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Clinical Observations

A Retrospective Study on Clinical Features of Childhood Moyamoya Disease

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ABSTRACT

Background: Childhood moyamoya disease (MMD) can lead to progressive and irreversible neurological impairment. Early age at onset is likely associated with a worst prognosis of the disease. The study aims to summarize the clinical characteristics of childhood MMD for supporting the diagnosis and treatment of early MMD.

Methods: A retrospective study was conducted on children aged zero to 16 years who were diagnosed with MMD in the Department of Neurology and neurosurgery of our hospital from October 2016 to April 2020. The clinical characteristics of children with MMD were summarized for analysis, and the distribution of sex and initial attack type among different age groups was determined by data comparison.

Results: The study surveyed 114 children (male to female sex ratio of 1:1.07) with MMD, and 6.1% of them had family history. The mean age of onset was 7.15 ± 3.30 years, and the peak age of onset was five to eight years. The most common initial attack type was transient ischemic attack (TIA) (62 cases, 54.4%) with limb weakness. The incidence of the initial attack type in the three age groups was varied ($P < 0.05$). The result of overall prognosis was good in 86 cases (89.6%).

Conclusions: In this study, MMD cases were mainly ischemic type and TIA was the most common initial attack type. Infant group was more prone to have cerebral infarction, whereas preschool and school-age groups tended to have TIA. The treatments and prognosis of the studied MMD cases were achieved with good outcomes.

Introduction

Moyamoya disease (MMD) is a rare cerebrovascular disease associated with vessel lesion (mainly stenosis), occlusion of the anterior circulation artery, and abnormal network like vessels in the skull base, which can cause recurrent stroke in children.[1] The diagnosis of MMD is increasing with the development of neuroimaging technology. The peak onset of MMD in childhood was mainly concentrated in those aged approximately five to nine years. Children with MMD usually show an arterial ischemic stroke or transient ischemic attack (TIA). The disease can present with headache, cognitive decline, or other symptoms of pre-circulation ischemia, including aphasia, dysarthria, hemiplegia, and epilepsy. The disease is also induced by hyperventilation, such as fatigue or crying.[2] With the diverse symptoms listed, children with MMD have a poorer quality of life, which brings a heavy burden to their families. Early diagnosis is essential for effective management of MMD. So far, vascular reconstruction surgery is the most effective treatment for MMD, and the current medical treatment is still unable to stop the progression of arterial disease.[3] This retrospective study collected and analyzed the clinical data of children with MMD, by examining age of onset, gender, clinical manifestations, treatment performance, and prognosis evaluation, which could be

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useful information to better understand the characteristics of the disease and provide supports on improving the clinical treatment and management of children with MMD.

Methods

Patients

A total of 114 children aged zero to 16 years diagnosed with MMD from October 2016 to April 2020 participated in the study. The data of these participants was stored in the electronic medical record database of the First Affiliated Hospital of Zhengzhou University. Inclusion criteria are the following: (1) the participants are aged 16 years or less and (2) it conforms to the criteria of the treatment and diagnosis guidelines of MMD in 2012. Exclusion criteria are as follows: (1) the participants have secondary MMD caused by meningitis, Down syndrome, systemic vasculitis, hyperthyroidism, neurofibromatosis, leptospirosis infection, or prior skull radiation therapy and (2) the data of the participants are incomplete. All patients were enrolled with the informed consent of their parents or legal guardian, and the study was approved by the Ethics Committee of Scientific Research and Clinical Trials of the First Affiliated Hospital of Zhengzhou University (2020-KY-500).

Data collection

The clinical data of the patients were collected, including gender, age of onset, initial symptoms, family history, condition of intracranial unilateral or bilateral vessels, condition of posterior cerebral artery, treatment, and prognosis. Initial attracks were classified into six categories: TIA, cerebral infarction, cerebral hemorrhage, headache, seizure, and asymptomatic disease.[4] According to the age of onset, the patients were divided into three groups: the infant group (onset age less than three years), the preschool group (onset age approximately three to six years), and the school age group (onset age approximately seven to 16 years). The neurological status and its functional performance were assessed using modified Rankin scale (mRS) in a follow-up investigation. Outpatient or telephone follow-up was conducted at three months, six months, and every 12 months after the operation. The occurrence of cerebral infarction and adverse events was investigated. The neurological status (mRS score) at the last survey was examined and classified as either good (mRS score less than or equal to 2) or poor (mRS score greater than or equal to 3).[5]

Statistical analysis

All statistical analyses were performed using SPSS (version 26.0, IBM). Measurement data were described in the form of mean ± S.D. ($\overline{X} \pm S$). Categorical variables were presented as counts (with percentages). Pearson chi-square test or Fisher exact test was used to compare categorical variables, as appropriate. Kruskal-Wallis rank sum test was used for grade data. P value < 0.05 was considered statistically significant.

