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Case Report

Case of *de novo* cerebral microbleeds in ischemic-type pediatric moyamoya disease

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ABSTRACT

Background: Studies on pediatric patients with moyamoya disease who presented with *de novo* cerebral microbleeds (CMBs) are extremely rare.

Case Description: Herein, we report a 7-year-old boy with moyamoya disease who had *de novo* CMBs during treatment. He presented with transient left-side motor weakness and was diagnosed with moyamoya disease. He underwent revascularization surgery on the right cerebral hemisphere. Six months after the surgery, he presented with transient right-side motor weakness and MRA revealed progression of stenosis in the left middle cerebral artery. After another 3 months, three *de novo* CMBs were identified. He underwent revascularization surgery on the left side. The symptom disappeared completely after surgery and no additional *de novo* CMBs were identified 1 year after surgery.

Conclusion: This is the first report on *de novo* CMBs in pediatric patients. Although the significance of *de novo* CMBs in pediatric patients is completely unknown, attention should be paid to not only ischemic stroke but also hemorrhagic stroke. Although the short-term course is good in the current case, follow-up period is too short to assess for rebleeding and long-term follow-up is still important. Further, more cases should be collected.

Keywords: *De novo* cerebral microbleeds, Pediatric moyamoya disease, periventricular anastomosis

INTRODUCTION

Cerebral microbleeds (CMBs) are commonly detected on T2*-weighted imaging (T2*WI) and susceptibility-weighted imaging (SWI) in patients with moyamoya disease.[7,9-14,16-19] Asymptomatic CMBs can be a predictor of hemorrhagic stroke in adult patients with moyamoya disease.[14,17] In addition, *de novo* CMBs can be observed during follow-up.[9,14,21] However, there are several unclear points about this notion. Hemorrhagic stroke is primarily attributed to long-term hemodynamic stress in dilated and fragile moyamoya blood vessels, which are commonly adult-onset.[7,14,20] Therefore, almost all studies on microbleeds have targeted adult patients with moyamoya disease. Transient ischemic attack (TIA) or ischemic infarcts are common in pediatric patients with moyamoya disease. However, hemorrhage is not.[1-4] Therefore, there are extremely few reports on CMBs in pediatric patients with moyamoya disease, and previous studies have not assessed for *de novo* CMBs. Herein, we report a case of *de novo* CMBs during treatment in a pediatric patient with moyamoya disease.

CASE DESCRIPTION

A 7-year-old boy initially presented with transient left-side motor weakness and then visited the pediatric department of a local hospital. He was diagnosed with moyamoya disease based on magnetic resonance angiography (MRA) results [Figure 1a] and was then referred to the neurosurgical department of our hospital. Repeat TIA did not occur, and the patient was then followed up in the outpatient department. Right middle cerebral artery (MCA) stenosis progressed during the 1-year follow-up [Figure 1b]. Hence, the risk for TIA gradually increased. Single-photon emission computed tomography with iodine-123 iodoamphetamine (^{123}I-IMP SPECT) revealed preserved cerebral blood flow (CBF) and a significant decrease in vascular reserve in the right hemisphere [Figure 1c and d]. The patient underwent direct and indirect revascularization surgery on the right cerebral hemisphere. The symptoms disappeared after surgery, and the patient was followed up again in the outpatient department. He presented with transient right side motor weakness 6 months after surgery. MRA revealed good angiogenesis from the external carotid system to the right cerebral hemisphere and progression of stenosis in the left MCA [Figure 2a]. ^{123}I-IMP SPECT showed preserved CBF and a significant decrease in vascular reserve in the left hemisphere [Figure 2b and c]. T2*WI and SWI revealed the absence of CMBs in the left hemisphere [Figure 3a and b]. However, three *de novo* CMBs were identified after 3 months [Figure 3c and d]. No cerebral aneurysm was detected on digital subtraction angiography of the left internal carotid and left vertebral arteries [Figure 4a and b]. The abnormal collaterals from the anterior choroidal artery form periventricular anastomosis, which continued to the MCA through the medullary artery [Figure 4a-c]. The CMBs occurred on the peripheral side of the abnormal collaterals. In addition to the exacerbation of ischemic symptoms due to left MCA stenosis, the patient was considered at risk for hemorrhagic stroke. Thus, he underwent direct and indirect revascularization surgery on the left side. The symptom disappeared completely after surgery, and magnetic resonance imaging showed good angiogenesis from the external carotid system to the left cerebral hemisphere [Figure 5a]. No additional de novo CMBs were identified 1 year after surgery [Figure 5b and c]. Further, MRA revealed

