CLINICAL VIGNETTE

Management of Symptomatic Bilateral Renal Artery Stenosis

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Presentation

An 84-year-old female with a long-standing history of poorly controlled blood pressure presented to the emergency department with sudden shortness of breath. She woke up the morning of admission and "felt [she] was suffocating." Her blood pressure was 176/93mmHg on admission, and her symptoms rapidly improved with intravenous Furosemide. Her blood pressure remained persistently elevated with systolic blood pressure greater than 220mmHg, so she was transferred to the ICU and was initiated on a Nicardipine IV infusion. She did not have headache, chest pain, vision changes, or hematuria.

Home medications included Torsemide 10mg daily, Metoprolol 300mg daily, and Irbesartan 150mg twice daily. Her cardiologist told her she was "the most difficult hypertensive patient [she had] treated in fifty years." Numerous antihypertensive medications had been used in the past. She had no prior episodes of sudden shortness of breath, as well as no prior admissions for hypertensive urgency/emergency or other cardiovascular history. Past medical history was significant for a stable lung nodule, prior thyroidectomy for multinodular goiter, GERD, and a traumatic hip fracture after a fall. She was allergic to Penicillin. She had no family history of premature CAD or sudden death. She lives alone and has a daughter who is accompanying her. No tobacco, alcohol, or recreational drug use.

On physical exam, she was afebrile with normal respiratory rate and oxygen saturation. Heart rate was 68 bpm. She was a well appearing woman who appeared comfortable and younger than her stated age. Her mucus membranes were moist; she had no scleral icterus and cranial nerves were intact. A retinal exam was not performed. Her JVP was not distended; carotid upstrokes were brisk without bruits. She had a regular rate and rhythm with no additional heart sounds. There was a mid-peaking II/VI systolic murmur best heard at the left sternal border. Lungs were clear to auscultation. Her abdomen was soft and non-tender with no organomegaly. Aorta was non-palpable, and no abdominal bruits were heard. She had palpable femoral and pedal pulses with no leg edema. Skin was warm and well-perfused with good capillary refill. Neurologic exam was unremarkable.

Her EKG on admission showed sinus arrhythmia at 68 without ST-T changes. Chest X-ray showed bilateral coarse ground glass opacities without infiltrate or effusion. Laboratory data was significant for a white blood cell count of 12,000, Creatinine of 1.7, BNP of 399, and troponin of 0.2.

Hospital course

The patient continued to feel well with no recurrence of dyspnea. Blood pressure control slightly improved on Carvedilol, Nicardipine, and Irbesartan, but systolic blood pressure readings remained >160mmHg. Creatinine remained stable at 1.7. An echocardiogram showed mild aortic stenosis, normal left ventricular systolic function with an ejection fraction of 65%, moderate left atrial dilation, and moderate concentric left ventricular hypertrophy. A renovascular duplex showed normal velocities in the mid-segments of both renal arteries, but the ostia were not well visualized. Cardiac biomarkers continued to rise with the troponin increasing from 0.2 to 0.63 to 7.0.

Her preference was to undergo non-invasive ischemic evaluation, so she underwent a Regadenoson SPECT, which revealed inferolateral ischemia. She underwent coronary angiography and was found to have a severe focal stenosis in the proximal circumflex coronary artery corresponding to her area of ischemia. A drug-eluting stent was deployed at the lesion with a satisfactory result.

Since her clinical presentation of pulmonary edema, refractory hypertension and renal insufficiency were all suggestive of bilateral renal artery stenosis, and the ostia of both renal arteries were poorly visualized on ultrasound, an aortic angiogram at the level of the renal arteries was performed. This revealed severe bilateral renal artery stenosis with a 90% ostial stenosis on the left and 99% subtotal occlusion on the right.

She returned several days later for planned revascularization of her renal arteries, which she underwent via left radial artery access. Stents were placed in the proximal segments of both renal arteries with a satisfactory angiographic result (Figures 1-3). A subsequent renovascular duplex showed widely patent renal arteries. Her blood pressure improved on carvedilol and Losartan; a low dose nifedipine was later added to her

regimen. Her creatinine the day prior to intervention increased to 2.4, and four days post renal artery revascularization dropped to 1.2. She continues to do well with no recurrence of symptoms.

