Concurrent Moyamoya Disease and Graves’ Thyrotoxicosis: Case Report and Literature Review

Ai-Ling Shen¹, Shan-Jin Ryu², and Shinn-Kuang Lin¹

Abstract- Coexistence of thyrotoxicosis and moyamoya disease is extremely rare. A 23-year-old woman who had a history of migraine, suffered from frequent right carotid transient ischemic attacks, followed by an ischemic stroke after taking ergotamine for migraine. Magnetic resonance angiography revealed a tubular stenosis of the right internal carotid artery (ICA) and bilateral strictures of the supraclinoid segments of the ICAs. A concomitant thyrotoxicosis was found. A second stroke occurred three weeks later, when the dosage of antithyroid medication was increased and phenylpropanolamine-containing cold remedies were taken. Moyamoya disease was confirmed by cerebral angiography which showed irregular tubular stenosis of the right cervical ICA just above the bifurcation and nearly complete occlusion of bilateral supraclinoid ICAs with collateral flows from posterior circulation. The complexity of the cerebral hemodynamics of this patient is discussed.

Key Words: Moyamoya disease, Graves’ thyrotoxicosis, Migraine, Stroke, Ergotamine, Phenylpropanolamine

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INTRODUCTION

Moyamoya disease is a disorder characterized by bilateral stenosis or occlusion of the terminal internal carotid artery and proximal portion of the anterior and middle cerebral arteries, accompanied by “moyamoya” network collaterals in the vicinity. Moyamoya disease is one of the important causes of either ischemic or hemorrhagic stroke in young patients. The incidence and prevalence of moyamoya disease is higher in Asian countries. Moyamoya phenomenon is used to describe the extensive collateralization of the circle of Willis arteries associated with severe unilateral or bilateral internal carotid artery stenosis or occlusion in the presence of conditions such as sickle cell disease, atherosclerosis, cranial irradiation, fibromuscular dysplasia, neurofibromatosis, dissecting aneurysm, and arteriovenous malformation. Graves’ disease is an autoimmune disorder presented as hyperactivity of the sympathetic...
nervous system. Graves’ disease mainly affects female patients and is not uncommon in Taiwan. However, coexistence of symptomatic moyamoya disease and Graves’ thyrotoxicosis is extremely rare. Only five such patients have been reported in English literature\(^2\). We report a young woman with concurrent moyamoya disease and Graves’ thyrotoxicosis who developed two episodes of ischemic stroke.

**CASE REPORT**

A 23-year-old woman had suffered from intermittent throbbing headache for five years. In a three-week period prior to her first hospitalization, she experienced several episodes of transient (of one hour duration) weakness and numbness in her left limbs with mildly slurred speech. At admission, she reported that she had taken two tablets of dihydroergotamine mesylate, containing 5 mg ergotamine each, for an attack of migraine-like headache before sleep. The following morning she noted a persistent weakness of the left limbs. She was subsequently admitted to the neurology ward. On admission, her blood pressure was 138/54 mmHg and pulse rate was 113/min. Bilateral upper cervical bruits were noted and a systolic cardiac murmur was audible at her left upper sternal border. The muscle power in her left upper limb was 4/5 (Medical Research Council of Great Britain), and of the left lower limb, was 4+/5. Laboratory investigations including routine hemogram, ESR, biochemistry, fibrinogen, proteins C and S, homocysteine, ANA, C3, C4, antithrombin III, and antiphospholipid antibodies were all within normal ranges. Her electrocardiogram showed sinus tachycardia. Transthoracic echocardiography revealed mitral valve prolapse. Her serum triiodothyronine (T3) was 5.76 nmol/L (reference range 0.93 - 2.52), the free thyroxine (FT4) was > 111 pmol/L (reference range 10.96 - 23.99), and her thyroid stimulating hormone (TSH) was < 0.03 mU/L (reference range 0.25 - 4). The titer of microsomal antibody was 1:1024. The results of thyroid sonography and aspiration cytology study were suggestive of an autoimmune thyroid disease. Duplex sonography study did not show atherosclerotic change of the carotid arteries but demonstrated smaller caliber of the right internal carotid artery (ICA) with reduced volume flow, and markedly accelerated flow in bilateral superior thyroid arteries (Fig. 1C) (Table 1). Brain magnetic resonance (MR) imaging showed small infarcts in the right centrum semiovale (Fig. 1A). MR angiography revealed segmental narrowing of the right cervical ICA and strictures at the supraclinoid portion of bilateral ICAs. Stricture at the origins of bilateral anterior cerebral arteries (ACA) and middle cerebral arteries (MCA) of the left side was evident (Fig. 1A).

