

Neurol Med Chir (Tokyo) 50, 668~674, 2010

Familial Moyamoya Disease Associated With Graves' Disease in a Mother and Daughter

—Two Case Reports—

Hiroshi TOKIMURA, Kenichiro TAJITSU*, Hiroshi TAKASHIMA**,
Takahisa HIRAYAMA*, Masahiro TSUCHIYA,
Kenji TAKAYAMA***, and Kazunori ARITA

Departments of Neurosurgery and **Neurology and Geriatrics,
Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima;
*Division of Neurosurgery, Sendai Shimin Hospital, Satsumasendai, Kagoshima;
***Sendai Neurosurgical Clinic, Satsumasendai, Kagoshima

Abstract

A mother and daughter presented with a rare combination of moyamoya disease and Graves' disease. A 19-year-old woman experienced numbness in her right hand due to cerebral infarction during therapy for Graves' disease. Cerebral angiography demonstrated stenoses of the bilateral internal carotid arteries and net-like abnormal collateral vessels indicative of moyamoya disease. Her 52-year-old mother with a history of Graves' disease presented with left hemiparesis due to intracerebral hemorrhage; she recovered after hematoma evacuation. Postoperative angiography demonstrated stenoses of the bilateral internal carotid arteries and net-like abnormal collateral vessels indicative of moyamoya disease. Another otherwise healthy daughter manifested slight stenosis of the left internal carotid artery. After cerebral revascularization surgery the patients were able to return to their normal daily lives. These familial cases of moyamoya disease and Graves' disease indicate hereditary involvement in both diseases.

Key words: moyamoya disease, hyperthyroidism, Graves' disease, cerebral infarction, genetic factor

Introduction

Moyamoya disease is characterized by progressive occlusion of the terminal portion of the internal carotid artery associated with the formation of collateral abnormal vessels at the base of the brain.⁵⁾ Although the mechanism(s) underlying the vascular changes are unknown, hereditary factors appear to be involved because 10% of Japanese

patients have a familial history of moyamoya disease.²⁸⁾ Graves' disease is an autoimmune disorder presenting as thyroid gland hyperactivity; its underlying mechanisms also remain to be elucidated. Patients with coexisting moyamoya disease and Graves' disease are rare; with only 22 cases reported to date.^{6,8,10,12-15,17,19,22,23,26-28)}

We encountered a Japanese mother and daughter with moyamoya disease associated with Graves' disease, and discuss the possible association between the two diseases.

Received December 21, 2009; Accepted February 5, 2010

Case Reports

We retrospectively reviewed data recorded in the medical charts of a Japanese mother and daughter with the rare combination of moyamoya disease and Graves' disease. Both patients had undergone cerebral revascularization surgery between May 2003 and February 2009 at Sendai Shimin Hospital. We also studied magnetic resonance (MR) angiograms of the mother's other healthy daughter.

Case 1: The affected 19-year-old daughter was admitted with exophthalmos and tachycardia to another hospital specializing in the treatment of thyroid diseases. Laboratory studies revealed thyrotoxicosis; the thyroid-stimulating hormone (TSH) receptor antibody value was 86.2%, the TSH level was 0.03 μ U/ml, the free tri-iodothyronine (FT3) level was 30.0 pg/dl, and the free thyroxine (FT4) level was 6.0 ng/dl. Immediately after thyroidectomy, she reported numbness of the right hand that remained unrelieved for 3 months and she was admitted to our hospital. Prior to this admission she had not experienced any symptoms suggestive of cerebrovascular accidents.

