STM JOURNALS

Journal of Nursing Science & Practice
ISSN: 2249-4758 (online), ISSN: 2348-957X (print)
Volume 4, Issue 2
www.stmjournals.com

Moyamoya Disease: A Cerebral Disorder of Children

Vishali Galhotra*, Gaurav Kohli, Manu Kohli
[1]Dept. of Medical Surgical Nursing, L.L.R. Institute of Nursing, Moga (Pb.), India
[2]Dept. of Community Health Nursing, M.M. Institute of Nursing, M.M. University Mullana, Ambala (Haryana), India
[3]Dept. of Mental Health Nursing, Mai Bhago College of Nursing, Tarantaran (Punjab), India

Abstract

Moyamoya disease is an increasingly recognized arteriopathy associated with cerebral ischemia and has been associated with approximately 6% of childhood strokes. It is characterized by chronic progressive stenosis at the apices of the intracranial internal carotid arteries (ICA), including the proximal anterior cerebral arteries and middle cerebral arteries. Occurring in tandem with reduction in flow in the major vessels of the anterior circulation of the brain, there is compensatory development of collateral vasculature by small vessels near the carotid apices, on the cortical surface, leptomeninges, and branches of the external carotid artery supplying the dura and skull base. Moyamoya is an increasingly recognized entity associated with cerebral ischemia. Diagnosis is made from clinical and radiographic findings. Surgical revascularization is recommended for definitive treatment of children with moyamoya syndrome. Moyamoya is an increasingly recognized cause of stroke in both children and adults. Patients with certain conditions such as Down's syndrome19 and sickle cell disease may be particularly at risk for moyamoya. Characteristic radiographic findings confirm the diagnosis, and recognition of the disease early in its course, with prompt institution of therapy, is critical in order to achieve the best outcome in patients. Revascularization surgery appears to be effective in preventing stroke in patients with moyamoya.

Keywords: *Cerebral, ischemia, stroke, collateral vasculature*

**Author for Correspondence* E-mail: tandonvg12@gmail.com, gauravkohli78@gmail.com

INTRODUCTION

When we hear that someone has or had, or is at risk for, a stroke, we tend to immediately picture an older person. "After all," we may think, "a stroke is something our parents and grandparents might face not our children." Unfortunately, pediatric stroke is a very real risk for many kids with certain cerebrovascular disorders, including Moyamoya disease. The name "moyamoya" means "puff of smoke" in Japanese and describes the look of the tangle of tiny vessels formed to compensate for the blockage [1]. The disease primarily affects children, but it can also occur in adults. Moyamoya disease is a cerebro vascular condition that predisposes affected patients to stroke in association with progressive stenosis of the intracranial internal carotid arteries and their proximal branches. Reduced blood flow in the major vessels of the anterior circulation of the brain leads to compensatory development of collateral vasculature by small vessels near the apex of the carotid, on the cortical surface, leptomeninges, and branches of the external carotid artery supplying the dura and the base of the skull. In rare cases, this process also involves the posterior circulation, including the basilar and posterior cerebral arteries. Moyamoya disease is a rare, progressive cerebrovascular disorder caused by blocked arteries at the base of the brain in an area called the basal ganglia [2]. Although "spontaneous occlusion of the circle of Willis" has recently been suggested as an alternative to the more evocative name "moyamoya," the International Classification of Diseases recognizes "moyamoya" as the specific name for this condition. Patients with the characteristic moyamoya vasculopathy who also have well recognized associated conditions are categorized as having the

moyamoya disease. By definition, the pathognomonic arteriographic findings are bilateral in moyamoya disease, although the severity can differ between sides. Patients with unilateral findings have the moyamoya syndrome, even if they have no other associated risk factors. However, contralateral disease eventually develops in up to 40% of patients initially presenting with unilateral findings [3].

ETIOLOGY

Etiology of the disease is still unknown. A genetic mode of inheritance is considered possible because of the higher incidence of the disease in Japan and Korea and the familial occurrence among the Japanese as well as in Caucasians [4]. The condition is believed to be hereditary and linked to q25.3, on chromosome. In Japan the overall incidence is higher (0.35 per 100,000). In North America, women in the third or fourth decade of life are most affected. Moyamoya can be either congenital or acquired. Patients with Down syndrome, neurofibromatosis type 1, or head trauma can develop moyamoya malformations. It is more common in women than in men, although about a third of those affected are male [5].

