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Moyamoya Disease: A Comprehensive Case Report and Review of Clinical Presentation, Diagnosis, and Management Approaches"

Charanya A.G.*1, Shoba S.P.1, Sneha.V1, Keren Ann George2
1-Department of Pharmacy Practice, Affiliated to "The Tamil Nadu Dr. MGR Medical University", Chennai, Tamil Nadu, India.
2-Department of Pharmacy Practice, Affiliated to "The Tamil Nadu Dr. MGR Medical University", Chennai, Tamil Nadu, India.

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ABSTRACT
Moyamoya disease(MMD) is a rare disease which causes cerebrovascular steno-occlusion which is characterized by progressive stenosis of the internal carotid artery. The clinical presentation is well described and it affects both the pediatric and adult population, and may lead to ischemic or hemorrhagic stroke, headache, epilepsy or transient ischemic attack. Despite their rarity, MMD is well described in the medical literature. Herein we present the case report of a 17-year-old female patient diagnosed with moyamoya disease. The patient presented with symptoms and the further investigations, such as cerebral digital subtraction angiography showed ICA occlusion consistent with MMD. The detailed analysis of her case, provides both knowledge and insight to the presentation and the medical and surgical management and multidisciplinary approach for this rare and challenging condition.

Keywords: Moyamoya disease, Internal carotid artery, Case Report,Encephalo-Duro-Arterio-Myo Synangiosis

I. INTRODUCTION:

Moyamoya disease (MMD) is a cerebrovascular steno-occlusive condition characterized by progressive stenosis of the terminal portion of the internal carotid artery and the formation of an abnormal network of dilated, fragile perforators at the base of the brain.[1]Adult moyamoya disease and syndrome are rare disorders with significant morbidity and mortality. Since the 1950s, this rare disease has been reported in Japan and gradually has gained recognition around the world. Suzuki and Takaku first published the term "moyamoya disease" in an English-language journal in 1969.[2]In the 1970s, the Japanese Ministry of Health and Welfare organized the Research Committee on Moyamoya Disease (RCMD) to provide cohesive diagnosis, treatment, and prevention methods. This research group first established the guidelines for diagnosis of MMD in 1978, and has revised them since then on 5 occasions.[3]

The term characterizes the obscured hazy angiographic appearance of collaterals "MoyaMoya vessels (hazy puff of smoke)" resulting from insufficiency in the circle of Willis. The incidence of MMD is high in East Asian populations but low in European and North American populations. The Ministry of Health and Welfare of Japan has defined 4 types of moyamoya disease (MMD): ischemic, hemorrhagic, epileptic, and "other".[4] The ischemic type has been shown to predominate in childhood, while the hemorrhagic type is more often observed in the adult population. The highest prevalence of MMD is found in Japan, with a higher female to male ratio.

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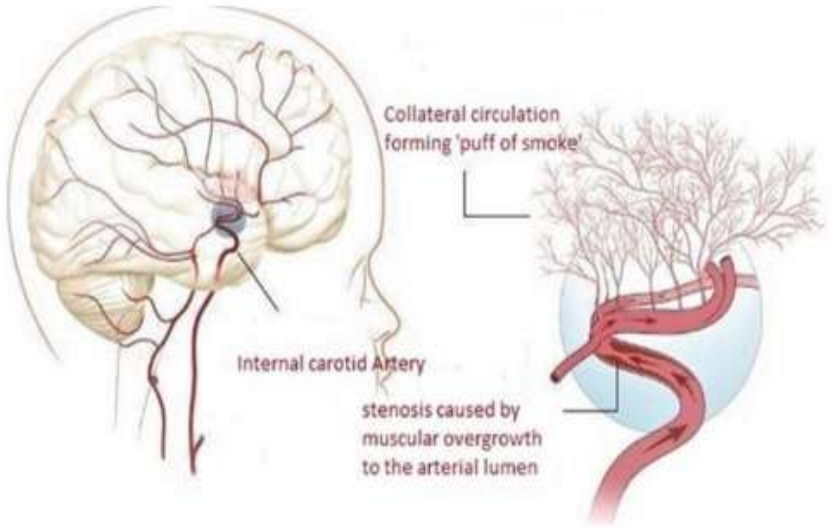

Figure 1: Stenosis found in the Internal Carotid Arteries (ICAs) and hazy network of basal collaterals.[21]

During autopsy, intracerebral hematoma is found and most commonly serves as the major cause of death in patients with MMD. Moyamoya vessels at the base of the brain are composed of medium-sized or small muscular arteries emanating from the circle of Willis, mainly the intracranial portions of ICAs, anterior choroidal arteries, and posterior cerebral arteries, forming complex channels that connect with distal positions of the MCAs. Off of these channels are small tortuous and dilated vessels that penetrate into the base of the brain at the site of the thalamoperforate and lenticulostriate arteries. On angiography, there is the characteristic stenosis or occlusion bilaterally at the terminal portion of the ICAs as well as the moyamoya vessels at the base of the brain.

