Conclusions—In pediatric-onset moyamoya disease, asymmetrical involvement of bilateral ICAs and PCAs was common, leading to the diagnosis of this disease were analyzed. In the excluded from this review. In 71 patients, the initial angiograms moya-like vascular changes due to other known causes were also this disease by cerebral angiography before the age of 16 years 85 patients (30 males and 55 females) who were diagnosed with development of abnormal netlike vessels called moyamoya at the base of the brain.1 Previous studies have indicated that the posterior cerebral artery (PCA) is frequently affected in this disease,2–4 and we recently observed several patients with the more advanced ICA and PCA lesions on ipsilateral sides. To clarify this predominant involvement in the ipsilateral ICAs and PCAs, we examined angiograms in 85 patients with childhood onset of moyamoya disease.

Subjects and Methods

Patients

Between 1980 and 2000, cerebral angiograms were performed in 186 patients with idiopathic moyamoya disease. Excluding the 101 patients who were diagnosed at age >16 years, we selected 85 patients (30 males and 55 females) who were diagnosed with this disease by cerebral angiography before the age of 16 years (childhood-onset patients). Patients with nonidiopathic or moyamoya-like vascular changes due to other known causes were also excluded from this review. In 71 patients, the initial angiograms leading to the diagnosis of this disease were analyzed. In the remaining 14 patients who had been diagnosed before 1980 with childhood-onset moyamoya disease but had only been treated medically (without surgery), follow-up angiograms obtained between 1980 and 2000 were analyzed because the initial angiograms were unavailable, were not of sufficient quality, or lacked vertebral angiograms. All the angiograms reviewed in this study were preoperative and were obtained when the patients were aged between 1 and 35 years (mean, 10±6 years). Among the 85 patients, revascularization surgery was eventually performed in 60 of these patients, and the remaining 25 patients were conservatively treated.

Angiographic Evaluations

In all patients, selective internal and external carotid arteriography or common carotid arteriography on both sides and vertebral arteriography on at least 1 side were performed. We evaluated angiographic findings in both hemispheres of all 85 patients, using 2 angiographic staging systems for the anterior and posterior circulations. The ICA lesions were evaluated by a 4-stage angiographic classification scale that was modified from that proposed by Suzuki and Takaku1 (Table 1). We also classified the steno-occlusive lesions in the PCA into 4 stages, as defined in our previous study (Table 2).4 We examined whether lesions with more advanced ICA and PCA stages were on the same side.

Interobserver Agreement

First, angiographic findings were independently reviewed by 2 radiologists blinded to the patients’ identity. When interpretations
Lesions in Patients With Moyamoya Disease*

TABLE 1. Angiographic ICA Staging of Steno-occlusive Lesions in Patients With Moyamoya Disease*

<table>
<thead>
<tr>
<th>ICA Stage</th>
<th>Angiographic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild to moderate stenosis around carotid bifurcation with absent or slightly developed ICA moyamoya: almost all of both ACA and MCA branches are opacified in antegrade fashion</td>
</tr>
<tr>
<td>II</td>
<td>Severe stenosis around carotid bifurcation or occlusion of either of proximal ACA or MCA with well-developed ICA moyamoya: either ACA or MCA branches or both are clearly defective, but at least several of ACA or MCA branches remain opacified in antegrade fashion</td>
</tr>
<tr>
<td>III</td>
<td>Occlusion of both proximal ACA and MCA with well-developed ICA moyamoya: only a few of either ACA or MCA branches or both are faintly opacified in antegrade fashion through the meshwork of ICA moyamoya</td>
</tr>
<tr>
<td>IV</td>
<td>Complete occlusion of both proximal ACA and MCA with absent or small amount of ICA moyamoya: without opacification of either ACA or MCA branches in antegrade fashion</td>
</tr>
</tbody>
</table>

ICA moyamoya indicates moyamoya vessels at or around the terminal part of the ICA.