Results

Gender distribution

There were 114 children with MMD (55 males and 59 females). The male to female sex ratio was 1:1.07. The symptom of bleeding classifies the studied cases into two groups. There were children with bleeding (two males and seven females, male: female = 1:3.5) and children with no bleeding symptom (53 males and 52 females). The significant difference was unseen in gender distribution of MMD among the three groups ($P > 0.05$) (Table 1).

Age distribution

The age of 114 children with MMD ranged from one to 15 years, and the median age was six years. The average age of onset was (7.15 ± 3.30) years. There were seven cases (6.2%) in the infant group, 51 cases (44.7%) in the preschool group, and 56 cases (49.1%) in the school-age group. As shown in Fig 1, the peak age of onset was approximately five to eight years and the number of children with MMD is the largest in the approximately five- to six-year-old group. In this study, the number of children with MMD was less in the infant group (less than three years old) and in the school-age group after age eight years.

Clinical manifestations

TIA was the most common initial attack type found in 62 cases (54.4%), whereas other manifestations also occur, including infarction (26 cases, 22.8%), headache (14 cases, 12.3%), hemorrhagic blood (nine cases, 7.9%), asymptomatic (two cases, 1.7%), and seizure (one case, 0.9%) (Fig 2).

In the cohort with TIA, there were 42 cases of limb weakness (67.7%), six cases of syncope (9.8%), four cases of limb numbness (6.5%), three cases of involuntary movement (4.8%), three cases of speech disturbance (4.8%), two cases of facial droop (3.2%), one case of blurred vision (1.6%), and one case of walking instability (1.6%) (Fig 3). The main manifestations of infarction were limb weakness and speech disorder. The clinical manifestations of hemorrhagic blood group were headache and syncope. The statistical analysis showed that the incidence of initial attack type was different among the three studied groups ($P < 0.05$) (Table 2). Infant group was more prone to have cerebral infarction, whereas preschool and school-age groups tended to have TIA.

Surgical treatment and outcome

A total of 96 cases (46 males and 50 females) received surgical treatment. There were four cases from the infant group, 41 cases from the preschool group, and 51 cases from the school-age group. Of the treated cases, there were nine cases of hemorrhagic MMD, including three cases of basal ganglia hemorrhage, three cases of ventricular hemorrhage, two cases of parietal lobe hemorrhage, and one case of temporal occipital lobe hemorrhage. Cerebral magnetic resonance imaging showed that most of the infarcts were found in frontal temporal lobe, lateral ventricle, and basal ganglia region. Computed tomographic perfusion scan revealed the varied levels of cerebral blood flow insufficiency in the brain tissues.

For the 96 cases, indirect revascularization was performed in 59 cases and direct/combined revascularization was performed in 37 cases. The children who had bilateral surgery and had direct/combined revascularization on one side were classified in the direct/combined revascularization group. The results showed that

TABLE 1
Comparison of Gender Distribution of Moyamoya Disease in Different Age Groups (n, %)

Sex	Total	Infant Group	Preschool Group	School Age Group	*P* Value
	114	7	51	56	
Male	55	4 (57.1)	24 (47.1)	27 (48.2)	0.904
Female	59	3 (42.9)	27 (52.9)	29 (51.8)	