Renal artery stenosis

Background

The prevalence of renal artery stenosis may be as high as 40% in patients presenting with refractory hypertension.[1] Treatment options including renovascular revascularization have been fraught with uncertainty with several clinical trials not suggestive of benefit. However, bilateral renal artery stenosis remains a clinically relevant entity and is independently associated with an increase in mortality.[2] Causes of renal artery stenosis are fibromuscular dysplasia and atherosclerosis. More than 90% of cases of renal artery stenosis result from atherosclerosis. Fibromuscular dysplasia is usually due to medial fibroplasia – a connective tissue disorder involving the medial layer of vascular smooth muscle.[3] It disproportionately affects women under 50, and most commonly results in stenosis of the distal renal artery with a typical "beaded" appearance on angiography. Atherosclerotic renovascular disease on the other hand more commonly involves the proximal portion of the renal artery, and is associated with other atherosclerotic risk factors – advanced age, hypertension, hyperlipidemia, diabetes, and the presence of arterial atherosclerosis in other vascular territories.

Diagnosis

The diagnosis should be considered in those who have refractory hypertension despite being on numerous antihypertensive agents, onset of hypertension at <30 years of age, unexplained atrophic kidney or more than 1.5 cm size discrepancy between kidneys, unexplained renal dysfunction, sudden unexplained "flash" pulmonary edema and hypertensive urgency, development of new azotemia or worsening renal function after administration of Ace inhibitor or ARB, and in patients with multivessel coronary artery disease and peripheral artery disease (the coexistent incidence of RAS and CAD is up to 20%).[4] Renovascular duplex with high sensitivity and specificity is an inexpensive modality that can be beneficial in establishing kidney size, peak velocity (corresponding to the segment of highest stenosis), and other parameters that can indicate renal hypoperfusion such as resistive indices and the ratio of aortic to renal artery velocities. Alternative imaging modalities include CT angiography and MR angiography, although renal dysfunction might preclude the use of these tests. Renovascular ultrasound can be limited by body habitus or poor visualization. Doppler criteria for severe renal artery stenosis include a peak velocity of >200cm/s (or end-diastolic velocity >150cm/s) with evidence of post-stenotic turbulence, renal artery to aorta peak systolic velocity ratio >3.5. A resistive index >0.8 may be used to predict blood pressure response to renal revascularization.[5] Indications for renal artery ultrasound include refractory hypertension, abrupt worsening of previously well-controlled hypertension, hypertension with atherosclerosis of the abdominal aorta, and assessment of renal arteries after revascularization. Renal angiography remains the gold standard for the invasive assessment of hemodynamically significant renal artery stenosis.[6]

Treatment

The optimal treatment for renal artery stenosis remains unclear. Despite randomized clinical trials showing a lack of benefit with revascularization, they have been justly criticized for their porous enrollment criteria.[7] A prime reason is due to the sub-optimal definition of "severe" renal artery stenosis; for instance, angiographic renal artery stenosis does not necessarily correlate with hemodynamic severity as has been well-established in coronary literature. It is recommended that non-invasive assessment of severe RAS be associated with angiographic stenosis more than 70%, or with fractional flow reserve ≤0.9 at maximal hyperemia prior to revascularization.[5,8] The goals of treatment include improvement in blood pressure, prevention of renal failure, improvement in heart failure, and chronic angina.[5] Renal artery stenting is considered appropriate care in patients with a cardiac disturbance syndrome or flash pulmonary edema (class IB), patients with accelerated or resistant hypertension on more than 3 antihypertensive agents, including one diuretic and hypertension with medication intolerance (class IIB).[5] In the case of our patient, pulmonary edema and refractory hypertension despite being on maximal doses of 3 or more antihypertensive agents in the setting of bilateral severe renal artery stenosis is a Class I recommendation for renal artery stenting.[4] Renal revascularization remains the optimal treatment strategy in patients such as ours and should be considered when no alternative explanation exists in those with difficult to treat hypertension and unexplained pulmonary edema.

Figures

Figure 1. Aortogram showing severe bilateral renal artery stenosis.

