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Moyamoya Disease in Korea

Gyung Jong Yu, Soh Yeon Kim and Chang Jun Coe

Thirty eight cases of moyamoa disease, 21 children, 17 adults were encountered during a 16-year period at Yonsei University Medical Center. Clinical manifestations, together with computed tomography(CT) and angiographic findings were analyzed with a review of the literature. The mean age was 6.3±3.5 years in children and 36.8±9.9 years in adults. The majority of attacks occurred in spring in both adults and children. The most common chief complaint on admission was hemiparesis followed by convulsion in children, while in adults, loss of consciousness was most common followed by headache. Of transient neurologic deficits, hemiplegia was most common in children, while cranial nerve involvement was common in adults. Hemiplegia, also was the most common permanent neurologic manifestation in children, while hemiparesis and intellectual deterioration were the most common in adults. Of the children, 90.6% showed infarction on CT, while 88.2% of adults had hemorrhage. Bilateral occlusion of the carotid arteries was the most common site of lesions in both adults and children on cerebral angiogaphy.

Key Word: Moyamoya

"Moyamoya" was first described in the Japanese literature in 1957 by Kudo(1968) who noted an unusual angiogram of a boy showing a diffuse intracranial vascular network without the usual vascular pattern. Suzuki and Takaku (1969) suggested the term "moyamoya" which was derived from the angiogrphic appearance of cerebrovascular abnormalities with filling of the basal telangiectasia, producing a cloudy image resembling that of a puff of smoke in the air.

Until the 1960's, most of the reports of moyamoya disease considered it an entity peculiar to Japan. Since then, several authors have reported the disease occuring in other nationalities (Porr *et al.* 1974; Lichtor *et al.* 1987; Bruno *et al.* 1988; Makoy *et al.* 1977; Nishimoto *et al.* 1984; Maki *et al.* 1987). In the Far East region, moyamoya disease has also been reported to occur in Chinese(Lee *et al.* 1973) in addition to Japanese. In 1987, Choi (1987) presented a report on 289 caes of moyamoya disease in Korea.

The main features of moyamoya disease are bilateral occlusion of the internal carotid arteries with dilated collateral lenticulostriate and thalamoperforating arteries forming basal telangiectasia. The disease occurs bilaterally but is usually asymmetric and is followed later in the course by extensive formation of collteral vessels in the basal ganglia and upper brain stem. Choi (1987) categorized moyamoya disease into two types; typical moyamoya disease in which stenosis and occlusion of the internal carotid arteries(ICA) occur bilaterally, and atypical or moyamoya-like disease in which occlusion occurs unilaterally. We have reviewed our cases of moyamoya disease in patients admitted to Yonsei University College of Medicine and analyzed their age and sex distribution as well as clinical manifestations with radiologic features and residual neurologic deficits.

SUBJECTS AND METHODS

Thirty eight Patients (21 children and 17 adults) diagnosed at Yonsei University College of Medicine as having moyamoya disease, admitted during a 16-

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Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea
Address reprint requests to Dr. G J Yu, Department of Pediatrics, Yonsei University College of Medicine, CPO Box 8044, Seoul, Korea, 120-752

year peroid (1973~1988) were reviewed. The moyamoya patients were studied retrospectively for initial clinical symptoms, accompanying neurologic deficits, and types of involvement, that is ischemic or hemorrhagic. Cranial computerized tomography (CT) of the patients was evaluated and correlated with their cerebral angiographies. Those of ages less than 16 years were grouped as children while all greater than or equal to the ages of 16 years were grouped as adults.

RESULTS

Age and Sex

Of our case review, moyamoya disease frequently affected children at 4~5 years of age and adults in the fourth decade. Out of 38 patients, 21(55.3%) were less than 16 years of age. The mean age of the children was 6.3±3.5 years and that of adults was 36.8±9.9 years. Among the 14 male patients, 10 (71.4%) were under the age of 16 years. Eleven (45.8%) of the 24 female patients were under 16 years of age. The male to female ratio was 1 : 1.1 for patients under 16 years of age and 1 : 3.3 for adults (Table 1).

