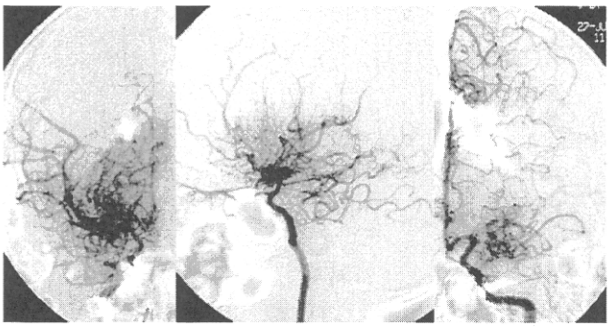

Fig. 4 Preoperative digital subtraction angiograms demonstrating steno-occlusive changes at the terminal portions of the bilateral internal carotid arteries as well as marked development of an abnormal vascular network at the base of the brain, which satisfied the diagnostic criteria of moyamoya disease.

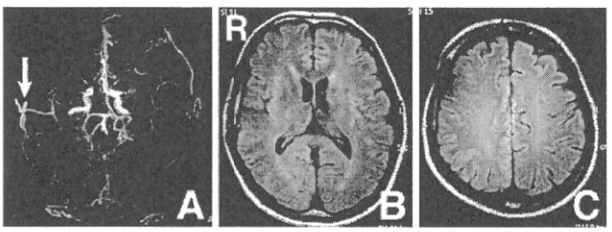

Fig. 5 Postoperative magnetic resonance (MR) angiogram (A) and fluid-attenuated inversion recovery MR images (B, C) 3 months after revascularization surgery demonstrating that the right superficial temporal artery-middle cerebral artery (MCA) bypass and the branches of right MCA were well visualized (arrow), and that ivy sign in the right hemisphere had disappeared.

temporal lobe. The temporary occlusion time was 25 minutes. EDMS and dural pedicle insertion were then performed. The patency of the STA-MCA bypass was confirmed by near-infrared indocyanine green videoangiography during surgery, and postoperative ^{123}I-IMP SPECT showed increased CBF on the operated hemisphere (data not shown). Blood pressure was strictly controlled under 140 mmHg until 48 hours after surgery to avoid symptomatic cerebral hyperperfusion. No antiplatelet agent was given postoperatively except for ibudilast. The patient did not suffer neurological deterioration due to TIA or cerebral hyperperfusion.

Postoperative MR angiography showed the apparently patent STA-MCA bypass as a thick highly dense vessel, and diffusion-weighted MR imaging showed no evidence of ischemic change. TIA completely disappeared postoperatively, and he was discharged without neurological deficit 12 days after surgery. Postoperative MR imaging and MR angiography 3 months after revascularization surgery demonstrated that the right STA-MCA bypass and the branches of right MCA were well visualized, and that the ivy sign in the right hemisphere had disappeared (Fig. 5) compared to the preoperative findings (Figs. 1B, C and 3A). He did not suffer further neurological events during the follow-up period of 2 years.

Discussion

The present extremely rare case of asymptomatic moyamoya disease subsequently manifested as TIAs, SAH, and ICH in a short period. The clinical course and neuroimaging findings suggested that the second TIA and SAH occurred simultaneously, and acute asymptomatic thalamic hemorrhage was also evident in the contralateral hemisphere that was probably formed within 3 weeks prior to the attack. Asymptomatic moyamoya disease carries a 3.2% annual risk for any stroke, including TIA, cerebral infarction, and intracranial hemorrhage.[6] Asymptomatic moyamoya disease was reported to carry relatively low risk for cerebrovascular events,[6,9,11] but our case manifested with dynamic changes in a short period.

The exact mechanism resulting in the various types of strokes in the present case at the same time is totally undetermined. The presence of hypertension may have contributed, at least in part, to the atherosclerotic changes in addition to the moyamoya disease, thus causing hemodynamic compromise associated with hemodynamic stress in the collateral vessels and abnormal vascular networks. Certain changes in the serum level of inflammatory molecules such as matrix metalloproteinases, implicated in the pathophysiology of moyamoya disease,[3] may also have participated in the simultaneous occurrence of TIA, SAH, and ICH. We also cannot completely rule out the possibility that the use of ibudilast, a non-selective phosphodiesterase inhibitor, may facilitate the occurrence of hemorrhage due to its actions of vasodilation and inhibition of platelet aggregation.

Surgical revascularization for ischemic-onset moyamoya disease is believed to prevent cerebral ischemic attack by improving CBF,[1,2,4,6,7] whereas revascularization surgery to prevent re-bleeding in hemorrhagic-onset patients is still controversial.[8] Direct revascularization surgery is reported to reduce moyamoya vessels and peripheral aneurysms,[4,7] suggesting the potential for improving hemodynamic stress in the collateral vessels with consequent reduced risk for re-bleeding. On the other hand, the risk for re-bleeding is not different between the surgically-treated and conservatively-treated groups.[12] To clarify this issue, a randomized controlled clinical trial for adult-onset hemorrhagic moyamoya disease is currently being undertaken to evaluate the effect of STA-MCA anastomosis for hemorrhagic-onset moyamoya disease in adults.[8]

The present case manifested as both hemorrhage and repeated TIAs due to the severe hemodynamic compromise in the right hemisphere, so we performed STA-MCA anastomosis with indirect pial synangiosis which resulted in favorable outcome. Early improvement of CBF in the affected hemisphere relieved his symptoms, and he has not experienced any cerebrovascular event since surgery. Based on these observations, early revascularization surgery can be recommended even for hemorrhagic-onset patients as long as ischemic symptoms and hemodynamic compromise are also evident. In fact, the final outcome of

revascularization surgery for hemorrhagic-onset moyamoya disease patients with ischemic symptoms was favorable in our series, despite the higher risk for postoperative transient cerebral hyperperfusion, as shown by our most recent report.[2)]

In conclusion, asymptomatic moyamoya disease may manifest with a dynamic course, so careful follow up is necessary. Simultaneous manifestation of ischemic attack, SAH, and ICH in a short period in our case may indicate the involvement of a specific biological background which could facilitate the occurrence of various types of cerebrovascular event in this rare entity.

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Address reprint requests to: Miki Fujimura, M.D., Department of Neurosurgery, Kohnan Hospital, 4-20-1 Nagamachi-minami, Taihaku-ku, Sendai 982-8523, Japan.
e-mail: fujimur@kohnan-sendai.or.jp

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Postoperative neurological deterioration in pediatric moyamoya disease: watershed shift and hyperperfusion

Clinical article

Toshiaki Hayashi, M.D., Ph.D.,[1] Reizo Shirane, M.D., Ph.D.,[1] Miki Fujimura, M.D., Ph.D.,[2] and Teiji Tominaga, M.D., Ph.D.[2]

Departments of Neurosurgery, [1]Miyagi Children's Hospital, and [2]Tohoku University Graduate School of Medicine, Sendai, Japan

Object. Young patients with moyamoya disease frequently exhibit extensive cerebral infarction at the time of initial presentation, and even in the early postoperative period. To investigate clinical characteristics in the early postoperative period, the authors prospectively analyzed findings of MR imaging, MR angiography, and SPECT before and after surgery. The authors focused in particular on how postoperative neurological deterioration occurred.

Methods. Between August 2005 and June 2009, 22 patients younger than 18 years of age with moyamoya disease were treated at Miyagi Children's Hospital. The mean patient age (± SD) was 8.58 ± 4.55 years (range 2–17 years). Superficial temporal artery–middle cerebral artery bypass and indirect bypass of encephalosynangiosis between the brain surface and the temporal muscle, galea, and dura mater were performed in 35 hemispheres. Magnetic resonance imaging and MR angiography were performed before surgery, at 7 days postoperatively, and 3–6 months after surgery. A ^{123}I-isopropyl iodoamphetamine SPECT scan was also obtained pre- and postoperatively.

Results. During the postoperative period, neurological deterioration was observed after 15 operations (10 cases of motor paresis, 1 of aphasia, and 4 of sensory disturbance) in 13 patients. All symptoms had resolved by the time of discharge, except in 2 patients who suffered cerebral infarction. All patients exhibited disappearance (94.3%) or reduction (5.7%) of transient ischemic attacks (TIAs) during the follow-up period. Perioperative studies revealed 2 different types of radiological findings, focal uptake decrease on SPECT indicative of cerebral ischemia due to dynamic change in cerebral hemodynamics caused by bypass flow, the so-called watershed shift, and perioperative edematous lesions on MR imaging due to cerebral hyperperfusion. The frequent occurrence of preoperative TIAs was significantly associated with watershed shift, whereas preoperative MR imaging findings and preoperative SPECT findings were not. Age at operation was the only factor significantly associated with postoperative hyperperfusion.

Conclusions. In young patients, moyamoya disease exhibits rapid progression, resulting in poor clinical outcome. The risk of postoperative neurological deterioration in very young moyamoya patients with frequent TIAs should be noted. The findings in this study showed that direct bypass is not completely safe in patients with moyamoya disease because it causes dynamic change in postoperative cerebral hemodynamics. *(DOI: 10.3171/2010.4.PEDS09478)*

Key Words • **bypass surgery** • **hyperperfusion** • **moyamoya disease** • **watershed shift**

Moyamoya disease is characterized by progressive arterial stenosis or occlusion of the intracranial ICAs and the development of extensive collateral vessels (moyamoya vessels).[20,21] It is a cause of stroke and TIA in both pediatric and adult patients. Surgery to revascularize the ischemic brain is a frequently recommended treatment option in this patient population. Both direct revascularization through STA–MCA bypass and various indirect methods have been performed, with varying success.[1,2,8,13,17,19–22] Surgical treatment of young children, however, is an issue of some concern. Young patients, and particularly young children, frequently exhibit extensive cerebral infarction at the time of initial presentation and even in the early postoperative period, despite the marked advances in recent surgical and perioperative treatment.[4,11,12,18,23] The longitudinal changes

Abbreviations used in this paper: ACA = anterior cerebral artery; ICA = internal carotid artery; IMP = isopropyl iodoamphetamine; MCA = middle cerebral artery; PCA = posterior cerebral artery; STA = superficial temporal artery; TIA = transient ischemic attack.

