

Moyamoya Syndrome as a Severe Cerebrovascular Complication of Mucopolysaccharidosis Type I: Clinical Presentation and Underlying Mechanisms

Le syndrome de Moyamoya, complication cérébrovasculaire majeure de la mucopolysaccharidose de type I: Aspects cliniques et mécanismes physiopathologiques

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A 24 years-old-women, with a medical history of recurrent pneumonia, splenomegaly, pancytopenia, deforming polyarthritis since childhood, ischemic stroke, and arterial hypertension was admitted to the internal medicine department with a suspicion of lysosomal storage disease. Clinical examination showed no evidence of neurological deficit, growth delay or intellectual impairment. Moreover, the cardiovascular examination revealed tachycardia (105/minute), a diastolic murmur consistent with aortic regurgitation, systolic hypertension (160/80 mmHg), and bilateral carotid bruits. Musculoskeletal examination showed deforming polyarthritis characterized by flexion contractures of both elbows, fixed deformities of both wrists, and involvement of both proximal and distal interphalangeal joints. Laboratory investigations revealed pancytopenia characterized by leukopenia ($2.5 \times 10^9/L$, normal range $4-10 \times 10^9/L$), neutropenia ($0.8 \times 10^9/L$, normal range $1.5-7 \times 10^9/L$), anemia (hemoglobin 9 g/dL, normal range 12–16 g/dL), and thrombocytopenia ($70 \times 10^9/L$, normal range $150-400 \times 10^9/L$). C-reactive protein was elevated at 40 mg/L (normal < 6 mg/L). Renal function was normal, with an estimated creatinine clearance of 95 mL/min/1.73 m² (normal range 90–120 mL/min/1.73 m²). Liver function tests were within normal limits, with aspartate aminotransferase at 25 IU/L and alanine aminotransferase at 28 IU/L (normal < 35 IU/L). Antinuclear antibodies and anti-cyclic citrullinated

peptide antibodies were negative. Gaucher disease and Niemann-Pick disease were excluded by enzymatic assays. The elevated C-reactive protein level was attributed to acute pneumonia occurring in the context of neutropenia. It may also have been partly related to the underlying inflammatory polyarthritis. In addition, the pancytopenia was considered to be secondary to hypersplenism.

The diagnosis of Mucopolysaccharidosis Type I (MPS I), particularly the attenuated MPS I phenotype (previously referred to the Scheie syndrome), was confirmed by alpha-L-iduronidase deficiency. Computed tomography angiography of the supra-aortic and cerebral vessels revealed bilateral stenosis of the internal carotid arteries associated with Moyamoya syndrome (occlusion of the intracranial internal carotid arteries on cerebral angiography with capillary collaterals resembling a puff of smoke or Moyamoya in Japanese), which was the underlying cause of the stroke [Figure 1]. Echocardiography revealed severe aortic regurgitation, valvular thickening, and hypertrophy of the left ventricle. The patient initiated enzyme replacement therapy with weekly Laronidase infusions (0.5 mg/kg/week), resulting in positive clinical outcomes. During follow-up (6 months), progressive clinical improvement was observed. Hematological parameters improved with partial

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resolution of pancytopenia: leukopenia ($3.5 \times 10^9/L$), anemia (hemoglobin 10 g/dL), and thrombocytopenia ($90 \times 10^9/L$). The patient also reported a reduction in arthralgia with mild improvement in joint mobility. Cardiac evaluation showed stabilization of the aortic regurgitation without further progression, and no new neurological events were documented.

MPS I is a rare lysosomal storage disorder caused by the accumulation of glycosaminoglycans (GAGs), leading to a multisystem disease. Neurological manifestations include hydrocephalus, spinal cord compression, and cognitive decline [1]. Cerebral arteriopathy in patients with MPS I may result from GAGs accumulation within the cerebrovascular system, predisposing them to arterial narrowing and recurrent strokes. Moyamoya syndrome is an under-recognized cerebrovascular complication in MPS I [2-4]. Cerebral revascularization represents a safe therapeutic strategy that may reduce the risk of future cerebrovascular events and should be strongly considered within the overall management guidelines for patients with MPS I [2, 5].

This case highlights the importance of a multidisciplinary approach, integrating musculoskeletal, hematologic, cardiovascular, and neurological findings in the diagnosis and management of MPS I. In attenuated phenotypes of MPS I, diagnostic delay is common, and the disease is frequently recognized in adulthood, which may expose patients to severe cardiovascular and neurological complications. Therefore, screening for cerebral arteriopathy and stroke should be considered in the management of patients with MPS I.



Figure 1. Computed tomography angiography of the supra-aortic and cerebral vessels showing long occlusions of both internal carotid arteries (black arrow) with extensive collateral vascular networks consistent with Moyamoya syndrome (red asterisk) in a patient with mucopolysaccharidosis type I.

Written informed consent of the patient was obtained

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