On admission her physical status was normal. Thyroid function studies showed slight hypothyroidism; the levels of TSH, FT3, and FT4 were 39.51 μ U/ml, 2.4 pg/dl, and 0.83 ng/dl, respectively. Other laboratory findings were normal. Neurological examination revealed dysesthesia of the 3rd-5th fingers of the right hand. MR imaging showed an infarction in the left parietal lobe (Fig. 1), and cerebral angiography demonstrated occlusion of the terminal portion of the bilateral internal carotid arteries and both middle cerebral (MCA) and anterior cerebral arteries. Net-like vessels were recognized around the circle of Willis (Fig. 2). These angiographic findings led us to diagnose stage 5 moyamoya disease,²⁵⁾ and 6 months later she underwent revascularization using a superficial temporal artery (STA) to MCA bypass on the left side. Six months after that operation a similar bypass was carried out on the right side. Postoperative MR angiography demonstrated adequate blood supply to the bilateral cerebral hemispheres via both STAs (Fig. 3). She suffered no ischemic attacks

during the immediate postoperative period and she was able to resume her normal daily life. No recurrence of cerebral ischemia has occurred in the 5 years since surgery.

Case 2: The 52-year-old mother of Case 1 had a past history of hypertension and hyperlipidemia; 18 years earlier she was diagnosed with hyperthyroidism with symptoms of tachycardia and excessive sweating. She underwent

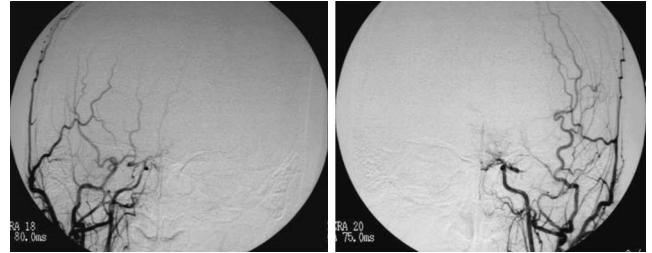


Fig. 2 Case 1. Preoperative right (left) and left (right) common carotid arteriograms, anteroposterior views, demonstrating stenosis of the terminal portion of the bilateral internal carotid arteries, occlusion of the middle and anterior cerebral arteries, and net-like abnormal collateral vessels around the circle of Willis.

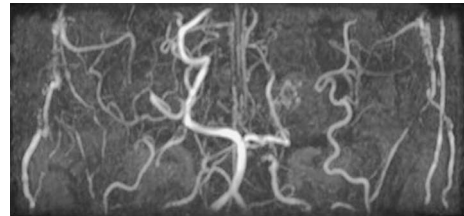


Fig. 3 Case 1. Postoperative magnetic resonance angiogram demonstrating many vessels in the area of the bilateral middle cerebral arteries through parietal branches of the superficial temporal arteries.

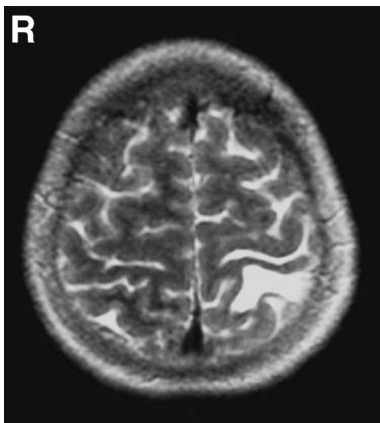


Fig. 1 Case 1. T₂-weighted magnetic resonance image demonstrating a hyperintense area in the left parietal lobe.

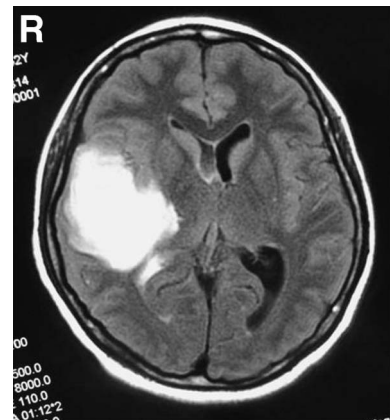


Fig. 4 Case 2. Fluid-attenuated inversion recovery magnetic resonance image demonstrating a hyperintense area in the right temporal lobe.

