Clinical Features of Hemorrhagic Moyamoya Disease in China

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OBJECTIVE: **To elucidate the clinical features of patients with hemorrhagic moyamoya disease (MMD) in China.**

METHODS: **We retrospectively reviewed 471 patients with hemorrhagic MMD at Beijing Tiantan Hospital. Clinical features and radiologic findings were analyzed.**

RESULTS: **The mean age at diagnosis was 35.3 ± 11.5 years, with 1 peak distribution in patients from 35 to 39 years of age. The ratio of women to men was 1.2:1. Familial occurrence was 3.8%. The primary symptoms at initial presentation were intraventricular hemorrhage (42.0%), intracerebral hemorrhage (23.6%), intracerebral hemorrhage with intraventricular hemorrhage (18.3%), and subarachnoid hemorrhage (16.1%). Before the diagnosis, 68 patients experienced a second episode of bleeding. Rebleeding tends to be common within 6 years after the first bleeding (83.8%). The second bleeding episode was characterized by a change in which hemisphere bleeding occurred in 7 patients (10.3%) and by the type of bleeding in 23 patients (33.8%). Most patients presented with Suzuki stage 3 or 4 MMD (61.7%). Posterior cerebral artery involvement was observed in 28 (18.4%) patients. Forty-three intracranial aneurysms were identified in 39 patients (8.3%).**

CONCLUSIONS: **A 1-peak pattern in age distribution and mild female dominance in sex distribution were observed in patients with hemorrhagic MMD. Rebleeding tends to be common within 6 years after the first bleeding; however, some cases of rebleeding occur after a long period. Furthermore, the second bleeding episode was characterized frequently by a change in hemisphere and the type of bleeding. Early surgical treatment in both hemispheres is recommended.**

INTRODUCTION

Moyamoya disease (MMD) is an unusual form of chronic, occlusive cerebrovascular disease characterized by bilateral stenosis or occlusion at the terminal portion of the internal carotid artery (ICA) and an abnormal vascular network at the base of the brain.[1] Ischemic type and hemorrhagic type occupy the main phenotypes of MMD in Asian populations: ischemic type is common in children, whereas hemorrhagic type is frequently diagnosed in adults.[2-4]

Epidemiologic features of MMD have been reported in various regions during the last 3 decades.[5] In Japan and South Korea especially, the incidence, prevalence, and patient characteristics have been well documented.[6,7] Recently, more and more hemorrhagic MMD instances have been detected in our hospital. However, to our knowledge, information of the clinical characteristics and natural history in Chinese patients is rare. Here, we retrospectively review the demographic data and clinical features of hemorrhagic patients treated at our institution over the last 30 years, which represents, to our knowledge, the largest group of hemorrhagic MMD patients in China.

Key words
- Clinical features
- Hemorrhage
- Moyamoya disease
- Rebleeding

Abbreviations and Acronyms
CT: Computed tomography
ICA: Internal carotid artery
ICH: Intracerebral hemorrhage
IVH: Intraventricular hemorrhage
MMD: Moyamoya disease
PCA: Posterior cerebral artery
SAH: Subarachnoid hemorrhage

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MATERIALS AND METHODS

Patient Selection

There were 1688 patients with MMD from the neurosurgical department of Beijing Tiantan Hospital from January 1984 to December 2015. Cerebral digital subtraction angiography or magnetic resonance angiography was carried out in all the patients. All patients were diagnosed according to the current diagnostic criteria: 1) stenosis or occlusion of the terminal internal carotid and the proximal middle and anterior cerebral arteries[8]; 2) unilateral or bilateral involvement; and 3) had experienced at least 1 intracranial hemorrhage which was verified by computed tomography (CT) scanning, magnetic resonance imaging, or lumbar puncture. Patients with a history of cranial irradiation and meningitis, brain tumor, Down syndrome, and neurofibromatosis type 1 were excluded.

Retrospective Chart Review

The Ethics Committee of Beijing Tiantan Hospital, Capital Medical University, Beijing, China, approved the study. Medical records and radiologic data were retrospectively reviewed. Clinical information on sex, age at diagnosis, ethnicity, family history, hypertension, diabetes mellitus, hyperlipidemia, smoking, alcohol use, thyroid disease, history of infection, arteriovenous malformation, cavernous hemangioma, aneurysms, past symptoms, and initial modified Rankin Scale score are shown in Table 1. The radiologic features of the initial hemorrhages were analyzed. The locations of hemorrhage include intraventricular hemorrhage (IVH), intracerebral hemorrhage (ICH), ICH breaking into ventricles, and subarachnoid hemorrhage (SAH). Analysis by conventional angiography was available in 441 patients (882 hemispheres), and the Suzuki stage of each hemisphere was investigated.[9]

RESULTS

General Patient Characteristics

We identified 1688 cases of MMD at Beijing Tiantan Hospital between January 1984 and December 2016. Among 1688 cases in total, 471 cases (27.9%) were diagnosed to have hemorrhagic MMD. The number of new patients diagnosed with hemorrhagic MMD in our hospital has increased significantly year by year (Figure 1). Most of the patients (468/471) were Han Chinese, 1 patient was Mongolian, 1 patient was Buyei, and 1 patient was Zhuang. Eighty-six patients were from Beijing, 81 patients were from Henan province, 73 patients were from Hebei province, 55 patients were from Shandong province, and 176 patients were from the other 21 provinces (Figure 2).

There were 213 men and 258 women, for a female/male ratio of 1.2:1.0. The mean patient age ± SD at diagnosis was 35.3 ± 11.5 years (range, 2–62 years). There were 46 patients less than 18 years of age (9.8%). One peak in age distribution was found in patients from 35 to 39 years of age (Figure 3). In female or male patients, one definite peak in age distribution was observed—a peak at 35–39 years of age; this was similar to the pattern of total age distribution. Of the 471 patients, 18 (3.8%) had familial

Table 1. Patient Characteristics at Admission (N = 471)

Characteristics	Value	%
Female/male ratio	258/213	
Mean age at diagnosis (years), mean ± SD	35.3 ± 11.5	
Age (years)		
≤18	46	9.8
>18	425	90.2
Ethnicity		
Han	468	99.4
Mongolian	1	0.2
Buyei	1	0.2
Zhuang	1	0.2
Family history	18	3.8
Vascular risk factors		
Hypertension	81	17.2
Diabetes	14	3.0
Hyperlipidemia	26	5.5
Smoking	47	10.0
Alcohol use	33	7.0
Thyroid disease	8	1.7
History of infection	12	2.5
Hepatitis B virus	9	1.9
Syphilis	1	0.2
Tubercle bacillus	1	0.2
Cysticercus	1	0.2
Polycystic kidney	2	0.4
Arteriovenous malformation	2	0.4
Cavernous hemangioma	1	0.2
From first bleeding to the diagnosis (months), mean ± SD	15.0 ± 32.1	
Total bleeding episodes (before diagnosis)		
1	403	85.6
2	57	12.1
3	10	2.1
4	1	0.2
Past symptom		
TIA	69	14.6
Stroke	89	18.9
Initial mRS (score <3)	363	77.1

Values are number of patients or as otherwise indicated.
TIA, transient ischemic attack; mRS, modified Rankin Scale.