Time of Initial Attack

Although no record has been made previously about the time of initial attack by other workers, there may be some relevance regarding the time of attack in relation to the attack itself. Eight (38.0%) of the children had their initial attack in spring with 6 (28.6%) in winter. In adults, 7 (41.1%) had their initial attack in spring and 5 (29.5%) had it in autum (Table 2).

Chief Complaint

The most common chief complaints in children on the first visit were hemiparesis (42.3%), convulsion (19.3%) and loss of consciousness (11.5%), headache (7.7%), vomiting (7.7%), and alternating hemiplegia (7.7%). In adults, the majority of patients were admitted in order of frequency (Table 3) due to loss of consciousness (33.3%) mostly due to intracranial hemorrhage, headache (33.3%), hemiparesis (16.7%), vomiting (12.5%) and convulsion (4.2%).

Initial Neurologic Manifestation

In some of the patients, the initial neurologic signs manifested by the disease were of the tran-

Table 1. Age and sex distribution in patients withmoyamoya disease

Age (years)	Male	Female	Total (%)
~ 5	5	9	14 (36.8)
6~10	3	1	4 (10.5)
11~15	2	1	3 (7.9)
16~20	0	2	2 (5.3)
21~25	0	0	0 (0.0)
26~30	0	1	1 (2.6)
31~35	2	3	5 (13.2)
36~40	1	3	4 (10.5)
41~45	1	2	3 (7.9)
46~50	0	0	0 (0.0)
51~55	0	1	1 (2.6)
56~60	0	1	1 (2.6)
	14	24	38(100.0)

Table 2. Month of attack

Month	Child (%)	Adult (%)
January	3 (14.3)	1 (5.9)
February	1 (4.8)	0 (0.0)
March	3 (14.3)	1 (5.9)
April	4 (18.9)	3 (17.6)
May	1 (4.8)	3 (17.6)
June	1 (4.8)	1 (5.9)
July	2 (9.5)	1 (5.9)
August	1 (4.8)	2 (11.7)
September	2 (9.5)	1 (5.9)
October	0 (0.0)	1 (5.9)
November	1 (4.8)	2 (11.7)
December	2 (9.5)	1 (5.9)
Total	21 (100.0)	17 (100.0)

Table 3. clinical feature of initial attack in children and adults

Initial Attack	Child (%)	Adult(%)
Hemiparesis	11 (42.3)	4 (16.7)
Convulsion	5 (19.3)	1 (4.2)
Loss of Consciousness	3 (11.5)	8 (33.3)
Headache	2 (7.7)	8 (33.3)
Nausea/Vomiting	2 (7.7)	3 (12.5)
Alternating Hemiplegia	2 (7.7)	0 (0.0)
Hemiparesis+Convulsion	1 (3.8)	0 (0.0)
Total	26 (100.0)	24 (100.0)

* Each patient have one or more symptoms at the time of admission

sient type which disappeared within a few days or so after onset, and others manifested persistent clinical symptoms. Some of the patients had more than one presenting symptom at the time of admission.

Three children (13.0%) and 5 adults (33.3%) had transient hemiplegia. One child (4.3%) also had transient ataxia as the initial neurologic manifestation. Children showed only VII cranial nerve palsy and although this was the most frequent cranial nerve involved in adults, VII, XII and II nerves were also involved in order of frequency (Table 2).

Nineteen (90.6%) of the children showed infarction on brain CT with only 2 (9.4%) of them showing hemorrhage. In contrast, 15 (88.2%) of the adults showed hemorrhage with only 2 (11.8%) of them showing infarction. The frontal cortex was the most frequent site of involvement in children (42.9 %) followed by the frontoparietal (14.3%), basal ganglia (14.3%), occipital (9.5%), parietal (4.8%) and temporoparietal (4.8%) areas. In contrast, intraventricular hemorrhage with spread into subarachniod space was the common site of involvement (Table 4) in adults.

