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CLINICAL VIGNETTE

Recurrent Renal Artery Stenosis in a Child with Multiple Renal Arteries: A Case Report and Review of Literature

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Case Report

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

The patient was treated with intravenous labetalol and transitioned to a labetalol infusion followed by a nicardipine infusion in the pediatric intensive care unit. He was gradually started on oral labetalol, nifedipine, hydrochlorothiazide, with as needed clonidine enabling discontinuation of his nicardipine and labetalol infusions. His oral antihypertensive regimen was 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, with hydralazine 10 mg for blood pressures > 140/90 mmHg. He required multiple hydralazine doses per day, with systolic blood pressures remaining in the 140s.

The causes of his severe hypertension were thoroughly evaluated. Laboratory tests included: normal CBC, metabolic panel, urinalysis, c-reactive protein, Hemoglobin A1C, thyroid function tests, complement levels, antinuclear antibodies, plasma renin activity, aldosterone levels, plasma and urine metanephrine and electrocardiogram.

Lipid panel showed elevated cholesterol of 213 mg/dL (reference: 112-207 mg/dL). Echocardiogram noted left ventricular wall thickness at 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 in both eyes. Renal duplex ultrasound (US) showed bilateral high-grade ostial stenosis of superior renal arteries. Computed tomography scan of chest, abdomen, and pelvis with contrast showed two renal arteries to the right kidney and three arteries to left kidney. The superior artery to the right kidney had ~ 70% stenosis at origin and the superior left renal artery had ~ 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 evaluation 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 attributed the abnormalities to inflammation rather than a hypercoagulable disorder. Renin levels were significantly elevated 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).

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 delayed perfusion of the left kidney likely due to stenosis of the multiple left renal arteries. Balloon angioplasty was performed on the bilateral superior renal arteries. Post intervention angiography demonstrated near-complete resolution of superior renal artery stenosis with less than 10% residual stenosis. After angioplasty, he was discharged on nifedipine monotherapy (60 mg daily). He received post-procedure enoxaparin for 48 hours and was then switched to daily aspirin 81 mg. His antihypertensive medications were weaned, and he was maintained on monotherapy with Nifedipine 30 mg daily.

In the months following discharge from the hospital his blood pressures gradually increased, requiring addition of labetalol, clonidine, and hydrochlorothiazide. About six months after his initial hospitalization, 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 renal artery compared to his post-angioplasty renal ultrasound, suggesting residual stenosis. Repeat renal angiography demonstrated mild stenosis of the right superior renal artery, and severe stenosis of the left superior renal artery. Repeat diagnostic aortogram showed stable minimal (<25%) narrowing of intra-abdominal aorta without significant difference in pressure

gradients. Balloon angioplasty was performed on the bilateral superior renal arteries with near complete resolution of stenosis bilaterally (Figure 1). Following the second angioplasty the patient's clonidine dose was reduced and hydrochlorothiazide was discontinued. He continues on nifedipine and labetalol with excellent blood pressure control.

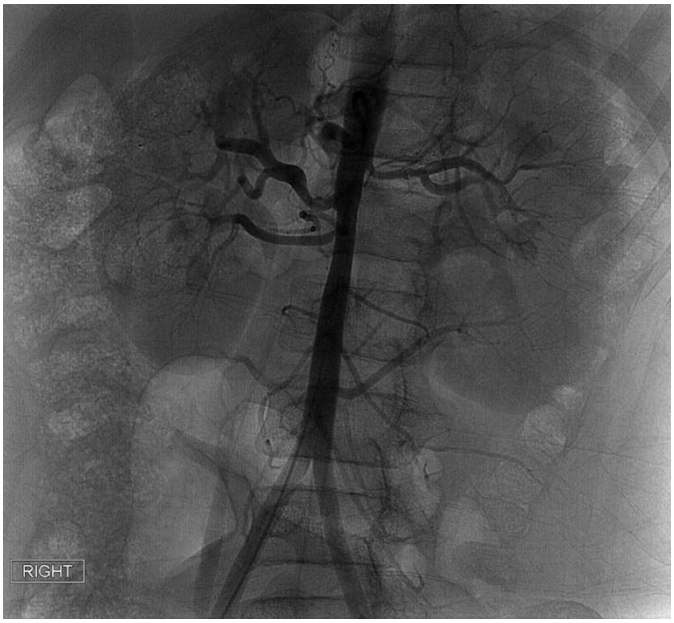

Figure 1: Post repeat angioplasty intervention angiography demonstrating improvement in stenosis of bilateral super renal arteries.

Discussion

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

FMD causes vessels stenosis and aneurysms through a non-inflammatory process which commonly involves the renal arteries.[4] Our patient is 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, such as cafe-au-lait macules, skinfold freckling, or neurofibromas. Inflammatory disorders such as Takayasu's arteritis was also considered unlikely, as it usually presents with elevated inflammatory markers in females around age 25.[5] Finally midaortic syndrome, or narrowing of the proximal aorta, leading to decreased blood flow to the kidneys and subsequent renovascular hypertension. Our patient had mild narrowing of the aorta (<25%) on imaging which may have contributed to inadequate flow through his abnormal renal arteries.

