Retina Brainteaser Cases…

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Conflict of Interest…

- I have no disclaimers or conflict of interests to report…..
- I'm not perfect…
- Some cases are more straight forward than others…
- I will email you my reference list if you want it….

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Case #1:

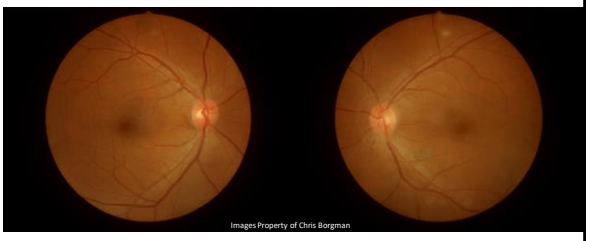
"Why does my uveitis keep coming back?"

Case History…

- 38 year old AF
- History of recurrent iritis q6 months x 2 years OS only
- Vietnamese immigrant; non-English speaking
- POH: (+)phaco OS 18 months prior secondary to PSC
- PMH: denies all
- FMH: unknown
- SH: unremarkable
- ALL: NKMA/NKDA

Exam…

- VA = 20/20 OD, 20/30+ OS (sc)
- EOM's/Pupils/CVF = WNL OU
- Adnexa = WNL
- Slit Lamp = OD WNL, OS had old corneal KP's, no current A/C rxn, stable PCIOL OS with no PCO
- IOP = 16 mmHg, 15 mmHg with Goldmann
- DFE: see pictures



Labwork ordered…..

- CBC with diff = WNL
- ESR = WNL
- RF = WNL
- ANA = WNL
- PPD = WNL
- Chest x-ray = WNL
- ACE, Lysozyme = WNL
- Lyme titers = non-reactive
- RPR =WNL
- HIV = WNL
- Toxocariasis titers = WNL
- Toxoplasmosis titers = IgG reactive, IgM non-reactive

Toxoplasmosis Iritis….

- Intraocular infection of the intracellular parasite *Toxoplasma gondii*
- Recurrent posterior uveitis; usually unilateral
- 90% posterior uveitis = toxoplasmosis
- Sx = floaters, blurry vision, pain, photophobia, veils, etc.
- Sn = iritis, vitritis, retinochoroiditis, retinal scars

- Most common onset = 20-40 years of age
  - Congenital possible too
- Posterior pole = 50% of cases

- Optic nerve involved in ~5% of cases
  - Aka = "toxoplasma neuroretinitis"

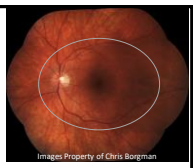
- HIV patients at highest risk when CD4 <250

- USA = 30% exposed
- Europe, Asia, Africa, S. America = 40-80% exposed

T. Gondii Life Cycle…

- T. Gondii life cycle:
  - Cats = definite host (needed)
- Humans more than likely get it from undercooked meat and/or contaminated drinking H20
- Direct exposure from cats themselves is possible but rarer…

T. Gondii Treatment…



- Observation only in most cases…
- If macula/ONH/vision threatened then Tx is indicated…
- <u>Vision Threating Defn:</u> any lesion within temporal arcades or adjacent to ONH

1. "Classic therapy" (pyrimethamine, sulfadiazine, prednisone)
   - Pyrimethamine can cause: leukopenia and thrombocytopenia, GI problems, dermatological problems too; hence #2 most common Tx now
2. Trimethoprim/sulfamethoxazole (Bactrim) and oral prednisone
3. Clindamycin and prednisone

- <u>Note:</u> Topical steroids (Pred Forte, Durezol) still important for anterior iritis

Ocular Toxoplasmosis Prevention…?

- Similar concept to recurrent HSV….
- <u>Trimethoprim/sulfamethoxazole (160-800 mg) PO q3 days</u>
- Decreased recurrent episodes from 23.8% to 6.6% over 20 month period
- Viewed as best with history of recurrency and/or scars adjacent to the fovea
- Promoting resistance???

Case #2:

"Doc, I can't see very well…"

Case History…

HPI: onset 5 days, OS>OD, D & N, h/o trauma with coat hanger 5 days earlier OS, (+)floaters/flashes OS>OD

POH: LEE 6-8 months; current Rx 2 months old

PMH: LME >4 years, (+) arthritis, (+) Sickle Cell (SC variant)

Meds: denies, vitamins only

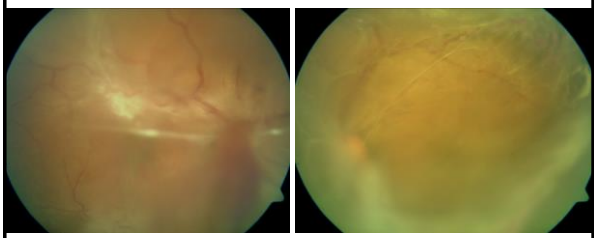
Allergies: PCN

SH: unremarkable

Exam…

- **VA's:**
  OD 20/50- (PHNI),
  OS 20/60- (PHNI)
- **EOM:** FROM OU
- **CVF:** FULL OU
- **Pupils:** equal, round, RL 4+ OU, (-)APD OU
- **SLE:** unremarkable OD, OS
- **Tonometry:** 14 mmHg OD, 13 mmHg OS
- **DFE:** see pics

DFE…



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SC Trait vs. SC Disease

- AA = normal
- AS = trait
- AC = trait
- SS = sickle cell disease (anemia)
- SC = sickle cell disease
- Spectrum of SCD: 80% AS, 4% SS, 2% SC, 14% other types

Sickle Cell Disease (SCD)

- Inherited disorder of Hemoglobin molecules
  - Most common hemoglobinopathy
- 60,000 people in U.S. with SCD (not trait)
- 8.0% of African Americans have sickle cell trait (AS)

Elagouz et al. "Sickle Cell Disease and the Eye: Old and New Concepts." Survey of Ophthalmology. July-August 2010;55:359-377.

Hemoglobin Review

- **Normal Hemoglobin**:
  - 2 α-chains and 2 β-chains
  - Hemoglobin A = normal; "adult"
  - Lifespan of 120 days
- **Sickle Cell Hemoglobin**:
  - Different combos of β-chains; α-chains are unchanged
    - β-chains are reduced/missing = Thalassemia
  - Hemoglobin S = abnormal
  - Hemoglobin C = abnormal
  - Lifespan of 16 days
    - Cleared by spleen much more quickly →severe anemia

Pathogenesis of SCD

•Low O2 environments →"sickling" → sticky → vascular occlusions

•Point mutation on hemoglobin β-chain
•Glutamate is replaced by Valine = SS
•Glutamate replaced by Lysine = SC
•Hb loses O2 →Valine/Lysine binds to open spot in molecule forming long rigid strands → sickle shape

•Occlusions cause tissue ischemia throughout body leading to various complications

Laboratory Testing

1. Sickledex test (screener)
   - •Identifies presence of Hb S (99% accurate)
     - •Sickle Cell Trait---may be NEGATIVE
       - •May be masked by normal Hb A molecule (rare)
2. Hemoglobin Electrophoresis
   - •Performed if Sickledex is positive or inconclusive
   - •Capable of identifying:
     - •Hb AA
     - •Hb AC
     - •Hb AS
     - •Hb SS
     - •Hb SC
     - •Hb Sthal variants

SC Retinopathy: Stage 1(Non-Proliferative)

1) Peripheral Retinal Arteriolar Occlusions
2) Salmon Patches (fresh intraretinal hemmorrhages)
3) Black Sunbursts (resorbed hemmorrhages associated with RPE hyperplasia)
4) Venous Tortuosity
5) Angioid Streaks (rarely can develop CNVM)

Alexander, Larry J. Primary Care of the Posterior Segment. "Sickle Cell Retinopathy." 2nd Edition. 2002. pgs 439-443.

SC Retinopathy: Stage 2 (Non-Proliferative)

•Arteriovenous anastomosis
  •Shunt vessels
  •Arterioles→ Venules

Duanes Clinical Ophthalmology: Diseases of the Retina. Vol 3:17. Sickle Cell Disease. 2008.

SC Retinopathy: Stage 3 (Proliferative)

•VEGF released from the retina in response to ischemia

•Seafan neovascularization proliferates
  •Most common in superior-temporal quad
  •Very similar to PDR in diabetics

•Tx: PRP laser to non-perfused retina, direct laser to feeder vessels and/or neo

•Alternate Tx: Avastin injections

•According to Massachusetts Eye and Ear Infirmary, 60% of sea-fan neo spontaneously regresses on it's own…

Risk of Converting to VH and RD from Stage 3	Timeframe
5.3%	6.3 years
2%	6.3 years

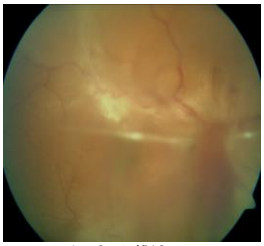
Regina et al. "Sickle Cell Disease and the Eye: Old and New Concepts." Survey of Ophthalmology. July-August 2003;53:398-377.

SC Retinopathy: Stage 4 (Proliferative) ---Vitreous Hemorrhage

- Risk of Vitreous Hemorrhage:
- SC---21-23%
- SS---2-3%

- Results from fibrous tissue traction on sea-fan neo which breaks and leaks into vitreous

- Tx: Usually monitored for 3-6 months. Non-clearing or sight-threatening →PPV



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SC Retinopathy:Stage 5 (Proliferative) ---Retinal Detachment

- Stems from fibrous scaffolding of seafan neovascularization which contracts/pulls on retinal tissue→RD

- Tx: RD repair surgery (scleral buckle, laser, cryotherapy)
- Scleral buckle in SCD has 70% chance of anterior segment necrosis
  - Non-SCD has only 5% chance
- Prognosis: guarded (depends on location, extent, etc.)

Alexander, Larry J. Primary Care of the Posterior Segment. "Sickle Cell Retinopathy." 2nd edition. 2002. pgs 639-643.

Systemic Complications

- Any one of these alone or in combo could be called **"sickle cell crisis"**

  - Organ Infarcts:
    - Lungs → pulmonary embolism
    - Spleen → increased risk of infection
    - Kidney
    - Liver → jaundice
  - Anemia
  - Gallstones
  - Stroke/CVA
  - Joint Pain
    - Arms, Legs, Chest, Abdomen
    - Can be severe

Current Systemic Tx Options

1. Pain Relievers---joint and bone pain
2. Blood transfusions---replaces defective RBC's, only cure available
3. Antiplatelet therapy---decreases risk of clotting
4. Anticoagulation---decreases risk of clotting
5. Thrombolytic agents---clear already blocked vessels
6. Gene Therapy---replacing defective Hb chains; area of research
7. Nitrous Oxide---induces vasodilation
8. Hydroxyurea---increases production of Hb-F via transcription
   - Hb-F has higher affinity for O2
   - Decreases chances that RBC's will sickle in low O2 environment

Hydroxyurea (HU) Therapy

- Harminder et al. found that Hb-F was increased from 12.83% to 19.17% in one year

- 20-25 mg/kg once daily dosing

- Mean overall Hb levels increased from 9.15g/dL to 9.98 g/dL

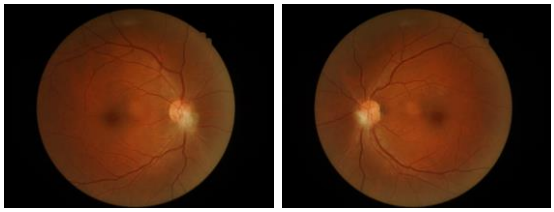
- Conclusion:
  - HU treatment resulted in ↑Hb-F levels, ↓SCD crisis, ↑ intervals between blood transfusions, and ↓hospital admissions.
    - Authors suggest increasing acceptance of HU therapy
    - Concurrent use of transfusions as needed

Singh H, Dulhani N, Kumar BN, Singh P, Tiwari P. Effective control of sickle cell disease with hydroxyurea therapy. Indian J Pharmacol [serial online] 2010 [cited 2010 Aug 31];42:32-5. Available from: http://www.ijp-online.com/text.asp?2010/42/1/32/2459

Back to the patient….