This article contains some figures that are displayed in color online but in black and white in the print edition.

that take place in cerebral hemodynamics after surgery have not been fully elucidated.[9] To investigate clinical characteristics in the early postoperative period, we prospectively analyzed the findings of MR imaging, MR angiography, and SPECT before and after surgery, and focused on how postoperative deterioration occurred.

Methods

Patient Population

Between August 2005 and June 2009, 22 patients younger than 18 years of age (8 boys and 14 girls) with moyamoya disease were treated at Miyagi Children's Hospital (Table 1). The mean patient age (± SD) was 8.58 ± 4.55 years (range 2–17 years). All patients satisfied the diagnostic criteria of the Research Committee on Spontaneous Occlusion of the Circle of Willis of the Ministry of Health, Labor, and Welfare of Japan. Among 22 consecutive patients, the onset of symptoms was ischemic in 16 and marked by seizures in 6. Two patients had neurological symptoms (mild hemiparesis) at the time of admission. All patients underwent combined direct and indirect bypass. In total, 35 sides were treated. Of the 35 hemispheres, frequent preoperative TIA (more than 2 episodes during the preceding month) and/or preoperative cerebral infarction during the month preceding surgery was seen in 11 hemispheres.

Surgical Procedure

The majority of the patients were treated by the same surgeon (T.H.). The details of the surgical technique used in these patients are described elsewhere.[5,19] Briefly, both direct STA–MCA bypass and indirect bypass of encephalosynangiosis between the brain surface and the temporal muscle, galea, and dura mater were performed mainly toward the frontotemporoparietal region. The initial surgery in each patient was performed in the dominant hemisphere, as determined by the clinical symptoms and findings of SPECT. If dominance was unclear, the left side of the brain usually was selected for the first surgery. The second surgery, for the contralateral side, was usually performed 3 months after the initial surgery. If the patients were young (3 years of age or less) and suffered cerebral infarction, the surgery was performed as soon as possible to prevent additional infarction.

All patients were registered for this study based on clinical manifestations, MR imaging and MR angiography findings, and results of SPECT studies. The MR imaging and MR angiography studies were performed before surgery, at 7 days postoperatively, and 3–6 months after surgery. Cerebral perfusion was measured for all patients with ^{123}I-IMP SPECT pre- and postoperatively. A postoperative SPECT study was performed at 3 or 4 days after surgery to assess early postoperative changes, and again 3–6 months after surgery to assess the effectiveness of the operation. Cerebral vasodilatory capacity was also assessed after an intravenous injection of acetazolamide (20 mg/kg; maximum dose 1 g) preoperatively and 3–6 months after surgery, unless a severe decrease in uptake was observed in resting SPECT studies.

TABLE 1: Summary of findings in 35 surgically treated hemispheres in 22 pediatric patients with moyamoya disease*

Variable	No. of Hemispherest
sex	
M	12 (8)
F	23 (14)
onset	
ischemia	24 (16)
seizure	11 (6)
preop condition	
neurological symptoms	
yes	3 (3)
no	32 (19)
frequent TIA/INF	
yes	11 (8)
no	24 (14)
preop MRI findings	
cerebral lesion	
yes	13 (9)
no	22 (13)
INF	12 (8)
ICH	1 (1)
MMVs	
minimal	13
marked	22
ACA depiction	
good	17
poor	18
MCA depiction	
good	16
poor	19
A_1	
occlusion	28
stenosis	7
M_1	
occlusion	31
stenosis	4
PCA lesion	
yes	6
no	29
periop neurological symptoms	
yes	15 (13)
no	20 (9)
periop MRI findings	
INF	
yes	2 (2)
no	33 (20)
edematous lesion	
yes	7 (5)
no	28 (17)

(continued)

TABLE 1: Summary of findings in 35 surgically treated hemispheres in 22 pediatric patients with moyamoya disease* *(continued)*

Variable	No. of Hemispheres†
condition at FU	
neurological worsening	
yes	2 (2)
no	33 (20)
TIA	
no	33 (20)
decreased	2 (2)
seizure	
no	35 (22)
yes	0
new lesion on FU MRI	
no	33 (20)
yes	2 (2)

* FU = follow-up; ICH = intracerebral hemorrhage; INF = infarction; MMV = moyamoya vessel.
† Numbers in parentheses represent the number of patients.

Findings on MR Angiography

The findings evaluated on preoperative MR angiography of the treated hemisphere included extent of moyamoya vessels and involvement of the MCA, ACA, and PCA. The extent of moyamoya vessels was classified as absent, minimal, or marked. The MCA and ACA involvement was classified as normal, stenosis, or occlusion. The depiction of peripheral vessels of the ACA and MCA was also classified as good or poor.

Findings on SPECT Images

The cerebellum was considered as the reference region for visual inspection of basal and acetazolamide stress brain perfusion SPECT images. The SPECT images were assessed as exhibiting either "preserved" or "decreased" regional cerebral blood flow. Decreased cerebrovascular reserve was defined as cerebral perfusion on acetazolamide stress SPECT that fell into a lower color range than that in basal SPECT over at least one-third of any brain lobe. Postoperative SPECT studies were compared with preoperative basal SPECT to assess early postoperative changes (3 or 4 days after surgery) and the effectiveness of surgery (3–6 months after surgery).

Statistical Analysis

Ordinal logistic regression was used for the analysis of a total of 35 hemispheres, with SPSS version 16.0 J for Windows. For all tests, findings of $p < 0.05$ were considered significant.

Results

Table 1 presents a summary of neurological condition and MR imaging and SPECT findings for all patients. Preoperative cerebral lesions were seen in 13 hemispheres (cerebral infarction in 12 and an old intracranial hemorrhage in 1). All of the hemispheres exhibited moyamoya vessels on MR angiography (minimal in 13, marked in 22). The majority of hemispheres exhibited occlusion of the proximal portions of both A_1 and M_1. Stenosis of the PCA was seen in 6 hemispheres. Preoperative SPECT studies revealed decreased cerebral perfusion in 25 hemispheres (Table 2). All 35 hemispheres exhibited decreased cerebrovascular reserve.

During the postoperative period, neurological deterioration was observed following 15 operations (9 cases of motor paresis, 1 of aphasia, 4 of sensory disturbance, and 1 of motor paresis and aphasia) in 13 patients (Table 3). All symptoms resolved by the time of discharge, except in 2 patients who suffered cerebral infarction and exhibited mild left hemiparesis and motor aphasia. Postoperative SPECT studies performed 3 or 4 days after surgery (perioperative SPECT) revealed an increase in uptake in 15 of 25 hemispheres that exhibited decreased cerebral perfusion on preoperative SPECT, whereas 7 of 10 hemispheres with preserved cerebral perfusion preoperatively exhibited no apparent changes (Fig. 1). High uptake was clearly observed in 1 patient. On the other hand, although some increase in uptake was seen around the site of anastomosis, a focal decrease in uptake away from the site of anastomosis was seen in 12 hemispheres (Fig. 2). Of the 12 hemispheres that exhibited a decrease in uptake, 2 had defects in uptake that were subsequently found to represent cerebral infarction on MR imaging studies (Fig. 3).

The onsets of symptoms indicative of infarction were 6 hours and 2 days after surgery, respectively. The 2 patients involved were each 3 years of age. Postoperative MR imaging studies performed 7 days after surgery revealed 9 additional lesions compared with the preoperative studies. Two were cerebral infarctions, whereas 7 were focal lesions located adjacent to the site of anastomosis that did not exhibit high signal intensity on diffusion weighted images, but did so on T2-weighted and FLAIR images due to the brain edema caused by cerebral hyperperfusion (Fig. 4). All patients but 1 showed the high uptake adjacent to the lesion on SPECT images. All of the edematous lesions resolved during the follow-up period without any significant findings on MR imaging studies. Follow-up MR imaging studies revealed no significant additional lesion, except in 2 patients with cere-

TABLE 2: Summary of SPECT findings in 35 hemispheres in 22 patients with moyamoya disease

SPECT Findings	Cerebral Perfusion	
	Preserved	Decreased
preop	10	25
periop changes		
increased uptake	1	15
decreased uptake	2	10
no change	7	0
FU		
preserved perfusion	10	23
decreased perfusion	0	2

TABLE 3: Characteristics of 13 patients with moyamoya disease and postoperative ischemic symptoms*

Case No.	Age (yrs)	Symptom	WS	HP	Recent TIA	Preop INF	Area of Decreased Uptake	
							On Preop rSPECT	On Preop sSPECT
1	3	LE paresis	no	no	no	yes	ACA–MCA	
	3	hemiparesis	yes (INF)	no	yes	yes	MCA–PCA	
2	3	aphasia	yes (INF)	no	yes	yes	MCA–PCA	
3	5	sensory	no	no	no	yes	hemisphere	
4	7	hemiparesis	no	no	yes	yes	hemisphere	
	8	hemiparesis	yes	no	yes	no	ACA–MCA	
5	9	hemiparesis	yes	no	yes	no	MCA–PCA	
6	10	UE paresis	no	yes	yes	no	ACA–MCA	
7	10	sensory	no	no	no	no	NS	ACA–MCA
8	12	sensory	yes	no	no	no	MCA	
9	13	sensory	no	no	no	no	MCA	
10	14	hemiparesis	no	yes	no	no	MCA	
11	14	hemiparesis	no	yes	no	yes	MCA–PCA	
12	15	hemiparesis	no	yes	no	no	NS	ACA–MCA
13	17	hemiparesis, aphasia	no	no	no	no	NS	ACA–MCA

* HP = hyperperfusion; LE = lower extremity; NS = not significant; rSPECT = rest SPECT; sensory = sensory disturbance; sSPECT = acetazolamide stress SPECT; UE = upper extremity; WS = watershed shift.

bral infarction on postoperative MR imaging. The MR angiography findings revealed significant development of indirect pial synangiosis as well as patent STA–MCA bypasses in all hemispheres. Follow-up SPECT studies demonstrated improvement of both cerebral perfusion and cerebrovascular reserve in all hemispheres but 2 that exhibited additional cerebral infarction on MR imaging studies. Even the hemispheres with postoperative cerebral infarction exhibited improvement of cerebrovascular reserve, except in the infarcted regions.

