Renovascular Hypertension & Secondary Causes of Hypertension

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Our patient, Ms. X

• 34 year old female in usual state of good health until two years ago, suddenly developed onset of hypertension with blood pressures of 150/100

• PMH: rosacea, mild Raynaud’s disease, genetic hearing loss

• PSH: Umbilical repair, tonsilectomy, wisdom teeth extraction

• Placed on Norvasc, 10mg po qd and Toprol XL 50mg po qd with moderate control

• Meds: Norvasc, Toprol XL, Folic acid, ASA

• SH: single, physical therapist, non-smoker, drinks 2-3 times/week

• PE: P72, BP 142/100, R12, no cervical bruits, no flank/abdominal bruits, palpable femoral, popliteal, and pedal pulses bilaterally
Disorders associated with secondary hypertension

1. **Primary renal disease** — both acute and chronic renal disease, particularly with parenchymal disorders, tumorectomy, nephrectomy, or vascular disorders, angioplasty

2. **Oral contraceptives** — often raise the BP within the normal range but can induce overt hypertension, stop medication

3. **Pheochromocytoma** — About ½ of patients have paroxysmal HTN, most of the remaining have what appears to be essential HTN, medications, surgery

4. **Primary hyperaldosteronism** — surgery

5. **Cushing’s syndrome** — medications, surgery

6. **Other endocrine disorders** — both hypothyroidism & hyperthyroidism, hyperparathyroidism — medications, surgery

7. **Sleep apnea syndrome** — surgery

8. **Coarctation of the aorta** — surgery
Clinical clues for causes of secondary HTN

- elevated plasma Cr and/or an abnormal urinalysis → primary renal disease
- paroxysmal elevations in BP, especially if associated with headache, palpitations, and sweating → pheochromocytoma
- low-renin forms of HTN, especially with unexplained hypokalemia and metabolic alkalosis → primary hyperaldosteronism
- cushingoid facies, central obesity, ecchymoses, and muscle weakness → Cushing’s syndrome
- obese individuals who snore, awake with headache, daytime somnolence → sleep apnea syndrome
- decreased or lagging peripheral pulses and a vascular bruit over the back → coarctation of the aorta
- an elevated plasma TSH level or suggestive symptoms → hypothyroidism
- unexplained hypercalcemia → primary hyperparathyroidism
Radiographic findings in several causes of secondary HTN

Arteriogram showing bilateral renal artery stenosis in 19yo female who has Takayasu’s arteritis

Abdominal CT scan shows large and invasive left aldosterone-secreting adrenocortical carcinoma

MRI demonstrates severe aortic coarctation
Our patient, Ms. X

- Initial workup of HTN included:
  - electrolytes were all normal, creatinine of 0.7
  - renal vein renin was 2.2 (within normal limits)
  - aldosterone level was 15 (upper limit of normal)
  - normetanephrine and metanephrine were normal
  - renal ultrasound was unremarkable

- Switched PCP → got an MRA which showed a high grade stenosis in the middle portion of her right renal artery, aortic and iliac arteries appeared completely normal.

- Lesion initially thought to be not amenable to angioplasty and recommended to undergo aorto-renal bypass with saphenous vein. Now here for second opinion.
• Excluding obesity and alcohol abuse, renovascular hypertension is the most common correctable cause of secondary HTN

• Incidence varies with the clinical setting
  - <1% of patients with mild HTN
  - 10 – 45% of white patients with severe or malignant HTN
  - generally less common in black patients

• Radiographic testing for renovascular disease is indicated only in patients in whom the history is suggestive AND in whom a corrective procedure will be performed if significant renal artery stenosis is detected.
When renovascular HTN should be suspected

- severe or refractory HTN, including retinal hemorrhages or papilledema; bilateral renovascular disease may be present in those patients who also have a plasma creatinine (Cr) >1.5 mg/dL.

- acute rise in blood pressure over a previously stable baseline — this includes renovascular disease superimposed upon underlying and often well-controlled essential HTN.

- proven age of onset <20 (especially if before puberty) or >50.

- acute elevation in the plasma Cr that is either unexplained or occurs after the institution of therapy with an ACE inhibitor (in the absence of an excessive reduction in blood pressure).
When renovascular HTN should be suspected, cont.

- moderate to severe HTN in a patient with diffuse atherosclerosis or an incidentally discovered asymmetry in renal disease.

- systolic-diastolic abdominal bruit that lateralizes to one side (Se = 40%, Sp = 99%).

- negative family history for HTN.

