Hypertension: Routine Screening Detects Rare Causes

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Major Point of Discussion
A routine evaluation for hypertension, when combined with a careful history and physical examination, will lead to diagnosis of even rare forms of hypertension

Outline for Discussion
- Diagnosis of hypertension
- Important history & physical findings
- Workup
- 3 Routine cases
- 4 Interesting / instructive cases

Is the patient hypertensive?
- Definition of hypertension in children:
  - Now based on age and height percentiles (NHBPEP 2004)
  - average BP measured at rest on 3 or more separate occasions

Is the patient hypertensive?
- Normal BP
  - SBP and DBP <90%ile for age, sex, height
- Prehypertensive
  - SBP and DBP 90-95%ile
- Hypertension
  - >95%ile
  - Stage 1 hypertension: 95 to 99%ile + 5 mm Hg
  - Stage 2 hypertension: >99%ile + 5 mm Hg

There's an app for that...
BP measurement in children

- Annually after age 3
- Oscillometric measure >90% ile should be repeated by auscultation
- Seated, feet on floor, arm supported, cubital fossa at heart level, right arm preferred

BP measurement in children <3 years old

- Prematurity, VLBW, NICU admission
- Congenital heart disease
- Recurrent UTI, hematuria, proteinuria
- Family Hx congenital renal disease

BP measurement in children <3 years old

- Solid organ transplant
- Malignancy or BMT
- Rx with medications known to increase BP
- Systemic illnesses associated with HTN
- Increased intracranial pressure

What evaluation will be helpful?

- History and physical exam remain the most reliable diagnostic tools
- Everything else is to confirm your suspicions!

Patient history

- Symptoms of hypertension
- Symptoms of renal diseases
- Sleep history (sleep apnea)
- Obesity
Patient history (cont’d)
- Symptoms of other diseases: poor weight gain, flushing, tachycardia, palpitations, excessive sweating, muscle cramps, weakness, constipation, arthritis, arthralgias, rash, edema, abdominal pain

Patient history (cont’d)
- History of medications, OTC drugs, illegal/recreational drugs, oral contraceptives

Family history
- Hypertension, cardiovascular /atherosclerotic disease, particularly in younger people
- Obesity, diabetes mellitus, renal disease, malignancies, siblings, cousins with similar problems

Physical exam
- Measure BP in all 4 extremities and assess peripheral pulses
- Vital signs: tachycardia, postural hypotension

Physical exam (cont’d)
- Abdomen: palpable mass, epigastric or flank bruit
- Genitalia: virilization, ambiguous genitalia
- Extremities: joint swelling or inflammation, muscle weakness, edema, tetany

Physical exam (cont’d)
- Growth data/general appearance: growth retardation, truncal obesity, evidence of syndromes
- Skin: pallor, flushing, acne, hirsutism, striae, cafe-au-lait spots, neurofibromas, adenoma sebaceum, butterfly rash
- Chest: heart murmur, irregular heart sounds
Physical exam (cont’d)
- Look for evidence of chronic (as opposed to new onset) hypertension:
  - Optic fundus
  - Cardiac (LVH)
  - Renal (hematuria, proteinuria, edema)
  - CNS (evidence of previous strokes)

Baseline evaluation: identifiable causes and comorbidities
- Urinalysis
- Plasma electrolytes, BUN, creatinine, renin, fasting lipid profile
- CBC
- EKG / echocardiogram
- Renal ultrasound with Doppler
- Retinal exam

Indications for Treatment
- Symptomatic HTN
- Secondary HTN
- Target-organ damage
- Diabetes (Type 1 or 2)
- Persistent HTN despite non-pharmacologic measures

Baseline evaluation (cont’d)
- Further evaluation depends on results of history, physical, baseline tests

Case 1
- A 14 year old boy was participating in screening exam for his high school football team and noted to have a blood pressure of 138/89. The school will not allow him to participate until his blood pressure is evaluated by his primary care provider. He is in good general health and has no relevant past medical history. His father is 40 years old and being treated with enalapril for hypertension. On exam, both height and weight are >95%ile. With the exception of mild obesity, his physical exam is unremarkable.

