

Improvement of Cerebral Arterial Stenosis Associated With Basedow's Disease

—Case Report—

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Abstract

A 29-year-old female presented with Basedow's disease manifesting as sudden vomiting, diarrhea, fever over 38°C, transient aphasia, and numbness in her extremities. These symptoms were considered due to cerebral ischemia at a local clinic. Magnetic resonance angiography indicated stenosis of the bilateral distal internal carotid arteries and the bilateral proximal anterior cerebral and middle cerebral arteries. Thyroid swelling and exophthalmos were observed. She was transferred to our hospital. Endocrine function tests showed hyperthyroidism. The diagnosis was Basedow's disease. Her symptoms disappeared after receiving intravenous drip infusion of fluid replacement, and antithyroid and antiplatelet medication. After she became euthyroid, cerebral angiography and magnetic resonance angiography revealed improvement of the stenosis of the cerebral arteries. Stenosis of the terminal portion of the internal carotid artery associated with Basedow's disease is extremely rare. Conservative treatment mainly including antithyroid medications for Basedow's disease, and antiplatelet drugs and intravenous replacement fluid for the ischemic manifestations should be the first choice of treatment unless immediate vascular reconstruction is necessary.

Key words: Basedow's disease, stenosis, cerebral artery, antithyroid therapy

Introduction

Basedow's disease manifests as a type of thyrotoxicosis with diffuse goiter, and is an autoimmune disease caused by thyroid-stimulating immunoglobulin, an autoantibody against the thyroid gland.¹⁾ Basedow's disease may sometimes be complicated by thyroid crisis; i.e., acute exacerbation of hyperthyroidism. In addition, this disease increases the tonus on the sympathetic nerves. Basedow's disease is very rarely associated with stenosis of the terminal portion of the internal carotid arteries (ICAs).^{4-6,9,10,13,15)} Recently, we treated a patient with thyroid crisis complicated by ischemic manifestations, and thorough investigations revealed concomitant stenosis of the terminal portion of the ICAs. Treatment for Basedow's disease also led to improvement of the stenosis of the terminal portion

of the ICAs.

Case Report

A 29-year-old woman was admitted to a local clinic on July 22, 2001 due to sudden vomiting, diarrhea, fever over 38°C, transient aphasia, and numbness in her extremities. The initial diagnosis was cerebral ischemia due to dehydration, and the manifestations gradually improved after conservative treatment with intravenous replacement fluid. Computed tomography and magnetic resonance (MR) imaging did not reveal any particular abnormalities, but MR angiography indicated stenosis of the bilateral distal ICAs and the bilateral proximal anterior cerebral arteries (ACAs) and middle cerebral arteries (MCAs) (Fig. 1). Physical examination found a thyroid mass measuring 5 cm in width (Fig. 2) and exophthalmos.

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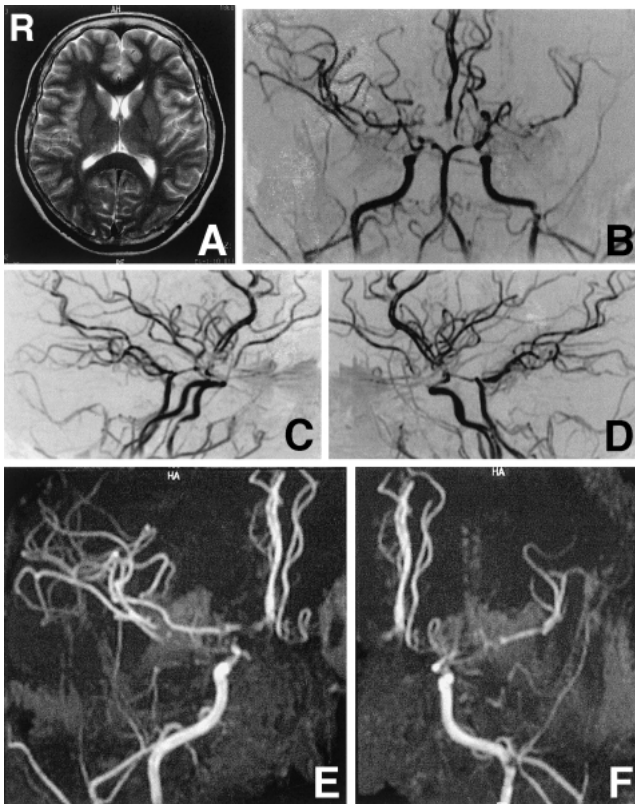


