Clinical Ocular Grand Rounds
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CASE 1

Case History
- 38 black male, complaining that the vision in his right eye is blurry.
  - Got the current Rx 3 weeks previously, and started out good but in last couple of days OD vision has become blurry
- Medical Hx: no current health concerns and no medications
Entrance Skills

- VA's: OD: 20/25, OS: 20/20
- Pupils: PERI
- CVF: full to finger count
- EOM's: FROM
- Amsler: central metamorphopsia OD
- HVF: 10-2 (see VF)

Which of the following OCT's goes with this patient?
Lid Nevi

- Lid nevi:
  - congenital or acquired
  - occur in the anterior lamella of the eyelid and can be visualized at the eyelid margin.
- The congenital eyelid nevus is a special category with implications for malignant transformation.
- With time, slow increased pigmentation and slight enlargement can occur.
- An acquired nevus generally becomes apparent between the ages of 5 and 10 years as a small, flat, lightly pigmented lesion.
Congenital Nevus

• The nevus is generally well circumscribed and not associated with ulceration.
• The congenital nevus of the eyelids may present as a "kissing nevus" in which the melanocytes are present symmetrically on the upper and lower eyelids.
  – Presumably this nevus was present prior to eyelid separation.

Congenital Nevus

• Most nevi of the skin are not considered to be at increased risk of malignancy.
  – However, the large congenital melanocytic nevus appears to have an increased risk of malignant transformation of 4.6% during a 30 year period.

Acquired Lid Nevi

• Acquired nevi are classified as:
  – junctional (involving the basal epidermis/dermis junction), typically flat in appearance
  – intradermal (involving only the dermis), tend to be dome shaped or pedunculated
  – compound (involving both dermis and epidermis) tend to be dome shaped
CHRPE vs Nevus

Nevi Trivia

- 31% of choroidal nevi show slight enlargement over time without the transformation to a melanoma (Ophthalmology 2011)
- The prevalence of choroidal nevi in the white U.S. population ranges from 4.6% to 7.9%
  - If it is assumed that all choroidal melanomas arise from preexisting nevi, then the published data suggest a low rate (1/6845) of malignant transformation of a choroidal nevus in the U.S. white population. (Ophthalmology 2005)
- Choroidal melanoma risk for metastasis, ranging from 16% to 53% (at 5 years of follow-up) depending on the size of the tumor at the time of diagnosis. (Arch Ophthamol 1992)

TFSOM—“To Find Small Ocular Melanoma”

Thickness: lesions >2mm
Fluid: any subretinal fluid (suggestive of serous retinal detachment)
Symptoms: photopsia, vision loss
Orange pigment overlying the lesion
Margin touching optic nerve head

- None of these factors = 3% risk of a nevus converting to melanoma in five years.
- One of these factors = 8% risk of conversion in five years.
- Two or more factors = 50% risk of conversion in five years.
For any changes noted during the course of follow-up, refer the patient to a retinal practice or an ocular oncology service.
Case

- 65 yr old white male
  - Notices spot in vision in his left eye
  - Diabetes for 15 years
- Vision: 6/6 (20/20) and 6/12 (20/40)
- Dilated exam:
  - Large lesion noted in left eye (not noted in exam 6 months previously)
  - See photo

Ocular Tumors

- Astrocytic Hamartoma
- Amelanotic Melanoma
- Retinoblastoma
- Metastatic Choroidal Tumor

Choroidal Melanoma OCT and FAF
Choroidal Melanoma Metastases

• 80 to 90% of metastases from uveal melanoma occurred in the liver, less common sites being the skin and lung.

Latest Development

• September 4, 2014, the US FDA approved a new therapy for patients with advanced melanoma.
• The treatment, Keytruda (pembrolizumab), proved so successful in a large Phase 1 clinical trial that the drug was granted breakthrough therapy designation by the FDA, meaning that it was fast tracked for approval.