Case 1
- Is the patient hypertensive?
- What are possible causes?
- What evaluation will be helpful?
- Is treatment needed?
- In particular, what do you need to do prior to participation in sports?
- What is the best form of treatment for this patient?
Classification of sports according to cardiovascular demands (based on combined static and dynamic components).

Sports participation
- Stage 1 hypertension in the absence of end organ damage, including LVH or concomitant heart disease, should not limit a person's eligibility for competitive athletics.

Case 2
- A 12-year-old girl is in the clinic for a routine visit. Her blood pressure is 124/82 on initial measurement, and 2 subsequent measurements show similar values. She states she is somewhat tired, and has been for several months. She occasionally complains of leg cramps after exercising. Her past history is significant for 5 urinary tract infections (2 suggestive of pyelonephritis) between the ages of 4-9, but she has had no infections for 3 years. Family history is unremarkable. On exam, height and weight are both 5-10%ile for age. Skin and mucous membranes are slightly pale. Lungs are clear, but the precordium is hyperdynamic, with a questionable S3 gallop. Abdomen is soft and nontender. She has Tanner 1 sexual development. Extremities are normal.

Case 3
- A six-year-old boy is noted to have a blood pressure of 140/90 during a routine exam. He complains of headaches at school, and occasional blurred vision when playing with friends. Past history and family history are unremarkable. On exam, his lower extremity blood pressures are 100/60 in both legs. His femoral pulses are present but difficult to detect. The remainder of his exam is unremarkable.

Case 2
- Is the patient hypertensive?
- What are possible causes?
- What is significant about the past history?
- Does her presentation suggest a cause for her hypertension?
- What evaluation will be helpful?
- Do you think that the lab evaluation will be abnormal?
- Is treatment needed?
- What is the best form of treatment for this patient?
Case 3
- Is the patient hypertensive?
- What are possible causes?
- What evaluation will be helpful?
- Is treatment needed?
- Is this a hypertensive emergency?
- What is the best form of treatment for this patient?

Things you’ll only see once (But don’t want to miss)
- Liddle’s Syndrome
- Glucocorticoid-remediable hyperaldosteronism
- Interrupted aortic arch
- Pheochromocytoma

A Liddle Bit of Renin
- 6 year old boy: BP’s 143-161/71-81 on several occasions over 2 months
- Family history: paternal grandfather hypertensive, father hypertensive (since age 11)
- Patient history: unremarkable

A Liddle Bit of Renin (cont’d)
- Height and weight 50%ile
- BP
  - RA 139/80
  - LA 139/79
  - RL 161/71
  - LL 143/81
- Unremarkable physical exam

A Liddle Bit of Renin (cont’d)
- Urinalysis: normal
- Plasma electrolytes: K=3.8
- Plasma renin=0.58 ng/ml/hr
  - (reference range 0.65-3.20)
- Uric acid: 2.5 mg/dl (normal 3.5-8.5)
- Echocardiogram: normal, no LVH

What Makes Renin Low?
- Too much “downstream” hormone
- Mineralocorticoid
- Mineralocorticoid-like substances
- Too much fluid
- Too much salt
Sorting out Low Renin Hypertension

- Family history of hypertension
- Serum K+
- Response to diuretics: spironolactone,amiloride, loops
- Urine steroid profile

Liddle's Syndrome

- Autosomal dominant
- Resistant to spironolactone
- Sensitive to amiloride
- Genetically transmitted defect in amiloride-sensitive sodium channel in collecting duct (basically, channel is “too open”)

All in the Family

- 2.5 yo boy with BP’s 134-148/90-94
- Asymptomatic
- Family history: significant
- Height and weight 50% ile
- Unremarkable physical exam