Of 22 consecutive patients with 35 surgeries, all exhibited disappearance (33 hemispheres, 94.3%) or reduction (2 hemispheres, 5.7%) of TIAs during the follow-up period (3–6 months after surgery).

Risk Factors for Perioperative Deterioration

Perioperative neurological deterioration (that is, occurring within 2 weeks of surgery) was detected in 15 hemispheres in 13 patients (Table 3). All symptoms were resolved by the time of discharge, except those in 2 pa-

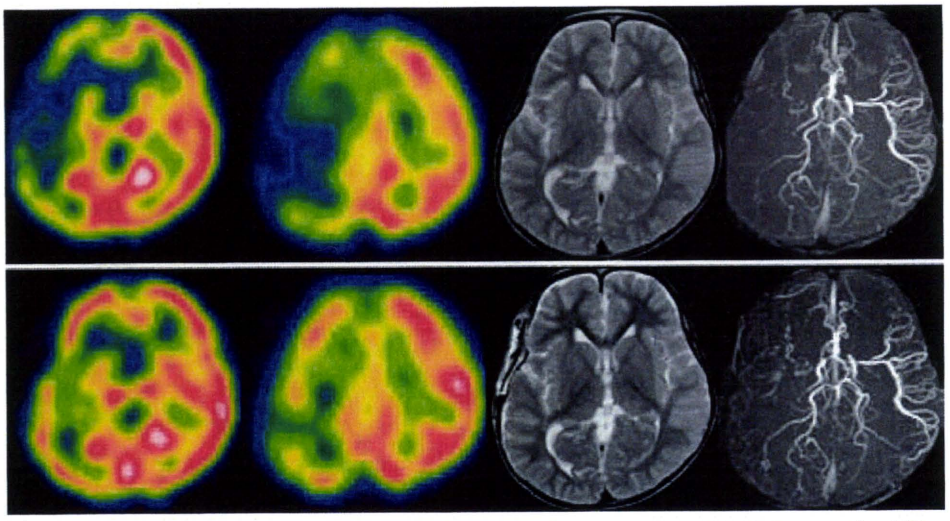

Fig. 1. Preoperative **(upper)** and postoperative **(lower)** images obtained in a 3-year-old girl. Preoperative MR angiography study showed minimal moyamoya vessels with poor depiction of the MCA in the right hemisphere. Postoperative SPECT study obtained 3 days after surgery revealed improvement of right cortical uptake. On postoperative T2-weighted MR imaging and MR angiography studies obtained 1 week after surgery, the right STA–MCA bypass and the branch of the right MCA were well visualized, and no significant postoperative lesion was seen.

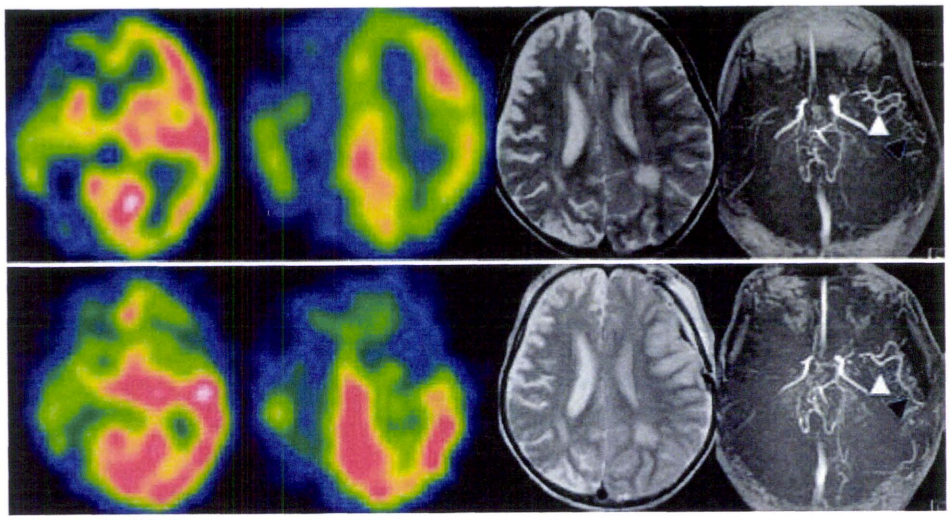

FIG. 2. Preoperative **(upper)** and postoperative **(lower)** images obtained in a 3-year-old girl, demonstrating watershed shift. Preoperative MR imaging revealed cerebral infarction in the right hemisphere. Preoperative MR angiography revealed marked moyamoya vessels, with good depiction of the MCA in the left hemisphere. Postoperative SPECT study obtained 3 days after left direct and indirect bypass was performed revealed improvement of left occipitotemporal uptake, with focal hyperperfusion and marked decrease in uptake in the left frontal region. On postoperative T2-weighted MR imaging obtained 1 week after surgery, an ischemic change is noted in the left frontal subcortical area. Postoperative MR angiography revealed increased signal intensity in the lower branch of the left MCA *(black arrowheads)* and decreased signal intensity in the upper branch of the left MCA *(white arrowheads)*.

tients found to have cerebral infarction on MR imaging studies. Perioperative studies revealed 2 different types of radiological findings: perioperative focal uptake decrease on SPECT study, indicative of cerebral ischemia (5 patients), and perioperative edematous lesions on MR imaging study (4 patients). On ordinal logistic regression analysis, frequent preoperative TIA and/or preoperative cerebral infarction during the month preceding surgery was significantly associated with a focal decrease in uptake on perioperative SPECT studies, whereas preop-

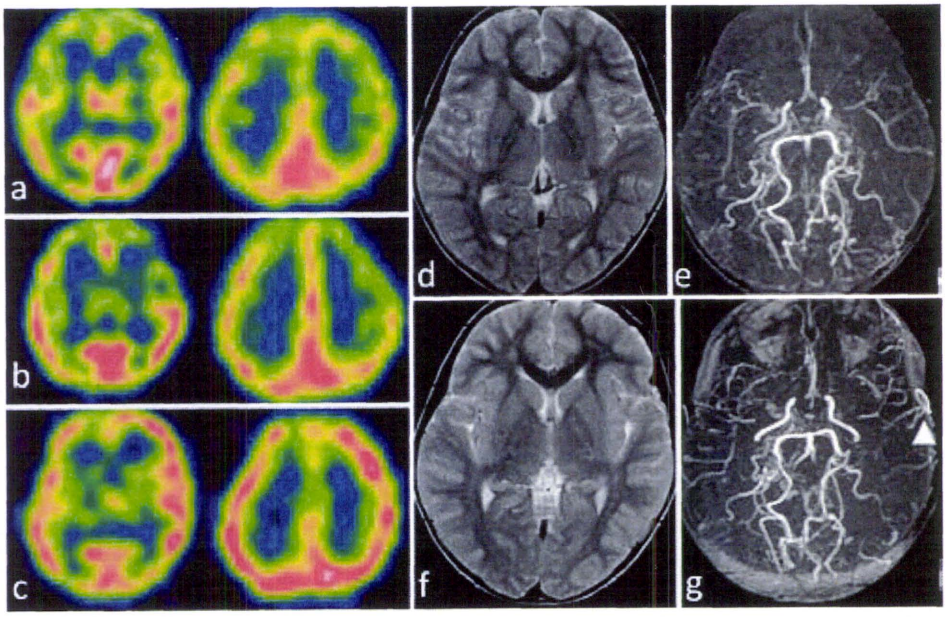

FIG. 3. Preoperative and postoperative findings in a 5-year-old girl. Preoperative MR angiography revealed marked moyamoya vessels with poor depiction of the MCA in the left hemisphere **(e)**. Preoperative SPECT study revealed a mild decrease in uptake bilaterally in the frontal area **(a)**. Postoperative SPECT performed 3 days after left direct and indirect bypass revealed a decrease in uptake in the left frontal region **(b)**. Follow-up SPECT study performed 3 months after surgery revealed marked improvement of left cortical uptake **(c)**. Follow-up MR imaging **(f)** performed 3 months after surgery revealed no significant lesion other than the preoperative one **(d)**. Signal intensity of the left STA–MCA bypass *(white arrowhead)* and depiction of the left MCA were more prominent on follow-up MR angiography **(g)** than on preoperative MR angiography **(e)**. Decreased depiction of moyamoya vessels was also noted.

