Fibromuscular Dysplasia: 
A Rare Case of Renal Artery Stenosis Presenting with Stroke

ABSTRACT
Fibromuscular dysplasia (FMD) is a noninflammatory, nonatheromatous, systemic disease of unknown etiology that is rarely seen in children. The association of renal artery stenosis and stroke is not well established and adequately evaluated in children. We, herein, report a case of a pediatric FMD patient with a complex clinical presentation characterized by stroke and persistent hypertension, due to its rarity.

KEY WORDS: Fibromuscular dysplasia, Stroke, Hypertension, Children, Renal artery stenosis

INTRODUCTION
Fibromuscular dysplasia (FMD) is a noninflammatory, nonatheromatous, systemic disease of unknown etiology mainly affecting medium- and small-sized arteries especially in adult women. This entity is rarely seen in children (1). The estimated incidence of childhood arterial ischemic stroke associated with renal arteriopathy and FMD is approximately 1:300000 per year (2). This condition is typically associated with stenotic lesions in the renal, cerebral and cardiac arteries causing a characteristic “string of beads” appearance on angiography (1,3-5). The most commonly described form of FMD is medial fibroplasia/dysplasia typically affecting young adult females with renal and cerebral vessel involvement, refractory hypertension (HT) and stroke. Although the association between renal arteriopathy and stroke in adults is relatively well established, the relationship between renal arteriopathy and childhood stroke has not been adequately evaluated (6). Herein, we describe a pediatric FMD patient with a complex clinical presentation characterized by seizure, weakness of left side of the body and persistent HT.

CASE
A previously healthy eight-year-old girl was admitted for complaints of headache, focal seizure and weakness involved left side of the body and face as well as decreased level of consciousness. There was no recent trauma and drug use. The family history was unremarkable and not specified a stroke or cardiovascular event at an early age. Consanguinity was determined between the parents. On physical examination, she had a weight of 24 kg (25p-50p) and a height of 130 cm (75p). Vital parameters were as follows; body temperature: 36.5 °C, heart rate: 92/min, respiratory rate: 26/min, blood pressure (BP): 165/102 (>99p/ >99p), oxygen saturation: 98% and capillary refill...
time: 2 seconds. She was lethargic with a Glasgow coma scale of 13. Her neurological examination revealed hemiparesis on the left side including face, extensor plantar response and increased deep tendon reflexes on the left. Other system examinations were normal. Initial laboratory tests; white blood count: 12.900/mm³, hemoglobin: 11.4 gr/dl, platelet count: 318.000/mm³, c-reactive protein: 0.89 mg/dl, glucose: 72 mg/dl, creatinine: 0.5 mg/dl, aspartate aminotransferase: 27 u/l, alanine aminotransferase: 13 u/l, sodium: 140 mmol/l, potassium: 3.5 mmol/l, calcium: 9.6 mg/dl, phosphate: 3.5 mg/dl, triglycerides: 77 mg/dl, low and high density lipoproteins: 65 and 47 mg/dl, blood gas values pH: 7.39, PCO₂: 42.5, cHCO₃⁻: 25.6, SO₂: 97.3, lactate: 0.79, base excess: 0.6. Coagulation parameters were as follows; prothrombin time: 13.3 seconds, partial thromboplastin time: 22.7 seconds. Chest x-ray and electrocardiogram were normal. The urine panel tests which were all negative to rule out vasculitis. We had a rather high suspicion of secondary HT as eye fundoscopy was compatible with stage 1 hypertensive retinopathy. Due to the persistence of HT, propranolol (1 mg/kg/day) was added to the treatment and the dose increased to 2 mg/kg/day.

In this particular patient, we suspected renovascular HT and cerebrovascular stroke caused by FMD. Consequently, renal artery Doppler ultrasound (US) showed that right kidney size (long axis: 67 mm) was smaller than left (long axis: 88 mm). Additionally a higher peak systolic flow was detected in the proximal part of the right renal artery secondary to the suspected renal artery stenosis. Also, no renal or adrenal masses were found on ultrasonographic examination. Renal magnetic resonance angiography revealed focal narrowing of the renal artery (Figure 3). In addition, due to uncontrolled hypertension, losartan (1 mg/kg/day, P.O.) was also added to the treatment. Conventional angiography and balloon angioplasty were performed without complications in the same setting (Figure 4A,B). Initially prescribed captopril treatment was continued due to prompt correction of renal artery pathology and also, normal serum creatinine and serum potassium levels. On follow-up, propranolol was discontinued due to the control of BP. However, she needed to continue two antihypertensive drugs. An electroencephalography obtained revealed right hemispheric focal spikes. Therefore, carbamazepine was started and phenytoin was gradually tapered. Enoxaparin therapy was switched to acetylsalicylic acid (4 mg/kg/day) within the first month of follow-up. The patient was enrolled in a physical therapy and rehabilitation program. Antiphospholipid antibody, antithrombin III, protein C, protein S, fibrinogen and homocysteine values were within the normal ranges. The results of hemoglobin electrophoresis was normal. Factor V Leiden mutation and prothrombin gene mutation were not detected. Four months after discharge, our patient’s BP was monitored with a 24-hour ambulatory blood pressure measurements [mean arterial BP was 82 mmHg (SDS: 0.7) at all time, 84 mmHg (SDS: 0.0) at daytime and 70 mmHg (SDS: 0.24) at nighttime]. Hemiparesis also improved apparently as well as no new seizures and stroke attacks were observed. At the sixth month of follow-up, she was

Figure 1: A) Apparent Diffusion Coefficient Mapping and B) Magnetic Resonance B1000 Imaging shows diffusion restricted lesion.
able to walk with no seizures or stroke attack. Currently, she is on carbamazepine (20 mg/kg/day), captopril (1 mg/kg/day), losartan (1 mg/kg/day) and acetylsalicylic acid (3 mg/kg/day) treatment with no symptoms.