SYMPTOMS

A comprehensive list of Moyamoya disease symptoms includes [6]:

1. stroke: there are two types of stroke:
    - An ischemic stroke occurs when a brain artery has been blocked.
    - A hemorrhagic stroke occurs when an artery rupture or leaks.
2. Recurrent transient ischemic attacks: also known as TIAs or mini strokes.
3. hemiparesis
4. seizures
5. disturbed consciousness
6. speech deficits
7. sensory impairments
8. involuntary movements
9. vision problems
10. Endocrine dysfunction
11. Decline in the IQ of children

PATHOPHYSIOLOGY

The disease Moyamoya appears to look like a "puff of smoke" because the arteries are thinned which makes the blood leak out of the arteries causing pressure to the brain resulting with headaches. The pathogenesis of moyamoya disease is unknown. The gene ring (RNF213) has been implicated in the pathogenesis of this disease. A number of factors have been postulated as playing a role in the pathogenesis of moyamoya disease. Fibroblast growth factor has been proposed as a possible mediator of the neovascular response. There is some evidence to show that CSF (cerebro spinal fluid) bFGF (Basic fibroblast growth factor) may play a role in the pathogenesis of the disease. Transforming growth beta factor 1 (TGF beta 1), a factor involved in angiogenesis and expression of connective tissue genes, was also shown to be elevated in the disease [7]. An unknown CSF protein has been detected in some patients with moyamoya. Further analysis of this protein may reveal a clue by which the molecular mechanism of moyamoya disease may be elucidated. The role of prostaglandin in the pathogenesis of the disease has been studied. These studies have shown that the arterial smooth muscle cells in moyamoya activate cox2 in response to inflammation, and produce excess PGE. This can cause an increase in vascular permeability and decrease the tone, which may promote intimal thickening. A possible role for infection in the pathogenesis has been proposed. The evidence is still inconclusive but some studies have suggested a relationship with Epstein-Barr virus infection. This was based on the increased presence of EBV (Epstein-Barr virus) DNA and antibody in patients with moyamoya [8].

DIAGNOSTIC EVALUATION

Moyamoya should be considered — and diagnostic evaluation initiated — in patients, particularly children, presenting with acute neurologic deficits or unexplained symptoms referable to cerebral ischemia. A delay in diagnosis results in a delay in treatment, increasing the risk of permanent disability from stroke. It is critically important to refer patients with moyamoya, or suspected moyamoya, to centers experienced in the care of such patients. Any patient with unexplained symptoms suggestive of cerebral ischemia should be considered as possibly being at risk for moyamoya. Although the differential diagnosis for these symptoms is broad, the

presence of moyamoya can be readily confirmed by means of radiographic studies. Radiographic evaluation of a patient suspected of having moyamoya usually requires several studies [9].

COMPUTED TOMOGRAPHY

Computed tomography (CT) in a patient with moyamoya disease may show small areas of hypo density suggestive of hemorrhage or of a stroke in the cortical watershed zones, basal ganglia, deep white matter, or per ventricular regions. However, the CT scan can be normal, particularly in patients presenting solely with TIAs. CT angiography can show the intracranial stenosis seen in moyamoya. Thus, CT angiography should be considered when magnetic resonance imaging (MRI) is not readily available and a diagnosis of cerebral occlusive vasculopathy is being considered [10].

MAGNETIC RESONANCE IMAGING

The widespread availability of MRI and magnetic resonance angiography has led to the increasing use of these methods for primary imaging in patients with symptoms suggestive of moyamoya. An acute infarct is more likely to be detected with the use of diffusion-weighted imaging, whereas a chronic infarct is more likely to be seen with T1- and T2-weighted imaging. Diminished cortical blood flow due to moyamoya can be inferred from fluid-attenuated inversion recovery (FLAIR) sequences showing linear high signals that follow a sulcal pattern, which is called the "ivy sign". The finding most suggestive of moyamoya on MRI is reduced flow voids in the internal, middle, and anterior cerebral arteries coupled with prominent flow voids through the basal ganglia and thalamus from moyamoya-associated collateral vessels. These findings are virtually diagnostic of moyamoya [10].

ANGIOGRAPHY

Formal angiography should consist of a full five vessel or six-vessel study that includes both external carotid arteries, both internal carotid arteries, and one or both vertebral arteries, depending on the collateral patterns seen. In a study of 190 patients undergoing diagnostic angiography, complication rates among patients with moyamoya were no higher than those among patients with other forms of cerebrovascular disease. The definitive diagnosis is based on a distinct arteriographic appearance characterized by stenosis of the distal intracranial internal carotid artery, extending to the proximal anterior and middle arteries. Disease severity is frequently classified into one of six progressive stages that were originally defined in 1969. Development of an extensive collateral network at the base of the brain along with the classic "puff of smoke" appearance on angiography is seen in the intermediate stages of the Suzuki grading system. Imaging of the external carotid arteries is essential to identify any preexisting collateral vessels so that surgery, if performed, will not disrupt them. Aneurysms, as well as the rare arterio venous malformation known to be associated with certain cases of moyamoya, are also best detected by means of conventional angiography [11].

