38-Year-Old Woman With Hypertension, Headaches, and Abdominal Bruit

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A 38-year-old woman presented to her local clinic for recurrent episodes of headache of several weeks’ duration. Evaluation revealed a blood pressure of 202/136 mm Hg. The patient was prescribed 37.5 mg of triamterene with 25 mg of hydrochlorothiazide (1 tablet) twice daily and 50 mg of atenolol once daily.

Her blood pressure remained elevated, and her headaches persisted. She was referred to the hypertension clinic for further management.

The patient’s medical history was remarkable for preeclampsia during her second pregnancy 9 years previously. She smoked half a pack of cigarettes per day for 15 years. Her alcohol use was limited to social gatherings and consisted of 1 to 2 drinks monthly. She exercised regularly and had a balanced low-salt diet. Essential hypertension was common on her maternal side.

On physical examination, the patient’s blood pressure was 172/100 mm Hg (both arms), and her heart rate was 90 beats/min. Findings on funduscopic examination were normal. Cardiac examination revealed a grade 2/6 systolic ejection murmur at the right upper sternal border. Abdominal examination was remarkable for a systolic-diastolic bruit present over the right midabdomen without palpable masses. No evidence of pitting edema was observed, and findings on lung examination were normal.

Initial work-up included the following (reference ranges shown parenthetically): hemoglobin, 14.1 g/dL (12.0-15.5 g/dL); creatinine, 0.8 mg/dL (0.7-1.2 mg/dL); sodium, 139 mEq/L (135-145 mEq/L); potassium, 4.2 mmol/L (3.6-4.8 mmol/L); bicarbonate, 29 mEq/L (22-29 mEq/L), and calcium, 9.5 mg/dL (8.9-10.1 mg/dL). Findings on electrocardiography were normal.

1. On the basis of this patient’s clinical context, which one of the following is the most likely diagnosis?
   a. Anxiety
   b. Essential hypertension
   c. Secondary renovascular hypertension due to atherosclerotic renal artery stenosis
   d. Secondary renovascular hypertension due to fibromuscular dysplasia (FMD)
   e. Hypertension associated with renal insufficiency

Anxiety can be associated with episodes of dramatic but temporary elevations in blood pressure. This patient’s hypertension appears to be persistently elevated, which argues against this diagnosis.

Essential hypertension commonly occurs in middle-aged people who are usually asymptomatic with normal findings on physical examination.1 Secondary hypertension, defined as the presence of a specific condition known to cause hypertension, may affect up to 10% of hypertensive patients. It commonly presents as resistant hypertension, defined as an inability to control blood pressure despite the concurrent use of 3 antihypertensive agents, one of which is a diuretic.2 Our patient’s severe stage 2 hypertension (defined as a systolic blood pressure ≥160 mm Hg and/or a diastolic blood pressure ≥100 mm Hg), young age, and inadequate response to blood pressure therapy argued against essential hypertension and raised suspicion for secondary causes.

Renovascular hypertension results from critical stenosis of the renal arteries. When the stenosis is sufficiently severe (ie, causing ≥75% diameter reduction), renal hypoperfusion ensues, leading to up-regulation of renin in the affected kidney. Consequent stimulation of angiotensin II and aldosterone leads to vasoconstriction and salt retention, respectively, which play a central role in the development of renovascular hypertension. Abdominal bruits, particularly those that have a diastolic component and lateralize to the renal areas, are suggestive of renal artery stenosis. Our patient’s clinical presentation was highly suggestive of renal artery stenosis. Although atherosclerotic renal artery stenosis usually occurs in elderly patients with cardiovascular comorbid conditions such as hyperlipidemia and coexisting atherosclerotic vessel disease, fibromuscular dysplasia commonly affects young women with a history of smoking.3 Considering our patient’s age, sex, and history of smoking, renovascular hypertension due to renal artery stenosis secondary to fibromuscular dysplasia was the most likely diagnosis. Hypertension associated with renal insufficiency was less likely given the negative findings on physical examination, normal kidney function, and absence of significant proteinuria on urinalysis.