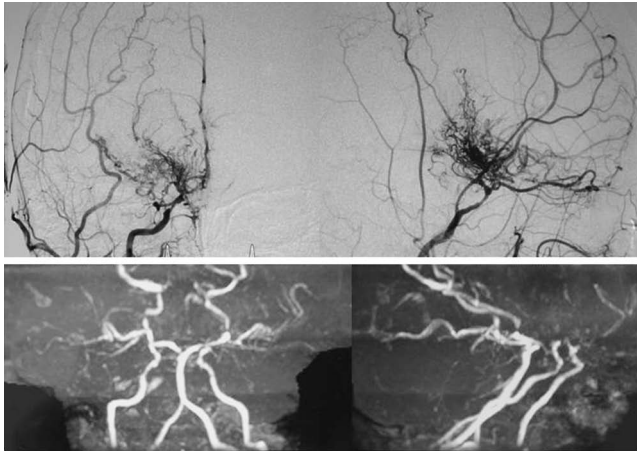


Fig. 5 Right common carotid arteriograms, anteroposterior view (upper left) and lateral view (upper right), demonstrating stenosis of the terminal portion of the internal carotid and anterior cerebral arteries, occlusion of the middle cerebral artery, and net-like abnormal collateral vessels around the circle of Willis. Magnetic resonance angiograms demonstrating these findings bilaterally (lower row).

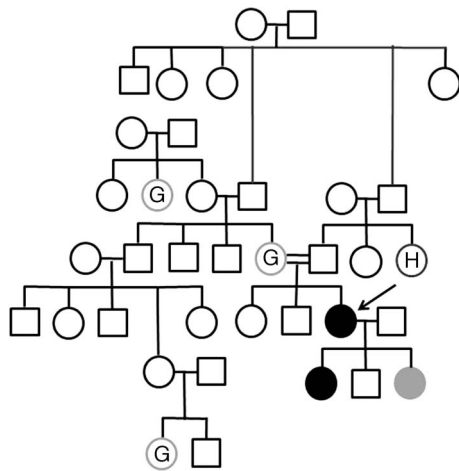


Fig. 6 Family pedigree of the patients. Circles and squares indicate female and male, respectively. The arrow indicates the proband, the 52-year-old mother (Case 2). Closed circles identify the mother (Case 2) and daughter (Case 1) who presented with combined moyamoya and Graves' diseases. "G" and "H" indicate individuals with thyroid tumor and hypothyroidism, respectively. Gray circle identifies another daughter with stenosis of the left internal carotid artery.

thyroidectomy which relieved her symptoms. She suffered sudden onset of left hemiparesis and was admitted to a local hospital in April 2008. The diagnosis was cerebral hemorrhage in the left temporal subcortical region and the hematoma was evacuated. She was subsequently admitted to our hospital for further assessment and treatment.

On admission her physical status and laboratory data were normal. Neurological examination revealed no pareses but detected left upper quadrihemianopsia. MR

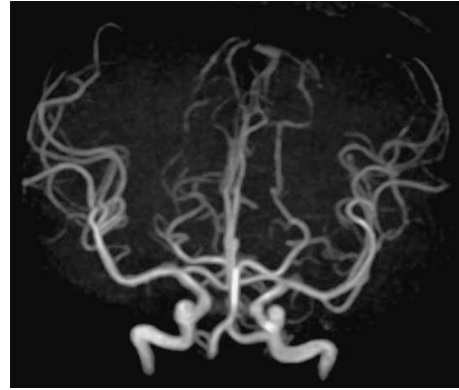


Fig. 7 Magnetic resonance angiogram of another daughter at 21 years old demonstrating slight stenosis at the siphon of the left internal carotid artery.

imaging disclosed hyperintensity in the right temporal region due to cerebral hemorrhage (Fig. 4). Bilateral carotid angiography demonstrated stenoses of the terminal portion of the internal carotid and anterior cerebral arteries, and occlusion of the MCA. Well-developed moyamoya vessels were seen at the base of the cerebrum (Fig. 5). Anomalous MR angiography findings were present bilaterally (Fig. 5). The angiographic diagnosis was stage 3 moyamoya disease.²⁵⁾ Six months after the onset of her subcortical hemorrhage she underwent STA-MCA anastomosis on the right side. She manifested no postoperative neurological deficits. After the operation she was able to return to her normal daily life. She is currently scheduled for revascularization on the left side.

