Pediatric Neurology 75 (2017) 48–54

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Transient Ischemic Attack in Pediatric Patients With Moyamoya Disease: Clinical Features, Natural History, and Predictors of Stroke

Meng Zhao MD [a,b,c], Dong Zhang MD [a,b,c], Shuo Wang MD [a,b,c], Yan Zhang MD [a,b,c], Rong Wang MD [a,b,c], Jizong Zhao MD [a,b,c,*]

[a] *Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China*
[b] *China National Clinical Research Center for Neurological Diseases, Beijing, China*
[c] *Center of Stroke, Beijing Institute for Brain Disorders, Beijing, China*

ABSTRACT

BACKGROUND: Despite being the most common presentation in children with moyamoya, transient ischemic attack (TIA) in children has rarely been described. The aim of this study is to describe the clinical characteristics of TIAs in children with moyamoya and explore the risk factors for stroke after TIA. **METHODS:** We reviewed 696 consecutive patients with moyamoya vasculopathy (155 pediatric patients and 541 adults) admitted to our hospital from 2009 to 2015 to identify pediatric patients with moyamoya with an initial presentation of TIA. We defined recurrent TIAs that involve more types of symptoms or symptom extensions as symptom progression. The risk factors for subsequent stroke were analyzed using time-to-event analyses. **RESULTS:** We identified 60 pediatric patients with moyamoya who had presented with TIA (initial presentation age, 10.0 ± 3.5 years). Motor weakness (n = 51 [85%]) was the most common initial presentation. During follow-up, 55 patients (91.7%) had recurrent TIAs and 14 (23.3%) had subsequent strokes. We identified female gender (hazard ratio, 5.08; 95% confidence interval, 1.40-18.47; $P = 0.01$), Suzuki grade greater than 3 (hazard ratio, 4.01; 95% confidence interval, 1.16-13.82; $P = 0.03$), and symptom progression (hazard ratio, 5.31; 95% confidence interval, 1.65-17.14; $P = 0.01$) as independent predictors of future stroke events. **CONCLUSIONS:** Transient ischemic attacks have a relatively high recurrence rate in children with moyamoya and are associated with subsequent stroke. We identified the female sex, Suzuki grade greater than 3, and symptom progression as independent predictors of future strokes.

Keywords: transient ischemic attack, pediatric, moyamoya disease, stroke, risk factors; Suzuki grade

Pediatr Neurol 2017;75:48–54

Introduction

Although transient ischemic attack (TIA) in adults is well studied and considered to herald stroke,[1] TIA in children has rarely been described.[2,3] Although certain TIA characteristics have been found to predict stroke in adults, they are not verified in children.[1] Studies suggest moyamoya disease is one of the primary causes of TIA in children,[3,4] and subsequent strokes are the leading cause of poor outcomes in these patients. Revascularization might be effective in stroke prophylaxis for children with moyamoya presenting with TIA, yet the timing for surgery is vague, as stroke risk stratification for these children is not well established.[5] Moreover, TIAs in pediatric patients with moyamoya have not been specifically studied. TIA characteristics and risk factors of subsequent stroke events in this distinct patient group remain unknown.

Therefore, we studied the clinical characteristics of TIAs in children with moyamoya and to explored the predictors

Article History:
Received May 7, 2017; Accepted in final from June 30, 2017

* Communications should be addressed to: Dr. Zhao; Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University. NO.6 Tiantanxili, Dongcheng District, Beijing 100050, China.
E-mail address: zhaojz205@163.com

0887-8994/$ — see front matter © 2017 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2017.06.020

of subsequent strokes to guide management decisions in these patients.

Methods

Study population

We reviewed 696 patients with consecutive moyamoya vasculopathy (155 children and 541 adults) admitted to Beijing Tiantan Hospital from 2009 to 2015 to identify pediatric patients with moyamoya disease with TIA as their initial presentation. Neurologists or neurosurgeons made the moyamoya disease diagnoses via computed tomography angiography (CTA) or digital subtraction angiography (DSA). We excluded patients (1) whose initial presentation was not TIA; (2) with no DSA data; and (3) diagnosed as the quasi-moyamoya disease (moyamoya syndrome, atherosclerosis, autoimmune disease, meningitis, neurofibromatosis type I, radiation for brain tumor, Down syndrome, sickle cell disease, Marfan syndrome, tetralogy of Fallot, diabetes mellitus Ia, Fanconi anemia, and others) according to the moyamoya diagnostic criteria.[5] TIA was defined as neurological dysfunction caused by a focal brain ischemia with symptoms lasting less than 24 hours, irrespective of ischemic lesions detected by brain imaging. All TIAs were diagnosed by neurologists or neurosurgeons. Electrocardiogram and CTA were performed on admission. The study was conducted according to the Declaration of Helsinki and approved by the Beijing Tiantan Hospital Research Ethics Committee. All patients or their legal guardians provided written informed consent for this study.