OTHER DIAGNOSTIC TECHNIQUES

Other diagnostic evaluations that may be useful in evaluating patients with moyamoya include electroencephalography (EEG) and cerebral blood-flow studies. Specific alterations of EEG recordings, which are usually observed only in children, include posterior or centrotemporal slowing, a hyperventilation- induced diffuse pattern of monophasic slow waves (called "build-up"), and a characteristic "rebuild-up" phenomenon, which looks identical to the build-up slow waves seen in patients without moyamoya, but differs in the timing of its presentation [11]. Build-up occurs during hyperventilation, whereas rebuild-up occurs after hyperventilation and indicates a diminished cerebral perfusion reserve. Techniques such as transcranial Doppler, perfusion CT, xenon-enhanced CT, positron-emission tomography, magnetic resonance perfusion imaging, and single-photon-emission CT with acetazolamide challenge have all been used in the evaluation of patients with moyamoya. These imaging studies may help to quantify blood flow, serve as a baseline before the institution of treatment, and occasionally aid in treatment decisions [12].

TREATMENT

Medical R_x

Medical therapy has been used in patients with moyamoya, particularly when surgery has been considered to present a high risk or the patient has had relatively mild disease, but there are few data showing either its short-term or long-term efficacy. A large survey from Japan showed no significant differences in outcome between medically and surgically treated patients with moyamoya, although a more recent review revealed that 38% of 651 patients with moyamoya who were initially treated medically ultimately underwent surgery because of progressive symptoms. Anti platelet agents have been used to prevent emboli from micro thrombi formed at sites of arterial stenosis a possible cause of ischemic symptoms in patients with moyamoya — and these agents, although not used universally, are used routinely in patients in many operative series [13]. Anticoagulants such as warfarin are rarely used, although there has been some experience with low molecular weight heparin. Calcium-channel blockers may be useful in ameliorating intractable headaches or migraines, which are commonly seen in patients with moyamoya, and these agents may be effective in reducing both the frequency and the severity of refractory TIA. Because calcium-channel blockers may cause hypotension, they must be used with caution in this patient population [14].

SURGERY

The arterio pathy of moyamoya affects the internal carotid artery while sparing the external carotid artery. Surgical treatment of patients with moyamoya typically uses the external carotid artery as a source of new blood flow to the ischemic hemisphere. Two general methods of revascularization are used: direct and indirect [14]. In direct revascularization, a branch of the external carotid artery (usually the superficial temporal artery) is directly an astomosed to a cortical artery. Indirect techniques involve the placement of vascularized tissue supplied by the external carotid artery (e.g., dura, temporalis muscle, or the superficial temporal artery itself) in direct contact with the brain, leading to an in growth of new blood vessels to the underlying cerebral cortex. Historically, direct procedures have been used in adults for whom an immediate increase of blood flow to the ischemic brain is a major benefit [15]. Augmentation of cerebral blood flow usually does not occur for several weeks with indirect techniques. However, direct bypass is often technically difficult to perform in children because of the small size of both donor and recipient vessels, making indirect techniques appealing. Nonetheless, direct operations have been successful in some children, and indirect procedures have been successful in some adults. There is considerable debate about the relative merits and shortcomings of the two approaches; in fact, some centers advocate a combination of direct and indirect approaches [16].

THERAPIES

Rehabilitation with physical therapy, occupational therapy, and speech therapy should be considered, depending on the neurological impairment. The extent of therapy can range from bedside treatment to full, comprehensive inpatient rehabilitation. The latter would include physical, occupational, speech, and cognitive therapy. The condition of the patient, including active co morbidities, dictates his or her involvement in rehabilitation therapy [17].

CONCLUSION

Moyamoya is an increasingly recognized cause of stroke in both children and adults. Patients with certain conditions such as Down's syndrome19 and sickle cell disease may be particularly at risk for moyamoya. Moyamoya was initially recognized as an angiographic pattern. Attempts to classify it into a primary disease form and a secondary form associated with other diseases have led to criterion for its diagnosis being adopted. There is evidence to show linkage of moyamoya to several chromosomes and it is likely to have heterogeneous loci. A role for various growth factors and proteins in its pathogenesis has been proposed and the role, if any, played by infections remains to be elucidated. Better methods for studying the cerebral blood flow and screening have been devised. A number of surgical procedures have been developed for revascularization and there is controversy regarding the timing and the surgical procedure to be used. There is some evidence to show that the pathogenesis may vary in

different races. Moyamoya is an interesting disease and its study may help understand the genetics and the pathogenesis of vasoocclusive diseases in children. Identification at early stage can enhance positive outcome of medical treatment. Surgical intervention includes direct and indirect revisualization.