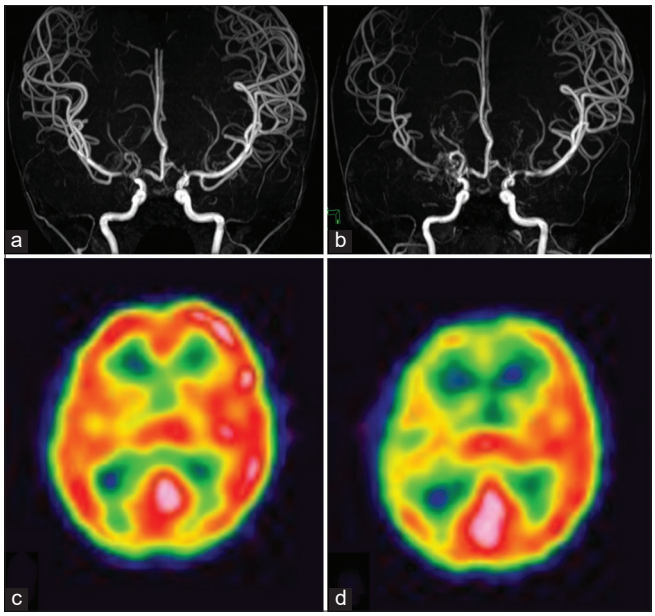

Figure 1: (a) Initial magnetic resonance angiography (MRA) showed stenosis in the terminal portion of the bilateral internal carotid artery. (b) MRA performed after 1 year revealed progression of stenosis in the right middle cerebral artery. (c and d) Single-photon emission computed tomography with iodine-123 iodoamphetamine revealed preserved cerebral blood flow and a significant decrease in vascular reserve in the right hemisphere.

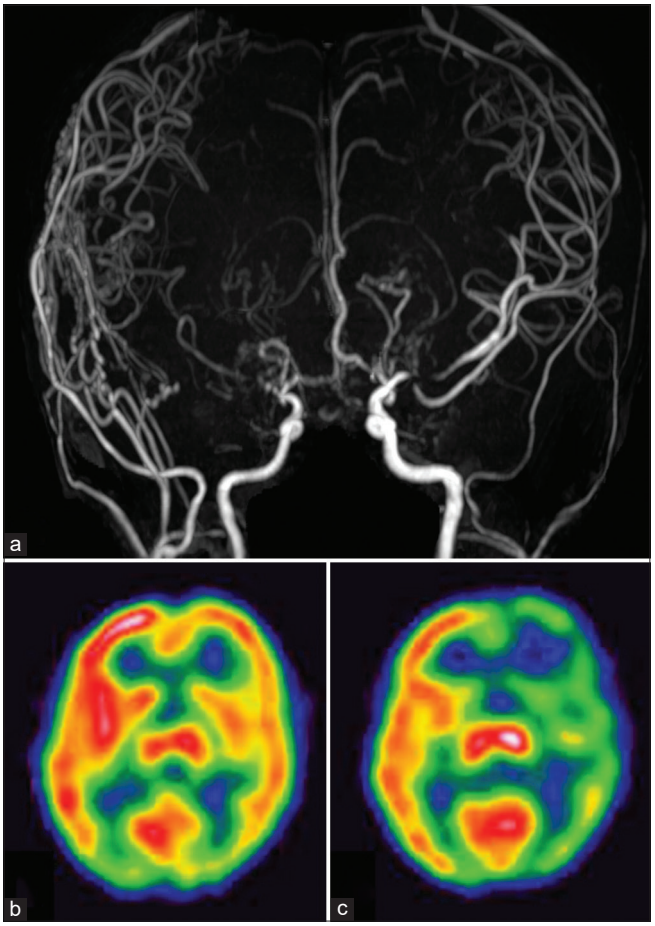

Figure 2: (a) Magnetic resonance angiography revealed good angiogenesis from the external carotid system to the right cerebral hemisphere and progression of stenosis in the left middle cerebral artery. (b and c) Single-photon emission computed tomography with iodine-123 iodoamphetamine showed preserved cerebral blood flow and a significant decrease in vascular reserve in the left hemisphere.

