Fibromuscular dysplasia as a cause of stroke in a 9-year-old girl

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Fibromuscular dysplasia is a rare, idiopathic and nonatheromatous disease. It is rarely encountered as a cause of stroke in children. We report a nine-year-old girl with stroke in whom extensive fibromuscular dysplasia of intracranial vessels was established. She also had familial combined hyperlipidemia as an additional risk factor. This case suggests that additional risk factors like hyperlipidemia in cases with fibromuscular dystrophy may facilitate the occurrence of stroke at early ages.

Key words: fibromuscular dysplasia, stroke, child

Stroke is increasingly recognized in children. The reported incidence for pediatric stroke is about 3 per 100,000 children per year[1]. Sensitive neuroimaging techniques and molecular testing for genetic prothrombotic risk factors have contributed to a rising number of cases. Congenital heart malformations, hematological disorders like sickle cell anemia, infections, and collagen tissue disorders are the main predisposing conditions for ischemic stroke in children, but about half of the ischemic strokes occur in previously healthy children[2]. Vascular, intravascular and embolic risk factors contribute to ischemic stroke in children. Regarding the vascular disorders, arteriopathies, vasospastic disorders, vasculitis, and systemic vascular diseases are the most common causes[3]. Fibromuscular dysplasia (FMD) is a non-inflammatory, non-atherosclerotic arteriopathy that involves small- and medium-sized vessels. It is a diagnosis made based on the appearance of vessels on angiography or on pathology. The most frequently affected vessels are renal arteries followed by internal carotid, intestinal and iliac arteries[4]. When cephalic arteries are affected, it may be a cause of cerebral ischemia. It is an uncommon cause of stroke in children, and a 10-year retrospective study including 27 children with ischemic stroke showed that FMD was the cause of stroke in two cases (7%)[5]. Here, we report a case of a childhood stroke caused by FMD of the right carotid, middle and anterior cerebral arteries. She also had hyperlipidemia as an additional risk factor.

Case Report

A nine-year-old girl presented with sudden-onset right-sided weakness. She was previously healthy and had no history of recent trauma, infection or vaccination. There was no family history for premature stroke, myocardial infarction or deep venous thrombosis.

The patient was afebrile and vital signs were normal. Blood pressure was 90/60 mmHg. On neurologic examination, she was fully conscious and cooperative. Cranial nerve examination revealed left central facial paralysis. Strength in the right upper and lower extremities was normal (5/5), but greatly diminished on the left (1/5). Deep tendon reflexes were hyperactive on the left and left plantar response was extensor. Skin examination revealed no signs of café- au-lait spots, neurofibromas or freckling of the groin or the axilla. The remainder of the physical examination revealed no pathological finding.

Diffusion-weighted magnetic resonance imaging revealed diffusion restriction in the right putamen, nucleus caudatus and posterior limb

of the internal capsule consistent with acute infarction (Fig. 1). Time of flight magnetic resonance angiography (MRA) showed beading and decrease in caliber in the right supraclinoid segment of the carotid artery and middle cerebral artery (Fig. 2). In the superior-anterior part of the M1 segment of the middle cerebral artery, there seemed to be a second lumen with a signal intensity lower than of the primary lumen but higher than of the parenchyma. These findings suggested dissection superimposed on FMD in the middle cerebral artery, which compromised the origin of the lenticulostriate arteries and led to striatocapsular infarct. Digital subtraction angiography (DSA) performed one week after the MRA showed the typical "string of beads" appearance of FMD in the right supraclinoid segment of the carotid artery, M1 and M2 segment of middle cerebral artery, and A1 segment of anterior cerebral artery (Fig. 3). Dissection, however, was not confirmed. It was assumed that the dissected intima had sealed during the interval between the MRA and the DSA or that the second lumen appearance resulted from motion artifacts. Abdominal magnetic resonance imaging of the patient was normal.