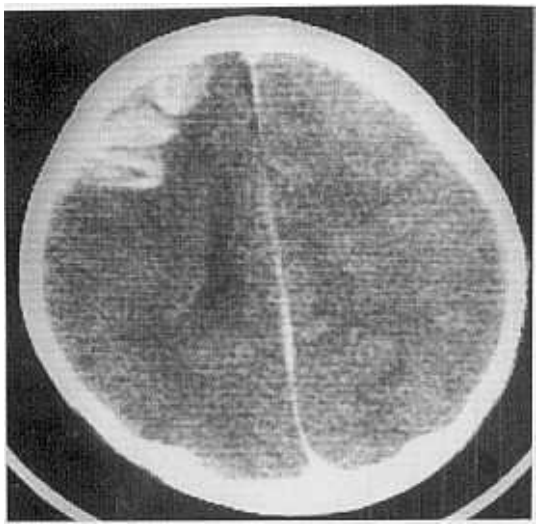

Fig. 1. Brain Computer tomography showing high density area due to hemorrhage from moya-moya vessels.

Management

Encephalodurosynangiosis (EDAS) was performed on 6 children (28.6%) and 1 adult (5.9%). All of the patients either improved, did not have recurrences or had no further progression of the disease after treatment with EDAS.

Fifteen children (71.4%) and 12 adults (70.6%) recived conservative management. Among them, 2 adult patients had hematoma due to intracerebral hemorrhage which were removed. Ventriculoperitoneal shunts were performed on 3 adults who developed hydrocephalus associated with intraventricular hemorrhage (Table 8).

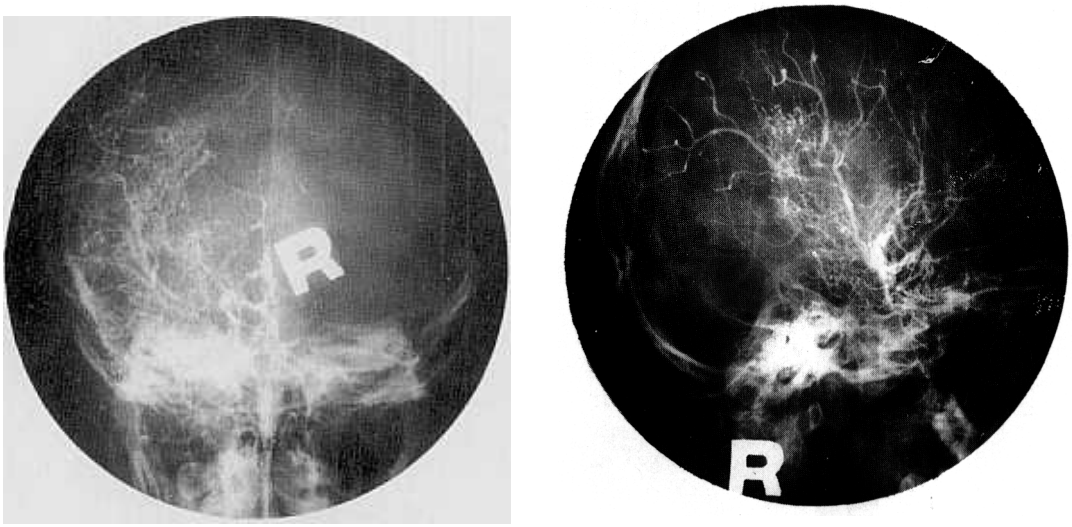

Fig. 2. Anteroposterior and lateral view of right angiography showing moyamoya vessles.

