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Clinical and angiographic findings in Moya Moya

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Patient: Female, 40
Final Diagnosis: Moya-Moya Disease
Symptoms: Blurred vision • headache • lethargy
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Rare disease
Background: Moya Moya is a cerebrovasculopathy of the terminal internal carotid arteries and the proximal anterior and middle cerebral arteries. It is comparatively more common in Japan compared to Western countries.
Case Report: We present a patient of South-East Asian origin diagnosed with Moya Moya, confirmed on magnetic resonance angiography and later computerized tomography angiography. She was managed conservatively through medical management and lifestyle advice, and has now been enlisted into the national Moya Moya database in the UK.
Conclusions: We believe this report will help advance our understanding on Moya Moya and help to elucidate the importance of a combined medical and radiological approach to this condition.

MeSH Keywords: Moya Moya Disease – diagnosis • Cerebrovascular Disorders • Brain Ischemia

Abbreviations: **EMS** – encephalomyosynangiosis; **EDAS** – encephaloduroarteriosynangiosis; **ACA** – anterior cerebral artery; **MCA** – middle cerebral artery; **ICA** – internal carotid artery; **CSF** – cerebrospinal fluid; **MRI** – magnetic resonance imaging; **MRA** – magnetic resonance angiography

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Background

Moya Moya is a cerebrovasculopathy that results in stenosis of the terminal internal carotid arteries and the proximal anterior and middle cerebral arteries [1,2]. This results in collateral vascularization at the base of the brain, which on cerebral angiography appears as a 'puff of smoke', which is termed Moya Moya in Japanese [1,2].

It is important to distinguish Moya Moya disease from the Moya Moya syndrome. The latter entity consists of patients who have the characteristic Moya Moya findings but with comorbidities such as Down syndrome, sickle cell disease, neurofibromatosis type 1, and in those patients who have received cranial radiotherapy for tumors [3].

Extensive research has been undertaken to elucidate the etiology and pathogenesis of the disease. Autopsy and biopsy samples have shown fibrocellular thickening of the intimal layer with thinning of the tunica media [4,5]. There has, however, been no evidence of atherosclerosis or inflammatory changes; rather, smooth muscle hyperplasia, mural thrombi and lipid deposits have been the cause for occlusion [6,7]. The basal Moya Moya collateral vessels are very thin and have been found to demonstrate microaneurysms that are vulnerable to rupture [3,8].

It is not fully understood why these changes occur, but Moya Moya patients display elevated levels of basic fibroblast growth factor, transforming growth factor β-1, hepatocyte growth factor, vascular endothelial growth factor, matrix metalloproteinases, intracellular adhesion molecules, and hypoxia-inducing factor 1α [3,9–12]. CSF analysis of these patients displays elevated levels of cellular retinoic acid-binding protein-I; *in vitro* studies have shown that this leads to reduced negative feedback normally relayed by retinoic acid on growth factor-stimulated smooth muscle cell proliferation and could be the cause of the thickened intima [13].

In Japan, 10% of patients with Moya Moya have first-degree relatives with the disease compared to 6% in the USA. This suggests a strong genetic predisposition to the disease [3,14]. Linkage analysis studies have found associations with *loci* on chromosomes 3, 6, 8, and 17 [3,15–17]. However, environmental factors that play an equally important role make Moya Moya most likely a polygenetic disease [3].

Case Report

A 40-year-old female patient of South-East Asian descent presented with a 12-hour history of severe left-sided temporal headache. She had associated left eye pain, blurry vision, and chemosis with longstanding lethargy. She did not complain of any scalp tenderness or jaw claudication but did recall that 10 months before she had an episode of dysphasia that lasted for 30 minutes, but with no focal-associated neurological signs.

During childhood, the patient recalled that she had frequent headaches and early myopia, for which she had a CT angiogram of her cerebral vasculature in Chennai, which was reported as normal.

The patient's medical history consists of migraine and episodes of uveitis, a dendritic corneal ulcer, and left nasolacrimal duct blockage in 2005, for which she had dacrocystorrotomy. She is a non-smoker, drinks alcohol occasionally, and works in the medical profession.

On examination her GCS was 15/15. Power in all 4 limbs was 5/5. Reflexes were mildly brisker in the right arm compared to the left arm, tone was normal throughout, as was sensation and proprioception. The left pupil was fixed, dilated, and injected. Fundoscopy revealed a normal retina.

On auscultation, her heart sounds were normal, her chest was clear, and her abdomen was soft and non-tender; with no organomegaly and with normal bowel sounds.

