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Prevalence of Autoimmune Disease in Moyamoya Disease Patients in Central Chinese Population

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Abstract

Background: The etiology of Moyamoya Disease (MMD) remains to be unclear. An immunogenic role has been hypothesized but not confirmed. We attempted to investigate the clinical features of autoimmune diseases in MMD patients in central China to further understand the pathogenesis of MMD.

Methods: Retrospective clinical features analysis of patients with angiographically identified MMD was conducted and compared with the general Chinese population.

Results: Type 1 diabetes mellitus (immune-mediated disease) was found in 18 (5.8%) patients, significantly higher comparing with the Chinese general population (P<0.001, 5.8% *vs.* 1.3%, χ^2 test). The prevalence rate of Graves' disease (20/312) in Central Chinese population was significantly higher than that in Chinese general population (P<0.001, 6.4% *vs.* 0.34%, χ^2 test). The prevalence of autoimmune thyroiditis was not significantly different than in the Chinese general population (P=0.112, 5.5% *vs.* 1.5%, χ^2 test). Overall, autoimmune disease was associated with Moyamoya disease in 68 out of 312 (21.8%).

Conclusion: This study suggested that higher prevalence of autoimmune disease in MMD and autoimmune abnormality might associate with MMD, further supported autoimmune component to the pathogenesis of Moyamoya.

Keywords: Moyamoya disease; Autoimmune disease; Type 1 diabetes mellitus

Introduction

Moyamoya Disease (MMD) is a disorder characterized by stenosis or occlusion of the terminal portion of the internal carotid artery and the proximal portion of the anterior and/or middle cerebral arteries, and is accompanied by the formation of "Moyamoya" like collateral vessels, and a leading cause of stroke in children and young adults [1-5]. Moyamoya has been described in all races and ethnicities around the worldwide, with existing differences of race and region [1,3]. While the etiology of Moyamoya remains to be unclear [1,3]. Previous studies have reported that its pathogenesis is related to genetics, inflammation, immune stimulation, etc. [2,4]. Patients with Moyamoya syndrome also present with comorbidities such as various autoimmune diseases [2-6]. An immunologic basis has been suggested, and recent studies indicated an association between Moyamoya and autoimmune diseases, including Graves' disease, diabetes mellitus and systemic lupus erythematosus [2,4,7]. Such cases may provide new insights into the pathogenesis of these concurrent conditions. An immunogenic role has been hypothesized but not confirmed [2,4,7-9]. It is necessary for investigating more patients with this dual condition, and obtaining more evidence of immunogenic background.

Until now, the epidemiological features of autoimmune disease in Moyamoya disease have not been reported in Central Chinese Population [9]. In this study, we focused on the prevalence of autoimmune diseases among Moyamoya with co-existing diseases. We attempted to investigate the epidemiological features of autoimmune diseases in Moyamoya disease patients in central China to further understand the pathogenesis of Moyamoya disease.

Materials and Methods

A retrospective hospital discharge data was reviewed on patients who met inclusion criteria. A search of clinical database was performed for patients seen at our institution from January 2017 to July 2023, with the diagnosis of Moyamoya disease based on the guidelines set by the Research Committee on MMD of the Japanese Ministry of Health and Welfare [7]. This study

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also received approval from the local medical ethics committee and every participant signed the informed consent form. The prevalence of comorbidity was compared with that of the general population in China, according to national statistics.

Definition of autoimmune disease

Autoimmune disease was identified according to ICD-9 and ICD-10 coding. For autoimmune thyroid disease, patients were required to both have a diagnosis of Hashimoto's thyroiditis or Graves' disease and have previously documented elevated thyroid antibody studies. Individuals with abnormal thyroid autoantibodies and no autoimmune diagnosis were not considered to have autoimmune disease. A thyroid level (TSH and free/total T4) were not verified, nor was therapeutic intervention. Autoimmune disease in first-degree relatives was obtained solely from clinical documentation review and required a biological parent with a documented autoimmune disorder. Autoimmune disease of any other kind was identified as well as according to ICD-10 coding.

Statistical analysis

IBM SPSS 26.0. (Chicago, IL, USA) was used to analyze statistical data. Mean, median and Standard Deviation (SD) was used to indicate frequency. Continuous variables were compared employing χ^2 test or Fisher exact test among groups, and Statistical differences were identified significant with a P value <0.05.