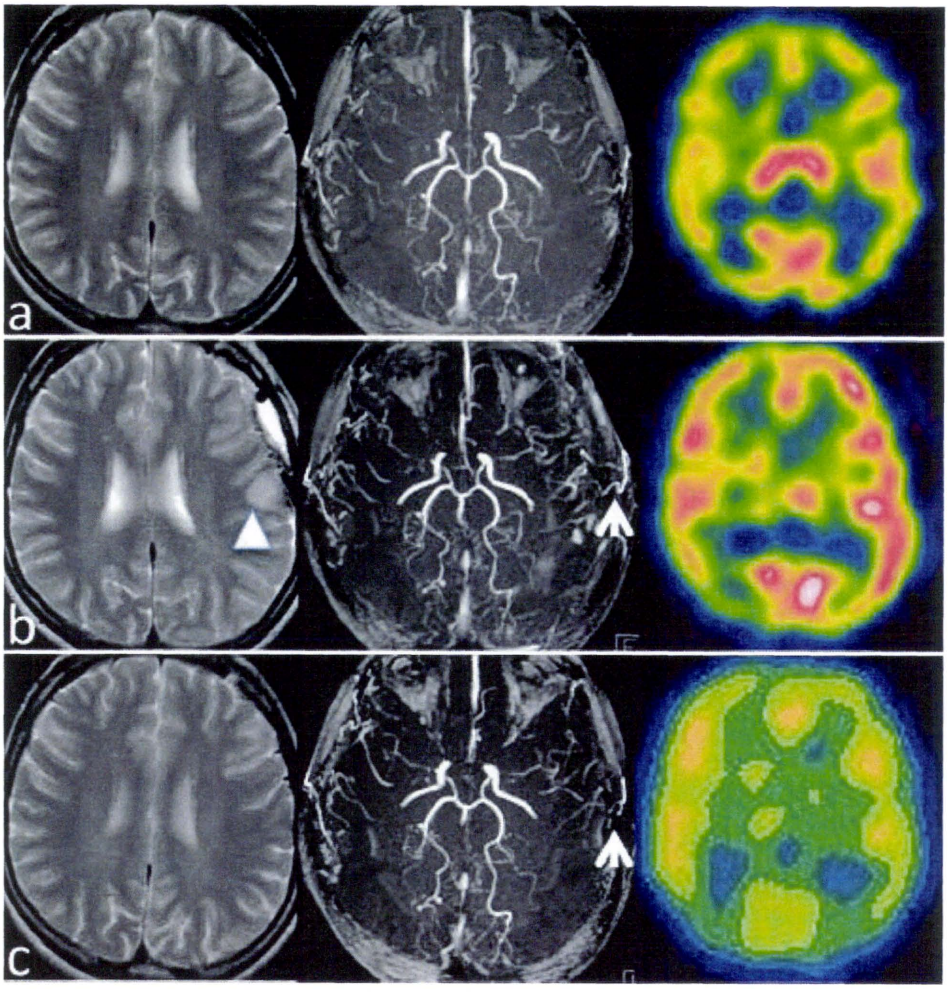

Fig. 4. Preoperative **(a)**, perioperative **(b)**, and follow-up **(c)** images obtained in a 17-year-old girl who had previously undergone bypass surgery in the right hemisphere and who this time underwent left direct and indirect bypass. Preoperative T2-weighted MR imaging revealed no significant cerebral lesion **(a)**. Preoperative MR angiography revealed minimal moyamoya vessels, with poor depiction of the MCA in the left hemisphere. Postoperative T2-weighted MR imaging performed 7 days after surgery revealed a hyperintense area in the left parietal region *(arrowhead;* **b**). An MR angiography study disclosed an apparently patent STA–MCA bypass *(arrow)* with increased intensity in the left MCA. A SPECT study performed 3 days after surgery revealed improvement of uptake in the left hemisphere, with an area of focal hyperperfusion in the left parietal region corresponding to the hyperintense area. Follow-up studies performed 3 months after surgery revealed disappearance of the hyperintense area and focal hyperperfusion **(c)**. Signal intensity of the STA–MCA bypass *(arrow)* was less prominent than in the acute postoperative period.

erative MR imaging findings and preoperative SPECT findings were not (Table 4). On the other hand, age at operation was the only factor significantly associated with postoperative edematous lesions (Table 5).

Discussion

In young patients, moyamoya disease exhibits rapid progression, resulting in poor clinical outcome. Several reports have shown that subsequent preoperative infarction occurred significantly more often in the younger patient group.[4,12,16,18,23] These findings indicate the need for early surgery in young patients with moyamoya disease.

On the other hand, despite the marked advances in recent surgical and perioperative treatment,[10] young patients sometimes suffer cerebral infarction in the early postoperative period. In our series, postoperative transient neurological symptoms were observed during the perioperative period in 15 (42.9%) of 35 surgeries, and 2 patients (5.7% of 35 hemispheres, 9.1% of 22 patients) exhibited postoperative cerebral infarction. Taki et al.[23] also reported that postoperative neurological deficits were observed during the acute stage after surgery in 16 (59.3%) of 27 pediatric patients who underwent both direct and indirect bypass, whereas postoperative infarction was seen in one of 27 hemispheres. Kim et al.[12] found that the rate of surgery-related infarction was 28 (13.7%) of 204 in pediatric moyamoya patients who underwent indirect bypass, whereas Scott et al.[18] found that it was 11 (4%) of 271. It is interesting that the rate of postoperative stroke differs between Asian and American series. It seems that the patients in Asian countries showed a more aggressive clinical course.

TABLE 4: Characteristics of hemispheres with uptake decrease on perioperative SPECT

Characteristic	Periop Uptake Decrease		p Value
	+ (12 sides)	– (23 sides)	
mean age in yrs	6.98 ± 4.13	9.44 ± 4.42	0.638
ischemic onset	8	15	0.857
preop INF	4	8	0.061
marked MMVs	11	11	0.100
A_1 occlusion	11	17	0.907
M_1 occlusion	13	18	0.745
poor ACA depiction	6	12	0.161
poor MCA depiction	6	13	0.447
PCA lesion	2	4	0.113
basal SPECT decrease	12	13	0.269
recent TIA/INF	7	4	0.018*

* Statistically significant.

The mechanism of postoperative deterioration in these patients has remained undetermined due to the lack of postoperative cerebral blood flow analysis and also the absence of MR studies during the acute stage after direct and indirect bypass. Cerebral hyperperfusion or cerebral ischemia after surgery has been reported to be a cause of transient neurological deterioration.[3,6,7,14,15,23] To address this issue, we prospectively performed ^{123}I-IMP SPECT scanning within 4 days of surgery, and MR imaging studies 1 week after surgery in 35 treated hemispheres in patients with childhood moyamoya disease. Our findings suggested that 2 different mechanisms might have contributed to neurological deterioration in the early postoperative period. One is focal decrease in cerebral perfusion remote from the site of anastomosis detected on perioperative SPECT studies, whereas the other is edematous lesions at the site of anastomosis detected on MR imaging studies (Fig. 5). Although underlying ischemia due to a preoperative condition could have contributed to the postoperative ischemic symptoms,

TABLE 5: Characteristics of hemispheres with edematous lesion on perioperative MRI

Characteristic	Periop Edematous Lesion		p Value
	+ (7 sides)	– (28 sides)	
mean age in yrs	13.91 ± 2.68	7.27 ± 3.81	0.008*
ischemic onset	5	18	0.960
preop INF	1	11	0.846
marked MMVs	5	17	0.796
A_1 occlusion	5	23	0.585
M_1 occlusion	6	25	0.776
poor ACA depiction	3	15	0.739
poor MCA depiction	3	16	0.500
PCA lesion	1	5	0.655
basal SPECT decrease	4	21	0.227
recent TIA/INF	1	10	0.209

* Statistically significant.

9 of 15 hemispheres with postoperative clinical deterioration showed these conditions.

Recently, postoperative hyperperfusion syndrome has come to be considered the cause of postoperative focal neurological symptoms, despite the relatively low flow revascularization obtained by surgery for moyamoya disease.[4,5,14,15] This syndrome appears as focal edema on MR imaging, whereas in SPECT studies a marked increase in uptake is noted at the lesion. However, symptoms resolved within a period of several minutes to 2 weeks, with minimal or no significant findings on follow-up MR imaging. Fujimura et al.[3] reported that the incidence of symptomatic hyperperfusion is as high as 38.2% in patients with adult-onset moyamoya disease, and 5.9% in those with childhood moyamoya disease. Although edematous lesions detected on MR imaging do not always cause neurological symptoms, the incidence of postoperative edematous lesions on MR imaging was 20% in our study. On the other hand, our SPECT studies performed early in the postoperative period revealed a decrease in uptake in 14 of 35 surgically treated hemispheres, including 2 hemispheres that exhibited cerebral infarction. This focal decrease in cerebral perfusion on perioperative SPECT studies has never been previously reported.

Our findings indicated that not only improvement, such as increase in perfusion flow in any cerebral region, but also worsening can occur after revascularization surgery. Because the region adjacent to the site of anastomosis exhibited an increase in uptake on SPECT, and MR angiography revealed a marked increase in signal intensity of the anastomosed vessels, obvious causes of deterioration such as occlusion of the STA–MCA bypass could be ruled out. Intraoperative causes of neurological deterioration such as effects of anesthesia, hypotension, and temporary occlusion of a cortical vessel or sacrifice of its small branches were unlikely to have caused the deficits, because in each case the patient awoke satisfactorily and deterioration occurred hours to days later. The dynamic change in postoperative hemodynamics due to bypass flow was considered to be the cause of this deterioration. Heros et al.[6] first reported the possibility that a change in the flow pattern after STA–MCA bypass causes ischemic symptoms. They speculated that shifts in the watershed region resulting from the new flow pattern after bypass grafting may play an important role in the origins of postoperative neurological deficits. They confirmed filling of the flow pattern by the graft on digital subtraction angiography, and concluded that the MCA division remote from the anastomosis had in effect become the "distal field" or "watershed" area of the MCA territory now supplied by the graft. The graft, by reversing flow patterns, induced relative hypoperfusion in the remote territory of the MCA that gradually improved as flow through the graft increased.

