Case Report

A Case of Atherosclerotic Moyamoya Syndrome

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Moyamoya disease is an idiopathic, noninflammatory, nonatherosclerotic, progressive, occlusive disease of the cerebral vasculature with a particular predilection for the circle of Willis and the arteries that arise from it.

The term moyamoya disease is reserved for the idiopathic, sometimes familial variety of the disease. However numerous other conditions mimic the angiographic appearance of moyamoya disease. In that case, we use the designation moyamoya syndrome or phenomenon or pattern. These diseases include atherosclerosis, sickle cell vasculopathy, neurofibromatosis type 1, Down syndrome, Turner syndrome and Allagille syndrome.

Here we present a case of an adult male presenting with seizures caused by an infarct due to atherosclerosis induced Moyamoya syndrome.

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Case Report

A 38 year old, hypertensive, diabetic male presented with a history of acute onset seizure like movements of the lower left part of his face for the past 24 hours. There was no associated loss of consciousness, weakness of limbs, difficulty in swallowing, slurred speech, sensory abnormalities or any other abnormal movements. There was no history of any such occurrence in the past or among his close family members. He was a smoker, smoking around 3-5 cigarettes/day and was also poorly compliant with his antihypertensive and antidiabetic medications.

General examination was unremarkable except for a blood pressure of 160/96 mm Hg and random capillary blood glucose of 312 mg/dL.

Neurological examination revealed a rapid jerky movement of the lower left part of his face with tensing movements of the jaw suggestive of seizures. The rest of the examination was unremarkable.

Considering his risk factors and the acuity of onset, we considered a vascular lesion and an urgent noncontrast CT brain was done. This revealed a hypodense lesion in his right frontal region suggestive of an infarct.

His complete blood count, liver function tests and serum electrolytes were unremarkable. HIV 1 and 2, hepatitis B and hepatitis C serologies were non reactive. FBS and PPBS were 210 mg/dL and 396 mg/dL respectively. His fasting lipid profile was remarkable for an LDL cholesterol of 168 mg/dL.

The patient was started on levetiracetam and once the seizures were controlled, an MRI brain (plain+contrast) with MR angiography of brain and neck vessels was obtained (Fig 1).

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Editor's Comment :

- **Atherosclerosis is common in the Indian population and the cause of substantial cardiovascular morbidity and mortality. This usually manifests in the form of large vessel ischemic strokes, intracerebral bleeds, acute coronary syndromes and peripheral arterial disease.**
- **Moyamoya syndrome is a relatively uncommon presentation of this atherosclerotic process, but the widespread prevalence of this atherosclerosis merits consideration of this entity in the differential diagnosis.**
- **Due consideration will allow quicker diagnoses and faster treatments, thereby facilitating better outcomes for patients.**

The MRI brain showed diffusion restriction of the right frontal region with perilesional edema. Contrast imaging showed mild gyriform enhancement. The lesion was hypointense on ADC (apparent diffusion coefficient) mapping with the ADC in ischemia limit suggestive of a subacute infarct.

MR angiography showed decreased flow in the middle cerebral arteries (MCA) bilaterally, more on right side. The circle of Willis lacked artery-to-artery anastomosis. Few small vessel signals and neovascularization were seen near the circle of Willis.

Considering the possibility of moyamoya syndrome, we obtained a digital subtraction angiography (DSA) of the arch of aorta, its branches and the cerebral vasculature (Fig 2).

The DSA revealed 48% diffuse narrowing of the right internal carotid artery with severe (78%) narrowing of its supraclinoid part. The left internal carotid artery showed severe (76%) narrowing of its supraclinoid part. The A1 segment of the right anterior cerebral artery (ACA) and M1 segment of the right middle cerebral artery (MCA) were markedly narrowed with a few thin and slender branches of M2 and M3 segments of the right MCA visualized. The A2

