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Moyamoya Disease in a Child with Glycogen Storage Disease Type Ia

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Abstract

A three-year-old child affected by glycogen storage disease (GSD) type Ia presented with acute hemiplegia secondary to Moyamoya disease. So far, the association of moyamoya with GSD Ia had only been reported twice. The rarity of both conditions makes their association unlikely to be a

chance event and an etiological relationship between them must be considered.

Key words: Moyamoya disease - Glycogen storage disease type Ia

Abbreviations

EDAMS: encephaloduroarterio- MRI: magnetic resonance
myosynangiosis imaging
ICA: internal carotid artery TIA: transient ischemic attacks
MCA: middle cerebral artery GSD: glycogen storage disease

Moyamoya disease is a cerebrovascular disease characterized by repeated cerebral ischemic attacks with progressive occlusion of both internal carotid arteries (ICA) and of their branches and formation of an exuberant collateral network of blood vessels at the base of the brain. It has been first described in Japan as primitive arteriopathy but the disorder may also develop as secondary phenomenon of vascular occlusion in several conditions and it has been reported in children both as a primary phenomenon or associated with underlying disease (1, 8, 9). We report on a child with moyamoya disease and GSD type Ia.

Case history and results

This caucasian boy developed normally until the age of 37 months, when, following a mildly febrile pharyngitis he presented one evening a transient weakness of the left side of the body and was found on awakening the following morning with a left-sided paralysis. Since the age of two, his parents recorded bouts of painless hypotonia of the left arm related to "pulled elbow" and retrospectively interpreted as transient ischemic attacks (TIA). Examination showed a bright child with a left-sided hemiplegia and pyramidal tract signs predominating in the lower limb. The abdomen was enlarged with a voluminous soft liver reaching 16 centimeters below the costal margin (which had never been noted before). Blood pressure was 120/80, cardiac and vascular examination were normal. Laboratory investigations showed normal values for serum glucose, electrolytes, urea, bilirubin and cholesterol. WBC count was 7.700/mm³ with 66 % neutrophils; platelets: 534.000/mm³; hematocrit: 32.4 %; prothrombin: 93 %; activated partial prothrombin time: 56 sec (N: <70). Bleeding time was 9 min. Abnormal serum values were recorded for triglycerids: 5.9 mmol/l (N: 0.55 - 1.70), lipoprotein a: 0.81 g/l (N <0.3), SGOT: 100 U/l and SGPT: 70 U/l (N: 5-20). CSF was normal.

Cerebral MRI showed on T₂-weighted sequences an increased cortical signal of the right paracentral lobule and a more limited symmetrical lesion on the left side. Partial obstruction of the lumen of the right transverse sinus was seen on MRI angiography. These findings were interpreted as cortical softening following partial thrombosis of the right transverse sinus. Liver biopsy showed macrovesicular steatosis of hepatocytes with normal Kupffer cells, suggestive of GSD. The diagnosis of GSD type Ia was confirmed by the enzymatic assay (deficiency of glucose-6-phosphatase hepatic activity). Molecular study of the glucose-6-phosphatase gene showed that the child was homozygous for the Q 347 X mutation, previously described by Lei et al (7). As the child was able to tolerate a 15-hour fast, he was just given cornstarch (1.5 g/kg) at every meal. The hemiplegia progressively resolved and he was left within two months with a mild motor deficit limited to the left leg. The following months, he episodically presented transient difficulties to hold an object in his hand, right or left. Nine months after the hemiplegia, MRI showed bilateral symmetrical frontoparietal atrophy sequelae of the softening and increased visibility of the vascular network in the deep cerebral white matter and the basal ganglia on both sides, suggestive of moyamoya disease (Fig. 1). This was confirmed by angiography, showing severe stenosis of both ICA at the level of the siphon with no flow through the right middle cerebral artery (MCA) and minimal flow through the left anterior cerebral artery and distal MCA (Fig. 2). An important anastomotic network through telangiectatic lenticulostriate arteries was developed on both sides. Vertebral injection showed contribution to the extensive deep collateral vessels through thalamic and posterior choroidal vessels. The angiography did not confirm the thrombosis of the right transverse sinus. Following these findings, the initial frontoparietal softening was retrospectively interpreted as secondary to arterial occlusion. Despite treatment with nimodipine 15 mg/day, repeated TIA affecting the left arm led to perform an indirect revascularization procedure by a right encephaloduroarteriomyosynangiosis (EDAMS). This was followed 36 hours later by complete flaccid left-sided hemiplegia related to postsurgical cerebral edema. Pyracetam (900 mg/day) was added to nimodipine 30 mg/day. The left-sided hemiplegia disappeared within two months. Protein S, protein C and antithrombin III plasma concentrations were normal or slightly increased (130 % of controls), anti-cardiolipine IgG antibody was not detected in the serum. At the age of 5 years, contralateral TIA occurred with paralysis of the right arm and aphasia and EDAMS was performed on the left side.

