Moyamoya Syndrome Associated with Graves' Disease: A Case Report and Review of the Literature

Shaneela Malik, MD,* Andrew N. Russman, DO,† Angelos M. Katramados, MD,† Brian Silver, MD,† and Panayiotis D. Mitsias, MD, PhD†

We report a patient and critically review the literature in order to define the demographic, clinical, neuroradiologic, and treatment features of moyamoya syndrome (MMS) in the setting of Graves' disease (GD). We performed a comprehensive English language Medline search using the keywords "moyamoya," "Graves' disease," and "thyrotoxicosis." We included all patients with angiographic findings consistent with MMS. A 23-year-old woman with active GD presented with intermittent confusion and right arm paresis. Brain magnetic resonance imaging revealed acute left and chronic bilateral hemispheric infarcts. Cerebral angiography revealed multivessel intracranial occlusive disease. Initial treatment with plasmapheresis plus aspirin stabilized the patient's neurologic deficits. Antithyroid treatment plus subsequent surgical encephalomyosynangiosis resulted in prolonged neurologic stability. We studied 30 patients (27 women [90%], 23 of Asian descent [77%]), with a mean age of 29 ± 11.6 years. Hemiparesis (n = 12; 40%) was the leading clinical sign, and ischemic infarction was the most frequent neuroimaging finding (n = 26; 87%). Treatment regimens included antithyroid medications alone (n = 5; 17%), antithyroid plus antiplatelet agents (n = 9; 30%), neurosurgical revascularization after antithyroid medication (n = 11; 37%), and plasmapheresis in the acute thyrotoxic state (n = 2; 7%). Most patients had good short-to-medium term outcome (n = 14; 78% of reported outcome). Plasmapheresis-treated patients achieved neurologic stabilization and had good outcomes. MMS, an infrequent complication of GD, typically affects young women. Our findings indicate that plasmapheresis can stabilize the neurologic picture in the acute phase, and that antithyroid and antiplatelet therapy, combined with revascularization surgery, may improve long-term outcomes. Further work is needed to establish an optimal treatment strategy. **Key Words:** Cerebrovascular disease—stroke—thyrotoxicosis—treatment—plasmapheresis.
Published by Elsevier Inc on behalf of National Stroke Association

Moyamoya syndrome (MMS) is an increasingly recognized cause of stroke in children and young adults. MMS is characterized by spontaneous, progressive occlusion of the terminal portions of the bilateral intracranial internal carotid arteries and the proximal portions of their major branches, as well as abnormal vascular networks in the vicinity of the occlusive lesions in the arterial phase. MMS may present with ischemic or hemorrhagic infarcts and transient ischemic attack (TIA).[1,2] The pathology of MMS was first described by Takesuchi and Shimizu in 1957.[3] The term "moyamoya" was first used by Suzuki and Takaku[4] to describing the characteristic angiographic appearance of the small vessels at the base of the brain in affected patients. Several variants of MMS do not completely fulfill all of the diagnostic criteria and present mainly with unilateral disease.[5] The pathophysiology of MMS is incompletely understood. MMS has been linked

From the *Department of Neurology, University of Virginia Health System, Charlottesville, Virginia; and †Stroke and Neurovascular Center, Henry Ford Health System, Detroit, Michigan.
Received December 19, 2009; accepted March 9, 2010.
Address correspondence to Shaneela Malik, MD, University of Virginia Health System, Department of Neurology, PO Box 800394, Charlottesville, VA 22908-0394. E-mail: sm4qn@virginia.edu.
1052-3057/$ - see front matter
Published by Elsevier Inc on behalf of National Stroke Association
doi:10.1016/j.jstrokecerebrovasdis.2010.03.006

