Article published online: 2022-08-16

Case Report

Coexisting Moyamoya Syndrome and Type 1 Diabetes Mellitus: A Case Report and Review of the Literature

Abstract

Moyamoya disease (MMD) is an incompletely understood malady that affects many age groups, primarily in a bimodal age distribution. We present a patient with the association of type 1 diabetes mellitus (type 1 DM) and MMD followed by a review of the existing literature. We found five papers that describe this association, in the form of one case report, one case series, and three retrospective reviews. Despite a poor understanding of the underlying pathophysiology, a clear association between autoimmune conditions and MMD appears to exist. Clinicians who manage such patients ought to be vigilant and have a high index of suspicion when young patients with type 1 DM present with new onset of neurological symptoms.

Keywords: *Chorea, external carotid–internal carotid bypass, hemiballismus, moyamoya disease, type 1 diabetes mellitus*

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Introduction

Moyamoya disease (MMD) is a progressive idiopathic intracranial occlusive disease that primarily affects bilateral terminal internal carotid arteries (TICAs), proximal middle cerebral arteries (MCA), and anterior cerebral arteries. Affected patients present with symptoms related to regional cerebral ischemia in the form of transient ischemic attacks, stroke, and seizures. Some patients present with cognitive decline, personality changes, and movement disorders. Headache is another important clinical feature that occurs due to the dilatation of meningeal collaterals. Intracranial hemorrhage usually occurs due to neovascularization or rupture of flow-related aneurysms, especially in the posterior circulation.[1] Although MMD occurs at all ages, it usually follows a bimodal distribution, affecting children aged <10 years or adults in their 40s. Females and persons of Asian ancestry are affected more commonly.[2-5]

The exact pathogenesis of MMD remains poorly understood. Familial MMD shows an autosomal-dominant inheritance pattern with incomplete penetrance. Chromosome 17q25 has been implicated in the development of MMD.[6] Recent reports have described associations with various autoimmune disorders.[7-10] Diffuse hyperplasia of the smooth muscle cells occurs in the affected arteries, without any atherosclerotic or inflammatory changes.[11] We present the clinical, imaging, cerebral hemodynamic features and management approach in a patient with type 1 diabetes mellitus (DM), alopecia areata, and MMD along with a review of the available literature.

Case Report

A 21-year-old Malay woman presented with hemiballismus involving the left upper and lower limb for 2 days. Although the movements had reduced in intensity, they occurred even during sleep. She was diagnosed with type 1 DM at the age of 9 years when she presented with diabetic ketoacidosis. Her acute episode was treated, and he was started on insulin for long-term control. She was subsequently diagnosed with alopecia areata, bronchial asthma, and vitiligo.

Blood sugar on hospital arrival was 28 mmols/L (normal range 4.0–7.8 mmols/L). Magnetic resonance (MR) imaging of the brain showed abnormal signals in the right basal ganglia [Figure 1a] while computerized tomographic angiography demonstrated

How to cite this article: Bolem N, Nga VD, Chou N, Yeo TT, Lin J, Sharma VK. Coexisting moyamoya syndrome and type 1 diabetes mellitus: A case report and review of the literature. Asian J Neurosurg 2020;15:194-7.

Submission: 12-07-2019 **Accepted:** 11-09-2019
Published: 25-02-2020

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Access this article online

Website: www.asianjns.org

DOI: 10.4103/ajns.AJNS_218_19

Quick Response Code:

severe steno-occlusive disease of both TICAs [Figure 1b] with numerous collaterals in Moyamoya pattern. Blood tests for vasculitic disorders (including erythrocyte sedimentation rate, systemic lupus erythematosus panel, rheumatoid factor, and antinuclear antigen) were unremarkable.