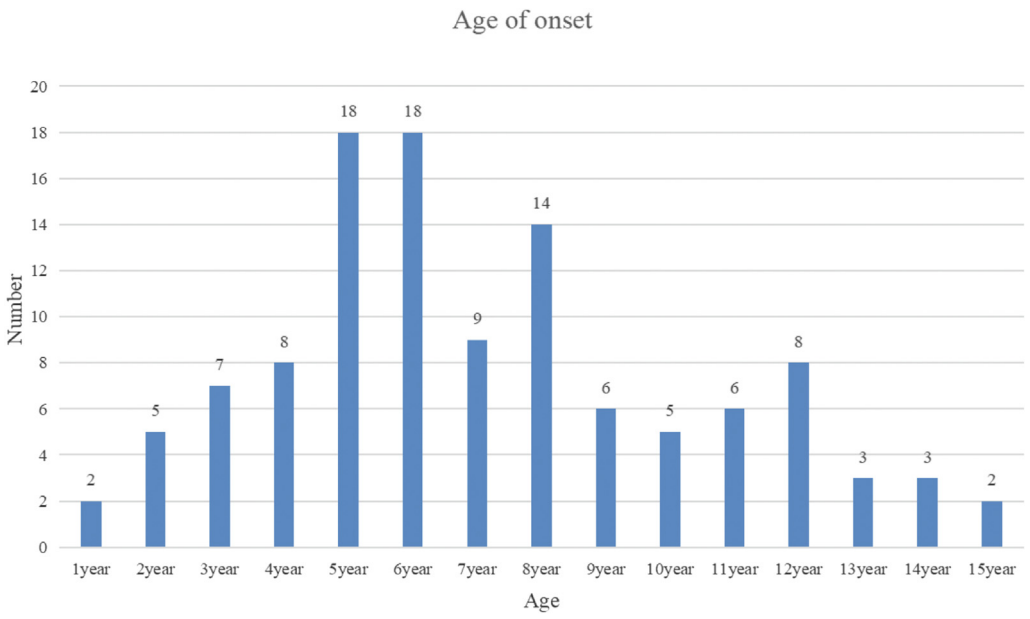

FIGURE 1. Age distribution of the patients. The color version of this figure is available in the online edition.

there was no statistical significance in the prognosis between the two groups ($P > 0.05$) (Table 3).

Of the 96 children, 57 received unilateral surgery and 39 received bilateral surgery. A total of 135 cerebrovascular reconstructions were conducted. Direct revascularization (anastomosis of superficial temporal artery to middle cerebral artery [STA-MCA] branch) was performed in two cases. There were 93 cases of indirect revascularization, including 67 cases of encephaloduroarteriosynangiosis (EDAS), seven cases of encephalomyosynangiosis (EMS), and three cases of encephaloduroarteriomyosynangiosis. Multiple burr-hole operation (MBH) was performed in 16 cases, and combined vascular reconstruction was done in 40 cases, including 11 cases of EDAS+dural reversal, five cases of EMS+dural reversal, five cases of EDAS+MBH, eight cases of EDAS+EMS+dural reversal, one case of EDAS+MBH+dural reversal, three cases of STA -MCA branch anastomosis + EDAS, one case of STA-MCA branch anastomosis + EMS, and six cases of STA-MCA branch anastomosis + EMS + dural turnover.

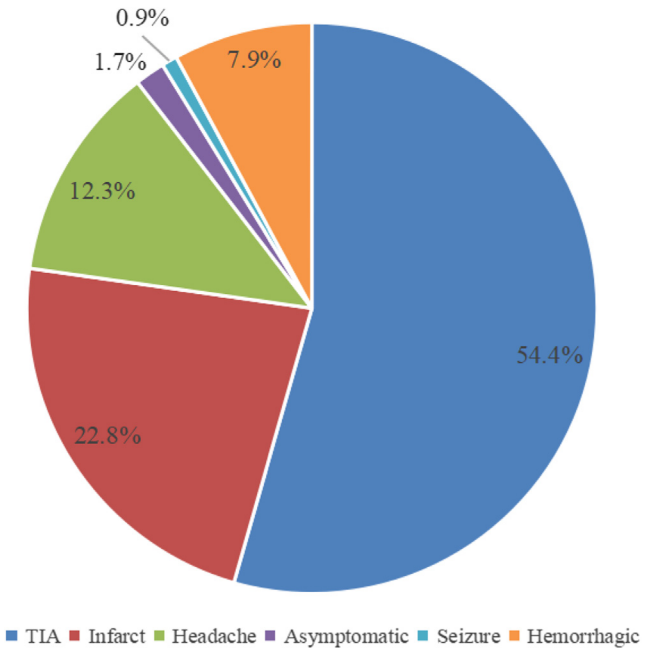

FIGURE 2. Disease type manifested at the initial attack. The color version of this figure is available in the online edition.