ACKNOWLEDGEMENT

With profound gratitude we express our heartfelt veneration toward our invaluable family members and friends for enlightening guidance, interest, valuable suggestions and consistent encouragement at all stages of work. We deeply appreciate their untiring and outstanding contribution, encouraging words for compiling the review paper.

METHOD

Review was undertaken using the following databases, pub med, CINAHL, MEDLINE, Newspaper, National, International Journals, and Magazines of Punjab regarding Moyamoya disease.

CONFLICT OF INTEREST STATEMENT

All contributors of this review articles did not have any financial difficulty to carry out this review of Moyamoya Disease: A cerebral disorder of children. There was not any hindrance to write and publish an article**.**

Source of Funding Statement: Self

Ethical Clearance: Since it is a self review paper, ethical; clearance not needed.

REFERENCES

1. Suzuki J, Takaku A. Cerebrovascular "Moyamoya" Disease. Disease Showing Abnormal Net-like Vessels in Base of Brain. *Arch Neurol.* 1969; 20(1): 288–299p.
2. Fukui M. Guidelines for the Diagnosis and Treatment of Spontaneous Occlusion of the Circle of Willis ("Moyamoya" Disease). *Clin. Neurol. Neurosurg.* 1997; 99(1): 238–240p.
3. Kawano T, Fukui M, Hashimoto N, *et al.* Follow-up Study of Patients with "Unilateral" Moyamoya Disease. *Neurol. Med. Chir*. (Tokyo) 1994; 34: 744–747p.
4. Hirotsune N, Meguro T, Kawada S, *et al.* Long-term Follow-up Study of Patients with Unilateral Moyamoya Disease. *Clin. Neurol. Neurosurg.* 1997; 99(1): 178–181p.
5. Karasawa J, Kikuchi H, Furuse S, *et al.* Treatment of Moyamoya Disease with STA-MCA Anastomosis. *J. Neurosurg.* 1978; 49: 679–688p.
6. Malek AM, Connors S, Robertson RL, *et al.* Elevation of Cerebrospinal Fluid Levels of Basic Fibroblast Growth Factor in Moyamoya and Central System Disorders. *Pediatric. Neurosurg.* 1997; 27: 182–189p.
7. Hojo M, Hoshimaru M, Hoshimaru M, *et al.* Cerebrospinal Fluid Associated with Moyamoya Disease: Report of Three Cases. *Neurosurgery* 1999; 45: 170–173p.
8. Yamamoto M, Aoyogi M, Fukai N, *et al.* Increase in Prostaglandin E (2) Production by Interleukin-1 Beta in Arterial Smooth Muscle Cells Derived from Patients with Moyamoya Disease. *Circ. Res.* 1999; 85: 912–918p.
9. Tanigawara T, Yamada H, Sakai N, *et al.* Studies on Cytomegalovirus and Epstein Barr Virus Infection in Moyamoya Disease. *Clin. Neurol. Neurosurg.* 1997; 99(2): 225–228p.
10. Natori Y, Ikezaki K, Matsushima T, *et al.* Angiographic Moyamoya, its Definition, Classification and Therapy. *Clin. Neurol. Neurosurg.* 1997; 99(2): S168–172p.
11. Kuwabara Y, Ichiya Y, Sasaki M, *et al.* Cerebral Hemodynamica and Metabolism in Moyamoya Disease – A Positron Emission Tomography Study. *Clin. Neurol. Neurosurg.* 1997; 99(2): 74–78p.
12. Liu HM, Peng SS, Li VW. The Preoperative and Postoperative Cerebral Blood Flow and Vasoreactivity in Childhood Moyamoya Disease. *Keio J. Med.* 2000; 49(1): A86–89p.
13. Takeuchi K, Shimizu 1. K. Hypoplasia of the Bilateral Internal Carotid Arteries. *Brain Nerve* 1957; 9: 37–43p.
14. Suzuki J, Takaku A. Cerebrovascular "Moyamoya" Disease: Disease Showing Abnormal Net-Like Vessels in Base of Brain. *Arch. Neurol.* 1969; 20: 288–99p.

15. Fukui M. Guidelines for the Diagnosis and Treatment of Spontaneous Occlusion of the Circle of Willis (‘moyamoya’ disease). *Clin. Neurol. Neurosurg.* 1997; 99(2): 238–240p.
16. Kelly ME, Bell-Stephens TE, Marks MP, *et al.* Progression of Unilateral Moyamoya Disease: A Clinical Series. *Cerebrovasc. Dis.* 2006; 22: 109–15p.
17. Smith ER, Scott RM. Progression of Disease in Unilateral Moyamoya Syndrome. *Neurosurg. Focus.* 2008; 24(2): 17p.

