Paradoxical symptomatic cerebral blood flow decreases after combined revascularization surgery for patients with pediatric moyamoya disease: illustrative case

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BACKGROUND Transient neurological deficits (TNDs) develop after cerebral revascularization in patients with moyamoya disease (MMD). The authors report a rare pediatric MMD case with extensive decreased cerebral blood flow (CBF) and prolonged TNDs after combined revascularization.

OBSERVATIONS A 9-year-old boy presented with transient left upper limb weakness, and MMD was diagnosed. A right-sided combined surgery was performed. Two years after the surgery, frequent but transient facial (right-sided) and upper limb weakness appeared. The left internal carotid artery terminal stenosis had progressed. Therefore, a left combined revascularization was performed. The patient's motor aphasia and right upper limb weakness persisted for approximately 10 days after surgery. Magnetic resonance angiography showed that the direct bypass was patent, but extensive decreases in left CBF were observed using single photon emission tomography. With adequate fluid therapy and blood pressure control, the neurological symptoms eventually disappeared, and CBF improved.

LESSONS The environment of cerebral hemodynamics is heterogeneous after cerebral revascularization for MMD, and the exact mechanism of CBF decreases was not identified. TNDs are significantly associated with the onset of stroke during the early postoperative period. Therefore, appropriate treatment is desired after determining complex cerebral hemodynamics using CBF studies.

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KEYWORDS cerebral blood flow; combined revascularization surgery; moyamoya disease; transient neurological deficits; pediatrics

Moyamoya disease (MMD) is characterized by stenoocclusive changes at the terminus of the bilateral internal carotid artery (ICA) and the development of basal collateral networks. Direct and indirect combined revascularization surgeries were established for effective treatment, and these surgeries comprise a superficial temporal artery (STA) middle cerebral artery (MCA) bypass for direct bypass and the placement of the vascularized pedicle using temporal muscle, dura mater, and periosteum for indirect bypass. Evidence shows that these treatments reduce cerebral ischemia and the risk of future hemorrhagic events. However, transient neurological deficits (TNDs), such as numbness or weakness in the extremities, aphasia, and dysarthria, are well-recognized major events that develop in the early postoperative period. Cerebral blood flow (CBF) studies indicated that these symptoms were caused by focal hyperperfusion as a result of rapid increase in blood flow due to the direct bypass. CBF studies also showed that TNDs may occur in patients without focal

ABBREVIATIONS CBF = cerebral blood flow; DSA = digital subtraction angiography; FLAIR = fluid-attenuated inversion recovery; ICA = internal carotid artery; MCA = middle cerebral artery; MMD = moyamoya disease; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; PCA = posterior cerebral artery; POD = postoperative day; SPECT = single photon emission computed tomography; STA = superficial temporal artery; TIA = transient ischemic attack; TND = transient neurological deficit.

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hyperperfusion, and the pathophysiology of TNDs was not fully elucidated.8,10,14 Notably, a focal reduction in CBF after combined revascularization for pediatric MMD was rarely reported.15 We report a pediatric patient who had prolonged transient motor aphasia and motor weakness in the upper extremities as TNDs after combined revascularization with decreased CBF.

Illustrative Case
A 9-year-old right-handed boy presented to a physician with reports of transient left upper limb weakness. A diagnosis of MMD was suspected on magnetic resonance angiography (MRA), and digital subtraction angiography (DSA) was subsequently performed. MMD was diagnosed based on the criteria of the Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis (Fig. 1A).16 No significant ischemic lesions were observed on fluid-attenuated inversion recovery (FLAIR) using magnetic resonance imaging (MRI) (Fig. 1B). However, single photon emission computed tomography (SPECT) showed a marked decrease in CBF within the right MCA territory (Fig. 1C). Therefore, antiplatelet therapy was started. Direct and indirect combined revascularization on the right side was implemented. SPECT approximately 2 weeks after surgery showed improvement in the CBF of the right MCA territory. The patient was discharged without any TNDs or new strokes during the postoperative course.

Approximately 2 years after surgery was performed on the right side, the patient developed an intermittent weakness of the right side of the face and upper limbs. MRA revealed that the stenosis of the left ICA terminal had progressed without posterior cerebral artery (PCA) involvement (Fig. 2A, arrow). No new cerebral ischemic lesions were found on FLAIR (Fig. 2B), but left cerebral revascularization and fluid replacement treatment were urgently planned because of the high frequency of transient ischemic attacks (TIAs).