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See end of article for correct answers to questions.

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Duplex renal artery sonography revealed single main renal arteries bilaterally with elevated velocity in the midright renal artery consistent with stenosis. The renal parenchyma appeared normal. The right and left kidneys measured 11.2 cm and 12.2 cm in diameter, respectively.

2. Which one of the following would be the most appropriate next step in the investigation and management of this patient’s hypertension?
   a. Magnetic resonance angiography
   b. Computed axial tomography of the abdomen and pelvis
   c. Renal angiography
   d. Captopril renography
   e. Renal vein renin ratio

Magnetic resonance angiography has been used as a noninvasive imaging modality in identifying renal artery stenosis. Limitations include high cost and inadequate views of peripheral renal artery branches, which can be involved in FMD. Magnetic resonance angiography provides a specificity of 88% and a sensitivity of 78% and does not allow for therapeutic intervention.

Computed axial tomography of the abdomen and pelvis is an appropriate diagnostic modality to identify renal carcinoma. It also allows for evaluation of the adrenal glands, which are associated with pheochromocytoma and primary aldosteronism. However, it provides no information about the etiology of the renal artery stenosis in our patient.

Renal angiography is the most effective diagnostic and therapeutic modality currently used for evaluation and management of renal artery stenosis. It allows for direct visualization of the renal arteries and intervention with angioplasty or stent placement. Given our patient’s high pretest probability for renal artery stenosis, renal angiography, rather than any form of noninvasive testing (including duplex sonography), could have been considered as an initial test.

Captopril renography is a noninvasive diagnostic test used to establish the diagnosis of renal artery stenosis. Renal artery stenosis decreases renal blood flow, which triggers renin release and thereby leads to increased angiotensin II levels. These increased levels cause efferent arteriolar vasoconstriction, which helps to maintain the glomerular filtration rate (GFR). The administration of captopril, an angiotensin-converting enzyme inhibitor (ACEI), decreases angiotensin II levels, leading to less efferent arteriolar vasoconstriction and a drop in the filtration rate. Therefore, captopril is able to target the kidney that has the lower GFR as a result of significant stenosis. This test provides no information about the cause of the stenosis. Moreover, when compared with renal angiography, which is considered the gold standard, the sensitivity and specificity of this test are 74% and 59%, respectively.

The calculation of a renal vein renin ratio entails measurement of plasma renin activity (PRA) in both renal veins and in the inferior vena cava. The renal vein renin ratio can be calculated using the following formula: (PRA of Affected Side/PRA of Lateral Side)/(PRA from Inferior Vena Cava). This test presumes that plasma renin activity will be higher in the renal effluent from the affected ischemic kidney than from the nonaffected kidney. A ratio of greater than 1.5 with lateralization to the affected side is considered “abnormal” and is highly predictive of a beneficial blood pressure response to either revascularization or nephrectomy of a small, atrophic kidney. However, two-thirds of patients with renal vein renin ratios of less than 1.5 will also improve with surgery, suggesting that a negative test, in the appropriate clinical setting, should not preclude consideration of nephrectomy. This test was unnecessary in our patient because her hypertension duration of less than 5 years and the etiology of her renal artery stenosis are commonly associated with favorable blood pressure outcomes.

The patient underwent renal angiography, which showed stenosis of the right main renal artery secondary to FMD. Transluminal balloon angioplasty was performed.

3. Which one of the following is the most likely outcome of renal artery angioplasty in this patient?
   a. Cure of hypertension
   b. Improved blood pressure control
   c. Greater number of complications than with vascular surgery
   d. Negligible risk for restenosis
   e. Decreased risk of ACEI-induced acute kidney injury

Intervention with the goal of curing hypertension as an alternative to lifelong medical treatment is a common approach in young patients. However, in the most recent series, the reported cure rates did not exceed 50%. Therefore, improved blood pressure control is the most likely outcome of renal artery angioplasty.

