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Case Report

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Renal Artery Stenosis Presenting with Resistant Hypertension in Children and Adolescents: A Report of Five Cases

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Abstract

We aimed to present five patients presenting with hypertension and diagnosed as renal artery stenosis. Five patients with renal artery stenosis were studied retrospectively. Two of our cases were diagnosed as fibromuscular dysplasia, other cases were diagnosed as Takayasu arteritis and Moyamoya disease, and one of them had congenital vascular abnormality. Renovascular hypertension is one of the most important causes of secondary hypertension in children, and renal artery stenosis constitutes a significant proportion of renovascular disease. We must consider renal artery stenosis in children presenting with resistant hypertension.

Keywords: Children, hypertension, renal artery stenosis

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INTRODUCTION

Hypertension in children and adolescents is a serious public health problem which occurs in 1%-5% of all children and adolescents (1). Hypertension can be classified as primary or secondary. Most cases of childhood hypertension are considered as secondary. Renovascular disease is one of the most common etiologies of secondary hypertension. Renal artery stenosis (RAS) constitutes a significant proportion of renovascular diseases. Most of the cases are caused by fibromuscular dysplasia (FMD). Vasculitis like Takayasu arteritis (TA), Moyamoya disease, and congenital vascular abnormalities must be considered in the differential diagnosis of hypertension secondary to renovascular disease.

CASE PRESENTATION

Case 1

An 11-year-old girl was admitted to the hospital with headache. Physical examination was normal. Blood pressure was 150/100 mm Hg. In the follow-up, she had resistant hypertension and was treated with combined antihypertensive therapy (amlodipine besylate, enalapril maleate, doxazosin mesylate, atenolol). Complete blood count and urinalysis were normal. Laboratory findings revealed hypokalemia, metabolic alkalosis, and normal renal function tests. The 24-hour urinary potassium and chloride excretions were normal, and we excluded primary tubular diseases like Bartter syndrome. Acute phase reactants, rheumatoid factor (RF), antinuclear antibody (ANA), anti-double stranded DNA antibody (anti-dsDNA), and anti-neutrophilic cytoplasmic antibody (ANCA) were negative. Plasma renin and aldosterone levels were high (79.6 ng/mL and 790 pg/mL respectively). In the differential diagnosis, renovascular disease and reninoma were considered because of hyper-reninemic hypertension. Systemic vasculitis and collagen tissue diseases were not considered because there were no clinical findings implicating systemic vasculitis and collagen tissue diseases, and acute phase reactants and autoantibody tests were normal. Abdominal angiography demonstrated calcified aneurysm, surface irregularity, occlusions, and collaterals up to the interlobar arteries along the left renal artery (Figure 1a).

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In thoracic computed tomography angiography, major vascular abnormalities were not detected, and TA was excluded. With these findings, FMD was strongly considered in our patient. Blood pressure was kept under control with medical treatment.

Case 2

A three-year-old boy presented with vomiting. Physical examination was normal. Blood pressure was 145/100 mm Hg and could be controlled with two antihypertensive drugs (amlodipine besylate and doxazosin mesylate). Complete blood count and urinalysis were normal. Laboratory findings showed hypokalemia, hyponatremia, and normal renal function tests. Acute phase reactants, RF, ANA, anti-dsDNA, and ANCA were negative. Renal ultrasound revealed that the left kidney was too large for his age, and parenchymal echogenicity was increased. CT angiography demonstrated a stenotic segment in the right renal artery and post-stenotic dilatation behind that part. In selective renal angiography, left renal artery was normal, and subtotal occlusion was determined in the middle part of the right renal artery (Figure 1b). Because of his age, congenital vascular abnormality was considered as a cause of RAS. Stenosis of right renal artery was completely dilated through balloon angioplasty, and he did not need antihypertensive therapy one month after the angioplasty.

Case 3

A 16-year-old girl was admitted to the hospital with headache. Blood pressure measured in the right arm was 180/110 mm Hg. She was treated with amlodipine besylate and enalapril maleate to normalize her blood pressure. In the physical examination, blood pressure could not be measured in the left arm, and pulses were weak. Complete blood count, urinalysis, and renal function tests were normal. Acute phase reactants, RF, ANA, anti-dsDNA, and ANCA were negative. CT angiography revealed bilateral RAS (Figure 1c), and thoracic CT angiography revealed complete stenosis of the left subclavian artery (Figure 2). TA was diagnosed. The stenosis was fully dilated with balloon angioplasty, and the patient did not need further medical treatment.

