SYSTEMIC CONDITIONS WITH OCULAR INVOLVEMENT

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Disclosure Statement:
No financial disclosures
Hypertension

- Incidence: 70 million people in the US have HTN (29% of the population)
- Only 52% have their HTN under control
- Risk of:
  - heart attack
  - stroke
  - chronic heart failure
  - kidney disease
- Each increase of 20 mmHg systolic or 10 mmHg diastolic doubles the risk of complications
Hypertension

- Treatment reduces risk
  - 40% reduction in CVA
  - 25% reduction in MI
  - 50+% reduction in heart failure
Hypertension

- Essential HTN
  - Most common (90-95%)
  - Risk factors: sedentary lifestyle, smoking, alcohol, stress, obesity

- Secondary HTN
  - Results from identifiable cause: kidney disease, Cushings, thyroid disorder, pregnancy, drugs

- Malignant HTN (BP >210/130)
  - Immediate referral for BP lowering
  - 80% of pts with malignant htn die within 1 year
  - 95% mortality rate within 3 years
Hypertensive Retinopathy

• Clinical findings:
  • Retinal artery attenuation & straightening
  • Retinal artery nicking & crossing changes
  • Flame-shaped hemorrhages
  • Cotton wool spots
  • Retinal edema (rare)
    • Macular star
  • Disc edema
Hypertensive Retinopathy

• Keith-Wagener-Barker Classification System

• Grade 1
  • Mild arteriolar narrowing
  • No ocular symptoms
  • No systemic involvement

• Grade 2
  • AV crossing changes
  • Arteriolar light reflex
  • No ocular symptoms
  • No or minimal systemic involvement
Hypertensive Retinopathy

- Grade 3 (mild angiospastic retinopathy)
  - Retinal hemorrhages
  - Cotton wool spots
  - Exudates (macular star) (symptomatic)
  - Cardiac, cerebral or renal dysfunction common
- Grade 4 (severe hypertensive retinopathy)
  - Severe grade 3 signs and papilledema
  - Cardiac, cerebral and renal dysfunction are more severe
Hypertension

JNC 8 Practice guidelines (2013) / changes from JNC 7

• Changes to more lenient systolic BP values
• Results from 5 key trials
  • Showed a reduction in cerebrovascular events, heart failure, and overall mortality in patients treated to DBP target level.
  • In younger patients, elevated DBP is a more important cardiovascular than SBP.
Hypertension

JNC 8 Practice guidelines (2013) / changes from JNC 7

- Pts 60+yo with no DM or CKD, goal BP <150/90
- Pts 18-59 without mj comorbidities & pt 60+ with DM+/- CKD, goal BP <140/90
- When starting tx in AA pts s CKD, use CCB & thiazides instead of ACE inhibitors
- ACE inhibitors & ARBs rec for all pts with CKD
- ACE inhibitors & ARBs should not be used simultaneously
Hypertension

• JNC 8 Practice guidelines
• Lifestyle Changes
  • Dietary Approaches to Stop Hypertension (DASH)
  • Weight loss
  • Reduce sodium intake (<2.4g/d)
  • 30-minutes of aerobic activity most days of the week
Hypertension

- JNC 8 Practice guidelines
- Initial drugs of choice:
  - thiazide diuretic (hydrochlorothiazide)
    - Reduces sodium & water thus decreases blood volume
  - calcium channel blocker (verapamil, diltiazem)
    - Relaxes arteriolar & cardiac smooth muscle thus decreasing BP
  - angiotensin-converting enzyme (ACE) inhibitor (lisinopril, captopril)
    - Relaxes blood vessels by blocking formation of enzymes which narrow blood vessels
  - angiotension receptor blocker (ARB) (losartan)
    - Relaxes blood vessels by blocking formation of enzymes which narrow blood vessels
Hypertension

- Additional medication classes:
  - Beta blockers (atenolol)
    - Reduces workload on heart, causing decreased heart rate
  - Renin inhibitors (aliskiren)
    - Renin (enzyme) produced by kidneys which starts the hypertensive cascade
Hypertension

JNC 8 Hypertension Guideline Algorithm

Adult aged ≥ 18 years with HTN
Implement lifestyle modifications
Set BP goal, initiate BP lowering medication based on algorithm

General Population
(no diabetes or CKD)

Diabetes or CKD present

Age ≥ 60 years
Age < 60 years

BP Goal < 150/90
BP Goal < 140/90

Nonblack
Black

Initiate thiazide, ACEI, ARB, or CCB, alone or in combo
Initiate thiazide or CCB, alone or combo

All Ages
Diabetes present
No CKD

BP Goal < 140/90

Initiate ACEI or ARB, alone or combo w/another class

At blood pressure goal?