**DISCUSSION**

The most interesting aspect of this case is the manifestation of signs of acute stroke and persistent HT on initial clinical presentation that directed us to diagnose FMD as a result of renal examination and imaging studies. On the occasion of this case, we emphasize the importance of the management of pediatric FMD patients who manifest with acute stroke and persistent hypertension.

Pediatric stroke is a rare condition with an incidence of 0.6 to 7.9 per 100,000 children per year (1,7-9). Furthermore, pediatric stroke is rare but a significant cause of short-and long-term morbidity and mortality in children. It can be divided into three categories: arterial ischemic stroke (AIS), hemorrhagic stroke and cerebral sinovenous thrombosis (9). This case report also focuses on FMD as one of the causes of AIS.

**Figure 2:** 3D Time-Of-Flight brain magnetic resonance angiography shows sequentially narrowed and normal calibrated areas on middle cerebral artery M1-M2 segments.

**Figure 3:** Renovascular magnetic resonance angiography shows narrowness on proximal part of the right renal artery.

**Figure 4:** Appearance of angiography of renal artery A) Before and B) After angioplasty. Normal calibrated renal artery is shown after angioplasty.
There are no specific criteria for the diagnosis of FMD and it may be difficult to distinguish from other causes of AIS in children. The diagnosis of FMD depends on the clinical findings, angiographic appearance and, if possible, pathological findings. The clinical presentation may vary from an asymptomatic condition to multiorgan disease including renovascular HT, AIS, cranial hemorrhage due to arterial dissection and abdominal pain or claudication. The disease can mimic vasculitis such as polyarteritis nodosa, giant cell arteritis or Takayasu arteritis (1,5). Our patient manifested with the symptoms of arterial insufficiency of brain and arterial occlusion of kidney. She presented with headache, seizures and other signs of stroke as well as persistent HT. On follow-up, no evidence of intracranial bleeding was observed and thus the patient was considered to have an ischemic stroke. Although vasculitis was not definitely ruled out, the lack of inflammatory markers and no involvement of the skin and joints excluded the diagnosis of vasculitis in this patient. Due to the lack of underlying cardiac disease and family history of stroke and myocardial infarction at an early age, embolism was not considered primarily.

Fibromuscular dysplasia mostly affects the middle or distal parts of the renal artery followed by the middle and distal portions of the carotid and vertebral arteries bilaterally. This entity is characterized by “string of beads” appearance on angiography. However, there are also rare types, as in our case, that the appearance of a typical “string of beads” was so prominent, especially in young girls aged between 5 and 15 years (4, 6). In this case, we observed a unilateral stenotic area in the proximal part of the renal artery and focal segmental irregularities in the deep part of the middle cerebral artery. Moyamoya disease is another condition that needs to be evaluated in the differential diagnosis. Bilateral and progressive narrowing and collateral formation in internal carotid artery and its major branches as well as circle of Willis are characteristics of this disease (10). In our patient, because of unilateral and nonprogressive course as well as the absence of the characteristic angiographic appearance suggesting formation of collaterals, moyamoya disease was not considered (Figure 2).

Severe HT with acute neurologic symptoms is usually the most complicated and difficult clinical scenario, as the differential diagnosis includes AIS, hemorrhagic stroke, head trauma and hypertensive encephalopathy. It has been reported that the signs such as headache, confusion, nausea and vomiting usually abate after the blood pressure is lowered and that the edema was resolved in patients with stroke and head trauma. Although HT is a common situation following stroke, its optimal management is controversial, especially in children. HT can result from the stress of stroke, full bladder, pain, preexisting hypertension, a response to hypoxia or increased intracranial pressure. HT usually resolves after the management of edema in stroke and this creates a dilemma for the diagnosis and treatment (11,12). Our patient was initially considered as having HT associated with stroke and edema. Consequently, renal artery Doppler US and renal MR angiography were performed for persistent HT and showed renal artery stenosis compatible with FMD.

Disease-specific treatment is not yet available. According to the clinical condition of the patient, anticoagulation and antiplatelet therapy as well as percutaneous angioplasty are the treatment of choice. Percutaneous angioplasty, anticoagulation and antiplatelet therapies are especially recommended for patients with transient ischemic attack or stroke (1). The goal of treatment is the control of BP and preventing the complications associated with HT in FMD patients. The initial treatment may also be percutaneous balloon angioplasty (4). Our patient had persistent HT despite antihypertensive drugs. Therefore, we performed balloon angioplasty without stent implantation. The need for antihypertensive drugs was partially reduced after angioplasty and BP has been kept under control with two antihypertensive drugs and monitored closely for possible angioplasty needs.

In conclusion, stroke is an unusual condition in childhood. Moreover, FMD is a very rare cause of childhood stroke. In cases with treatment-resistant HT and stroke, FMD should be kept in mind in the differential diagnosis. Early diagnosis and appropriate treatment may prevent complications and may be life-saving. Furthermore, conventional angiography and percutaneous angioplasty may be an effective method of choice for the diagnosis and treatment.

REFERENCES