Table 4. Type and site of involvement by computed tomography

Site	Infarction		Hemorrhage	
	Child (%)	Adult (%)	Child (%)	Adult (%)
Frontal	9 (42.9)			1 (5.9)
Temporal				1 (5.9)
Parietal	1 (4.7)	1 (5.9)*		1 (5.9)
Occipital	2 (9.5)			
Thalamus				1 (5.9)
Basal ganglia	3 (14.3)			2 (11.7)
Frontoparietal	3 (14.3)			
Temporoparietal	1 (4.8)			1 (5.9)
Intraventricular			2 (9.4)	7 (41.1)
Hydrocephalus				1 (5.9)**
Normal		1 (5.9)		
Subtotal	19 (90.6)	2 (11.8)	2 (9.4)	15(88.2)

* : Associated with abnormal calcified density
**: Associated with subarachnoid hemorrhage

Table 5. Site of occlusion by angiograpy

Site of occlusion	Child (%)	Adult (%)
Left ICA	2 (9.5)	1 (5.9)
Right ICA	2 (9.5)	2 (11.8)
Bilateral ICA	12 (57.0)	8 (47.0)
Left MCA	0 (0.0)	1 (5.9)
Right MCA	1 (4.8)	3 (17.6)
Bilateral ACA+MCA	1 (4.8)	0 (0.0)
Left ACA+MCA	0 (0.0)	1 (5.9)
Right ICA+Left PCA	1 (4.8)	0 (0.0)
Bilateral ICA+ACA+MCA	1 (4.8)	0 (0.0)
Normal	1 (4.8)	1 (5.9)
Total	21 (100.0)	17 (100.0)

ICA=Internal Carotid Artery
ACA=Anterior Cerebral Artery
MCA=Middle Cerebral Artery
PCA=Posterior Cerebral Artery

Table 6. Transient neurologic manifestation in children and adults

Transient Neurologic Manifestation	Child	Adult
Hemiparesis	3	5
Ataxia	1	0
Cranial Nerve II	0	1
VI	0	1
VII	1	2
XII	0	2
Change in Mentality	2	4
Neck Stiffness	1	4
	8	19

* Each patient may have one or more symptoms at the time of admission

Sequelae

The sequelae remaining after an attack were as diverse as the presenting neurologic manifestations and each patients sometimes had more than one type of sequelae. Hemiplegia remained permanently after the initial attack in 16 children (76.2%) and 3 children (14.3%) developed seizures. Ataxia remained in 2 children (9.5%) and 1 other child (4.8 %) developed cranial nerve paisy. Dysarthria was present in 1 child (4.8%) and 1 child (4.8%) had permanent aphasia. Four children (19.0%) had no sequelae while 2 children (9.5%) died during hospitalization (Table 7).

Ten of the adult patients (58.8%) had hemiplegia and 4 adults (23.5%) had intellectual deterioration. One patient (5.9%) had cranial nerve palsy, 1 (5.9 %) had cerebellar ataxia and 1 (5.9%) had hydrocephalus. There was also 1 patient each with dysesthesia, aphasia and seizure. Four patients (23.5%) had no neurologic sequelae and 3 patients (17.6%) died during hospitalization.

Table 7. Rate of sequelae occurrence after moyamoya disease

Sequelae	Chil (%)	Adult (%)
Heimparesis	17 (51.6)	9 (40.0)
Cranial Nerve VII	1 (3.2)	1 (4.0)
Cerebellar	2 (6.5)	1 (4.0)
Dysesthesia	0 (0.0)	1 (4.0)
Change in Mentality	0 (0.0)	4 (16.0)
Aphasia	1 (3.2)	0 (0.0)
Seizure	3 (9.7)	1 (4.0)
Hydrocephalus	1 (3.2)	0 (0.0)
Dysarthria	1 (3.2)	0 (0.0)
None	4 (12.9)	4 (16.0)
Expire	2 (6.5)	3 (12.0)
	31 (100.0)	25 (100.0)

* Each patient may have one or more sequelae

Table 8. Type of management in children and adults with moyamoya disease

Management	Child (%)	Adult (%)
Encephalodurosynagniosis	6 (28.6)	1 (5.9)
Conservative	15 (71.4)	12 (70.6)
Hematoma Evacuation		2 (11.8)
Ventriculoperitoneal shunt		3 (17.6)
Bilateral Sympathetic Ganglionic Block		1 (5.9)
	21 (100.0)	17 (100.0)

DISCUSSION

In 1956, Kudo (1968) first noted an unusual pattern of diffuse intracranial vascular network without the usual cerebral vascular pattern. It was later reported by several authors, the majority of whom were Japanese (Suzuki *et al.* 1983; Takeuchi 1961; Nishimoto *et al.* 1966; Nishimoto *et al.* 1968).