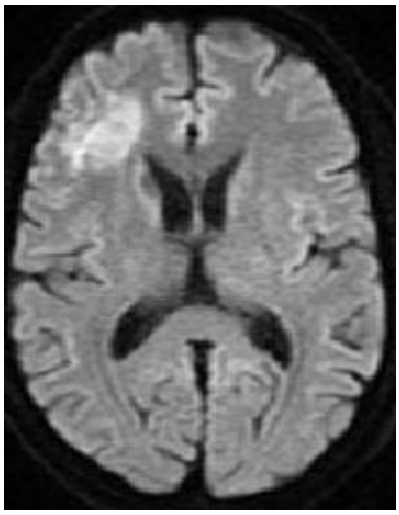

Fig 1 — MRI brain showing hyperintense lesion in the right frontal area

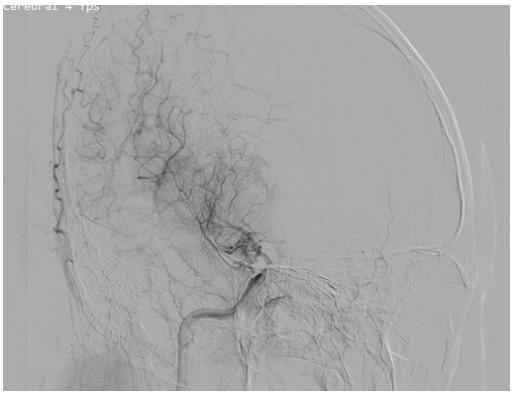

Fig 2 — DSA images showing typical puff of smoke appearance of the cerebral vasculature

and A3 segments of the right ACA were filled by the left ACA through the anterior communicating artery. The filling of the left posterior cerebral artery (PCA) was through the left posterior communicating artery from the left internal carotid artery. Extensive collaterals from the PCA through the posterior communicating arteries on both sides and, in addition, branches of the external carotid artery were seen supplying the brain in the MCA territories. This gave the 'puff of smoke' appearance suggestive of a moyamoya syndrome.

The patient was diagnosed as a case of facial seizures secondary to stroke due to moyamoya syndrome caused by atherosclerosis.

He was managed with long acting insulin analogues and human regular insulin transitioned into oral hypoglycemic agents, statins, calcium channel blockers and levetiracetam. He was then referred to neurosurgery for management of his moyamoya syndrome.

Discussion

Moyamoya disease, first characterized by Suzuki and Takaku in 1969, is characterized by a chronic, progressive occlusion of the supraclinoid part of the internal carotid arteries with reduction of blood flow in the anterior circulation.This leads to the development of collateral vasculature near the apex of the carotid, on the cortical surface, leptomeninges and branches of the external carotid artery supplying the dura and base of skull. In rare cases, the disease process may affect the posterior circulation as well[1,5].

The characteristic angiographic appearance of the abnormally dilated collaterals, after which the entity is named, has been likened to that of 'something hazy, like a puff of cigarette smoke' which in Japanese is moyamoya. Different workers have tried to rename the disease but the International Classification of Diseases (ICD) 10th revision endorses the term moyamoya disease[1].

It must be kept in mind that moyamoya is simply an angiographic appearance, referring to the 'puff of smoke' appearance of the collateral vessels. Moyamoya disease refers to the idiopathic, sometimes familial, noninflammatory, nonatherosclerotic variety. Moyamoya syndrome refers to a vasculopathy with the characteristic angiographic appearance developing in the background of a number of well characterized conditions which include atherosclerosis, diabetes mellitus, sickle cell syndrome, Graves disease, antiphospholipid antibody syndrome, Down syndrome, Allagille syndrome etc[2].

The idiopathic variety has a strong geographical and familial predilection and commonly affects people of Japanese and Korean ancestry. The incidence in East Asia is almost 10 times that of Western countries[3]. It usually affects females more than males and in Japan, moyamoya disease is the most common pediatric cerebrovascular disease with a prevalence of approximately 3/100,000 children. The epidemiological data on moyamoya syndrome, pertaining to India is not well known but case series from a number of centres across the country are gradually becoming available[8,9].

Moyamoya disease is familial in almost 10% cases in Asia and in 6% in North America. A polymorphism R4810K in the gene RNF 213 at chromosome 17q25.3 is a genetic susceptibility factor for East Asian populations. HLA A*24, B*46,B*54,6q25 etc have also been identified as risk factors[1,6].

The etiopathogenesis of moyamoya disease involves stenosis beginning at the distal intracranial internal carotid artery (ICA) at the bifurcation. This then progresses to involve the proximal ACA and MCA. The posterior circulation is involved in the later stages. The stenotic process is accompanied by collaterals developing at the base of the brain and the lateral ventricles which perfuse and nourish the threatened brain. Finally, the anterior and middle cerebral circulations are supplied and reinforced by dural and extracranial arterial networks.