Results

Basic clinical features

Three hundred and twelve people were included in the study. Gender was predominantly female (65.1%, n=202). The median age at onset was 32 years (from 5 to 65 years). Incidence rates varied with age, with two peaks, at ages 5 to 10 and 35 to 50 years. The female-to-male was 1.9 to 1. 8 pairs of patients had a family history of Moyamoya disease (mother-daughter). 82.1% (256/312) of patients were diagnosed with bilateral Moyamoya disease (definite cases), and 17.9% (56/312) of patients with lateral Moyamoya disease at diagnosis.

The first symptoms on admission of patients mainly include the following: TIA in 88 (28.2%), cerebral infarction in 68 (21.8%), headache or dizziness in 46 (14.7%), hemorrhage in 33 (10.6%), memory deterioration in 18 (5.8%), cognition impairment in 19 (6.1%), and asymptomatic patients comprised 40 (12.8%) of the total number of patients. Clinical characteristics of patients were shown in Table 1.

Risk factors for cerebrovascular events

Cerebrovascular risk factors are shown in Table 2. We found that 14.4% (45/312) of patients were current or former smokers, 20.8% (65/312) had hypertension, 19.6% (61/312) had hyperlipidemia, and 6.4% (20/312) had type 2 diabetes. The cerebrovascular risk factors were compared with the prevalence rate of Chinese population. The prevalence of hyperlipidemia in our cohort did not differ significantly compared to the general population in China. At the same time, the study did not find significant differences between hypertensive patients and smokers.

Autoimmune disease

Previous studies have suggested that an abnormal autoimmune is a potential causative factor for Moyamoya disease. In this study, we focused on the prevalence of autoimmune diseases among

Table 1: Characteristics and presentation of Moyamoya disease patients in population of Central China.

Clinical features and presentation of Moyamoya disease patients	
Sex	N=312 (%)
Female	213 (68.3)
Male	99 (31.7)
Average age at presentation	33.5 ± 16.2 (years)
Race/ethnicity	
Han	298 (95.5)
Tujia	5 (1.6)
Miao	3 (0.9)
Manchu	2 (0.6)
Other	4 (1.3)
Type (laterality)	
Unilateral	53 (17.0)
Bilateral	259 (83.0)
Presentation	
TIA	88 (28.2)
Infarction	68 (21.8)
Headache or dizziness	46 (14.7)
Hemorrhage	33 (10.6)
Memory deterioration	18 (5.8)
Cognitive impairment	19 (6.1)
Asymptomatic	40 (12.8)

ICA: Indicates Internal Carotid Artery; MCA: Middle Cerebral Artery; TIA: Transient Ischemic Attack

Moyamoya with co-existing diseases. We found high rates of type 1 diabetes mellitus (immune-mediated disease) and Graves' disease in our cohort (Table 2). Type 1 diabetes mellitus was found in 18 (5.8%) patients, significantly higher comparing with the Chinese general population (P<0.001, 5.8% *vs.* 1.3%, χ^2 test) (Table 2). The prevalence rate of Graves' disease (20/312) in Central Chinese population was significantly higher than that in Chinese general population (P<0.001, 6.4% *vs.* 0.34%, χ^2 test). The prevalence of autoimmune thyroiditis was not significantly different than in the Chinese general population (P=0.112, 5.5% *vs.* 1.5%, χ^2 test). Other autoimmune diseases included systemic lupus erythematosus (3 cases). Fifteen patients (13.9%) had various autoimmune diseases, significantly higher than the estimated prevalence of autoimmune diseases in the Chinese general population of 2.4% (P<0.001, 13.9% *vs.* 2.4%, χ^2 test). Overall, autoimmune disease was associated with Moyamoya disease in 68 out of 312 (21.8%) patients (Table 2). In addition, a higher proportion of women suffer from autoimmune diseases (F:M ratio=213:99, 2.15:1).

Discussion

Moyamoya has been described in all races and ethnicities around the worldwide, with existing differences of race and region [3-8]. The pathogenesis of Moyamoya remains to be unclear [1,3,8]. Moyamoya presenting concurrently with other diseases has been reported in several studies in the literature, including sickle cell disease, Down syndrome, and neurofibromatosis type 1 [4,7,9]. Such cases may provide new insights into the pathogenesis of these concurrent conditions. A genetic or immunogenic role has been hypothesized but not confirmed [1,2,7,9]. It is necessary for investigating more patients with this dual condition, and obtaining more evidence of

Table 2: Vascular risk factors and prevalence of autoimmune disease in 312 Moyamoya disease patients (5-65 years) when compared with the general Chinese population.

Comorbidities	Number of patients N=312 (%)	Prevalence in general Chinese population (%)	*P* value
Current or previous smoker	38 (12.2)	16.1 [10]	0.301
Hypertension	49 (15.7)	18.8 [11]	0.875
Hyperlipidemia	40 (12.8)	13.8 [11]	0.932
Type 1 diabetes mellitus	18 (5.8)	10.4 [12]	0.633
Autoimmune disease of any other kind	30 (9.8)	2.4 [13,14]	<0.001
Autoimmune type 1 diabetes mellitus	22 (7.1)	1.2 [13,14]	<0.001
Thyroid disease			
Graves' disease	20 (6.4)	0.34 [14,15]	<0.001
Hashimoto thyroiditis	17 (5.5)	1.5 [14,15]	0.096

immunogenic background.

In this study, we provided some features of Moyamoya disease patients in central China. The prevalence of MMD was significantly higher; especially type 1 diabetes and Graves' disease. The epidemic proportion of overall autoimmune diseases in MMD was up to 21.8%, which was similar to the results of previous studies in other regions. The findings further demonstrated the close correlation between MMD and autoimmune diseases. It is worth noting that autoimmune abnormalities may be related to Moyamoya disease, which suggested abnormal autoimmune mechanism may be a potential factor of Moyamoya disease.

Previous studies have indicated multiple autoimmune diseases associated MMD [2,6,9,16]. Moreover, several studies indicated that the disease progress course in MMD is associated with the presence of thyroid autoantibodies [2,17,18]. Multiple intracranial arterial stenoses and Graves' disease may occur simultaneously [2,9,16]. In this idiopathic MMD study, prevalence of autoimmune disease was roughly 21.8%, which is similar to other reported prevalence in MMD patients which ranged from 14% to 33%. Literature on autoimmune disease in pediatric-onset MMD is much sparser and mainly smaller case series. This hypothesis may be supported by several reports that other autoimmune disorders, such as systemic lupus erythematosus, type 1 diabetes, and antiphospholipid syndrome, were reported to be associated with Moyamoya syndrome [2,6,9,16].

In this study, prevalence of total autoimmune thyroid disease (Graves' disease and thyroiditis) was significantly higher in this cohort study than in the Chinese general population. The positive correlation between the levels of free thyroxine and both homocysteine and methylmalonic acid suggested that thyrotoxicosis may induce intracranial artery vessel changes in MMD [7,16-18]. Because hyperthyroxinemia above physiological dose has been implicated in patients with ischemic stroke and lacunar infarction, this would be an important factor in the pathophysiology of Moyamoya angiopathology [2,6,9,19]. Therefore, we considered that the vessel changes in the present case are due to an autoimmune-mediated mechanism, including other autoimmune disorders, or are a mere coincidence, and that the symptoms occurred because of the progression of the vessel changes. Previous studies have suggested that vasculitis caused by antithyroid drugs may be related to changes in intracranial arteries. Propylthiouracil has been reported to cause vasculitis in patients with hyperthyroidism [16]. The possibility of a mere coincidence of Graves' disease and these vascular changes should also be considered. The cerebral hemodynamic changes caused by thyrotoxicosis are thought to be the cause of infarction [19]. In a thyrotoxic state, excessive production of thyroid hormones is thought to increase brain metabolism and oxygen consumption, leading to brain perfusion injury [16,19]. Due to the reduced cerebral perfusion reserve capacity of Moyamoya disease, cerebral perfusion injury is thought to occur more frequently in this condition [6,9,19]. In addition, it has been reported that induced hypercoagulability during thyrotoxicosis may influence ischemic events [19]. These factors may explain why the patients reviewed tended to experience ischemic events rather than hemorrhagic events. The possibility of thyrotoxicosis should be considered in patients with Graves' disease when cerebral ischemia symptoms increase during follow-up.

This study has several limitations due to the single medical center. In addition, the sensitivity and specificity of the ICD code for identifying Moyamoya and autoimmune disease are unknown. Despite these limitations, our results only represent the prevalence of autoimmune disease in Moyamoya disease from the population composition of central China. Future studies should involve in multiple medical centers and more races.

