Multiple Intracranial Arterial Stenoses in Association with Thyrotoxicosis: A Case Report

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Abstract- A 26-year-old young man, had Graves' disease in hyperthyroid state, presented with frequent episodic transient left hemiparesis and mild slurred speech lasting for few minutes to 2 hours for one month. Infarction at posterior limb of right internal capsule was found on brain MRI. Angiography revealed multiple intracranial arteries stenoses around the circle of Willis. After treatment with propylthiouracil and aspirin, his thyroid function returned to normal and the patient remained free from stroke.

Key Words: Graves' disease, Thyrotoxicosis, Multiple intracranial stenoses, Stroke

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INTRODUCTION

Stroke is a heterogeneous disease with a variety of pathophysiologic mechanisms. It is known that occulusive diseases occurring in intracranial vessels are more common than those occurring in extracranial vessels in Taiwanese compared to Caucasian stroke patients[1]. The association of multiple intracranial arterial stenoses with Graves' disease is rare in patients with stroke. Only few cases, and exclusively in female, had been reported in the literature[2-7]. Graves' disease is an autoimmune disorder characterized by hyperthyroidism due to circulating autoantibodies acting on thyroid-stimulating hormone (TSH) receptor. We reported a case of young man who had ischemic stroke caused by multiple intracranial arterial stenoses around the circle of Willis in association with Graves' disease in hyperthyroid state.

CASE REPORT

A 26-year-old young man had episodic transient left hemiparesis and mild slurred speech lasting for few minutes to 2 hours for one month. Before this admission, he had heat intolerance, excessive sweating and palpitation for several months. There was also body weight loss and hand tremor. Reviewing his history, he denied illicit drug used. He was not alcoholic or a smoker. Family history for stroke was negative.

On admission, his blood pressure was 160/90 mmHg (blood pressure returned to normal after discharge), heart rate was 112 beats/minute. An enlarged thyroid gland was palpated and bruit on neck was heard during the physical examination. His skin showed generalized hyperpigmentation. The neurological examination performed on admission demonstrated no neurolog-

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ical deficits except for fine postural tremor on both hands.

Laboratory studies revealed normal complete blood count, liver and renal function tests, electrolytes, lipid profile and fasting blood glucose. Venereal Disease Research Laboratory (VDRL), anti-β2 glycoprotein 1 IgG and Human Immuodeficiency virus (HIV) titer was negative. Prothrombin time, activated partial thromboplastin time (APTT), erythrocyte sediment rate (ESR), fibrinogen, protein C, protein S and anti-thrombin III assessment, all within normal limit. Thyroid function test revealed thyrotoxicosis state (free-thyroxin: 2.22 ng/dl, total thyroxin: 29.6 ug/dl, triiodothyronine: 486 ng/dl, thyroid-stimulating hormone: 0.003 uIU/ml). Thyroid-binding inhibitory immunoglobulin (TBII) and anti-microsomal antibody titer were positive whereas anti-nuclear antibody titer was negative. Tc-99m thyroid scan showed diffuse goiter with homogenous increased uptake. Cardiovascular examination was normal except tachycardia.

Brain MRI demonstrated recent infarction at posterior limb of right internal capsule. Cerebral angiography revealed multiple intracranial artery stenosis (Figure) Carotid duplex showed no significant stenosis in common and internal carotid arteries.

The patient was followed up at out patient clinic and treated with propylthiouracil (PTU) for his thyroid disease and aspirin for secondary stroke prevention after discharge. His thyroid function returned to normal after six-month treatment and he remained stroke-free during the following eight months.

DISCUSSION

Intracranial arterial stenoses are more prevalent in Asian stroke patients, but the etiology still remains unknown. The association of multiple intracranial arterial stenoses with Graves' disease is not common but had been reported in the literature. Only 10 cases had been reported and the majority of the patients were Asian, Tendler et al[4] described two Caucasian women with this medical situation. Although Wakamoto[7] reported a case with intraventricular hemorrhage, most of the cases presented as transient ischemic attack or infarction and the patient always had favorable outcome after treatment of the underlying thyroid problem. The ischemic symptoms will recur while the patient remains in thyrotoxicosis[3]. Reviewing the cases reported, all the patients involved were female in gender. This interesting case was reported because of its rarity and that this was the first case

