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# Moyamoya Disease: an Elusive Diagnosis

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## Introduction

Moyamoya disease is an idiopathic vasculopathy, affecting vessels of Circle of Willis.1 It usually manifests as stroke, but can also cause seizures and cognitive impairment.2 Ischemic strokes are common in children and hemorrhagic strokes in adults.1 We describe our experience with moyamoya disease in four patients who presented with ischemic strokes, at an academic tertiary care center and emphasize that this diagnosis should be considered in young patients, especially children, who present with stroke.

## Patients and Methods

Patients with final diagnosis of moyamoya disease were searched by ICD-9 coding system of the hospital medical records. Four patients were identified over a period of 10 years (January 1st, 1991 to December 31st, 2001). Their demographic characteristics, clinical features/presentation, laboratory, electrophysiological and radiological investigations were recorded and analyzed.

## Results

Four patients of moyamoya disease were admitted to our hospital over the last 10 years. Ages ranged from 9 months to 25 years (mean age 9 years). Three were females, all below 10 years and one male. All patients presented with sudden hemiparesis, one with recurrent alternating events. Two patients had seizures at presentation and one additional patient developed seizures during hospital stay. One patient had a fulminant course, deteriorated rapidly after admission and died within three weeks of clinical onset of illness. Two patients underwent synangiosis (one encephaloduroarteriosynangiosis; EDAS and the other encephalomyoduroarteriosynangiosis; EMDAS) but long-term follow up was not available. All patients had normal complete blood count (CBC), renal function, and electrolytes. Anti-nuclear antibodies (ANA), anticardiolipin antibodies (aCLA) and erythrocyte sedimentation rate (ESR) were done in three patients and were normal. Anti double stranded DNA (anti-ds DNA) was tested in one patient and was normal. In another patient, sickling test was normal. Lumbar puncture was done in one case, which was significant with slightly raised proteins. Electroencephalography (EEG) was performed in three patients, who had seizures, and all showed focal abnormalities. One had bitemporal spikes, one had asymmetric slowing and one had diffuse slowing with asymmetric suppression. CT scan was done in two patients and was normal in one and showed a large infarction in territory of left middle cerebral artery (MCA) in the other. All four patients underwent magnetic resonance imaging (MRI) and all showed infarctions. The locations were bilateral parietal in one, bilateral basal ganglia and left frontoparietal in one (Figure 1) and single subcortical infarcts in two patients. There was no evidence of arteriovenous malformation (AVM) or tuberous sclerosis on MRI. Four

vessel conventional angiography was done in three patients which showed either obliteration or stenosis of distal internal carotid arteries, proximal middle and anterior cerebral arteries and small collateral blood vessels, giving typical 'puff of smoke' appearance (Figures 2, 3 and 4). In the fourth patient magnetic resonance angiographhy (MRA) brain, showed obliteration of distal internal carotid, proximal middle cerebral and anterior cerebral arteries, and low signals on T1 weighted images in the basal ganglia.

**Discussion**

Moyamoya disease is an idiopathic vasculopathy of the circle of Willis, which affects mainly children and young adults.1 First described by Takeuchi and Shimizu in Japan in 19553, it has since been described in other geographical locations including North America4, Europe5 and the Indo-Pakistan subcontinent.6-9 Though an uncommon cause of ischemic as well as hemorrhagic stroke in young patients, stroke is the most common clinical manifestation of this entity.2 Moyamoya disease accounts for 10% to 20% of arterial infarcts in children.10 About 85% of patients with moyamoya disease present with stroke. Three quarters of the strokes are ischemic.2 Hemorrhage is more common in older patients.1 Seizures and cognitive impairment have been reported in 7.5% of the patients.3 Headache, psychiatric symptoms and movement disorders are uncommon symptoms. All of our patients presented with ischemic strokes. In addition three patients had seizures, one had multifocal and two had generalized tonic clonic seizures, at some point in their disease course.

Annual incidence of moyamoya disease is estimated at one per million population, with peak age incidence below the age of ten years. However, another small peak is well described during the 3rd decade of life.1 The disease is slightly more common in females.2 About 10% of patients have a positive family history of moyamoya disease.1 Three of our four patients were females and presented during childhood. None had a family history of moyamoya.

The basic pathologic process in affected vessels is smooth muscle cell proliferation and migration to intima. However, the cause of the disease is unknown. The process affects primarily large caliber cerebral blood vessels of the Circle of Willis and results in narrowing of distal internal carotid arteries (ICAs) early in the disease course, followed by that of proximal middle cerebral arteries (MCAs), anterior cerebral arteries (ACAs) and posterior cerebral arteries (PCAs). A collateral basal circulation develops, which gives a typical 'puff of smoke' appearance on cerebral angiography, the hallmark of this entity.1 This appearance prompted Suzuki to give this entity the name moyamoya, a Japanese word, meaning 'vague or hazy puff of smoke'.3 As the disease progresses, the basal network becomes less and less pronounced. The definite diagnosis requires angiographic findings (bilateral occlusion or stenosis of terminal ICAs, proximal ACAs and proximal MCAs, and bilateral abnormalities of basal vascular network and collaterals) which are not secondary to other known processes i.e. CNS infections, sickle cell disease, thalassemia, tuberous sclerosis, neurofibromatosis, vasculitis, connective tissue disease and AVM.1 A comparison of MRA with conventional angiography found it to be a useful noninvasive technique to screen and follow patients with moyamoya

disease.11-14 MRA has also been recommended as a definitive noninvasive diagnostic procedure for children.1 In our series, in three patients the diagnosis was established on the basis of DSA and in one patient on the basis of findings of MRI/MRA. Currently surgical cerebral revascularization either through extracranial-intracranial bypass (EC-IC bypass) or synangiosis, is considered to be the mainstay of therapy.1 This procedure reduces the rate of stroke recurrence. Two of our patients underwent surgical intervention without immediate complications, but long-term follow up is not available. In addition conservative/medical treatment such as antiplatelet agents, have been used in patients with ischemic strokes or transient ischemic attacks (TIAs). Steroids may be helpful, especially during the acute phase of recurrent hemiparesis and in patients who present with abnormal involuntary movements.1 Although an uncommon disease, moyamoya should be considered in all children presenting with stroke and in young adults in whom the etiology of stroke is unclear.

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