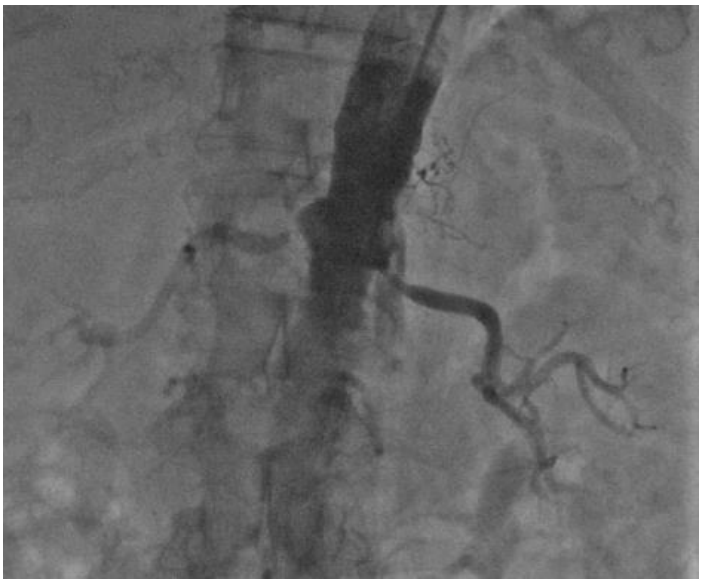


Figure 2. Right renal artery after stent placement.

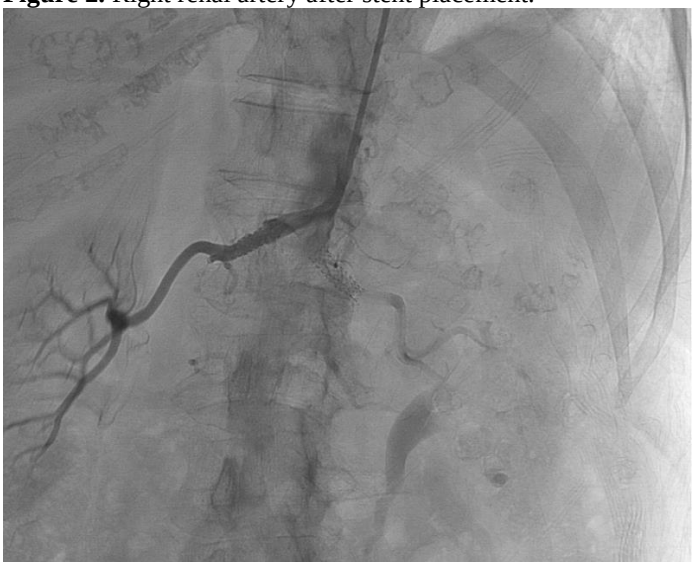
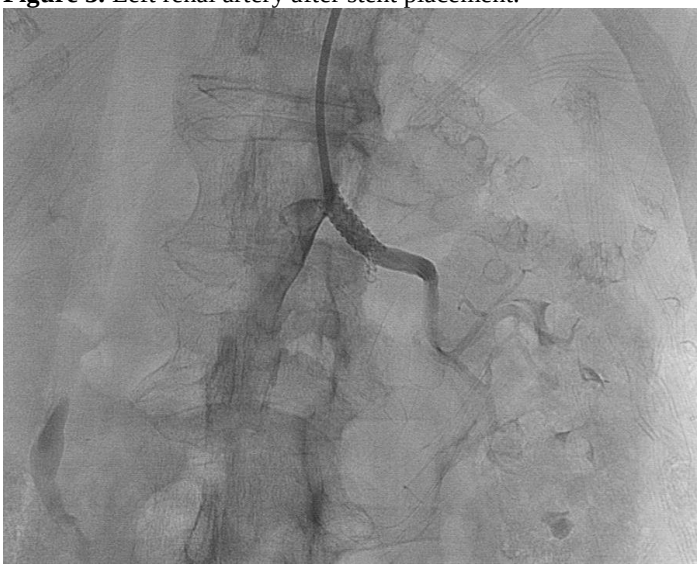


Figure 3. Left renal artery after stent placement.



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