Recurrent renal artery stenosis in a child with multiple renal arteries: case report and review of literature

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Abstract

We report a case of a 10-year-old male who presented with hypertensive emergency in the setting of idiopathic bilateral renal artery stenosis with multiple renal arteries. After failed medical management, he underwent angioplasty of the bilateral superior renal arteries twice. This highlights the need for a multidisciplinary approach in treatment.

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Abstract

Introduction: Bilateral renal artery stenosis is a rare cause of severe pediatric hypertension. Definitive treatment remains challenging.

Case Presentation: We report a case of a previously healthy 10-year-old male who presented with hypertensive emergency and was found to have idiopathic bilateral renal artery stenosis with multiple renal arteries and mild midaortic syndrome. After failed medical management, he underwent angioplasty of the bilateral superior renal arteries twice prior to resolution of the stenosis bilaterally.

Conclusion: This case highlights the need for a multidisciplinary approach in treatment of these patients and the risk of recurrence of stenosis and hypertension following angioplasty.

Case Report

Case:

A 10-year-old previously healthy male presented with one day of abdominal pain and vomiting and two weeks of intermittent headaches. He was found to have severe hypertension with blood pressure of 225/150 mmHg. He had no personal or family history of hypertension. He had not seen his pediatrician in over one year. His body mass index was normal. His cardiac and respiratory exam were within normal limits.

The patient was treated with intravenous labetalol and subsequently transitioned to a labetalol infusion followed by the addition of a nifedipine infusion in the pediatric intensive care unit. He was gradually started on oral labetalol, nifedipine, hydrochlorothiazide, and with clonidine as needed, allowing for discontinuation of his nifedipine and labetalol infusions. His oral antihypertensive regimen was later titrated to labetalol 200 mg three times a day, clonidine 0.1 mg in the morning and 0.2 mg in the evening, nifedipine extended release 60 mg twice a day, hydrochlorothiazide 12.5 mg daily, and as needed hydralazine 10 mg for blood pressures > 140/90 mmHg. He continued to require multiple hydralazine doses per day, with systolic blood pressures remaining in the 140s.

The patient underwent a thorough investigation for the causes of his severe hypertension. Laboratory tests showed normal hemoglobin and platelet counts. His serum electrolytes, kidney function panel (SCr 0.4 mg/dl, BUN 8 mg/dl), plasma renin activity and aldosterone levels were normal. Urinalysis, erythrocyte sedimentation rate, c-reactive protein, Hemoglobin A1C, thyroid function tests, complement levels, antinuclear antibodies, plasma and urine metanephrine and electrocardiogram were normal.

Lipid panel screening for metabolic syndrome showed an elevated cholesterol level of 213 mg/dL (reference: 112-207 mg/dL). Echocardiogram demonstrated left ventricular wall thickness upper limit of normal. Magnetic resonance angiography of the brain demonstrated tortuosity of the posterior cerebral artery greater than expected for age and multiple chronic microhemorrhages, likely secondary to chronic severe hypertension. Ophthalmology exam showed mild hypertensive changes including arterial attenuation and vascular tortuosity of both eyes. A renal duplex ultrasound (US) showed bilateral high grade ostial stenosis of superior renal arteries bilaterally. Computed tomography scan of chest, abdomen, and pelvis with contrast showed two renal arteries to the right kidney and three arteries to left kidney (Figure 1). The superior artery to the right kidney suggested ~ 70% stenosis at origin and the superior left renal artery demonstrates ~ 80% stenosis at its origin. The inferior arteries to both kidneys were patent without obvious stenosis. There was also a diminutive third left renal artery. Hypercoagulable workup showed elevated factor VIII activity (245%), low
protein C clottable activity (40%), low antithrombin III (92%), normal antithrombin III antigen (101%),
and low partial thromboplastin time (28.2 seconds). Hematology was consulted and the abnormalities were
attributed to inflammation rather than a hypercoagulable disorder. Renin levels from both renal veins (right
renal vein 17.3 ng/mL/hr, left renal vein 9.0 ng/mL/hr) and from the inferior vena cava (16.3 ng/mL/hr)
were significantly elevated.

Due to poor blood pressure control despite multiple antihypertensives, aortogram and angiography were
performed. Aortogram showed mild narrowing of the intra-abdominal aorta (<25%) and severe (>90%)
stenosis of the bilateral superior renal arteries at the level of the ostia. There was also delayed perfusion
of the left kidney likely due to stenosis of the multiple left renal arteries (Figure 2). Balloon angioplasty
was performed of the bilateral superior renal arteries. Post intervention angiography demonstrated near-
complete resolution of superior renal artery stenosis with less than 10% residual stenosis (Figure 3). After
his angioplasty, he was discharged on nifedipine monotherapy (60 mg daily). He received enoxaparin for 48
hours after his procedure and was then switched to aspirin 81 mg daily. His antihypertensive medications
were weaned, and he was maintained on monotherapy with Nifedipine 30 mg daily.