Our findings are the first to confirm a postoperative change in flow pattern, the so-called watershed shift, caused by direct bypass. A source of emboli arising from local problems at the site of anastomosis, such as intimal tags left within the lumen of the vessel or endothelial injury, could also have caused the cerebral infarction due to embolism. Lacking early postoperative digital subtraction angiography studies, we could not conclude but only

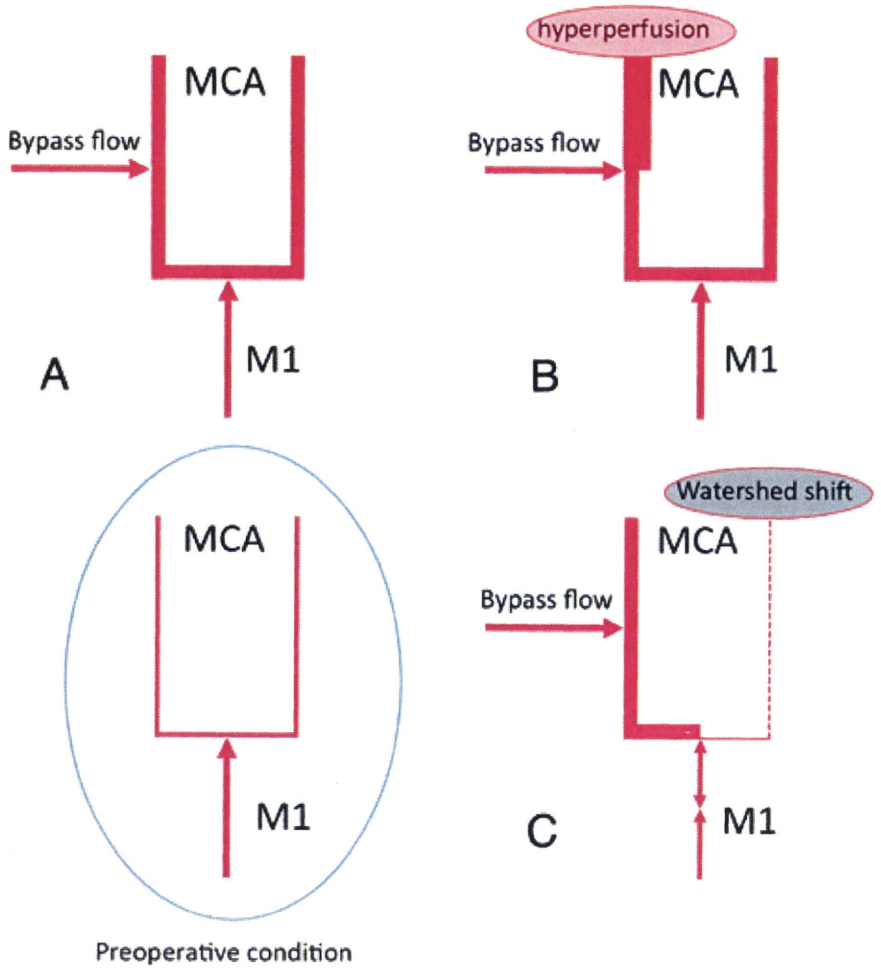

Fig. 5. Schematic drawings of postoperative hemodynamic changes. **A:** Ideal increase in MCA flow with direct bypass. **B:** Excessive flow from direct bypass causes hyperperfusion. **C:** The graft, by reversing flow patterns, induces relative hypoperfusion in the remote territory of the MCA.

speculate on the postoperative condition. However, the pattern of infarction was not that caused by occlusion of a branch of the MCA, which would have yielded a wedge-shaped region of infarction including white matter, but instead was that caused by decrease in perfusion pressure resulting in subcortical laminar necrosis. Infarction was not observed distal to the site of anastomosis.

The risk factor for decrease in focal perfusion that we identified, the watershed shift, was frequent preoperative TIAs and/or preoperative cerebral infarction during the month preceding surgery, whereas preoperative MR imaging and SPECT findings were not risk factors for this. Previous reports also showed that the frequent occurrence of preoperative TIA is an important indicator of instability of cerebral hemodynamics.[10,23] Because the graft, by reversing flow patterns, induced relative hypoperfusion in the remote territory of the MCA, ischemic attacks indicative of decreased perfusion with unstable hemodynamics in the territory of the ICA should be considered a risk factor. Although not significant in this study ($p < 0.15$), depiction of PCA and moyamoya vessels, which are important collateral pathways in the ICA territory, may also affect hemodynamics.[13,15] On the other hand, because low perfusion preoperatively as demonstrated on SPECT studies was not a risk factor, low cerebral perfusion alone cannot be considered a risk factor for watershed shift. Additional study with larger numbers of patients will settle this important issue. On the other hand, age was the only risk factor for hyperperfusion in our study. The mechanism underlying hyperperfusion in moyamoya disease also remains unclear. Duration of preoperative ischemia may affect postoperative cerebral hyperperfusion. Investigation of a larger number of patients is required to determine this mechanism.

Among the many different methods of treatment for moyamoya disease, our choice for its initial treatment is both direct (STA–MCA bypass) and indirect (encephalomyodurogaleosynangiosis) bypasses. The advantages of this procedure include both immediate improvement of cerebral hemodynamics by STA–MCA anastomosis and subsequent development of marked collateral circulation by the indirect pial synangiosis. During the early postoperative period, STA–MCA bypass should improve cerebral hemodynamics and reduce ischemic symptoms. However, it should be noted that direct bypass is not a completely safe procedure in moyamoya disease. In our

patients, watershed shift did not always cause infarction, although it did occur in 2 patients, each of them 3 years of age and with marked preoperative cerebral infarction. Because the infarctions occurred within 3 days of surgery, and hyperperfusion syndromes have been reported more than 3 days after surgery,[4,14,15] the possibility of watershed shift should be considered until the flow through the graft bypass gradually increases. The more aggressive double STA–MCA bypass, which can increase perfusion flow in both the anterior and posterior MCA territories, should be considered to reduce the risk of watershed shift in high-risk patients. It should be noted that once permanent neurological deficits have developed, there is little chance for surgical treatment to improve neurological status.

Conclusions

In young patients, moyamoya disease exhibits rapid progression, resulting in poor clinical outcome. The risk of postoperative neurological deterioration in very young moyamoya patients with frequent TIAs should be noted. Our findings showed that direct bypass is not a completely safe procedure in moyamoya disease, because it causes dynamic changes in postoperative hemodynamics due to bypass flow.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Hayashi, Fujimura. Acquisition of data: Hayashi, Shirane. Analysis and interpretation of data: Hayashi. Drafting the article: Hayashi. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Hayashi. Administrative/technical/material support: Hayashi, Shirane. Study supervision: Tominaga.

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Address correspondence to: Toshiaki Hayashi, M.D., Ph.D., Department of Neurosurgery, Miyagi Children's Hospital, 4-3-17 Ochiai, Aoba-ku, Sendai, 989-3126 Japan. email: hayashi@nsg.med.tohoku.ac.jp.

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CASE REPORT

Unilateral moyamoya syndrome involving the ipsilateral anterior and posterior circulation associated with paroxysmal nocturnal hemoglobinuria

Shunji Mugikura · Shuichi Higano · Miki Fujimura
Hiroaki Shimizu · Shoki Takahashi

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Abstract Moyamoya refers to a phenomenon of stenoocclusive changes at or around the terminal part of the internal carotid artery (ICA). Moyamoya vessels develop in patients with (moyamoya syndrome) or without (moyamoya disease) various underlying diseases or conditions. Recent evidence shows that stenoocclusive lesions tend to involve the ipsilateral ICA system and posterior cerebral artery (PCA) predominantly in moyamoya disease. A 53-year-old Japanese woman with paroxysmal nocturnal hemoglobinuria presented with cerebral infarction from stenoocclusive involvement in the ipsilateral ICA and PCA associated with moyamoya vessels; she had no contralateral vascular lesion. Although predominant involvement of the ipsilateral ICA and PCA was associated with underlying disease (moyamoya syndrome) in the present case, it is a characteristic finding of moyamoya disease. We discuss the possible pathogenesis of the vascular changes of this case.

