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Case Report

Resolution of white matter hyperintensity after surgical revascularization in moyamoya disease – A report of three cases

Yuichiro Koga, Shusuke Yamamoto, Satoshi Kuroda

Department of Neurosurgery, University of Toyama, Toyama, Japan.

E-mail: Yuichiro Koga - ichikoga@med.u-toyama.ac.jp; Shusuke Yamamoto - shuyama@med.u-toyama.ac.jp; *Satoshi Kuroda - skuroda@med.u-toyama.ac.jp

***Corresponding author:**
Satoshi Kuroda,
Department of Neurosurgery,
University of Toyama, Toyama,
Japan.

skuroda@med.u-toyama.ac.jp

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ABSTRACT

Background: Moyamoya disease often presents white matter hyperintensity (WMH) lesions on fluid-attenuated inversion recovery (FLAIR) images, which is generally accepted as irreversible. We, herein, describe three cases of moyamoya disease with WMH lesions that regressed or disappeared after surgical revascularization.

Case Description: This report included two pediatric and one young adult case that developed transient ischemic attacks or ischemic stroke due to bilateral Moyamoya disease. Before surgery, five of their six hemispheres had WMH lesions in the subcortical and/or periventricular white matter on FLAIR images. The lesions included morphologically two different patterns: "Striated" and "patchy" morphology. In all of them, combined bypass surgery was successfully performed on both sides, and no cerebrovascular events occurred during follow-up periods. On follow-up magnetic resonance examinations, the "striated" WMH lesions completely disappeared within six months, while the "patchy" WMH lesions slowly regressed over 12 months.

Conclusion: Based on radiological findings and the postoperative course of the WMH lesions, the "striated" WMH lesions may represent the inflammation or edema along the neuronal axons due to cerebral ischemia, while the "patchy" WMH lesions may represent vasogenic edema in the white matter through the blood-brain barrier breakdown. Earlier surgical revascularization may resolve these WMH lesions in Moyamoya disease.

Keywords: Cerebral ischemia, Moyamoya disease, Revascularization, White matter hyperintensity

INTRODUCTION

Moyamoya disease is characterized by chronic, progressive stenosis of the terminal portion of internal carotid arteries (ICAs) and its main branches, and the anterior and middle cerebral arteries, respectively.[10,16] In patients with Moyamoya disease, the reduction of cerebral perfusion pressure usually causes cerebral infarction in the cerebral cortex and watershed zone.[10,16] Recent studies have also shown that the integrity of the normal-appearing white matter is impaired in hemodynamically compromised areas and is closely related to cognitive dysfunction in Moyamoya disease.[1,2,4,7,8,14] Furthermore, a certain subgroup of moyamoya patients also carries the white matter hyperintensity (WMH) lesions on fluid-attenuated inversion recovery (FLAIR) images or T2-weighted magnetic resonance imaging (MRI) and may be a predictive marker for future ischemic events.[19] Interestingly, some WHM lesions in moyamoya patients

reversibly diminish after surgical revascularization.[3,5,9,13,15] However, the pathophysiology of WMH lesions in moyamoya disease remains obscure. We, herein, describe three rare cases of moyamoya disease with WMH lesions that remarkably diminished or disappeared after successful surgical revascularization. We also precisely analyzed the images to improve our knowledge of their pathophysiology.

CASE PRESENTATION

Case 1

A 13-year-old girl presented with transient weakness of the right extremities. Neurological examinations on admission revealed no neurological deficits. Cerebral angiography showed severe stenosis of the terminal portion of the ICA on both sides. The perforating arteries were markedly dilated [Figures 1a and b]. N-isopropyl-I-123-p-iodoamphetamine (^{123}I-IMP) single-photon emission computed tomography (SPECT) showed cerebral blood flow (CBF) reduction in the ICA territories on both sides [Figure 1c]. T1-weighted MRI demonstrated multiple flow voids due to the dilated perforating arteries [Figure 1d]. FLAIR images showed the WMH lesions on both sides [Figure 1e]. The WMH lesions included anatomically two morphologies, including "patchy (arrows)" and "striated (arrowheads)" patterns [Figure 1e]. Diffusion-weighted MRI found no abnormality in the white matter [Figure 1f]. She was diagnosed with moyamoya disease and successfully underwent superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis and encephalo-duro-myo-arterio-pericranial synangiosis (EDMAPS) on both sides.[11,12] Postoperative course was uneventful, and transient ischemic attacks (TIAs) completely disappeared. CBF was restored to the normal level [Figure 1g]. Follow-up MRI revealed that the "striated" WMH lesions disappeared and the "patchy" WMH lesions diminished six months after surgery [Figure 1h], followed by further reduction of the "patchy" WMH lesions 12 months after surgery [Figure 1i].