Six angiographic stages have been described, from Stage 1, which reveals a narrowing of the carotid forks, to Stage 6, in which the moyamoya vessels disappear and collateral circulation is produced solely from the external carotid arteries.[5]

The diagnostic criteria for MMD according to Fukui et al. involved three criteria: 1) The stenotic occlusion of the terminal ICA and the proximal portion of anterior and/or middle cerebral arteries, 2) Abnormal vascular network evidenced in the arterial phase in proximity to the occlusion, and 3) Bilateral involvement.[6]

EPIDEMIOLOGY:

The incidence of MMD exhibits significant regional differences, with a high incidence in East Asia and a low incidence in other regions. According to previous studies, the prevalence of MMD is 10.5/100,000 individuals and the incidence rate is 0.94/100,000 individuals in Japan[7]; in South Korea, the prevalence rate is 16.1/100,000 and the incidence rate is 2.3/100,000 individuals.[8] The incidence of MMD was as low as 0.09/100,000 individuals in other regions, including North America, but it has exhibited an upward trend in the US. [9]In Nanjing (China), the prevalence of MMD in the time frame of 2000–2007 was 3.92/100,000. [10]According to the most recent study, 2,430 cases of MMD have been reported in China since 1976.[11]

Worldwide, the age of onset of MMD is significantly bimodal in distribution, with a bimodal peak consisting of a major peak in the first decade of life and a moderate peak in the late 20 to 30s.[11] Of note, geographic differences in sex distribution have been observed. In foreign populations, the incidence of MMD in females was reported to be higher than that in males with the male-to-female ratio ranging from 1:1.8 to 1:2.2 [7-10]; however, the sex ratio is 1:1 in China.[10]

ETIOLOGY:

Moyamoya disease may be linked to inherited conditions and associations**,** including:

- Sickle Cell Disease or trait
- Down Syndrome (Association)
- Neurofibromatosis type 1 (Association)

Acquired conditions:

- Head and/or neck irradiation
- Chronic meningitis
- Skull base tumor

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- Atherosclerosis of skull base arteries
- Arteriosclerosis
- Cerebral vasculitis.[12]

PATHOPHYSIOLOGY:

The pathophysiology of MMD remains unclear, though genetic predisposition is theorized in East Asian countries. Mutations in BRCC3/MTCP1 and GUCY1A3 genes are implicated in Moyamoya syndrome. Affected individuals are found to have concentric and eccentric fibro cellular thickening of intima within the intracranial portion of ICA. In a study involving the Midwestern US population, an unusually high prevalence of type 1 diabetes, autoimmune thyroid disorders, and other autoimmune disorders were found in the moyamoya cohort which may point towards an autoimmune association. Chronic brain ischemia resulting from the narrowing is believed to be causing an overexpression of proangiogenic factors (fibroblast growth factor and hepatocyte growth factor) which, in turn, would cause the development of a fragile network of collateral vessels.[12]

The basic pathology of MMD mainly includes intimal fibrous hyperplasia of the intracranial arterial stenosis, irregular proliferation of the inner elastic layer, thinning of the middle layer of the vessel wall and reduction of the outer diameter of the blood vessel. A high-resolution MRI cohort study indicated that most patients with MMD had a contractile remodeling at the distal end of the ICA and a long concentric enhancement.[13] This result is consistent with the thickening of the arterial intima and the thinning of the tunica media detected by vascular pathology.

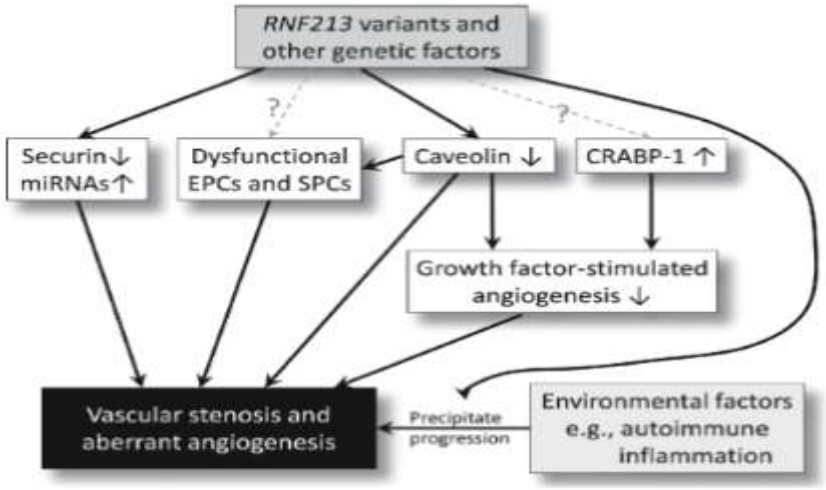

Figure 2: The pathophysiology of Moyamoya Disease.[20]

