# CASE REPORTS

## RECURRENT STROKES SECONDARY TO MOYAMOYA PHENOMENON IN A CHILD WITH DOWN'S SYNDROME

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## ABSTRACT

A 6 year-old girl with Down's syndrome presented to the paedriatic emergency department with sudden onset weakness of the left half of body. Evaluation leads to the eventual diagnosis of stroke secondary to Moyamoya syndrome. This is an unusual presentation of stroke and highlights the need to expand the differential diagnosis to include rare diseases in children with predisposing conditions. This case highlights the relationship between trisomy 21 and Moyamoya syndrome.

**Keywords:** Moyamoya syndrome, Stroke, Trisomy 21.



## CASE REPORT

A 6 years old girl with Down's syndrome presented to the paedriatic department of CMH Quetta with sudden onset right hemipariesis. She had past history of left hemipariesis, diagnosed as ischemic stroke 4 months back. She was born to parents with consanguinous marriage. Birth history was unremarkable. There was no history of similar illness in other siblings.

On examination she was normotensive and afebrile. The child was sitting comfortably on the stretcher with her mother present beside her. The child had typical facial characteristics of trisomy 21. Her speech was delayed. Motor testing revealed a fluctuating 4/5 grade strength of her right upper extremity and right lower extremity. Long-tract signs included an equivocal right toe and a down-going left toe. She walked towards her mother with a slight limp favoring the right side.

Routine laboratory serum studies revealed slightly raised TLC (13.1 x 109/L). CT scan revealed chronic infarct in the right cerebral hemisphere and haemorrhagic infarct in the left cerebral hemisphere in distribution of left middle cerebral artery (MCA). MRI of the brain was performed in 1.5 Tesla Philips. SE and FSE sequences were used to obtain T1, T2WI and FLAIR images in different planes. MR angiogram was performed using 3D TOF technique and MIP images were obtained. MRI revealed areas of chronic infarcts with associated early encephalomalacia changes and gliosis in left frontal region and left basal ganglia (fig-1). Small areas of chronic infarction and gliosis were also noted along right centrum semiovale. MR angiography revealed marked narrowing of supraclinoid and intracavernous portion of left internal carotid artery and nonvisualization of right middle cerebral artery and anterior cerebral (A-1 segment) arteries (fig-2). Basal collaterals were noted, characteristic of Moya Moya-syndrome (fig-3). Vertebrobasilar circulation appeared normal. Hematological investigations revealed normal hematocrit, ESR, normal clotting time and sickling test was negative. 2D echo was unremarkable. As such, no primary cause was found for the patient's disease. The differential diagnosis included transient ischemic attacks, ischemic stroke, dissection, hypoglycemia, cardiac source emboli, hypercoaguable states. The patient was given aspirin 81 mg poqd and

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physical therapy. She was discharged home and was lost for followup.

Fairly well circumscribed abnormal signals involving cortex and white matter are noted in left frontal lobe extending into left lentiform nucleus, in territory of left MCA.

Abnormal signal intensity area is noted in periventricular white matter and centrum semiovale on right side in territory of right MCA appearing hyperintense on T2WS and FLAIR sequences suggesting chronic infarct with gliosis.

## DISCUSSION

Moyamoya disease is a progressive vasculo-occlusive disease involving the circle of Willis, typically the terminal ICA. The term Moyamoya has its origin from a Japanese, meaning "puff of smoke" was first described by Suzuki and Takaku in 1969[1]. The term Moyamoya refers to the appearance on angio-graphy of abnormal vascular collateral networks that develop adjacent to the stenotic vessels. The steno-occlusive areas are usually bilateral, but unilateral involvement does not exclude the diagnosis.

The term Moyamoya disease should be reserved for an idiopathic, sometimes familial, condition, which leads to characteristic intracranial vascular changes. Numerous entities have been described which mimic the appearance, in which case the term Moyamoya phenomenon, syndrome or pattern is used.

Pathologically, Moyamoya disease is characterized by intimal thickening in the walls of the terminal portions of the internal carotid vessels bilaterally. The proliferating intima may contain lipid deposits. The anterior, middle, and posterior cerebral arteries that emanate from the circle of Willis may show varying degrees of stenosis or occlusion. The cause of Moyamoya disease is not known. The disease is believed to be hereditary. Mineharu suggested that familial Moyamoya disease is autosomal dominant[2,3]. Many disease states have been reported in association with Moyamoya disease, including the following:

- Immunologic -Graves disease / thyrotoxicosis.
- Infections - Leptospirosis and tuberculosis.
- Hematologic disorders - Aplastic anemia, Fanconi anemia, sickle cell anemia, Congenital syndromes - Apert syndrome, Down syndrome, Turner syndrome, Marfan syndrome, tuberous sclerosis, (Neurofibromatosis Type 1).
- Vascular diseases - Atherosclerotic disease, coarctation of the aorta and fibromuscular dysplasia, radiation injury and hypertension.

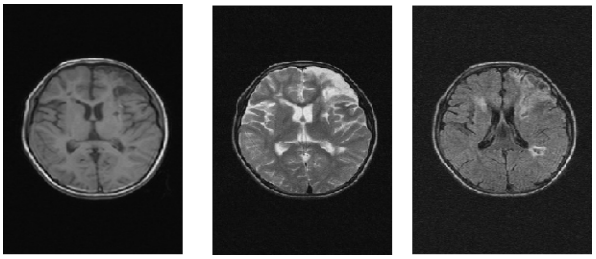

**Figure-1: MRI brain axial T1WS, T2WS & FLAIR sequences.**

In the presence of these risk factors, the condition is referred to as Moyamoya syndrome.