Complete blood count, coagulation parameters, antiphospholipid antibodies, antithrombin III, protein C, protein S, and homocysteine were normal. Factor V Leiden, methylenetetra

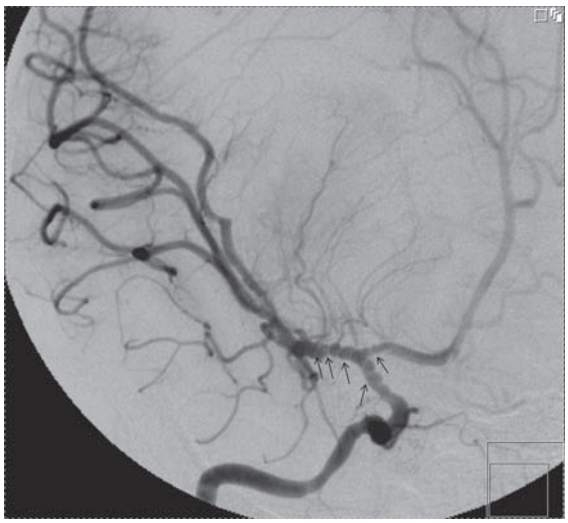

Figure 1. Transverse diffusion-weighted isotropic image shows an area of infarction in the right putamen (arrow).

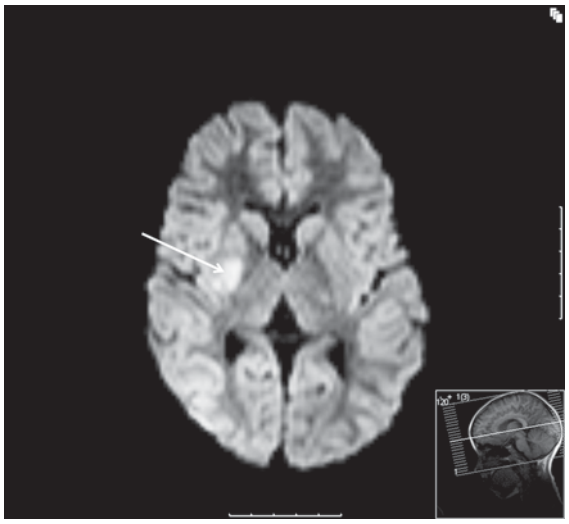

Figure 2. Source image for the cerebral time of flight magnetic resonance angiography. The beaded appearance (small arrows) of the middle cerebral artery is quite characteristic of FMD, whereas the second lumen appearance (thick arrow) suggests a dissection.

hydrofolate reductase and prothrombin G20210A mutations were negative. Serum cholesterol, triglyceride and low- and high-density lipoproteins (LDL, HDL) were 303 mg/dl (122-209), 122 mg/dl (35-114), 221 mg/dl (60-150), and 58 mg/dl (35-84), respectively. Cardiac examinations including echocardiography and electrocardiography were normal. The lipid profile of both parents also showed increased levels of cholesterol, triglyceride and LDL. Familial combined hyperlipidemia was suggested, and a low- cholesterol, low-saturated fat diet was started.

Aspirin at a dosage of 3 mg/kg/day was started for its antiplatelet effects, and physical rehabilitation was instituted for hemiparesis. No further strokes appeared in the follow-up period of six months, and at present, she has mild hemiparesis and is able to walk independently.

Discussion

Fibromuscular dysplasia (FMD) is a systemic arteriopathy that has a predilection for renal arteries followed by cervicocranial vessels. One autopsy study showed that the prevalence of FMD is 1.1% in the general population[6]. The etiology of the disease is still unknown. FMD is classified histologically according to

whether it predominantly affects the arterial media, intima or adventitia. Medial dysplasia is the most common histologic type followed by intimal and adventitial fibroplasia. In medial dysplasia, the media of the artery has both very thin and thick areas without inflammatory cells. In intimal fibroplasia, the intima is very thick with circumferential collagen deposition. Finally, in adventitial fibroplasia, dense collagen replaces the fibrous tissue of the adventitia[7]. It is reported in association with connective tissue disorders like Ehlers-Danlos syndrome and alpha-1-antitrypsin deficiency[8,9]. Familial cases have also been described leading to suspicion of a genetic disorder. In our case, there was no family history of FMD and there was no finding of a connective tissue disorder on physical examination. Although we did not measure the activity of alpha-1-antitrypsin, the patient showed no signs like cirrhosis or emphysema that are typically associated with this condition. FMD should also be differentiated from the vasculopathy of neurofibromatosis, especially since both can affect cranial and renal arteries and cause similar symptoms.