Case 4

An eight-year-old boy was admitted to the hospital with vomiting, somnolence, cognitive deficit, and weakness in the right arm. Right-sided hemiparesis was identified by clinical examination. Blood pressure was 200/145 mm Hg, and he was diagnosed as having a hypertensive emergency. Firstly, he was treated with intravenous antihypertensive drugs (sodium nitroprusside and esmolol hydrochloride) and in the follow-up, amlodipine besylate, propranolol, doxazosin mesylate, and minoxidil were used to keep the blood pressure under control. His complete blood count, liver and kidney function tests, electrolytes, thyroid function tests, and urinalysis were normal. A CT did not show hemorrhagia, hydrocephalia, or a shift at the central line. Multiple small infarcts in the left temporo-occipital region were detected by cerebral magnetic resonance imaging (MRI). After that, conventional angiography was performed. Severe stenosis of the internal carotid arteries with multiple collateral vessel formations typical of Moyamoya disease (Figure 3) and bilateral stenosis of the renal arteries (Figure 1d) were demonstrated by cerebral and renal angiographies, respectively. He was diagnosed with Moyamoya disease. His blood pressure was kept under control with medical treatment. Revascularization was not essential for stenosis of the internal carotid arteries and right renal artery; however, it was essential for the left renal artery. Revascularization procedure could not be performed in this patient because he was lost to follow-up. This case was previously published (2).

Case 5

A 16-year-old girl presented with diplopia and dizziness. Blood pressure was 200/122 mm Hg. She had malignant hypertension and was treated with an intravenous antihypertensive drug, esmolol hydrochloride, first and then followed by combined oral antihypertensive therapy (amlodipine besylate, doxazosin mesylate, atenolol, nifedipine, alpha methyldopa, spironolactone, minoxidil). Her complete blood count, liver and kidney function tests, electrolytes, thyroid function tests, and urinalysis were normal. Acute phase reactants, RF, ANA, anti-dsDNA, and ANCA were negative. CT angiography revealed complete stenosis of the proximal part of the right renal artery and mild stenosis of the left renal artery. By conventional renal angiography, the degree of stenosis of the right renal artery and left renal artery were found to be 90% and 70%, respectively (Figure 1e). Cranial MRI showed microangiopathic changes due to earlier intracranial hemorrhages. Thoracic CT angiography showed no major vascular abnormalities; hence, TA was excluded. With these findings, FMD was strongly considered in our patient. Her blood pressure could not be kept under control with medical treatment. Bilateral stenosis could not be dilated by balloon angioplasty or stent placement, and finally, the patient was referred to a transplant center for renal auto-transplantation.

Main Points

- Renovascular disease is one of the most common etiology in secondary hypertension.
- Renal artery stenosis must be considered in children presenting with severe hypertension.
- Fibromuscular dysplasia is the most common cause of renal artery stenosis.
- Radiological examination and presence of systemic involvement is important for differential diagnosis.

DISCUSSION

Renovascular hypertension is one of the most common (25%) etiologies of severe hypertension in children. FMD, vasculitic diseases, Moyamoya disease, and congenital vascular abnormalities must be considered in the differential diagnosis.

FMD is a type of noninflammatory arteriopathy that affects all arteries, most commonly the renal and internal carotid arteries. The presence of FMD may cause arterial stenosis, occlusion, dis-