- Sickle cell SC → highest risk of retinopathy
- Set up with retinal specialist who recommended PPV OU
- Patient no-showed to surgery date
- Has not returned calls/letters
- "Unless your patient is too young or cognitively impaired to know better, you can't care more for him than he cares for himself."
  - Drs. Joe Sowka and Alan Kabat

New Case: 39 YO AAM
What is going on here?



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Persistent Fetal Vasculature…

- Defn: Failure of hyaloid vasculature to undergo programmed involution
- Anterior, posterior, combined forms
- 3% of all full term infants have some form of PFV
- MOA: dysregulation of apoptosis
- Unilateral (89-98%)
- Bilateral (2-11%)
- The nomenclature changed from PHPV to PFV in 1997
  - Reflects the inclusion of pathology throughout this system:
    - Vasculature
    - Iris
    - Lens
    - Vitreous
    - Retina
    - Macula
    - Optic nerve

Case #3:
"Doc, my vision is patchy…"

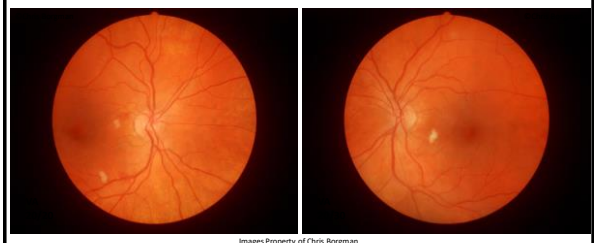
Case History…

- 31 YO WF
- CC: "blurry/patchy vision" OS>OD, onset 3-4 weeks, spots missing in vision OS>OD, sudden onset
- (-) DM, (-)HTN, (-)tobacco
- LME = unknown, long time per pt
- (-) head, chest, or ocular trauma, (+)broken femur
- Meds = oxycodone PRN, Ca pill, Vit D
- ALL = NKMA

Exam…

- VA = 20/20 OD, 20/30 OS, PHNI OS (sc)
- EOM's = WNL
- Pupils = WNL
- CVF = WNL
- Amsler = "patchy" vision paracentrally L >R
- MR: OD plano 20/20 slow
  OS pl – 1.00 x 090 20/20-2 slow
- SLE: WNL OU
- IOP = 16 mmHg OU
- DFE: see pics

DFE…



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Labwork….

- CBC with diff, ESR, FBS, HbA1c, ANA, RF, ANCA, RPR, Hepatitis panel, HIV, ANA, Lyme titer, BMP, thyroid panel, lipid panel, Protein S & C, ANCA, anticardiolipin, antiphospholipids, PT/PPT
- ALL WNL!!!

➢Remember, patient had femur fracture from football accident 3-4 weeks prior…

Purtscher-like Retinopathy…

- Purtschers Retinopathy = retinal hemorrhages, CWS, ONH edema in patients with severe head trauma or compressive chest trauma
  - 83-92% cases have intraretinal hemorrhages & CWS
  - When non-traumatic case, called "Purtscher's-Like"
- Average age = 34 YO
- 60% male
- 60% bilateral, 40% unilateral
- Sx start within 24-48 hours to 2 days usually
- VA = 20/20 → NLP reported
- Central scotoma in 93% cases
  - Paracentral > arcuate> peripheral

Purtscher's-Like Retinopathy Potential Causes…

- Acute pancreatitis
- Pancreatic cancer
- Renal failure
- Autoimmune diseases
- Pregnancy complications (preeclampsia, HEELP, amniotic fluid embolus, etc.)
- Multiple Myeloma
- Thrombotic Thrombocytopenia purpura
- Childbirth
- Long bone fractures
  - Femurs, shoulder joints

Pathophysiology?

- MOA: truly unknown
  - Leading theory → pre-capillary arteriolar occlusion due to embolization from air, fat, granulocyte, platelets, fibrin other leuko-aggregates formed after complement activation
  - Noticeably, visible retinal emboli are absent!
  - Air emboli from chest compression syndrome

Fat Emboli? How?

- Systemic embolism may stem from:
  - Patent foramen ovale
  - AV pulmonary shunts
  - Persistent ductus arteriosus
- "Fat emboli are commonly released from the intramedullary fat into the venous circulation after long bone fracture, surgery, and pancreatitis…such emboli would be more likely to occlude the smaller 5 um retinal capillaries at the time of injury." --- Agrawal & McKibbin (2006)
  - Fat emboli = 5-10 um
  - Precapillary arterioles = 45 um
  - Retinal capillaries = 5 um

Management…

- FANG
  - Arteriolar occlusions
- ICG
  - Evidence for choroidal hypoperfusion
- Follow up:
  - 1 month
  - 2-3 months
  - 6-12 months
- Treatment:
  - Monitor
    - Resolution in 1-3 mo typically
  - Corticosteroids (no statistically significant difference in studies)
  - Hyperbaric oxygen

Back to patient…

- Failed to return as directed…
- Did see retinal specialist who confirmed PLR

Case #4:

