Moyamoya syndrome associated with neurofibromatosis type I in a pediatric patient

Síndrome de moyamoya associada a neurofibromatose tipo I em paciente pediátrico

Luiz Guilherme Darri哥o Júnior1, Elvis TerCI Valera2, André de Ab0im Machado3, Antonio Carlos dos Santos4, Carlos Alberto Scrideli5, Luiz Gonzaga Tone6

Department of Pediatrics, Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (FMRP-USP), Ribeirão Preto, São Paulo, Brazil

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INTRODUCTION

Neurofibromatosis type 1 (NF-1) is a multisystemic genetic disorder that displays important cutaneous manifestations such as café-au-lait spots, freckles and neurofibromas. Despite variable clinical expression, mutation of the NF-1 gene is considered to be the most common de novo spontaneous autosomal dominant genetic alteration in human beings, with complete penetrance.1 The incidence of NF-1 is approximately one in 2,500 births, affecting all races. About 80,000 cases are estimated to exist currently in Brazil, and about 1.5 million worldwide.1,2

The NF-1 gene is located on the long arm of chromosome 17, and more precisely, in the 17q11.2 band. This gene codes for neurofibromin, a protein that acts during nervous tissue growth remodeling.3 Recent studies have also demonstrated the presence of neurofibromin on the walls of vascular endothelial cells and in vascular smooth muscle cells.3

Moyamoya disease (MMD) is a rare inherited cerebral disorder of unknown etiology characterized by obliteration of the internal carotid artery and its branches, with the concomitant development of an abnormal network of collateral vessels. Moyamoya syndrome (MMS), an acquired form of MMD, also displays the angiographic pattern of MMD, although it is usually associated with different risk factors such as NF-1, Down syndrome and previous cranial irradiation, among others.4 Associations between NF-1 and vascular disorders are not uncommon, although associations between NF-1 and specific cerebrovascular disorders such as MMS are far less frequent.5,6

The objective of this study was to report on the case of a patient with NF-1 and MMS. This paper also provides a brief review of the main clinical and radiological aspects of this association. We conduct-
ed a systematic search in the PubMed, Cochrane Library, Lilacs (Literatura Latino Americana e do Caribe em Ciências da Saúde) and SciELO (Scientific Electronic Library Online) databases. The results obtained are shown in Table 1.

**CASE REPORT**

An eight-month-old Afro-descendant girl was referred to the emergency room of the University Hospital due to convulsive 5-10 minute seizures characterized by mucosal pallor, clonic movement to the right and right-sided head version. The patient presented postictal somnolence. No fever was observed at the time of the seizures. A cerebrospinal fluid tap yielded normal results. Brain magnetic resonance imaging (MRI) revealed asymmetry of the hemispheres, with hemiatrophy on the left (Figure 1A) and signs of internal carotid occlusion in the supraclinoid and basilar portions, with marked collateral circulation through perforating vessels, with a moyamoya pattern (Figures 1B to 1F). Hemiparesis was most evident in the right upper limb.

A diagnosis of ischemic stroke was made based on the clinical and radiological findings. Thrombophilia testing was negative. At one year and eight months of age, she was referred to the medical genetics service due to the presence of skin lesions, delayed motor development and facial dysmorphism. Physical examination revealed several café-au-lait spots (larger than 0.5 cm) and cutaneous neurofibromas. At two years of age, the patient presented facial paralysis with slight facial asymmetry of peripheral pattern. Her mother also fulfilled the diagnostic criteria for NF-1. The girl is the first child of non-consanguineous healthy parents. Regarding her neuropsychomotor development, she was able to hold her head up at the age of seven months, spoke her first words at the age of one year and seven months and sat up unsupported at the age of one year and nine months. The child is currently under clinical surveillance, and persists with motor deficits.

**DISCUSSION**

NF-1 occurs most frequently during childhood, and its diagnosis is based on the clinical criteria established by the National Institutes of Health (NIH) Consensus Development Conference. For a definitive diagnosis of NF-1, two or more of the following clinical character-

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**Figures 1A-1F.** Magnetic resonance imaging performed with Philips 3.0 Tesla apparatus showing FLAIR (fluid-attenuated inversion recovery) images (A), T2 (B), post-contrast T1 (C and D) and angioresonance of intracranial and cervical vessels (E and F). Asymmetry of the brain hemisphere can be seen in A, with marked atrophy on the left, distortion of the gyri and prominence of the sulci, involving the cortex and the left frontotemporal-parietal white matter, while sparing the ipsilateral occipital region (large arrow). B, C and D show exuberant tortuous collateral circulation above the occlusion of the supraclinoid internal carotids. E and F show occlusion of the internal carotids in the supraclinoid region and above the basilar artery, associated with exuberant and tortuous collateral circulation in perforating vessels (dotted and small arrows).
and particularly surgical revascularization in order to increase the blood flow to the hypoperfused cortex.³,⁶

**CONCLUSION**

The present report describes an additional case of associated NF-1 and MMS in a pediatric patient. Although this association is relatively uncommon, MMS is a potentially severe disease that may evolve with an unfavorable neurological course. Thus, the hypothesis that this association may be present should be considered in cases of patients with NF-1 and focal neurological symptoms, so that proper care can be promptly provided.

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Address for correspondence:
Luiz Guilherme Darrigo Júnior
Rua do Professor, 904
Jardim São Luiz — Ribeirão Preto (SP) — Brasil
CEP 14020-280
Tel. (+55 16) 38022651
E-mail: guimedicina@gmail.com