Although duplicate renal arteries are typically considered a normal variant we consider whether duplicated renal arteries increase the likelihood of developing renovascular hypertension. Seventy percent of individuals have a single renal artery with about 30% having accessory renal arteries. Multiple renal arteries are unilateral in 30% of patients and bilateral in approximately 10%.[6,7] Our patient has three left renal arteries and two right renal arteries. The bilateral superior arteries were stenosed. 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 somewhat patent bilateral inferior renal arteries explain his normal renal function. There are reports of hypertension due to secondary hyperaldosteronism in the setting of accessory renal arteries, in patients 21 to 40 years old.[8]

The underlying mechanism in renovascular hypertension involves decreased perfusion to the kidney and activation of the renin-angiotensin-aldosterone system.[9] 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 suggests bilateral stenosis in the renal arteries.[10] Our patient had normal levels of systemic renin and aldosterone but renin elevation on 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 our 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 suggests percutaneous transluminal renal angioplasty (PTRA) is an appropriate treatment option for pediatric renovascular hypertension due to Takayasu arteritis and fibromuscular dysplasia. However it remains unclear if this is ideal treatment option for idiopathic Renal Artery Stenosis (RAS).[11] The literature on renal artery angioplasty for pediatric renovascular hypertension shows that angioplasty overall success rate is 58%.[12] Another article reports less than 10%, complete resolution of hypertension with revascularization in patients with atherosclerotic RAS, with ~ 50% full response in patients with FMD.[13] Ileorenal bypass or renal artery reimplantation, especially in the setting of midaortic syndrome, may be effective for patients who do not improve from PTRA.[3] This may be a future consideration for our patient if blood pressure control worsens 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 highlights some obstacles to treatment of RAS in pediatric patients, the risk of recurrent hypertension, and the possible need for multiple interventions.

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REFERENCES

1. **Grinsell MM, Norwood VF**. At the bottom of the differential diagnosis list: unusual causes of pediatric hypertension. *Pediatr Nephrol*. 2009 Nov;24(11):2137-46. doi: 10.1007/s00467-008-0744-y. Epub 2008 Mar 5. PMID: 18320238; PMCID: PMC2755748.
2. **Villegas L, Cahill AM, Meyers K**. Pediatric Renovascular Hypertension: Manifestations and Management. *Indian Pediatr*. 2020 May 15;57(5):443-451. Epub 2020 Mar 12. PMID: 32221053.
3. **Sayed A, Elsharkawi H, Awad AS, Emil E, El-Sayed H**. Case report: Bilateral renal artery stenosis in a 7-year-old child. *Methodist Debakey Cardiovasc J*. 2014 Jul-Sep;10(3):190-2. doi: 10.14797/mdcj-10-3-190. PMID: 25574348; PMCID: PMC4280245.
4. **Swinford RD, Ingelinger JR**. Evaluation of hypertension in childhood diseases. Barratt TM, Avner ED, Harmon WE (eds). *Pediatric Nephrology*. (4th ed). Baltimore: Lippincott Williams and Wilkins, 1999; p.1007.
5. **Alnabwani D, Patel P, Kata P, Patel V, Okere A, Cheriyath P**. The Epidemiology and Clinical Manifestations of Takayasu Arteritis: A Descriptive Study of Case Reports. *Cureus*. 2021 Sep 15;13(9):e17998. doi: 10.7759/cureus.17998. PMID: 34667674; PMCID: PMC8519497.
6. **Deshpande SH, Bannur BM, Patil BG**. Bilateral multiple renal vessels: a case report. *J Clin Diagn Res*. 2014 Jan;8(1):144-5. doi: 10.7860/JCDR/2014/6893.3800. Epub 2014 Jan 12. PMID: 24596748; PMCID: PMC3939528.
7. **Standring S**. *Gray's Anatomy: The Anatomical Basis of the Clinical Practice*.39th edition. Edinburg: Elsevier Churchill Livingstone; 2008. p. 1231.
8. **Chan PL, Tan FHS**. Renin dependent hypertension caused by accessory renal arteries. *Clin Hypertens*. 2018 Nov 1;24:15. doi: 10.1186/s40885-018-0100-x. PMID: 30410790; PMCID: PMC6211501.
9. **Nair R, Vaqar S**. Renovascular Hypertension. 2022 Nov 7. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 31869068.
10. **Patel PA, Cahill AM**. Renovascular hypertension in children. *CVIR Endovasc*. 2021 Jan 7;4(1):10. doi: 10.1186/s42155-020-00176-5. PMID: 33411105; PMCID: PMC7790992.
11. **Zhu G, He F, Gu Y, Yu H, Chen B, Hu Z, Liang W, Wang Z**. Angioplasty for pediatric renovascular hypertension: a 13-year experience. *Diagn Interv Radiol*. 2014 May-Jun;20(3):285-92. doi: 10.5152/dir.2014.13208. PMID: 24675165; PMCID: PMC4463347.
12. **Giavroglou C, Tsifountoudis I, Boutzetis T, Kiskinis D**. Failure and success of percutaneous angioplasty in a hypertensive child with bilateral renal artery stenosis. *Cardiovasc Intervent Radiol*. 2009 Jan;32(1):150-4. doi: 10.1007/s00270-008-9350-4. Epub 2008 Apr 29. PMID: 18443856.
13. **Trinquart L, Mounier-Vehier C, Sapoval M, Gagnon N, Plouin PF**. Efficacy of revascularization for renal artery stenosis caused by fibromuscular dysplasia: a systematic review and meta-analysis. *Hypertension*. 2010 Sep;56(3):525-32. doi: 10.1161/HYPERTENSIONAHA.110.152918. Epub 2010 Jul 12. PMID: 20625080.