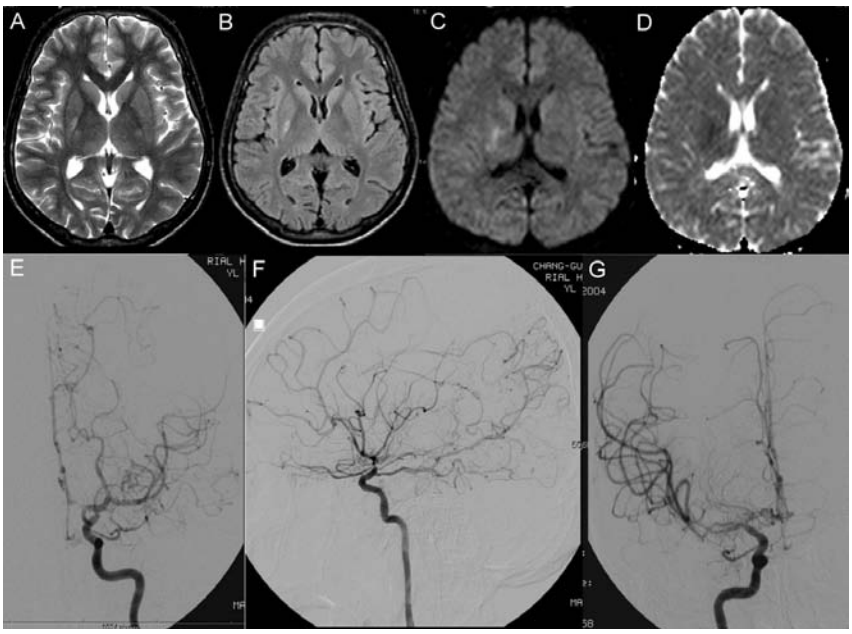

Figure. High-signal lesion was noted in right internal capsule posterior limb at T2 weighted image (A), FLAIR (B) and Diffusion weighted image (C). This lesion appeared dark in ADC map (D) denoting recent ischemic stroke. The PA (E) and lateral views (F) of the angiography on the left internal carotid artery (ICA) showed marked narrowing of left distal ICA, middle cerebral artery (MCA) M1 and anterior cerebral artery (ACA) A1 segments with leptomeningeal collaterals from the left poeterior cerebral artery. The stenosis in the right MCA M1/2 segments was also noted in the PA view of the angiogram on the right ICA (G).

involved in male gender.

Our case did not meet the full diagnostic criteria for moyamoya disease, in that there was no obvious abnormal, net-like or smoke-like appearance in the basal ganglia on cerebral angiography, but other clinical and angiographic features were consistent with this condition. Kataoka et al.[5] suggested that moyamoya disease may include some variant types that do not completely fulfill the diagnostic criteria but exhibit the same pathophysiological features as moyamoya disease. Our case may represent one of these variant types or may simply reflect early stage of definite moyamoya disease.

The relationship between intracranial arterial stenoses and Graves' disease remains unclear. Several hypotheses of the coexistent conditions had been proposed.

Most patients presented their neurologic symptoms while in thyrotoxicosis and recovered after the thyroid problem had been treated. In some patients, the recurrent neurologic symptoms coincided with the recurrence of thyrotoxicosis[3].

Carotid intima-media thickness was observed to be associated with thyroid hormone in linear relationship[8]. Hyperthyroidism also showed significant increase stiffness in carotid artery, which may reflect the harmful effect of hyperthyroidism on arterial wall[9-10]. In addition, thyroid hormones increase the sensitivity of sympathetic nervous system, which may be responsible for the pathological change in cerebral arteries[3]. Therefore, hyperthyroidism may increase the risk of stroke and possibly explain the stenotic change of arteries in our patient. However, intracranial arterial stenoses cannot be observed in general population of hyperthyroidism. The exact association of arterial stenosis and excess thyroid hormone remains to be elucidated.

Tendler et al.[5] suggested the possibility of a common pathophysiological mechanism, involving T cell dysregulation, in Graves' disease and moyamoya disease. Therefore, Graves' disease could be associated with the causal mechanism of moyamoya disease.

Although difficult, it is equally important to determine whether the apparent link between Graves' disease and moyamoya disease or a moyamoya variant represents a mere chance association. Obviously, the study of more cases is necessary to shed light on the relationship between the two diseases.

Successful treatment with surgical bypass procedures had been reported in intractable case. However, most of the cases reported had improvement of neurologic symptoms after antithyroid therapy. So, medical treatment might be the first choice of the treatment. But given the rarity of this combined entity and limited clinical experience, efforts to identify the best management paradigm are difficult. It is mandatory to maintain long-term follow up in patients to understand the natural history of this medical situation.

In conclusion, multiple intracranial arterial stenoses and Graves' disease may occur simultaneously and it is practical to consider patients with both multiple arterial stenoses and Graves' disease as being at risk for ischemic cerebrovascular events. Maintaining normal levels of thyroid hormone is necessary and treatment with surgical procedure might be considered in intractable cases.

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