

Analysis of Relationship between Brain Ischemia and Angiographic feature in Childhood Moyamoya DiseaseZHANG Zhiying¹, WANG Li², WU Jun¹, XU Yuming^{3,*}

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Abstract: In 39 patients with childhood-onset moyamoya disease, angiograms were reviewed for stenooclusive lesions, and CT scans, MR images, or both were reviewed for the sites and extent of cerebral infarction. The relationship between the angiographic and CT/MR findings was examined. The prevalence and degree of stenooclusive lesions of the posterior cerebral artery (PCA) significantly correlated with the extent of lesions around the terminal portion of the internal carotid artery (ICA). The prevalence of infarction significantly correlated with the degree of stenooclusive changes of both the ICA and PCA. Infarctions tended to be distributed in the anterior borderzone in less-advanced cases. Our results indicate that progressive changes of the anterior and posterior circulations are associated with the distribution of cerebral infarction, culminating in a patchily disseminated infarction on CT and MR studies in late stages of the disease.

[ZHANG Zhiying, WANG Li, WU Jun, XU Yuming. **Analysis of Relationship between Brain Ischemia and Angiographic feature in Childhood Moyamoya Disease.** *Life Sci J* 2012;9(4):1208-1211] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 180

Keywords: brain ischemia; cerebral angiography; moyamoya disease

1. Introduction

Moyamoya disease is a rare cerebrovascular occlusive disorder of unknown origin (1–4). It is divided into two types according to whether the onset occurs in childhood or adulthood (5). The main features of moyamoya disease are bilateral stenooclusive changes at and around the internal carotid artery (ICA) bifurcation along with a distribution of abnormal netlike vessels in the basal regions, called moyamoya (3). Although changes similar to those around the ICA can also be found in the posterior circulation, few reports have dealt with the posterior circulation in this disease (6, 7). In childhood-onset moyamoya disease, progression of cerebral infarction is considered to occur with an advancing stenooclusive process. However, no large-scale study has been undertaken to evaluate how the severity of stenooclusive vascular lesions in the anterior and posterior cerebral circulations is related to the development of cerebral infarction. Recent evidence indicates that the frequency of cerebral infarction positively correlates with the progression of posterior cerebral artery (PCA) lesions (7), but the relationship between the location and extent of infarction and the degree of stenooclusive PCA changes remains to be defined.

We studied the relationship between changes in the posterior and anterior circulations on angiograms and the frequency and extent of cerebral infarction on CT scans and MR images, or both, in 39 patients with childhood-onset moyamoya disease.

2 Methods

Between 1999 and 2011, 39 patients with children seen at our institution were confirmed to have moyamoya disease at angiography. 13 patients were male and 26 female; all patients were under 14 years of age (mean, 8 ± 3 years) at the onset of symptoms. The average interval from the onset of symptoms to angiography was 5 years. None of the 39 patients had any other underlying disease, consistent with a diagnosis of idiopathic moyamoya disease. The initial manifestations of disease were transient ischemic attack or cerebral infarction in 36 patients; the other three patients presented with intraventricular hemorrhage at the age of 6 years, thalamic hemorrhage at the age of 6 years, and putaminal hemorrhage at the age of 10 years, respectively.

All 39 patients underwent cerebral angiography, including bilateral internal and external or common carotid arteriography, and unilateral or bilateral vertebral arteriography. All 39 patients were examined by CT ($n = 39$), and 27 additionally underwent MR imaging. All CT and MR studies analyzed were performed within 1 month of cerebral angiography.

We applied two angiographic staging systems for the anterior and posterior circulations. We classified stenooclusive changes of the supraclinoid ICA into six angiographic stages as defined by Suzuki et al (3): stage I, narrowing of the carotid bifurcation only; stage II, dilatation of the main cerebral arteries with appearance of moyamoya vessels at or around the

terminal part of the ICA (ICA moyamoya); stage III, partial disappearance of the middle (MCA) and anterior (ACA) cerebral arteries with intensification of ICA moyamoya at the base of the brain; stage IV, advanced stenocclusive changes in the ICA (ACA and MCA are traced very dimly or in a completely different shape through the mist of the ICA moyamoya) with a small amount of ICA moyamoya; stage V, absence of the ACA and MCA with further reduction of the ICA moyamoya; and stage VI, blood supply only from the external carotid artery and almost complete disappearance of ICA moyamoya

The leptomeningeal collateral circulation frequently develops from the cortical branches of the PCA and from the posterior pericallosal arteries. The leptomeningeal collateral circulation from the PCA was subjectively classified into one of the following four grades according to its extent: good, cortical branches in all three frontal, parietal, and temporal lobes being more or less opacified; moderate, cortical branches in two of the three lobes opacified; poor, cortical branches in either the parietal or the temporal lobe opacified; none, no substantial collateral circulation.