Data review and clinical follow-up

We reviewed the clinical data including clinical records and brain images for each patient. Baseline information was recorded on admission according to a protocol that included demographic data, vascular risk factors, and TIA symptoms. Two independent interventional neurologists were enrolled to review radiological examinations including DSA, MRI, CTA, and CT perfusion images. In this study, CT perfusion abnormalities included prolonged mean transit time or time to peak and decreased cerebral blood flow. Individuals with an abnormality of at least one of these parameters on a CT perfusion study were considered to have cerebral hypoperfusion. 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. Previous clinic records of other hospitals were also obtained, and the information of initial clinical presentation was required and reviewed thoroughly. The follow-up data were ascertained either by face-to-face clinical reviews or telephone interviews by neurologist residents. We conducted the last follow-up in May 2016. We inquired about (1) information of stroke events (ischemic or hemorrhagic); (2) information about symptoms of recurrent TIA; and (3) death events. Stroke was defined as a new symptomatic neurological deterioration lasting at least 24 hours or causing death that could not be attributed to a nonvascular cause.[6] TIA fluctuations were defined as the complete remitting and relapsing of TIA for two times or more within the first 24 hours of the initial TIA.[7] TIA fluctuations do not count as recurrent TIAs. Symptom progression included new types of symptoms (e.g., first TIA involved only motor symptoms, recurrent TIA symptoms had sensory or language symptoms) and symptom extensions (e.g., first TIA involved arms, recurrent involved arms and legs) in recurrent TIAs.

Statistical analysis

We performed univariate and multivariate time-to-event analyses to identify risk factors associated with subsequent stroke. The time of initial TIA presentation was time zero. The censoring events occurred when a participant was event free at the last follow-up or when the patient underwent revascularization. We dichotomized age at 11 years to explore the difference between adolescents and nonadolescents. We also conducted an analysis treating age as a continuous variable. Potential risk factors associated with a future stroke risk were assessed in univariate analyses using log-rank tests. We then employed Cox proportional hazards models for multivariate analyses. Candidate variables for multivariate modeling included all risk factors with $P < 0.20$ for association with future stroke. Hazard ratio (HR) were reported in a final model that includes only the variables with significant P values. Data were analyzed using the R statistical program (R core team; version 3.3.1; Vienna, Austria). Statistical significance was set at $P < 0.05$.

Results

Clinical characteristics

Sixty pediatric patients with TIA and moyamoya disease (10.0 ± 3.5 years at presentation) were included in this study. Baseline and TIA characteristics of these patients are detailed in Table 1. TIAs occurred most often in early school aged children (six to ten years, n = 28 [46.7%]), followed by occurrence in adolescents (11 to 18 years, n = 26 [43.3%]) and in toddlers (two to five years, n = 6 [10.0%]). No infant patients (zero to one year) were identified (Fig 1). The female-to-male ratio was 1.2:1. No patient had a history of hypertension, diabetes, smoking, or a family history of moyamoya disease. Because we excluded patients with quasi-moyamoya, disorders such as hyperthyroidism, sickle cell anemia, autoimmune disease, and congenital heart disease were not detected in our cohort.

According to DSA examinations, 36 patients (60.0%) had moyamoya diseases presented as Suzuki grade greater than 3; five patients (8.3%) exhibited unilateral moyamoya disease. Meanwhile, spontaneous collateral vessel formation from the ophthalmic artery or external carotid artery occurred in 25 patients (41.7%). Thirty-one patients (51.7%) in our cohort underwent CT perfusion examination on admission, and most

TABLE 1.
Patient Clinical Characteristics

Characteristic	No. (%) of Patients
Total number	60
Age*	10.0 ± 3.5
Female	27 (45.0)
Symptoms	
Motor weakness	51 (85.0)
Sensory dysfunction	7 (11.7)
Language disturbance	15 (25.0)
Visual disturbance	3 (5.0)
Altered mental status	4 (6.7)
Dizziness	8 (13.3)
Headache at presentation	5 (8.3)
Duration of TIA,* minute	
<1	2 (3.3)
1-4	14 (23.3)
5-9	21 (35.0)
10-29	14 (23.3)
30-59	5 (8.3)
≥60	4 (6.7)
Suzuki grade	
1	0 (0)
2	1 (1.7)
3	23 (38.3)
4	17 (28.3)
5	18 (30.0)
6	1 (1.7)
TIA fluctuations	6 (10.0)
Symptom progression†	18 (30.0)

TIA = transient ischemic attack.
* At initial presentation.
† Recurrent TIA.