"While finding where the water leaks, you find smoke" - A Case Report: Incidental finding of Moyamoya for a Filipino worked up for Subarachnoid Hemorrhage

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ABSTRACT

Moyamoya Disease was initially reported in 1957 as vessels resembling a puff of smoke, alongside hypoplasia of bilateral internal carotids. The true incidence remains elusive. Genetic studies point to familial occurrence of the disease, however some studies refute this, claiming that environmental factors are to blame. The treatment strategies remain an enigma, more so in our country where data is scarce. We present a case of an asymptomatic Moyamoya disease incidentally diagnosed in the work - up of Subarachnoid Hemorrhage. The basis of the management is being provided.

Keywords: Moyamoya disease, intracranial aneurysm, headache

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INTRODUCTION

Moyamoya is a Japanese word meaning puffy, obscure, or hazy like a puff of smoke in the air. Thus, the term was used to describe the smoky angiographic appearance of the vascular collateral network.[1]

It has been used to refer to an extensive basal cerebral rete mirabile (a network of small anastomotic vessels at the base of the brain, around and distal to the circle of Willis, associated with segmental stenosis of both internal carotid arteries. This form of cerebrovascular disease is predominant but not limited to the Japanese[2]. Originally considered to affect predominantly persons of Asian heritage, but now observed around the world in people of many ethnic background[3, 4].

We treated a patient who presented with Subarachnoid hemorrhage with incidental Moyamoya disease, and was discharged in good functional status.

Case Presentation

A 39 year old female, right handed, with a degree in education, currently working as an online tutor.

Seven hours prior to admission, while watching a movie alone, the patient suddenly felt pulsating headache, that initially started on both frontal area, radiating to the back and to the nape. This was rated to be 10/10, and described to be the worst headache of her life. She tried to contain the pain for approximately 30 minutes because she was into the movie, until she could no longer tolerate, she went to the bathroom to void, thinking that voiding would help ease the pain. To her dismay, the pain persisted, she went back to her seat. The person seated 2 seats away noticed her agonizing in pain, and offered to bring her to the clinic.

She was then brought to the mall clinic, where her blood pressure was noted to be 150/100, she was given clonidine 75 mcg sublingually, and was allowed to rest in the clinic. While she was resting, she felt nauseated, and vomited previously ingested food, approximating 200 cc. Due to the persistence of the pain, she was advised ER consult.

She was brought to a nearby emergency room (3 hours PTA). On the assessment of the ER physician, the patient was advised admission, however she opted to transfer to our institution.

The patient has no known co morbidities, the family history reveals both her parents are of pure Filipino origin. Her mother has hypertension, while her father has type 2 diabetes mellitus, and neither has suffered a stroke. The nearest relative who suffered a stroke is a paternal uncle who had a stroke in his 60s. Social history includes an eight pack per year smoking history, consuming 8-10 sticks per day for the past 17 years, and an occasional alcoholic beverage drinker, consuming one to two glasses of wine a week.

The physical exam reveals an awake lady, not in acute cardiorespiratory distress, with regular respirations, and spontaneous movements of all extremities. Vital Signs: blood pressure: 110/80, heart rate: 62 beats per minute, respiratory rate: 18, temperature 37.1 degrees Celsius and saturating 97% at room air. The rest of her physical examination, as well as her neurologic examination were all normal, except a nuchal catch.

At the emergency room, neuroimaging with a CAT scan was done, and revealed a subarachnoid hemorrhage. The patient was then referred to interventional radiology for conventional four vessel angiogram, and possible coiling. Neurosurgery service was also informed for possible clipping of the aneurym. The angiogram revealed an A1 secular aneurysm measuring 3.54 mm x 2.73 mm and a neck of 1.95 mm with a teat-like extension note at its fundus denoting recent site of rupture. An ACOM saccular aneurysm measuring 3.26 mm x 2.12 mm with a 2.31 mm neck. There was a severe narrowing noted at the take off site of the proximal M1 segment of the left middle cerebral artery. This is fair but slightly restricted ante-grade flow into the more distal branches of the left middle cerebral artery. There are multiple ill defined vessels around the distal supraclinoid segment of the left internal carotid artery and around the stenotic area in the proximal left middle cerebral artery they represent Moyamoya veessels.

The A1 aneurysm was coiled using GDC 10 360 4 mm x 8 cm and GDC 10 360 3mm x 6 cm, which showed complete occlusion of the lumen of the aneurysms on check angiograms. In consultation with the family of the patient, a decision to clip the ACOM aneurysm, was made. The question then was whether a by-pass procedure will be done.

Discussion

First described in 1957 as "hypoplasia of the bilateral internal carotid arteries,"[5] Moyamoya disease is thought to be an abnormal proliferation of thalamoperforating vessels occurring in the Japanese population. It was later learned that the associated network of abnormally dilated collateral vessels on angiography was later likened to "something hazy, like a puff of cigarette smoke," which is, in Japanese, Moyamoya.[6]

The disease was originally considered to affect predominantly persons of Asian heritage but is now observed around the world in people of many ethnic backgrounds, with [7] an incidence of 0.086 case per 100,000 persons. The incidence ratio in the United States is: 4.6 Asian Americans, 2.2 Blacks, and 0.5 for Hispanics[8]. In the East Asian area, the incidence is 3.16 - 10.5 per 100,000[9] with a bimodal presentation: children (5 years old), and adults (mid 40s) presentation; and a sexual predilection: twice as many female to male [10,11]

The most common presentations are typically localized to the regions of the brain supplied by the internal carotid arteries and middle cerebral arteries: frontal, parietal and temporal lobes. Others may present as seizures, visual deficits, syncope, or personality changes that can be mistaken for psychiatric illness [12]. It is common in adult patients with Moyamoya disease to present with a hemorrhagic stroke with the location of hemorrhages in descending order: intraventricular, intraparenchymal, subarachnoid[13]. Less common presentations would be headache, or choreiform movements.