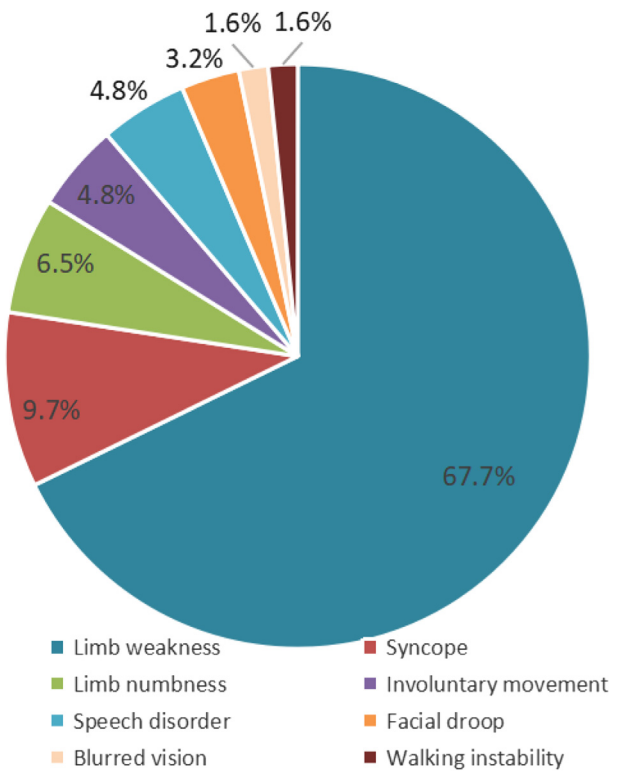

FIGURE 3. The different manifestations in the cohort of transient ischemic attack (TIA). The color version of this figure is available in the online edition.

TABLE 2
Comparison of Initial Attack Type Seen in Children With Moyamoya Disease in Different Age Groups (n, %)

Item	Total	Infant Group	Preschool Group	School Age Group	*P* Value
	114	7	51	56	
Disease type					0.006*
TIA	62	2 (28.6)	29 (56.9)	31 (55.4)	
Infarction	26	4 (57.1)	14 (27.5)	8 (14.3)	
Hemorrhage	9	0 (0.0)	1 (1.9)	8 (14.3)	
Headache	14	0 (0.0)	5 (9.9)	9 (16.0)	
Seizure	1	0 (0.0)	1 (1.9)	0 (0.0)	
Asymptomatic	2	1 (14.3)	1 (1.9)	0 (0.0)	

Abbreviation:
TIA = Transient ischemic attack
* Significant at the $P < 0.05$ level.

Perioperative complications, which are the weakness of one limb and aphasia, were undetectable in six children with MMD (including two cases of TIA) after surgical treatment. Two cases of cerebral infarction showed better pronunciation and cognitive improvement after symptomatic treatment. One case of epilepsy did not have seizure after the application of antiepileptic drugs; another case showing poor incision healing after surgery was further treated with external fixation material.

Prognosis

The outcomes of the surgical treatments were followed up in the 96 cases. The prognosis was achieved with good score in 86 patients (mRS score less than or equal to 2), whereas the prognosis of 10 patients was with poor score (mRS score greater than or equal to 3). Eighty five patients participated in the review study after surgery. The TIA symptom disappeared by one month after surgery in two cases, and TIA disappeared by three months after surgery in one case. The muscle strength of the left side was improved after rehabilitation in nine cases. Three cases showed residual fine motor impairment of the affected hands. Another three cases had memory loss. One case with seizure and one case with postoperative convulsion were treated with antiepileptic drugs, and the frequency of convulsions was reduced after the antiepileptic drug treatment. The rest of the cases were improved to varied degrees; 11 cases were followed up by telephone survey, in which no MMD-associated symptom was reported. By six months after the operation, 78 cases received medical examination. Digital subtraction angiography examination was conducted in 59 cases, and the results showed that the surgical area could see obvious vascular compensation network generation, bypass blood vessel patency and provide a good blood supply to the skull (Fig 4). By four months after surgery, two cases had TIA once and one case had cerebral hemorrhage. Two cases had cerebral infarction by five months after operation. Eighteen cases were followed up by telephone without any symptom.