Urinalysis: normal
- Plasma electrolytes: K=3.2
- Plasma renin=0.2 ng/ml/hr
  - (reference range 0.65-3.20)
- Echocardiogram: normal, no LVH
Family Hx Significant for HTN

Glucorticoid Remediable Aldosteronism
- Autosomal dominant
- "Too much" mineralocorticoid
- A very interesting mutation

Glucorticoid Remediable Aldosteronism
- Angiotensin II → Zona Glomerulosa
- ACTH → Zona Fasciculata
  - Aldosterone
  - Cortisol

Glucorticoid Remediable Aldosteronism
- Zona Glomerulosa
  - Aldosterone
  - Aldosterone Synthetase
  - 11-beta hydroxylase
- Zona Fasciculata
  - Cortisol

Glucorticoid Remediable Aldosteronism
- Zona Glomerulosa
  - Aldosterone
  - Aldosterone Synthetase
  - 11-beta hydroxylase
  - code
- Zona Fasciculata
  - Cortisol
  - 11-beta hydroxylase
  - regulator
Glucorticoid Remediable Aldosteronism

Zona Glomerulosa  
Aldosterone Synthetase  
Aldosterone  
ACTH controlled Mineralocorticoid

Zona Fasciculata  
11-beta hydroxylase  
regulator

Too Healthy: Version 1.0
- 12 year old boy, increased BP noted in science class: measuring each other's BP's
- Past history: small VSD
- Family History: unremarkable

Too Healthy: Version 1.0
- height >95% ile, weight 75% ile
- BP: RA 154/81, LA 159/75, RL 161/71, LL 150/72
- Tall, thin, healthy
- Bruit on left side of abdomen
- NORMAL FEMORAL PULSES!

Too Healthy: Version 1.0
- Urinalysis: normal
- Plasma electrolytes: normal
- Plasma renin=9.4 ng/ml/hr (reference range 0.65-3.20)
- Echocardiogram: small VSD, no LVH
- Renal US: normal including Doppler

What Makes Renin High?
- Renal parenchymal damage (scars, glomerulonephritis)
- Poor renal perfusion: renal artery stenosis, coarctation of aorta

- Family History
  - Abnormal PE
    - Virilization
    - Hypogonadism
    - Low K+
  - Normal PE
    - 11 Beta Hydroxylase Deficiency
    - 17 Alpha Hydroxylase Deficiency
    - Apparent Mineralocorticoid Excess (AME)
Abnormal Renal Ultrasound
  Abnormal Echocardiogram
    High Renin Hypertension
      Abnormal Kidneys
        Abnormal Vessels
      Indeterminate Vessels
      LVH
      Coarctation, Other structural defect
        Further Imaging
        Angiogram

There Must Be A Reason!
- MR renal angiogram: normal renal arteries and kidneys
- MR of chest: narrowing of aorta in area of ligament arteriosus, enlarged internal mammary arteries

Too Healthy: Version 2.0
- 17 year old boy with BP's as high as 200/130 over the past year
- No performance enhancing drugs
- Has “hard time” gaining weight

Too Healthy: Version 2.0
- Complains of headaches during strenuous activity, improves with rest
- Occasional palpitations and flushing during sports, none at rest
- Family history: PGGF on dialysis

Too Healthy: Version 2.0
- height 25% ile, weight 10% ile
- BP: RA 181/92, LA 164/108, RL 175/94, LL 189/97
- Thin, very athletic, healthy
Too Healthy: Version 2.0

- Urinalysis: normal
- Plasma electrolytes: normal
- Plasma renin: normal
- Echocardiogram: normal, no LVH
- Renal US: reported as normal by outside hospital

Too Healthy: Version 2.0

- Repeat ultrasound (in order to check Doppler): 3 x 4 cm mass adjacent to upper pole of left kidney
- 24 hour urine: elevated epinephrine, norepinephrine, dopamine, combined metanephrines, VMA

Major Points

- Patient history, family history, physical exam, and baseline evaluation will determine need for further evaluation and/or referral
- More likely to be a secondary cause in younger, thinner, healthier children