"Moya" than meets the eye: neurofibromatosis type 1 associated with Moyamoya syndrome

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ABSTRACT

Moyamoya syndrome (MMS) is an uncommon association of neurofibromatosis type 1 (NF1). We describe a seven-year-old chinese girl with NF1 and unilateral MMS with multiple hyperintensities on T2-weighted magnetic resonance (MR) images. The ischaemic lesions in the ipsilateral white matter were hypointense on fluid attenuated inversion recovery (FLAIR) MR images, in contrast to the hyperintense "unidentified bright objects" (UBOs) of NF1. Neuroradiologists should be aware of associated MMS in NF1 patients, and distinguish the effects of ischaemia from UBOs, especially on FLAIR MR imaging.

Keywords: cerebral ischaemia, cerebrovascular disease, magnetic resonance imaging, Moyamoya syndrome, neurofibromatosis, phacomatoses

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INTRODUCTION

Neurofibromatosis type 1 (NF1) is the most common neurocutaneous disease, and patients with NF1 may present with a variety of central nervous system complaints, such as seizures, learning disability and attention-deficit disorder. Intracranial lesions associated with NF1 include optic gliomas, sphenoid wing dysplasia, "unidentified bright objects" (UBOs) and cerebrovascular lesions such as Moyamoya syndrome (MMS) and aneurysms.[1-3] We present a case of NF1 with unilateral MMS.

CASE REPORT

A 7-year-old Chinese girl presented with cutaneous stigmata of multiple café-au-lait spots, axillary freckling, Lisch nodules, and mild learning difficulties with visual-spatial incoordination. Magnetic resonance (MR) imaging of the brain showed multiple small foci of T2 prolongation in the left frontal, occipital and temporal lobe white matter (Fig. 1a), as well as both globus pallidi and cerebellar hemispheres. These lesions were hypointense on T1-weighted (T1-W) images, did not show any mass effect, and did not enhance after intravenous contrast injection. However, on fluid-attenuated inversion recovery (FLAIR) sequences, the left-sided white matter lesions were hypointense, compared to the hyperintense lesions in the

