

Renal Artery Fibromuscular Dysplasia

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Abstract

Pediatric renal artery fibromuscular dysplasia (FMD) is a systemic noninflammatory, non-atherosclerotic vascular disease, presenting primarily in young children with hypertension. The renal, mesenteric, extracranial carotid, intracranial carotid, and aorta are the most common sites of lesions. Common radiologic presentations include focal segmental stenosis and a string of beads appearance, although less common presentations such as dissection, tortuosity, and aneurysm should raise suspicion of renal artery FMD. Due to its vague clinical and radiologic presentation, diagnosis of renal artery FMD in children is often delayed and thus should be considered in the differential diagnosis of renovascular hypertension.

Keywords: Vascular, Multisystem, Non-Inflammatory

Case Summary

A preteen patient was referred to the emergency department by the primary care physician for headaches. The patient's blood pressure (BP) was 170s/100s mm Hg on amlodipine; there was no papilledema or neurologic findings. Post-angioplasty, the BP was 120s/70s with no medications.

Imaging Findings

Renal artery US is usually the first imaging modality utilized for suspected renovascular hypertension. The renal color Doppler examination revealed an elevated peak systolic velocity of 305 cm/s in the left main renal artery (Figure 1). Catheter angiogram and CT angiogram showed a region of focal stenosis with a "string of beads" appearance (Figure 2). Renal angiography confirmed the string of beads appearance in the left renal artery (Figure 3). No dissections or aneurysms

were noted. After renal angioplasty, an increased luminal diameter was noted.

Diagnosis

Renal artery fibromuscular dysplasia (FMD).

Differential diagnosis in children includes Takayasu arteritis, Kawasaki disease (KD), neurofibromatosis, Grange syndrome, Williams syndrome, and Alagille syndrome.

Discussion

FMD is a systemic noninflammatory, non-atherosclerotic vascular disease of small and medium-sized vessels. FMD can affect any vascular bed, although it most commonly affects the renal arteries. Pediatric FMD also affects the mesenteric arteries, carotid arteries, and the aorta, resulting in the deposition of collagen and the degeneration of elastic fibrils.¹

Renal artery FMD is the most common cause of renal artery stenosis in children, although it is often undiagnosed due to its vague symptoms at presentation. Pediatric renal artery FMD presents with secondary hypertension due to renal artery stenosis. Symptomatic presentation can also include headache, dizziness, abdominal bruit, and flank pain.¹ There is a 3:2 ratio of girls to boys being diagnosed, and the mean age at diagnosis is 8.4±4.8 years.¹ This is unlike the adult form of FMD, in which the ratio of females to males is 9:1, suggesting a unique clinical manifestation for pediatric FMD.²

FMD lesions are classified as unifocal or multifocal. Unifocal FMD lesions can present as a solitary lesion (<1 cm of stenosis) or a segment of tubular stenosis (>1 cm of stenosis) and are more common in pediatric patients than adults.³ Multifocal lesions (≥2 stenoses) present with the classic "string of beads" appearance with successive regions of stenosis and dilation. Segmental weakening of the vessel wall may also result in aneurysm formation, tortuosity, and dissection, although rare in pediatric cases.

FMD lesions are also classified by the arterial layer affected, including the intima, media, or adventitia. Pediatric FMD most commonly presents with intimal fibroplasia, presenting with focal

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Figure 1. Doppler US image showing elevated peak systolic velocity in the left main renal artery (normal 60-100 cm/s) of 305 cm/s (arrow, right upper image).