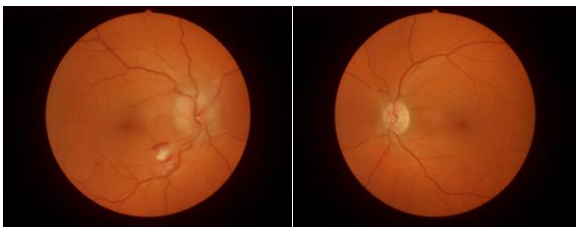
"Doc, I don't feel so good…"

Case History…

- 43 year old WM
- Referred for vision loss and HA after being admitted to hospital, onset 1 week, OD > OS, D = N
- LME = doesn't remember; long time ago
- BS = 600+
- HbA1c = 18.6%.....wow!
- BP = 200/120
- Also, hypertriglyceridemia and hypercholesterolemia
- CT/CTA = WNL OU in emergency room

Exam…

- BCVA = 20/50 OD, 20/20 OS
- EOM's = WNL OU
- Pupils = PERRLA, (+)mild APD OD
- CVF = WNL OS, inf nasal restriction OD
- HVF = WNL OS, central and inf nasal defects OD
- Adnexa/SLE = WNL OU
- DFE: see pictures
- IOP = 19 mmHg OU via Goldmann
- ESR and CRP = WNL in ER department work-up



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Diabetic Papillopathy….

- Defn: optic disc edema in a DM patient with minimal or mild optic nerve dysfunction
- Some suggest is on mild end of NAION spectrum
  - Typically more peri-papillary hemorrhages than NAION
- 70% have Type 1 DM
- 60% are unilateral; 40% bilateral
- No specific Tx for edema; treat DME if present; spontaneous recovery usually occurs over several weeks to months
- May have permanent visual field or acuity defects
- Control underlying systemic issues (BS, BP, BC, etc.)
- FANG can differentiate between DM papillopathy and NVD
  - Rarely needed…

Back to patient…

- Sent to retina given proximity of exudate and CWS to macula….
- FANG ruled out CSME → retina chose to monitor
- Patient returned 2 months later
- VA = 20/25-2 OD, 20/20 OS
- Dramatically improved optic nerve swelling on OCT and exam
- Monitor q6 months given BS levels

Case #5:

"Doc, I can't breathe very well…"

Case history #1…

- 64 year old white female
- "Vision…is…blurry……OS……I can't breathe very well…"
- Stopped exam → sent patient to ER in wheelchair

Case History #2….4 weeks later

- Chest CT in ER showed numerous masses → stage 4 lung cancer
  ---Smoker x 50+ years, 1-2 packs/day
- Full body scans revealed metastasis to liver, brain, brainstem, neck, chest, spine, and abdomen → EVERYWHERE!
- Refused chemo, started radiation

Choroidal Metastasis OS

---Sup/Temp with exudative RD involving fovea

Choroidal Metastasis…

- Women > Men (70%:30%)
- Average age = 50-60 years of age
- Men = Lung Cancer
- Women = Breast Cancer
- Most common intraocular malignancy
- Usually amelanotic, shallow, oval/round mass
  - "leopard spots" = macrophages containing lipofuscin
- 90+% are posterior to equator of eye!……..why?
  - Choroid is highly vascularized!
- Less than 10% have metastasis from sites other than lungs or breasts
- Sx = blurred vision, floaters, VF defects, metamorphopsia, asymptomatic
- SRF and serous retinal detachments are found in 91% of cases
- History of malignancy in 65-75% of patients

Types of Retinal Metastasis…

- Choroid is most common site of metastasis to eye
  - Breast carcinoma = 39-49% of uveal metastases
  - Lung carcinoma = 21-29%
  - GI Tract = 4%
  - Kidney, skin (melanoma), prostate, pancreas, thyroid, testes …
- In 17-18% of cases the primary metastasis site remains unknown

"Ocular ultrasound is really important with metastases because they tend to be echogenic, whereas melanoma tends to be echolucent."
--- Carol Shields, MD (Wills Eye Hospital)

Most important differentials…

- Amelanotic choroidal melanoma/nevus
- Choroidal hemangioma
- Lymphoma
- Choroidal osteoma
- Disciform macular scarring
- Posterior scleritis
- CHRPE
- Rhegmatogenous RD

Is color of mass important?

- Some tendencies but <u>not</u> specific in all cases…
  - Pale-yellow = lung/breast cancer
  - Dark grey/Brown = cutaneous melanoma
  - Orange/red = renal cell or thyroid carcinoma
  - Pink/Yellow-orange = carcinoid tumors

Choroidal Metastasis Treatment…

- Ocular:
  - External-beam radiotherapy
  - Chemotherapy
  - Hormonal therapy
  - Plaque radiotherapy
  - Enucleation
  - Any combination of the above
- Systemic:
  - Left to oncologist….radiation, chemotherapy, surgery, etc.
- Sometimes ocular tissues are simply monitored for response to systemic treatment
- Life expectancy strongly considered too!

Prognosis…

- Ocular metastasis carries an exceedingly poor systemic prognosis…
- Life expectancy = 12-21 months (gross mean)
- Bleak outlook overall…
- Ocular oncology referral

Back to the patient…

- Patient declined chemotherapy, agreed with radiation Tx
- Referred to local retina specialist too…
- Given spread to entire body specialist wanted to monitor with systemic treatment only first given bleak outcome
- Patient died 4 months later…

<u>Case #6:</u>

"Doc, I feel great and don't have any problems…"

Chief Complaint:

- 10 YO AAF; First eye exam ever
- Failed school screening
- Referral said OD>OS blurriness
- Patient denied any difficulties with vision
  - A's and B's for grades; "does very well"
- Father had never noticed any problems before