Discussion

Stroke is one of the major causes of death in children. Most strokes in children result from diverse arterial diseases, of which MMD, as a pediatric arterial disease, is the most common one.[6,7] MMD is a type of nonatherosclerotic cerebrovascular structural lesion, characterized by the formation of abnormal vascular

TABLE 3
Summary of Clinical Characteristics of Children With Moyamoya Disease After Surgical Treatment (n, %)

Project	Total	Indirect Revascularization	Direct/Combined Revascularization	*P* Value
Sex		59	37	0.594
Male	46	27 (58.7)	19 (41.3)	
Female	50	32 (64.0)	18 (36.0)	
Age				
Infant group	4	2 (50.0)	2 (50.0)	0.638
Preschool group	41	26 (63.4)	15 (36.6)	0.734
School age group	51	31 (60.8)	20 (39.2)	0.885
Family history	7	6 (85.7)	1 (14.3)	0.243
Disease type				
TIA	52	31 (59.6)	21 (40.4)	0.687
Cerebral infarction	21	14 (66.7)	7 (33.3)	0.579
Cerebral hemorrhage	9	4 (44.4)	5 (55.6)	0.458
Seizure	1	0 (0.0)	1 (100.0)	0.385
Headache	13	10 (76.9)	3 (23.1)	0.218
Asymptomatic	0	0	0	
Unilateral and bilateral vascular involvement				1.000
Unilateral	8	5 (62.5)	3 (37.5)	
bilateral	88	54 (61.4)	34 (38.6)	
Involve the posterior cerebral artery				
Yes	20	12 (60.0)	8 (40.0)	0.880
No	76	47 (61.8)	29 (38.2)	
Prognosis				0.658
mRS score $\leq$2	86	54 (62.8)	32 (37.2)	
mRS score $\geq$3	10	5 (50.0)	5 (50.0)	

Abbreviations:
mRS = Modified Rankin scale
TIA = Transient ischemic attack

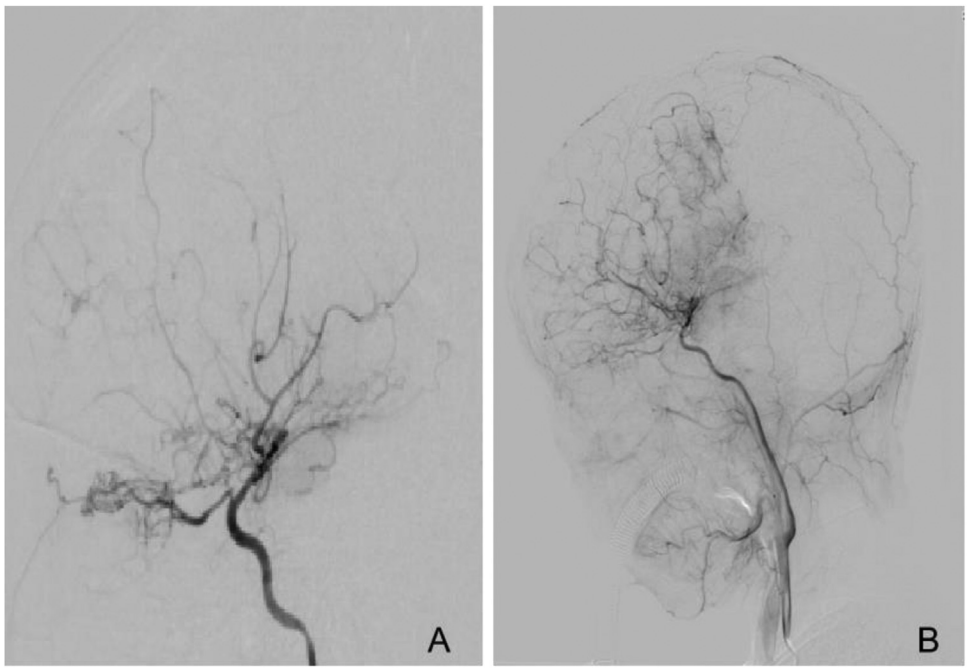

FIGURE 4. Comparison of digital subtraction angiography (DSA) before and after surgery. (A) The end of the internal artery in the left side of DSA was occluded before surgery, and smoky vessels were visible around it. (B) After DSA, the left external carotid artery compensates for blood supply to the left temporal parietal lobe through the bone window area.

network due to progressive stenosis or occlusion of bilateral internal carotid artery terminal, anterior cerebral artery, and initial segment of middle cerebral artery accompanied by compensatory hyperplasia of the skull base.[8] The unilateral vascular lesions could increase and further evolve into bilateral lesions over time.[1] These pathologic vascular features are known as moyamoya syndrome (MMS), which is also associated with many other disorders (either acquired or genetic, such as sickle cell disease, neurofibromatosis type 1, or trisomy 21).[9] The difference of clinical manifestations between MMS and MMD was not significant. Atherosclerosis and hyperthyroidism were the most common symptoms.[10] We excluded patients with Down syndrome and other diseases by screening the results of clinical manifestations, laboratory tests, chromosome analysis, and genetic examination in this investigation.