Key words Moyamoya · Posterior circulation · Paroxysmal nocturnal hemoglobinuria · Thrombosis

S. Mugikura (✉) · S. Higano · S. Takahashi
Department of Diagnostic Radiology, Tohoku University, School of Medicine, Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan
Tel. +81-22-717-7312; Fax +81-22-717-7316
e-mail: mugi@rad.med.tohoku.ac.jp

M. Fujimura · H. Shimizu
Department of Neurosurgery, Tohoku University, School of Medicine, Sendai, Japan

H. Shimizu
Department of Neuroendovascular Therapy, Tohoku University, School of Medicine, Sendai, Japan

Introduction

Moyamoya refers to a phenomenon of stenoocclusive changes at or around the terminal part of the internal carotid artery (ICA). Moyamoya vessels develop in patients with (moyamoya syndrome) or without (moyamoya disease) various underlying diseases or conditions.[1–3]

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired stem cell disorder of an abnormal clone in the bone marrow. It characteristically manifests as chronic hemolytic episodes, intermittent hemoglobinuria, neutropenia and/or thrombocytopenia, and intravascular thrombosis.[4,5] Although cerebral venous or arterial thromboses are sometimes associated with PNH and are major contributors to mortality,[5,6] an association with moyamoya syndrome has been reported in only one case.[7]

We report an additional patient with PNH who developed cerebral infarction associated with unilateral moyamoya phenomenon involving the ipsilateral ICA system and posterior cerebral artery (PCA) without a contralateral vascular lesion. Although predominant involvement of the ipsilateral ICA and PCA was associated with underlying disease, it is a characteristic finding of moyamoya disease.[8,9] We discuss the possible pathogenesis of the vascular changes in our case.

Case report

In June 2007, a 52-year-old Japanese woman with anemia and transient sensory disturbance in the left upper and lower limbs was admitted to a local hospital. Laboratory examination revealed typical hemolytic

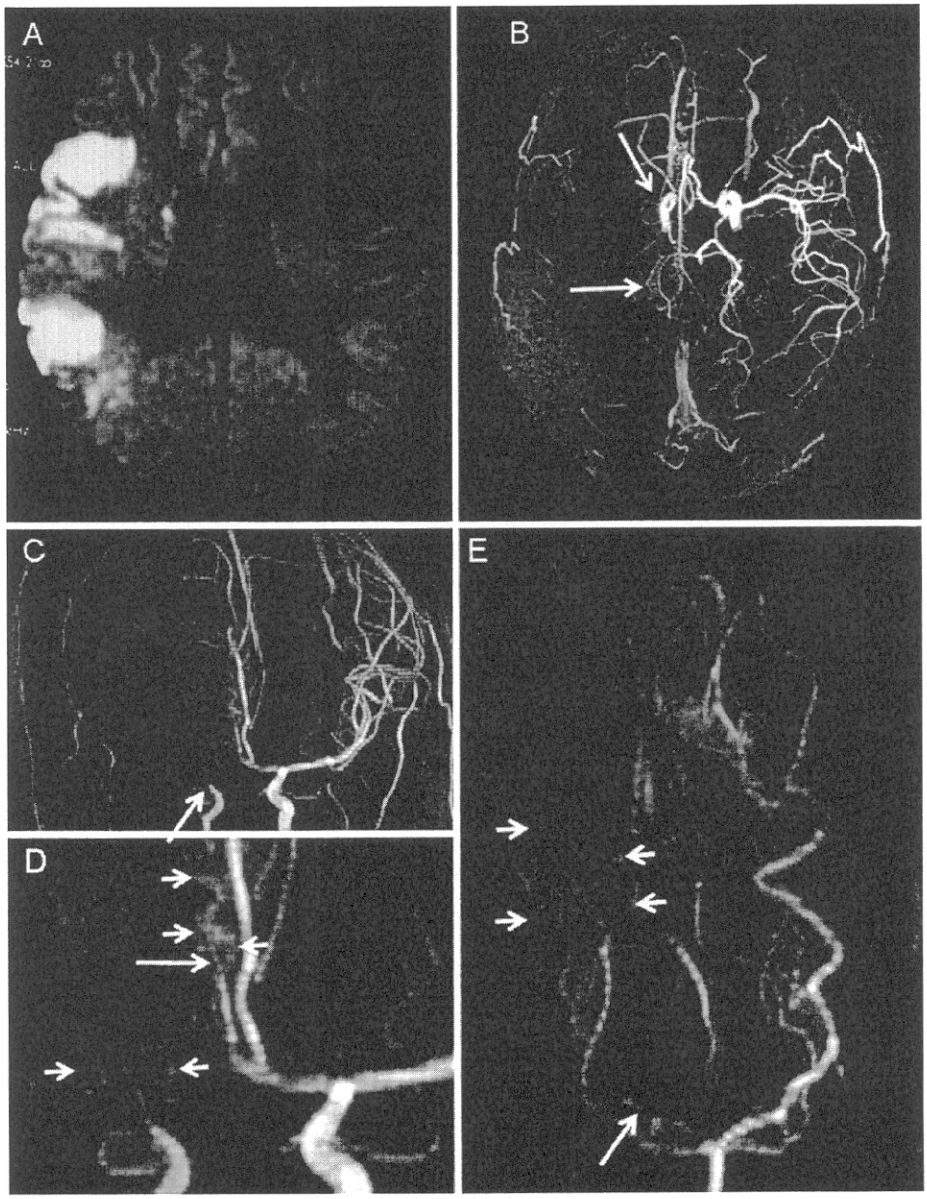

Fig. 1. A 53-year-old Japanese woman with paroxysmal nocturnal hemoglobinuria presented with left hemiparesis following stroke and underwent magnetic resonance imaging (MRI) and MR angiography (MRA) the same day. **A** Axial diffusion-weighted MRI shows infarction in the territory of the right middle cerebral artery. **B** Axial time-of-flight 3-tesla (T) MRA shows advanced stenoocclusive lesions at and around the terminal part of the internal carotid artery (ICA) (*top arrow*) and in the proximal part of the posterior cerebral artery (*bottom arrow*) in the right cerebral hemisphere. Note there is no apparent stenoocclusive lesion in the arteries of the contralateral left cerebral hemisphere. **C, D** A partially collapsed coronal 3-T MRA of the anterior circulation and a magnified image show near-occlusion at the supraclinoid portion of the ICA (*arrow*, **C**) without visualization of the middle cerebral artery or of proximal part of the anterior cerebral artery in the right. Moyamoya vessels at and around the terminal part of the right ICA are also seen (*short arrows*, **D**). Note that the distal part of the right anterior cerebral artery, presumably filled via the anterior communication artery, is also stenotic (*long arrow*, **D**) with development of moyamoya vessels (*short arrows*, **D**) and no stenoocclusive lesions in the left ICA system. **E** Partially collapsed coronal 3-T MRA of the posterior circulation shows advanced stenosis in the proximal part of the right posterior cerebral artery (*long arrow*) with development of moyamoya vessels (*short arrows*). No stenoocclusive lesion is seen in the left posterior cerebral artery

anemia (leukocyte count 2160/mm^3, hemoglobin 8.8 g/dl, platelet count 13.5 × 10^3/mm^3, and lactate dehydrogenase (LDH) 901 IU/l. Bone marrow examination revealed hypercellularity in the erythroid series. Cytogenetic studies of bone marrow cells showed normal female karyotype (46XX). PNH was diagnosed by flow cytometric measurement of glycosylphosphatidylinositol (GPI)-anchored markers on erythrocytes. At follow-up, her anemia had not progressed.

In November 2007, at age 53, she presented with sudden stroke and left hemiparesis. Hyperintensity in the right middle cerebral artery territory on T2- and diffusion-weighted magnetic resonance imaging (MRI) suggested recent infarction (Fig. 1A). MR angiography (MRA) (3 tesla) showed stenoocclusive lesions in the distal part of the right ICA and proximal parts of the anterior, middle, and ipsilateral PCAs and the development of moyamoya vessels (Fig. 1B–E). No stenoocclusive lesion was found in the ICA system or the PCA on the left. Laboratory examination showed slight progression of anemia (hemoglobin 7.7 g/dl) and hypercoagulability (thrombin antithrombin III complex 6.3 ng/ml—normal <3.2 ng/ml).

A large infarction in the right cerebral hemisphere and associated high probability of hemolytic crisis during bypass surgery precluded surgical revascularization. She received only antiplatelet drugs. At the 2-year follow-up, MRI showed no additional infarction, and MRA revealed no progression of the stenoocclusive lesions.

Discussion

We reported a 53-year-old Japanese woman with PNH who presented with cerebral infarction as a result of unilateral moyamoya phenomenon involving the ipsilateral ICA and PCA and with no contralateral vascular lesion. A 17-year-old Taiwanese girl with PNH has been reported with the moyamoya phenomenon involving bilateral ICAs without a PCA lesion.[7]

We considered the mechanism triggering the development of the moyamoya phenomenon in our case and that of the Taiwanese girl with PNH[7] as well as diseases other than PNH that underlie the moyamoya phenomenon, including various prothrombotic disorders (e.g., thrombocytopenic purpura, protein S deficiency, antiphospholipid syndrome, plasminogen deficiency).[1,2] We suspect that the moyamoya phenomenon likely develops from chronic ischemia owing to a prothrombotic mechanism. Indeed, in our case, the molecular markers in the blood for prothrombosis were high (thrombin antithrombin III complex level of 6.3 ng/ml).

Based on this hypothesis of a prothrombotic mechanism, we further speculate that in the present case thrombosis initiated in the supraclinoid ICA might have spread to the ipsilateral proximal PCA via the posterior communicating artery and caused the stenoocclusive ICA and PCA lesions associated with moyamoya vessels.

The predominant involvement of the ipsilateral ICA and PCA found in this case with PNH has been reported as an angiographic characteristic of moyamoya disease.[8,9] In a previous study of 85 Japanese patients with moyamoya disease, angiographic laterality in individual patients was common in both ICA and PCA systems, with a significant probability for lesions with more advanced ICA and PCA lesions to be on the same side.[8] In addition, two Japanese children were reported who had initial involvement of moyamoya phenomenon in the ipsilateral ICA and PCA without any contralateral lesions.[9] Although unexplained, such angiographic similarity might indicate a similar pathogenesis of moyamoya phenomenon in the present case and moyamoya disease. This hypothesis is consistent with the results of a recent prospective study in which prothrombotic disorders were detected in moyamoya disease and moyamoya syndrome.[10] Those results and frequent association of the moyamoya phenomenon with blood dyscrasia,[1,2,7] including that in the present case, suggest a latent prothrombotic mechanism as a common pathogenesis for the moyamoya phenomenon in moyamoya disease and some other moyamoya syndromes.

