Long-term effects of indirect bypass surgery on collateral vessel formation in pediatric moyamoya disease

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Object. The authors investigated whether revascularization surgeries in children with moyamoya disease could reduce abnormal collateral formations in the posterior circulation; long-term follow-up angiography was performed to assess status.

Methods. In six patients who underwent indirect bypass surgery in childhood, long-term follow-up angiography studies were obtained between 7 and 12 years after surgery. All six patients presented with ischemic symptoms at onset of disease between 2 and 7 years of age. Ischemic insults did not occur after surgery in any patient. In five cases, the angiographically documented stages advanced bilaterally, and in three cases the angiography revealed nearly occluded intracranial carotid arteries bilaterally. In all sides in these five cases, the collateral circulation through the grafts developed well, and collateral formation from the lenticulostriate arteries and from the anterior choroidal artery decreased according to the natural advancement of disease. There was no reduction in the collateral formations from the posterior circulation, however, in four of these five cases.

Conclusions. Although the data cannot directly indicate that the patients in this study remain at potential risk of developing hemorrhage in the future, these facts should be considered when evaluating the efficacy of revascularization surgeries, because the hemorrhagic potential of abnormally dilated collateral vessels from the posterior circulation would increase as the advancement of the disease.

Keywords • moyamoya disease • collateral vessel • hemorrhage • angiography • revascularization surgery • pediatric neurosurgery

MOYAMOYA disease is a progressive occlusive cerebrovascular disease characterized by bilateral stenosis of the ICAs and the development of compensatory collateral vessels.25–27 It most often affects pediatric patients, but its presentation in the adult population is common. The clinical signs and symptoms are different in pediatric and adult patients. Whereas pediatric patients likely present with ischemia-related symptoms, adult patients often present with intracerebral hemorrhage.

During the last 20 years, several types of revascularization surgery have been undertaken in patients with moyamoya disease, especially pediatric patients.10,11,15,20,23 The authors of certain reports demonstrated the efficacy of these surgeries in preventing ischemic insults.1,4,8,9,12,16,18,22,24 On the other hand, it remains controversial whether revascularization surgeries effectively prevent future hemorrhage in adult patients.3,4,13,17 Because abnormally dilated collateral vessels, including aneurysm formations, have been considered the source of hemorrhage in adult patients,6,14,17,22,29 their angiographically documented reduction is necessary to prevent hemorrhagic potential. These issues are common among patients who undergo revascularization surgeries in childhood and have grown to adulthood.

There have been few reports, however, concerning long-term angiographic follow up in pediatric patients maturing into adulthood. Little is known about the long-term temporal profile of collateral formations, especially those arising in the posterior circulation, which would be responsible for hemorrhagic potential in adulthood.2,7,28 Thus, in this study we investigated, using long-term follow-up angiography, whether revascularization surgeries in childhood could reduce abnormal collateral formations from the posterior circulation.

Clinical Material and Methods

Between 1984 and 2002, we treated 23 pediatric patients who had moyamoya disease. Long-term follow-up angiographic studies were performed in six patients more than 7 years after revascularization surgery. The clinical data obtained in these patients are summarized in Table 1. All six patients presented with ischemic symptoms as the...
Collateral vessel formation in moyamoya disease

In the angiographic studies, the degree and temporal changes of abnormal collateral vessels were estimated compared with those on preoperative angiograms. The following were examined: 1) the severity of the angiographically documented stages; 2) the abnormal basal collateral vessels from the LSAs (basal moyamoya); 3) the abnormal collateral vessels from the AChA and dilation of the AChA; 4) the collateral vessels through the graft; 5) the collateral vessels from the OphA; 6) the abnormal collateral vessels from the PChA; 7) the abnormal collateral vessels from the posterior PerA; and 8) the leptomeningeal collateral vessels from the PCA.

The postoperative collateral circulation through the graft was estimated according to the method of Matsushima, et al., as follows: A, collateral formation supplied more than two thirds of the MCA distribution; B, between one third and two thirds of MCA distribution; and C, slight or no collateral formation. Basal moyamoya vessels were graded as 0 (absent), 1 (few), and 2 (dense), as reported by Morioka, et al.

Additionally, the degree of development of the collateral vessels from the AChA and PChA was graded as 0 (none), 1 (mild), and 2 (marked). The degree of development of the collateral vessels from the OphA was graded using the scale applied to basal moyamoya vessels. The degree of development of the collateral vessels from the PerA and the PCA was estimated in the same manner as for the choroidal arteries.

