

## A Case of Neurofibromatosis type 1 with Moya Moya Disease

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### Abstract

A 5 years old boy with multiple café au lait spots came with intermittent weakness of the right side of the body and seizures. The child had global developmental delay. His MRI and MRA showed thickening of the optic nerves, abnormal signal in multiple areas of the brain with non-visualization of the left middle cerebral artery. The child was diagnosed to have neurofibromatosis type 1 with seizures with bilateral optic glioma with Moya Moya disease.

### Keywords

Neurofibromatosis type 1 with Moya Moya Disease, Cerebral Vasculopathy

### Introduction

Neurofibromatosis type 1 is an autosomal dominant disease. Vasculopathies are increasingly being reported in this disease in recent years. This case report is done to support the previous studies and to think the association of the disease with vasculopathy.

### Case Report

A 5 years old boy, hailing from old town of Dhaka, came with the complaints of intermittent attacks of weakness of the right side of the body for 10 months. The weakness from attack lasted for several hours and recurred 2-3 times a month. He had seizures for the last 6 months. The seizure semiology consisted of crying for several minutes and then got weak. The attack rate was 4-5 times a month. There were no visual symptoms. The patient belongs to

non-consanguineous parents. The boy has 3 other siblings; all are healthy.

The child was delivered by normal vaginal delivery with no immediate complication. The child developed his social smile at the age of 5 months, held the neck at 7 months, sat at 12 months, walked at 2.5 years. The boy started



**Fig.1:5 years old child with 3 visible Café au Lait spots**

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babbling at 1 year, 1st word at 2 years. He could make only 2 words sentence. He could not memorize rhymes. On examination, he had 8 café-au-lait spots on the trunk and limbs. The long axis of these spots ranges from 7-10 mm (Fig. 1).

There was no bony deformity or skin nodule. His gait was normal. There was no Lisch nodule in the iris. His visual field examination was normal with normal eye movement. His fundus of the eye was normal. Other cranial nerve examination showed no abnormality. His sensations were intact including vibratory sensation and position sense. He had normal

muscle tone and power (5/5) all over. His deep tendon reflexes are 2+ all over. There were no cerebellar signs. He had normal gait with normal tandem walking.

His EEG was normal. His antinuclear antibody and antibody to double stranded DNA were negative. Other extensive work up for stroke were negative. The MRI of brain showed expansion of the orbital part of both the optic nerves which were also tortuous and buckled (Fig.2). There were abnormal signals in thalami, posterior limb of internal capsule, basal ganglia and cerebellar white matter. Magnetic Resonance Angiography showed left middle cerebral artery cannot be visualized (Fig.3).



**Fig. 2: MRI of the brain in T1 sequences showing transverse expansion with tortuosity of the optic nerve bilaterally.**



**Fig. 3: Magnetic resonance angiogram shows non visualized left middle cerebral artery with formation of a few collateral vessels.**

Finally diagnosed to have Neurofibromatosis 1 with Moya Moya Disease with bilateral optic glioma. The child has been given oxcarbazepine and was given referral to ophthalmology, pediatric oncology and neurosurgery. As there was no symptom, the ophthalmologist asked for 6 monthly follow up until the age of 10 years. The pediatric oncologist advised similarly. The neurosurgeon took the decision to go for pialsynangiosis for Moya Moya disease.

### Case Discussion

Neurofibromatosis type 1 (NF1) is the most common autosomal dominant condition affecting the nervous system with an incidence of 1 in 2500 to 3500. It was first described in 1882 and the diagnostic criteria were established in 1987 by National Institute of Health which set seven points for diagnosis:

1. Six or more café-au-lait macules larger than 5mm in greatest diameter in pre-pubertal individual or larger than 15 mm in post-pubertal individuals
2. Two or more neurofibromas of any type or one plexiform neurofibroma
3. Freckling in axillary and inguinal region
4. Optic glioma
5. Two or more Lisch nodules
- 6 A distinctive osseous lesion (e.g. sphenoid dysplasia or thinning of the long bone cortex with or without pseudothrosis)
7. A first degree relative (parent, sibling or offspring) with NF1. Two or more are required for diagnosis of neurofibromatosis type 1.

NF1 is a progressive autosomal dominant condition caused by mutation in NF1 gene on

chromosome 17. NF1 is also heterogeneous at the mutation level, with than 300 independent mutations having been reported in the gene.

Vasculopathy is under recognized in NF 1. In this disease, characteristic vascular lesions are distributed in renal arterial tree<sup>1</sup>; Symptomatic involvement is uncommon.<sup>1</sup> Vascular malformation of the intracranial circulation induces stenosis, occlusion, ectasia, fusiform aneurysm formation or arteriovenous fistula. Our case shows Moya Moya with supraclinoid internal carotid artery narrowing of the left side. Rosser et al<sup>2</sup> showed 353 children with NF1 underwent routine MRI screening and 8 (2.5%) had cerebral vessel abnormality. The mean age of cerebral vasculopathy was between 5.2 and 7.3 years.<sup>2,3,4</sup> There may be a lag of several months to years between radiologic manifestations and the development of ischemic symptoms. This shows the importance of radiologic surveillance. Though there is no consensus regarding the treatment of vasculopathy, revascularization operation and giving aspirin looks prudent.

The etiology of vascular disease in NF1 is not well understood. The neurofibromin protein has been shown to be expressed in the vascular endothelial cell layer as well as in the smooth muscle of the aorta and it is likely to be involved in the pathogenesis of vasculopathy in NF1.<sup>5, 6</sup> Smooth muscle cells that have lost NF1 exhibit an abnormal proliferative response to arterial injury, which may account for the development of obstructive vascular disease. The increased neo-intima formation in response to mechanical injury has been shown to be mediated by a molecular signaling pathway in NF1 +/- mice

molecular signaling pathway in NF1 +/- mice that is sensitive to the tyrosine kinase inhibitor imatinib.<sup>7</sup>

Optic pathway gliomas are regarded as benign tumors of the CNS originating from glial tissue. They are frequently asymptomatic as is our case but sometimes they manifest rapid growth, causing considerable visual dysfunction, neurologic deficit and endocrine disturbances. These tumors may arise in any part of the optic pathway. Typically, they appear in early childhood, with a peak between 4 and 5 years of age. Optic pathway gliomas constitute 2 to 5% of all brain tumors in children. They are the most common CNS tumors in children with NF1; their prevalence of about 15 to 20 %. Histologically, optic pathway gliomas are pilocytic astrocytomas.<sup>10</sup>

It is not known why some of these tumors grow aggressively whereas others remain clinically silent for many years. In fact, little is known about their natural course. General symptoms of increased intracranial pressure were more frequently observed on sporadic optic pathway gliomas in most studies (18/55 vs 6/51).<sup>12</sup> Decrease visual acuity was the most common clinical sign of optic pathway gliomas. Lund and Skovky, Kuenzle and colleagues found visual deterioration at the time of diagnosis in nearly 70% of the patients with NF1.<sup>11</sup> Changes on the fundus of the eye, optic atrophy and edema are the next most common signs in patients with optic pathway gliomas at the time of diagnosis. Bilateral optic nerve gliomas are specific for NF1.<sup>13</sup>

## Conclusion

It would be wise to go for MRI and MRA brain in all cases of Neurofibromatosis type 1 to pick up the vasculopathy early.

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