More than meets the eye
Role of vascular disease in glaucoma & retinal disease

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The questions that follow

- What's you Dxs or DDx?
- What tests would you order to identify underlying disease?
- How would you manage the glaucoma?
- Are you concern with the decreased vision OD? Would you order a MRI?
- Other in office tests tests?

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68 Jamaican female

- CC: mild decrease in vision OS X few months
- POHx:
  - ACIOL OS (slight de-centered)
  - Cataracts OD
  - Retinal break OS s/p laser
  - POAG OU (Takes timoptic BID)
- PMHx: PRE-DM X 1 yr
- IOP: 15mmHg OU

51 BM

- Vision decreased OD over the last 2 yrs
- PMHx: unremarkable
- BCVA:
  - 20/60 OD 20/20- OS
- P: (+) APD OD
- IOP: 38mmHg OD 27mmHg OS
- SLE: mild cataracts OU
**Sturge Weber Syndrome (SWS)**

*Encephalotrigeminal (facial) angiomatosis*

*Neuro-oculo-cutaneous* congenital *vascular hamartomas*

- Need not affect ALL 3 systems
  - CNS angiomata
  - Choroidal hemangioma (ipsilateral to PWS)
  - 50% of CH are associated with SWS
  - Most commonly DIFFUSE pattern
  - Various associated complications
  - PWS
    - Distribution along trigeminal nerve
    - Choroidal hemangioma is more common with lid involvement
    - Also increased likelihood of glaucoma

**SWS and association with glaucoma**

Pathophysiology:
- Abnormal development of anterior chamber
  - Abnormalities within the angle structures may be associated with decrease aqueous drainage (like in other congenital glaucoma)
- Mechanical pressure from CH pressure (onset of OAG late)

Treatement via unconventional path:
- (AH sip through tissue around area)

Conventional
- TM → Schlemm canal → episcleral venous plexus (via iridocorneal) → VV → ophthalmic (leave via sclera)

**Management of OUR patient**

- **SWS**
  - Glaucoma
    - Glaucoma work-up
    - Cosopt BID initiated
      - PG work well with THIS 2nd glaucoma but why is it NOT an ideal med in THIS case?
  - Retinal detachment/Choroidal menangioma
    - Ultrasound/FA CONFIRMED the dx
    - FA: hyperFL of large choroidal vessels with Fl staining entire lesion
    - UBM: solid moderate reflective tumor

**S/p AVT injection affect on permeability**

Pt will be undergoing external beam radiation to treat the choroidal hemangioma
54 BM
- Blurred vision at near
- No medical Hx
- BCVA: 20/20 OD, OS
- P: (+) APD OS
- POHx: Trauma OS ’04
  - Received stitches to the side of his head
- Gonio: Angle recession OS
- BP: 160/110 mmHg

20/20 and (+) APD...is that possible?
- Occupying ONH lesion
- Optic neuritis
- Neurological VFD
- And...

Follow up for our pt 1M later
- S/p Timoptic BID / Xalatan qhs OU
  - 15 mmHg OU
- BP Dx and managed...
  - Dxed with HTN through a PCP consultation and placed on meds
- BP today 133/86 mmHg
- F/u q3M

Relationship b/t glaucoma & vascular diseases (2010 Study)
- N= 76,000 glaucoma
- 50% had HTN
- 30% hyperlipidemia
- 30% had DM
- Other co-morbidities were also significantly higher in pts with glaucoma than does w/o glaucoma
- Glaucoma patients are significantly more likely to have co-morbidities. This can be life threatening or can affect the quality of life appreciably. Glaucoma pts should see PCP q12M

Hsing-Ching Lin Ophthalmology 2010
**HTN & glaucoma: Pathogenesis**

- HTN $\rightarrow$ arteriosclerosis $\rightarrow$ constriction of SPCA $\rightarrow$ ischemia $\rightarrow$ neural tissue loss
- This further may cause dysregulation
- Retinal vascular narrowing has been reported among glaucoma pts
  - Studies have shown that subjects with narrower retinal vessels were more likely to have glaucomatous ON

**Systolic BP and Glaucoma**

- IOP is positively (but weakly) correlated with BP
  - For every 10mm change in SBP, there is a 0.5mm change in IOP
  - Association between BP and the development of glaucoma is weak

**Glaucma and OBF**

Decrease in ocular flow have has been observed in pts with glaucoma & even believe to be associated with progression.