Left cerebral revascularization, consisting of STA-MCA single bypass plus encephalo-myo-synangiosis of the temporal region and encephalo-galeo-periosteal-synangiosis of the frontal region, was performed via two craniotomies. The precentral artery was
selected as the recipient of the direct bypass, and the time
required for the anastomosis was 16 minutes. The amount
of bleeding was 250 mL, but the patient’s hemoglobin level
did not drop below 10 g/dL. Therefore, a blood transfusion was
not required. No problematic findings were found on computed
tomography (CT) immediately after surgery, but the patient
developed symptoms of motor aphasia and right upper limb paresis. Because there was a possibility of cerebral ischemia and focal hyperperfu-
sion, the patient was treated with blood pressure control and fluid
therapy. The symptoms remained on postoperative day (POD) 1.
However, diffusion-weighted imaging was negative on MRI, and
the bypass was patent on MRA (Fig. 3A, arrow). SPECT was per-
formed on POD 3 because the patient had prolonged neurological
symptoms, and extensive decreases in CBF in the left MCA terri-
tory were observed (Fig. 3B). A CT at the same time as the
SPECT showed mild swelling of the temporal muscular flap that
was placed via the indirect method, but there was no apparent
brain compression. Another MRI was performed on POD 4, but
there were no cerebral ischemic lesions (Fig. 3C), and the bypass
was patent on the MRA (Fig. 3D, arrow). Antiplatelet therapy was
resumed. The patient’s neurological symptoms, including motor
aphasia and left upper limb paresis, persisted until POD 8 and
then started to improve. Figure 4 shows SPECT on POD 10; CBF
of the left MCA territory was improved. The patient’s neurological
symptoms completely resolved on POD 14, and the patient was
discharged from the hospital. A recheck DSA approximately 1
year after surgery showed good revascularization effect in the left
STA and in the other external carotid arterial systems (Fig. 5).

**FIG. 3.** Left cerebral revascularization, consisting of STA-MCA single bypass plus encephalo-myo-synangiosis of the temporal region and encephalo-
galeo-periosteal-synangiosis of the frontal region, was performed via two craniotomies. The patient developed motor aphasia and right upper limb aphasia immediately after surgery. A: MRA from POD 1 shows the patent bypass (arrow). B: SPECT on POD 3 shows extensive CBF decreases in the left MCA territory. C: MRI/MRA reexamination on POD 4 shows no acute cerebral infarction, and the bypass remained patent (D, arrow).

**FIG. 4.** The neurological symptoms of motor aphasia and left upper limb paresis persisted to POD 8 and then started to improve. SPECT on POD 10 shows improvement of the CBF of the left MCA territory. A: Ventricular level. B: Centrum Semiovale level.
The cause of TNDs after combined revascularization in patients is likely due to a wide range of CBF decreases. However, the exact mechanism of the decreases in CBF was not identified. The watershed shift phenomenon is a potential etiology.15,18,25,26 Tashiro et al.17 found that this phenomenon occurred in 10.9% of adult patients with MMD after STA-MCA bypass surgery. The anastomosed STA-MCA bypass flow conflicts with the recipient MCA flow in the proposed pathology, and the original MCA perfusion territory showed low perfusion during a CBF study due to the shift of the watershed territory. SPECT was not performed immediately before surgery in this case, and it cannot be compared with postoperative SPECT. Therefore, there is a lack of information to explain the watershed shift phenomenon. Notably, one case had effects other than the effects secondary to the changes in flow due to direct bypass and decreases in the CBF due to a direct compression of the brain because of swelling of the temporalis muscle flap that was placed during indirect surgery.27 This fact should be recognized because combined revascularization mainly uses the temporalis muscle. There was no swelling of the patient’s temporalis muscle flap on the CT performed simultaneously with POD 3 SPECT, but the patient had marked decreases in CBF.