In the months following the patient’s discharge from the hospital his blood pressures gradually increased, re-
quiring addition of labetalol, clonidine, and hydrochlorothiazide. About six months after his initial diagnosis,
24 hour ambulatory blood pressure monitoring showed severe systolic daytime and nighttime hypertension.
Repeat renal doppler ultrasound nine months after angioplasty showed increased velocities in the right re-
nal artery compared to his post-angioplasty renal ultrasound, suggesting residual stenosis. A repeat renal
angiography demonstrated mild stenosis of the right superior renal artery, and severe stenosis of the left
superior renal artery. A repeat diagnostic aortogram demonstrated stable minimal (<25%) narrowing of
intra-abdominal aorta without significant difference in pressure gradients. Balloon angioplasty was per-
formed on the bilateral superior renal arteries with near complete resolution of stenosis bilaterally (Figure
4). Following the second angioplasty the patient’s clonidine dose was reduced and his hydrochlorothiazide
was discontinued. He continues on nifedipine and labetalol with excellent blood pressure control.

Discussion

Hypertension affects approximately 1-5% of pediatric patients.1 Most cases in pediatrics are attributable
to a primary cause. About 10 % of children with secondary hypertension have a renovascular cause, the
most common of which is renal artery stenosis.2 Rarely, pediatric patients present with idiopathic renal
artery stenosis. The most common causes of renal artery stenosis in children include fibromuscular dysplasia
(FMD), Williams syndrome, and neurofibromatosis type 1, with the most common being FMD.3

FMD is a condition that causes vessels stenosis and aneurysms through a non-inflammatory process which
commonly involves the renal arteries.4 In our patient duplex renal ultrasound and angiogram were not
suggestive of focal or multifocal disease caused by FMD. Other causes of renal artery stenosis were also
considered. Neurofibromatosis was unlikely given the absence of physical exam findings consistent with this
syndrome, i.e. cafe-au-lait macules, skinfold freckling, or neurofibromas. Inflammatory disorders such as
Takayasü’s arteritis was also considered but was unlikely as it usually presents with elevated inflammatory
markers in females around age 25.5 Finally midaortic syndrome, or narrowing of the proximal aorta, leads
to decreased blood flow to the kidneys and subsequent renovascular hypertension. Our patient did had
mild narrowing of the aorta (<25%) on imaging which may have contributed to inadequate flow through his
abnormal renal arteries.

It is important to consider whether duplicated renal arteries increase the likelihood of developing renovascular
hypertension, although duplicate renal arteries are typically considered a normal variant. 70% of individuals
have a single renal artery whereas about 30% have accessory renal arteries. Multiple renal arteries are
unilateral in 30% of patients and bilateral in approximately 10%.6,7 In our case, the patient has three left
renal arteries and two right renal arteries. The superior arteries were stenosed bilaterally. The inferior
right renal artery appeared patent but the inferior left renal arteries likely had proximal stenosis given the
findings of delayed perfusion on angiography. The presence of at least somewhat patent inferior renal arteries
bilaterally likely explains why this patient had normal renal function. There are reports in older patients (21 and 40 years-old) of hypertension due to secondary hyperaldosteronism in the setting of accessory renal arteries. The underlying mechanism in renovascular hypertension involves decreased perfusion to the kidney and activation of the renin-angiotensin-aldosterone system. A renin ratio of > 1.5 between the main renal veins and a ratio of < 1.3 between the contralateral renal vein and the infra-renal inferior vena cava supports bilateral stenosis in the renal arteries. Our patient had normal levels of systemic renin and aldosterone but had evidence of renin elevation with renal vein sampling with a renin ratio ~1.9 between main renal veins and a ~0.9 ratio between contralateral renal vein and infra-renal inferior vena cava.

Treatment remains challenging and includes medical management, angioplasty, graft bypass, and vascular reimplantation. Although out patient’s blood pressure briefly improved after initial angioplasty, it remained difficult to control six months after his procedure, requiring increasing doses of antihypertensives. His blood pressure improved after second angioplasty. Literature review shows that percutaneous transluminal renal angioplasty (PTRA) is an appropriate treatment option for pediatric renovascular hypertension due to Takayasu arteritis and fibromuscular dysplasia however it unclear if this is an ideal treatment option for idiopathic Renal Artery Stenosis (RAS). A review of the literature on renal artery angioplasty for pediatric renovascular hypertension shows that the overall success rate of angioplasty is 58%. Based on another article, complete resolution of hypertension with revascularization is uncommon (<10%) in patients with atherosclerotic RAS whereas ~ 50% respond fully in patients with FMD. Ileorenal bypass or renal artery reimplantation, especially in the setting of midaortic syndrome, may be effective for patients who do not improve from PTRA. This may be a future consideration for our patient if blood pressure control worsens again following repeat angioplasty.

Conclusion

Pediatric patients rarely present with idiopathic bilateral renal artery stenosis. Although some patients benefit from angioplasty, our patient continued to have severe hypertension after initial angioplasty and required a second angioplasty to achieve blood pressure control. This report highlights the obstacles to treatment of RAS in pediatric patients, the risk of recurrent hypertension, and the possible need for multiple interventions.

References


Figure Legends:

Figure 1: Computed tomography scan demonstrating stenosis of right super renal artery (black arrow) originating from aorta

Figure 2: Pre-angioplasty angiography demonstrates narrowing of the abdominal aorta, severe stenosis of right superior renal artery with post-stenotic dilatation, stenosis of the left superior renal artery, and delayed perfusion of left kidney. The middle and inferior left renal arteries are difficult to visualize like due to delayed blood flow in the setting of stenosis.

Figure 3: Post-intervention angiography demonstrating improvement in stenosis of bilateral super renal arteries.

Figure 4: Post repeat angioplasty intervention angiography demonstrating improvement in stenosis of bilateral super renal arteries.