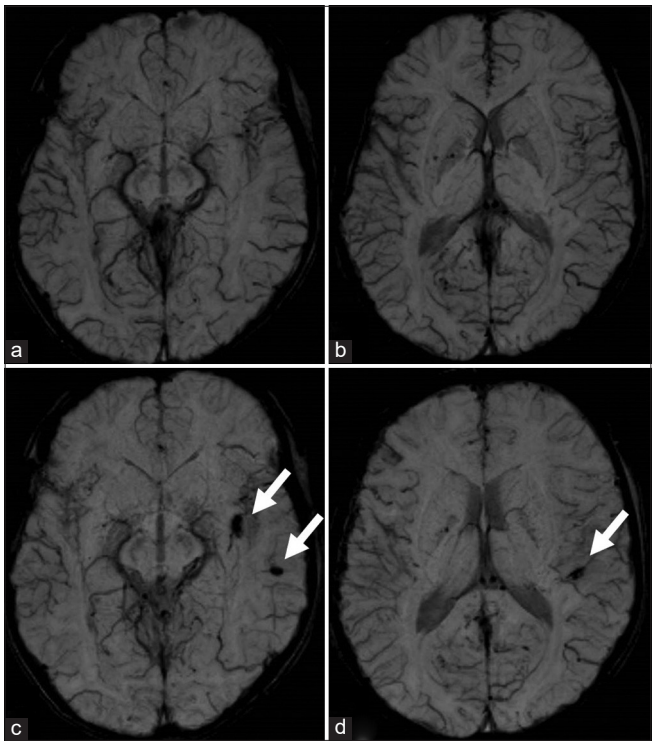

Figure 3: (a and b) Six months after the initial surgery, susceptibility-weighted imaging (SWI) revealed the absence of cerebral microbleeds (CMBs) in the left hemisphere. (c and d) Nine months after the initial surgery, SWI showed three *de novo* CMBs in the left hemisphere (white arrows).

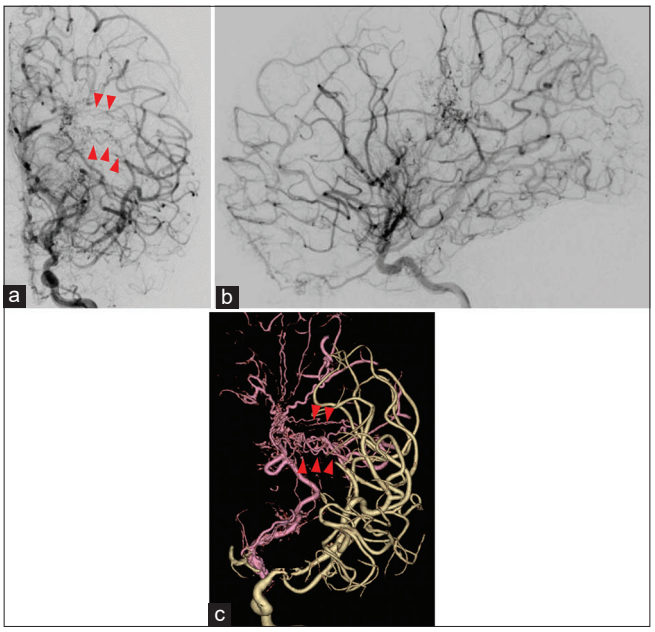

Figure 4: Anteroposterior (a) and lateral (b) views on the left internal carotid angiography revealed the absence of cerebral aneurysm. Left internal carotid angiography (a) and three-dimension reconstruction angiography (c) revealed the abnormal collaterals from the anterior choroidal artery form periventricular anastomosis, which continued to the middle cerebral artery through the medullary artery (red arrowheads).

shrinkage of the anterior choroidal artery and disappearance of abnormal collaterals [Figure 5d and e].

DISCUSSION

In adult moyamoya disease, intracerebral and intraventricular hemorrhage is a major symptom, and it can be caused by the rupture of dilated and fragile moyamoya vessels caused by long-term hemodynamic stress. Recently, it has been shown that moyamoya vessels flow back into the medullary artery through periventricular anastomosis and perfuse the cerebral cortex, and vulnerability of periventricular anastomosis is considered to be the cause of hemorrhage. Funaki *et al.* classified the periventricular anastomosis into three types according to the perforating artery: lenticulostriate, thalamic, and choroidal type.[5] In this case, the collateral network was the choroidal type. Although the appearance of the CMBs was not around the periventricular anastomosis, it was considered that there was a hemodynamic stress through this abnormal anastomosis. In recent years, attention has been paid to the relationship between moyamoya disease and CMBs. Kuroda *et al.* have reported that the annual risk of hemorrhagic stroke is 6.6% in adult patients with asymptomatic CMBs.[14] Revascularization can reduce hemodynamic stress in moyamoya vessels and the risk of hemorrhagic stroke.[6,8,20,21]