CASE 2
Case: Gonzalez

- 33 HF presents with a painful, red right eye
  - Started a couple of days ago, deep boring pain
  - Has tried Visine but hasn’t helped the redness
- PMHx: patient reports she has been diagnosed with rheumatoid arthritis 3 years ago
  - Takes Celebrex for the joint pain
  - Patient reports she occasionally gets a skin rash when she is outdoors in the sun
- POHx: unremarkable
- PMHx: mother has rheumatoid arthritis

- VA: 20/30 OD, 20/20 OS
- Pupils: PERRL –APD
- VF: FTFC OH
- EOM’s: FROM OU
- BP: 130/85 mm Hg RAS
- SLE: see picture
  - 2+ cells, mild flare
- IOP’s: 16, 16 mm HG
- DFE: see fundus photo

Etiologies of Cotton Wool Spots

<table>
<thead>
<tr>
<th>Vascular Occlusive Disease</th>
<th>Hypertension</th>
<th>Ocular Ischemic Syndrome</th>
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<tbody>
<tr>
<td>Autoimmune Disease e.g.</td>
<td></td>
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<tr>
<td>SLE</td>
<td></td>
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<tr>
<td>Pre-eclampsia</td>
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<tr>
<td>Neoplastic e.g. leukemia</td>
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<tr>
<td>Infectious e.g. HIV</td>
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<tr>
<td>Toxic e.g. interferon</td>
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Trauma

Hyperviscosity syndromes

Anterior Ischemic Syndrome
Antimalarials

- hydroxychloroquine more common and less toxic than more effective chloroquine
- usual dose is 200-400 mg/d @night with onset of action after a period of 2-4 months
- has mild DMARD effect, does not slow radiographic progression and has relatively slow onset of action, useful with other DMARD’s

Antimalarial Ocular Complications

- Have affinity for pigmented structures such as iris, choroid and RPE
- Toxic affect on the RPE and photoreceptors leading to rod and cone loss.
- Have slow excretion rate out of body with toxicity and functional loss continuing to occur despite drug discontinuation.

Question

Which of the following depicts a retina undergoing hydroxychloroquine toxicity?

ARMD  Macular Hole  OHS  Bull’s Eye Maculopathy
Question
Which OCT goes with a patient undergoing hydroxychloroquine toxicity?

Antimalarial Ocular Complications
- Toxicity can lead to whorl keratopathy, “bulls eye” maculopathy, retinal vessel attenuation, and optic disc pallor.
- Early stages of maculopathy are seen as mild stippling or mottling and reversible loss of foveal light reflex
- “Classic” maculopathy is in form of a “bulls eye” and is seen in later stages of toxicity
  - this is an irreversible damage to the retina despite discontinuation of medication

Antimalarials
Fabry Disease

- alpha-galactosidase-A deficiency.
  - insufficient breakdown of lipids, which build up to harmful levels in the eyes, kidneys, autonomic nervous system, and cardiovascular system.
- Fabry disease is one of several lipid storage disorders and the only X-linked lipid storage disease.
- Lipid storage may lead to impaired arterial circulation and increased risk of heart attack or stroke.
  - The heart may also become enlarged and the kidneys may become progressively involved.
- Other signs include decreased sweating, fever, and gastrointestinal difficulties.

Revised Recommendations on Screening for Retinopathy

- 2002 recommendations for screening were published by Ophthalmology
- Revised recommendations on screening published in Ophthalmology 2011;118:415-42
  - Significant changes in light of new data on the prevalence of retinal toxicity and sensitivity of new diagnostic techniques
  - Risk of toxicity after years of use is higher than previously believed
    - Risk of toxicity approaches 1% for patients who exceed 5 years of exposure

Revised Recommendations on Screening for Retinopathy

- Amsler grid testing removed as an acceptable screening technique
  - NOT equivalent to threshold VF testing
- Strongly advised that 10-2 VF screening be supplemented with sensitive objective tests such as:
  - Multifocal ERG
  - Spectral domain OCT
  - Fundus autofluorescence
Revised Recommendations on Screening for Retinopathy

