Moyamoya Disease and Down Syndrome

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Abstract. Moyamoya disease is an obstruction of the internal carotids and of the afferent and efferent channels of Willis polygon, which causes a collateral circulation, responsible for the typical angiographic image of a "puff of smoke" (Moyamoya, in Japanese). Its etiology is unknown, and it might be congenital or acquired. The clinical features are cerebral ischemia, recurrent transient ischaemic attacks, sensorimotor paralysis, convulsions and migraine-like headaches. We report a 2 years and 9 months old boy with Down syndrome and Moyamoya disease who presented with focal convulsions. [Indian J Pediatr 2005; 72 (8) : 697-699] *E-mail: m4deveci@yahoo.com*

Key words : Convulsions; Down syndrome; Moyamoya disease; Puff of smoke; Willis polygon.

Moyamoya disease is a chronic vasculopathy that leads to single or usually double sided blockage in intracranial zones of internal and external carotid arteries which are responsible for circulation in the frontal regions of the brain. "Moyamoya" is a Japanese word meaning "puff of smoke" and is used to identify classical angiographic look of multiple small intracranial vessels.^{1,2} This disease causes cerebrovascular insufficiency which leads to formation of reticular multiple anastomosis and collaterals between internal and external carotid arteries. Occurrence of this very rare disease accompanying with Down Syndrome is more frequent when compared to normal population.³

CASE REPORT

A male patient of 2 years and 9 months of age was admitted to our clinic with lower respiratory tract infection and focal convulsions. Patient had history of generalized convulsions on three different occasions. The patient was the ninth and the last child of a couple who were second degree relatives; and were approximately 47 years old. Seven sisters were alive and healthy. His brother (third child) had died due to an undiagnosed disease when he was only 20 days old.

On physical examination, child had facies suggestive of Down Syndrome (Fig. 1). On systemic examination, respiratory system revealed bilateral coarse crepitations, cardiovascular, gastrointestinal and genitourinary system examinations were normal. On neurological examination; left arm's activity was less than normal. A mild hypotonia was noticed in all other extremities, and a mild increase in deep tendon reflexes was observed. The laboratory findings revealed a normal urine analysis, while hemogram revealed hypochromic microcytic anemia.



Fig. 1.

Routine biochemical tests were normal; HbA1: 96.4% (N: 95.5-97.5%), HbA2: 3.6% (N: 2.5-4-5%), HbF: Negative (N: < 3%), HbS: Negative (N: Negative), Protein C: 73% (N: 70-140%), Protein S: 103% (N: 60-140%), Antithrombin III: %105 (N: 75-125%). No pathology was found in tests for inborn errors of metabolism. EEG was found to be showing fast baseline activity. In cranial MRI; parenchymal atrophy was observed in frontal and parietal regions, and hemorrhagic infarct zone was observed in right frontal region. With cranial MR angiography, there was gradual thinning in intracranial internal carotid artery. With A1-M1 cranial MR angiography; gradual thinning in intracranial internal carotid artery, occlusion in A1-M1, occlusion in posterior cerebral artery, vascular reticular formation on Willis polygon which was

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suspected to be because of Moya Moya, and recanalization of A2 segment *via* this vascular web were observed (Fig. 2).



Fig. 2.

DISCUSSION

When searching the reasons for repeated convulsions in the patient, we observed bilateral ischemic regions in cranial MR. After excluding cardiac, inflammatory, metabolic, hematolologic and cerebrovascular diseases which may cause cerebrovascular blockage; based on cranial MR angiography, Moyamoya disease was diagnosed.

Etiology of the disease is currently not clearly known. According to its relations with some HLA types such as HLA B51, the disease is thought to be having hereditary tendencies and having genetic factors in its pathogenesis. There are no clinical characteristic symptoms of the disease. In children, the disease usually causes transient ischemic attacks accompanying with hemiparesis, convulsions or other focal neurological findings. In the present case, seizures were the prominent symptoms. There may be intraventricular and subarachnoid hemorrhage. Imaging techniques are used in diagnosis.⁴ Multiple infarct and atrophic regions are observed in CT and MRI. Exact diagnosis is *via* cerebral angiography or MR angiography.⁵ Characteristic findings observed through these methods are occlusion in intracranial internal carotid artery and abnormal vascular reticulation. This abnormal vascular reticulation is called "Moyamoya vessels". These pathologies are usually bilateral. But if these are congenital or developing later are still a matter of discussion. This is because of the fact that the disease has two peaks: the first decade and the third decade. Also the disease is more frequent when accompanying with diseases like Down syndrome, neurofibromatosis and tuberous sclerosis. The patient was in first decade and had Down syndrome. In some cases with moyamoya disease, coexistence of protein C or S deficiency has been reported.⁶⁷ However, this case had normal protein C and

S levels.

It is hard to predict the prognosis, because the natural progress of the disease is currently unknown. In autopsies, serious occlusive changes are observed in intracranial internal carotid artery and arteries of Willis polygon. These changes are caused by intimal proliferation and subepithelial hyperplasia and fibrosis. Adventitia and media of the vessels are normal. There are no inflammatory cells or atheroma found on the vessels.

In medical treatment, steroids, and with some cases aspirin, ticlopidine, vasodilators and anticoagulants are used.⁸ There are various different modalities in surgery and satisfactory results are obtained by EDAS (encephaloduroarteriosynangiosis).^{9,10}

Moyamoya is a truly rare disease (with incidence of 1/ 1.000.000 a year), but its incidence in patients with Down syndrome has been noted to be three times the estimated incidence of moyamoya disease in the general population.¹¹ In an analysis of stroke in 37 children with Down syndrome, seven patients were found to have angiographic abnormalities consistent with moyamoya disease.¹² The abnormalities associated with Down syndrome may create a vulnerability for the development of moyamoya disease. Several proteins encoded on chromosome 21, including superoxide dismutase 1, interferon gamma receptor, cystathionine ß-synthase and á-chains of collagen type VI, are associated with an increased risk for vascular diseases.¹³⁻¹⁵

In conclusion, moyamoya disease should be considered in distinctive diagnosis of neurological abnormalities in patients with Down syndrome having multiple cerebral infarcts and related neurological findings. Magnetic resonance angiography is an important imaging technique for diagnosis of this condition.

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Moyamoya Disease and Down Syndrome

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