II. CASE PRESENTATION:

A 17-year-old female patient presented with complaints of left-sided upper limb weakness for the past 6 days then improved and again had multiple episodes. At the time of admission, she reported complete weakness and pain in her left upper limb and had no complaints of slurring of speech. On examination, the patient was conscious, oriented and afebrile. All the vitals were normal apart from systemic examination of the central nervous system which showed left upper limb (2/5) hand grip weakness and plantar was mute. The patient was advised to get admitted for further evaluation and management.

All the hematological investigations were within normal limits apart from the coronary risk profile. Her HDL cholesterol levels were found to be lower (47 mg/dl) and direct LDL cholesterol level was found to be a little higher (107 mg/dl) than the normal range (less than 100mg/dl). Her Echo revealed normal LV systolic function (EF-66%) and no RWMA. On the post-admission day, the patient underwent the diagnostic procedure, Cerebral digital subtraction angiography which revealed bilateral ICA occlusion intracranially with filling of distal vessels through collaterals, consistent with MOYA MOYA DISEASE. Her dsDNA, p-ANCA and c-ANCAs were found to be negative.

Initially she was started on Inj. Dexa-4mg, T.ecospirin-75mg, Inj. Strocit-500mg, Inj.pan-40mg , C.Remylin AX-1 cap. The patient has

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undergone elective EDAMS (Right Encephalo-Duro-Arterio-Myo Synangiosis). During the procedure under ETGA, the head turned to the left, scalp mused+ flap raised preserved STA. The frontal branch is identified and preserved. Temporalis stripped from pericranium. Free bone flap craniotomy was done. The frontal branch ofthe Superficial Temporal Artery (STA) along with the cuff coagulated and cut. Distally and rotated into the defect and sutured to dural edge. Temporalis muscle, overlaid; hemostasis secured. Temporalis fascia sutured to dural margins bone flap placed over and anchored loosely with titanium miniplates and screws. Hemostasis reconfirmed. Dressed and taped. Intra-op and post-op periods were uneventful. Post-operative CT-brain (plain) was done which showed Diffuse hypodense areas noted in the Right frontal and parietal lobes-S/O old infarcts. Post right temporal craniotomy status, post-operative changes in the form of soft tissue thickening with extra calvarial air pockets in the right temporal scalp region and minimal extra-axial hemorrhage in the surgical bed, Pneumocephalus noted in bilateral frontal region- post operative changes.

Post-op, the patient was started on Inj.Dexa-4mg, Inj. Levipil-250mg, Inj.Supacef-1.5gm, Inj.Paracetamol-1gm, Inj.Tramadol-50mg, Inj.pan-40mg and de-escalated on the following days T.strocit-500mg, T.Ultracet-1 tab, Cap.Remylin AX-1 cap, T.pan-40mg, T.Dexa-4mg, T.Strocit plus-1 tab, T.Stil OZ-50mg, T.Naprosyn-250mg sos. The patient was neurologically and hemodynamically stable. Since then, the patient improved symptomatically and was discharged with C.Remylin AX-1cap, T.Pantop-40mg, T.Stil OZ-50mg, T.Levipil-500mg and T.Ultracet-1 tab.

III. DISCUSSION:

Moya Moya disease (MMD) is a type of chronic cerebrovascular occlusion disease, which frequently occurs in the East Asian population, including pediatric and adult patients, and may lead to ischemic or hemorrhagic stroke, headache, epilepsy or transient ischemic attack. The prevalence of the disease ranges from 3.2 to 10.5 per 100,000 population and is found to be more common among Asian origin people. About 57% of the affected patients are Asianand 71% are female. In a study conducted by Berry JA et al., (2020) stated that MMD has an almost 2:1 female-to-male ratio in the adult population.[14]

Although the disease may be seen in any age group, it is more common in people from 5-15 years and 30-40 years of age. Both adults and children may present with different clinical findings. Usually, children may present with hemiparesis, monoparesis, sensory impairment, involuntary movements or seizures etc., and adults may experience hemorrhage(can be subarachnoid, intraventricular or intracerebral) in sudden onset and symptoms as same as children. Similarlya study by Sarah Lee et al., (2017) An international multicenter stroke database showed that 90% of MMD patients initially presented with ischemic stroke, 7.5% with a transient ischemic attack, and 2.5% with hemorrhagic stroke.[15]

Family history is present in about 10-15% of the patients. Risk factors include Down syndrome, sickle cell anemia, congenital heart disease, fibromuscular dysplasia activated protein c resistance, head trauma, familial cause (10%) and genetically susceptibility loci have been found on 3p,6p,17q,and band 8q23. A genomic-wide association study identified RNF213 as the first gene associated with moyamoya.