• Parafoveal loss of visual sensitivity may appear before changes are seen on fundus evaluation
  • Many instances where retinopathy was unrecognized for years as field changes were dismissed as "non-specific" until the damage was severe
  • 10-2 VF should always be repeated promptly when central or parafoveal changes are observed to determine if they are repeatable
  • Advanced toxicity shows well-developed paracentral scotoma

Paracentral Scotomas

• SD-OCT can show localized thinning of the parafoveal retinal layers confirming toxicity
  – not appreciable with time-domain OCT
  – changes maybe visible prior to VF defects
• Fundus autofluorescence may reveal subtle RPE defects with reduced autoFL or show areas of early photoreceptor damage
• MF-ERG can objectively document localized paracentral ERG depression in early retinopathy
Normal Retina: VF/OCT/ERG

Mild Maculopathy

Bull’s Eye Maculopathy
Revised Recommendations on Screening for Retinopathy

<table>
<thead>
<tr>
<th>Factors Increasing Risk of Retinopathy</th>
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<tbody>
<tr>
<td>Duration of use</td>
<td>&gt; 5 years</td>
</tr>
<tr>
<td>Cumulative Dose</td>
<td>&gt; 1000 g (total)</td>
</tr>
<tr>
<td>Daily Dose</td>
<td>&gt; 400 mg/day</td>
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<tr>
<td>Age</td>
<td>Elderly</td>
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<tr>
<td>Systemic Disease</td>
<td>Kidney or liver dysfunction</td>
</tr>
<tr>
<td>Ocular Disease</td>
<td>Retinal disease or maculopathy</td>
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• older literature focused on daily dose/kg
• newer literature emphasizes cumulative dose as the most critical factor
  – initial baseline
    • within 1 year of beginning medication
  – then screening for toxicity should be initiated no later than 5 years after starting the medication

CASE 3
Case

- 65 year old Caucasian patient presents with sudden onset loss/blurring of vision in the right eye
- PMHx: HTN for 15 years, takes “water pill”
- VA’ s: 6/18 (20/60) OD, 6/7.5 (20/25) OS
- Pupils: PERRL – APD
- CVF: Inferior defect right eye, no defects noted in the left eye

Vision Loss Without Pain: Diabetes/Diabetic Retinopathy

- Microvascular complications resulting in capillary closure & abnormal permeability
- S&S include;
  - blurring of vision (maculopathy and refractive error shifts),
  - sudden drop in vision (vitreous heme),
  - dot and blot hemes,
  - exudate,
  - cotton wool spots,
  - neovascularization (iris, retina and disc)

VEGF and DME
Aug. 10, 2012: FDA approves Lucentis to treat diabetic macular edema

- The drug’s safety and effectiveness to treat DME were established in two clinical studies involving 759 patients who were treated and followed for three years.
  - patients were randomly assigned to receive monthly injections of Lucentis at 0.3 milligrams (mg) or 0.5 mg, or no injections during the first 24 months of the studies
  - after 24 months, all patients received monthly Lucentis either at 0.3 mg or 0.5 mg
- Results:
  - 34-45% of those treated with monthly Lucentis 0.3 mg gained at least three lines of vision compared with 12-18% of those who did not receive an injection.

What’s New?

- Sept. 16, 2014 -- Regeneron Pharmaceuticals, Inc. announced that the FDA has granted EYLEA™ (aflibercept) Injection Breakthrough Therapy designation for the treatment of diabetic retinopathy in patients with diabetic macular edema (DME).
- Sept 29, 2014: The FDA approved Ozurdex (dexamethasone intravitreal implant) for the general patient population being treated for DME
- Sept 29, 2014: The FDA approved Iluvien (fluocinolone acetonide implant) for the treatment of DME in patients previously treated with corticosteroids who did not have a significant increase in IOP

Question

When would you prescribe a final spectacle Rx for a patient who is being treated for DME with anti-VEGF medications?