The incidence of MMD varies in different ethnic groups, but is typically seen in East Asia, like Japan, South Korea, and China.[11] An epidemiologic survey conducted from 2002 to 2006 showed that the incidence and prevalence were 0.94 of 100,000 and 10.5 of 100,000 respectively.[12] In South Korea, the incidence of MMD increased from 6.5/100,000 in 2005 to 18.1/100,000 in 2013.[13] These results suggest that the diagnosis of the disease has been increasing with the development of imaging technologies and genetic counseling. The current publications reported 12 clinical studies of MMD in children (Table 4). According to the existing data, the average age of onset is aprroximately 6.15 to 13.6 years. The onset age in our study is similar to that in previous studies, in which the average age of onset of MMD in children is 7.15 ± 3.30 years. The onset age of MMD is bimodal: aprroximately five to 10 years and 45~49 years.[25] Other clinical study reported that the onset age of patients with MMS could be unimodal.[10] The peak of onset in this study was approximately five to eight years, consistent with previous reports.

It is noticeable that the ratio of male to female in children with MMD was varied in current reports. The Japanese study shows that the incidence is mainly female,[24] whereas the studies in the United States and China do not observe the trend.[5,16] In this study, the difference was not detected in the distribution of gender. The familial occurrence of MMD was also considered as the range was 6.9%~13.9% in published data. In this study, 6.1% had a family history, which was underestimated since the family history of all the studied cases was not complete.

The common features of MMD in children are crying, excessive exercise, and excessive breathing. Hyperventilation can cause vascular dilation to compensate for chronic cerebral ischemia, leading to hypoperfusion in other vulnerable areas.[26] MMD is a progressive process in children, when unilateral lesions can be transformed into bilateral lesions. Children with MMD are at lifelong risk of suffering recurrent strokes, which have a negative impact on neurocognition and function. A study showed that children with MMD had a lower quality of life than healthy controls, similar to that of children with chronic disease and children without MMD stroke.[27] The existing publications indicated that children mainly manifesting cerebral ischemia were mostly characterized by TIA and infarction, and those manifesting by parietal limb weakness or hemiplegia, by headache, speech disorder, involuntary movement, and seizure. Intracranial hemorrhage is relatively rare in children.[17,19,22] TIA was also the most common clinical manifestation in our cohort, followed by infarct, and hemorrhagic type was relatively rare. The statistical analysis between different age groups showed that cerebral hemorrhage was more frequently seen in the school-age group, suggesting that this symptom could be age related.

Medical intervention helps with children in MMD. Studies have shown that 37% of children receiving conservative treatment had neurological impairment of varying degrees with lower quality of life during follow-up observation.[28] On the other hand, the risk of stroke was found to be reduced during the follow-up of patients with postoperative MMD.[29] However, early surgical treatment is more effective for preventing the onset of irreversible neurological impairment in children with MMD. Recent studies have shown that 82.7% (177 of 214) of children with MMD receiving surgical treatment achieved good outcomes, which is significantly higher than those who received conservative treatment.[5] At present, there are

TABLE 4
Summary of Studies Demonstrating the Clinical Features of Moyamoya Disease in Children