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Fig. 1 MRI T₁-weighted sequences: increased visibility of the deep vascular network in the basal ganglia and white matter.

Discussion

Our patient had clinically asymptomatic GSD Ia that was fortuitously discovered after admission for acute ischemic stroke due to moyamoya disease (demonstrated 9 months later). The child was normoglycemic at the time of the stroke and during the subsequent TIA which occurred on the other side. Furthermore, he was able to tolerate prolonged fasting as previously observed in some patients with GSD Ia (5). No coagulation defect could be responsible for the stroke; thrombocytopenia was documented several times after the stroke but with increased bleeding time in favor of an hypocoagulatory state and dysfunction of platelets aggregation, as frequently encountered in this type of GSD in which bleeding tendency is a frequent manifestation (3). The child also had hyperlipemia and hypertriglyceridemia but the arterio-

graphic findings were not those encountered in this situation and were typical of moyamoya disease (12). In connection with this, Lee et al (6) have shown that, in spite of hyperlipemia, vascular endothelial function was not impaired in GSD Ia patients.

The association of GSD Ia and moyamoya has been previously reported by Sunder in a 17-year-old boy with acquired hemiplegia followed by TIA and severe stenosis of both carotid arteries with abundant collateral network of deep-penetrating vessels (11). Another child with acute hemiplegia and GSD type Ia has been reported by Fine et al (2). Although no arteriographic demonstration was available, this patient might also have had moyamoya on clinical presentation with several episodes of amaurosis suggestive of TIA following acute hemiplegia. The rarity of both conditions makes their association a non-fortuitous event and one must consider a relationship between them. In a GSD Ia teenage girl with pulmonary hypertension, Pizzo described anatomic vascular changes with medial hypertrophy and intimal fibrosis (10). These data have been recently confirmed (4). Similar pathologic findings have been described in cerebral vessels of patients with moyamoya (9), confirming the hypothesis of a relationship between both conditions. Circulating vasoactive agents normally removed or altered by the liver might lead to a primary vasoconstrictive process (4, 10). Nevertheless, vascular changes are not usually recorded in GSD Ia, and patients with pulmonary hypertension had no neurological manifestations (4, 10).

Furthermore, Pizzo reported that the brain was normal on post-mortem examination (10). Although a very uncommon association, GSD Ia may be considered a possible cause for moyamoya and it would be justified to look for this arteriopathy in every child with GSD Ia and unexplained normoglycemic neurological deficits.

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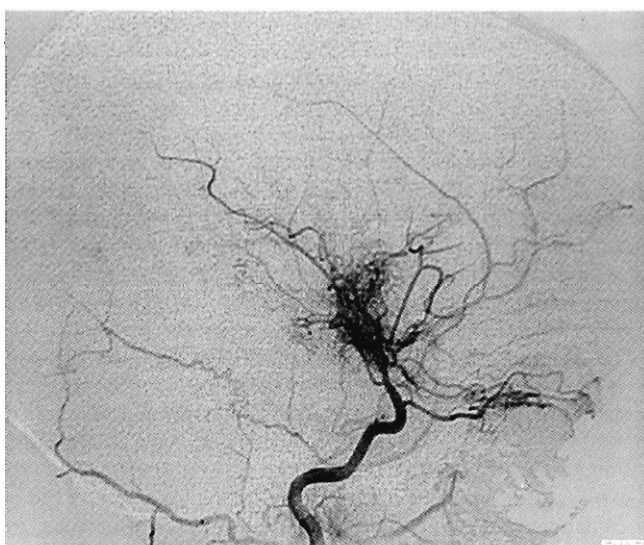


Fig. 2 Right carotid internal arteriography: stenosis of the carotid siphon with no flow through the right MCA and telangiectatic lenticulostriate arteries (moyamoya).