical Features:
 - a) Normal undilated examination on postoperative day
 - b) Delayed onset of painless visual loss between one and 14 days after surgery (may be asymptomatic in mild cases)
 - c) Relatively mild anterior chamber and vitreous inflammation, without hypopyon.
 - d) Retinal vascular occlusions associated with sectoral intraretinal hemorrhage in areas of nonperfusion (often along venules)
 - e) Peripheral retinal involvement in all cases, with macular ischemia in advanced disease
 - f) Sectoral retinal vasculitis and vascular occlusion on fluorescein angiography, corresponding to areas of hemorrhage
5. Poor visual results common, often complicated by **neovascular glaucoma**.
6. Negative extensive intraocular and systemic workups.

- C. Cause of the disease is not definitively known, but associated with **intraocular use of Vancomycin**
1. Most likely a type 3 hypersensitivity reaction to intraocular vancomycin; only agent common to all cases
 2. Similar to rare reports of leukocytoclastic vasculitis and Henoch-Schönlein purpura secondary to vancomycin, both of which are mediated by antibody/antigen complex deposition causing small-vessel vasculitis occurring one to two weeks after initiation of intravenous vancomycin
- D. Management
1. Consider high-dose systemic, periocular and intraocular corticosteroids
 2. Consider early anti-VEGF treatment with PRP to non-perfused regions.
 3. Consider systemic antiviral therapy if acute retinal necrosis is suspected.
 4. Avoid intravitreal vancomycin if possible.
 5. Consider ocular and systemic workup for masquerade syndromes.
- E. Prevention
1. Delay or avoid fellow eye surgery if HORV presents in the first eye.
 2. Avoid intraocular adjuvant medications if HORV develops in the first eye.
 3. Reconsider using vancomycin with close sequential bilateral cataract surgery, especially if immediate sequential same-day bilateral surgery is performed.
 4. Be aware that in addition to delayed onset, HORV may **not** cause symptoms in the first eye, and a **dilated retinal examination** may be the only way to detect it.
 5. Consider cefuroxime or moxifloxacin as alternatives to Vancomycin.
- F. Prognosis
1. Visually devastating, carries a high risk of neovascular glaucoma.
 2. 22 eyes (61%) were 20/200 or worse, and 8 eyes (22%) were NLP
- G. Use of Vancomycin after CE
1. The rate of acute-onset postoperative endophthalmitis after cataract surgery generally is reported between approximately 0.03% and 0.2%
 2. How Intracameral Vancomycin Prophylaxis Emerged
 - a) In 2007, the European Society of Cataract and Refractive Surgeons (ESCRS) published results from a large prospective, randomized, multicenter study demonstrating that prophylactic intracameral **cefuroxime** injection (1 mg/0.1 ml) given at the end of cataract surgery reduced the risk of postoperative endophthalmitis fivefold.
 - (1) This study has been criticized on multiple grounds, including the limited spectrum of activity of cefuroxime, the high rate of endophthalmitis in eyes not randomized to receive intracameral cefuroxime (approximately 0.2%), the use of topical levofloxacin 0.5% beginning 24 hours after surgery (as opposed to the same day), and the use of multiple surgical techniques.
 - b) The percentage of cataract surgeons using prophylactic intracameral antibiotics routinely during cataract surgery more than doubled from 15 percent in 2007 to 36 percent in 2014.
 - c) US surgeons mostly use off-label moxifloxacin or vancomycin, usually mixed by the operating room staff the day of surgery, because the commercial formulation of intraocular cefuroxime used in the ESCRS study is not available in the United States.
 - d) Effectiveness of ICA'S to reduce rate of endophthalmitis

1. Yes!! Endophthalmitis rate of 0.06% before ICA dropped 6-fold to 0.01% with ICAs (Tan, et al J Cat Refractive Surg 2012)
 2. No! 75,000 cases, topical fluoroquinolone antibiotic drops were used routinely before and after surgery, POE 0.02% rate without ICA (Rudinsky, Ophthalmology 2014)
 3. Yes!! 16,000 eyes, POE rates dropped 22 fold, primarily with **cefuroxime** (Shornstein, AAO 2014)
 4. Yes! Reduction in endophthalmitis rates with no cases of medication toxicity in almost 10,000 eyes (Rush, J Ophthal 2015)
 5. No! Mayo Clinic, 2018: topical fluoroquinolone antibiotic drops were used routinely before and after surgery, POE 0.02% rate without ICA (50,000 cases)
- e) *** These studies are limited and likely flawed relating to their study designs in which, generally, an earlier cohort of patients who underwent surgery without intracameral antibiotics is compared with a later cohort of patients who underwent surgery with intracameral antibiotics. Endophthalmitis rates may decline over time for many reasons other than the use of intracameral antibiotics, including improvements in surgical technique, equipment, and other factors.****
3. Routine use may increase the risk of medication toxicity, drug contamination, and promote vancomycin resistance.
The Controversy Continues:
 - a) Schwartz, Flynn et al 2017 Ophthalmology: “In summary, the routine use of prophylactic intra- cameral antibiotics during cataract surgery, although enticing as a strategy to reduce infection rates, has incompletely proven efficacy, increased costs, possible serious risks to the individual patient, and larger risks to the population as a whole by potentially contributing to antibiotic resistance.”
 - b) Naserri, Wells, et al 2017 Ophthalmology: “Nonetheless, after the creation of a joint task force with member solicitation of large cataract and retina societies, Witkin et al report HORV in 36 eyes of 23 patients worldwide spanning an 11-year period. By contrast, it has been estimated that the expanded use of ICAs could prevent 2000 cases of POE annually in the United States alone. Although HORV is likely extremely rare compared with POE, the uniformly poor outcome and bilateral risks reported with vancomycin-associated HORV should point surgeons toward intracameral alternatives such as cefuroxime or moxifloxacin, whose efficacy and safety have been broadly reported.”
- H. The American Society of Retinal Specialists (ASRS) is collecting information about suspected cases of HORV, at this link: <http://goo.gl/vst6yR>

V. Small Intraocular Foreign Body

- A. Incidence among eyes with open-globe injury is 16% in the United States
- B. History is most important!!!
 1. Most common cause is hammering
 2. Incidence decreasing at the workplace and increasing in the home.
 3. Most patients are male, between 21 and 40 years old
 4. Protective eyewear (3 mm of polycarbonate) prevents virtually all injuries
- C. In case of doubt, it is advisable to err on the side of an IOFB presence.

- D. **NB:** The most common cause for litigation against the ophthalmologist/optometrist in a trauma case is a missed IOFB. It is important to remember that the patient may be unaware of any object entering (or even striking) the eye, and the vision may be unaffected initially.
- E. Examination:
1. Slit lamp examination
 - a) Seidel testing should be performed to aid in identifying leaking wounds.
 - b) The anterior chamber should be evaluated for depth, cell, hypopyon, fibrin, hyphema, and/or lens material.
 - c) The iris should be examined for transillumination defects prior to dilation, which may suggest a potential IOFB.
 - d) Important clues:
 - (1) A corneal entry wound and a hole in the iris provide trajectory information.
 - (2) IOFBs transversing the lens are **less** likely to cause major retinal damage
 - (3) A **smaller** wound size usually means **deeper** penetration
 2. The indirect ophthalmoscope through a dilated pupil may allow direct visualization of the IOFB.
 3. Gonioscopy and scleral depression are **not** recommended
- F. Ancillary Testing
1. **CT scans** are the imaging study of choice for IOFB localization.
 2. Plain x-ray is useful if a metallic IOFB is present and a CT scan is unavailable
 3. MRI is generally **not** recommended for metallic IOFBs
 4. Ultrasound is a useful tool in localizing IOFBs
- G. Management:
1. A posterior segment IOFB requires a vitrectomy.
 - a) Retained metallic IOFBs can result in **chalcosis** and **siderosis** with retinal toxicity
 - b) Glass IOFBs, which account for 6% to 9% of all IOFBs, can be observed if there is no other significant structural damage.
- H. Prognosis
1. Endophthalmitis, corneal scarring, elevated intraocular pressure, cataract, retinal detachment, proliferative vitreoretinopathy, and metallosis (eg, chalcosis, siderosis) are possible complications
 2. The prognosis is generally relatively good.: over one half of eyes with IOFB injury regain/retain reading vision