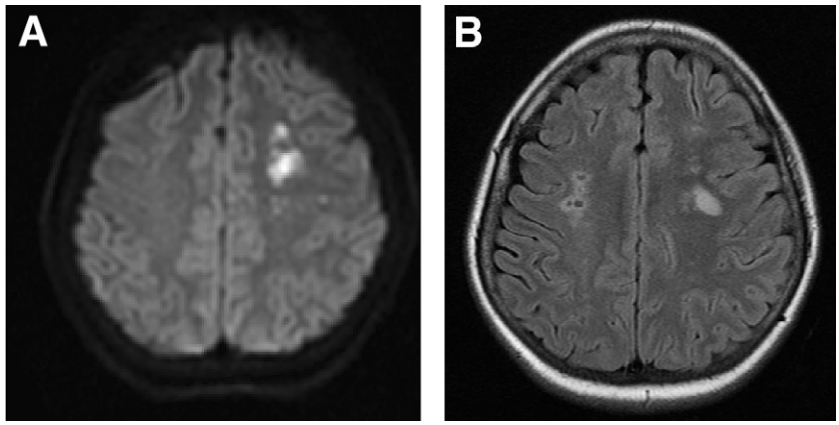

Figure 1. *Axial brain MRI. (A) Diffusion-weighted image showing an acute frontal lobe infarct. (B) T2-weighted FLAIR image showing multiple bilateral frontal lobe infarcts of varying ages.*

to several distinct clinical conditions, including sickle cell disease, systemic lupus erythematosus, Down syndrome, and fibromuscular dysplasia.[6]

Graves' disease (GD) is an autoimmune antibody-mediated disease of the thyroid gland that can lead to the development of MMS.[7] The exact frequency of MMS in GD is unknown but appears to be low. The demographic, clinical, and pathophysiologic features, as well as treatment options in patients with an extensive intracranial occlusive process and autoimmune thyroid disease have been poorly elucidated to date.

In this article, we report one patient with GD and MMS who we treated, and then systematically analyze the cases reported in the literature to clarify the demographic, clinical, neuroradiologic, and prognostic features of MMS in association with GD, and define a treatment algorithm for these patients.

Methods

We reviewed our clinical experience with a patient with GD and MMS. In addition, we performed a comprehensive Medline search for pertinent articles using the key words "moyamoya disease," "thyrotoxicosis," and "Graves' disease." We also reviewed the references cited in those articles for any specific citations or case histories. Only English language articles were reviewed. All cases with sufficient clinical and angiographic data that used standard criteria for the diagnosis of GD and MMS[1,8] were included in this study.

Results

Case Report

A 23-year-old woman presented with progressively increasing right arm weakness of 2 days duration, along with fluctuating confusion, facial numbness, and difficulty with speech for 3 weeks. She had been diagnosed with GD 5 months before presentation. Examination revealed exophthalmus and flaccid paralysis of the right arm. Brain magnetic resonance imaging (MRI) showed acute ischemic infarctions in the left hemisphere (Fig 1A) and multiple bilateral hemispheric ischemic infarctions of varying age (Fig 1B). Magnetic resonance angiography (MRA) demonstrated a tapering occlusive process of the bilateral intracranial internal carotid arteries (ICAs) and significant narrowing of the bilateral proximal posterior cerebral arteries (PCAs), proximal right middle cerebral artery (MCA), and right anterior cerebral artery (ACA) (Fig 2A). Catheter angiography demonstrated near occlusion of the bilateral carotid arteries distal to the ophthalmic artery (Fig 2B and C). An extensive laboratory investigation, including studies for potential autoimmune or hypercoagulable states, was unremarkable. She had a free thyroxine (T4) level of 5.64 ng/dL and a thyroid-stimulating hormone (TSH)

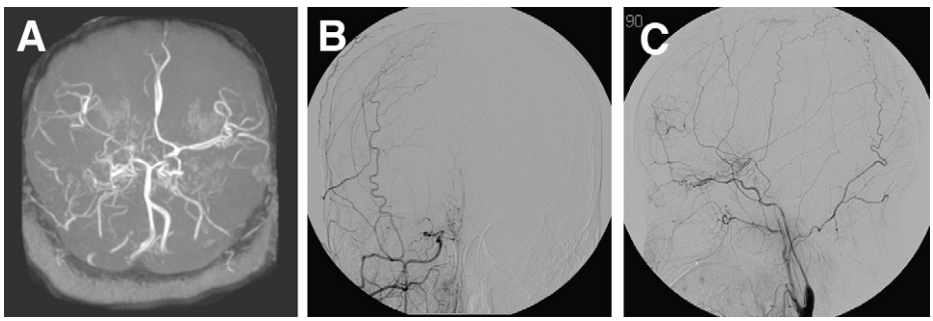

Figure 2. *Cerebral angiography. (A) Intracranial MRA demonstrating narrowing of bilateral supraclinoid ICA and PCA and right MCA and ACA occlusions. (B) Right common carotid angiogram (AP view) showing ICA occlusion. (C) Left common carotid angiogram showing ICA narrowing near the ophthalmic artery.*