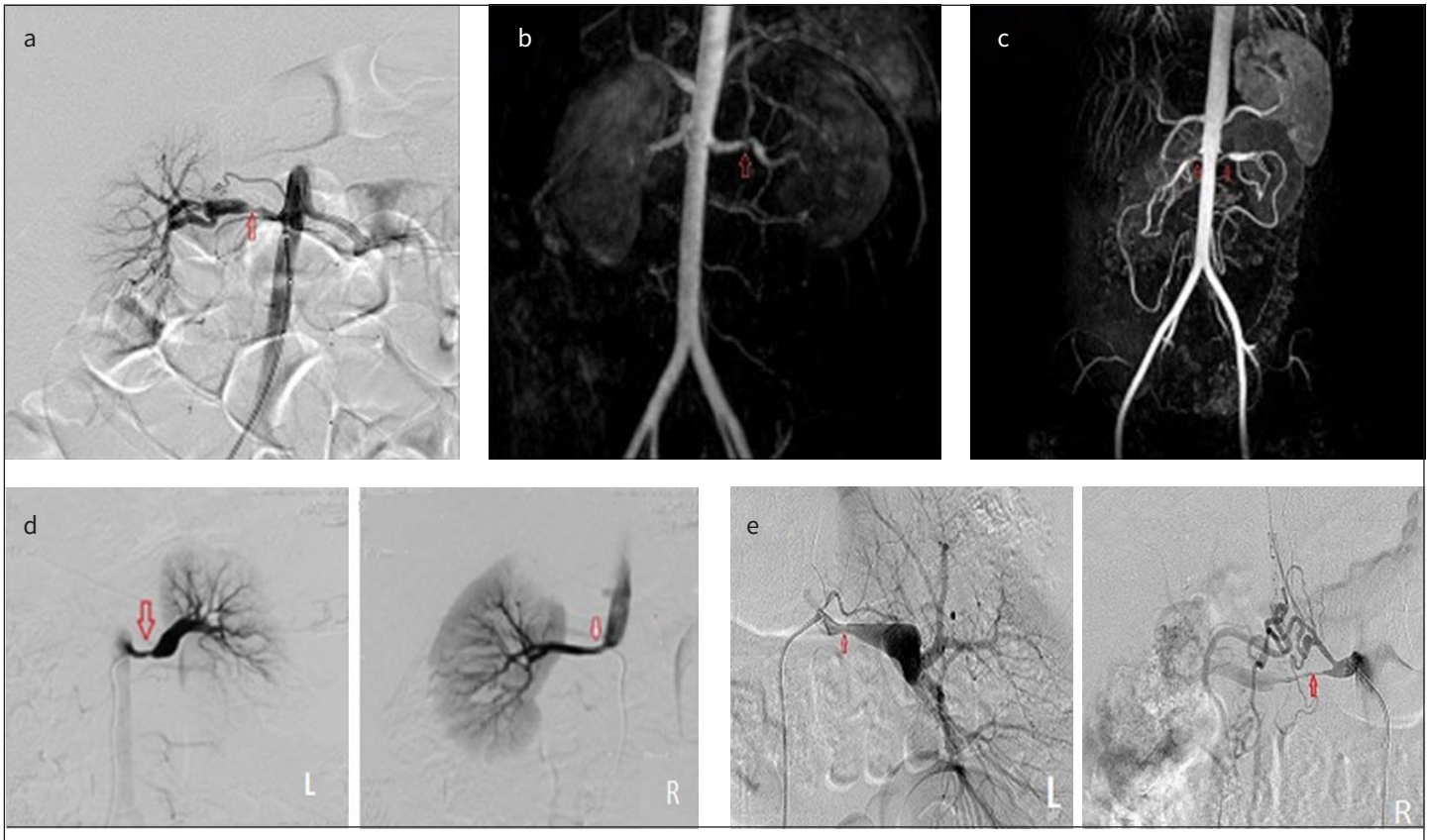

Figure 1. a-e. a) Conventional renal angiography showed stenosis of the left renal artery (Case 1). b) CT angiography showed stenosis of the right renal artery (Case 2). c) CT angiography showed bilateral renal artery stenosis (Case 3). d) Conventional renal angiography showed bilateral renal artery stenosis (Case 4). e) Conventional renal angiography showed bilateral renal artery stenosis (Case 5).

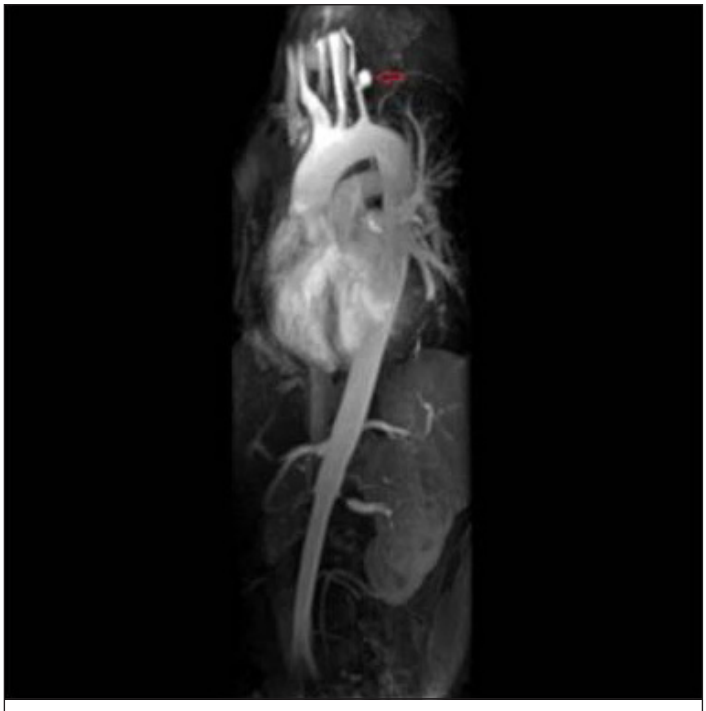

Figure 2. CT angiography showed complete stenosis of the left subclavian artery (Case 3).