Histopathology of the stenotic vessels reveals endothelial hyperplasia, intimal thickening, duplication of theinternal elastic lamina and attenuation of the tunica media. The moyamoya collaterals on histopathology show fibrinoid necrosis, fragmentation of elastic lamina and microaneurysm formation. The latter may explain why some patients present with intracranial hemorrhages. On the other hand, some of the collaterals on histopathology show collapsed and thrombosed lumens, perhaps accounting for the ischemic symptoms. Moyamoya syndrome secondary to atherosclerosis shows the characterstic atheromatous changes in addition to many of the findings present in the idiopathic variety.

Clinical presentation varies between ischemia and bleeding manifestations. Pediatric patients classically present with ischemic features specially TIA and infarcts. This may be precipitated by seemingly minor events such

as crying and induction of anesthesia for minor surgical procedures. The presumed mechanism is that normal cortical vessels, already maximally dilated due to chronic ischemia, may constrict in response to lowered arterial CO_2 levels due to hyperventilation, thus causing infarction. Dehydration and bleeding due to any cause, renders the patient unusually susceptible to ischemic symptoms. Older patients usually present with intracranial bleeds. The usual location is intraparenchymal (mostly basal ganglionic), intraventricular and often subarachnoid. In fact, moyamoya should be in the differential for CADASIL and all nonhypertensive spontaneous intracrebral hematoma especially primary intraventricular hemorrhage[1,5,9].

Headache is also a common symptom in moyamoya syndrome, caused by dural nociception by the dilated collaterals. It is migraine like and often resistant to both medical therapy and revascularization procedures.

Diagnosis is suggested by CT and MRI imaging of the brain and cerebral vasculature but diagnosis is confirmed by conventional catheter angiography. It is believed that advances in noninvasive neurovascular imaging will eventually allow it to reach the same level of diagnostic certainty as that of the latter. The disease severity is also determined at the time of diagnosis using the Suzuki system developed in 1969[1,5,7].

EEG is a helpful adjunct since it shows the characteristic 'build up' and 're-build up' phenomenon induced by hyperventilation. This finding, characteristic of moyamoya disease is thought to arise from reduced arterial CO_2 tension, which causes vasoconstriction of previously maximally dilated normal cerebral vessels and leads to cerebral ischemia. PET CT and SPECT studies are also used.

Treatment of moyamoya disease or syndrome is complex and involves both medical and surgical components. It is ideally suited to centres that deal with these cases in large volumes and have developed considerable clinical expertise in the same.

Medical therapy involves antiplatelet agents for prevention of ischemia developing from microthrombi in arterial stenoses. Calcium channel blockers may also be used for the moyamoya headache. But it should be remembered that these often induce hypotension that is potentially deleterious and might cause infarcts. Potential new agents include angiogenic growth factors and gene therapy.

Neurosurgery is the mainstay of therapy and involves creating anastomoses between the blood starved arteries of the circle of Willis and the external carotid circulation. Surgical options include the direct bypass procedures like STA-MCA bypass and indirect ones like EDAS (encephalo-duroarteriosynangiosis), EMS (encephalomyosynangiosis) and multiple burr hole procedures.

At present, hybdrid procedures involving both methods are being used at multiple centres. This is more beneficial for children with moyamoya disease where the donor vessels are quite thin and patency is an issue.

Surgery should be recommended for all symptomatic patients with angiographically proven moyamoya disease. It is unclear at this time whether the same can be recommended for atherosclerotic moyamoya syndrome. Controversy exists as to the optimal management of these patients and the means by which it should be done – medical or surgical. Endovascular procedures have been tried but have had high rates of recurrence and complications. However, in case of symptomatic ischemia and hemorrhage, neurosurgical referral for revascularization procedures may be recommended. Optimized management of the underying atherosclerotic risk factors must not be overlooked in these patients.

It should thus be remembered that atherosclerotic vasculopathy can present as a moyamoya syndrome, especially in the Indian population. In such cases, a secondary cause should be sought after in order to exclude a potentially treatable disorder. Since the Indian population is a high risk population with respect to lifestyle diseases like atherosclerosis, diabetes, hypertension, coronary artery disease and stroke, proper evaluation of an atherosclerotic etiology is crucial. This becomes more important if the patient has underlying risk factors for atherosclerosis as in our case – diabetes, dyslipidemia, hypertension and smoking.

In such cases, prompt confirmation of diagnosis using angiographic methods and prompt referral to neurosurgery will help reduced the morbidity and mortality associated with this disease.

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