The family pedigree of this patient reveals 3 women with thyroid tumors and one with hypothyroidism (Fig. 6). Her grandfathers were brothers with the same parents. She has 3 children, one son and 2 daughters. The daughter with no symptoms of moyamoya disease or Graves' disease underwent MR angiography at the age of 21 years, which revealed slight stenosis in the cavernous portion of the left internal carotid artery (Fig. 7).

Discussion

The familial occurrence renders our two patients distinct from previously reported patients with the combination of moyamoya disease and Graves' disease. Another daughter of the proband patient manifested internal carotid artery stenosis. Based on these observations, we suggest that genetic factors are important in the coexistence of moyamoya disease and Graves' disease. If a single genetic factor was involved in the present family, the inheritance pattern of Graves' disease should be autosomal dominant with incomplete penetrance. We posited that the inheritance pattern of moyamoya disease with Graves' disease may point to a mitochondrial origin; our observations suggest that like Graves' disease it is autosomal dominant with incomplete penetrance.

Some genetic factors are involved in the pathogenesis of moyamoya disease. Microsatellite linkage analyses identi-

fied at least 3 genetic loci on chromosomes 3p16 (MYMY1), 17q25 (MYMY2), and 8q23 (MYMY3). The responsible genes associated with the 3 loci remain to be identified.^{9,18,21} Although the 2 diseases present with different main symptoms, 2 genes are reported to cause moyamoya disease. Mutations in smooth muscle alpha-actin (*ACTA2*) have been reported as a causative factor in coronary artery disease, stroke, moyamoya disease, and thoracic aortic disease.⁷ The specific *ACTA2* mutation p258R>H or C is strongly associated with young age at the onset of stroke and moyamoya disease. *ACTA2* mutations increase the vascular proliferation of smooth muscle cells. However, the patients with Schimke immuno-osseous dysplasia identified by genetic study did not demonstrate any association with Graves' disease.^{2,3} Besides Graves' disease, moyamoya disease has also been documented to occur in association with other disease entities including Down syndrome, sickle cell anemia, aplastic anemia, systemic lupus erythematosus, antiphospholipid syndrome, ulcerative colitis, Apert syndrome, neurofibromatosis, and tuberous sclerosis.^{4,10}

Graves' disease is an autoimmune disorder in which TSH receptors are targeted by various auto-antibodies, resulting in the excessive production and release of thyroid hormones. The consequent hyperthyroid state leads to multi-organ physiologic disorders. Autoimmune thyroid diseases including Graves' disease and Hashimoto's thyroiditis are attributable to interactions between environmental and genetic factors. The identified susceptibility gene loci are human leucocyte antigen (HLA)-DR, a quintet of non-HLA genes that includes the cytotoxic T lymphocyte antigen (CTLA-4), CD40, protein tyrosine phosphatase-22 (PTPN22), thyroglobulin, and the TSH receptor gene. However, the gene responsible for Graves' disease remains to be identified.¹¹ A gene locus of autoimmune thyroid disease spans 8q23-q24, a site that is very close to the locus of MYMY3.²⁰ Therefore, if the disease-associated locus is single, the gene locus in our family may map to 8q23-q24. Graves' disease has also been reported to occur in association with ulcerative colitis, inflammatory bowel disease, pulmonary hypertension, aplastic anemia, primary sclerosing cholangitis, retroperitoneal fibrosis, membranous glomerulonephritis, myasthenia gravis, cerebral venous thrombosis, thyroid and breast carcinoma, and moyamoya syndrome.⁸

Most associations between Graves' disease and moyamoya disease involve immunologic factors, but our current findings suggest that moyamoya disease may have a strong genetic relationship with Graves' disease. Although moyamoya disease and Graves' disease have their origin in independent genetic or immunological factors, we posit that the presence of Graves' disease or the hyper-immune state may facilitate arterial narrowing in individuals with genetic factors involved in the manifestation of moyamoya disease. Although hereditary and immunologic factors are involved in both moyamoya disease and Graves' disease, only 22 patients with moyamoya disease and Graves' disease have been reported.^{6,8,10,12-15,17,19,22,23,26-28}