Because TNDs may be caused by direct bypass flow and CBF decreases, the relationship between indirect procedures and TNDs is interesting. Previous studies by our group demonstrated that compression of the temporalis muscle flap that is used in indirect surgery was significantly associated with TNDs.28 We revealed the relationship between the sulcal hyperintensity sign on FLAIR images after indirect surgery and the occurrence of TNDs.29 Sakamoto et al.30 reported that TNDs were observed more frequently in patients receiving indirect surgery than patients receiving direct bypass. Although these previous studies did not verify the fluctuations in CBF, the results suggested that the causes of TNDs were complex. Because the temporal muscle and galea that are placed on the brain surface via indirect surgery are not present in the physiological environment, these techniques may cause inflammation and head trauma.31 MRI FLAIR revealed that the sulcal hyperintensity signals were due to changes in the composition of cerebrospinal fluid and development of inflammatory responses.32 These findings support the hypothesis that inflammation is an etiology of TNDs. However, the authors also noted that focal hyperperfusion on SPECT and TNDs after combined surgery was not a significant pathological condition, but it was similar to posterior reversible encephalopathy syndrome and vascular edema.33 Rapid changes in focal CBF due to direct bypass and direct stimulation of the brain in combined revascularization and changes in the composition of cerebrospinal fluid due to indirect surgery may be microenvironments that induce an impaired blood–brain barrier and endothelial injuries.34 This environment may induce hyperpermeability of the vasculature, which results in CBF decreases and intravascular dehydration. From a radiological perspective, the MCA appeared spastic after surgery compared to the other vascular systems in the MRA findings (Fig. 3A). Therefore, the pathophysiology of decreased CBF and TNDs may also be related to the pathology of reversible cerebral vasoconstriction syndrome caused by endothelial injury.35

The policy of our institution on preoperative infusion and oral antiplatelet drugs should be described. The Anesthesiology Department instructs patients to fast after dinner the day before surgery. Patients
receive intravenous extracellular fluid at a maintenance dose for volume replacement to prevent dehydration from the afternoon of the day before surgery. We administer aspirin preoperatively in most patients as an antiplatelet therapy. Aspirin administration should be discontinued on the third day before surgery because of the risk of excessive intraoperative bleeding and postoperative bleeding, except for patients who are likely to have severe cerebral ischemia before surgery.36

The details regarding blood pressure and fluid therapy should be valuable lessons from this case. First, the preoperative baseline blood pressure of this 9-year-old patient was 110/70 mm Hg, which was normotensive. Ischemic attacks may be avoided by maintaining preoperative baseline blood pressure during the perioperative period of cerebral revascularization for MMD.37 The autoregulatory response to hypotension is definitely lower in children than adults, which increases its importance.38 Lee et al.39 investigated intraoperative functional autoregulation using near-infrared spectroscopy and showed that postoperative TIA was more frequent when it was impaired. However, they could not set a goal for postoperative target blood pressure because of age and individual differences in autoregulation. Therefore, we set the lower limit of the perioperative blood pressure control target for patients with ischemic-type pediatric MMD as the preoperative baseline value. Only a few survey results in adults were reported in the setting of the upper limit of postoperative blood pressure.40 According to these results, the upper limit of systolic blood pressure was approximately 130 to 140 mm Hg. However, we adopted an additional 20% of the preoperative value because of the lower baseline blood pressure reference values in children than adults and because postoperative hyperperfusion syndrome and cerebral hemorrhage are definitely less common in children than in adults.41

Fluid management is also extremely important for prevention of postoperative cerebral ischemia in MMD. Sufficient intravenous administration of extracellular fluid avoids postoperative hypotension and hypovolemia.40 Unlike adults, pediatric patients receive 1 to 1.5 times the normal maintenance rate converted by body weight.42 We do not measure central venous pressure in our routine. However, the total balance among oral intake, total infusion volume, and urine output is controlled to avoid negative values. Blood pressure control and fluid therapy should always be administered at least during the appearance of TNDs. Our previous study showed that the average duration of appearance of TNDs was 8.2 days (range 2 to 16).10 Notably, the postoperative inflammatory response peaked at 2 to 3 days and normalized at approximately 7 days. Management should be strengthened during this time because extracellular fluid leakage causes hypotension and intravascular dehydration. The blood pressure management and fluid therapy strategy prevented the progression of stroke to a unique postoperative CBF condition in this case. With the discovery of extensive CBF decreases in SPECT on POD 3, the permissive hypertension blood pressure management strategy was certainly considered. However, we did not choose the intention hypertensive policy because of the safety issues of continuous hypertension administration to pediatric patients and the lack of prior literature on its use. Sufficient fluid therapy was provided instead.

Lessons
The treatment strategy for these cases is important. However, no progression to stroke was observed in this patient after he received sufficient fluid replacement and normotensive blood pressure control, and the imaging findings and the patient's symptoms eventually resolved. In situations in which the pathophysiology has not been fully elucidated, strict perioperative management may be required with frequent CBF studies to manage cerebral ischemia and focial hyperperfusion.

References


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

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