Author (Year)	Region	Subjects (Number)	Age	Sex (Female: Male)	Family History	Disease Type	Treatment	Prognosis
Singhi et al.[14]	India	Children with MMD (23)	The median (range) age: 5 (7.5 months-10.5 years) years	0.28:1	/	/	Indirect surgical revascularization procedure: 3 (13.0%) Conservative: 20 (87.0%)	Of the 18 patients, 12 (66.7 %) had residual neurological deficit
Kainth et al.[15]	USA	Children with MMD (2236)	/	1.07:1	/	TIA: 68 (3.1%) Ischemic stroke: 175 (7.8%) Hemorrhagic stroke: 33 (1.5%) Other: 1958 (87.5%)	/	Minimal disability: 2090 (93.5%) Moderate to severe disability: 116 (5.2%) Died in hospital: 30 (1.3%)
Bao et al.[16]	China	Children with MMD (288)	The mean (range) age: 8.0 (0.5-17.9) years	0.97:1	27 (9.4%)	TIA: 183 (61.4%) Ischemic stroke: 43 (14.9%) Hemorrhage: 12 (4.2%) Headache: 37 (12.8%) Syncope: 2 (0.7%) Seizure: 6 (2.0%) Asymptomatic: 1 (0.3%)	Surgical: 288 (100%)	2 patients (3.3%) died; mRS score: 0 and 1: 249 (86%)mRS score 2 or 3: 31 (11%)mRS score 4 or 5: 6 (2%)
Liu et al.[17]	China	Children with hemorrhagic MMD (30)	The mean (range) age : 12.6 ± 3.1 (4-16) years	1:2	/	/	Bilateral revascularization surgery: 30 (100%)	1 patient (3.3%) died mRS scores 0 and 1: 23 (83%) mRS score 2 and 3: 3 (10%) mRS score 4: 1 (3.3%)
Zhao et al.[18]	China	Adolescents with MMD (95)	The mean age: 13.1 ± 2.3 years	0.98:1	/	Ischemic: 71 (74.7%) Hemorrhage: 10 (10.5%) Headache: 9 (9.5%) Seizures: 5 (5.3%)	Indirect bypass: 53 (55.8%) Direct/combined bypass: 42 (44.2%)	/
Gaillard et al.[19]	USA	Children with familial moyamoya (18; including 2 cases of MMS)	The mean (range) age: 8.1 (2-20) years	1:1	/	Ischemic: 12 (67%) Asymptomatic: 6 (33%)	Surgical: 18 (100%)	mRS scores: postoperative mean 0.4 (range 0-2)
Tho-Calvi et al.[20]	UK	Children with moyamoya (88; including 31 cases of MMS)	The median (range) age: 5.1 (0.3-16.4) years	/	/	Ischemic stroke: 36 (40.9%) TIA: 29 (33.0%) Hemorrhage: 1 (1.1%) Headache: 10 (11.4%) Seizures: 4 (4.5%) Hemichorea: 2 (2.3%) Asymptomatic: 6 (6.8%)	Surgical: 55 (62.5%) Conservative: 33 (37.5%)	Surgical patients: good: 23 poor: 29 Conservative patients: good: 16 poor: 17
Zhang et al.[21]	China	Children with MMD (115)	The mean (range) age : 7.3 ± 4.0 (1.21-17.37) years	0.85:1	13 (11.3%)	TIA: 63 (54.78%) Headache: 31 (26.96%) Infarction: 16 (13.91%) Seizure: 3 (2.61%) Hemorrhage: 1 (0.87%) Asymptomatic: 1 (0.87%)	Encephaloduro arteriosynangiosis: 115 (100%)	The mean short-term (about 5 years) and long-term (about 10 years) mRS scores after surgery were 0.61 ± 1.18 and 0.57 ± 1.16.
Cai-Xia et al.[22]	China	Children with MMD (14)	The mean (range) age: 6.15 (21 months-13 years) years	1.33:1	/	Limb weakness or hemiplegia: 8 (57.14%) Twitch: 2 (14.29%) Unclear vision: 2 (14.29%) Conscious disturbance after headaches and vomiting: 1 (7.14%) Hearing loss: 1 (7.14%)	Conservative: 14 (100%)	1 Patient died; 4 patients suffered hemiplegia; 2 walked unsteadily; the others suffered no hemiplegia
Ge et al.[23]	China	Children with hemorrhagic MMD (46)	The mean (range) age: 13.6 ± 3.6 (2-18) years	1.19:1	2 (4.3%)	/	Surgical: 36 hemispheres Conservative: 53 hemispheres	mRS score (mean ± S.D.): 126.1 ± 96.0
Zheng et al.[5]	China	Children with MMD (303)	The mean age: 9.4 years	1.10:1	21 (6.9%)	TIA: 148 (48.8%) Infarction: 62 (20.5%) Hemorrhage: 38 (12.5%) Headache: 36 (11.9%) Seizure: 16 (5.3%) Asymptomatic: 3 (1.0%)	Combined bypass: 17 (6.0%) Direct bypass: 47 (16.7%) Indirect bypass: 150 (53.2%) Conservative: 68 (24.1%)	mRS score of 82.7% (177/214) who underwent surgical treatment was 0-1