The clinical profiles of the 24 patients, including ours, are summarized in Table 1. All patients except one were

female; 22 presented with ischemic symptoms and 2 with hemorrhage. Most patients with moyamoya disease experience ischemic attacks in infancy and childhood; hemorrhages tend to be seen in older patients.¹⁶ In the subgroup of patients with moyamoya disease associated with Graves' disease, the average age of those with ischemia was 28.6 ± 11.3 (standard deviation); the 2 patients with intracranial hemorrhage were 19 and 52 years old. Computed tomography (CT) and/or MR imaging studies showed that 19 patients had cerebral infarction, 2 presented with intracerebral hemorrhage, and 2 manifested no lesions compatible with neurologic events. Angiography showed classical moyamoya vessels in 19 patients and moyamoya phenomenon, e.g., uni- or bi-lateral internal carotid artery stenosis not associated with classical moyamoya vessels, in 5. Cerebrovascular accidents occurred in 21 patients when they were thyrotoxic. Vascular events may be triggered by the hemodynamic changes that have been reported in patients with thyrotoxicosis.²⁴ The onset of moyamoya disease and Graves' disease was simultaneous in 13 patients, and 6 patients with a past history of cerebrovascular accidents manifested worsening of moyamoya disease during thyrotoxicosis. The onset of moyamoya disease occurred during diagnostic procedures, therapy, and Graves' disease recurrence in 3 patients. Only 2 patients presented with moyamoya disease long after the diagnosis of Graves' disease.

Immunological disorders and hereditary factors are thought to be involved in the development of cerebral artery stenosis in moyamoya disease; hypermetabolism due to excessively high levels of thyroid hormone may be an important promoting factor of arterial stenosis in patients with coexistent moyamoya disease and Graves' disease. Hyperplasia of the cerebral arterial wall may be attributable to the hypermetabolism-induced increase in the cerebral blood flow and to direct hormonal effects in thyrotoxicosis.²⁴ In addition, thyroid hormones are thought to increase regional sensitivity to the sympathetic nervous system; this may contribute to pathologic changes seen in the internal carotid arteries of these patients.¹³

Of the 24 documented patients, including ours, 12 received antithyroid therapy and revascularization surgery, 11 underwent medical treatment of hyperthyroidism only, and one patient received no treatment; 17 patients had a good recovery, 4 were moderately disabled, and one patient died. After treatment 19 patients experienced no recurrence of cerebrovascular events, and no outcome information was provided for the remaining patients. As the neurological condition of treated patients improved with remission of hyperthyroidism, optimal hormonal control during the perioperative period is important.^{13,27,29} Revascularization surgery was performed 1 to 4 months after the start of intensified medical treatment for Graves' disease.¹⁰ We suggest revascularization surgery after control of Graves' disease as the first line of treatment.

Among patients with moyamoya disease, the incidence of familial occurrence is 10-15%. The clinical characteristics of familial moyamoya disease include female preponderance and younger age at onset.²² The clinical characteristics of familial Graves' disease include familial occur-

Table 1 Summary of clinical findings in 24 patients with moyamoya disease associated with Graves' disease