Yes

No

Reinforce lifestyle and adherence
Titrate medications to maximum doses or consider adding another medication (ACEI, ARB, CCB, Thiazide)

At blood pressure goal?

Yes

No

Reinforce lifestyle and adherence
Add a medication class not already selected (i.e. beta blocker, aldosterone antagonist, others) and titrate above medications to max (see back of card)

At blood pressure goal?

Yes

No

Reinforce lifestyle and adherence
Titrate meds to maximum doses, add another med and/or refer to hypertension specialist

Lifestyle changes:
- Smoking Cessation
- Control blood glucose and lipids
- Diet
  - Eat healthy (i.e., DASH diet)
  - Moderate alcohol consumption
  - Reduce sodium intake to no more than 2,400 mg/day
- Physical activity
  - Moderate-to-vigorous activity 3-4 days a week averaging 40 min per session.

Strategy
Description

A
Start one drug, titrate to maximum dose, and then add a second drug.

B
Start one drug, then add a second drug before achieving max dose of first

C
Begin 2 drugs at same time, as separate pills or combination pill. Initial combination therapy is recommended if BP is greater than 20/10 mm Hg above goal

Initial Drugs of Choice for Hypertension
- ACE inhibitor (ACEI)
- Angiotensin receptor blocker (ARB)
- Thiazide diuretic
- Calcium channel blocker (CCB)

Card developed by Cole Glenn, Pharm.D. & James L Taylor, Pharm.D.
Hypertension

• JNC 8 Practice guidelines
• Moved away from assumption that lower BP will improve outcomes regardless of type of agent used.
• Focuses on reducing cardiovascular risk.
• May lead to less use of anti-htn meds in younger patients
  • Less potential for adverse events that limit adherence
Case Report

- 40 yow referred by ED
- painful HAs behind eyes
- blurred vision OS
- BP 215/104
Case report: malignant HTN

BCVA 20/15

BCVA 20/30-
Case report: malignant HTN

- H/o IgA nephropathy (Berger’s disease)
- HTN previously well-controlled; however, now:
  - proteinuria & increased creatinine values
  - dialysis / kidney transplant?
  - elevated BP
Malignant HTN: 6 week f/u

20/100 (down from 20/15)  20/30 (stable)

Pt reports difficulty with medication compliance; BP 170/108.
Malignant HTN: 10month f/u

20/20

Current treatment options?
Retinal Plaques

• 3 types of emboli
  • Cholesterol (Hollenhorst) ~ 80%
  • Fibrinoplatelet = 14%
  • Calcific = 6-9%

• All types share strong association to cardiovascular disease
Cholesterol (Hollenhorst)

- Most common (80%)
- Typically at bifurcations, mobile
- Rarely cause occlusion
- Shiny, yellowish color
- Ipsilateral carotid artery plaque
Fibrino-platelet

- Typically within arterioles (not at bifurcation)
- Dull white-grey (linear)
- Often associated with carotid disease or mitral valve insufficiency
- Risk of RAO
Calcific

- Typically within arterioles (not at bifurcation)
  - Immobile
- Highest systemic risk (often cause BRAO)
- Serious complication of calcific cardiac valve disease
  - May be presenting feature of severe cardiovascular disease in need of early surgical correction
Retinal Plaques

- Almost 20% of patients with retinal emboli have carotid stenosis >75%
- Increased risk of strokes
- HH plaques have increased mortality rates:
  - 15% at 1 year
  - 29% by 3 years
  - 54% by 7 years
Case report: Hollenhorst Plaque

65 yom, asymptomatic
BMI 28, chol 319, trig 688, A1c 10.0%, BP 185/106

Acuities 20/20 OD & OS
Normal carotid duplex 3 yrs prior
Case report: Hollenhorst Plaque

• Carotid duplex ordered:
  • Bilateral calcified and noncalcified atherosclerotic plaques of the ICA with bilateral stenosis of more than 70%.
• Referred to vascular surgeon; reports 2 episodes of blurred vision OS in past month
  • CEA vs stent
  • Continue asa & statin