Case History

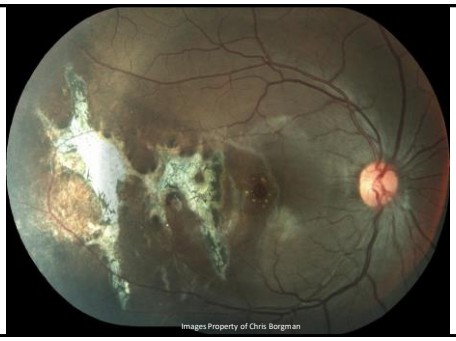
- POH: (-)injuries, (-)surgeries, (-)strab, (-)Rx before, (-)trauma
- PMH: denies all, sees PCP yearly, full term baby with no problems during delivery, normal milestones
- FOH: (+) grandmother with borderline POAG
- FMH: denies all
- MEDS: denies all
- ALL: NKMA, NKDA

Ocular Exam Continued…

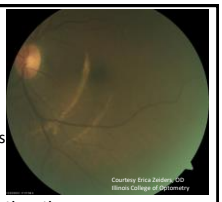
Refraction: OD: +1.50-1.50x180 20/80
OS: +0.75 sph 20/20

OD	Slit Lamp Exam	OS
Clear	**Lids/Lashes**	Clear
Clear	**Conjunctiva**	Clear
Clear	**Cornea**	Clear
4+ T/N	**Angles**	4+ T/N
D & Q	**A/C**	D & Q
Clear, Brown	**Iris**	Clear, Brown
Clear	**Lens**	Clear

Tonometry: 20 mmHg OU via Goldman



Choroidal Rupture



- Tear in choroid, Bruch's membrane, and RPE layers
- Typically follows blunt trauma
  - 5% of time ; M>>F
- May acutely be covered by hemorrhage or commotio retinae (Berlin's Edema)
- Yellow or white crescent shaped streak
- Concentric to optic nerve

Rupture Mechanism of Action

•Two Types of Choroidal Rupture:
- •1)**Direct**---site of injury, usually parallel to ora serrata, more anterior
- •2)**Indirect**---contrecoup injury, typically posterior pole, "classic rupture"

Choroidal Rupture Complications…

- CNVM
  - Occurs in 5%-10% of rupture cases
  - Months to years after trauma (up to 37 years) (avg 7-8 months) (81% within one year)
  - FANG/ICG and/or OCT to help with Dx
  - Usually anterior to RPE in neurosensory space
- Scar Tissue of Retina/Rupture Site
  - Fully scarred 3-4 weeks after trauma
  - Usually have to wait for hemorrhages to reabsorb in order to have clear view

Choroidal Rupture Treatment…

1. **Monitor with Amsler Grid**
   - q6-12 months
   - No Tx if no CNVM
2. **Laser Photocoagulation**
   - Juxtafoveal and extrafoveal CNVM
3. **Photo-Dynamic Therapy**
   - Subfoveal CNVM
4. **Surgical Removal of CNVM**
   - Subfoveal CNVM
5. **Anti-VEGF Agents** (Avastin, Lucentis)
   - Subfoveal CNVM

Choroidal Ruptures and Final Visual Acuity

- Ament et al. studied 111 indirect ruptures (2006)…
- Final Acuity Results ≥1.5 Years:

	Peripheral CR	Macular CR	(-) CNVM	(+) CNVM
Total (n)	34	73	99	12
Final VA ≥ 20/40	59%	22%	38%	8%

- **CNVM Likelihood:** older age, length of CR (not width), macular rupture location
- **Poor Prognosis with:** macular rupture location, (+) CNVM, ↓ baseline VA

Traumatic Macular Holes…

- **83%** macular holes are idiopathic
  - Tend to be gradual formation over weeks to months
- **5%-15%** holes due to trauma (TMH)
  - Coincide with traumatic event; immediate formation
- **95%** achieve hole closure with surgery

Mechanism of Action…

- Very similar to choroidal rupture MOA
- Anteroposterior compression of globe → stretches retinal tissues
- **2 Theories:**
  1. Immediate Tear of Retina --- immediate hole upon trauma
  2. Tangential Vitreous Traction --- delayed/slow hole formation
- **Treatment:**
  - PPV with Fluid-Gas Bubble Exchange
  - "Tamponade"

TMH Monitoring Only Outcomes…

- Yamashita et al. studied 18 total eyes with TMH
- 44% showed spontaneous closure within 8.4 months (Japanese studies)
- Other 2 studies show range of 10-67% spontaneous closure of TMH
- **Final VA same as with surgery**

- Problem: Which pts will close spontaneously?

TMH Surgical Outcomes…

- Yamashita et al. combined 2 studies (39 eyes total) (2002)…
  - 95% achieved hole closure with surgery
  - 77% had final VA of ≥20/40
  - Surgery = faster closure of hole
  - Surgery has no affect on final VA
  - Monitor for several months in acute setting then surgery for traumatic macular holes
  - Chronicity may play a role as well

Patient outcome…

- Sent to retinal specialist….
  - Declined further surgery given lack of clear timeline of trauma
- Youngest of 7 children…
- Vaguely remembers trauma with roller skate to same eye as a child at the hands of an older sibling…
- (-) CNVM----------Tx = monitor only
- Polycarbonate for protection at all times
- Be aware of child abuse in odd cases like this…

Case #7:

"Doc, I have this occasional flash in my eye."

Exam…

- 53 YO AF (Vietnamese migrant) (limited English)
- CC: "mild flashing lights" OD, onset few years, worse when bending over, (+)PVD in previous records OD
- PMH: denies, LME 6 months prior
- FMH: (+)HTN
- SH: unremarkable
- Meds: BC pill
- ALL: NKMA

Exam…

- VA = 20/20 OD, 20/20 OS (cc)
- EOM/Pupils/CVF = WNL OU
- SLE = mild pinguecula OU temporally
- Tonometry = 15 mmHg OD, 14 mmHg OS with Goldmann
- DFE = see pictures…

DFE…

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DFE 2 months later…

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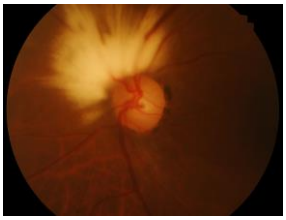
Huh? What is going on here?