Case 2

A 10-year-old girl complained of transient weakness of the right extremities and severe headache attacks. Neurological examinations on admission revealed no neurological deficits. Cerebral angiography showed severe stenosis of the terminal portion of the ICA on both sides. The perforating arteries were markedly dilated [Figures 2a and b]. ^{123}I-IMP SPECT showed CBF reduction in the ICA territories on both sides [Figure 2c]. FLAIR images showed the WMH lesions on both sides. The WMH lesions included morphologically two patterns: "Patchy" and "striated" patterns [Figure 2d]. She was diagnosed with moyamoya disease and successfully underwent STA-MCA anastomosis and EDMAPS on both sides. The postoperative course was uneventful, and CBF improved to the normal level [Figure 2e]. TIAs and headache attacks completely disappeared after surgery. Follow-up MRI revealed that the "striated" WMH lesions disappeared, and the "patchy" WMH lesions diminished five months after surgery [Figure 2f]. The "patchy" WMH lesions disappeared 12 months after surgery [Figure 2g].

Case 3

A 22-year-old male suddenly developed visual field disturbance and numbness in the right arm. Neurological examinations on admission revealed the right homonymous hemianopsia and sensory disturbance of the right extremities. Magnetic resonance angiography showed severe stenosis of the terminal portion of the bilateral ICA and the left posterior cerebral artery [Figure 3a]. ^{123}I-IMP SPECT showed CBF reduction in the whole cerebral hemispheres on both sides [Figure 3b]. T1-weighted MRI found cerebral infarction in the left parieto-occipital lobe. FLAIR images demonstrated the WMH lesions in the right subcortical and periventricular white matter, including the "patchy" and "striated" lesions [Figure 3c]. He was diagnosed with moyamoya disease and successfully underwent STA-MCA anastomosis and EDMAPS on both sides. The postoperative course was uneventful, and he was free from any cerebrovascular events during the follow-up. Cerebral hemodynamics were restored to normal levels except in the areas of cerebral infarction four months after surgery [Figure 3d]. Follow-up MRI showed that the "striated" WMH lesions completely disappeared and the "patchy" WMH lesions diminished four months after surgery [Figure 3e], followed by a further decrease in the volume of "patchy" WHM lesions 12 months after surgery [Figure 3f].

DISCUSSION

All three moyamoya patients presented here had a severe CBF reduction in the ICA territory, which resulted in a loss of hyperfrontality characteristic of children and young adults. FLAIR images demonstrated the hyperintensity lesions in the subcortical and/or periventricular white matter in five of six involved hemispheres. Interestingly, the WHM lesions could be divided morphologically into two patterns: the "patchy" and "striated" morphology, although there were no reports that denoted their morphology in the past. The "patchy" WMH lesions were found in the subcortical and/or periventricular white matter, while the "striated" WMH lesions were found only in the periventricular white matter. All three patients successfully underwent combined bypass surgery.[11] Several months later, CBF markedly improved, and the hyperfrontality was restored. Along with the normalization of cerebral hemodynamics, the WHM lesions gradually diminished

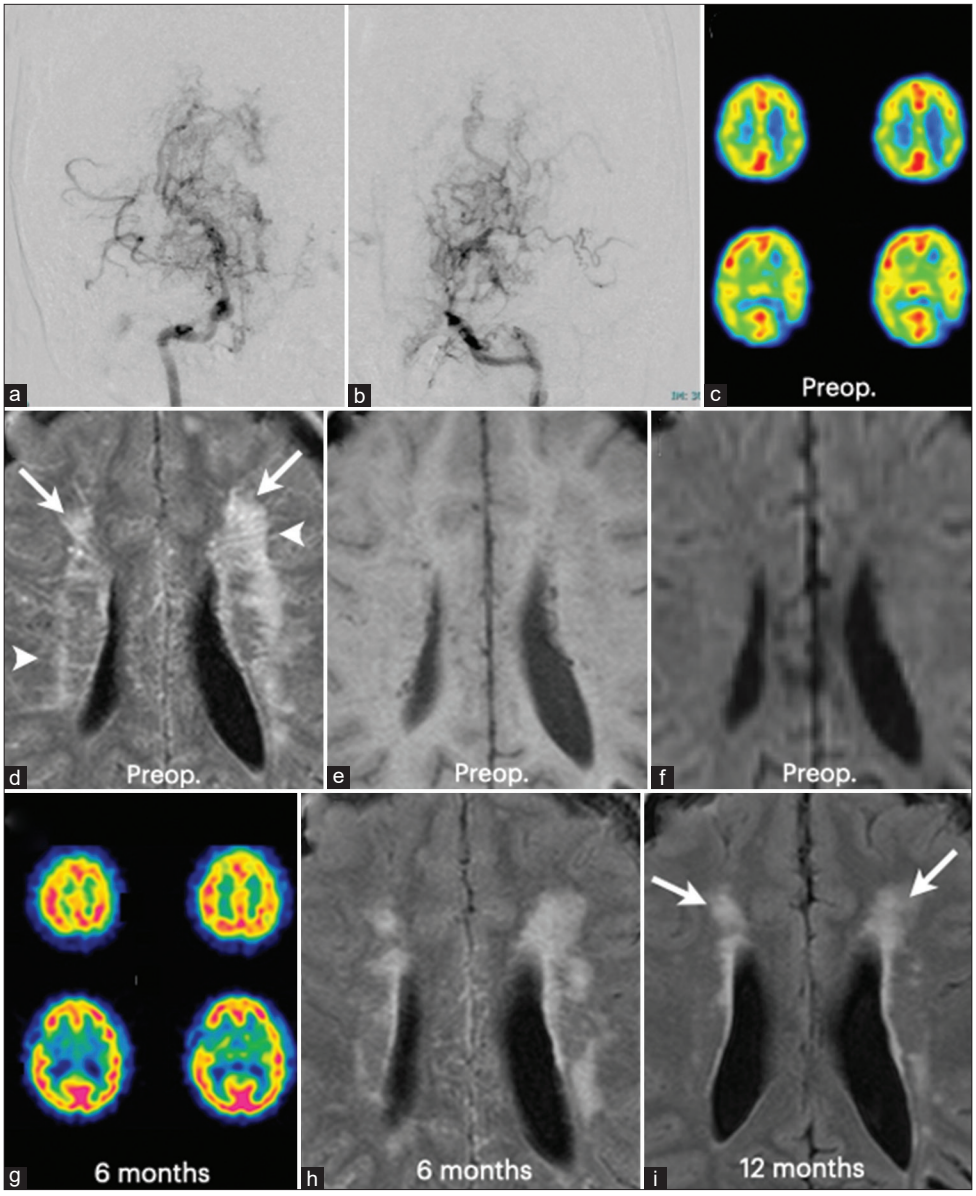

Figure 1: Radiological findings of a 13-year-old girl with moyamoya disease (Case 1). (a) Right internal carotid angiography demonstrated typical findings of moyamoya disease, including severe stenosis of the supraclinoid portion of the internal carotid artery and the horizontal portions of the anterior and middle cerebral arteries. (b) Left internal carotid angiography also showed very similar findings. Note the markedly dilated perforating arteries on both sides. (c) Single photon emission computed tomography (SPECT) demonstrated cerebral blood flow reduction in the internal carotid artery territories on both sides. (d) Fluid-attenuated inversion recovery (FLAIR) image showed the "patchy" hyperintensity lesions (arrows) in the periventricular white matter and also the "striated" hyperintensity lesions (arrowheads) in the periventricular white matter. The "striated" lesions appear to radiate from the lateral ventricles. (e) These hyperintensity lesions on FLAIR image cannot be detected on T1- weighted MRI. (f) Diffusion-weighted MRI did not identify them. (g) Cerebral blood flow almost normalized 6 months after combined bypass surgery on both sides. (h) The "striated" hyperintensity lesions completely disappeared 6 months after surgery. (i) The "patchy" hyperintensity lesions regressed 6 months after surgery and further diminished 12 months after surgery(arrows)

or disappeared within 12 months. However, we observed a significant difference in the resolution of WHM lesions between the "patchy" and "striated" lesions. The "striated" WMH lesions almost completely disappeared 4–6 months