Transcranial Doppler (TCD) ultrasonography revealed multiple waveform patterns in the MCA regions due to various collaterals, consistent with Moyamoya pattern. Her vasodilatory reserve in both MCAs, evaluated during the hypercapnic challenge, showed an exhausted response with paradoxical reduction of the flow velocities (Reversed Robin Hood syndrome).[12] Mean flow velocity (MFV) in the right MCA reduced from 32 cm/s to 23 cm/s during 30 s of voluntary breath holding while the MFV of the left MCA reduced from 36 cm/s to 32 cm/s during the same period [Figure 2].

Treatment with intravenous insulin and oral clonazepam gradually reduced the hemiballistic movements. Clonazepam was gradually tapered during the following 2 weeks. She underwent an uneventful right superficial temporal artery-to-MCA bypass (STA-MCA) surgery after 2 weeks. However, she developed mild left hemiplegia on the 5th postoperative day. Although MR imaging of the brain showed an acute infarction in the right MCA territory, the STA-MCA bypass was patent [Figure 3]. With rehabilitative physiotherapy, she recovered rapidly and became independent for all activities of daily living during the next 2 weeks. TCD performed 4 months after the surgery revealed normal vasodilatory reserve in the right MCA (breath holding index 0.8; normal >0.69). However, the left MCA still showed an impaired response (breath holding index 0.13). Left EC-IC indirect bypass surgery was performed on the left side 6 months later, which improved the vasodilatory reserve on the left side also. She has remained well during the follow-up during the past 1 year.

Discussion

Our patient presented with hemiballismus. We believe that the right basal ganglia lesion occurred due to a combination of hyperglycemia and MMD-induced ischemia.[13]

An extensive literature search in "PubMed," "Google Scholar," and "Scopus" using the terms such as "Type 1 Diabetes Mellitus," "Moyamoya disease," and "Moyamoya disease and autoimmune diseases" revealed 5 publications between 2012 and 2016 that included 1 case series, 1 case report, and 3 retrospective reviews of individual patient data.[14-18]

The case report from Japan in 2015 described a young woman who developed stroke symptoms after 26 years with type 1 DM. She was investigated and found to have a concurrent MMD. Interestingly, Moyamoya cases related to autoimmune conditions in Japan are surprisingly rare given the relatively higher incidence of MMD in Japan.[14]

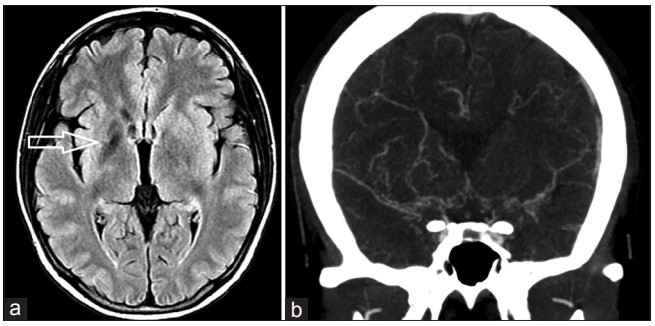

Figure 1: Magnetic resonance imaging of the brain at the time of presentation. Axial fluid-attenuated inversion recovery sequence shows an abnormal signal in the right basal ganglia (a). Computerized tomographic angiography performed on day 2 (b) revealed Moyamoya pattern of collaterals in the regions of both terminal internal carotid arteries and middle cerebral arteries

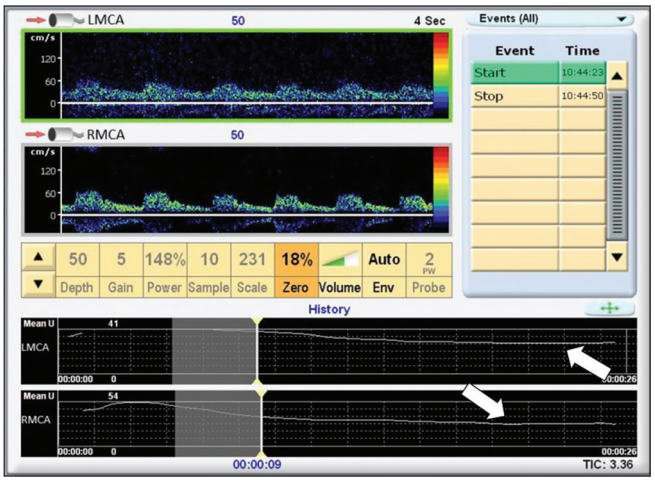

Figure 2: Continuous monitoring of blood flow in both middle cerebral arteries with transcranial Doppler during the hypercapnic challenge shows paradoxical reduction of flow velocities (arrows)