Endovascular procedures are associated with fewer overall periprocedural complications compared with surgical revascularization. In younger patients, bleeding, prolonged wound healing, and infections may complicate the postoperative course and lengthen the time to full recovery, thus favoring endovascular procedures as the first-line revascularization approach.

Risk of restenosis is not negligible: it may occur in up to 25% of treated patients within 6 months of the procedure. In these patients, renal artery imaging is advisable and follow-up angioplasty may be considered.

In patients with bilateral renal artery stenosis, ACEI-induced relaxation of the efferent arteriole affects the entire renal mass, thus leading to reduced glomerular capillary hydrostatic pressure and a decrease in GFR. An increase in...
creatinine level has been reported in one-third of patients in whom revascularization may allow for use of an ACEI. Consequently, ACEI therapy is frequently viewed as a double-edged sword and thus is not considered in these patients who would otherwise benefit from this treatment for either control of hypertension or optimal management of cardiac and/or renal disease. It is frequently ignored that a decrease in GFR is not specific to ACEI. Loss of poststenotic function occurs as a result of the lowering of blood pressure, which is effectively achieved in renovascular hypertension with ACEI therapy. Therefore, monitoring of renal function and kidney size is crucial during long-term hypertension therapy in patients with known renal artery stenosis and coexisting risk factors for ACEI-induced deterioration of renal function, including preexisting renal insufficiency; heart failure; and concurrent use of diuretics, vasodilators, or nonsteroidal anti-inflammatory drugs. Revascularization should be considered if early signs of renal impairment occur (typically, an increase over baseline >30% in creatinine level or a potassium level >5.5 mmol/L). In patients who, as our patient, have unilateral renal artery stenosis, the contralateral, unaffected kidney may compensate for the hemodynamic and blood pressure–lowering effects of ACEI therapy, and detectable changes in GFR are rarely encountered.

Transluminal balloon angioplasty resulted in immediate arterial dissection, which extended to the secondary branches, resulting in ischemia and infarction of the affected renal tissue. Attempts to recanalize the true lumen were unsuccessful. The patient was admitted to the hospital with severe and persistent abdominal pain, which improved with analgesia. Findings on a follow-up electrolyte panel were all normal. The kidney size from pole-to-pole was 11.4 cm on the affected right side and 13.3 cm on the unaffected left side. The dissection could not be visualized with duplex renal artery sonography, and no flow disturbance was noted. The patient's blood pressure remained elevated at 154/86 mm Hg.

4. Which one of the following is the next best step in management of this patient's hypertension?
   a. Addition of an ACEI
   b. Indefinite anticoagulation for renal infarction
   c. Addition of a calcium channel blocker
   d. Observation only
   e. Initiation of statin therapy

The hypertension associated with unilateral renal artery stenosis is primarily driven by increased levels of angiotensin II and so can be effectively controlled with ACEI therapy. Our patient developed renal infarction, in which sudden elevations in blood pressure are likely mediated by renin. Therapy with an ACEI or an angiotensin II receptor blocker should be the initial choice in the absence of contraindications. Indefinite anticoagulation is not indicated for kidney infarction that develops as a consequence of renal artery dissection. Long-acting dihydpyridine calcium channel blockers have been used for management of essential hypertension. Although they may help control this patient's blood pressure, an ACEI or an angiotensin II receptor blocker is preferred because of the presence of 2 high-renin coexisting comorbid conditions: renal artery stenosis and renal infarction. Observation only is not an option for this patient in whom control of hypertension was inadequate before the procedure and could have worsened as a consequence of renal infarction.

Statin use has been shown to be effective in patients with atherosclerotic renal artery stenosis because it reduces the atherosclerotic burden. Because FMD-associated renal artery stenosis is much rarer, similar studies for FMD are unavailable.