Stenosis occurs in the distal internal carotid artery and often involves the proximal anterior and middle cerebral arteries. Pathologic analysis has revealed that affected vessels do not show arteriosclerotic or inflammatory changes leading to occlusion. Rather vessel occlusion results from a combination of hyperplasia of smooth muscle cells and luminal thrombosis. The media is often attenuated, with irregular elastic lamina. Caspase dependent apoptosis has been implicated as a contricontrubitory mechanism, the associated degradation of the arterial wall[14]

Genetic factors appear to play a major role in Moyamoya. The proportion of patients who have affected first degree relatives is 10% in Japan and 6% in the United States. Associations with loci on chromosomes 3, 6, 8 and 17, as well as specific HLA haplotypes have been described[15,16]. Literature search reveals that these haplotypes have been conducted only in East Asian population, and in series, no Filipino patient was included.

Familial cases appear to be polygenic or inherited in an autosomal dominant fashion with incomplete penetrance.[17]Ringfinger 213 (RNF 213) gene in the 17q25-ter region was identified as the strongest susceptibility gene for MMD in East Asian People but not for South Asians[18]. p.R4810K variant was identified in 95% of patients with familial MMD, 80% in sporadic MMD, and 1.8% in control subjects[19]. The p.R4810L RNF213 variant is related to the ischemic type of MMD, while the non p.R4810L RNF213 variants particularly A4399T, were associated with the hemorrhagic type of Moyamoya disease[20] Securing decreesing normal Identical twin with only one affected sibling would point to environmental factors[21], contesting the genetic theory.

Smooth muscle progenitor cells collected from the peripheral blood of patients with MMD showed that the SPC in MMD group tended to make more irregularly arranged and thickened tubules, as well as express differential genes compared to that of the healthy controls. Endothelial progenitor cells (EPCs) originate from the bone marrow and help maintain the vasculature and blood flow in infarcted areas[22]. EPC potentially contribute to the neovascularization at the ischemic brain injury site in patients with MMD[23]. However, the EPCs were noted to have defective angiogenic functions in MMD. Aberrant angiogenesis was an active angiogenetic process that may cause both stenosis through the proliferation of endothelial and or smooth muscle cells and abnormal collateral formation[24].

The natural history of Moyamoya disease is variable. Disease progression can be slow with rare, intermittent events or fulminant, with rapid neurologic decline[25,26]. However, regardless of the course, Moyamoya progresses in the majority of patients. A 2005 report indicated that the rate of disease progression is high even among asymptomatic patients, and that medical therapy alone does not halt disease progression[27]. It has been estimated that up to two thirds of patients with Moyamoya have symptomatic progression over a 5 year period.

Asymptomatic adult Moyamoya disease is not a permanent disease. In particular, reduced cerebrovascular reserve capacity is an indication of Moyamoya disease progression[28].

The outcome is poor without treatment. In contrast the estimated rate of symptomatic progression is only 2.6% after surgery, according to a meta analysis involving 1156 patients[29]. In general, neurologic status at the time of treatment more than the patient's age predicts long term outcome. Thus early diagnosis of Moyamoya coupled with expeditious institution of therapy is of paramount importance.

The diagnosis of Moyamoya was first established in Japan, the most recent revision of this first diagnostic criteria is contained in the Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis; Health Labour Sciences Research Grant for Research on Measures for Intractable Diseases: Guidelines for diagnosis and treatment of Moyamoya disease. This was published in 2012. The diagnosis of Moyamoya disease required the bilaterality of the vessels.

In 2016, the Korean Stroke Society published a new guideline[30]. The diagnostic criteria for definitive MMD were revised to include patients with unilateral terminal ICA steno - occlusion. Definitive diagnosis of MMD requires catheter angiography in unilateral cases, while bilateral cases can be promptly diagnosed by either catheter or MRA.

Asymptomatic Moyamoya disease is defined as Moyamoya vessels without neurological deficit and ischemic or hemorrhagic episodes[31]

In patients where surgery appears to present a high risk or when patient has mild disease, medical management is employed. Approximately 38% of medically managed patients underwent surgery for worsening symptoms[32] In patients that present Anti platelet agents have been used to prevent emboli from micro thrombi at sites of arterial stenosis, anticoagulants are rarely used. Calcium Channel blockers may be useful in ameliorating intractable headaches or migraines[33]

Surgical therapies uses the external carotid artery as a source of new blood flow.

Direct: a *branch of the external carotid artery* (superficial temporal artery) is directly anastomosed to a cortical artery.

Indirect: placement of *vascularized tissue* supplied by the external carotid artery in direct contact with the brain

The bypass procedure does not come without complication, with post operative stroke with permanent neurologic deficits occurring in 1.6-16%. Hemodynamic status of patient is the most important factor, the other two being advanced Suzuki stage and lower cerebral blood flow[34].

The rate of asymptomatic Moyamoya disease developing ischemic stroke is 0.8%, while 2.5% would develop a hemorrhagic stroke[35].

The impracticality to screen the general population for asymptomatic Moyamoya disease as well as for asymptomatic intracranial aneurysms robs us of the information of the actual prevalence of these conditions, much more leaves us at an enigma of the incidence of these two diseases occurring concurrently in a patient.

This case report aims to contribute data into this void of information.

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