CT and MR studies were reviewed to determine the location and number of cerebral infarctions. The number of infarctions was counted according to the regions involved, as described below. One continuous lesion involving two or more adjacent zones was regarded as two or more infarctions. Zones in the hemisphere were divided into the following eight regions: the territory of the ACA; the anterior half of the territory of the MCA (ant-MCA); the posterior half of the territory of the MCA (post-MCA); the territory of the PCA; the basal ganglia; and the thalamus. The ant-MCA and post-MCA were divided at the central sulcus, and the temporal lobe was included in the post-MCA.

Angiographic findings and CT and MR images were evaluated by two radiologists blinded to the patients' identity. CT and MR images were interpreted without knowledge of the angiographic findings. When interpretations were inconsistent, the final evaluation was reached by consensus. The interobserver agreement between the two radiologists was good: 94% in the interpretation of CT scans, MR images, or both, and 84% in the interpretation of angiograms.

The data were analyzed statistically by one of three methods: Spearman rank correlation, Mann-Whitney U-test, or Kruskal-Wallis rank test. Values of $P < .05$ were considered statistically significant.

3 Results

Of the 39 patients, 22 (56%) were found to have stenocclusive lesions in one or both PCAs; 35 PCAs (45%) in 78 sides showed stenocclusive changes. The relationship between the ICA and the PCA stages of stenocclusive lesions is summarized in Table 1. The

degree of stenocclusive PCA changes significantly correlated with ICA stage (Spearman rank correlation, $P < .0001$). Of the 19 sides with the most advanced stages involving the anterior circulation (ICA stages V or VI).

Leptomeningeal Collaterals from the PCA

Among the 78 sides, leptomeningeal collaterals from the PCA were seen in 42 sides (53%). These collaterals were scant in sides with ICA stage I and tended to be best developed in sides with ICA stage II or III. As the ICA stage advanced from III to VI, the degree of leptomeningeal collaterals from the PCA decreased significantly (Spearman rank correlation, $P < .0001$). Of seven sides with ICA stage VI, representing the most advanced disease, only one (14%) had collaterals, which were very poorly developed. Also, there was a significant negative correlation between the PCA stage and the degree of leptomeningeal collaterals from the PCA (Spearman rank correlation, $P < .0001$). (show in Fig 1).

Brain ischemia

Brain ischemia was demonstrated in 36 (46%) of 78 hemispheres. There was a significant positive correlation between the ICA staging and the number of infarcted regions (Spearman rank correlation, $P < .0001$). Furthermore, except for the ACA territory, the more advanced the ICA stage, the more posterior regions were involved (Kruskal-Wallis rank test, $P = .0005$).

The frequency of cerebral infarctions in the five regions other than the ACA territory significantly correlated with PCA stage. Furthermore, except for the ACA territory, the more advanced the PCA stage, the more posterior regions were involved (Kruskal-Wallis rank test, $P < .0001$). Among the 9 sides with PCA stage 2, and the ant-MCA and post-MCA regions were more frequently involved than in PCA stage 1.

Table 1. Click on image to view larger version

ICA stage of stenocclusive lesions (side)		PCA stage of stenocclusion lesions			
		1	2	3	4
I	4	3	1	0	0
II	8	7	0	1	0
III	36	15	6	15	0
IV	13	4	3	5	1
V	4	1	0	1	2
VI	3	0	0	2	1
Total	78	30	10	24	4

Note number indicate the number of sides according to stage

Fig 1

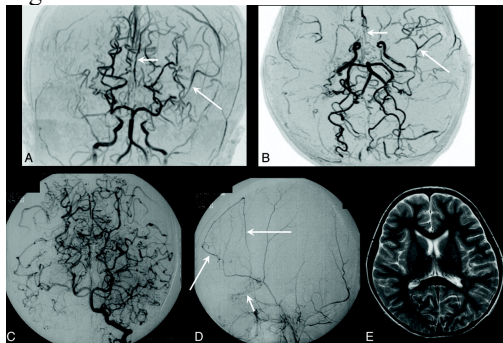


Fig 1 . A 7-year-old girl (diagnostic age group, 4–7 years) who had recurrent transient left hemiparesis for 5 years was diagnosed with Moyamoya disease, which manifested clinically as TIA. *A* and *B*, time-of-flight MR angiograms show advanced steno-occlusive changes at or around the terminal part of the right ICA, with poorly visualized ACA and MCA branches (ICA stage III, right). Moderate steno-occlusive changes at or around the terminal part of the left ICA with relatively good visualization of the ACA (*small arrows*) and MCA (*large arrows*) cortical branches (ICA stage II) are seen on the left. No steno-occlusive lesions are seen bilaterally in the posterior cerebral artery (PCA stage 1, bilaterally). *C*, Anteroposterior view of the vertebral angiogram shows no steno-occlusive lesions bilaterally in the PCA and well-developed leptomeningeal collateral circulation to the anterior circulation. *D*, Left lateral external carotid angiogram shows dilated anterior branches of the middle meningeal artery providing transdural collaterals to the contralateral frontal region (*large arrows*), with the medial branches of the maxillary artery providing transdural collaterals to the right anterior basal region (*small arrow*). Two transdural collaterals can be seen on the right, and none are seen on the left (anteroposterior view of the left external carotid angiogram, not shown). *E*, T2-weighted MR image shows no infarction bilaterally. Note that in this patient, the steno-occlusive changes do not involve the PCA, even in the right hemisphere, where ICA lesions are advanced (stage III).