- Biggest differential Dx = Cotton Wool Spot
- "Myelinated nerve fiber layers can be confused with cotton wool spots…If uncertainty persists, photograph the lesion and reappoint the patient for re-evaluation. Cotton wool spots fade over several weeks, whereas myelinated nerve fiber layers do not."
  - The Handbook of Ocular Disease Management: 10th Anniversary Edition. Review of Optometry; April 15, 2008; 46A-47A.

NFL Myelination…

- "Normal myelination typically progresses from the chiasm to the optic nerve from the eighth month of gestation until birth and then stops at the lamina cribrosa." --- Shelton JB, et al. JAMA Ophthalmol. (2013)
- Congenital mainly
- Progression/Regression has been documented too

Worst NFL Myelination I've seen…



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Case #8:

"Doc, I need my DOT form filled out today."

Case History…

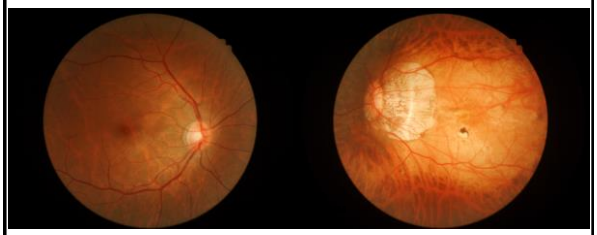
- 38 year old WF
- CC: "failed my DOT test and need this form filled out"
- "Vision OD is fine but my OS is bad" (stable for years)
- POH: OS has been bad since car accident when she was 1-2 YO
- PMH: unremarkable
- FMH: unremarkable
- Meds: denies
- ALL: NKMA/NKDA

Exam:

- 20/20 OD, 20/HM OS (PHNI)---cc
- EOM's = WNL OU
- Pupils = mild APD OS
- CVF = WNL OD, some nasal hemifield difficulty OS
- Adnexa/SLE = WNL OU
- IOP = 11 mmHg OD, 13 mmHg OS
- DFE: see pictures

- Refraction: OD -4.75 -1.25 x 090 20/20
  OS +/-6.00 sph 20/HM

DFE…



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Post-Dilated Retinoscopy…

- OD: -4.75 -1.25 x 090 20/20

- OS: -29.00 sph ! 20/800

- Myopic Degeneration OS = Dx

Myopic Degeneration

- F>M
- Usually > 6.00 D myopia

- Complications:

1. Retinal breaks
   - Increased risk of RD's, tears, etc.
2. Choroidal neovascular membranes
   - 5-10% of cases with axial length >26.5 mm
3. Fuch's spots
   - Previous CNVM and/or subretinal hemorrahges
4. Posterior staphylomas
5. Lacquer cracks --- breaks in Bruch's membrane complex; 4% eyes
6. PVD
   - Occurs at earlier age
7. Diffuse pigmentary alteration/chorioretinal degeneration
8. Lattice Degeneration --- not more common in myopic degeneration
9. Increased glaucoma risk?

Treatments?

- Controversial…
- Myopia control???
  - Spectacles: single vision vs. MF's
  - CL's: single vision vs. MF's
  - Ortho-K
  - Atropine/Pirenzepine
- Scleral reinforcement???
- CNVM:
  - Laser photocoagulation
  - Anti-VEGF agents

Case #9:

The case of misdiagnosis…

Case History…

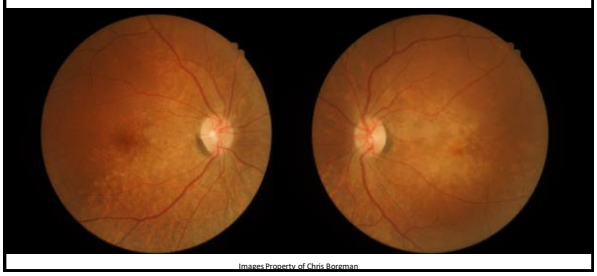
- 49 YO AAF

- CC: "doing well….just want Rx updated"
- POH: history of "*dominant/familial drusen*" , (-)trauma
- PMH: (+)bilateral hearing loss since birth
- FMH: unremarkable
- SH: unremarkable
- ALL: denies

Exam…

- VA = 20/20 OD, OS (cc)
- EOM's = WNL OU
- Pupils = WNL OU
- CVF = WNL OU
- Refraction:
  - OD: -1.75 – 0.75 x 090 20/20
  - OS: -1.75 – 1.25 x 060 20/20
- SLE = WNL OU ; early cataracts OU
- Tonometry = 18 mmHg OU with Goldmann

DFE…



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Diagnosis in the past…

- Dominant Drusen = previous diagnosis

- Differentials now…
  - Usher's Syndrome with RP
  - Syphilitic Chorioretinopathy
  - Rubella Retinopathy

Electrophysiological & Lab Tests…

- ERG = normal

- CBC with diff = WNL
- FTA-ABS = negative
- RPR = negative/non-reactive
- Rubella IgG = positive
  - (greater than 10 = positive/immune)
    - Patient's level was 13.8

Dx = Rubella Retinopathy…

- *Toga viridiae* family → found only in humans
- Respiratory tract transmission
- Consequence of rubella infection in utero
  - Ocular & systemic complications possible
- Last major worldwide pandemic was 1963-65 (50 YO today)
  - 10% of all pregnant women infected, 30% of those pregnancies resulted in CRS
- Triad: heart disease, deafness, & cataracts
- 70-90% of worldwide population has antibodes to Rubella
- 95% of US population is seropositive due to vaccines…
- Risk of malformations during pregnancy = first 16 weeks is largest risk
  - 90% → 2-10 weeks
  - 34% → 11-12 weeks
  - 17% →13-16 weeks
  - 3% → 17-18 weeks
  - 0% → 19+ weeks