Case No.	Author (Year)	Age (yrs)/ Sex	Symptom	Age at VA (yrs)	Age at Graves' (yrs)	CT/MR imaging findings	Angiographic findings	Thyroid condition at VA	Treatment	Outcome	Recurrence
1	Kushima et al. (1991) ⁽³⁾	26/F	ischemia	21	21	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	GR	-
2	Matsumoto et al. (1992) ⁽¹⁷⁾	22/F	ischemia	22	17	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	GR	-
3		35/F	ischemia	34	35	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & STA-MCA bypass	MD	-
4	Liu et al. (1994) ⁽⁵⁾	28/F	ischemia	28	28	infarction	moyamoya disease	thyrotoxic	-	ND	ND
5	Tandler et al. (1997) ⁽²⁶⁾	37/F	ischemia	37	37	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	GR	ND
6	Leno et al. (1998) ⁽⁴⁾	47/F	ischemia	38	47	ND	moyamoya disease	thyrotoxic	antithyroid therapy	GR	ND
7		21/M	ischemia	21	21	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	MD	-
8	Wakamoto et al. (2000) ⁽²⁹⁾	19/F	hemorrhage	19	19	hemorrhage	intracranial arterial stenosis	thyrotoxic	antithyroid therapy	GR	-
9	Kim et al. (2001) ⁽²⁾	37/F	ischemia	37	34	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	ND	ND
10	Nakamura et al. (2003) ⁽⁹⁾	23/F	ischemia	19	23	infarction	intracranial arterial stenosis	thyrotoxic	antithyroid therapy & STA-MCA bypass + EMS	GR	-
11		54/F	ischemia	54	42	infarction	intracranial arterial stenosis	normal range	antithyroid therapy & STA-MCA bypass + EMS	GR	-
12	Urku et al. (2004) ⁽²⁷⁾	45/F	ischemia	45	45	normal	intracranial arterial stenosis	normal range	antithyroid therapy	GR	-
13		22/F	ischemia	19	22	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & STA-MCA bypass + EMS	MD	-
14	Im et al. (2005) ⁽¹⁰⁾	14/F	ischemia	8	16	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & EDAS	GR	-
15		22/F	ischemia	20	22	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & STA-MCA bypass + EMS	MD	-
16	Golomb et al. (2005) ⁽⁶⁾	25/F	ischemia	25	25	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & STA-MCA bypass + EDAS	GR	-
17		10/F	ischemia	10	10	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & revascularization	GR	-
18	Hsu et al. (2006) ⁽⁸⁾	40/F	ischemia	40	40	infarction	intracranial arterial stenosis	thyrotoxic	antithyroid therapy	D	NA
19	Sasaki et al. (2006) ⁽²²⁾	27/F	ischemia	27	27	normal	moyamoya disease	thyrotoxic	antithyroid therapy & EDAS	GR	-
20		16/F	ischemia	16	16	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & EDAS	GR	-
21	Shen et al. (2006) ⁽²³⁾	36/F	ischemia	36	34	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	GR	-
22		23/F	ischemia	23	23	infarction	moyamoya disease	thyrotoxic	antithyroid therapy	GR	-
23	Present Case 1	19/F	ischemia	19	19	infarction	moyamoya disease	thyrotoxic	antithyroid therapy & STA-MCA bypass	GR	-
24	Present Case 2	52/F	hemorrhage	50	30	hemorrhage	moyamoya disease	normal range	antithyroid therapy & STA-MCA bypass	GR	-

Age at Graves': age at diagnosis of Graves' disease, age at VA: age at onset of vascular accident, CT: computed tomography, EDAS: encephalo-duro-arterio-synangiosis, EMS: encephalo-myo-synangiosis, D: dead, GR: good recovery, MD: moderately disabled, MR: magnetic resonance, NA: not applicable, ND: not described, STA-MCA: superficial temporal artery-middle cerebral artery, VA: vascular accident.

rence with incidence of 2–3%, male preponderance, younger age at onset, and autoimmune and allergic disorders in relatives. The clinical symptoms do not affect the prognosis.¹⁾ In the family reported here, the daughter was young (19 years) at the onset of both diseases, 3 relatives had a past history of Graves' disease, and one relative had hypothyroidism.

The present report includes a mother and daughter with moyamoya disease associated with Graves' disease. Another daughter manifested internal carotid artery stenosis. Further clinical and genetic studies of related patients presenting with the rare coexistence of moyamoya disease and Graves' disease are underway to discover clues for the etiology and pathophysiology of both diseases.