Lately however, it has been reported to occur in other races as well including whites (Poor *et al.* 1971; Lichtor *et al.* 1987; Bruno *et al.* 1988; Hoare *et al.* 1974), Asians (Lee *et al.* 1973) and blacks (Makoyo *et al.* 1977). This "unusual" pattern of vascular network was first named "moyamoya" by Suzuki and Takaku (1969) which is the Japanese word for something hazy, like a puff of smoke, referring to the abnormal appearance of net-like vessels at the base of the brain on angiography. The etiology of moyamoya disease has still not yet been defined; hence, the name moyamoya is appropriate. Suzuki and Kodama (1983) noted the disease has two peak ages; one in the first decade and the other in the 4th decade. The mean ages of the patients were 6 years 4 months for children and 36 years 9 months for adults in our investigation, which are similar to those reported by Maki and Enomoto (1988) whose peak ages were 5 years 4 months for children and 36 years 5 months for adults. The male to female ratio according to Nishimto (1984) was 1 : 1.65, while in our study the male to female ratio was 1 : 1.1 for children and 1 : 3.3 for adults. We observed that the majority of attacks occured in spring in both children and adults. Although there have been no reports of seasonal variation in this disease, precipitating factors may be aggaravated during certain seasons, leading to the onset of disease.

Maki and Enomoto (1988) have suggested that infarction tends to occur more in the male and hemorrhage in the female. However, we were not able to observe these differences in our cases. Instead, the dominant symptoms occuring in children differed from those symptoms arising in adults. Symptoms arising from infarction such as hemiplegia and seizures predominated in children. Headache seemed to occur with a certain frequency together with vomiting and dysesthesia. Transient neurologic symptoms, that is, alternating hemiplegia, arising sequentially in both extremities also occurred in children. Most of the symptoms in adults were related to intracranial hemorrhage, with loss of conciousness being the predominant symptom. Headache, hemiparesis, convulsion and vomiting were also symptoms manifestated by adults with intracranial hemorrhage. The site of infarction in our cases occuring most frequently in the frontal region in contrast to the temporal area suggested by Suzukui and Kodma (1983). The extent of intracranial lesion did not correlate with clinical manifestations.

Intracerebral hemorrhage arose most commonly within the ventricles and in the basal ganglia. Suzuk and Kodoma (1983) have suggested that intracerebral and intraventricular hemorrhage may be caused by rupture of small aneurysms near the wall of the lateral ventricle.

Furthermore, repeated angiograms have supported this argument and have strongly suggested that small vessels near the ventricular wall rupture, causing these hemorrhages. As the name of the disease was derived from the angiographic appearance, angiography is mandatory in the diagnosis of moyamoya disease. On serial angiography, dynamic

changes can be observed at the bases of the brain.

Suzuki and Kodama (1983) have suggested that the basal moyamoya vessels represent collateral channels formed as a result of stenotic change in the internal carotid artery bifurcation. They have observed two kinds of collateral pathways from the extracranial to the intracranial arteries. Ethmoidal moyamoya is seen as net-like vessels in the orbit perfused from the ophthamic artery, posterior and anterior ethmoidal arteries and the external carotid arteries. Vault moyamoya develps from transdural anastomoses derived from the middle meningeal and superficial temporal arteries. In both these kinds of collateral pathways, Suzuki and Kodama (1983) observed that the moyamoya vessels tend to grow in direct proportion to the severity of the staging of the disease, while in the adults, there was a poor correlation in this respect. Maki and Enomoto (1988), however, focused on the extent of stenosis or obstruction instead and have classified it into three subgroups. Type I stenosis or obstruction present in the anterior half of the circle of Willis, type II for stenosis or obstruction extending to the posterior communicating arteries in addition to type I changes, and type III for the same lesion present in the entire circle of Willis and the posterior cerebral arteries. We have observed that it was more practical and easier to classify moyamoya disease according to the latter using the degree of stenosis present in the vessels rather than according to the presence of collateral vessels. In our cases, we noted that among 21 children in whom angiography was done, 20 of them could be classified as type I with 1 child each being types II and III. Among the 17 adults with angiography, all were classified as type I. hence, symptoms seem to begin to appear even before the disease could progress beyond type I in most of the cases.

