Case Report: Moyamoya Disease in a Caucasian Infant with Early and Severe Clinical Presentation

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Abstract: Moyamoya disease is a chronic progressive cerebrovascular disease of the arteries around the circle of Willis with prominent arterial collateral circulation. We describe a 15 month old Caucasian female infant, who was admitted to our hospital due to left hemiparesis. Magnetic resonance imaging demonstrated occlusion at the terminal portion of the internal carotid artery, at the proximal portion of the anterior and middle cerebral arteries and stenosis of posterior cerebral arteries bilaterally. Magnetic resonance angiography and conventional cerebral angiography revealed the characteristic abnormal vascular network known as "puff of cigarette smoke". An extensive laboratory workup was performed to rule out underlying diseases such as coagulopathy, autoimmune or infectious diseases. The infant underwent a surgical procedure of bilateral neurosurgical revascularization, encephalomyosynangiosis, initially on the right and then on the left cerebral hemisphere. Clinical improvement was gradually noticed after the surgery. Our patient is a rare case of MMD as she is non-Asian, with early and severe clinical presentation, and extended radiological lesions at the time of diagnosis.

Keywords: Moyamoya, stroke, cerebrovascular, encephalomyosynangiosis, carotid occlusion.

INTRODUCTION

Moyamoya disease (MMD) is a rare idiopathic cerebrovascular disorder, which is characterized by progressive stenosis or occlusion of the distal internal carotid artery (ICA) and proximal cerebral arteries, with an extensive network of cerebral collaterals [1]. MMD, which has been named after the Japanese word "Moyamoya" meaning a puff of smoke in the air, is described mainly in Japan and other Asian countries and characterized by the smoky angiographic appearance of the vascular collateral network. In this case study we describe a young European female diagnosed with MMD.

CASE REPORT

A 15 month old Greek female was presented to our hospital due to sudden onset of left hemiparesis. Her parents recalled an episode of transient paresis of her left leg one month ago that was not further investigated, but her neonatal and past medical history were otherwise unremarkable. On physical examination, there were noted neurological signs compatible with left hemiparesis, such as diminished muscular strength and tone of the left side, normal examination of the cranial nerves and equal sized pupils.

The patient underwent a full laboratory investigation, including full blood count, biochemical tests, clotting screening and tests for autoimmune and metabolic disorders, which was within normal limits, an echocardiography that was unremarkable and a non-enhanced computed tomography (CT) that revealed hypo dense areas in the frontoparietal and occipital regions in the right cerebral hemisphere.

She was further investigated with a magnetic resonance imaging (MRI), revealing well-defined wedge-shaped hyperintensities in bilateral frontal, parietal, parieto-occipital, basal ganglia and subcortical white matter, suggestive of acute and chronic ischemic lesions (Figure 1). Basal ganglia collaterals were noted and therefore MMD was considered as a possible diagnosis.

Magnetic Resonance Angiography (MRA) images through the circle of Willis revealed near-complete occlusion of both supraclinoid internal carotid arteries (ICAs), middle, anterior and right posterior artery (Figure 2). The collateral "Moyamoya vessels" in the basal ganglia resembled a 'puff of smoke'.

Following the MRA, a conventional cerebral angiography (CCA) was performed, that revealed near-complete occlusion of both supraclinoid ICAs, anterior cerebral arteries and right posterior artery (Figures 3 and 4). Both anterior cerebral arteries seemed to fill from the collaterals. Vascular channels in the skull-
base region (leptomeningeal collaterals) and basal ganglia resembled a ‘puff of smoke’. External carotid arteries (ECA), common carotid arteries and the basilar system were normal. All laboratory and imaging findings were compatible with MMD.

**Figure 1:** Axial T2 weighted image shows multiple hyperintense lesions in the right frontal, parietal, and parito-occipital lobe. A small high signal lesion is also noted at the left parietal lobe.

**Figure 2:** Magnetic resonance angiography of the circle of Willis reveals occlusion of supraclinoid internal carotid arteries bilaterally and the middle, anterior and right posterior artery.

During her hospitalization, the patient had another major ischemic stroke that presented with right hemiparesis, therefore she was administered antiplatelet and antiepileptic medication. She also underwent encephalomyosynangiosis, an indirect revascularization surgical procedure, initially on the right and one month later on the left cerebral hemisphere. However, even after the second operation, the child had a new stroke presented as an episode of jaw’s focal convulsions making her unable to swallow.

**Figure 3:** Left internal carotid angiogram confirms a) subclinoid occlusion of the left internal carotid (black arrow) and reveals vascular collateral network called puff of smoke (red arrow) b) occlusion of the left middle cerebral artery (red arrow) and stenosis of the anterior cerebral artery (black arrow).

It was not until two months later that our patient showed signs of gradual clinical improvement, such as minimal movements of the right hand and leg and ability of swallowing but not drinking. She was discharged after 5 months of hospitalization, followed thereafter on the outpatients’ neurohabitation and physiotherapy department.
Figure 4: Right internal carotid angiogram reveals stenosis of anterior cerebral artery (arrow).

DISCUSSION

Moyamoya disease was first described in Japan in 1957. Many similar cases have been reported, mainly in Japan and other Asian countries, but less frequently in North America and Europe. The annual incidence of MMD is estimated at 0.35 to 0.94 per 100,000 population, with a female predominance. Age distribution of MMD varies with a higher peak reported in the 45-49 year old group and a lower peak in the 5-9 year old group. To the best of our knowledge, our patient is the youngest European child with MMD referred to literature, with severe clinical presentation and extended radiological lesions.