Among the brain vessels, the most commonly involved vessels are extracranial carotid arteries followed by vertebra-basilar and intracranial carotid arteries. The involvement is often bilateral[10]. The reports describing patients with extensive intracranial involvement are scarce[11,12]. Our case is remarkable for the extensive unilateral involvement of the intracranial carotid artery, middle cerebral artery and a portion of the anterior cerebral artery. On the other hand, the most common presentation of FMD is renovascular hypertension secondary to renal artery involvement. This is particularly important because the coexistence of focal neurological deficits and hypertension is important. The blood pressure of the case at presentation was normal and the measurements during follow-up were in normal limits for her age group. Blood pressure measurements of cases with FMD at certain intervals are important because one large study of 40 patients with intracranial FMD demonstrated renal involvement in 5 of 16 patients investigated with renal arteriograms[13,14].

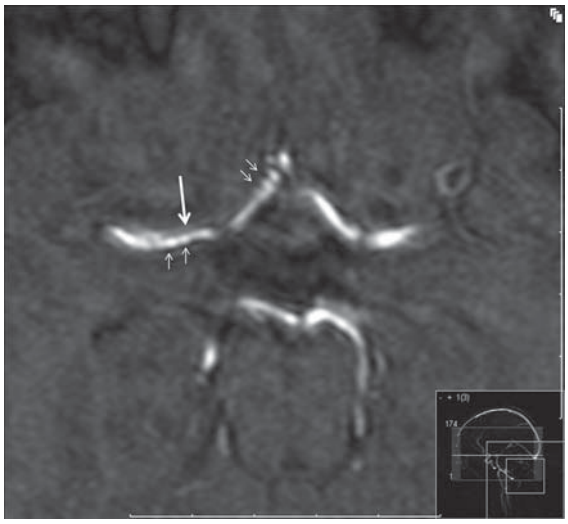

Figure 3. Right carotid angiography obtained in the right oblique projection shows the classic beaded appearance consistent with FMD (arrows).

Fibromuscular dysplasia (FMD) is associated with an aneurysm in 20-40% of cases. It also predisposes to dissection[15]. On the other hand, luminal narrowing may lead to transient ischemic attacks and cerebral infarction. In the conventional angiographic study of the patient, no finding of an aneurysm or dissection was observed, and luminal narrowing was suspected as the cause of the ischemic infarct. Although the prevalence of FMD in autopsy series is 1.1%, every case with FMD is not symptomatic. This suggests that there may be predisposing factors that may facilitate the occurrence of symptoms. Atherosclerosis as a cause of stroke in children is rare as compared to adults[16]. In children, the lipoprotein abnormality may lead to occlusive cerebrovascular atherosclerosis leading to ischemic stroke[17]. The patient was also diagnosed as familial combined hyperlipidemia, and we suggest that this finding facilitated the occurrence of ischemic stroke as an additional risk factor to FMD.

Magnetic resonance angiography (MRA) is an important diagnostic tool for FMD, but the exact diagnosis is established with conventional angiography. The "string of beads" appearance is characteristic for FMD, and the angiographic appearance in our case was in harmony with FMD. The treatment options include antiplatelet agents, anticoagulant agent and surgical treatment. If there is severe stenosis or the drug therapy fails, surgical treatment is considered. Our case was treated with aspirin, because the stenosis was not severe and symptoms were not progressive.

In conclusion, increasing awareness of stroke

in children has increased our knowledge about the etiology, diagnostic methods and treatment options for cases. FMD as a cause of stroke is rarely encountered in children, and this report adds a new childhood case of FMD with extensive intracranial vessel involvement. FMD should be considered in the differential diagnosis of childhood stroke cases. Additional risk factors like hyperlipidemia in cases with FMD may facilitate the occurrence of stroke at early ages.

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