**So what is Vascular Dysregulation?**

- Impairment of normal autoregulation mechanism
  - Vessels do not constrict/dilate properly in order to provide adequate blood flow
    - It may lead to decreased blood flow into the eye & glaucomatous damage
  - This can be an affect of localized ocular disease or overall vascular disease can lead to dysregulation

**Hypotension & glaucoma**

- Reduction in systemic BP has a deleterious effect, creating insufficient perfusion pressure to ON
  - Ischemia can lead to glaucomatous damage
    - pts with glaucomatous & associated VLD are more likely to have underlying hypotension, compared to pts with glaucoma & no associated VFD
    - Ocular perfusion pressure is associated with decrease blood flow
  - Barbados Eye Study
    - Low SBP was a risk factor for incidence of OAG
  - EMGT: Low SBP was a predictor for progression

**We have all experienced dysregulation...**

- Ever felt the following
  - Cold extremities
  - Reduced sensation of hunger OR...
  - Migraines...while working with your kids on their homework
    - OK this one may be SELF induced REGULATION
**Ocular Perfusion Pressure and Glaucoma Progression**

**OPP in EMGT**
- Randomized clinical trial comparing no treatment to treatment for initially diagnosed glaucoma (entire cohort followed for progression)
  - In patients with higher baseline IOP:
    - h/o CVD increased risk (HR 2.75, CI 1.44-5.26)
    - Lower SPP increased risk (HR 1.55, CI 1.02-2.35)
  - In patients with lower baseline IOP:
    - Higher systolic BP decreased risk (HR .44, CI .2-.97)


**The First Charge**
- There is no accurate, repeatable, verifiable method of measuring blood flow to the optic nerve head.
- The instruments purported to do so do not agree.
- We have no means of measuring blood flow to the nerve in a clinically useful fashion

**Consensus Points**
- Blood Pressure is positively correlated with IOP.
- It is unclear whether the level of BP is a risk factor for having or progressing OAG in an individual patient.
- Lower OPP is a risk factor for primary OAG.
- OBF parameters measured with various methods are impaired in OAG, especially in NTG

Hayreh SS. Trans Am Acad Ophthalmol 1974; 78:240-54

**Conclusion**
- “The relationship among BP, IOP and development of OAG is complex and requires further investigation.”


**RTC for evaluation of glaucoma**
- Treated with Alphagan BID (highest IOP was 19)
- PMHx: HTN but very compliant with meds
- Takes systemic b-blocker at night
- BP: 126/60 mmHg
- BCVA: 20/20 OD, OS
OD is showing progression

Managing HTN & managing OAG may be challenging

- **First**, lower IOP (17 is too high for this pt)
- **Second**, consider increasing perfusion (but remember that it may be at the consequence of lowered IOP)
  - Anti-glaucoma meds that affective diurnal/nocturnal IOP curves
    - Those who are less likely to have transient spikes
  - What about non-selective b-blockers (Timoptic) vs selective (Betoptic)
    - B-blockers may decrease perfusion via vessel constriction
    - How is his systemic b-blocker affecting IOP & should you stay away from ocular b-blocker in these pts?

**OD OS**

Is decreases perfusion the cause for progression?

What is her OPP (ocular perfusion pressure)?

**BP 126/60mmHg**

**IOP is 17mmHg**

Ocular perfusion pressure measured as DPP (diastolic perfusion pressure) 60-17= 43 mmHg

May be important to look at perfusion in the future...particular for cases that progress despite low IOP.

EMGT establish that lower systolic BP was predictor for glaucoma progression

**Travoprost**

Travoprost Reduces and Sustains Habitual IOP-lowering

**Managing HTN & managing OAG may be challenging: Continuation**

- Exercise can increase blood flow
- Talk to PCP about HTN medications
- Can pt take Medications during the day rather than at night ???
  - May have a (+) affect on OAG BUT (-) affect on CVD
REview

- Lower IOP improves OPP
- Higher systemic BP improves OPP but don’t necessarily want to raise BP
  - Stroke #3 cause of death in US behind CVD and CA!
- Avoid drugs that lower systemic BP beyond patient’s desired systemic control
- Avoid nocturnal hypotension

MAPEC 2011

- The thought behind the study
  - Previous large population-based, long-term outcome studies found that sleep-time BP level is more sensitive predictor of risk of dying from CVD THAN BP level measured during the daytime
  - Some pts do not experience 10-20% decrease in BP at night (NON-DIPPERS)
  - 5 yr study used 48hr ambulatory BP monitoring perform in yearly intervals to determine if AM vs PM dosing would affect CVD/BP
  - There are variable BP measurements in AM/PM

MAPEC study

- RESULTS: There should be a shift from taking HTN meds at night instead of AM in order to protect (CVD) the pt
  - PM dosing:
    - Kept BP in normal range throughout the day
    - Pts had normal daytime BP
    - Provided protection against CVD complications
    - A decreases risk of cardiovascular related death, myocardial infarction and stroke were noted among pts taking PM dosing
    - Pts with PM dosing had 1/3 the # of CVD related complications

Take Home Points

- The role of blood supply as a risk factor in glaucoma is poorly understood and remains controversial
- Be aware of vascular health issues in our glaucoma patients
  - Blood pressure
  - Sleep apnea
  - dyslipidemia

- Encourage good lifestyle habits
  - Diet
  - Exercise
  - Avoid headstands with yoga
  - Stop smoking
- Refer for appropriate evaluation and management of possible risk factors
  - Blood pressure: avoid nocturnal hypotension
  - Sleep apnea
  - Vasospasm

58 AA Female

- PMHx: T2DM X 6 yrs
- POHx: LEE 2 yrs ago
- IOP: 25mmHg OD 22mmHg OS
- Pachs: 500 OD 508 OS
**Why the discrepancy?**

Varying approaches for:
- diagnosis of condition (i.e., diabetes, glaucoma),
- assessment criteria, and
- statistical approaches.