The diagnosis was done based on the cerebral digital subtraction angiography revealed bilateral ICA occlusion intracranially with the filling of distant vessels through collaterals, consistent with Moya Moya disease - Gupta A, et al., (2020) also suggest that gold standard investigation for Moya Moya disease is cerebral angiography. [16]

The management is based on two types i.e., medical and surgical management. Medical management includes two phases which are an acute and chronic phase. Management of acute cases of ischemic stroke due to MMD is symptomatic. Aspirin should be given to children with acute anterior ischemic stroke due to MMD. Similarly our patient is also treated with aspirin due to stroke-like symptoms such as left-sided weakness associated with pain. Surgery is beneficial over conservative management in the recurrence of stroke. In the case of children with MMD takes a rapid course and has a poor prognosis. Therefore, surgical revascularization is recommended in MMD at a young age.

Zhang H et al., (2019) suggest that the surgical indirect revascularization is based on a variety of tissues used as a source of blood supply, mainly including encephaloduromyoarteriosynangiosis, encephaloduromyoarteriopericranial synangiosis, encephalomyosynangiosis etc., in our patient elective EDAMS procedure(Right encephalo-Duro-Arterio-myosynangiosis) is done in order to

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improve the quality of life of the patient by reducing the clinical symptoms. [17]Gupta A et al., (2020) suggest that indirect revascularization depends on the formation of new vessels, which can take months to form and it is also dependent on age, with children showing better results than adults.[16]

Deng et al., (2018) state that indirect revascularization is easy to perform compared to direct revascularisation procedures, which shortens the operation time and reduces intraoperative complications.[18]

A study conducted on the long-term surgical outcome of Indirect revascularization surgery in young patients with Moyamoya disease by Eun Jin Ha et al., (2023) showed that out of 1417 patients 88% of them had favourable clinical outcomes and there was no hemorrhagic event. He also concluded that Indirect revascularization surgery could provide satisfactory long-term outcomes and prevent recurrent stroke in young patients.[19]

IV. CONCLUSION:

Moya Moya disease (MMD) is a chronic and progressive cerebrovascular occlusion disease. The incidence of the disease is higher in the East Asian population and to more common in female than male patients. MMD is the main cause of cerebral stroke in both the young and adult population. Still, the pathogenesis of moyamoya disease is not completely known. Increasing knowledge about the disease helps in early diagnosis and prevention of adverse effects. A multidisciplinary approach involving neurology, neurosurgery and other supportive care to patients, helps in optimizing the treatment regimen, management and improving the patient's quality of life.

In the case of management, surgical management provides satisfactory long-term outcomes and also prevents recurrent stroke attacks in young patients. Medical management is given usually as a symptomatic treatment. Therefore, Surgery is beneficial over conservative management in the recurrence of stroke. Ongoing trials and genetical studies, help in providing novel treatment approaches for MMD.

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AUTHOR'S CONTRIBUTION
A G, S P and S V collected the full details of the case, wrote and prepared the final draft of the manuscript. performed a critical review of the manuscript. helped to draft the manuscript. All authors contributed to the article and approved the submitted version.

DECLARATION BY AUTHORS
ETHICAL APPROVAL AND CONSENT TO PARTICIPATE:
Not applicable.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest.

CONFLICT OF INTEREST:
The authors have declared no conflict of interest.

ABBREVIATIONS
MMD:Moyamoya disease;
ICA:Internal Carotid Artery;
MCA: Middle Cerebral Artery;
STA: Superficial Temporal Artery;
HDL: High Density Lipoprotein;
LDL: Low Density Lipoprotein;
p-ANCAs: Perinuclear-Antineutrophil Cytoplasmic Antibodies;
c-ANCAs: Cytoplasmic- Antineutrophil Cytoplasmic Antibodies;
EDAMS: Encephalo-Duro-Arterio-Myo Synangiosis.

V. SUMMARY

Moyamoya disease with bilateral ICA occlusion present challenges due to their impact on the occlusion in collaterals in brain and provides weakness. Although advancement in the medical and surgical managements are available, early and timely diagnosis increasing knowledge and multidisciplinary approach involving neurology, neurosurgery and other supportive care to patients, helps in optimizing the treatment regimen, management and improving the patient's quality of life.

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