*Modified from the staging system proposed by Suzuki and Takaku.1 When the proximal ACA was hypoplastic, stagings were determined by evaluating the proximal MCA involvement, opacification of MCA branches, and degree of development of ICA moyamoya.

were inconsistent, the final evaluation was reached by consensus. The initial interobserver agreement in interpreting angiograms by 2 radiologists was 91%.

Statistical Analysis

We examined whether lesions with more advanced ICA and PCA stages were on the same side on 3×3 tables with 2-tailed probabilities from Fisher’s exact test using PROC PHREG/Exact of the SAS statistical software package (SAS Institute Inc).5 Probability values <0.05 were considered significant.

Results

When positive laterality in individual patients was defined as the presence of a difference by ≥1 stage between the stages on both sides, there were lateralities in the ICA stages and in the PCA stages in 40 (47%) and 27 patients (32%), respectively.

Table 3 shows the relationship between laterality in the ICA stage and that in the PCA stage in all 85 patients. Most cases with laterality in the ICA stage showed no laterality of the PCA stage or had the more advanced PCA stage on the same side as the more advanced ICA stage. There was a significant tendency that the more advanced ICA and PCA stages were on the same sides (Table 3; P=0.024). Lateralities in both ICA and PCA lesions were found in 17 patients. In 14 (82%) of the 17 patients, the more advanced side of the ICA lesions was identical to that of the PCA lesions, while it was contralateral in 3 (18%). Among all 85 patients, there were 7 patients who showed a bilateral difference of ≥2 stages in the degree of ICA involvement. Among them, the more advanced side of the ICA lesions was identical to that of the PCA lesions in 3, was contralateral in 0, and was bilaterally the same as the PCA stages in 4 (including 2 patients without PCA involvement on either side). The Figure shows a typical case with more advanced ICA and PCA lesions on ipsilateral sides.

Forty of 58 patients with no laterality in the PCA stage were scored as PCA stage 1 (no PCA involvement) on both sides. PCA stage 1 on both sides was seen in 19 (48%) of 40 patients with laterality in ICA stages and in 21 (47%) of 45 without laterality in ICA stages. When the analysis was limited to 45 patients with unilateral or bilateral PCA lesions (excluding 40 patients with PCA stage 1 on both sides), the trend that the lesions with more advanced ICA and PCA stages were on the ipsilateral side was more probable in the statistical analysis (Table 3; P=0.006).

Discussion

Angiographic laterality in individual patients was common in both ICA and PCA systems (47% in ICA and 32% in PCA systems), with a significant probability for lesions with more advanced ICA and PCA stages to be on the same side. In the literature, similar characteristics were also shown in 2 childhood “unilateral” moyamoya cases, both of whom had steno-occlusive changes in the ipsilateral ICA and PCA without lesions in the contralateral ICA or PCA.6 The trend was also supported by the evidence in our study that in patients with positive laterality in ICA involvement by ≥2 stages, there were no cases who had lesions with more...
advanced PCA stages on the sides contralateral to the more advanced ICA involvement.

When we excluded 40 patients with PCA stage 1 on both sides, the trend that lesions with more advanced ICA and PCA stages were on the ipsilateral side was more probable in the statistical analysis. The difference in probability should be related to the high frequency of PCA stage 1 on both sides not only in patients without laterality in ICA stages (47%) but also in patients with such laterality (48%). We assumed that even in the patients with laterality in the ICA stages, if there were less advanced ICA stages, there was a tendency not to have any steno-occlusive PCA lesions (PCA stage 1, bilaterally). Indeed, a previous study has indicated that in hemispheres with the less advanced ICA lesions (Suzuki’s stage I to III), 75% of hemispheres did not demonstrate steno-occlusive PCA lesions (PCA stage 1), in contrast to the hemispheres with the more advanced ICA lesions (Suzuki’s stage IV to VI) revealing only 13% of hemispheres without PCA involvement.

Previous reports also showed positive correlation of the severity of ICA and PCA lesions in the ipsilateral hemispheres. Although the present study was not based on temporally serial angiographic findings in each patient, we speculate that steno-occlusive lesions might initially involve the ICA, and, with advances in the ICA lesions, involvement of the ipsilateral PCA might follow. If that is the case, even a patient without PCA lesions may develop steno-occlusive changes over time, which requires further study. Under this hypothesis, the hemisphere with a higher risk of progression to infarction and/or ischemia could be predicted by considering the predominant involvement in the ipsilateral anterior and posterior circulations. Thus, information on vascular changes might suggest the appropriate therapeutic strategy.