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Paradoxical Association of Moyamoya Syndrome With Large Middle Cerebral Artery Aneurysm and Subarachnoid Hemorrhage

—Case Report—

Hidenori ENDO, Miki FUJIMURA, Takashi INOUE, Hiroaki SHIMIZU*, and Teiji TOMINAGA*

Department of Neurosurgery, Kohnan Hospital, Sendai, Miyagi;
**Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi*

Abstract

A 69-year-old woman was admitted to our hospital because of fluctuating dysarthria during the past 2 months. Magnetic resonance imaging revealed old cerebral infarction of the left cerebral hemisphere with acute subarachnoid hemorrhage in the left sylvian fissure. Cerebral angiography showed a large saccular aneurysm, 14 mm in diameter, at the bifurcation of the left middle cerebral artery (MCA) in association with moyamoya vasculopathy with atherosclerosis, including steno-occlusive changes at the bilateral terminal internal carotid arteries and abnormal net-like vessels at the base of the brain. She underwent microsurgical neck clipping of the large aneurysm followed by superficial temporal artery-MCA anastomosis without complication. Intraoperative findings showed no evidence of aneurysm rupture, suggesting that the subarachnoid hemorrhage was due to the intrinsic pathology of moyamoya vasculopathy. The postoperative course was uneventful, and the patient was discharged without neurological deficit. Association of moyamoya syndrome with large MCA aneurysm is extremely rare, and formation of large aneurysm at the vascular territory of an occluded vessel is apparently unique.

Key words: moyamoya syndrome, large cerebral aneurysm, middle cerebral artery aneurysm, subarachnoid hemorrhage

Introduction

Moyamoya disease is a progressive, occlusive cerebrovascular disease with unknown etiology characterized by bilateral steno-occlusive changes at the terminal portion of the internal carotid artery and abnormal vascular network at the base of the brain.[1,2] Moyamoya disease is frequently associated with intracranial aneurysms located within the abnormal basal network or the circle of Willis, probably as a result of the intrinsic pathology of moyamoya disease such as hemodynamic stress and fragile structure of the collateral vessels.[4,5,7,8] Most saccular aneurysms on the circle of Willis are located on the posterior circulation, and the association of moyamoya disease with middle cerebral artery (MCA) aneurysm is rare.[5] Furthermore, the association of moyamoya vasculopathy with large MCA aneurysm has not been reported previously. Here we report a rare case with adult onset moyamoya syndrome associated with large MCA aneurysm and subarachnoid hemorrhage (SAH).

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Case Report

A 69-year-old woman was admitted to our hospital because of fluctuating dysarthria during the past 2 months. She had never complained of severe headaches. Magnetic resonance (MR) imaging incidentally found acute SAH along the left sylvian fissure (Fig. 1A, B). MR imaging also showed old cerebral infarction in the left posterior watershed area without recent cerebral infarction (Fig. 1C, D). Cerebral angiography showed a large saccular MCA aneurysm (14 mm diameter) with bleb at its posterior aspect, in association with steno-occlusive changes of the bilateral terminal internal carotid arteries and abnormal net-like vessels at the base of the brain (Fig. 2A). Atherosclerotic changes were found in the intracranial major arteries, leading to the diagnosis of moyamoya syndrome (akin-moyamoya disease) associated with atherosclerosis.[11] Severe stenosis of the distal M1 segment, just proximal to the large aneurysm, was also observed (Fig. 2B). Collateral circulation for the cerebral blood flow from the external carotid artery was not detected (not shown). Xenon single photon emission computed tomography (SPECT) demonstrated that the cerebral blood flow and cerebral vascular reactivity were markedly com-

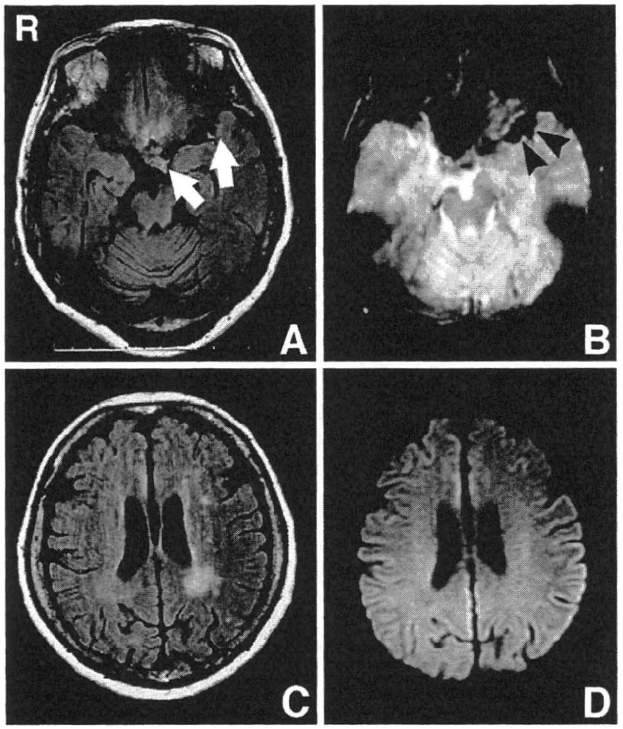

Fig. 1 Preoperative magnetic resonance images showing an area of high intensity on the fluid-attenuated inversion recovery (FLAIR) image (A, *arrows*) and low intensity on the T_2*-weighted image (B, *arrowheads*) in the left sylvian fissure indicating recent subarachnoid hemorrhage, and an area of high intensity on the FLAIR image (C) in the left posterior watershed area without abnormal signal on the diffusion-weighted image (D) indicating past history of cerebral infarction.

promised in the left cerebral hemisphere (not shown). Surgery was performed to inspect the source of silent bleeding and to prevent future ischemic stroke.

Left fronto-temporal craniotomy was performed. SAH was observed on the brain surface (Fig. 3A). The left sylvian fissure was split with evacuation of SAH in the fissure (Fig. 3B). Fragile microvessels had developed within the sylvian fissure. The aneurysm was carefully detached from the surrounding structure to observe the bleb on its posterior aspect (Fig. 3C). Inspection of the aneurysm found no evidence of recent rupture (Fig. 3D). Aneurysm clipping using multiple clips was performed with preservation of the M_2 portion and perforators (Fig. 3E). The distal M_1 portion had atherosclerotic appearance, which might correspond to the angiographic stenotic lesion. The parent artery (M_1 portion) was not occluded throughout the clipping procedure because the intra-aneurysmal pressure was relatively low for the size of the aneurysm. Motor evoked potentials monitored during clipping remained consistently normal. Superficial temporal artery (STA)-MCA single anastomosis was uneventfully performed to prevent future ischemic stroke (Fig. 3F).

MR imaging on the day after surgery revealed no ischemic or hemorrhagic complications (Fig. 4A, B). Posto-

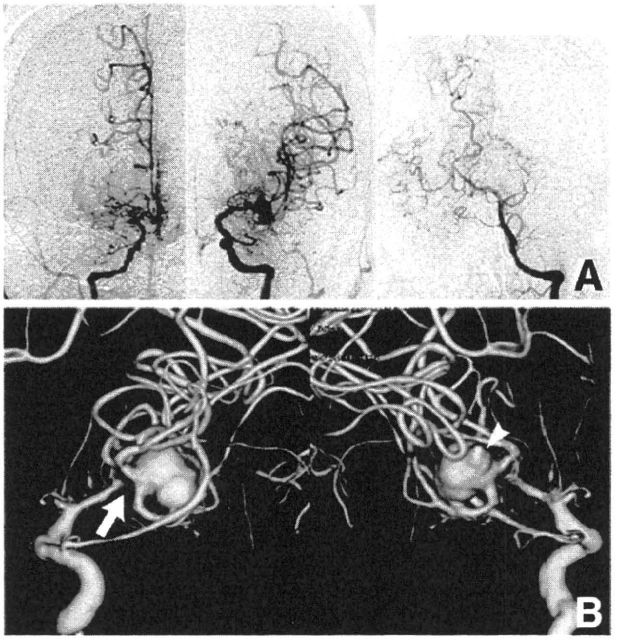

Fig. 2 A: Preoperative cerebral angiograms showing multiple steno-occlusive changes around the circle of Willis with net-like moyamoya vessels and a left large middle cerebral artery aneurysm. B: Three-dimensional digital subtraction angiograms revealing severe stenosis of distal M_1 segment (*arrow*) and bleb at the posterior aspect of the aneurysm (*arrowhead*).

perative *N*-isopropyl-p-[^{123}I]iodoamphetamine SPECT findings during the acute stage after revascularization surgery showed significant improvement of cerebral blood flow in the left cerebral hemisphere (not shown). Her blood pressure was strictly controlled to avoid symptomatic cerebral hyperperfusion.[2] The patient was discharged 3 weeks after surgery without neurological deficit. Cerebral angiography 6 months after surgery revealed the patent STA-MCA bypass with no aneurysm filling (Fig. 4C–E). No anterograde blood flow from M_1 was evident due to the contribution of the bypass flow to the distal MCA territory. No cerebrovascular event occurred during the follow-up period of 6 months.