![Figure 1](image.png)

**Figure 1.** (A) A coronal T2-weighted magnetic resonance (MR) image shows a small infarct (arrow) at the right centrum semiovale. (B) MR angiography demonstrates reduced caliber of the right internal carotid artery (ICA) and strictures of both bilateral distal ICAs and proximal middle cerebral arteries. (C) Duplex sonography shows significantly accelerated turbulent flow in the left superior thyroid artery.
Table 1. Velocities of each artery from carotid and transcranial duplex sonographies of the patient during first admission

<table>
<thead>
<tr>
<th></th>
<th>Right side</th>
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<th>Left side</th>
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<tr>
<td></td>
<td>PS (cm/s)</td>
<td>ED (cm/s)</td>
<td>MV (cm/s)</td>
<td>RI</td>
<td>FV (ml/min)</td>
<td>PS (cm/s)</td>
<td>ED (cm/s)</td>
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<td>0.77</td>
<td>66</td>
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<tr>
<td>ECA</td>
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<td>68</td>
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<td>131</td>
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<td>0.76</td>
<td>212</td>
<td>181</td>
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<td>116</td>
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</table>

CCA: common carotid artery; ICA: internal carotid artery; ECA: external carotid artery; VA: vertebral artery; STA: superior thyroid artery; IVA: intracranial vertebral artery; PS: peak systolic velocity; ED: end diastolic velocity; MV: mean velocity; RI: resistance index; FV: flow volume.

* Reference range: 26±9 cm/s

Figure 2. Follow-up brain computed tomography shows a new infarct at the right middle cerebral artery territory.

Figure 3. Digital subtraction angiography reveals tubular stenosis of the right internal carotid artery (arrowheads) (A) with bilateral intracranial moyamoya disease (B,C).
cerebral arteries (MCA), and prominent posterior circulation were observed. The findings of MR angiography are compatible with moyamoya disease (Fig. 1B). The patient received aspirin 100 mg/day, propiothiouracil 150 mg/day and propranolol 30 mg/day. She was discharged with minimal weakness in the left limbs one week after admission.

For a better control of hyperthyroidism, the dosage of propiothiouracil was increased to 300 mg/day ten days after discharge. Thirteen days after her discharge, she had a common cold and took a phenylpropanolamine (PPA) containing cold medicine obtained from a drugstore. She then noticed an increase of her left side weakness and was readmitted. A brain CT showed infarcts in the right temporal, frontal, and parietal lobes (Fig. 2). Digital subtraction angiography (DSA) revealed irregular tubular stenosis of the right cervical ICA just above the bifurcation and nearly complete occlusion of bilateral supraclinoid ICAs with tortuous collaterals supplying bilateral ACAs and MCAs. Some hazy net-like moyamoya vessels were observed (Fig. 3). The dosage of propiothiouracil was reduced to 150 mg/day. Ticlopidine (250 mg/day) was prescribed to replace aspirin. The left hemiparesis improved gradually and in a follow up examination two years later, only minor weakness of the left hand was noted.

**DISCUSSION**

Migraine-like headache has been reported to occur in 21% of patients with moyamoya disease. Down shift of this borderline perfusion state in the affected brain region could be a trigger for migraine with aura in susceptible patients. Recurrent ischemic stroke and TIA are common presentation of moyamoya disease in young adults. In our patient, the presentation of recurrent right carotid TIAs before first complete stroke is indicative of unstable cerebral hemodynamic state. Ergotamine, a commonly used ergot derivative for relieving migrainous headache, has vasoconstrictive effect and may increase sympathomimetic tone. Certain sympathomimetic drugs such as cocaine, amphetamine, and PPA were known to cause vasoconstriction as well. Patients with moyamoya disease are particularly at risk of developing symptoms of cerebral perfusion deficit after exposure to those sympathomimetic drugs. In our case, the cause-and-effect relationship between the use of ergotamine and the first stroke is very likely. A similar causal relationship is also observed between PPA-containing cold remedies and her second stroke.