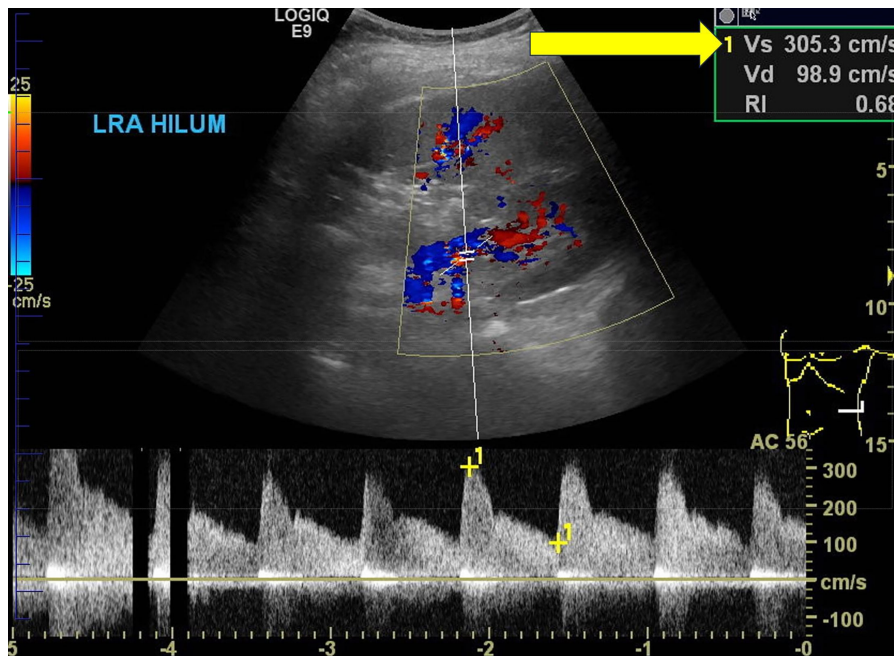
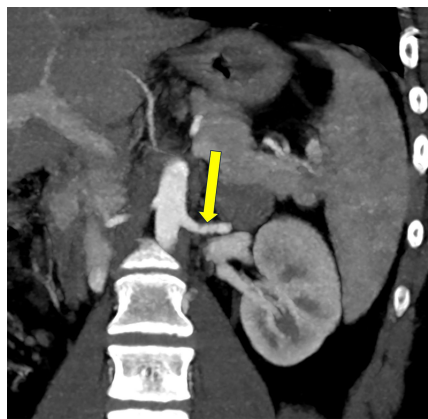


Figure 2. CTA image showing undulating irregular pattern of the left renal artery (arrow).



narrowing due to collagen deposition, which projects into the lumen.¹ Medial hyperplasia presents most commonly in adults with the “string of beads” appearance. Adventitial hyperplasia is extremely rare, making up <1% of total FMD cases. The pathophysiology is related to dense fibrosis that results in long, smooth, tubular narrowing of the vessel. In some cases, there is a short

segment narrowing. Beading is absent in these patients.

FMD is a condition with an unknown etiology and can present sporadically or in families. No genetic abnormalities have been identified in adult or pediatric patients with FMD. Thus, the differential diagnosis for this condition is broad. In general, the conditions in the differential diagnosis can be distinguished from FMD by vascular and anatomic imaging.

Takayasu arteritis is another cause of renovascular hypertension in children that is more commonly diagnosed in Asia and South Africa.⁴ Takayasu arteritis presents acutely with an early systemic phase, characterized by fever, arthralgias, weight loss, and fatigue. Imaging in the early phase may demonstrate arterial wall thickening and enhancement on CT and MRI (fat-suppressed T2 images). In the chronic phase, children present with progressive vascular lesions including arterial stenosis, occlusion, aneurysm formation, and dilation of the aorta and its branches. These lesions may require

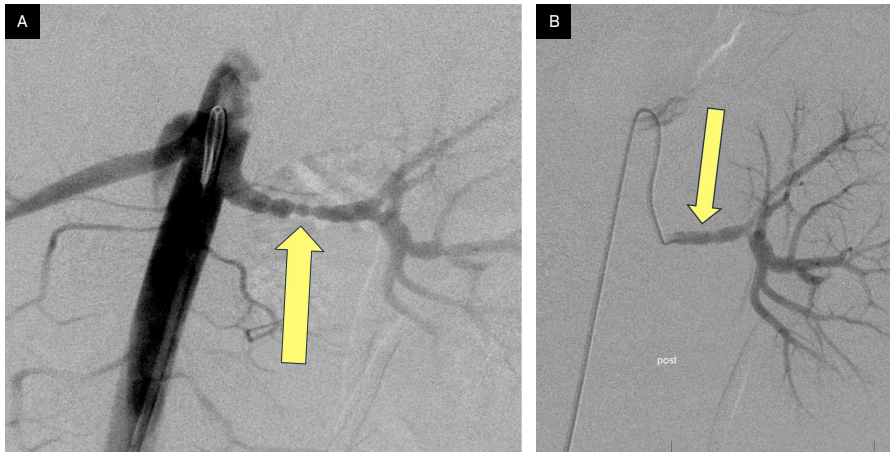
treatment using endovascular therapy or vascular surgery.