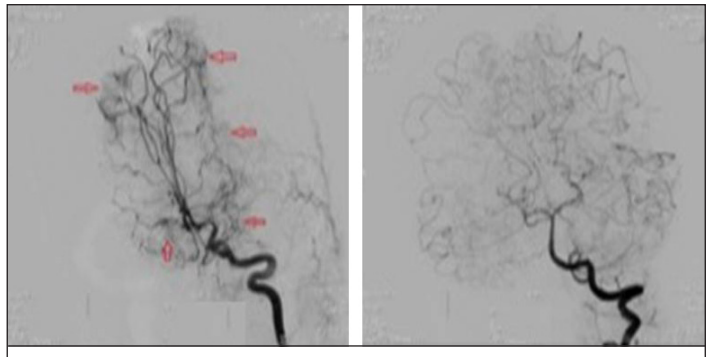

Figure 3. Conventional cerebral angiography showed normal vertobrobasilar system and severe stenosis of the internal carotid arteries with multiple collateral vessel formation typical of moyamoya disease.

section, or aneurysmal dilatation. Renal involvement occurs in approximately 60-70% cases of FMD and is one of the most common causes of severe hypertension in childhood. FMD is classified into focal and multifocal disease. The focal disease is usually caused by intimal hyperplasia; the classic string of beads appearance is seen in the multifocal disease, and it is caused by medial hyperplasia (3). Histopathological examination is the gold standard in the diagnosis of FMD; however, unfortunately none of our cases had renal artery biopsy. Once we excluded other differential diagnoses, FMD was a strong consideration in our patients.

TA is a type of large vessel vasculitis that mainly affects the aorta with its large branches. It is a granulomatous inflammation

Table 1. Patients' characteristics and treatment

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Female	Male	Female	Male	Female
Age (years)	11	3	16	8	16
Presenting symptom	Headache	Vomiting	Headache	Vomiting, somnolence, cognitive deficit, weakness in the right arm	Diplopia and dizziness
Diagnosis	Fibromuscular dysplasia	Congenital vascular anomaly	Takayasu arteritis	Moyamoya disease	Fibromuscular dysplasia
Medical treatment	Amlodipine besylate, enalapril meleate*, doxazosin mesylate, atenolol*	Amlodipine besylate, doxazosin mesylate	Amlodipine besylate, enalapril meleate	Sodium nitroprusside, esmolol, amlodipine besylate, propranolol, Doxazosin mesylate*, minoxidil*	Esmolol, amlodipine, Doxazosin mesylate*, atenolol*, nifedipine*, alphamethyldopa, spironolactone*, minoxidil
Surgical treatment	-	Balloon angioplasty	Balloon angioplasty	-	Balloon angioplasty, stent placement

*Antihypertensive drugs that are currently taken

causing thickening of the artery walls, stenosis, occlusions, and aneurysmal dilatations (4). According to the EULAR/PRINTO/PRES criteria, the presence of an angiographic abnormality, aneurysm/dilatation, narrowing, occlusion or thickened arterial wall not due to FMD or arteriosclerosis as demonstrated by conventional angiography or spiral CT angiography is the mandatory criteria for the diagnosis of TA along with pulse deficit or claudication, systolic blood pressure difference in any extremity (>10 mm Hg), vascular bruits or palpable thrills over large arteries, arterial hypertension (systolic and/or diastolic blood pressure >95th centile for patient's age, sex, and height), and elevated acute phase reactants. TA is diagnosed if the mandatory criteria plus one of the other five criteria exists (5). Our patient had angiographic abnormality as the mandatory criteria and two of other five criteria (arterial hypertension and systolic blood pressure difference in the upper extremities), and therefore, was diagnosed as TA. Sixty percent of the patients with TA have RAS, and it is associated with severe hypertension. If hypertension cannot be controlled with medical treatment, revascularization procedures such as percutaneous transluminal angioplasty or surgical revascularizations should be considered (6).

Moyamoya is a rare, progressive, and chronic cerebrovascular disease. It is characterized with occlusive/stenotic lesions of the internal carotid arteries and anterior and middle cerebral arteries. The best diagnostic clue, which is the outgrowth of small vessels appearing like a puff of smoke in the radiological images, was also demonstrated in patient 4 with cerebral angiography that was previously published (2). In Moyamoya disease, usually intracranial steno-occlusions are present, and extracranial involvements are rarely seen. The most common extracranial vascular involvement is RAS. The presence of RAS in Moyamoya disease can cause renovascular hypertension.

Polyarteritis nodosa (PAN) is a primary necrotizing vasculitis that affects medium sized visceral arteries and their branches. It is triggered by viral infections most commonly by hepatitis B virus (7). According to the EULAR/PRINTO/PRES criteria, the mandatory criteria and at least one of the above five criteria must be present for a diagnosis of PAN; histopathology or angiographic anomalies (mandatory criteria), skin involvement, muscle pain/muscle sensitivity, hypertension, peripheral neuropathy, renal involvement (5). None of the patients in our cohort met the diagnostic criteria for PAN.

CONCLUSION

We should consider the diagnosis of RAS in patients with severe high blood pressure in children and adolescents. Radiological examination and presence of systemic involvement is important for differential diagnosis.

Informed Consent: Written informed consent was obtained from the parents of the patients who participated in this case.

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