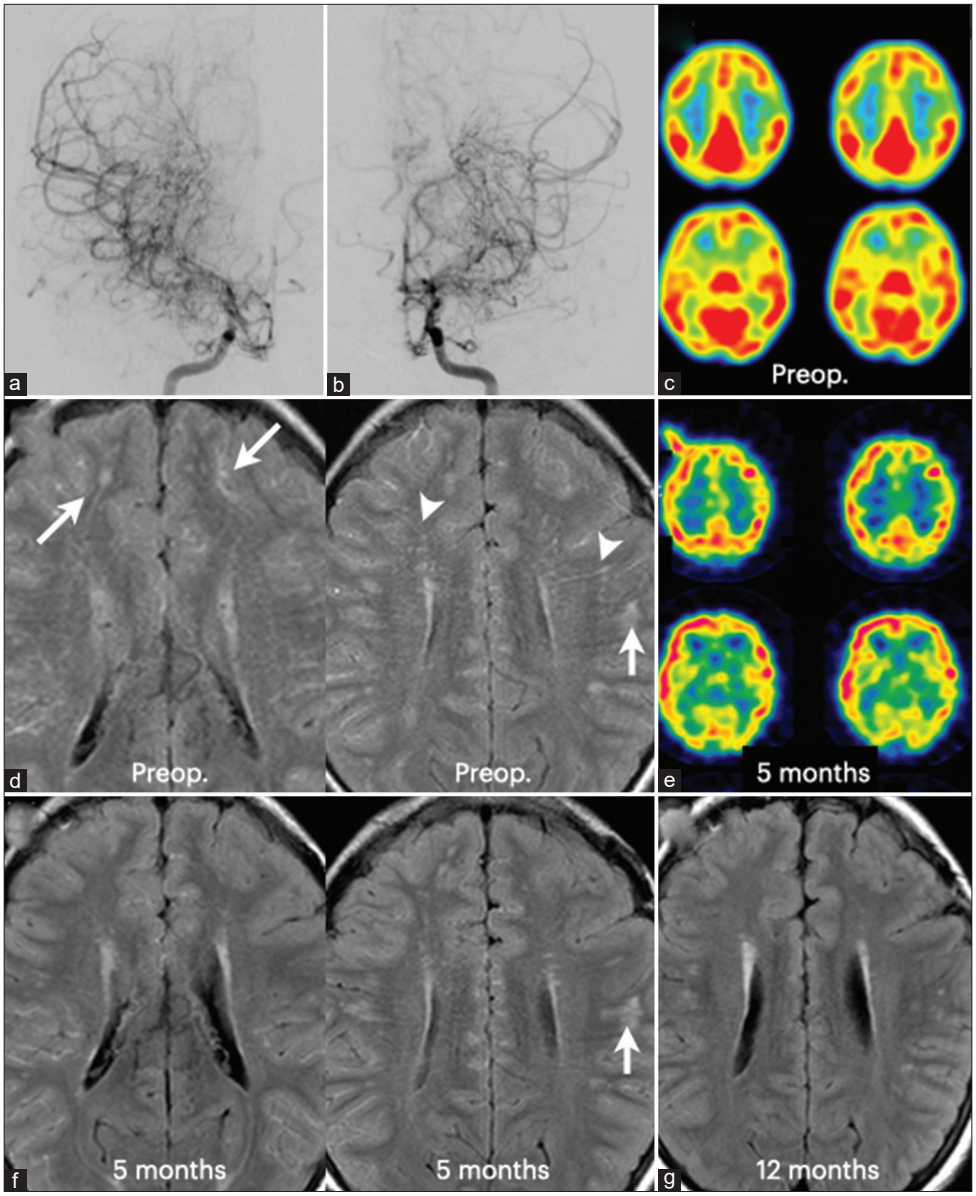

Figure 2: Radiological findings of a 10-year-old girl with moyamoya disease (Case 2). (a) Right nternal carotid angiography demonstrated typical findings of moyamoya disease, including severe stenosis of the supraclinoid portion of the internal carotid artery and the horizontal portions of the anterior and middle cerebral arteries. (b) Left internal carotid angiography also showed very similar findings. Note the markedly dilated perforating arteries on both sides. (c) Single photon emission computed tomography (SPECT) demonstrated cerebral blood flow reduction in the frontal lobe on both sides. (d)Fluid-attenuated inversion recovery (FLAIR) image showed the "patchy" hyperintensity lesions (arrows) in the subcortical white matter and also the "striated" hyperintensity lesions (arrowheads) in the periventricular white matter. The "striated" lesions appear to radiate from the lateral ventricles. (e) Cerebral blood flow almost normalized 5 months after combined bypass surgery on both sides. (f) The "striated" hyperintensity lesions completely disappeared 5 months after surgery. The "patchy" hyperintensity lesions disappeared in the frontal pole on both sides 5 months after surgery, but was still observed in the left frontal subcortex (arrow). (g) The lesion completely disappeared 12 months after surgery

after surgery, whereas the "patchy" ones regressed 4–6 months after surgery, but some of them were still observed 12 months after surgery.