Immune System & Rubella…

- Non-immune maternal exposure to Rubella virus during 1st trimester of pregnancy
  - If mother has immunity then risk of is virtually nil
- Organogenesis occurs 1-8 weeks of gestation
- Maternal IgG is only Ig that can cross placenta…however, this occurs around 8 weeks at the earliest…
  - Max IgG from mother around 32 weeks gestation
  - IgM too large…never crosses placenta
  - IgA only for mucosal surfaces….does not cross placenta
  - Endogenous IgG synthesis at 24 weeks gestation by fetus
- An acquired infection around this time (**1st trimester**) can easily affect the vulnerable fetus due to "no defense"
  - Biggest risk to fetus is here
  - Most active organogenesis and most rapid cell division here

Rubella Pathogenesis…

- Reduced organogenesis:
  1. Cellular deficiency → tissue destruction/scarring
     - Decreased growth rate
     - Shortened survival time
  2. Endothelial cell damage → vascular damage
- Notably, inflammation does not seem to play a role in pathogenesis
- Risk of CRS after re-infection is only 5-8%

Congenital Rubella Syndrome

1. Congenital cardiopathy
   - 30% of cases
2. Sensorial deafness
   - Most common
   - 60% of CRS cases
3. Ocular defects (30-40% of CRS cases)
   - Salt 'N Pepper Retinopathy – 60% of CRS
   - Nuclear Cataracts – 27% of CRS cases; must be ≤6 weeks gestation
   - Microphthalmia – 10-20% cases
   - Iris atrophy -- notoriously poor dilators; difficult phaco
   - Glaucoma –10-15% cases
   - Strabismus/Amblyopia
   - Hyperopia > myopia (shorter eyeballs)

Salt 'N Pepper Retinopathy

- Pathognomonic for prenatal rubella infection
- Pigmentary retinopathy of RPE
  - Neural retina = unaffected
  - Choroid = unaffected
- 40-60% of CRS cases
- Non-progressive (vast majority)
- Electroretinogram (ERG) = normal too
- Visual acuity not affected
  - CNVM possible

FAF vs. FANG in Dx of Rubella Retinopathy…

- "…fundus autofluorescence (FAF) can sensitivity and noninvasively highlight areas of dysfunctional RPE. Thus, FAF in the absence of FANG can be sufficient to establish the diagnosis of rubella retinopathy."
  - Goldberg N, et al. (2009)

Rubella Retinopathy Expectations

- RPE pigmentary changes & hearing loss → Think Rubella!
- Good vision is the rule
- ERG = normal
- Dilation can be difficult…..may need multiple mydriatics…
  - Iris atrophy 2' poor development of iris dilator muscles
- When in doubt…consider IgG/IgM
  - Rule out syphilis!
- Ask about maternal infections during utero….a lot of patients are aware!

MMR Vaccine and Seropositivity

- MMR = measles, mumps, rubella
  - Given within first year of life in developed countries now
  - Repeat around 15 years old too
- ***"…confirmation by RT-PCR, serum rubella IgM or persistently high levels of IgG were not useful since laboratory evidence of rubella virus must be obtained in the first year of life to be informative."***
  - **Tamayo MT, et al. (2013)**
- IgG will be persistently high in anyone who has been given the MMR vaccine in past
  - What about my patient then???

Case #10:

- "Doc, I'm having trouble reading for quite some time now."

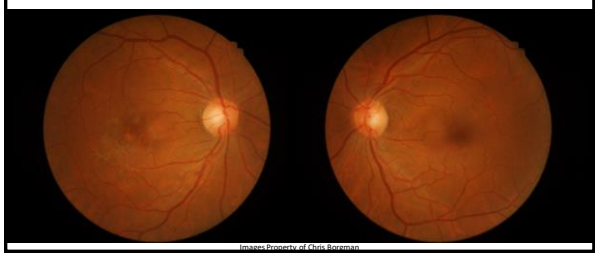
Case History

- 62 YO AAM
- "Blurry vision"
- HPI: OD only, onset "some time ago", constant, gradual until it stabilized
- PMH: denies ; LME unknown
- Meds: denies all
- All: NKDA
- SH: every day smoker

Exam

- BCVA: 20/40 OD, 20/20 OS
- CVF, Pupils, EOM's = WNL OU
- Slit lamp = WNL OU
  - Some minor cataracts OU
- Tonometry = 9 mmHg OD, 10 mmHg OS
- DFE: see pics

DFE…



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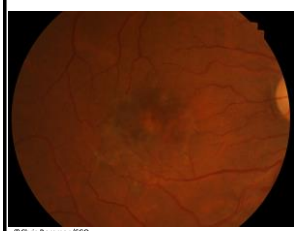
Macula Close up…



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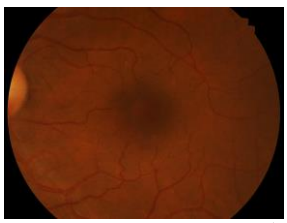

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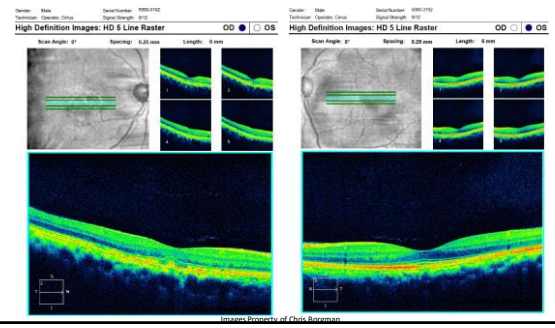

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Polypoidal Choroidal Vasculopathy

- Controversial overall…
- Idiopathic; aka---"posterior uveal bleeding syndrome"
  - Technically classified under "ARMD"
- Typically unilateral ; M = F
- Main differential Dx = ARMD!!!
  - Younger age of onset than ARMD
  - Persons of "color" more often ; Asians > African-Americans ??
    - Only 8-13% of Caucasians with CNVM
  - *Lack of drusen!*
  - Characteristic FANG/ICG and OCT findings;
    - ICG is more helpful than FANG!
- "Typically has a relapsing-remitting course with chronic, multiple, recurrent serosanguinous detachments of the RPE, neurosensory retina, and subretinal NVM."