Discussion

A review found that 56% of the aneurysms associated with moyamoya disease occurred around the circle of Willis, 22% on the peripheral collateral vessels, and 18% in the basal ganglia.[5] Aneurysms around the circle of Willis predominantly developed in the posterior circulation, and only 2 of the 73 aneurysms within the circle of Willis arose on the MCA (2.7%), indicating that the association of moyamoya disease with MCA aneurysm is relatively rare, probably due to the lower hemodynamic stress on the MCA bifurcation in moyamoya disease. Few cases have discussed the size of the aneurysms, and moyamoya disease in association with large MCA aneurysm was unknown. The present case was considered to be

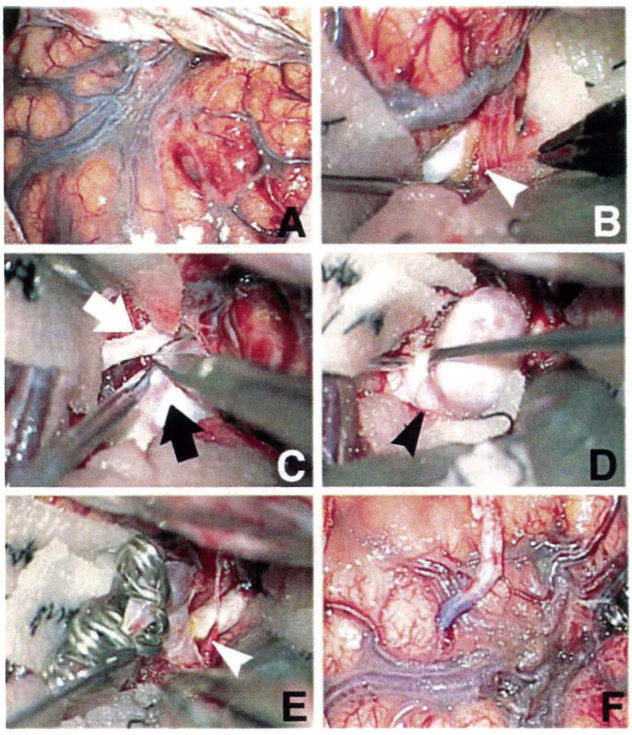

Fig. 3 Intraoperative photographs showing subarachnoid hemorrhage on the brain surface (A), evacuation of the thin subarachnoid hemorrhage (*arrowhead*) surrounding the aneurysm (B), M_2 segment (*white arrow*) separated from the aneurysm (*black arrow*) (C), little evidence of recent rupture around the aneurysm with the bleb (*arrowhead*) (D), clipping was performed using multiple clips, and atherosclerotic change of the distal M_1 portion (*arrowhead*) (E), and superficial temporal artery-middle cerebral artery single anastomosis was performed (F).

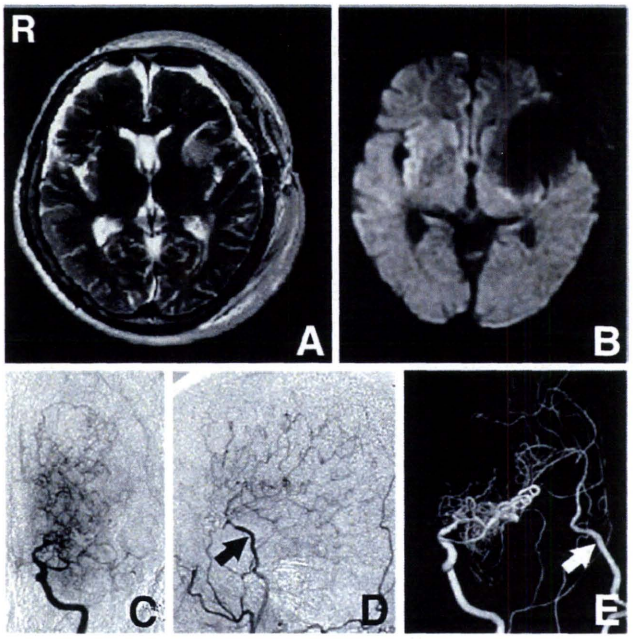

Fig. 4 A, B: T_2-weighted (A) and diffusion-weighted (B) magnetic resonance images obtained on the day after surgery showing no ischemic or hemorrhagic complications. C–E: Left internal carotid angiogram (C), left external carotid angiogram (D), and three-dimensional digital subtraction angiogram of the left common carotid artery (E) obtained 6 months after surgery showing no aneurysm filling, patent superficial temporal artery-middle cerebral artery bypass (*arrow*), and no antegrade blood flow from M_1 due to the contribution of the bypass flow to the distal middle cerebral artery territory.

moyamoya syndrome with a background of atherosclerosis, but also represents large cerebral aneurysm of the MCA associated with moyamoya vasculopathy.

The present case was considered to develop cerebral ischemia and SAH in a relatively short period. Most patients with hemorrhagic-onset moyamoya disease have intracerebral hemorrhage (ICH) or intraventricular hemorrhage (IVH).[6] In contrast, the clinical manifestations of hemorrhagic moyamoya disease associated with intracranial aneurysms tend to be SAH (74%) rather than ICH (34%) or IVH (29%).[5] The incidence of aneurysm rupture associated with moyamoya disease is unclear. In the present case, the intraoperative findings indicated that the cause of SAH was not related to aneurysm rupture. Disruption of the transdural anastomosis is a possible cause of SAH.[10] The incidence of disease progression in adult moyamoya disease was proven to be higher than recognized before.[9] Atherosclerotic background of the disease might be involved in the disease progression in our case.

The underlying mechanism of this rare association is totally undetermined. Based on the observation that the peculiar hemodynamic stress in moyamoya disease contributes to the formation of cerebral aneurysm at the circle of the Willis,[5,7,8] the formation of large MCA aneurysm at the vascular territory of occlusive vessel is apparently unique. Furthermore, the intraoperative findings showed relatively low intra-aneurysmal pressure and no evidence of aneurysm rupture. These findings might support the idea of initial occurrence of the cerebral aneurysm with subsequent development of moyamoya vasculopathy. Whether this association was incidental or had a shared background remains unclear. Recent studies have shown the importance of inflammatory response in the pathogenesis of cerebral aneurysm and moyamoya angiopathy.[1,3] Therefore, inflammatory response might be one of the potential mechanisms of this rare association.

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Address reprint requests to: Miki Fujimura, M.D., Ph.D., Department of Neurosurgery, Kohnan Hospital, 4-20-1 Nagamachi-minami, Taihaku-ku, Sendai 982-8523, Japan.
e-mail: fujimur@kohnan-sendai.or.jp

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Efficacy of Revascularization Surgery for Moyamoya Syndrome Associated With Graves' Disease

Hidenori ENDO, Miki FUJIMURA, Kuniyasu NIIZUMA*, Hiroaki SHIMIZU*, and Teiji TOMINAGA*

Department of Neurosurgery, Kohnan Hospital, Sendai, Miyagi;
**Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi*

Abstract

Appropriate management of moyamoya syndrome associated with Graves' disease is undetermined because of the rarity of this combination. Patients tend to present with cerebrovascular events such as transient ischemic attack (TIA) in a thyrotoxic state, which is relieved by proper antithyroid therapy. Four patients with moyamoya syndrome associated with Graves' disease were successfully treated with revascularization surgery on 5 hemispheres among 58 consecutive patients (2–62 years old, mean 34.4 years) with moyamoya disease in 80 hemispheres treated from March 2004 to May 2007. Three patients presented with TIA, and one patient presented with intracerebral hemorrhage. Three patients were thyrotoxic at the onset of the cerebrovascular events. All patients underwent revascularization surgery after normalization of thyroid function. Euthyroid state was strictly maintained perioperatively. One patient developed symptomatic cerebral hyperperfusion, which was resolved by blood pressure control. Postoperative courses of the other patients were uneventful, and all 4 patients have remained neurologically stable after discharge. Cerebrovascular reconstruction surgery is a successful treatment option for moyamoya syndrome associated with Graves' disease. Timing of surgery during the euthyroid state and perioperative management considering the thyroid function and the cerebral hemodynamic change are the keys to successful surgical treatment.

Key words: moyamoya disease, Graves' disease, hyperthyroidism, extracranial-intracranial bypass, cerebral hemodynamics

Introduction

Moyamoya disease is a progressive, occlusive cerebrovascular disease with unknown etiology characterized by bilateral steno-occlusive changes at the terminal portion of the internal carotid artery and abnormal vascular network at the base of the brain.[18] Quasi-moyamoya disease or moyamoya syndrome is the rarely observed characteristic moyamoya vasculopathy associated with conditions such as sickle cell disease, Down's syndrome, and neurofibromatosis type 1.[17] Several cases have been reported of the coexistence of moyamoya vasculopathy and Graves' disease, which is a female-dominant autoimmune thyroid disease causing hyperthyroidism.[5–7,9,10,12,13,16,19–21] Surgical revascularization for moyamoya disease prevents cerebral ischemic events by improving cerebral blood flow (CBF), and superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis with or without indirect pial synangiosis is generally used as the standard surgical treatment.[1] Application of this revascularization surgery to the treatment of moyamoya syndrome associated with Graves' disease is still undetermined because of the rarity of this combination. Ischemic symptoms may be reversible after the medical treatment of hyperthyroidism.

Here, we review 4 cases of moyamoya vasculopathy and Graves' disease successfully treated by revascularization surgery, focusing on perioperative management.

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Materials and Methods

A total of 58 consecutive patients (2–62 years old, mean 34.4 years) were treated for moyamoya disease in 80 hemispheres by the same surgeon (M.F.) in Tohoku University Hospital from March 2004 to May 2007. Four patients treated in 5 hemispheres