Fig. 1 A: T₂-weighted magnetic resonance (MR) image showing no distinct flow void in the cerebral basal ganglia. B-F: Initial MR angiograms showing stenosis of the bilateral distal internal carotid arteries and the bilateral proximal anterior cerebral and middle cerebral arteries (B: posteroanterior view; C: lateral view, right to left; D: lateral view, left to right; E, F: contrast views).

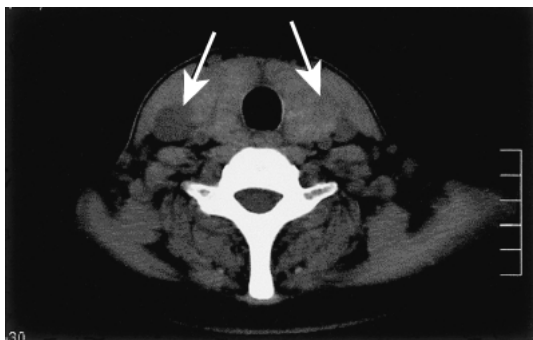


Fig. 2 Computed tomography scan showing a thyroid mass (arrows) measuring 5 cm in width.

She was transferred to our hospital on August 8.

On admission, hematological examination found thyroid-stimulating hormone (TSH) 0.03 μ U/ml (normal 0.34–3.5 μ U/ml), free T₄ 6.0 ng/dl (normal 0.9–1.8 ng/dl), free T₃ 25.19 ng/dl (normal 2.2–4.1 ng/dl), and anti-thyroglobulin antibody 480% (normal <180%). The diagnosis was Basedow's disease based on these results and the physical findings. Moreover, we believed that she had initially suffered thyroid crisis that was later complicated by cerebral ischemic manifestations due to dehydration. Her symptoms of vomiting, diarrhea, fever, numbness in the extremities, and aphasia completely disappeared after treatment with thiamazole (15 mg/day) and aspirin (81 mg/day). She was discharged from our hospital on August 27 with maintenance treatment of thiamazole (15 mg/day) and aspirin (81 mg/day). Follow-up hematological examination revealed TSH 0.01 μ U/ml, free T₄ 0.92 ng/dl, and free T₃ 3.18 ng/dl on January 20, 2002, indicating remission of Basedow's disease.

She was re-admitted into our hospital for extensive investigations with cerebral angiography. No specific physical characteristics were recognized except for goiter and exophthalmos. Cerebral angiography revealed stenosis of the right distal ICA and slight stenosis of the right proximal ACA and the left proximal MCA. Nevertheless, no collateral blood flow from the external carotid artery system or the ophthalmic artery, or distinct basal moyamoya vessels were observed (Fig. 3A, B). Concurrent MR angiography demonstrated similar findings, except that the stenosis of the terminal portion of ICA was better than at the initial MR angiography (Fig. 3C–E). Based on these findings, the arterial stenosis had apparently improved with the treatment for Basedow's disease, so we considered this stenosis as a secondary change caused by Basedow's disease. Single photon emission computed tomography (SPECT) using technetium-99m-ethylcysteinate dimer showed only a slight reduction in the reserve capacity from the left parietal lobe to the occipital lobe, so bypass surgery was not indicated. She was discharged on February 1 with maintenance therapy of thiamazole (15 mg/day) and aspirin (81 mg/day). Currently, Basedow's disease remains in remission with no signs of cerebral ischemia.