ARMD vs. PCV

ARMD	PCV
Older patients	Younger patients
Caucasians	Non-white races
Drusen present	Drusen absent
Macular location	Extra-macular; peripapillary
Indistinct lesions	Distinct lesions
Genetic background differs	Genetic background differs
---	Choroidal vascular hyperpermeability

- Although, these are different pathologies….."PCV is a type of choroidal neovascularization. Hence, PCV is currently categorized as a phenotype of age-related macular degeneration (AMD)."
  - Honda S, et al. (2014)

PCV Associations/Risk Factors…

- Hypertension (41-45%)
- Smoking
- Elevated CRP
- h/o CSCR
- Myopic degeneration w/ staphyloma

PCV Stages…

1. Orange/Red lesion in choroid/sub-RPE layers
2. Pigment Epithelial Detachment with +/- SRF
3. Subretinal fibrinous material after resolution
   - My patient likely is in this stage

Treatment…

- Very similar to wet ARMD and dry ARMD…
  - Anti-VEGF injections
  - Photo-dynamic therapy
  - Combo: PDT & Anti-VEGF = added benefit!
  - If inactive, monitoring retina q6 months is appropriate
- "Patients found to have exudative, hemorrhagic retinopathy, without signs of active inflammation or precursors to ARMD, should be considered suspicious for IPCV."

---Handbook of Ocular Disease, *Review of Optometry* (2013)

Case #11:

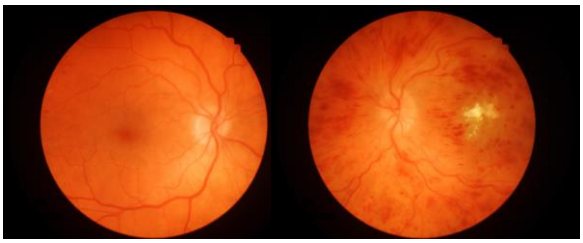
- "Doc, I lost vision in my left eye 4 months ago…..will it ever come back?"

Case History

- 48 YO WF
- CC: sudden, painless vision loss OS only x 4 months
- PMH: Type II DM, HTN, ↑ triglycerides, ↑ cholesterol, mild kidney failure,
- FMH: unremarkable
- SH: (-)tobacco, (-)EtOH, (-) Drug Abuse
- ALL: PCN
- Has had coronary stenting 2 years prior and DM foot surgery

- VA: 20/20 OD, 20/400- OS
- (+)APD OS
- CVF = WNL OD, UTT OS
- IOP = 18 mmHg OU

Dx = CRVO OS



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Next steps…

- Sent to retina for anti-VEGF injections
  - Unfortunately, no improvement noted after 4 months of Tx
- PCP ordered additional labwork:
  - Monoclonal antibody testing

Multiple Myeloma…

- Multiple myeloma is a neoplastic plasma-cell disorder resulting from malignant plasma cells in the bone marrow
  - Plasma cells are of B-cell lineage…
- 1.4% of all cancers
  - 10-15% of hematological cancers
  - 1.5-2.0% of cancer related deaths
  - Life expectancy = 3-4 yrs post-diagnosis (60-70% cases)

3 Main Stages in MM Spectrum…

1. **Monoclonal Gammopathy of Undetermined Significance (MGUS)**
   - 1% chance of developing MM in 1 year
2. **Smoldering Multiple Myeloma (SMM)**
   - 10% chance of developing MM in 1 year
3. **Multiple Myeloma (MM)**

Plasma Cell Disorder	Serum monoclonal protein (g/dl)	Clonal bone marrow plasma cells (%)	End organ damage present?
MGUS	<3	<10	(-)CRAB
SMM	>3	>10	(-)CRAB
MM	>3	>10	(+)CRAB

- End Organ Damage = CRAB
  - HyperCalcemia
  - Renal failure
  - Anemia
  - Bone lesions

Hyperviscosity???

- MM can cause a hyperviscosity syndrome secondary to the paraproteinemia associated with the disease.
  - Excess production of antibodies from abnormal plasma cells
    - AKA: monoclonal protein → paraproteinemia

Ocular Concerns…

- Retinal vein occlusions!
- Multiple myeloma should be considered as a differential diagnosis in young patients (<50 YO) with retinal vein occlusions, even if other risk factors for venous occlusion like hypertension, diabetes mellitus and hypercholesterolemia are present.
  - Borgman CJ. Clin Exp Optom. 2016

Systemic findings… All from monoclonal protein

- Spontaneous bone fractures
- Spinal cord compression
- Osteolytic lesions
- Renal failure
  - 15-25%
  - Secondary to hypercalcemia
    - Which is secondary to osteoclast bone resorption
- Anemia
- Recurrent infections
- Thromboembolism
  - Monoclonal proteinemia

MM Treatment

- Currently, MGUS and SMM do <u>not</u> represent an indication for treatment, as no clear benefit of treatment has been found in these patients, as with patients with multiple myeloma.
- When staged at MM:
  - Immunomodulatory agents
  - Corticosteroids
  - Stem-cell transplantation
  - Chemotherapy
  - Anticoagulation

Thanks!

- Questions? Accolades?
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- Complaints?
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