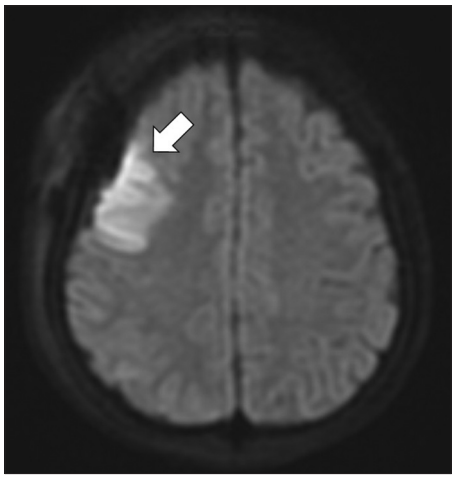

Figure 3: Magnetic resonance imaging performed on day 5 after right superficial temporal–middle cerebral artery bypass surgery. Restricted diffusion is noted in the right middle cerebral artery territory

Hughes *et al*. described 4 women with type 1 DM and MMD, 3 in their 20 s and one in 36 years of age at the time of diagnosis.[15] Two of them also had Grave's

disease and one suffered from concomitant systemic lupus erythrosis (SLE). Bilateral TICAs were affected in 3 of them. All patients presented with cerebral ischemic symptoms.

In a retrospective analysis of Western Chinese population, Chao *et al*. described 142 patients with MMD, of which 18 (12.7%) suffered from some kind of autoimmune disorder.[16] While 7% patients suffered from type 1 DM, gestational diabetes occurred in 8.3%, showing considerably higher prevalence of autoimmune conditions among the normal Chinese population (1.2% and 0.34%, respectively).[19] Similar higher prevalence of type 1 DM was reported among the MMD patients in the Mayo Clinic database from 1980 to 2011 (8.4% compared to 0.4% among the general US population).[17,20] A significant relationship was also noted between MMD and thyroid disorders in that database (Grave's disease in 2.1% and thyroiditis in 14.9% vs. 0.43% and 7.6%, respectively, in the General US population). On the contrary, a recent US study of predominantly Caucasian patients from Kentucky region explored the relationship between MMD and autoimmune disorders in 31 patients. Although such disorders were noted in 26% patients, no significant association was noted with DM. Even the severity of DM and Suzuki grade of MMD.[18]

Higher prevalence of autoimmune disorders suggests that they may contribute toward the development of MMD. Although type 1 DM and Grave's disease[21] seem to have the strongest association, other conditions such as SLE,[7] Polyarteritis nodosa, Sneddon syndrome and Antiphospholipid syndrome,[10,22] Anti-Ro and Anti-La antibodies[23] have also been reported to coexist with MMD in relatively higher prevalence. Although cerebral vasculitis occurs in some of the autoimmune disorders, it is usually transient and often responds to corticosteroids and other immune modulators. However, whether the commonly used immunomodulatory therapy for various autoimmune disorders provide any benefit to MMD remains unknown. Perhaps, a large multinational longitudinal registry of patients with MMD with autoimmune disorders may provide answers to this important question and open some treatment avenues for patients with MMD.

Conclusion

The etiopathogenesis of MMD remains poorly understood. The limited available data suggest that patients with MMD should also be considered for investigation for common autoimmune conditions, especially DM and Grave's disease.

Acknowledgments

We would like to thank all medical personnel involved in the patient's care and rehabilitation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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