Coexistence of thyrotoxicosis and moyamoya disease is extremely rare. Kushima et al reported their first two patients in 1991, and stated that the coexistence of these two diseases may not be so rare as three cases of thyrotoxicosis with cerebrovascular moyamoya phenomenon had been reported in the Japanese annual meeting. However, before this case there had been only five patients reported in English literature, when searched using the Medline system. Table 2 summarizes the clinical features of all reported patients. All of the patients were young females. Most of the cerebrovascular events were associated with thyrotoxicosis. In previous reports, the diagnosis of either stroke from moyamoya disease or hyperthyroidism, preceded the

<table>
<thead>
<tr>
<th>Author</th>
<th>Patient Age / sex</th>
<th>Sequence of diagnosis</th>
<th>TIA Headache</th>
<th>Bruit R / L</th>
<th>Recurrent stroke</th>
<th>Prognosis</th>
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<td>-</td>
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<td>37 Y/ F</td>
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<td>+</td>
<td>+ / -</td>
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<td>47 Y/ F</td>
<td>1) Stroke and moyamoya variety, 2) Hyperthyroidism</td>
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<td>-</td>
<td>-</td>
<td>good</td>
</tr>
<tr>
<td>Lin et al</td>
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<td>1) Stroke, hyperthyroidism, and moyamoya disease</td>
<td>+</td>
<td>+</td>
<td>+ / +</td>
<td>good</td>
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TIA: transient ischemic attack; R: right; L: left; Y: year; F: female
other by several months to years. In our patient, these two diagnoses were made almost simultaneously. Two patients had a history of TIA, and three suffered from a headache during an acute stroke. Cervical bruits, signs of hyperthyroidism, were described in only two patients, including ours. Two patients experienced repeated strokes. Our patient has all the features described in the table. All the patients had favorable short-term outcomes.

The etiology of moyamoya disease is still unclear although an autoimmune process has been implicated. Cellular proliferation with vascular dysregulation in moyamoya and immunologic stimulation of the thyroid in Graves’ disease, have been proposed to have a common pathogenetic link involving T-cell dysregulation(4). Some authors have postulated that thyroid hormones might augment vascular sensitivity to the sympathetic nervous system, and thus foster the pathologic process of the arterial wall in moyamoya disease(5). An increased collateral flow through the external carotid artery (ECA) might additionally increase the flow in the superior thyroid artery. Is it possible that a long-standing increase of blood flow into the thyroid gland also stimulates an overgrowth of thyroid gland?

The effect of thyrotoxicosis on the cerebral hemodynamics in patients with moyamoya disease is complex. Cerebral blood flow increases in thyrotoxicosis(6). The flow velocity of MCA also increases linearly with serum T3 level(7). Theoretically, increased flows in ECA due to hyperthyroidism provide more collateral flows to a certain extent in patients with moyamoya disease. However, oversensitivity to sympathetic tone in severe thyrotoxicosis may result in an intracranial vasoconstriction, which carries a negative effect to cerebral perfusion(8). Thyrotoxicosis is correlated with cerebrovascular events. The first patient in Tendler’s report developed stroke soon after treatment of thyrotoxicosis(9). A second stroke occurred in our patient shortly after the dosage of medication was increased. Although concomitant PPA-containing cold remedies might have also participated in causing the second stroke, sudden surge of thyroid hormone might have caused unexpected changes to the cerebral hemodynamics.

In conclusion, an underlying moyamoya disease and a more recent thyrotoxicosis, may contribute to the development of a migraine-like headache in this patient. Ergotamine, a vasoconstrictive agent, may further induce the first episode of ischemic stroke. Rapid alteration of cerebral hemodynamics, due to an improvement in thyrotoxicosis by increasing the dosage of antithyroid medication and the use of PPA-containing cold remedies, precipitated the second ischemic stroke. This case report demonstrates the importance of checking the thyroid function in young stroke patients with moyamoya disease, especially in those patients who have concomitant upper neck bruits. In the presence of moyamoya disease, the cerebral hemodynamic responses to certain common pharmacological agents, including medications for thyrotoxicosis, migrainous headache, and common cold, are complex in all aspects. Further research is necessary to better understand the probable common pathogenesis of moyamoya disease and Graves’ thyrotoxicosis.

REFERENCES