As aforementioned, the WHM lesions in moyamoya patients may sometimes be reversible and disappear or diminish after surgical revascularization.[3,5,9,13,15] Judging from the figures

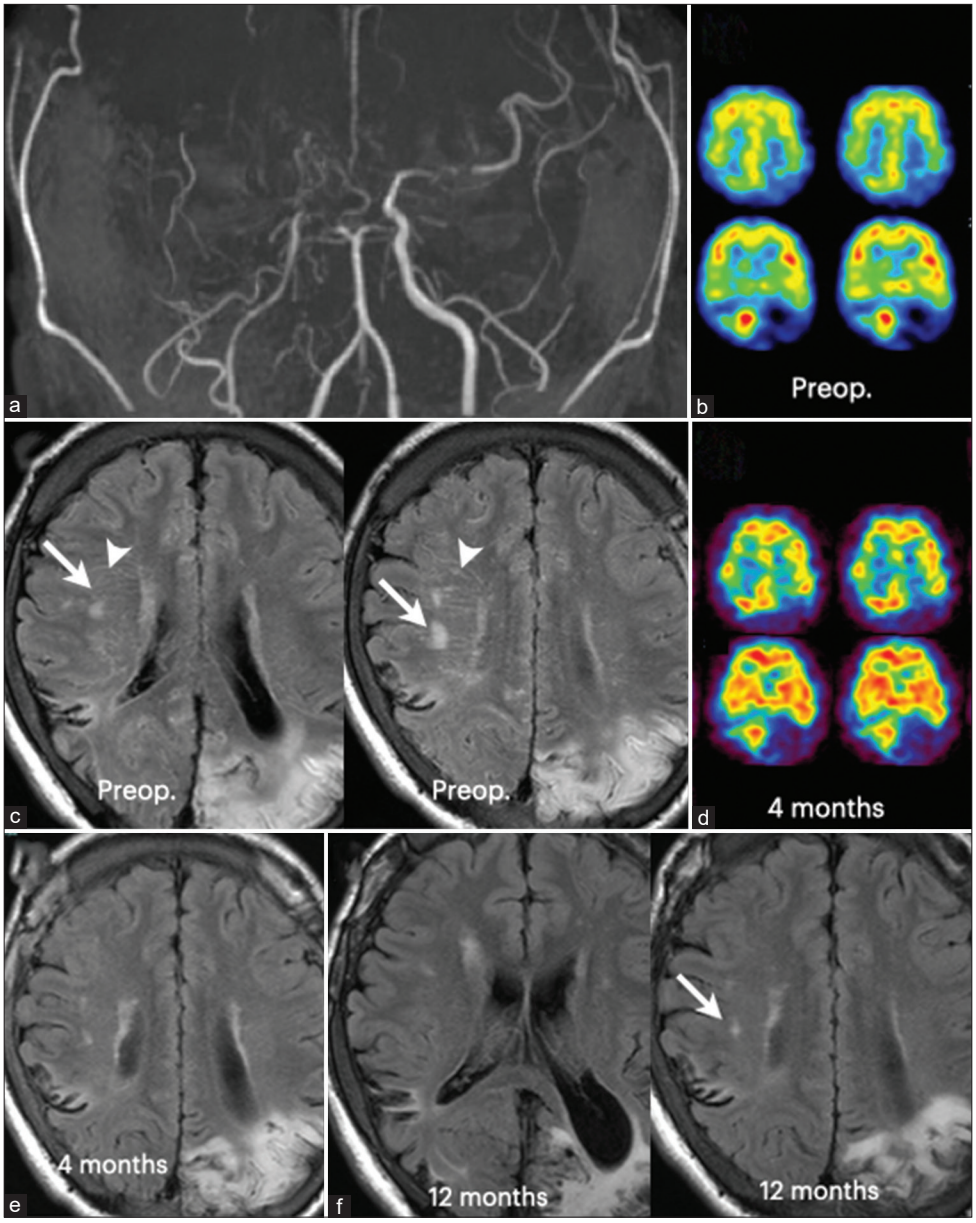

Figure 3: Radiological findings of a 22-year-old male with moyamoya disease (Case 3). (a) MR angiography demonstrated typical findings of moyamoya disease, including severe stenosis of the supraclinoid portion of the internal carotid artery on both sides. (b) Single photon emission computed tomography (SPECT) demonstrated cerebral blood flow reduction in the cerebral hemispheres on both sides. (c) Fluid-attenuated inversion recovery (FLAIR) image showed the "patchy" hyperintensity lesions (arrows) in the right periventricular white matter and also the "striated" hyperintensity lesions (arrowheads) in the right periventricular white matter. The "striated" lesions appear to radiate from the right lateral ventricles. Note cerebral infarction in the left occipital lobe.(d) Cerebral blood flow almost normalized 4 months after combined bypass surgery on both sides, except for the left occipital lobe. (e) The "striated" hyperintensity lesions completely disappeared 4 months after surgery. The "patchy" hyperintensity lesions regressed 4 months after surgery. (f) But, they were still observed in the right side 12 months after surgery (arrow).

presented by previous investigators, their WMH lesions can be categorized into the "patchy" lesions in our report. On the other hand, there are no articles that mention the "striated" lesions in moyamoya disease. Suzuki *et al*. reported the WMH lesions different from the "patchy" morphology. They found the linear structures in the white matter with hyperintensity

on T2-weighted MRI and FLAIR images and named them "medullary streak."[15] The morphology is very similar to the "striated" WMH lesions in our report. They speculated that these lesions were the stagnated cerebrospinal fluid or the vasogenic edema around the perivascular space. Originally, however, the enlarged perivascular space or medullary streak is defined as a small (<3 mm) punctate or linear hyperintensities on T2-weighted imaging with corresponding hypointensities on T1/FLAIR imaging due to the existence of cerebrospinal fluid.[6,15,18] Hence, it is unlikely that the striated lesions seen in the white matter are enlarged perivascular spaces. Indeed, in our three cases, the lesions could not be detected on T1-weighted MRI and showed hyperintensity on FLAIR images.