Unfortunately, angiography is not always safe in this disease, especially in hemorrhagic cases, and recent advances in radiologic techniques have made it possible for diagnosis of moyamoya disease without using invasive techniques. CT scans are useful in evaluating the type and site of lesion but the moyamoya vessels are not visualized on CT scans. However, with the aim of later generation CT scanners, it is possible for direct visualization of the moyamoya vessels. In our cases, with the aim of an experienced radiologist, it was possible to diagnose the disease even without angiography. However, in this cases, an experienced radiologist is mandatory.

Magnetic resonance imaging (MRI) has recently been used increasingly in the diagnosis of moyamoya as it is less invasive and more informative (Maki *et al.* 1987). Moyamoya vessels may be directly visualized together with infarction and hemorrhage. The technique of ^{133}Xe inhalation has recently been used to study regional cerebral blood flow in moyamoya disease. Takeuchi *et al.* (1985) studied regional blood flow in patients with moyamoya disease and noted that the mean hemispheric blood flow was lower in the upper frontal region compared to the relatively high flow in the posterotemporal and occipital regions. Nishimoto *et al.* (1979) reported that CO_2 reactivity in mean hemispheric blood flow presented at less than 40 mmHg of $PaCO_2$ (hypocapnia) in most of the patients with moyamoya disease. Hence, hyperventilation seems to precipitate an attack in patients with moyamoya disease.

Maki and Enomoto (1988) summarized the pathologic findings of moyamoya disease as concentric intimal hyperplasia of cerebral vessels with fragmentation and lamination of internal elastic lamina, and medial and adventitia thinning of the cerebral arteries with lipid deposition being present in the intima and with internal elastic lamina being follded centripetally.

Pathologically, there was no inflammatory or artherosclerotic changes observed. Furthermore, there was no pathological difference between adult and child types of moyamoya disease. Pathologic change were more remarkable in the distal portions of the carotid arteries and proximal portions of the anterior and middle cerebral arteries. Our study did not include pathology of specimens.

Treatment of moyamoya disease has been limited to symptomatic or both medical and surgical fields. The aim of surgical treatment is to supply blood to the brain suffereing from ischemia. Two methods have been tried, one of which is to facilitate blood supply through the original channel and the other to increase the blood supply via the external carotid artery. The first superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis was carried out in 1971 (Karyenbuhl 1975). Since then, Matsushima *et al.* (1981) have deviced a new method called "encephaloduroarteriosynangiosis" (EDAS) and this is recently being used. EDAS seems to an effective way of preveting further progression of the disease as noted in our 7 cases who recieved EDAS. All of them either had improvement of symptoms or had no further progression of the disease. Matsushima *et al.* (1985) performed indirect revascularization on pediatric patients with

moyamoya disease with good collateral formation in about 80% using EDAS, and encephalomyosynangiosis(EMS). Hence, although EDAS is a recent surgical procedure, there seems to be no differences in the effect on coll-ateral formation by the procedure itself. No autopsy has yet been performed on the patients who recieved EDAS, thus preventing knowledge of whether further damage is done to the parts of the brain supplied by the moyamoya vessels after surgery.

The sequelae remaininhg after an attack in the patients moyamoya disease were related to the lesion and the site of lesion formed by the disease itself, either from infarction or hemorrhage. Most of the patients, children and adults alike, did not recover from their sequelae to their fullest potential as before their attack.

As of yet, all treatment in moyamoya disease is symptomatic. Thus, efforts should be made to define the etiology so as to provide a way to specify prophylactic and/or radical treatment in patients with moyamoya disease.

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