References

- 1) Akamizu T, Nakamura Y, Tamaoki A, Inaba Y, Amino N, Seino Y: Prevalence and clinico-epidemiology of familial Graves' disease in Japan based on nationwide epidemiologic survey in 2001. *Endocr J* 50: 429–436, 2003
- 2) Boerkoel CF, Nowaczyk MJM, Blaser SI, Meschino WS, Weksberg R: Schimke immuno-osseous dysplasia complicated by moyamoya phenomenon. *Am J Med Genet* 78: 118–122, 1998
- 3) Boerkoel CF, Takashima H, John J, Yan J, Stankiewicz P, Rosenbarker L, Andre JL, Bogdanovic R, Burguet A, Cockfield S, Cordeiro I, Frund S, Illies F, Joseph M, Kaitila I, Lama G, Loirat C, McLeod DR, Milford DV, Petty EM, Rodrigo F, Saraiva JM, Schmidt B, Smith GC, Spranger J, Stein A, Thiele H, Tizard J, Weksberg R, Lupski JR, Stockton DW: Mutant chromatin remodeling protein SMARCA1 causes Schimke immuno-osseous dysplasia. *Nature Genet* 30: 215–220, 2002
- 4) Cramer SC, Robertson RL, Dooling EC, Scott RM: Moyamoya and Down syndrome. Clinical and radiological features. *Stroke* 27: 2131–2135, 1996
- 5) Fukui M: Guidelines for the diagnosis and treatment of spontaneous occlusion of the circle of Willis ('moyamoya' disease). Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan. *Clin Neurol Neurosurg* 99 Suppl 2: S238–240, 1997
- 6) Golomb MR, Biller J, Smith JL, Edwards-Brown M, Sanchez JC, Nebesio TD, Garg BP: A 10-year-old girl with coexistent moyamoya disease and Graves' disease. *J Child Neurol* 20: 620–624, 2005
- 7) Guo DC, Papke CL, Tran-Fadulu V, Regalado ES, Avidan N, Johnson RJ, Kim DH, Pannu H, Willing MC, Sparks E, Pyeritz RE, Singh MN, Dalman RL, Grotta JC, Marian AJ, Boerwinkle EA, Frazier LQ, LeMaire SA, Coselli JS, Estrera AL, Safi HJ, Veeraraghavan S, Muzny DM, Wheeler DA, Willerson JT, Yu RK, Shete SS, Scherer SE, Raman CS, Buja LM, Milewicz DM: Mutations in smooth muscle alpha-actin (ACTA2) cause coronary artery disease, stroke, and moyamoya disease, along with thoracic aortic disease. *Am J Hum Genet* 84: 617–627, 2009
- 8) Hsu SW, Chaloupka JC, Fattal D: Rapidly progressive fatal bihemispheric infarction secondary to moyamoya syndrome in association with Graves thyrotoxicosis. *AJNR Am J Neuroradiol* 27: 643–647, 2006
- 9) Ikeda H, Sasaki T, Yoshimoto T, Fukui M, Arinami T: Mapping of familial moyamoya disease gene to chromosome 3p24.2-p26. *Am J Hum Genet* 64: 533–537, 1999
- 10) Im SH, Oh CW, Kwon OK, Kim JE, Han DH: Moyamoya disease associated with Graves disease: Special considerations regarding clinical significance and management. *J Neurosurg* 102: 1013–1017, 2005
- 11) Jacobson EM, Tomer Y: The genetic basis of thyroid autoimmunity. *Thyroid* 17: 949–961, 2007
- 12) Kim JY, Kim BS, Kang KJ: Dilated cardiomyopathy in thyrotoxicosis and moyamoya disease. *Int J Cardiol* 80: 101–103, 2001
- 13) Kushima K, Satoh Y, Ban Y, Taniyama M, Ito K, Sugita K: Graves' thyrotoxicosis and moyamoya disease. *Can J Neurol Sci* 18: 140–142, 1991
- 14) Leno C, Mateo I, Cid C, Berciano J, Sedano C: Autoimmunity in Down's syndrome: Another possible mechanism of moyamoya disease. *Stroke* 29: 868–869, 1998