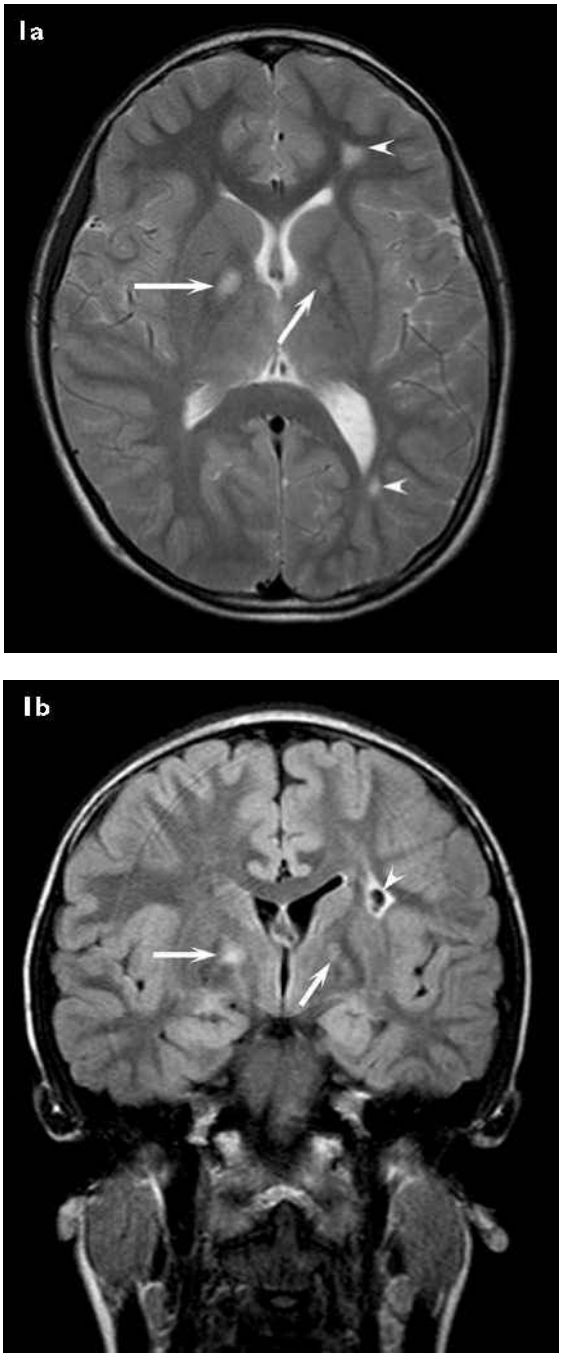

Fig. 1 Initial MR images of the patient obtained at 7 years of age. (a) Axial T2-weighted MR image shows multiple small foci of T2 prolongation in the left frontal and occipital lobe white matter (arrowheads) as well as both globus pallidi (arrows). (b) Corresponding coronal FLAIR image shows that the left-sided white matter lesion is hypointense (arrowhead), compared to the hyperintense UBOs in the basal ganglia (arrows).

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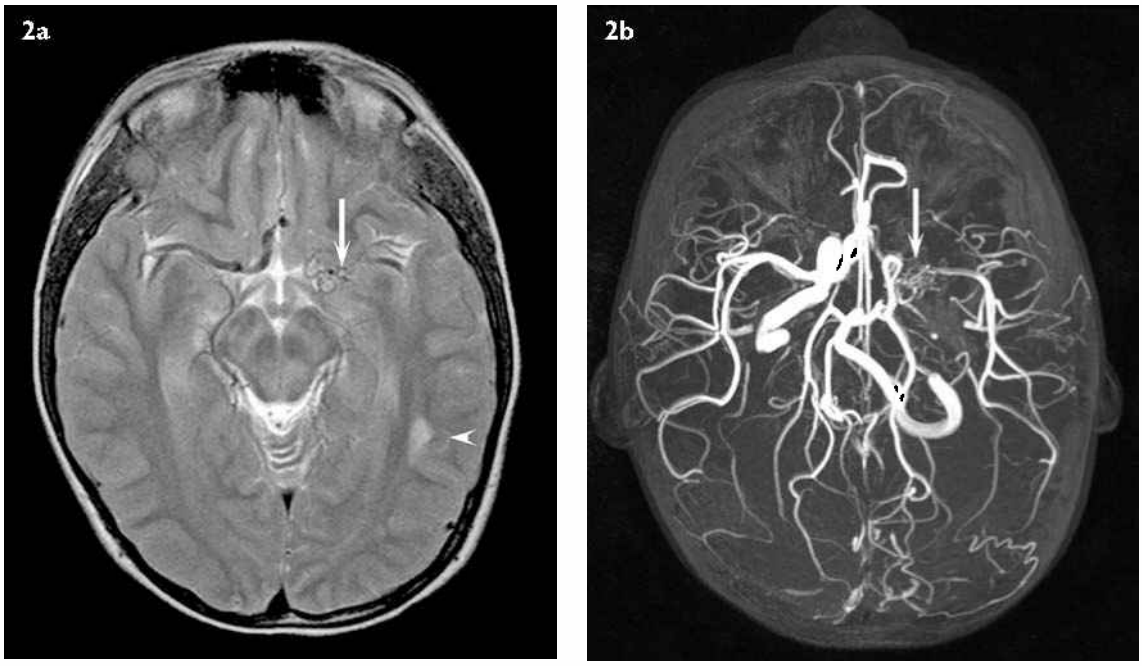

Fig. 2 MR images taken four years later. (a) Axial T2-weighted MR image shows multiple serpiginous basal flow voids (arrow) consistent with collateral arteries from unilateral MMS and an ipsilateral hyperintense lesion in the temporal lobe white matter (arrowhead); (b) Maximum intensity projection MR angiography confirms occlusion of the terminal left ICA and severe stenosis of the proximal middle cerebral artery with multiple basal collateral arteries (arrow).

basal ganglia and cerebellum (Fig. 1b).