The natural history of MMD tends to be progressive. The vascular pathology usually worsens with extensive intracranial large artery occlusion and collateral circulation. Patients often suffer cognitive and neurologic decline due to repeated ischemic stroke or hemorrhage. MMD may have a more rapid progression and a worse prognosis in younger than in older children, especially in children less than three years old mainly because of preoperative infarctions [1].

Regarding the pathogenesis of MMD, the thickened intima, luminal thrombosis and angiogenesis seems to have a critical role [2]. High levels of fibroblast growth factor and transforming growth factor beta-1, which may stimulate arterial growth and neovascularization, have been found in the vascular intima, media, and smooth muscle among patients with MMD. Autoimmune disorders and thrombophilia have been associated with some cases as the underling mechanism, while in others a potential genetic association to chromosome 17 has been demonstrated [3]. Although the mode of inheritance is not established, one study suggested that familial MMD is an autosomal dominant disease with incomplete penetrance, suggesting that genomic imprinting and epigenetic modification may account for the predominantly maternal transmission and elevated female to male incidence ratio. There are two distinguishable forms of MMD, the primary or true MMD and the secondary or Moyamoya syndrome. Primary MMD accounts for idiopathic, as in our case, or familiar forms while secondary form is associated to congenital heart disease, atherosclerosis, infectious diseases, hematologic conditions such as sickle cell diseases and beta thalassemia, factor XII deficiency, metabolic diseases, homocystinuria, vasculitis and autoimmune diseases, systemic lupus erythematosus, Grave’s disease, antiphospholipid antibody syndrome, connective tissue disorders and neurocutaneous syndromes, neurofibromatosis type 1, vasospasm after subarachnoid hemorrhage, cranial trauma, and brain tumors.

The clinical manifestations of MMD vary and include transient ischemic attack (TIA), ischemic stroke, hemorrhagic stroke, and epilepsy. Ischemic cerebrovascular events, either TIA or infarction, are more prevalent than hemorrhagic events in children, nevertheless symptoms such as headache, chorea, cognitive or psychiatric changes can be noticed. The diagnosis of MMD is based on the clinical presentation and radiological findings. Head CT and brain MRI are important studies for the detection of brain infarction and hemorrhage in patients with MMD, while noninvasive and conventional angiographic studies can demonstrate stenosis or occlusion of the circle of Willis vessels. However, the conventional cerebral angiography remains the gold standard imaging technique for the diagnosis of MMD. The characteristic angiographic appearance of bilateral stenosis affecting the distal internal carotid arteries and proximal circle of Willis vessels, along with the presence of prominent basal collateral vessels is typical for MMD. The angiography of our patient revealed occlusion of both ICAs, middle, anterior and right posterior artery and the presence of the collateral "Moya Moya vessels".

Diagnostic criteria for idiopathic MMD have been established by a Japanese research committee including stenosis or occlusion at the terminal portion of
the ICA and at the proximal portion of the anterior and middle cerebral arteries on MRA, abnormal vascular networks in the basal ganglia on MRA and exclusion of conditions such as arteriosclerosis, autoimmune disease, brain neoplasm, Down syndrome, head trauma and neurofibromatosis [4].

The management of the patients with MMD is focused initially on the revelation of the underlying condition as well as on the conservative prevention of new ischemic episodes and emboli, using antiplatelet agents or anticoagulants. Aspirin has been used in the treatment of patients with asymptomatic or mildly symptomatic ischemic disease. On the other hand, oral anticoagulants are seldom used in children with ischemic MMD because of the risk of hemorrhage after incidental trauma and because of the difficulty in maintaining therapeutic levels.

For patients with symptomatic MMD a surgical revascularization procedure is required, with risk of perioperative stroke rate estimated in 4.4% and the postsurgical improvement in about 85% [5]. Surgical techniques can be divided into direct, indirect and combined revascularization procedures. Superficial temporal artery to middle cerebral artery bypass or middle meningeal to middle cerebral artery bypass are the most common direct techniques. Direct methods are technically difficult to perform in children because of the small size of donor and recipient vessels. Indirect techniques include encephaloduroarteriosynangiosis, encephalomyosynangiosis, encephaloarteriosynangiosis and omentum transplantation. Our patient underwent encephalomyosynangiosis, a procedure involving the placing of temporalis muscle in direct contact with the brain in order to promote vascularization to the underlying cerebral cortex. Although she experienced a postoperative stroke she showed a gradual clinical improvement in the following months of her hospitalization.

In summary, strong clinical suspicion for MMD should be erased in the case of a child presented with a cerebrovascular event, without underlying condition or any risk factors. The disease should prompt suspicion even in younger children of Caucasian origin, bearing in mind that MMD although rare, can affect children on non-Asian origin.

An angiography can demonstrate the specific radiological findings and is essential for the confirmation of the diagnosis. In final, surgical treatment, which consists of direct or indirect vascularization, remains the treatment of choice for symptomatic patients with considerable good outcome.

ABBRIVEATIONS

MMD = Moyamoya disease
ICA = Internal carotid artery
CT = Computed tomography
MRI = Magnetic resonance imaging
MRA = Magnetic resonance angiography
CCA = Conventional cerebral angiography
ECA = External carotid artery

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