Discussion

Table 1 shows the 14 reported cases of Basedow's disease associated with stenosis of the terminal portion of ICA including moyamoya disease.^{4–6,9,10,13,15} In the present case, MR angiography revealed steno-

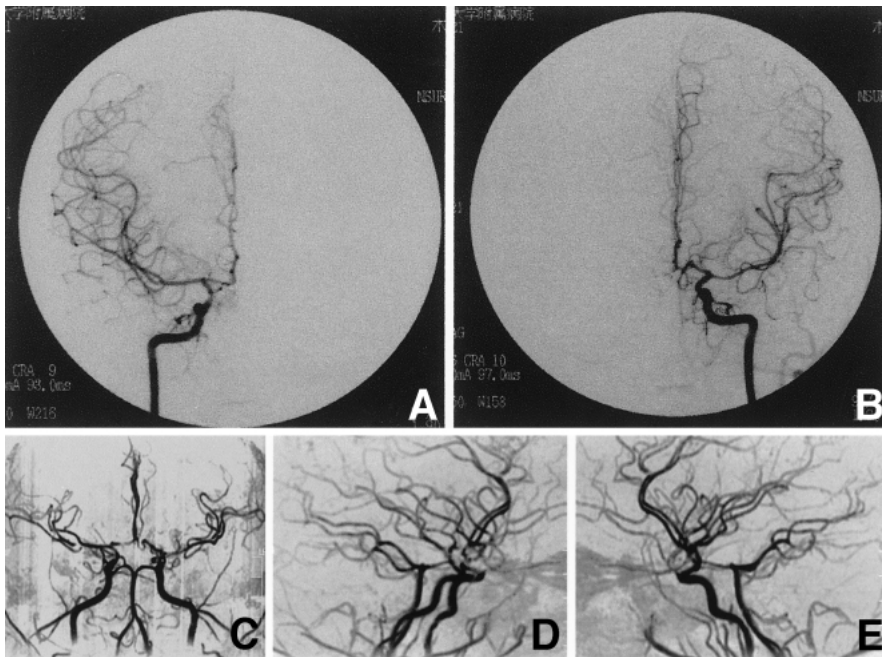


Fig. 3 A, B: Right (A) and left (B) internal carotid angiograms 6 months after the onset revealing stenosis of the right distal internal carotid artery (ICA) and slight stenosis of the right proximal anterior cerebral artery and the left proximal middle cerebral artery without collateral flow or basal moyamoya vessels. C–E: Magnetic resonance (MR) angiograms 6 months after the onset showing improvement of the terminal stenotic findings of the ICA compared with the initial MR angiogram (C: posteroanterior view; D: lateral view, right to left; E: lateral view, left to right).

sis of the bilateral distal ICAs, and the bilateral proximal ACAs and MCAs. Moyamoya disease was considered in the differential diagnosis. Nevertheless, MR imaging did not reveal distinct flow void in the cerebral basal ganglia. Accordingly, the diagnostic criteria for moyamoya disease were not fulfilled.¹⁸⁾ However, not all cases of moyamoya disease meet the diagnostic criteria initially, as neuroimaging may start to reveal the diagnostic criteria as the disease progresses.^{3,12,16)} Moreover, patients with a family history of moyamoya disease have a high incidence of multi-factorial hereditary diseases including thyroid gland disorders.¹¹⁾ Therefore, extra attention should be paid to the diagnosis and careful follow up is essential.

Table 1 also shows that all patients are female, possibly because females in their twenties are one of the most likely groups to develop Basedow's disease.⁴⁾ Except for our case, only one case has shown imaging evidence of improvement in the vascular stenosis before and after the treatment for Basedow's disease.¹⁵⁾ Furthermore, as shown in Table 1, improvement of the cerebral ischemic manifestations was observed in most patients with treatment for Basedow's disease, indicating that improvement of the clinical manifestations resulted from improvement in the cerebral blood flow. Thorough investigations are required if cerebral ischemia is suspected in patients with Basedow's disease, beginning with meticulous MR imaging and MR angiography. Thyroid crisis may be induced if cerebral angiography is performed in a patient with

untreated Basedow's disease.¹⁵⁾ Therefore, we did not initially perform cerebral angiography in our patient.