### TABLE 1

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Type</th>
<th>Age (yrs) at Onset</th>
<th>Admission Findings</th>
<th>Angiographic Stage*</th>
<th>Op (yrs)</th>
<th>Follow Up (yrs)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8, F</td>
<td>TIA (lt)</td>
<td>7</td>
<td>none</td>
<td>normal</td>
<td>rt II–III</td>
<td>EDAS</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>6, M</td>
<td>TIA (rt)</td>
<td>6</td>
<td>none</td>
<td>normal</td>
<td>lt normal</td>
<td>EDAS</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>3, F</td>
<td>TIA (complete stroke)</td>
<td>2</td>
<td>rt hemiparesis, speech disturbance</td>
<td>infarct (lt frontoparietal)</td>
<td>rt II</td>
<td>EDAS</td>
<td>16</td>
</tr>
<tr>
<td>4</td>
<td>9, F</td>
<td>TIA (rt)</td>
<td>7</td>
<td>none</td>
<td>normal</td>
<td>rt II</td>
<td>EDAS</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>4, F</td>
<td>headache</td>
<td>2</td>
<td>none</td>
<td>infarct (lt occipital)</td>
<td>rt III</td>
<td>EDAS</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>4, M</td>
<td>TIA (rt)</td>
<td>3</td>
<td>none</td>
<td>normal</td>
<td>rt III</td>
<td>EDAS</td>
<td>12</td>
</tr>
</tbody>
</table>

* Stage assessed using the classification of Suzuki and Takaku. See text for definition of stages. Abbreviation: CT = computerized tomography.
Results

Clinical Status

No patient received antiplatelet agents such as aspirin. Only one patient (Case 3) suffered hypertension and received medication to control it. In five of the six patients, normal development and absence of neurological deficits were demonstrated. All patients are doing well in school and social life. The remaining patient exhibited right-hand and speech disturbances but does not require assistance in daily activities; these neurological deficits were present preoperatively. There was no episode of stroke in any case between the perioperative periods and the time of writing.

Follow-Up MR Imaging Findings

Follow-up MR imaging was performed in all cases 12 to 18 years postoperatively. In all cases, no additional asymptomatic lesions were noted during the observation period.

Follow-Up CBF Findings

In all cases, CBF studies were performed 9 to 16 years postoperatively. In three patients, no definite perfusion defect was observed, and no abnormality was documented on MR imaging. In three patients areas of definite hypoperfusion were revealed, but these corresponded with the infarct areas on MR images.

Follow-Up Angiographic Findings

Long-term follow-up angiography was performed in all cases, and the intervals from the operation to the angiographic studies ranged from 7 to 12 years. In Case 1, the disease was unilateral at first and the patient underwent one-sided revascularization surgery; however, 4 years later the disease showed bilateral involvement, and the patient underwent revascularization surgery on the contralateral side. Thus, the actual duration from surgery to angiography was 8 and 4 years, respectively, according to side involved. The findings of long-term follow-up angiography are summarized in Table 2.

Only in the patient in Case 4 were bilateral, stabilized, angiographically documented stages present. On the right side of the circulation, where only faint collateral formation was noted, the progression of moyamoya disease was only slight and normal circulation from the ICA to the ACA and MCA was still preserved 12 years after surgery. There were no significant changes of collateral vessel formation.

In the other five cases, the angiographically documented stages advanced bilaterally and in three cases the angiography revealed nearly occluded ICAs bilaterally. In all sides of these five cases, the collateral circulation through the grafts developed well (Grade A in eight sides and Grade B in two sides). The collateral formations from the ethmoidal arteries and/or OphAs diminished in two cases. In one of these cases, both ICAs disappeared completely. In the other two cases, the collateral formation progressed after surgery. In one case, there was no obvious change.

In the nine sides of these five cases, collateral formation of the LSAs decreased after surgery. The results were the same for the collateral formations derived from the AChA, but the changes were more marked for these collateral vessels. In all nine sides, however, the natural progression of moyamoya disease might have been responsible for the reduction in these collateral vessels because the ICAs were nearly occluded in these sides.

In three of these five cases, the leptomeningeal collateral formations from the PCA also decreased. In the remaining two cases these collateral vessels were not so prominent on the preoperative angiograms. On the contrary, there was no reduction in the collateral formations from the PChAs and the PerAs in four of these five cases (Figs. 1–3). Only in the patient in Case 5 were angiographically documented reduction of these collateral formations demonstrated (Figs. 4 and 5).

Discussion

Although the number of cases was limited in this study,
indirect bypass surgery failed to reduce the abnormal collateral formations from the posterior circulation, especially those involving midline structures, during long-term observation.