- 15) Liu JS, Juo SH, Chen WH, Chang YY, Chen SS: A case of Graves' diseases associated with intracranial moyamoya vessels and tubular stenosis of extracranial internal carotid arteries. *J Formos Med Assoc* 93: 806–809, 1994
- 16) Maki Y, Enomoto T: Moyamoya disease. *Childs Nerv Syst* 4: 203–212, 1988
- 17) Matsumoto K, Nogaki H, Yamamoto K, Sasabe F, Morimatsu M: [A case of moyamoya disease complicated with Basedow disease]. *No Socchu* 14: 409–413, 1992 (Japanese)
- 18) Mineharu Y, Liu W, Inoue K, Matsuura N, Inoue S, Takenaka K, Ikeda H, Houkin K, Takagi Y, Kikuta K, Nozaki K, Hashimoto N, Koizumi A: Autosomal dominant moyamoya disease maps to chromosome 17q25.3. *Neurology* 70: 2357–2363, 2008
- 19) Nakamura K, Yanaka K, Ihara S, Nose T: Multiple intracranial arterial stenoses around the circle of Willis in association with Graves' disease: Report of two cases. *Neurosurgery* 53: 1210–1214, 2003
- 20) Sakai K, Shirasawa S, Ishikawa N, Ito K, Tamai H, Kuma K, Akamizu T, Tanimura M, Furugaki K, Yamamoto K, Sasazuki T: Identification of susceptibility loci for autoimmune thyroid disease to 5q31-q33 and Hashimoto's thyroiditis to 8q23-q24 by multipoint affected sib-pair linkage analysis in Japanese. *Hum Mol Genet* 10: 1379–1386, 2001
- 21) Sakurai K, Horiuchi Y, Ikeda H, Ikezaki K, Yoshimoto T, Fukui M, Arinami T: A novel susceptibility locus for moyamoya disease on chromosome 8q23. *J Hum Genet* 49: 278–281, 2004
- 22) Sasaki T, Nogawa S, Amano T: Co-morbidity of moyamoya disease with Graves' disease. Report of three cases and a review of the literature. *Intern Med* 45: 649–653, 2006
- 23) Shen AL, Shan-Jin R, Shinn-Kuang L: Concurrent moyamoya disease and Graves' thyrotoxicosis: Case report and literature review. *Acta Neurol Taiwan* 15: 114–119, 2006
- 24) Sokoloff L, Wechsler RL, Mangold R, Balls K, Kety SS: Cerebral blood flow and oxygen consumption in hyperthyroidism before and after treatment. *J Clin Invest* 32: 202–208, 1953
- 25) Suzuki J, Takaku A: Cerebrovascular "Moyamoya" disease showing abnormal net-like vessels in base of brain. *Arch Neurol* 20: 288–299, 1969
- 26) Tandler BE, Shoukri K, Malchoff C, MacGillivray D, Duckrow R, Talmadge T, Ramsby G: Concurrence of Graves' disease and dysplastic cerebral blood vessels of the moyamoya variety. *Thyroid* 7: 625–629, 1997
- 27) Utku U, Asil T, Celik Y, Tucer D: Reversible MR angiographic findings in a patient with autoimmune Graves disease. *AJNR Am J Neuroradiol* 25: 1541–1543, 2004
- 28) Wakai K, Tamakoshi A, Ikezaki K, Fukui M, Kawamura T,

- Aoki R, Kojima M, Lin Y, Ohno Y: Epidemiological features of moyamoya disease in Japan: Findings from a nationwide survey. *Clin Neurol Neurosurg* 99 Suppl 2: S1-5, 1997
- 29) Wakamoto H, Ishiyama N, Miyazaki H, Shinoda A, Tomita H: [The stenoses at the terminal portion of the internal carotid artery improved after initiation of antithyroid therapy: A case report]. *No Shinkei Geka* 28: 379-383, 2000 (Japanese)

Address reprint requests to: Hiroshi Tokimura, M.D., Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima, Kagoshima 890-8520, Japan.
e-mail: hiroshitok@nag.bbiq.jp