Has since had bilateral CEA
Case report: Hollenhorst Plaque

6 month follow-up
Case report

- 61 yom c floaters
- BMI 30
- Chol 228
- Trig 183
- A1c 6.0%
- HTN 134/78

- Bipolar II

Pt admits h/o IV cocaine & heroin use
Case report: Talc retinopathy

20/20

20/20
Case report: Talc retinopathy
Retinal Vein Occlusions

- 16.4 million people in the world have RVO
  - BROV accounts for 70% of RVOs
- BRVO risk factors
  - HTN
  - DM
  - Dyslipidemia
  - cigarette smoking
  - cardiovascular & renal disease
- Common retinal vascular disorder: prevalence 1/1000 persons
  - Macular edema is mj complication that can lead to blindness
Retinal Vein Occlusions

- Required Testing
  - BP
  - FBS/A1c
  - CBC
  - Lipid profile
  - Carotid duplex
- Additional Testing
  - Cardiac eval
  - Labs: ANA, RF, FTA/ABS, ESR
Central Retinal Vein Occlusions

Most common etiologies vary with age at presentation

- Under age 50
  - hyperlipidemia
  - head trauma
  - oral estrogen (BCP)

- Over age 50
  - HTN
  - DM
  - Chronic lung disease
Case Report

OD 20/30

OS 20/50

75 you, DM, HTN, hypercholesterolemia
Case Report: HRVO

OS 20/60

BMI 38

Allergies: COMPAZINE, SIMVASTATIN, NIACIN, PRAVASTATIN, LOVASTATIN
Case Report: HRVO

Post-Avastin #7, Lucentis #2, & FLT #2
Case Report: HRVO

OS: Post-Avastin #7, Lucentis #2, & FLT #2

Follow-Up #3 - 2/5/2013

IR 30° [HS]

Center: 172 μm
Central Min: 165 μm
Central Max: 326 μm
Circle Diameters: 1, 3, 6 mm ETDRS

OCT 21° (6.0 mm) ART (9) Q: 20 [HS]
Retinal Vein Occlusions

- CRUISE (Central Retinal vein occlusion Study)
  - anti-VEGF therapy proven successful
  - 392 patients, ranibizumab Qmx6, then PRN
  - followed Q3m
- HORIZON-RVO
  - open-label CRUISE, decreased mean tx of 3.5 a-VEGF
  - fewer tx needed but more frequent f/u required
- RETAIN-RVO
  - open-label HORIZON-RVO
  - VA gains sustainable x 2 yrs on PRN dosing
Retinal Vein Occlusions

- **COMRADE-C**
  - directly compared ranibizumab vs dexamethasone implant (Lucentis more effective)
- **CRYSTAL**
  - to assess longer term efficacy & safety of ranibizumab
  - #of injections similar c/s macular ischemia
  - monthly monitoring
- **BRIGHTER**
  - anti-VEGF c/s laser superior to focal laser alone

Timeline to treatment is critical

What about 90-day glaucoma?
Retinal Artery Occlusion

- CRAO/BRAO are the ocular equivalent of a cerebral infarction in the anterior circulation
- Up to 24% of patients with RAO have concomitant cerebral infarctions on MRI of brain
- Management of RAO focused on secondary prevention of vascular events
  - Cerebral ischemia
  - Myocardial infarction
  - Cardiovascular death
CRAO

- Ave. age of patients with CRAO is 58.5 years
  - Typically transient acute embolization
- In younger patients, incidence is 1/50,000, typically inflammatory arterial occlusion (persistent blockage)
  - anticardiolipin antibodies
  - rheumatic heart disease
  - aortic or mitral regurgitation
  - systemic lupus erythematous
  - homocystinuria
Case Report

Sudden vision loss OD x 10 days

83 yof, nursing home resident

CF @ 1ft OD, 20/30 OS +RAPD OD
Case Report: CRAO
Retinal Artery Occlusions

- Required testing
  - BP
  - Labs
    - ESR *stat (r/o GCA, ~2-5%)
    - FBS
    - CBC
    - Lipid profile
    - PT/PTT
    - ANA/RF
  - Carotid duplex
  - Cardiac eval
CRAO

• No current therapeutic intervention to improve visual outcome
• Management of CRAO should be focused on secondary prevention of vascular events:
  • cerebral ischemia
  • myocardial infarction
  • cardiovascular death

What about our patient?
Sickle Cell Disease

- WHO report: 270 million people worldwide (7% of the population) carry genes for abnormal hemoglobins (Hb)
- SCD affects ~100,000 Americans
- SCD occurs among ~1 out of every 365 Black births
- SCD occurs among ~1 out of every 16,300 Hispanic-American births
- ~1 in 13 Black babies is born with sickle cell trait (SCT)
Sickle Cell Disease