These characteristics in the relationship between the anterior and posterior circulations have not been demonstrated in other diseases that cause steno-occlusive vascular lesions in the central nervous system. In most other diseases with steno-occlusive change in the anterior circulation, the ipsilateral posterior circulation may develop more collateral pathways to compensate for decreased blood flow along with progressive involvement of the anterior circulation. Why does the PCA on the side with more severe involvement of the ICA tend to be affected to a greater degree in moyamoya disease? Although this question remains to be settled, we propose 2 hypotheses for this relationship between anterior and posterior circulations. The first is related to hemodynamic stress to the vascular endothelium. When the ICA is affected by steno-occlusive changes, the leptomeningeal collaterals from the ipsilateral PCA would develop to compensate for the reduced anterior circulation, as recent angiographic studies of childhood-onset moyamoya disease have described.

Increased blood flow through the PCA may cause hemodynamic stress to the vascular endothelium of the PCA, possibly resulting in steno-occlusive changes in that vessel on the side of the ICA involved.

The alternative hypothesis to explain this relationship between anterior and posterior circulations is based on previous electron microscopic study of the distribution of adrenergic nerve fibers. The ICA and proximal parts of the anterior cerebral artery (ACA) and middle cerebral artery (MCA) are innervated by the adrenergic nerve fibers from the superior cervical ganglion, and it has been supposed that hypertonicity of the fibers may cause constrictive narrowing of the distal ICA. The system from the superior cervical ganglion on 1 side proceeds backward from the distal ICA to the ipsilateral PCA via the posterior communicating artery. If hypertonicity of the system was involved in the pathogenetic mechanism of this disease, the PCA on the same side could also be affected after ICA involvement, but to a lesser degree. Thus, the fact that the more advanced sides of ICA and PCA lesions were frequently identical in this disease may be explained by this hypothesis.
In this study we introduced a new classification of steno-occlusive changes in the ICA by modifying the staging system proposed by Suzuki and Takaku. Their classification system was based mainly on temporally serial angiographic changes in intensification and decrease in moyamoya vessels. In brief, moyamoya vessels initially develop as occlusive changes in the ICA progress, then moyamoya vessels subsequently decrease when occlusive changes in the ICA become extremely severe. Although their classification system is widely known, its application to individual cases, ie, evaluation of intensification and minimization in moyamoya vessels, is often difficult on a single angiographic examination without the administration of temporally serial examinations in that individual. To evaluate angiographic staging more easily without temporally serial angiograms, in this study we reclassified the ICA system not on the basis of the degree of the development of moyamoya vessels but mainly on the severity of steno-occlusive lesions of the proximal part of the ACA/MCA and the degree of antegrade opacification of their branches.

In regard to moyamoya vessels, the ICA staging system adopted in this study generally corresponds to Suzuki’s staging, as follows: ICA stage I in this study corresponds to Suzuki’s stage I without moyamoya or stage II with “initiation” of moyamoya vessels; ICA stages II (Figure, panel B) and III (Figure, panel A) in this study correspond to Suzuki’s stage III with “intensification” of moyamoya or stage IV with “minimization” of moyamoya; ICA stage IV in this study corresponds to Suzuki’s stage V with “reduction” of moyamoya or stage VI with “disappearance” of moyamoya. In regard to PCA staging, we used the classification adopted in the previous study, which was devised mainly on the basis of steno-occlusive PCA lesions along with the degree of PCA moyamoya vessels.

In conclusion, our study shows that asymmetrical involvement of bilateral ICAs and PCAs was common, and the ipsilateral ICA and PCA tended to be predominantly involved in childhood-onset moyamoya disease.

References
Predominant Involvement of Ipsilateral Anterior and Posterior Circulations in Moyamoya Disease
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