The patient was prescribed 100 mg of losartan with 25 mg of hydrochlorothiazide, in addition to 50 mg of atenolol daily, and her blood pressure normalized. She continued with the same antihypertensive regimen but was lost to follow-up. She presented to the clinic 2 years later with hypertensive urgency (blood pressure, 201/110 mm Hg). Labetalol was initiated. Duplex renal artery sonography showed an atrophic right kidney measuring 7.6 cm in length, with marked thinning of the parenchyma. The right renal artery had a normal blood velocity. A nuclear medicine renal scan showed 19% renal function on the right side and 81% on the left side. Renal vein renin sampling showed renin levels in the right renal vein that were markedly higher than those in the left renal vein and inferior vena cava, with a renal vein renin ratio of 2.1, with lateralization to the right.

5. On the basis of the data provided, which one of the following is the next best step in management of this patient's refractory hypertension?
   a. Medical management
   b. Follow-up angiography with angioplasty
   c. Nephrectomy via laparotomy
   d. Laparoscopic nephrectomy
   e. Observation

Pursuing further medical management at this time is a good option but alone is unlikely to improve the patient's hypertension given the evidence of an atrophic, nonfunctioning right kidney. Performing follow-up angiography with angioplasty will not yield any helpful results because the right kidney has already atrophied and revascularization is unlikely to reverse the loss of function in that kidney.

Nephrectomy remains the treatment of choice for management of renovascular hypertension secondary to a high renin state due to an atrophic kidney. Laparotomy is a more
invasive surgical procedure that requires a longer hospital stay and has a higher complication rate than laparoscopy. Therefore, laparoscopic nephrectomy is the best next step in treating this patient’s hypertension. Observation alone is unacceptable because of the patient’s poorly controlled hypertension.

The patient underwent laparoscopic nephrectomy without any associated complications. Her blood pressure improved dramatically with losartan therapy (25 mg/d) and remained adequately controlled (112/70 mm Hg) at 12-week follow up. The creatinine level was unchanged (0.8 mg/dL).

**DISCUSSION**

Our case highlights several important clinical pearls. First, FMD is prevalent in women with a history of smoking and predominantly affects the mid-to-distal portions of renal arteries. In contrast, atherosclerotic lesions are typically ostial, occur in elderly patients with a history of cardiovascular risk factors, and require aggressive management of risk factors even after successful revascularization. As for the diagnosis, noninvasive testing is widely accepted as the first step, with renal angiography frequently being limited to those with positive findings on preliminary studies, despite the fact that the diagnostic accuracy of commonly used tests varies widely. With respect to treatment, pharmacologic management with either an ACEI or an angiotensin II receptor blocker is the first line of treatment. Because of the risk of teratogenicity, these agents should not be used in patients of child-bearing age who desire to become pregnant. Previous studies have reported poor pregnancy outcomes in women with renovascular hypertensive; however, both maternal and fetal outcomes improved in subsequent pregnancies after either revascularization or excision of the small, poorly functioning kidney. Revascularization is also often offered to patients with an increased likelihood of cure, such as those who are young and have recent-onset hypertension. Serious complications, such as renal artery dissection, may occur on rare occasions, and 17% to 25% of patients are at risk of developing restenosis within 6 months of the procedure. Judicious use of follow-up imaging studies, coupled with close blood pressure monitoring, may facilitate timely recognition and treatment of both early complications and unfavorable clinical outcomes. Finally, for highly selected patients with small, atrophic kidneys and resistant hypertension, unilateral nephrectomy (of the atrophic kidney) may improve blood pressure control without adverse effects on renal function. Blood pressure improved in 78% of patients whose “pressor” kidney was removed.

Renal artery stenosis secondary to FMD is the second most common cause of renovascular hypertension after atherosclerotic renal artery stenosis. Factors that should prompt clinical suspicion of renal FMD include young age, female sex, history of smoking, no family history of essential hypertension, and an abdominal bruit. Management includes medical therapy, revascularization, and, in rare cases, unilateral nephrectomy. Patient prognosis is generally good, but annual renal imaging studies are crucial in monitoring the long-term effects of FMD on renal artery patency and kidney size.

**REFERENCES**


Correct answers: 1, 2, 3, 4, 5, 6