Clinical Characteristics and Natural History of Quasi-Moyamoya Disease

Meng Zhao, MD,*,†,‡ Zhiqin Lin, MD,*,† Xiaofeng Deng, MD,*,†,‡ Qian Zhang, MD,*,†,‡ Dong Zhang, MD,*,†,‡ Yan Zhang, MD,*,†,‡ Rong Wang, MD,*,†,‡ Shuo Wang, MD,*,†,‡ Zhongli Jiang, MD,*,† Hao Wang, MD,*,† and Jizong Zhao, MD*,†,‡

Background: Quasi-moyamoya disease (quasi-MMD) is a rare cerebrovascular disease and its clinical features and natural history remain unclear. The aim of the study is to describe the clinical characteristics and the natural histories of this disease, with analysis of the risk factors for future cerebrovascular events. *Methods:* We identified 64 patients with quasi-MMD from 693 moyamoya vasculopathy patients referred to our hospital between 2011 and 2015. Demographic data, associated disorders, clinical manifestation, angiographic findings, natural history, and risk factors for cerebrovascular events were analyzed. *Results:* Patients included in the study had a mean age of 31.5 years. A unimodal age distribution was noted. Atherosclerosis was the most frequently associated disorder. Forty-five (70.3%) patients had ischemic events as their initial clinical manifestation and 14 (21.9%) patients presented as hemorrhagic stroke. The majority of patients presented with Suzuki grades 3 and 4 (20.3% and 42.2%). The annual risk of cerebrovascular events was 19.4% per patient-year. Prior hemorrhage (HR 2.77, 95% CI 1.20-6.41) and ischemic stroke (HR 2.77, 95% CI 1.26-6.07) were 2 risk factors for future events. *Conclusions:* Several clinical characteristic differences were observed in our mainland China cohort compared with the Japanese and European cohorts. The annual risk of cerebrovascular events was relatively high in quasi-MMD patients. Patients with prior hemorrhage and ischemic stroke were inclined to have future cerebrovascular events. Close follow-up is needed for these patients. **Key Words:** Quasi-moyamoya disease—moyamoya disease—clinical characteristics—natural history.

From the *Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China; †China National Clinical Research Center for Neurological Diseases, Beijing, China; and ‡Center of Stroke, Beijing Institute for Brain Disorders, Beijing, China.

Received October 6, 2016; revision received November 19, 2016; accepted December 24, 2016.

Grant support: This study was supported by the "13th Five-Year Plan" on National Science and Technology supporting plan (2015BAI12B04), the National Natural Science Foundation of China (81371292), and the Beijing Municipal Administration of Hospitals' Mission Plan, Code: SML20150501.

Address correspondence to Jizong Zhao, MD, Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, No. 6 Tiantanxili, Dongcheng District, Beijing 100050, China. E-mail: zhaojz205@163.com.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.12.025

Introduction

Moyamoya vasculopathy is a disorder characterized by progressive narrowing or occlusion of the intracranial internal carotid artery (ICA), with formation of abnormal vascular collateral networks at the base of the brain.[1] This vasculopathy was first described by Takeuchi and Shimizu in 1957.[2]

Moyamoya disease (MMD) corresponds to isolated and primary moyamoya vasculopathy. Quasi-moyamoya disease (quasi-MMD) refers to moyamoya vasculopathy associated with various disease entities. Although terms like moyamoya syndrome, moyamoya phenomenon, and moyamoya-like vasculopathy all have been used to describe such disorder, it is clearly defined as quasi-MMD in the Guidelines for Diagnosis and Treatment of Moyamoya Disease.[3]

Despite major clinical and experimental advances in MMD, few researches put the spotlight on quasi-MMD.[4-7] A Japanese nationwide survey reported that the prevalence and annual incidence of quasi-MMD are approximately 10 times lower than those of MMD.[4] Because of its rarity, the clinical features and the natural history of this disease remain unclear. Thus, limitations to predict the prognosis and determine the treatment strategy still existed. Therefore, we conducted a study of the natural history and clinical characteristics of quasi-MMD to help elucidate the clinical features of this rare disease and to help guide management decisions in these patients.

