Posterior circulation in moyamoya

To The Editor: We read with great interest the article by Hishikawa et al.1 (Hishikawa T, Tokunaga K, Sugiu K, et al: Assessment of the difference in posterior circulation involvement between pediatric and adult patients with moyamoya disease. Clinical article. J Neurosurg 119:961–965, October 2013), which clearly shows the clinical significance of stenoo-cclusive posterior cerebral artery (PCA) lesions responsible for infarction development in both pediatric and adult patients. In moyamoya disease, the leptomeningeal collaterals from the PCA are actually the only effective collateral suppliers of blood to the anterior circulation because bilateral steno-occlusive involvement in the terminal internal carotid artery (ICA) and proximal anterior and middle cerebral arteries prevents the development of leptomeningeal collaterals from each other and collaterals through the circle of Willis. Therefore, the steno-occlusive changes to the PCA give rise to the development of infarction in this disease process.

We completely agree with the authors’ finding that even less advanced steno-occlusive lesions in the ICA are associated with ipsilateral steno-occlusive PCA lesions in pediatric patients, while the severity of the steno-occlusive lesions in the ICA and the prevalence of ipsilateral PCA lesions correlated positively in both pediatric and adult groups. We believe this finding indicates that the vascular changes in this disease affect the PCA earlier in children than in adults, although they initially affect the ICA, and then the PCA in both children and adults. In pediatric patients, specifically those younger than 4 years of age, the earlier the age of onset, the earlier is PCA involvement with resultant ischemic strokes, with infarctions rather than transient ischemic attacks, even in cases of less advanced ICA lesions.3 This supposition goes along well with the discovery by Miyatake et al. of the homozygous c.14576G>A variant of ring finger protein 213 (RNF213) in the severe form of moyamoya disease.2 The homozygous c.14576G>A variant varies from a homozygote type to a heterozygote or wild type, either of which exhibited less advanced PCA lesions than did the homozygote type. Therefore, we hypothesize that the different genetic variants of c.14576G>A of RNF213 may partly explain not only the difference in the age of onset—that is, pediatric or adult—but also the differential degrees of involvement that Hishikawa et al. found between the ICA and PCA.

Indeed, whether the pathomechanism of pediatric and adult moyamoya disease is the same has long been discussed.4 Some authors have speculated that individuals diagnosed in adulthood include patients whose disease process begins in childhood, based on serial follow-up angiograms showing that the disease progresses up to adolescence but stabilizes or progresses slowly after adulthood is reached,1 and the disease does not progress in most adult patients.3,6 In that case, the results of Hishikawa et al. might be interpreted as indicating that patients with later PCA involvement survive childhood and adolescence when the lifetime vascular demand is highest, without developing ischemic symptoms, and reach adulthood (adult-onset moyamoya disease). Conversely, for children with earlier PCA involvement, such patients are more likely to develop ischemic symptoms before they reach adulthood (child-onset moyamoya disease).

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Disclosure
The authors report no conflict of interest.

References

Response: We greatly appreciate the thoughtful comments offered by Drs. Mugikura and Takahashi. The anterior circulation (AC) has been reported to be involved in the origination of moyamoya disease based on the results of historical angioarchitecture analysis.3 A complementary relationship between the AC and the external carotid artery (ECA) system is involved in the pathophysiology of moyamoya disease.1 Suzuki and Takaku’s angiographic stages were graded based on a presumption of this complementary relationship and have traditionally played the leading role in evaluating disease progression. There is also a significant interaction between AC and posterior
circulation (PC) in moyamoya disease.\textsuperscript{4} Under the complex pathophysiological relationship linking AC, PC, and the ECA system in moyamoya disease, one patient may exhibit ischemic complications while another exhibits hemorrhagic complications. Moreover, one patient may develop symptoms during childhood while another does so during adulthood. This multiplicity of symptomatology in moyamoya disease is mysterious, and its mechanism has been debated for many years.

The PC functions as a main collateral pathway to the AC in moyamoya disease. The impact of the PC on hemodynamic ischemia is significantly greater than that of AC,\textsuperscript{5} but our investigation demonstrated that PC involvement was of little relevance to hemorrhagic-type moyamoya disease.\textsuperscript{2} In our patient cohort, the clinical significance of PC involvement in ischemic-type moyamoya disease was similar between pediatric and adult patients: 26\% of pediatric and 33\% of adult patients exhibited PC involvement. The only significant difference was that pediatric patients with PC involvement had significantly less advanced AC involvement than adult patients. If the interaction between the AC and PC started in childhood and progressed uniformly, the prevalence of adult patients with PC involvement would be higher than that of pediatric patients with PC involvement. Instead, the similarity in the prevalence of PC involvement in pediatric and adult patients in this study indicates the existence of distinct patterns of interaction between the AC and PC in moyamoya disease. The theory proposed by Drs. Mugikura and Takahashi is a valid explanation for our results and we completely agree with it.

There could be 2 patterns of interaction between the AC and PC: one an early form of interaction and the other a delayed form. In patients with an early interaction, PC involvement complicates less advanced AC involvement and causes symptoms during childhood. In patients with a delayed interaction, PC involvement correlates with advanced AC involvement and causes onset during adulthood.

Rapid developments in the realm of genetic analysis of moyamoya disease have been seen in recent years. In particular, the discovery of the \textit{RNF213} gene is noteworthy as a new approach to pathophysiology of moyamoya disease. The homozygous c.14576G>A variant of RNF213 has been reported to be correlated with a particular clinical phenotype of moyamoya disease—namely, younger age at onset, cerebral infarction, and PC involvement.\textsuperscript{3} The regulation of early and delayed interaction between AC and PC involvement by this variant of \textit{RNF213} genotype is one possible mechanism that could be responsible for the distinct patterns of interaction between the AC and PC in moyamoya disease. According to this hypothesis, pediatric patients without PC involvement might develop PC involvement in adulthood if they have the delayed-interaction pattern. In the light of this point, periodic and careful observation is important in pediatric patients with moyamoya disease.

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\textbf{Mammillary body angle and craniopharyngioma}

To \textbf{The Editor:} We read with great interest the article by Pascual et al.\textsuperscript{3} (Pascual JM, Prieto R, Carrasco R, et al: Displacement of mammillary bodies by craniopharyngiomas involving the third ventricle: surgical-MRI correlation and use in topographical diagnosis. Clinical article. \textit{J Neurosurg} 119:381–405, August 2013). We congratulate Prof. Pascual and his colleagues. They evaluated the diagnostic accuracy of MRI to define the precise topographical relationships between intraventricular craniopharyngiomas (CPs), the third ventricle, and the hypothalamus and provided novel methods, the type of mammillary body displacement, and the mammillary body angle (MBA), to differentiate primary third ventricular CPs and primary suprasellar CPs.

We would like to address two complementary issues with respect to the change in MBA: 1) The authors mentioned “In 69\% of pseudointraventricular cases the value of the MBA was greater than 120° (obtuse angle) and only 6\% of lesions belonging to this topographical category displayed an MBA less than 90°.” The exceptional case was described in a report by Dusick et al.\textsuperscript{1} In our series of CPs, there were cases in which the MBA measured less than 90° as well (Fig. 1A and B). We find the common point is that those tumors were located anterior to the pituitary stalk (preinfundibular type), which was confirmed intraoperatively in our cases. In this condition, the third ventricle floor (TVF) is intact, the tumor compresses the third ventricle anteriorly, or the origin of force

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