

Effective Surgical Revascularization Improves Cerebral Hemodynamics and Resolves Headache in Pediatric Moyamoya Disease

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Key words

- Bypass surgery
- Cerebral hemodynamics
- Headache
- Moyamoya disease

Abbreviations and Acronyms

ACZ: Acetazolamide
CBF: Cerebral blood flow
CVR: Cerebrovascular reactivity
EDAS: Encephalo duro arterio synangiosis
EDMAPS: Encephalo duro myo arterio pericranial synangiosis
MR: Magnetic resonance
PET: Positron emission tomography
SPECT: Single photon emission computed tomography
STA-MCA: Superficial temporal artery to middle cerebral artery
TIA: Transient ischemic attack



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INTRODUCTION

Moyamoya disease is an uncommon cerebrovascular disease that is characterized by progressive steno-occlusion of the supraclinoid internal carotid artery and its main branches within the circle of Willis. This occlusion results in the formation of a fine vascular network (the Moyamoya vessels) at the base of the brain. Clinical presentations of Moyamoya disease are very unique. Most children with Moyamoya disease develop transient ischemic attack (TIA) or cerebral infarction, whereas about half of adult patients develop intracranial bleeding, and half develop TIA or cerebral infarct (1). On the other hand, headache is one of the serious symptoms associated with Moyamoya

■ **BACKGROUND:** Headache is one of the major clinical presentations in pediatric Moyamoya disease. However, the clinical features and underlying mechanisms are not fully understood. This study aimed to clarify the clinical feature of headache in pediatric Moyamoya disease and the effect of surgical revascularization.

■ **METHODS:** This study included 29 pediatric patients who underwent superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis and indirect bypass for Moyamoya disease. Their medical records were precisely evaluated to identify the clinical features of their headache. The findings on magnetic resonance imaging, positron emission tomography, and single-photon emission computed tomography also were analyzed.

■ **RESULTS:** Preoperative headache was documented in 11 (38%) of 29 patients. The majority of them complained of severe headache in the frontal or temporal region in the morning. Headache was significantly related to more advanced disease stage and to the decreases in cerebral blood flow and its reactivity to acetazolamide. Surgical revascularization completely resolved headache in all 11 patients.

■ **CONCLUSIONS:** These findings strongly suggest that disturbed cerebral hemodynamics may play key roles in developing severe headache in pediatric Moyamoya disease. STA-MCA anastomosis and encephalo-duro-myo-arterio-pericranial synangiosis may be effective procedures to rapidly resolve headache by widely supplying collateral blood flow to the operated hemispheres.

disease, especially in pediatric patients. Typically, they present with migraine-like severe headache in the frontal area in the morning. They cannot go to school because of severe headache. Headache is often associated with vomiting and spontaneously resolves within several hours (1, 23, 27, 30, 35). Migraine-like headache is also observed in some adult patients with Moyamoya disease (27, 31, 35). According to previous studies, persistent cerebral ischemia may be closely related to the occurrence of headache in pediatric Moyamoya disease because surgical revascularization may improve or resolve it (30). However, there are almost no studies that denote the relationship between cerebral hemodynamics and headache in pediatric patients with Moyamoya disease. Therefore, the authors believe that it is important to explore the underlying

mechanism to establish more effective treatment and improve quality of life. Based on these considerations, this study aimed to clarify the role of cerebral hemodynamics in headache and to survey the effects of surgical revascularization on headache in pediatric Moyamoya disease.

PATIENTS AND METHODS

Patients

This study included 29 pediatric patients who were admitted because of Moyamoya disease and underwent surgical revascularization at Hokkaido University Hospital between 1997 and 2010. All of them were Japanese and met the guidelines for the diagnostic criteria of the Research Committee on Moyamoya Disease of the Ministry of Health, Labor, and Welfare of

Japan. There were 7 boys and 22 girls. Their ages ranged from 5 to 17 years, with a mean age of 10.0 years.

Before surgery, the frequency, timing, region, and severity of headache were precisely evaluated in all patients. Based on functional impairment, severity of headache was classified into 4 categories: 1) mild, patient is aware of a headache but is able to continue daily routine with minimal alteration; 2) moderate, the headache inhibits daily activities but is not incapacitating; 3) severe, the headache is incapacitating; and 4) status, a severe headache that has lasted more than 72 hours (4).