- moderate to severe HTN in patients with recurrent episodes of acute (flash) pulmonary edema or otherwise unexplained congestive heart failure.
Ms. X’s renal arteriogram

- Patent Left renal artery with normal branching pattern
- Single Right renal artery which has a high grade stenosis immediately proximal to the branching into the anterior and posterior divisions.
- Prominent filling of the superior polar artery which is supplying the adrenal trunk.
Differential Diagnosis

Unilateral renal lesion that may cause hypertension

A. Lesion of Renal Artery or Its Branches
   1. Aneurysm
   2. Arteriolar nephrosclerosis
   3. Arteritis (i.e., syphilis, polyarteritis nodosa, Takayasu's arteritis, thromboangiitis obliterans, rubella, idiopathic)
   4. Atherosclerosis
   5. AV malformation
   6. Congenital narrowing
   7. Dissection
   8. Fibromuscular hyperplasia
   9. Neurofibromatosis
   10. Perivascular fibrosis
   11. Thrombosis or embolism
   12. Trauma
Differential Diagnosis

Unilateral renal lesion that may cause hypertension

B. Renal Parenchymal Disease

1. Neoplasm (i.e., carcinoma, sarcoma, Wilms' tumor, metastasis)
2. Obstructive uropathy
3. Ptosis of kidney
4. Pyelonephritis

C. Renal Vein Thromboembolism

D. Renal Compression (Page Kidney)

1. Extrarenal mass (i.e., aortic aneurysm, retroperitoneal hematoma or neoplasm, peripelvic cyst)
2. Subcapsular hemorrhage
Imaging Modalities to evaluate secondary HTN

- Excretory Urography
- Ultrasonography
- Computed Tomography
- Magnetic Resonance Imaging
- Renal Arteriography
- Nuclear Medicine Scanning
- Venous Sampling
Excretory Urography

• **Advantages**
  - can identify large renal masses
  - can detect abnormal renal anatomy (contour, collecting system, or function)

• **Disadvantages**
  - does not assess abdominal and renal vasculature
  - does not optimally assess adrenal glands
  - can miss small renal masses
  - requires use of iodinated contrast material and ionizing radiation

Silverman, et.al.
Excretory Urography
(companion patient #1)

Typical findings:
• affected kidney decreased in size with a smooth contour.
• collecting system shows delayed opacification with, paradoxically, an increased density and delayed emptying of the contrast material

From UpToDate

Delayed calyceal appearance of the contrast media in the right kidney
Ultrasonography

• Advantages

- inexpensive

- no need for radiographic contrast material

- no ionizing radiation

- can be performed to determine size of kidneys and presence of collecting system dilatation

- identifies many renal and some adrenal masses

- easily visualizes perinephric fluid collections

- color-flow Doppler ultrasound has shown promise in identifying patients with RAS

Silverman, et.al.
• **Disadvantages**

  - limited evaluation of adrenal glands in some patients. can miss small adrenal masses
  - can miss small isoechoic renal masses
  - use of Doppler U/S for detection of RAS remains investigational
Ultrasonography
(companion patient #2)

Restrictive Index = \( \frac{(Systolic P - Diastolic P)}{Systolic P} \)

(Normal ~ 0.7)

Markedly elevated restrictive index

Dx: Renal artery stenosis
Computed Tomography

- Advantages
  - very sensitive in detecting renal or adrenal masses
  - adrenal CT does not require IV contrast material administration. CT can also identify extra-adrenal pheochromocytomas
  - often able to distinguish between benign and malignant adrenal masses
  - can identify renal subcapsular fluid collections or masses
  - can evaluate abdominal vasculature (i.e. RAS) with helical CT

Silverman, et.al.
Computed Tomography

- Disadvantages
  - cannot distinguish among most types of solid renal masses
  - some benign adrenal masses cannot be differentiated from malignant adrenal masses (both soft tissue attenuation)
  - aldosteronomas can be so small (<5mm) that they can be missed
  - cannot evaluate arteries unless helical vascular protocol used. Stenosis may be misevaluated due to limitations of the reconstruction algorithms. Stenosis in branch vessels may be missed
  - use of IV contrast is needed for assessment of renal parenchyma or vessels

Silverman, et.al.
Middle-aged male with a history of abdominal pain

Contrast-enhanced abdominal CT taken at the mid-renal level

4.5-cm mass located in the right renal hilum

An aneurysm was suspected so a renal angiogram was ordered.
Renal Angiogram of patient #3

Dx: Right renal artery aneurysm.

contrast filling a large renal artery aneurysm which arises at the bifurcation of the renal artery.

right renal arteriogram
CT Angiogram, 3D reconstruction
(companion patient #4)

19 year old female with Takayasu's arteritis

Bilateral renal artery stenosis

Discontinuity is observed in association with the R RAS as the attenuation of the stenotic segment falls below the threshold range

From Rubin, et.al.
Magnetic Resonance Imaging

• Advantages
  - permits good visualization of adrenal glands, kidneys, and retroperitoneum
  - can distinguish b/t many benign and malignant adrenal masses
  - can evaluate the abdominal vasculature
  - does not require use of ionizing radiation or iodinated contrast material