Materials and Methods

Patient Selection

The study was approved by the Beijing Tiantan Hospital Research Ethics Committee. From 2011 to 2015, a total of 693 patients were identified as moyamoya vasculopathy in the Tiantan Hospital Stroke Center moyamoya database. Of these patients, 64 were diagnosed with quasi-MMD based on the criteria prepared by the Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of Japan.[3] According to these criteria, patients were diagnosed with quasi-MMD if they had typical angiographic MMD features associated with disorders as follows: atherosclerosis, autoimmune disease, meningitis, neurofibromatosis type I, brain tumor, Down's syndrome, head injury, irradiation, Turner syndrome, Alagille syndrome, Williams syndrome, Noonan syndrome, Marfan syndrome, nodular sclerosis, Ito nevus, incontinence of pigment, Hirschsprung disease, diabetes mellitus IA, Prader–Willi syndrome, Wilms tumor, primary oxalosis, sicklemia, Fanconi anemia, spherocyte, eosinophilic granuloma, plasminogen abnormality II, leptospirosis, enterovirus infection, protein S deficiency, pyruvate kinase deficiency, fibrous dysplasia, polycystic kidney, retinitis pigmentosa, and oral contraceptives.[3] A universally accepted definition of atherosclerosis had not been established. Determination of atherosclerosis-associated quasi-MMD was performed by 2 authors (Y.Z. and R.W.) independent of each other. The criteria were developed primarily based on cerebrovascular imaging with supporting evidence from the patient's clinical profile. Any patient with a radiography demonstration similar to MMD and who met 3 of the following 4 qualifications was identified as an atherosclerosis-associated quasi-MMD patient: (1) imaging demonstrated eccentric calcified plaques in the intracranial vasculature or the carotid bifurcation; (2) confirmed atherosclerosis in other site; (3) unilateral stenosis; and (4) hyperlipidemia. Other concurrent disorders were confirmed by clinical test or by medical history.

Chart Review

We retrospectively reviewed the clinical records for each patient from presentation. Previous clinic records were also obtained and reviewed if necessary. Baseline information was noted at initial presentation including the following: age, sex, ethnicity, mode of presentation, hypertension, cerebral aneurysm, familial MMD, hyperlipidemia, diabetes mellitus, hyperthyroidism, significant alcohol and/or tobacco use, oral contraceptive use, autoimmune disease, and parental stroke history. Clinical onset symptoms were divided into ischemic symptoms (including transient ischemic attacks [TIAs] and stroke), hemorrhage (including subarachnoid hemorrhage [SAH], intracerebral hemorrhage [ICH], and intraventricular hemorrhage [IVH]), seizure, and headache. Headache was accounted as initial manifestation if it was the only symptom of the patient.

Radiological studies including digital subtraction angiography (DSA), magnetic resonance imaging (MRI), computed tomography angiography (CTA), and CT perfusion were evaluated. DSA was routinely performed on all the patients at admission to our hospital and repeated if necessary during their course of disease. Two independent and blinded interventional neurosurgeons (Y.Z. and R.W.) were enrolled to analyze angiography data for stenosis sites, extent of involvement, sources of collateral flow, and other cerebrovascular abnormalities. The angiographic stages of quasi-MMD were estimated according to the Suzuki angiographic stage classification.[1] Disagreements were resolved by consensus.

Clinical Follow-up

The follow-up period was defined as the time between the initial clinical presentation and the last clinical follow-up or revascularization, whichever occurred first. If a patient had had a diagnosed moyamoya before the referral to our hospital, we required the information of initial clinical presentation by doing a chart review of the patient's earlier clinical notes. Thus, the follow-up period was extended.

Trained study staff interviewed patients or their caregivers by telephone. We inquired about the following: