Approach to the Young Patient with New-Onset Hypertension

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Introduction

A 22-year-old white woman with no prior history of hypertension had elevated BP during a routine office visit in 2006. One week later, BP remained elevated. She was asymptomatic and did not have chest pain, dyspnea, headaches, palpitations, sweating, leg swelling, or leg cramps. She did not take any over-the-counter medications. She smoked heavily and drank alcohol (approximately 5–10 drinks weekly). She did not use illicit drugs. Family history was significant for hypertension in her father diagnosed in his mid-50s. Hypertension in a young patient is uncommon, but it is a growing clinical concern. Essential hypertension is also possible, because she is overweight and drinks alcohol in excess, but secondary causes should first be excluded in a young patient with recent-onset hypertension.

Initial Workup for Secondary Hypertension

Plasma metanephrines, plasma renin activity, serum aldosterone, thyroid stimulating hormone, and cortisol were normal. Kidney duplex ultrasound did not show any evidence of renal artery stenosis. Because of high clinical suspicion, computed tomography angiogram (CTA) was performed, and it showed duplicate renal arteries in each kidney with a 70% stenosis of the proximal left superior renal artery with a beaded appearance consistent with FMD. Remaining renal arteries were free of discernible disease.

What Is FMD?

FMD is an idiopathic, segmental, nonatherosclerotic, noninflammatory disease of the musculature of arterial walls that leads to stenosis of small- and medium-sized arteries (1). Diagnosis requires exclusion of renal artery spasm, arterial diseases of monogenic origin, and inflammatory arterial diseases. Prevalence of symptomatic renal FMD is approximately 0.4% in the general population. Symptomatic involvement of the cervicocranial vessels is less common (2). FMD has been shown to affect mainly women between 30 and 50 years of age (3). Lesions commonly involve the middle or distal thirds of the main renal artery, and there is often extension into the proximal portion of the first-level branches. Lesions are bilateral in 60% of patients. The pathogenesis of FMD is unknown; however, a positive family history is present in 7% of first or second degree relatives (3). A recent genetic association study identified a common variant rs9349379 located on chromosome 6 (PHACTR1) that increases the risk of FMD by approximately 40% (4).

The three main histologic types of renal FMD include intimal FMD (5%), medial FMD (>85%), and perimedial
FMD (10%) (1). There can be involvement of more than one layer in the same diseased artery. Similar lesions are seen with cervical or intracranial FMD, and lesions can be seen in the aorta (midaortic syndrome), mesenteric arteries, and iliac arteries. Three patterns of renal artery FMD include multifocal (“string of beads” appearance), unifocal (solitary stenosis < 1 cm in length), and tubular (stenosis ≥ 1 cm in length) (1). The two last categories differ only by the length of the diseased segment, and they may be grouped under the general term unifocal (3). The “string of beads” aspect accounts for >80% of patients, and its histologic substrate is medial FMD. Because FMD-related renal artery stenosis is now usually treated by percutaneous transluminal angioplasty (PTA) rather than surgery, the angiographic classification has replaced the histologic classification. Atherosclerotic renal artery stenosis usually occurs in the ostium or proximal part of the renal artery, and patients are more likely to be men, be older, be smokers, have diabetes, and have CKD.

**Screening for FMD**

Screening is recommended in patients who are hypertensive <30 years of age, especially women; patient who have severe hypertension (≥180/110 mm Hg), accelerated malignant hypertension, or resistant hypertension; patients with a small kidney without history of uropathy; patients with abdominal bruit without apparent atherosclerosis; patients with FMD in at least another vascular territory; and patients with hypertension who have a family history of FMD (1).

**Imaging to Detect FMD**

Renal Doppler is an inexpensive first-line test, but this is operator dependent, and negative results do not definitively exclude the diagnosis. Results should be confirmed by another imaging technique if positive. It is reasonable to order CTA or magnetic resonance angiography (MRA) first if results of duplex ultrasound are expected to be suboptimal (obese patients or poor local expertise) or when the degree of suspicion of FMD is high. CTA is our preferred imaging modality. FMD lesions are usually distal in the renal artery and often involve branch arteries, and they are better visualized on CTA. The gold standard is renal arteriography, and if the clinician has a high index of suspicion, a renal arteriogram should be performed to definitively exclude FMD (5).

**Subsequent Management**

A renal arteriogram was performed that showed an 85% stenosis of the left superior renal artery with an increased gradient. A PTA was performed, and subsequent gradient was diminished (Figure 1A). She remained off antihypertensive medications after the procedure.

**Management of FMD**

Smoking cessation should be strongly encouraged in patients with FMD, because smokers may have a more aggressive course (6). Renal FMD is now treated by PTA rather than surgery, and stenting is usually not recommended.
unless required for procedural dissection or in arteries that, despite initial success of angioplasty, immediately collapse back to their original size. Surgery should only be contemplated when stenosis is associated with a complex aneurysm and rarely where complex lesions of arterial bifurcations or branches occur (1). Revascularization is recommended in patients who are hypertensive to normalize BP, patients with drug-resistant hypertension or medication intolerances, and patients with kidney insufficiency or deterioration of kidney function that occurs after use of renin-angiotensin-aldosterone system blockade and with reduced kidney size downstream of the stenosis (1). The procedure should be performed by a multidisciplinary team with extensive experience. If revascularization is not performed, close clinical observation is required. BP and kidney function should be checked post-PTA at 1 month, and renal imaging should take place at 6 months or earlier if BP or serum creatinine is increasing.

Subsequent Clinical Course
She presented 5 years later with hypertensive emergency. CTA showed a recurrent stenosis of the superior left renal artery consistent with FMD. Renal arteriogram (2012) showed a 98% stenosis in the midpoint of the superior left renal artery with a beaded appearance consistent with FMD. PTA of left superior renal artery was performed with no significant stenosis after angioplasty. Right renal arteries and the inferior left renal artery were patent. BP improved, and she remained on amlodipine 5 mg daily for the next 2 years. She quit smoking and decreased her alcohol intake. Home BP readings started to increase, and medications were intensified. Examination was unremarkable aside from elevated BP of 166/106 mm Hg. Kidney function remained normal. Echocardiogram showed severe concentric left ventricular hypertrophy with an ejection fraction of 65% and moderate diastolic dysfunction. A third renal arteriogram showed no significant stenosis of the right main renal artery; however, there was a minimal beaded appearance consistent with FMD. Left main renal arteriography showed moderate stenosis proximally with web formation. A 12-mm Hg pressure gradient was present across the right main renal artery. After angioplasty, the arteriogram showed no residual stenosis (Figure 1B). BP medications were stopped, and normal BP was maintained for the next 2 years.

Natural History of FMD
The natural history of untreated FMD is unknown, because there is often a delay in diagnosis for years (3). Of 19 kidney donors with FMD at evaluation who nonetheless donated, 26% were observed over 7 years to have developed new-onset hypertension compared with 6% of 49 age- and sex-matched non-FMD donors (7). Another series of 42 patients with FMD and hypertension who were reimaged over 11 years showed that all of these patients had angiographic progression (8). An update from the US FMD Registry observed a high prevalence of aneurysm and dissection in patients with FMD and recommended a one-time cross-sectional imaging from head to pelvis with CTA or MRA (9).

Follow-Up 1 Year Later
BP normalized after three left renal angioplasty procedures, but in 2015, BP started to increase on three antihypertensive agents at maximal dosing. Repeat renal arteriography showed beading consistent with FMD in the right main renal artery and approximately 60% midrenal artery stenosis. A 9-mm Hg systolic pressure gradient was present across the right main renal artery. After angioplasty, the arteriogram showed no residual stenosis (Figure 1C). Left main renal arteriography showed a beaded appearance to the artery in keeping with FMD without a significant pressure gradient (1 mm Hg) across the mild area of stenosis present. Two weeks later, BP was 122/82 mm Hg on amlodipine 5 mg daily.

Does Restenosis Occur in FMD?
Restenosis after PTA is rare; however, if this occurs, the benefit of treatment is diminished. A systematic review of 47 angioplasty studies (in patients with FMD and hypertension who underwent PTA or surgical reconstruction) (10) showed that combined rates of hypertension cure were 46% and 58%, respectively, and that the probability of cure was negatively associated with age. Cure rates were only 36% and 54% after angioplasty and surgery, respectively. Combined risks of periprocedural complications were 12% and 17% after angioplasty and surgery, respectively, with less major complications after angioplasty than surgery (6% versus 15%, respectively).

Cervicocephalic FMD
BP was reasonable, but she had intermittent, mild vertigo for 4 months. CTA of the head and neck showed chronic dissection in the left vertebral artery with pseudoaneurysm formation at the transverse foramen of C1 and mild irregularity of the cervical carotid arteries consistent with FMD (Figure 1D). Screening is recommended for asymptomatic cervicocephalic lesions in renal artery FMD only if identification of lesions will alter future management. Patients with hypertension and cervicocephalic FMD should be screened for renal FMD (1). MRA or CTA is recommended to establish the diagnosis of FMD of the cervicocephalic arteries and detect intracranial aneurysms. Revascularization is only recommended for symptomatic carotid FMD lesions.

Disclosures
None.

References


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