The authors of several reports have demonstrated the efficacy of revascularization surgeries in reducing abnormal collateral formations.\textsuperscript{3,5,8,12,15,18,30} These effects have been observed shortly after surgery.\textsuperscript{3,5,8,12,30} Houkin, et al.,\textsuperscript{3} reported that significant changes in the abnormal collateral vessels were observed in 100% of pediatric cases and in 25% of adult cases after combined STA–MCA anastomosis and EDAS; however, they offered no detailed description of abnormal collateral vessels, and the duration between pre- and postoperative angiographic studies was not indicated.\textsuperscript{3} Yamada, et al.,\textsuperscript{30} reported on the efficacy of revascularization surgeries (EDAS) in reducing abnormal collateral vessels in pediatric patients; however, significant changes were only observed in basal moyamoya vessels, and there was no significant reduction in abnormal collateral vessels from the PCA. The follow-up periods were also less than 4 years. Irikura, et al.,\textsuperscript{5} reported on the EMS-induced reduction in abnormal collateral vessels from the choroidal arteries as well as basal moyamoya vessels in approximately two thirds of their pediatric patients; however, the reduction in leptomeningeal anastomosis from the PCA was less significant, and the follow-up periods were mainly less than 3 years.

Based on these data, the effect of revascularization surgeries on the reduction in anterior circulation of abnormal collateral vessels seemed to be definite, even shortly after surgery. Their effect on the reduction in abnormal posterior circulation collateral vessels, however, remains uncertain.
We also observed a reduction in abnormal collateral vessels on postoperative angiograms obtained within 1 year of surgery. The changes, however, were limited to basal moyamoya and collateral vessels from the AChAs (data not shown). Thereafter, as indicated in this study, these abnormal vessels would disappear according to the natural advancement of the disease, resulting in complete occlusion of ICAs. Thus, hemodynamic stress affecting these arteries that supply the midline structures might again increase after certain periods in which the effects of surgery could produce hemodynamic stability in these areas. According to the natural progression of the disease, the blood supply to these regions mainly depends on the collateral vessels deriving from the posterior circulation at advanced stages. Therefore, long-term observation, especially of these collateral formations, appears to be necessary.

The authors of several reports have indicated the source of intracerebral hemorrhage in moyamoya disease. The associated aneurysms in the circle of Willis or in the peripheral arteries have been attributed to hemorrhage.\(^{14,17}\) Such aneurysms, however, could not always be detected by angiography in all cases. In these cases, the rupture of abnormally dilated collateral vessels without aneurysm formation should be considered the major cause of hemorrhage.\(^{3,5,6,21}\) Morioka, et al.,\(^{22}\) insisted on the role of the AChA and posterior communicating arteries in hemorrhage risk. Irikura, et al.,\(^{6}\) also reported on the significance of abnormally dilated collateral vessels from the choroidal arteries in hemorrhagic potential. Despite the presence of aneurysm formation, hemodynamic stress may play an important role in the underlying mechanism of hemorrhage. Thus, because the progression of moyamoya disease could result in complete occlusion of ICAs, the hemorrhagic potential of abnormally dilated posterior circulation collateral vessels would increase as the disease advances.

Our data do not directly indicate that the patients in this study remain at potential risk of hemorrhage in the future. The fact that the revascularization surgery cannot always reduce the abnormal collateral formations form the posterior circulation, however, should be considered when evaluating the efficacy of the surgeries. The patients in this study are young (present age range 16–26 years). Since it was first indicated that the incidence of hemorrhage in moyamoya disease is high in middle-age adults,\(^{27}\) our observation period has not been long enough. Many patients who now undergo revascularization surgery in childhood live into their third to fourth decades of life.
Thus, further observation of these patients will allow us to determine the precise incidence of hemorrhage, and angiographic studies will help to elucidate these issues. It is also unclear whether different types of revascularization surgeries would have produced different results in the abnormal collateral vessels. Additionally, it remains uncertain whether additional surgical interventions would reduce abnormal collateral vessels. Direct bypass surgery performed in the posterior circulation might be an alternative strategy. In this study, however, the leptomeningeal collateral formations from the PCA decreased in certain cases. Despite these effects, the collateral formations derived from the PChAs and the PerAs did not decrease. Because these vessels supply the deep midline structures, the efficacy of a prophylactic anastomosis to the PCA remains unclear. An early indirect bypass surgery in the interhemispheric areas may be an alternative. Thus, additional surgeries in early childhood may be considered when follow-up angiography reveals the insufficient reduction of the posterior circulation collateral formations.

References

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