All studies have included adult patients. Asymptomatic CMBs can be a significant predictor of hemorrhagic stroke in adult patients with moyamoya disease. To the best of our knowledge, asymptomatic CMBs are extremely rare in pediatric patients, and there are only two reports, seven available cases.[17,19] There are even fewer studies on *de novo* CMBs. Kuroda *et al.* showed that the annual incidence of *de novo* microbleeds was 1.7% in adult patients.[14] However, there is no previous study on *de novo* CMBs in pediatric patients, and this is the first report on this condition. Thus, its significance is completely unknown. In the current case, *de novo* CMBs were characterized by the progression of stenosis in the left MCA. Pediatric patients with hemorrhagic moyamoya disease often presented with TIAs before the hemorrhage.[1,15] Ahn *et al.* reported that the mean duration of the symptoms before hemorrhage was 19.2 months.[1] Unlike adult cases, hemodynamic stress on the fragile moyamoya vessels of pediatric moyamoya disease should be short-term. In pediatric patients with moyamoya disease who present with TIA due to the relatively rapid progression of vascular stenosis, hemodynamic stress on the moyamoya vessels is increasing and some of the patients may present hemorrhagic events. *De novo* CMBs in pediatric patients with moyamoya disease may reflect such sudden hemodynamic stress. Although the short-term course is good

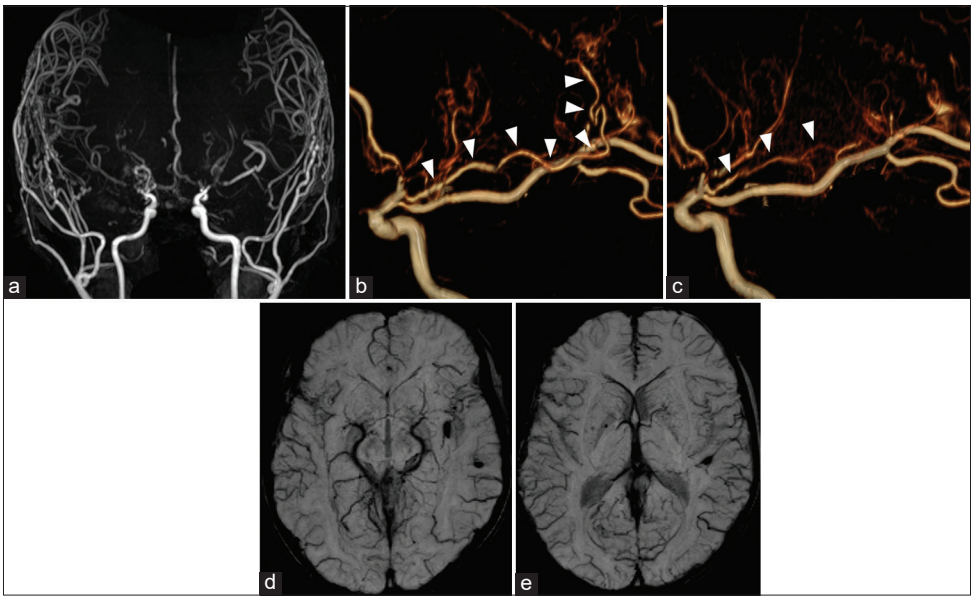

Figure 5: (a) Magnetic resonance angiography (MRA) showed good angiogenesis from the external carotid system to the bilateral cerebral hemispheres. (b and c) Susceptibility-weighted imaging revealed no additional *de novo* cerebral microbleeds 1 year after surgery. Postoperative MRA (e) revealed shrinkage of the anterior choroidal artery and disappearance of abnormal collaterals (white arrowheads) compared to preoperative MRA (d).

in the current case, follow-up period is too short to assess for rebleeding and long-term follow-up is still important. More cases of *de novo* CMBs in pediatric patients with moyamoya disease should be evaluated.

CONCLUSION

Herein, we report a case of *de novo* CMBs in a pediatric patient with moyamoya disease. The significance of *de novo* CMB is unknown because it is an extremely rare condition. However, attention should be paid to not only ischemic stroke but also hemorrhagic stroke. Hence, more cases should be collected.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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