Radiological Examinations

Before surgery, all patients underwent precise neuroradiological examinations, including magnetic resonance (MR) imaging, MR angiography, and cerebral angiography. Disease was classified into 6 stages according to Suzuki angiographic stage (33). Using ^{133}Xe or ^{123}I -IMP single-photon emission computed tomography (SPECT) or ^{15}O -gas positron emission tomography (PET), cerebral blood flow (CBF) before and after intravenous injection of 10 mg/kg acetazolamide was quantitatively measured, as reported previously (12, 15-18). In this study, the involved hemisphere was considered as the candidate for surgical revascularization when having impaired reactivity to acetazolamide (13, 28). Cerebrovascular reactivity (CVR) to acetazolamide was determined as follows: $\text{CVR}(\%) = 100 \times (\text{CBF}_{\text{ACZ}} - \text{CBF}_{\text{rest}}) / \text{CBF}_{\text{rest}}$, where CBF_{rest} and CBF_{ACZ} represent CBF before and after intravenous injection of acetazolamide, respectively. Because a normal CBF value dramatically changes with growth in children, CBF was rated as reduced when the value was lower than 80% of the cerebellum in each patient (9, 16, 26). CVR was rated as reduced when it was lower than 14% (17).

Surgical Procedures

The patients underwent superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis and encephaloduro-myo-arterio-pericranial synangiosis (EDMAPS) for surgical revascularization, as described previously (13, 28). Briefly, the skin incision was made along the course of the parietal branch of the STA

and extended upward to the midline near the bregma and then along the midline downward to the hairline. The parietal branch of the STA was dissected from the surrounding tissues, being kept patent, and the point where the STA crosses the skin incision. After the scalp flap was reflected laterally, the frontal branch of the STA was also dissected under a surgical microscope. The temporal muscle was dissected as widely as possible and was made as a vascularized flap. Then, the vascularized frontal pericranium was also dissected. A standard frontotemporal craniotomy was made, preserving the middle meningeal artery. The size of craniotomy was matched to that of the temporal muscle flap. Then, a medial frontal craniotomy was made separately, which should fit the size of the pericranial flap. The dura was incised, preserving the main branches of the middle meningeal artery. Subsequently, STA-MCA single or double anastomosis was performed in an end-to-side fashion with 10-0 or 11-0 nylon threads. The frontal branches of the MCA were usually used as the recipients of anastomoses because cerebral hemodynamics are impaired, especially in the frontal lobe, in Moyamoya disease. The clamping time was about 20 minutes. Then, the dural flaps were turned into the epiarachnoid space to make an indirect bypass. The dural opening through the frontotemporal craniotomy was covered with the temporal muscle flap. The dural opening through the medial frontal craniotomy was covered with the frontal pericranial flap. Cranioplasty was performed for both craniotomies, and the wound was closed. Total surgery time ranged from 5 to 7 hours. No blood transfusion was performed.

Follow-Up

After surgical revascularization, all patients were followed up in the outpatient clinic. The mean follow-up period was 85.3 ± 45.7 months, ranging from 3 months to 162 months. Episodes of TIA, cerebral infarction, and intracranial hemorrhage as well as the clinical features of headache during follow-up periods were precisely recorded. Overall clinical outcomes were classified into 4 categories: 1) excellent, preoperative symptoms (such as TIA) had totally disappeared without fixed neurological deficits; 2) good,

symptoms had totally disappeared but neurological deficits remained; 3) fair, symptoms persisted, albeit less frequently; and 4) poor, the symptoms remained either unchanged or worsened (20).

Cerebral angiography and blood flow study were repeated 3 to 6 months after surgery. Both MR imaging and MR angiography were performed every 6 or 12 months with a 1.5-T whole-body MR imager.

Statistical Analysis

Continuous variables were expressed as mean \pm SD. Statistical analysis was performed using a χ^2 test and a Kruskal-Wallis test as appropriate. The statistical level of significance was set at $P < .05$.

RESULTS

Clinical Results

STA-MCA anastomosis and EDMAPS were performed on 50 hemispheres of 29 patients. Perioperative ischemic stroke occurred in 3 (6.0%) of these 50 surgical procedures. Cerebral infarct developed in the ipsilateral hemisphere in 2 patients and in the contralateral hemisphere in another. However, their neurological sequelae completely disappeared within 30 days after surgery.

During follow-up periods, TIA completely disappeared in all but 1 patient. Only a 7-year-old girl continued to develop transient weakness of the bilateral legs for 1 year after surgery, although its frequency decreased markedly. No ischemic or hemorrhagic stroke occurred in 29 patients during follow-up periods. Therefore, clinical outcome was categorized as excellent in 26 patients (89.7%) and good in 3 (10.3%). Three patients categorized as having good outcomes had mild neurological sequelae because of their initial ischemic stroke, but were independent in their daily life.

Clinical Features of Preoperative Headache

Before surgery, headache was observed in 11 (37.9%) of 29 patients. Their clinical data are shown in Table 1. The clinical diagnosis was TIA in 10 patients and ischemic stroke in 1. The frequency of headache widely varied: once every day in 2 patients (18%), a few times per week in

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