ECG showed sinus rhythm and there were no abnormalities in her blood test, which included basic hematology and electrolytes, as well as a normal vasculitic screen. Lumbar puncture showed CSF oligoclonal bands, with a CSF WCC 2/μL (0–5/μL), RCC 3/μL (0/μL), CSF protein 36 mg/dL (15–45 mg/dL), and a CSF glucose of 43 mg/dL (40–85 mg/dL).

The report from the MRI head that was subsequently done indicated generalized vasculopathy with normal extracranial arteries but near occlusion of the internal carotid arteries as they enter the skull; there was an old left MCA territory infarct in the left corona radiate (Figure 1 and 2).

CT angiogram of the cerebral vasculature showed reduction in calibre of both clinoid and supraclinoid ICAs, with slightly more on the right. There was little or no opacification of the MCAs and ACAs. Furthermore, there was marked narrowing of the distal left PCA, with a myriad of fine and irregular appearing collaterals in the anterior perforated substance and related to the left choroidal fissure. The distal anterior cerebral arteries were reconstituted mainly via collaterals from the posterior circulation. There also appeared to be prominent leptomeningeal collateral vessels over the medial aspect of both frontal lobes and over both temporal lobes, at least some of which were arising from the middle meningeal arteries.

In summary, the appearances are in keeping with a widespread vasculopathy of the carotid vessels, with no visible flow in the left proximal MCA, but good collateralization distally.

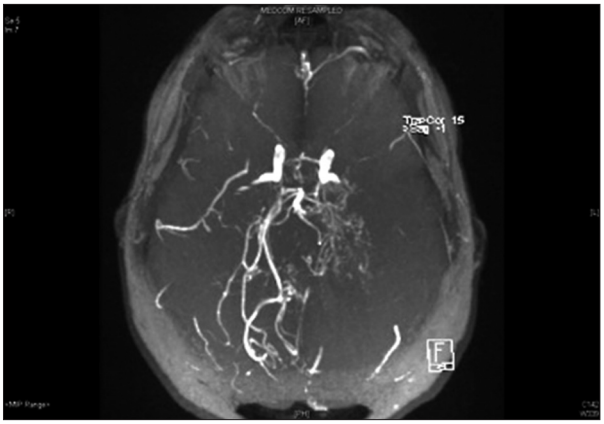

Figure 1. Magnetic resonance angiography: Time of Flight MR angiogram. MIP axial image showing occlusion at both distal ICAs and Moya Moya collateral vessels as a 'puff of smoke' on the left.

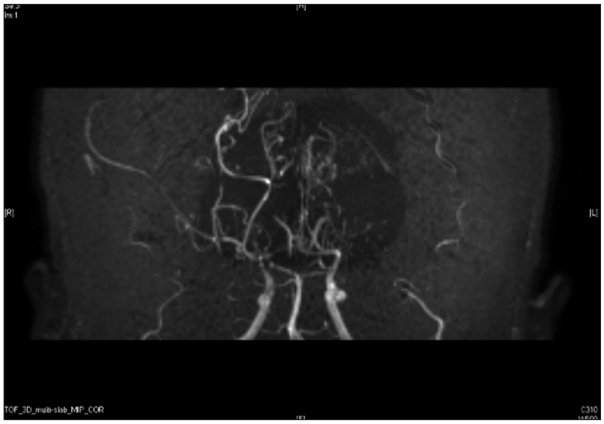

Figure 2. Magnetic resonance angiography: Time of Flight MR angiogram. MIP coronal image showing Moya Moya collateral vessels as a 'puff of smoke' on the left and reduced conspicuity of the left PCA.

Our immediate management for the patient was to initiate 300 mg aspirin for 2 weeks, with 40 mg prednisolone daily, for she which she was to wean off every 2–3 days. She was referred to the specialist Moya Moya centre at the National Hospital for Neurology and Neurosurgery. Subsequently, the patient has now been entered into the national Moya Moya database and her revised management plan is to continue with daily aspirin, advice on lifestyle factors to maintain a low blood pressure, and a suggestion to take migraine prophylaxis medication for any recurrent headaches. The steroid regimen was discontinued and she will now be followed up with yearly reviews.

Discussion

Takeuchi and Shimizu first described the disease in 1957 [18]. Moya Moya disease is more prevalent in the Asian population and is the most common cerebrovascular disease in Japanese children [3,19], with a reported prevalence rate of 0.003 [19]. The incidence rate in Japan is 0.35 per 100 000 compared to the American population of 0.086 cases per 100 000 persons [20,21]. However, Asian Americans have higher incidence-rate ratios in comparison to other ethnic subgroups: 4.6 for Asian Americans, 2.2 for blacks, and 0.5 for Hispanics, as compared with 1.5 for whites. There is a bimodal presentation of the disease, peaking at 5 and 40 years of age [21]. Women are twice as likely to be affected as males [20,21].