• Group of inherited red blood cell disorders
  • HbSS: sickle cell anemia (most severe form)
  • HbSC: usually a milder form of SCD
  • HbS beta thalassemia (types 0 and +)
  • HbAS: Sickle Cell Trait (SCT)
Sickle Cell Disease

- From 1989-1993, an average of 75,000 hospitalizations in the US (costing ~$475 million)
- Painful crises in 42% were the commonest reason for hospitalization
  - Pain is the result of obstruction of the microcirculation caused by sickled red blood cells
- Ophthalmology (76%) & Cardiology (64%) = most common referrals
  - Cardiomegaly, myocardial ischemia, biventricular dysfunction, pulmonary hypertension
Case report: Sickle Cell Retinopathy

25 yom inpatient: c/o new flashing lights x 3 days

HbSC on hydroxyurea with secondary pancytopenia & depression

Vsc 20/20-1 OD
   20/25-2 OS

EOMs full, pain on rt/lt and upgaze
Sickle Cell Retinopathy

Stage 3 sickle cell retinopathy

HRA2 04/30/2008, OS, #66 FA 2:42.40 55°Composite 85°

HRA2 04/30/2008, OS, #67 FA 4:41.73 55°Composite 85°x59°
Sickle Cell Retinopathy

- Sickle cell retinopathy more common in SC and S-β thalassemia
- SCR associated with vision loss in ≥ 10% of affected patients
  - Vitreous heme / RD
- Strong VEGF presence
# Blood Cell Types

<table>
<thead>
<tr>
<th>Red Blood Cells</th>
<th>White Blood Cells</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>anemia</em></td>
<td><em>leukopenia</em></td>
<td><em>thrombocytopenia</em></td>
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Pancytopenia = aplastic anemia
*decrease in all 3 blood cell types*
Leukemia

- Many types of leukemia exist
  - Acute lymphoblastic leukemia
  - Acute myeloid leukemia
  - Chronic lymphocytic leukemia (most common)
  - Chronic myeloid leukemia
  - More…
- Usually involves the white blood cells & bone marrow
  - WBC are potent infection fighters
- Treatment: some combination of chemo, radiation, targeted therapy, bone marrow transplant
Leukemia

- Symptoms
  - Easy bruising, pale skin, fever, enlarged spleen or liver
  - Frequent infections (sore throat, diarrhea)
  - Can be nonspecific
- Diagnosis based upon repeated CBC and bone marrow examination
- American Cancer Society estimates that 1/5 of patients with leukemia are not yet diagnosed
Case report
Leukemic retinopathy

- 74 yom, transferring care for DM
- No h/o retinopathy
- DM x 15 years, A1c ‘very low’, FBS ‘107/108’
- HTN
- A-fib
- CA: leukemia x 4 years, recently d/c Imbruvica
Leukemic retinopathy

- LR already present in ~50% of patients diagnosed with leukemia
- Retinopathy typically occurs in acute disease
  - Intraretinal hemorrhages: flame-shaped, Roth spots
  - Dilated & tortuous retinal vessels, with beading
  - Vascular sheathing
  - Sub-hyaloid & sub-ILM hemorrhages
- Labs: CBC, ESR, CRP, ANA
Leukemic retinopathy: 6m follow-up

20/20

20/20
Metastatic Disease

- Full medical history & physical exam
- CBC
- Liver/renal/thyroid function tests
- Chest CT
- Abdominal and pelvic ultrasound
- Mammogram

- Whole body CT scan & bone scan if above tests normal

- In lung CA, CA is diagnosed after dx of intraocular metastasis in 56% of cases
Case report: Metastatic disease
Metastatic retinopathy
Diabetes

• Incidence: 29.1 million people in US have diabetes (9.3% of the population)
  • 21.0 million are diagnosed
  • 8.1 million are undiagnosed
• Diabetic retinopathy is the most common retinal vasculopathy
• Risk for blindness, kidney failure, heart disease, stroke, amputation
DME

- **ETDRS (1990’s)**
  - Focal laser (FML) treatment for CSME
  - Reduced risk of moderate vision loss by 50%
  - Diffuse/chronic exudates respond poorly
- **Steroids (early 2000’s)**
  - Decreases permeability
  - At 2 yrs, laser more effective with fewer side effects than IV-triamcinolone
- antiVEGF
Case report

A1c 13.8%, oral medication
THANK YOU!