Four years later, the patient complained of worsening migrainous headaches. She did not experience any focal weakness or numbness, and neurological examination was unremarkable. On repeat MR imaging, it was noted that the normal signal voids of the terminal left internal carotid artery (ICA) and proximal middle cerebral artery were lost, and there were multiple serpiginous small basal collateral arteries typical of MMS (Fig. 2a). Review of the initial MR images four years ago showed that these abnormal vascular findings were present, but were not appreciated then. Neither the hypointense nor hyperintense lesions on FLAIR images had progressed in the interim.

MR angiography (Fig. 2b) and subsequent digital subtraction angiography confirmed occlusion of the terminal left ICA and severe stenosis of the proximal middle and anterior cerebral arteries, with multiple tiny basal collateral arteries. The right ICA and the posterior circulation were normal. Surgical revascularisation was carried out electively with a left encephalo-duro-arterio-synangiosis (EDAS). At three months follow-up, she remained well, with a reduction in the migraine frequency.

DISCUSSION

In our patient, the unilateral white matter hyperintensities on T2-weighted (T2-W) MR images were hypointense on FLAIR images and could be differentiated from the UBOs of NF1. UBOs are asymptomatic focal intraaxial lesions that are found in 60%–90% of NF1 individuals, and are typically located bilaterally in the cerebellum, brainstem, basal ganglia, thalami, and the cerebral white matter.[4] Pathologically, they correspond to vacuolar changes in the myelin sheath.[5] UBOs are focal areas of hyperintensity on both T2-W and FLAIR images, without any associated mass effect or contrast enhancement.[6] In our patient, multiple nonenhancing focal hyperintensities were found on T2-W MR images. On FLAIR images, however, those in the left cerebral white matter were hypointense, compared to the characteristic hyperintense lesions seen in the globus pallidi and cerebellum. In retrospect, these former lesions were not typical in their FLAIR appearance, and of locations for UBOs, and would have been consistent with chronic white matter watershed infarction from Moyamoya occlusive disease of the left ICA.

The subtle signs of unilateral MMS, as a cause of these lesions, were present but not appreciated on initial MR images. MMS is a chronic occlusive cerebrovascular disorder, and is characterised by angiographical findings of steno-occlusive changes in the circle of Willis, specifically involving the terminal portion of the ICA, proximal middle (MCA) and anterior cerebral arteries (ACA), with concomitant formation of profuse arterial collaterals at the base of the brain.[1,4] In children, ischaemic symptoms, such as recurrent transient ischaemic attacks and cerebral infarction, are common, while intracerebral, intraventricular or subarachnoid haemorrhage often occur

in adults due to rupture of the fragile collateral vessels. Headaches and seizures occur in both populations.[1] On conventional MR images, subtle signs of MMS, such as collateral vessels and loss of flow signal voids in the course of the ICA and MCA,[1] should be recognised in NF1 patients as a rare but characteristic association.

The prevalence of MMS in NF1 patients is estimated at 0.6%,[3] with about 30 cases reported in paediatric patients since 1976. The pathogenesis of NF1 vasculopathy may be related to altered function of neurofibromin, the NF1 gene protein product, and proliferation of vascular smooth muscle cells may result from the loss of neurofibromin expression in endothelial cells.[3] Interestingly, linkage studies have linked one of the genes for familial Moyamoya disease to chromosome 17q25, which is in close proximity to the NF1 gene on chromosome 17q11.2.[7] Further studies are needed to understand the association between these rare but interesting conditions. The treatment of MMS is primarily conducted using surgical revascularisation, to increase blood flow to the hypoperfused cortex. Indirect revascularisation procedures such as EDAS may be technically more feasible in young children, compared to direct superficial temporal artery-middle cerebral artery bypass.[1] MMS in NF1 patients is unilateral in up to 30% of cases,[8] but the observation that progression to bilateral Moyamoya occurs in 10%–100% of these patients[9] means that our patient may require long-term surveillance, and noninvasive perfusion studies may be helpful for assessment.[10,11]

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