4 Discussion

Moyamoya disease is characterized by bilateral stenoocclusive changes at or around the terminal part of the ICA, with the development of abnormal netlike vessels, called moyamoya, at the base of the brain (3). Previous studies have focused on stenoocclusive changes of the anterior circulation, and PCA involvement is not included in the diagnostic criteria for this disease (8). Only a few studies have evaluated the posterior circulation (6, 7), even though the PCA is frequently affected in this disease. We found stenoocclusive changes of the PCAs in 58% of the 69

patients, with involvement of 62 (45%) of 137 hemispheres. The frequency is generally consistent with the findings of previous studies (6, 7).

In our series, the frequency of PCA involvement positively correlated with the ICA stage. This finding agrees with the recent work of Yamada et al (7), although the frequency of PCA involvement we observed in hemispheres with the most advanced ICA stages was quite different from theirs. ICA stages V and VI in our study correspond to ICA stage 5 in the classification used by Yamada et al. In hemispheres with such advanced ICA stages, the frequency of stenoocclusive PCA changes was 95% among our cases, in contrast to 59% in the study of Yamada et al. Although we have no obvious explanation for this large difference, it might have resulted from the difference in age of disease onset between the two studies. In our study, all patients were under 15 years of age (mean, 6 ± 3 years) at onset, whereas the study of Yamada et al included patients with adult-onset disease, resulting in a mean onset age of 10 ± 12 years; the difference in onset age between the two studies is statistically significant (Welch's t-test; $P = .006$). We suspect, therefore, that vascular changes might progress faster in childhood (ie, the earlier the onset of disease, the faster PCA involvement may develop). Indeed, previous serial angiographic studies of patients with childhood-onset moyamoya disease have documented that the disease progresses up to adolescence but stabilizes or progresses very slowly after adulthood, and not all patients with moyamoya disease reach ICA stage V or VI (9).

We classified stenoocclusive changes of the PCA in accordance with the classification for the anterior circulation proposed by Suzuki et al (3). Their classification was based on the relationship between stenoocclusive changes of the main trunk and the intensification of and decrease in moyamoya vessels. In brief, collaterals, including moyamoya vessels, initially develop as occlusive changes of the ICA progress, and moyamoya vessels subsequently decrease when occlusive changes of the ICA become extremely severe. Such serial changes have been documented by follow-up angiograms (3). Although our PCA staging was not based on serial angiographic findings, the close relationship between ICA and PCA stages in our study supports that disease severity progresses in the posterior circulation in a similar manner to that in the anterior circulation. With progression of disease, occlusive changes are thought to occur initially in the proximal part of the PCA, with subsequent development of the PCA moyamoya (PCA stage 2) followed by gradual progression of stenoocclusive changes in the PCA and intensification of the PCA moyamoya (PCA stage 3). Finally, when the PCA is completely occluded, cortical branches are unopacified,

and the PCA moyamoya vessels decrease (PCA stage 4).

Cerebral infarctions in the MCA territory, the PCA territory were closely associated with stenocclusive changes in the PCA. Thus, when we see cerebral infarctions in the MCA territory, stenocclusive changes in the PCA are highly likely. Stenocclusive PCA changes are most probable, especially when the PCA territory is involved.

The positive correlation between the number of infarcted regions and ICA and PCA stage indicated a gradual extension of infarction in this disease. We postulate that the progression of stenocclusive PCA changes is closely related to such a pattern of development of cerebral infarction.

Kuroda et al (9) found that the occurrence of cerebral infarction did not correlate with stenocclusive ICA changes, but correlated with stenocclusive PCA changes, although stenocclusive ICA and PCA changes correlated with each other. In the present series, however, the frequency of cerebral infarction significantly correlated with the severity of both stenocclusive ICA and PCA changes. This discrepancy between the present study and that of Scott et al may reflect large difference in the frequency of PCA involvement in the hemispheres with the most advanced ICA stages, as noted above (95% vs 59%)(10).

Conclusion

We found that the severity of stenocclusive lesions in the PCA correlated positively with the severity of the stenocclusive ICA changes in childhood-onset moyamoya disease. Infarctions tended to be distributed in the anterior borderzone in the less advanced cases, while in the more advanced cases, lesions were additionally found posteriorly in the territory of the middle cerebral artery, the posterior borderzone, and the PCA territory.

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10/2/2012