Symptoms and signs of Moya Moya are categorized according to whether there is resulting ischemia from occlusion of the carotid vessels or hemorrhage of the vulnerable collateral vasculature [3]. Ischemic stroke and transient ischemic attacks are more common in children compared to adults, who are more likely to present with cerebral hemorrhage [22,23]. However, population studies have shown subtle differences between the Asian population and the rest of the world: a predilection for women in the non-Asian population, who tend to be afflicted with the ischemic symptoms more than hemorrhage, regardless of age [22,23].

Interestingly, CT angiogram in our patient showed a normal cerebral vasculature during her childhood, suggesting that she did not have congenital Moya Moya. The current episode of headache for which she presented with lasted 12 hours before admission. It is possible that obliteration of arteries could have happened concomitantly with the start of the headache. There was, however, no evidence of any arterial dissection in the vascular imaging.

The areas susceptible to infarction are at the watershed regions between the anterior, middle, and posterior cerebral arteries [3]. This involves the frontal, parietal, and temporal lobes. Ensuing symptoms can then be hemiparesis, dysarthria, aphasia, cognitive impairment, seizures, and ophthalmoplegia [3]. The likely sites for hemorrhages are intraventricular, subarachnoid, and intraparanchymal [3]. Headaches are also a common complaint, which can mimic migraines; they are believed to arise from dilatation of the meningeal and leptomeningeal vasculature [24].

Blood tests are usually nonspecific in Moya Moya, and the criterion standard investigation is angiography [25]. MRI and MRA are invaluable, and positive findings entail reduced blood flow in the internal carotid, middle cerebral, and anterior cerebral arteries, coupled with increased flow in the basal ganglia and thalamus due to the Moya Moya collaterals [3,26].

Suzuki developed a Moya Moya grading system, with increasing severity from grades 1 to 6 [1,3] (Table 1).

Table 1. Suzuki Grading System [1,3].

Grade	Description
1	Narrowing of ICA apex
2	Initiation of Moya Moya collaterals
3	Progressive ICA stenosis with intensification of Moya Moya-associated collaterals
4	Development of ECA collaterals
5	Intensification of ECA collaterals and reduction of Moya Moya- associated vessels
6	Total occlusion of ICA and disappearance of Moya Moya-associated collaterals

Grades 1–6 showing the increasing severity of Moya Moya.

Moya Moya is diagnosed with the conjunction of clinical and radiographic findings. Our patient's temporal headache, dysphasia, and evidence of progressive ICA stenosis with intensification of Moya Moya-associated collaterals on angiography place her in grade 3 of the Suzuki classification. We noted complete stenosis of her left proximal MCA compared to the right MCA, indicating asymmetric disease involvement, suggesting that awareness of unilateral angiographic findings in the diagnosis of Moya Moya can be crucial.

Medical treatment for Moya Moya involves maintaining a constant low blood pressure by use of antihypertensives, calcium channel blockers, and daily aspirin [3] as needed. For symptomatic Moya Moya patients, usually in grades 2 to 4, surgery is offered and has been reported to be very effective [25]; patients should have already experienced either stroke or hemorrhage [25].

The 2 types of surgery offered are differentiated into direct and indirect techniques. The direct form involves creating an anastomosis between the superficial temporal artery and the middle cerebral artery, resulting in immediate augmentation of cerebral blood flow [3,25]. Indirect techniques include encephalomyosynangiosis (EMS), which is essentially connecting the temporalis muscle to the brain surface to stimulate collaterals from the deep temporal artery [3,25].

Alternatively, encephaloduroarteriosynangiosis (EDAS) can be done, which is creating an artificial connection between the superficial temporal artery and the surface of the brain through burr holes [3,25]. This will produce arterial collaterals to supply regions of the brain that were not being perfused because of Moya Moya [3,25].

Encephaloduroarteriomyosynangiosis is a combination of EMS and EDAS [3,25]. This type of sophisticated neurosurgery has to be performed at a specialist Moya Moya center.

Conclusions

We have presented one of a very few cases in the literature of a patient of South-East Asian descent who has Moya Moya. It is important for practitioners to be alert to young patients presenting with symptoms of stroke, but without any underlying risk factors, and to consider the diagnosis of Moya Moya. Appropriate imaging must be done as soon as possible, with immediate transfer to a Moya Moya specialist center if Moya Moya is suspected.

Competing interests

There are neither any financial or non-financial competing interests in the publication of this manuscript.

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