Response to Letter Regarding Article, “Hemorrhagic Moyamoya Disease in Children: Clinical, Angiographic Features, and Long-Term Surgical Outcome”

We thank Dr Hanqiang Jiang for his thoughtful and constructive comments on our article. Given the limitation of the manuscript format, we were not able to show all the results in our manuscript.

Moyamoya disease (MMD) is a complicated cerebrovascular disease. Previous studies on adult MMD patients have considered the rupture of pseudo-microaneurysms, presence of moyamoya vessels, and the abnormal dilation of anterior choroidal artery and posterior communicating artery as the most possible causes for intracranial hemorrhage. Yet in the report of our pediatric case series, absence of the above features was also encountered in several children. Hence, we agree that further studies on the cerebral microbleeds may be helpful in a better understanding of the nature of bleeding in children with hemorrhagic MMD.

In our report, we show that revascularization surgery leads to significant decrease of moyamoya vessels (11/15, 73.3%), compatible to the previous observation by others that revascularization surgery accelerated the disappearance of moyamoya vessels and other occlusive changes in the distal internal carotid artery in adult patients. However, no significant improvement in anterior choroidal artery–posterior communicating artery dilation were seen in our pediatric patients. One patient in our study with intraventricular hemorrhage still suffered rebleeding of the same hemisphere located in the basilar ganglia after revascularization surgery and died. Similar to our results, the Japan Adult Moyamoya (JAM) Trial reported 42 patients with direct revascularization surgery, and 5 patients suffered rebleeding during the follow-up period.

Hence, we recognize that the revascularization surgery could not completely prevent recurrent hemorrhage, and the specific roles of the moyamoya vessels, anterior choroidal artery, posterior communicating artery need to be further investigated.

Recently, hemodynamic study on MMD found that hemodynamic stress was considered as the primary cause for the episode of bleeding in hemorrhagic MMD. However, in MMD patients, hemorrhage type and collateral pattern are individualized and complicated, and change of hemodynamic stress is more prone to ischemic stroke than to hemorrhage. A quantitative assessment of the cerebral hemodynamics by computed tomographic/magnetic resonance perfusion, single photon emission tomography, or positron emission tomography-computed tomography can only serve as a reference. As to the 374 children (ischemia 344; hemorrhage 30) in our study, decreased hemodynamic status was more prominent in the ischemia children (95.5% versus 21.7%; P<0.05) as revealed by positron emission tomography. Therefore, the relationship between the hemodynamic status and advent of intracranial hemorrhage remains unclear.

Recent studies from the perspective of gene mutations, molecular fingerprints of specific proteins to the change of vessel wall all indicated the distinctive features of hemorrhagic MMD. DNA sequence analysis of 170 MMD cases from Chinese Han population identified the relationship between RNF213 mutation and MMD susceptibility and also showed that R4810K and A4399T mutations were different between ischemic and hemorrhagic MMD. In 2013, Sigdel et al validated 165 antibodies-associated MMD and identified a subset of 6 candidate MMD-specific autoAbs, including APP, GPS1, STRA13, CTNNB1, ROR1, and EDIL3. As to the 6 proteins, antibody APP functioned as an increased risk of hemorrhage stroke. Our recent study on the high-resolution magnetic resonance imaging of the arterial vessel wall also showed that hemorrhagic MMD possessed some distinct features from the ischemic MMD, and all episodes of intracranial hemorrhage occurred in the patients without a plaque. Hence, larger case samples and more comprehensive studies are needed to further understand the pediatric hemorrhagic MMD in the future.

Disclosures

None.

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