References

1. Guidelines for diagnosis and treatment of moyamoya disease (spontaneous occlusion of the circle of Willis). Neurol Med Chir (Tokyo). 2012;52(5):245-66.
2. Santoro JD, Lee S, Wang AC, Ho E, Nagesh D, Khoshnood M, et al. Increased autoimmunity in individuals with down syndrome and Moyamoya disease. Front Neurol. 2021;12:724969.
3. Scott RM, Smith ER. Moyamoya disease and Moyamoya syndrome. N Engl J Med. 2009;360(12):1226-37.
4. El Ramahi KM, Al Rayes HM. Systemic lupus erythematosus associated with Moyamoya syndrome. Lupus. 2000;9(8):632-6.
5. Cramer SC, Robertson RL, Dooling EC, Scott RM. Moyamoya and Down syndrome. Clin Radiol Features Stroke. 1996;27:2131-5.
6. Bower RS, Mallory GW, Nwojo M, Kudva YC, Flemming KD, Meyer FB. Moyamoya disease in a primarily white, midwestern US population: Increased prevalence of autoimmune disease. Stroke. 2013;44(7):1997-9.
7. Tanaka R, Shimojima Y, Ueno KI, Takasone K, Ichikawa T, Kishida D, et al. Moyamoya syndrome related to systemic lupus erythematosus developing during pregnancy: a case-based review. Clin Rheumatol. 2020;39(12):3861-7.
8. Fukui M. Guidelines for the diagnosis and treatment of spontaneous occlusion of the circle of Willis ('Moyamoya' disease). Research committee on spontaneous occlusion of the circle of Willis (Moyamoya Disease)

of the ministry of health and welfare, Japan. Clin Neurol Neurosurg. 1997;99(Suppl 2):S238-40.

9. Li H, Zhang ZS, Dong ZN, Ma MJ, Yang WZ, Han C, et al. Increased thyroid function and elevated thyroid autoantibodies in pediatric patients with Moyamoya disease: A case-control study. Stroke. 2011;42(4):1138-9.
10. Cai M, Qian JC, Xu L, Rao KQ. Smoking trends from 1993 to 2008 and factors associated with smoking in rural area (of China). Chinese Rural Health Service Admin. 2010;5:364-367.
11. Wu N, Xie X, Cai M, Han Y, Wu S. Trends in health service needs, utilization, and non-communicable chronic diseases burden of older adults in China: Evidence from the 1993 to 2018 National Health Service Survey. Int J Equity Health. 2023;22(1):169.
12. Xu Y, Wang LM, He J, Bi Y, Li M, Wang T, et al. Prevalence and control of diabetes in Chinese adults. JAMA. 2013;310(9):948-58.
13. Ye L. The epidemiology of autoimmune disease. Foreign Medical Sciences (Section of Dermatology and Venereology). 1982;3:167-8.
14. Peng NC, Shi LX, Zhang Q, Xu SJ, Li H, Zhang M, et al. [An epidemiological survey of the prevalence of thyroid disease in mild iodine deficiency city after salt iodization]. Chin J Intern Med. 2013;52(1):16-20.
15. Li Y, Teng D, Ba J, Chen B, Du J, He L, et al. Efficacy and safety of long-term universal salt iodization on thyroid disorders: Epidemiological evidence from 31 provinces of mainland China. Thyroid. 2020;30(4):568-79.
16. Kainth D, Chaudhry SA, Kainth H, Suri FK, Qureshi AI. Epidemiological and clinical features of Moyamoya disease in the USA. Neuroepidemiology. 2013;40:282-7.
17. Sigdel TK, Shoemaker LD, Chen R, Li L, Butte AJ, Sarwal MM, et al. Immune response profiling identifies autoantibodies specific to Moyamoya patients. Orphanet J Rare Dis. 2013;8:45.
18. Lanterna LA, Galliani S, Zangari R, Conti L, Brembilla C, Gritti P, et al. Thyroid autoantibodies and the clinical presentation of Moyamoya disease: A prospective study. J Stroke Cerebrovasc Dis. 2018;27(5):1194-9.
19. Gill JH, Nam TK, Jung HK, Jang KM, Choi HH, Park YS, et al. Acute cerebral infarction combined with a thyroid storm in a patient with both Moyamoya syndrome and Graves' disease. J Cerebrovasc Endovasc Neurosurg. 2022;24(2):160-5.