Sato et al.[24]	Japan	Children with MMD (733)	/	1.71:1	102 (13.9%)	TIA: 382 (52.11%) Hemorrhagic: 56 (7.64%) Infarction: 195 (26.6%) Hemorrhagic infarct: 4 (0.55%) Epileptic: 39 (5.32%) Asymptomatic: 19 (2.59%) Other/unknown 38 (5.2%)	/	Good: 465 (63.61) Moderate: 204 (27.9) Poor: 62 (8.48)

Abbreviations:
MMD = Moyamoya disease
MMS = Moyamoya syndrome
mRS = Modified Rankin scale
TIA = Transient ischemic attack

three surgical methods for MMD treatment, including direct revascularization, indirect revascularization, and combined surgery. Direct revascularization is a direct vascular-to-vascular anastomosis of external carotid artery branches.[6] Indirect revascularization promotes the growth of blood vessels by attaching a vascularized graft from the external carotid artery to the surface of the cerebral cortex.[30] Direct vascular reconstruction requires high operational skills, and the thin blood vessels on the intracranial surface of children make the operation more difficult.[31] Indirect blood vessel revascularization is therefore commonly used, and a combined method is increasingly applied for many specific cases, with the combination of direct and indirect blood vessel revascularization or the combination of two or more indirect blood vessel revascularization to achieve better treatment outcome. In our case, indirect revascularization was used the most. The application of indirect revascularization showed advantage and efficiency to achieve good treatment outcomes.[32] Postoperative recovery and quality of life are also important factors, when postoperative ischemic events are the main concern in clinical prognosis.[5] A study covering 100 children with MMD showed that younger children were at higher risk of ischemia-related complications and older children showed better outcomes.[22] Bao's study showed that the surgical treatment could achieve good outcome in 84.2% of children with MMD.[17] In this study, 89.6% of 96 children treated by surgery had an overall good outcome. A further study found that both indirect and combined/direct vascularization improved symptoms, but there was no significant difference in prognosis. Notably, the follow-up time of this study is relatively short, so the outcome may be biased.

It is worth mentioning that one child in our group was found to have elevated blood pressure (the highest at 170/120 mm Hg) by five years after surgery. After admission, renal artery computed tomography angiography showed the following: (1) the left renal artery developed shallowly at the beginning, the proximal trunk lumen was occluded, and the distal lumen was weakly developed; (2) decreased perfusion and impaired function of the left kidney were detected; and (3) the right kidney supplied blood to both arteries. The causes of renal artery stenosis usually include atherosclerosis, myofibrodysplasia, and arteritis. In this work, it should be identified as the associated disease. Myofibrodysplasia lesions are different from MMD renal artery stenosis in imaging. The former lesions were mostly located in the distal one-third and distal branches of the renal artery with beadlike morphologic changes, whereas the latter lesions were located at the beginning of renal artery. The genetic test detected heterozygous mutation on RNF213 gene, known as a susceptibility gene for MMD.[33] Combined with clinical data and genetic test results, renal artery stenosis associated with MMD was identified. A report showed that renal artery stenosis was found in 7.9% of children with MMD, and 5.9% of patients with MMD developed renal vascular hypertension.[34] Analysis of the relationship between cerebral angiography stage and renal artery stenosis showed statistical significance. Research evidence suggested that p.R4810K can be the likely pathologic gene associated with MMD and systemic vascular diseases.[35] The genetic results of this child identified heterozygous variation of p.R4810K in RNF213 gene, which is not only involved in intracranial vascular lesions but also involved in renal arteries. At the case, the risk of extracranial vascular lesions could be possibly associated with the heterozygous variant of p.R4810K in RNF213 gene.

Conclusions

In our study, the male and female ratio of children with MMD was 1:1.07, the peak onset age was approximately five to eight years, and 6.1% of cases had a family history. TIA was the most

common initial attack type. MMD involves not only intracranial but also extracranial vessels. The clinical examination of extracranial vascular lesions of MMD could play a role in the accurate diagnosis and in-time treatment of the disease. Meantime, the examination of intracranial and extracranial vascular changes is also important in MMD diagnosis for preventing the incidence of stroke and other adverse events.

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