1. Anytime during the treatment
2. At the last treatment
3. 2 weeks after treatment
4. 3 months after treatment
Vision Loss Without Pain: Vein Occlusion

- Associated with:
  - hypertension,
  - coronary artery disease,
  - DM and
  - peripheral vascular disease.
- Usually seen in elderly patients (60-70), slight male and hyperopic predilection.
- Second most common vascular disease after diabetic retinopathy.

Branch Retinal Vein Occlusion: Signs/Symptoms

- BRVO: sudden, painless, visual field defect.
  - patients may have normal vision.
  - quadrantic VF defect,
  - dilated tortuous retinal veins with superficial hemes and CWS
  - typically occurs at A/V crossing (sup/temp)

BRVO

- BRVO more common than CRVO and has more favorable prognosis
  - Overall 50-60% of BRVO patients will maintain VA of 6/12 (20/40) or better
- Visual loss results from:
  - Macular edema
  - Foveal hemorrhage
  - Vitreous heme
  - Epiretinal membrane
  - RD
  - Macular ischemia
  - Neovascularization complications
Central Retinal Vein Occlusion: Signs/Symptoms

- CRVO: thrombus occurring at lamina is classical theory but new evidence indicates that the occlusion is typically in the optic nerve posterior to the lamina cribrosa
  - decreased VA ranging from near normal to hand motion with majority 6/60 (20/200) range
  - dilated tortuous vessels, with numerous retinal hemes and CWS

Central Retinal Vein Occlusion

- Visual morbidity and blindness are primarily from:
  - persistent macular edema,
  - macular ischemia and neovascular glaucoma
- CRVO’s can be ischemic or non.
  - Classical definition of ischemic is 10-disc area of non-perfusion found on angiography
  - RAPD and ERG maybe better predictor
  - VA's typically worse in ischemic
  - Increased number of cotton wool spots with decreased VA maybe predictive

Central Retinal Vein Occlusion

- Ischemic CRVO may lead to iris neovascularization and neovascular glaucoma
  - Estimated approx 20% of CRVO’s are ischemic with 45% of those developing neo
- Regular examinations (1-2 wks) to monitor for ischemia or neo development
  - should include gonio as angle neo can precede iris rubeosis
Vision Loss Without Pain: Artery Occlusion

• Primarily embolic in nature from cholesterol, calcifications, plaques.
• Usually occurs in elderly associated with:
  – hypertension (67%),
  – carotid occlusive disease (25%),
  – DM (33%) and
  – cardiac valvular disease.
• Sudden loss of unilateral, painless vision
  – defect dependent upon location of occlusion

Vision Loss Without Pain: Artery Occlusion

• BRAO typically located in temporal retinal bifurcations.

CRAO

• CRAO has profound vision loss with history of amaurosis fugax.
  – Vision is usually CF (count fingers) to LP (light perception) with positive APD.
  – Diffuse retinal whitening with arteriole constriction, cherry red macula.
Ophthalmic Emergency

- Treatment is controversial due to poor prognosis and questionable benefit.
- Treat immediately before workup, if patient presents within 24 hours of visual loss:
  - Digital ocular massage,
  - Systemic acetozolamide (500 mg IV or po),
  - Topical ocular hypertensive drops (Iopidine, B-blocker),
  - Anterior chamber paracentesis,
  - Consider admission to hospital for carbogen Tx (high carbon dioxide)

Quickie

Case History

- 60 yo WM
  - Type 2 DM: 4 years
  - Hypertension: 4 years
  - Bilateral PK’s secondary to keratoconus (has running suture OD)
  - Has history of steroid injections for lower back stenosis (with history of increased IOP up to 40 after injections)
  - VA(RGP): 20/25, 20/20-
  - IOP: OD: range 20-24, OS: range 17-20
Consider the below PSD plots.

Predict what TSNIT graphs you would obtain for this patient.
Comparing Rates of Adverse Reaction After Topical Antiglaucoma Medication Use by Self-Reported Allergy History

<table>
<thead>
<tr>
<th>Sulfa Allergy</th>
<th>CAI</th>
<th>PGA</th>
<th>Alpha 2</th>
<th>B Blocker</th>
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</thead>
<tbody>
<tr>
<td>Prior Sulfa vs other allergy</td>
<td>No difference</td>
<td>No difference</td>
<td>Significantly higher in Sulfa group</td>
<td>No difference</td>
</tr>
<tr>
<td>Prior allergy vs no allergy</td>
<td>Significantly higher in Sulfa</td>
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<td>Other allergy vs no allergy</td>
<td>Significantly higher in allergy</td>
<td>Significantly higher in allergy</td>
<td>No difference</td>
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A retrospective case-controlled cohort study via chart review performed on 1,287 patients with a diagnosis of glaucoma.
Self-Reported Sulfa-Allergic Patients

- had the highest rate of local adverse reactions to alpha2-adrenergic agonists
- lowest rate of local adverse reactions to topical beta-adrenergic blockers
- patients who reported allergies to any kind of medication were more likely to develop an adverse reaction to topical anti-glaucoma medications than patients who reported no allergies to medications

CASE 4

Arturo: 50 y/o Russian Male

- RK 1991 -> 20/20 with hyperopic correction: +5.50 -1.50X090
- TA: 32/18
- Pach
  - 544 μ
  - 558 μ
- Gonio –CBB
- PMHx
- meds
Case Courtesy of Dr. Mark Dunber

Question

A visual field is obviously required, but with the available data would you begin treatment for this patient?
1. No
2. Yes
1 Mo Later

- TA: 24,25 RE; 18 LE
  - (Initial IOP 32/18)

- How do you account for the difference?
- Illustrates the importance of establishing a baseline

Case Courtesy of Dr. Mark Dunber
Question

Based off the available data, what would you do?
1. Monitor in 1 month
2. Monitor in 3 months
3. Monitor in 6 months
4. Monitor in 1 year
5. Begin treatment right eye
6. Begin treatment in both eyes

CASE 5

Case Courtesy of Dr. Mark Dunbar
Case

- 30 WM presents with 2 weeks worsening vision OS
  - Was seen by neurologist 2 years previously for flashes, head CT was normal
  - Flashes continued for the two years
  - History of color blindness
  - Patient presents with pressure behind the eye and tightness with left eye movement for the past week
  - No vision changes with activity or movement
  - Denies history of trauma, redness, discharge or headache
- VA: 20/20 and 20/30
- External exam reveals no ptosis or resistance to retropulsion

Case

- PERRL with a left APD
- Hertel: Base of 102 and measurements of 19 and 18
- EOM: FROM though notes tight feeling in OS abduction
- IOP: 15 OU
- DFE: normal ONH appearance and fundus unremarkable
- HVF: inferior altitudinal defect OS

Case

- One week f/u:
  - Reports continued decreasing vision OS
    - Now 20/400
  - Increased left APD
  - Increased visual field defect
  - ONH swelling OS
Question
Which of the following MRI scans goes with this patient’s diagnosis?

Optic Neuritis

- Optic neuritis typically presents with a triad of symptoms:
  - loss of vision, dyschromatopsia and eye pain.
- The initial attack is unilateral in 70% of adult patients and bilateral in 30%.
- Associated visual symptoms are reduced perception of light intensity and Uhthoff's symptom (visual deficit induced by exercise or increased body temperature)
- The mean age of onset of optic neuritis is in the third decade of life

Optic Neuritis Treatment

- The ONTT showed that intravenous methylprednisolone followed by oral prednisone speeds the recovery of visual loss
- Oral prednisone was found to increase the risk of recurrent optic neuritis.
  - Thus, treatment with oral prednisone in standard doses is no longer advised.