KD is a necrotizing vasculitis presenting with systemic symptoms, including rash, fever, oral involvement (strawberry tongue, red and cracked lips), cervical lymphadenopathy, extremity changes (swelling and redness of hands and feet with peeling skin on the tips of fingers and toes), and conjunctivitis.⁵ The primary vascular presentation is coronary artery aneurysms that strongly suggest this diagnosis. KD may also present with renal artery stenosis and can be differentiated from FMD by clinical presentation, coronary artery involvement, histological analysis of affected vessels, and CTA, MR angiography (MRA), or catheter angiographic features.

Neurofibromatosis 1 (NF1) is an autosomal dominant neurocutaneous disorder characterized by café-au-lait macules, bone dysplasia, neurofibromas, and central nervous system (CNS) gliomas.⁶ NF1 vasculopathies are caused by dysregulation of the NF1 tumor suppressor gene that results in excessive smooth muscle in the arterial walls of all sized arteries. The kidneys are most affected by NF1 vasculopathy, leading to renovascular hypertension, which is often secondary to stenosis involving the abdominal aorta and proximal renal arteries. Other associations include aortic coarctation and pheochromocytoma, which can also result in severe hypertension.

Grange syndrome is a rare autosomal recessive condition characterized by early-onset vascular disease and variable penetrance of brachydactyly, syndactyly, bone fragility, and learning disabilities.⁷ The syndrome is caused by mutations in the YY1AP1 gene, which affects smooth muscle cells, resulting in stenosis and occlusion of arteries throughout the body. Vascular territories involved include the renal arteries, cerebrovascular disease that can lead to occlusions and Moya-moya disease, abdominal artery stenoses, and a wider variety of cardiac issues,

Figure 3. (A) Catheter angiography confirming irregular “string of beads” appearance of the left main renal artery. (B) Repeat angiography after angioplasty showing increased luminal diameter and improvement in wall contour.



coronary artery stenosis, and patent ductus arteriosus. Renal artery stenosis presents similarly to FMD with renovascular hypertension and stroke.

Other rare causes of pediatric renovascular hypertension include Williams syndrome, characterized by aortic stenosis, cardiovascular abnormalities, intellectual disability, and elfin facies, and Alagille syndrome, characterized by cholestasis, cardiovascular abnormalities, ophthalmologic abnormalities, vertebral defects, and characteristic facies.^{8,9}

Catheter-based angiography is the gold standard imaging modality for suspected renal artery FMD, with a sensitivity of nearly 100%.¹⁰ Noninvasive imaging studies include CTA, MRA, and duplex US. US is the initial diagnostic modality in the pediatric population and, with Doppler, can show the abnormal vascular anatomy and characterize the degree of vessel narrowing. Duplex US showing higher flow in regions of stenosis, as well as a reduction in kidney size, can indicate disease severity. CTA allows the visualization of calcifications that may differentiate FMD from atherosclerotic disease in the adult population but is not a factor in children. Contrast-enhanced MRA can be used when CTA is contraindicated. Catheter-based angiography is the gold standard for diagnosis as it has higher spatial resolution than CTA

and MRA, allowing earlier identification of disease, but is often reserved for cases of FMD requiring interventions such as angioplasty or rarely, stenting of stenotic lesions.

Due to the lack of randomized controlled trials comparing the effectiveness of FMD treatments and the variability of the disease course, treatment is highly dependent on symptomatic presentation. Antihypertensive agents are used for medical management of secondary hypertension, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, β -blockers, calcium channel blockers, and α -blockers.¹⁰ Pediatric patients with multiple renal involvement may require multiple antihypertensive agents. Aspirin or other antiplatelet drugs may be administered to prevent thrombosis of the affected vasculature.

Revascularization is effective in BP management of medically resistant renal artery FMD, including balloon angioplasty, stenting, and surgery, with or without combined medical therapy.¹¹ Balloon angioplasty (PTA) is preferred due to its less invasive nature, although surgery can be preferred in cases not well suited for PTA. Stenting is avoided in the pediatric population due to the risk of complications such as restenosis and growth-related issues.

Conclusion

Pediatric renal artery FMD is a systemic non-inflammatory, non-atherosclerotic vascular disease, presenting primarily in young children with hypertension. The renal, mesenteric, and extracranial carotid, intracranial carotid, and aorta are the most common sites of lesions. Common radiologic presentations include focal segmental stenosis and a string of beads appearance, although less common presentations such as dissection, tortuosity, and aneurysm should raise suspicion of renal artery FMD. Due to its vague clinical and radiologic presentation, diagnosis of renal artery FMD in children is often delayed and thus should be considered in the differential diagnosis.

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