A patient with Basedow's disease associated with cerebral arterial stenosis, as in our patient, requires that treatment for Basedow's disease or for cerebral ischemic manifestations should be prioritized. The cerebral ischemic manifestations may improve, as shown in Table 1. Therefore, conservative treatment with antithyroid medications for Basedow's disease, and antiplatelet drugs and intravenous replacement fluid for the cerebral ischemic manifestations should be the first choice of treatment unless immediate vascular reconstruction is necessary. Table 1 demonstrates that seven patients were undergone bypass surgery.^{4,9,10)} But it is difficult to say with certainty whether surgical revascularization is always necessary in such situations, as mentioned in comments of Nakamura's report.¹⁰⁾ In our patient, SPECT after the treatment for Basedow's disease showed mild reduction in the reserve capacity, and we are currently following up her condition by administering antithyroid medications and antiplatelet drugs without preventive revascularization surgery.

In the clinical cases of Basedow's disease patients, not only the ICAs, but also coronary arteries have shown the stenosis.^{2,14)} Moreover, in rare cases, an association between hyperthyroidism and coronary artery stenosis resulting in myocardial infarctions is considered.^{7,14)} The imbalance of autonomic nerve activity in hyperthyroidism is suggested to acceler-

Table 1 Summary of reported cases of Basedow's disease associated with stenosis of the cerebral arteries

Author (Year)	Age at onset of neurological symptoms/Sex	Neurological symptom before antithyroid therapy	Ischemia or hemorrhage	Improvement of neurological symptoms after antithyroid therapy
Moyamoya disease:				
Kushima et al. (1991) ⁵⁾	21/F	lt hemiparesis, speech disturbance	ischemia	+
Matsumoto et al. (1992) ⁹⁾	22/F	lt hemiplegia	ischemia	+
	35/F	difficulty of speech, slight impairment of consciousness, transcortical motor aphasia, minimal rt hemiparesis	ischemia (hemorrhagic infarction)	+ (after improvement, bypass surgery was performed for ischemia)
Liu et al. (1994) ⁶⁾	28/F	mild dysarthria, rt central facial palsy, rt hemiparesis and hemihypesthesia	ischemia	not described
Tendler et al. (1997) ¹³⁾	37/F	lt hemiparesis	ischemia	+
	38/F	dysarthria	ischemia	+
Ishikawa and Houkin (1998) ⁴⁾	28/F	lt hemiparesis, dysarthria	ischemia	not described
	33/F	not described	ischemia	not described
	5/F	not described	ischemia	not described
	38/F	not described	subarachnoid hemorrhage	not described
Stenosis of the terminal portion of the ICA:				
Wakamoto et al. (2000) ¹⁵⁾	19/F	slight impairment of consciousness, headache	intraventricular hemorrhage and ischemia	+
Nakamura et al. (2003) ¹⁰⁾	19/F	lt transient hemiparesis and hemihypesthesia	ischemia	+ (after improvement, bypass surgery was performed for ischemia)
	54/F	rt transient hemiparesis and hemihypesthesia	ischemia	not described (bypass surgery was performed for ischemia)
Present case	29/F	motor aphasia	ischemia	+

ICA: internal carotid artery.

ate the vasospasm of both ICA and coronary artery,^{15,17)} and the manifestations of the stenosis were improved by administrating of antithyroid drugs.^{7,15)} By contrast, the animal studies in the rats, concerning not with ICA, but with coronary arteries, have shown 5-hydroxytryptamine (5-HT)- and 9,11-dideoxy-11 α ,9 α -epoxymethanoprostaglandin F₂ α (U46619)-, one of thromboxane A₂ agonists, mediated contractile responses in coronary arteries proved uninfluenced by the hyperthyroid state,¹⁹⁾ even though thrombocyte-released vasoactive factors such as 5-HT and thromboxane A₂ have been proposed as the triggering stimuli for coronary spasm.⁸⁾ These results suggest angina pectoris occurring in hyperthyroidism is not accompanied by increased sensitivity to these vasoactive mediators.¹⁹⁾ This conclusion is contrary to the above-mentioned idea that the imbalance of autonomic nerve activity in hyperthyroidism may accelerate

the vasospasm. However, we can't conclude whether this is due to the different species between rats and humans or another possible mechanism exists. Further studies are necessary to conclude it.

Patients with Basedow's disease associated with stenosis of the terminal portion of ICA generally improve with treatment for Basedow's disease. However, periodical follow-up examination is necessary for patients with improved manifestations or vascular stenosis since suspected moyamoya disease may be confirmed in the future.

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