The "striated" WMH seen in our cases are more prominent in the periventricular white matter than the subcortical region of the white matter, and they always coexist with the patchy WMH. Although the pathophysiology of "striated" WMH lesions is still unclear, these observations strongly suggest that the "striated" WMH lesions may develop under the same conditions as the "patchy" ones. When the white matter is exposed to persistent cerebral ischemia, demyelination and axonal degradation occur quickly in the ischemic core, and remyelination has been observed in the peri-ischemic area.[17] Using myelin-sensitive MRI, Hara *et al*. reported the presence of myelin and axonal damage in the WMH lesions in moyamoya patients.[4] Therefore, the "striated" WMH lesions may indicate the expansion of inflammation or edema along the neuronal axons. In this context, it is possible to explain why the "striated" WMH lesions are detected as "hyperintensity" but not "hypointensity" on FLAIR images. Further radiological and histological studies are warranted to understand the underlying pathophysiology of the "striated" WMH lesions in moyamoya disease.

In this report, surgical revascularization significantly improved cerebral hemodynamics. Then, the "striated" WMH lesions completely disappeared 4–6 months after surgery, while the "patchy" WMH lesions slowly diminished or disappeared over 12 months after surgery. The fact strongly suggests that chronic cerebral ischemia plays an important factor in to development of these WMH lesions. In addition, the "striated" WMH lesions and the "patchy" WMH lesions always coexist before surgery. These facts provide us with an important clue to explain the mechanisms underlying the development of WMH lesions in moyamoya disease. Thus, the WMH lesions may develop in two steps: the "striated" WMH lesions first develop along the axons due to cerebral ischemia, and then the "patchy" WMH lesions develop due to the further expansion of inflammation and vasogenic edema, probably provoked by more dense or more prolonged ischemia. The blood–brain barrier (BBB) breakdown may be related to the underlying mechanism. Therefore, the "patchy" lesions would be a more severe phenotype than the "striated" lesions.

CONCLUSION

We reported three cases of moyamoya disease with reversible WMH lesions, including two different morphologies: the "striated" and "patchy" patterns. Following surgical revascularization surgery, the former completely disappeared within six months, while the latter slowly regressed but did not disappear over 12 months. Based on their radiological findings and postoperative course, the "striated" WMH lesions may represent the inflammation or edema along the neuronal axons due to cerebral ischemia, while the "patchy" WMH lesions may represent vasogenic edema in the parenchyma through the BBB breakdown. Earlier diagnosis and effective surgical treatment may be important to resolve the WMH lesions on FLAIR images.

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Ethical approval

The research/study was approved by the Institutional Review Board at Toyama University Hospital, number R2019057, dated August 30, 2019.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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