• Disadvantages
  - expensive
  - offers little imaging advantages over CT (other than the lack of need for contrast)
  - as with CT, RAS can be overestimated, underestimated, or missed

Silverman, et. al.
19 year old female with Takayasu’s arteritis with bilateral RAS

70 year old woman with atherosclerosis
Both renal arteries show significant stenoses just beyond the ostium
Renal Arteriography

- **Advantages**
  - still accepted as gold standard for evaluation of renal arteries and their branches
  - PCTA can be performed to treat a RAS immediately after diagnostic arteriogram

- **Disadvantages**
  - invasive procedure with small, but definite morbidity
  - required use of iodinated contrast and ionizing radiation
  - plays little or no role in evaluation of the adrenal glands or renal parenchyma

Silverman, et.al.
Young woman with R renal artery stenosis caused by fibromuscular disease
Nuclear Medicine Scanning

• Advantages
  - radionuclide renography with captopril can detect RAS in many patients
  - radioactive iodine-labeled metaiodobenzylguanidine (MIBG) is effective in detecting pheochromocytomas
  - does not require injection of iodinated contrast

• Disadvantages
  - radionuclide renography does not provide an anatomic picture of the renal vasculature
  - MIBG is not widely available

Silverman, et.al.
Nuclear scan
(companion patient #6)

BASELINE I-131 HIPPURAN RENOGRAM

normal and nearly symmetric uptake and clearance of radiotracer

visual findings are confirmed by the time-activity curves

From ACR Learning File
Nuclear scan
(companion patient #6)

I-131 HIPPURAN RENOGRAM FOLLOWING ORAL ADMINISTRATION OF 25 mg CAPTOPRIL

striking left renal tracer retention, with normal uptake and excretion on the right

asymmetrical findings are confirmed by the time-activity curves

Hemodynamically significant left renal artery stenosis

From ACR Learning
Venous Sampling

• Advantages

- adrenal vein (for aldosterone) permits distinctive identification of the hypersecreting adrenal gland in patients in whom cross-sectional imaging does not identity an adrenal aldosteronoma

- renal vein renin levels can be obtained from both kidneys in order to determine whether a visualized RAS is responsible for hypertension

• Disadvantages

- sampling of the R adrenal vein is extremely difficult (originates directly from the IVC and is difficult to cannulate)

- renal vein renin levels do not necessarily correlate with the likelihood of a successful angioplasty

Silverman, et.al.
Imaging Modalities to evaluate secondary HTN

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Back to our Patient:
Ms. X’s renal arteriogram

single Right renal artery which has a high grade stenosis immediately proximal to the branching into the anterior and posterior divisions.

Courtesy of Elvira Lang, MD
Diagnosis of Ms. X

• FIBROMUSCULAR DISEASE
  - more common in young women
  - subtypes based on the layer of the arterial wall involved:
    - medial fibroplasia
    - intimal fibroplasia
  - percutaneous angioplasty is the treatment of choice with low restenosis rate
  - surgical correction is preferred in those patients who fail or refuse angioplasty, since lifelong medical therapy is less desirable in the typically young patients with this disorder
Fibromuscular dysplasia: Medial Fibroplasia
(companion patient #7)

- most common subtype
- usually involves the distal two-thirds of the artery
- sometimes extends into branch vessels
- presents with alternating stenoses and small aneurysms of the renal artery.

From ACR Learning File

typical "string of beads appearance"
Fibromuscular dysplasia: Intimal Fibroplasia

(companion patient #8)

- most common cause of renal vascular hypertension in childhood
- presents as a symmetric band of narrowing with a poststenotic fusiform dilatation
Treatment of Ms. X

- kissing balloon/kissing guidewire assembly; balloon inflated twice to maximum of 6 atm and left inflated 20 min each
- good anatomic result without any impingement onto segmental branched artery
- successfully dilated to 5mm without residual pressure gradient

Courtesy of Elvira Lang, MD
Although most hypertensive patients have essential HTN, there are many causes of secondary hypertension, renovascular disease being an important common one that is correctable.

Suspect secondary HTN in patients based on clinical clues and order appropriate tests.

There are many imaging modalities to evaluate secondary hypertension.

For renovascular HTN, IVP is not recommended for screening. Renal arteries should be visualized directly by arteriography, MRA, CTA, or vascular US.

If a renal artery stenosis or occlusion is found → selective venous sampling may be performed to confirm the diagnosis (1.5x higher than IVC); patients with essential HTN may coincidentally have RAS.

Patients with true renovascular HTN generally benefit from either balloon angioplasty or surgical repair with renal artery bypass graft.
References

- American College of Radiology, Learning File.
- UpToDate Online.
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