Examples:
- Redefinition of primary open angle glaucoma: Rotterdam Eye Studies
- Ocular Hypertension Treatment Study (OHTS)
- European Glaucoma Prevention Study (EGPS)
- OHTS found DM pts to have thinner corneas

**OHTS results: Could DM be a good thing for glaucoma?**

- OHTS study methodological issues
  - Pts self reported their DM
- Selection was bias towards overall healthy DM population
  - EXCLUSION criteria was ANY sign of DR

OHTS in 2007 (OHTS prediction model applied to European Glaucoma Prevention Study control patients) concluded that Diabetes did NOT decrease or increase risk in EGPS

**Controversies about the direct correlation b/t glaucoma & DM**

- Longer duration of DM could make pt at risk for POAG
- Could it be that DM pts (compare to those w/o DM) get their EYE examine more often and consequently are more likely to have their glaucoma detected?
- Could it be related to the fact that DM pts have higher IOP but not exactly POAG?
  - Studies shown greater increase in IOP among DM pts compare to those w/o DM
  - OHTS found DM pts to have thicker corneas

**49 BM**

- Decreased VA X 4 days OD
- PMHx: unremarkable
- BCVA: 20/40 OD   20/25 OS
- BP: 135/80 mmHg
- P: +1 APD
- IOP: 20mmHg   26mmHg
SO WHAT TO DO?

PCP work up (PMHx: unremarkable)
Evaluation to retinal specialist for ?tx ME (VA 20/40)
Treatment of glaucoma OU (IOP 19/33)
Ischemic or non-ischemic (VA 20/40 & retinal presentation but +APD)

Is POAG a complication of VO: Fact or Fiction

- Studies report low incidence of POAG developing AFTER the RVO onset
  - Blue Mtn eye & Beaver Dam Studies & OHTS
- Pts are typically Dx with POAG or have risk factors (like large cups) prior to onset of RVO

Hence, it would seem that with regards to the relationship b/t POAG & RVO that the glaucoma was the PRIMARY event

Glaucoma & RVO: Pathophysiology

- Glacomatous damage at the level of the LC can result in a collapse CRV
- Increase in IOP can elicit pressure upon the CRV

OS Shows a Drance hemorrhage and IPP is 5mmHg higher than last visit
Disc Hemorrhages in OHTS

**Purpose:**
- To compare the rates of detection of ON hemorrhages by clinical examination and by review of ON photos
- To assess the incidence of and the predictive factors for ON hemorrhages
- To determine whether ON hemes predict the development of POAG in OHTS


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Results: Disc Heme in OHTS

- ON heme detected BEFORE POAG endpoint
  - 16% of hemes detected by exam
  - 84% of hemes detected by review of photos ALONE
- Presence of ONH increased risk of POAG developing by 6-fold
  - Median time to development of POAG after hem appears is 1 yr

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What the Drance Hemorrhage tells you...

**PATHOGENESIS?**
- Likely indicates active disease
- There may also be an increase likelihood of progression
  - Commonly associated with pre-existing VFD
  - True prevalence among glaucoma pts is not known
  - Reports of <10%
  - MORE COMMON IN LTG

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Case Presentation

- **BCVA:** 20/100 OD 20/40 OS
- **IOP:** 12mmHg 18mmHg
- **SLE:**
  - K: mild endothelial folds OD
  - trace C/F OD
  - NS OD > OS
- **Look at injection distribution...**
What did the doppler show?

Carotid stenosis

Clinical picture

**Anterior**
- IOP typically low
- Idiopathic uveitis
- Cataract
- Corneal edema
- Dilated episcleral vessels
- Neovascularization (in absence of DR)

**Posterior**
- Hemorrhages & CWS
- Dilated veins
- Macular edema
- Asymmetrical DR
- Embolic events
- AION
- Artery occlusion
- Retinal emboli

OIS: Ocular ischemic syndrome

OIS is commonly associated with carotid artery disease

DDx: may have common underlying risk factors but DIFFERENT w/u

**OIS**
- Mid-peripheral
- Dilated NON-tortuous veins
- Scares dot blot hemorrhages
- Associated anterior segment

**CRVO**
- Posterior pole
- Dilated tortuous veins
- Confluent superficial and intra-retinal hemorrhages

NVG can occur in these pts