Patients admitted with Moyamoya disease and Down syndrome were more likely to present with ischemic stroke and less commonly with hemorrhagic stroke (15.3% and 2.7%,

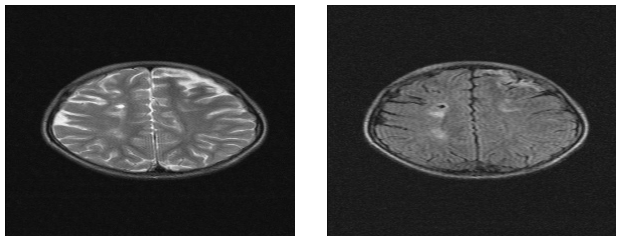

**Figure-2: MRI brain axial T2WS & FLAIR sequences.**

respectively)[4-6].

The condition was initially described in Japanese patients, where it is still most common, in which 7-10% of cases are familial with autosomal dominant inheritance pattern. Moyamoya disease occurs primarily in Asians but can also occur (with varying degrees of

severity) in whites, blacks, Haitians, and Hispanics. The female-to-male ratio of Moyamoya disease is 1.8:1. Moyamoya is a disease of children and young people, with a bi-modal age distribution, with the highest peak in the first decade and smaller peaks in the third and fourth decades. Ages for patients with Moyamoya disease range from 6 months to 67 years, Death in Moyamoya disease is usually from hemorrhage. The outcome of the disease depends on the severity and nature of the hemorrhage; the prognosis depends on recurrent attacks.

Presentation is to some degree age dependent. In children hemispheric ischaemic strokes are most pronounced, whereas in adults haemorrhage from the abnormal vessels is more common. Children may have hemiparesis, monoparesis, sensory impairment, involuntary movements, headaches, dizziness, or seizures. Mental retardation or persistent neurologic deficits may be present.

Misdiagnosis and delayed diagnosis of Moyamoya disease are particular pitfalls in the treatment of patients with this disorder. Atypical features such as young age and absence of obvious risk factors for stroke should raise suspicion of the disease. If an ischemic stroke that is being treated with antiplatelet agents or anticoagulants does not respond to therapy, then Moyamoya disease should be considered as a possible etiology. This is especially true if results of a hypercoagulability profile are unremarkable.

Several studies may be indicated in patients with Moyamoya disease. In a patient with stroke of unclear etiology, a hypercoagulability profile may be helpful. Significant abnormality in any of the following is a risk factor for ischemic stroke: Protein C and S, Antithrombin III, Homocysteine, Factor V Leiden. The erythrocyte sedimentation rate (ESR) can be obtained as part of the initial workup of possible vasculitis. However, a normal ESR does not rule out vasculitis. Thyroid function and thyroid autoantibody levels have been shown to be elevated in a significant percentage of pediatric patients with Moyamoya disease[7,8].

Cerebral angiography is the criterion standard for the diagnosis of Moyamoya disease. The following findings support the diagnosis:

- Stenosis or occlusion at the terminal portion of the internal carotid artery or the proximal portion of the anterior or middle cerebral arteries.
- Abnormal vascular networks in the vicinity of the occlusive or stenotic areas.
- Bilaterality of the described findings (although some patients may present with unilateral involvement and then progress).

Magnetic resonance angiography (MRA) is performed as it is radiation free procedure, however CT angiography is needed if surgery is planned. Any of the above findings on MRA may preclude the need for conventional angiography. MRI not only reveals areas of infarctions but also allows direct visualization of these collateral vessels as multiple small flow voids at the base of brain and basal ganglia. MR angiography is used to confirm the diagnosis and to see the anatomy of the vessels involved. It typically reveals the narrowing and occlusion of proximal cerebral vessels and extensive collateral flow through the perforating vessels demonstrating the classic puff of smoke appearance[9]. In the earlier stages of the disease, 3 DFT TOF technique, to avoid severity of stenosis and in the late stages, given the slow flow 2 DFT TOF technique is employed. IV contrast agent may be used to increase the intravascular contrast.

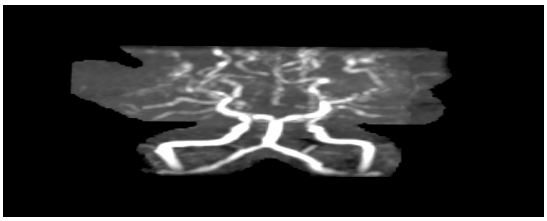

**Figure-3: MRA brain (axial image).**

Multiple tortuous irregular vessels are noted in vascular territories of ACA & MCA bilaterally suggestive of collateral formation.

Pharmacologic therapy for Moyamoya disease is primarily directed at complications of the disease. Rehabilitation with physical therapy, occupational therapy, and speech therapy should be considered, depending on the neurologic impairment. Surgical treatment may confer long-term benefits in severe disease[10]. Bypassing the occlusive segments is the aim of most surgical therapy.

Mortality rates from Moyamoya disease are approximately 10% in adults and 4.3% in children. About 50-60% of affected individuals experience a gradual deterioration of cognitive function, presumably from recurrent strokes. Patients with Moyamoya disease who present for treatment while symptoms are evolving have a better prognosis than do those who present with static symptoms (which probably indicate a completed stroke).

## CONCLUSION

Acute stroke is an infrequent disease of pediatric age group patients. The presence of Moyamoya syndrome should be considered in the evaluation of patients with Down Syndrome who present with transient ischemic attack-like symptoms or recurrent strokes.

## CONFLICT OF INTEREST

This case report has no conflict of interest to declare by any author.

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