Case Studies

Paradoxical Association of Symptomatic Local Vasogenic Edema with Global Cerebral Hypoperfusion after Direct Revascularization Surgery for Adult Moyamoya Disease

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> Background: Superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis is the standard treatment for Moyamoya disease (MMD). Cerebral hyperperfusion syndrome is a potential complication of this procedure and can cause local vasogenic edema and/or delayed intracerebral hemorrhage. Cerebral hypoperfusion is a contradictory postoperative pathophysiological condition implicated in MMD, but its association with symptomatic local vasogenic edema has not been reported. Case Report: A 31-year-old woman with MMD underwent left STA-MCA anastomosis 3 months after a minor completed stroke in bilateral hemispheres. Eight hours after the operation, the patient developed neurological deterioration of dysarthria and mono-paresis in her right hand. Magnetic resonance (MR) angiography showed apparently patent STA-MCA bypass, whereas MR imaging of fluid-attenuated inversion recovery demonstrated a local highsignal-intensity lesion at the vascular territory supplied by the bypass. The apparent diffusion coefficient value was significantly increased in this lesion, suggesting local vasogenic edema formation. N-isopropyl-p-[123] iodoamphetamine singlephoton emission computed tomography revealed global hypoperfusion in the left hemisphere. The administration of a free-radical scavenger and antiepileptic agent gradually relieved her symptoms, and MR imaging 1 month after surgery confirmed the complete disappearance of local vasogenic edema. Conclusions: Vasogenic edema may be associated not only with cerebral hyperperfusion but also with hypoperfusion after STA-MCA anastomosis for MMD. Although the exact mechanism of this rare association is unknown, the intrinsic vulnerability of intracranial vascular wall structures and the increased vascular permeability in MMD may partly explain the paradoxical association of hypoperfusion and local vasogenic

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edema. **Key Words:** Moyamoya disease—extracranial–intracranial bypass—vasogenic edema—hypoperfusion.

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Introduction

Moyamoya disease is a chronic, occlusive cerebrovascular disease characterized by bilateral steno-occlusive changes at the terminal portion of the internal carotid artery and an abnormal vascular network at the base of the brain.¹ Superficial temporal artery–middle cerebral artery (STA–MCA) anastomosis is generally employed as the standard management method for adult MMD.²⁻⁴

Cerebral hyperperfusion syndrome is one of the potential complications of STA–MCA anastomosis for adult MMD.⁵⁻⁷ Cerebral hyperperfusion is thought to cause local vasogenic edema and/or delayed intracerebral hemorrhage in the acute stage after surgery.^{6,7} Cerebral hypoperfusion is a contradictory pathophysiological condition that was also reported to occur after STA–MCA anastomosis for MMD.⁸ Significant cerebral hypoperfusion can cause cytotoxic edema and subsequent cerebral infarction, but its association with symptomatic local vasogenic edema has not been reported. We herein report an adult MMD case manifesting as the paradoxical association of symptomatic local vasogenic edema with global cerebral hypoperfusion after STA–MCA anastomosis.

Case Reports

Among 267 patients with MMD who underwent STA– MCA anastomosis on 361 affected hemispheres by a single surgeon (M.F.), 1 adult patient (.28%) developed the paradoxical association of symptomatic local vasogenic edema with global cerebral hypoperfusion after STA–MCA anastomosis.

This 31-year-old woman initially presented with aphasia and right-sided hemiparesis. Magnetic resonance (MR) imaging demonstrated acute infarction in both frontal and parietal lobes (Fig 1, A). Steno-occlusive changes at the terminal portion of the bilateral internal carotid arteries associated with abnormal vascular networks at the base of the brain were observed on cerebral angiography (Fig 1, B), leading to the definitive diagnosis of MMD. After 3 months of rehabilitation, her neurological status was partially relieved to a modified Rankin scale of 2, and N-isopropyl-p-[¹²³I] iodoamphetamine single-photon emission computed tomography (CT) revealed a significant decrease in cerebral blood flow (CBF) in the bilateral hemispheres, predominantly on the left side (Fig 1, C). She then underwent left STA–MCA anastomosis with



Figure 1. (A) Initial diffusion-weighted imaging showing infarctions in the bilateral hemispheres. (B) Preoperative bilateral carotid angiograms showing steno-occlusive changes at the terminal portion of the bilateral internal carotid arteries associated with the development of abnormal vascular networks at the base of the brain. (C) Preoperative N-isopropyl-p-[¹²³I] iodoamphetamine single-photon emission computed tomography demonstrating marked hemo-dynamic compromise in the bilateral hemispheres.

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Figure 2. (*A*) CT and (*B*-D) MR imaging 8 hours after left STA–MCA anastomosis. A low-density lesion in the left frontal lobe at the site of anastomosis is observed on CT (arrow in A). MR imaging demonstrating high-intensity signal on fluid-attenuated inversion recovery imaging at the site of anastomosis in the left frontal lobe (arrow in B), increase in apparent diffusion coefficient values (arrow in C), and slightly low-intensity signal on diffusion-weighted imaging (D). MR angiography demonstrating the apparently patent STA–MCA bypass (arrow in E). N-isopropyl-p-[¹²³I] iodoamphetamine single-photon emission CT 1 day after surgery showing global hypoperfusion in the left hemisphere (F). Abbreviations: CT, computed tomography; MR, magnetic resonance; STA–MCA, superficial temporal artery–middle cerebral artery.

encephalo-duro-myo-synangiosis successfully 3 months after the onset of the minor completed stroke. The stump of the parietal branch of superficial temporal artery was anastomosed to the M4 segment of the left middle cerebral artery, which supplied the frontal lobe. The diameter of the recipient artery was .8 mm, and the temporary occlusion time was 27 minutes. The patient did not develop neurological deterioration immediately after surgery. At 8 hours after surgery, however, dysarthria appeared along with mono-paresis in her right hand. A local lowdensity area in the left frontal lobe was noted on emergency CT (Fig 2, A). After CT examination, the patient presented a simple partial seizure in the right side of her face. Subsequent MR imaging of fluid-attenuated inversion recovery (FLAIR) demonstrated a local highintensity lesion at the vascular territory supplied by the STA-MCA bypass (Fig 1, B). The apparent diffusion coefficient of this lesion was significantly increased (Fig 2, C), and the diffusion-weighted imaging signal was slightly low (Fig 2, D), suggesting the formation of local vasogenic edema. MR angiography showed the apparently patent STA-MCA bypass as a thick high-signal intensity (Fig 2, E), but N-isopropyl-p-[123I] iodoamphetamine singlephoton emission CT on the same day indicated a paradoxical decrease in CBF in the entire left hemisphere (Fig 2, F). The administration of edaravone, a freeradical scavenger and antiepileptic agent, in addition to our standard perioperative management for MMD, such as minocycline hydrochloride, gradually relieved her

symptoms during the next 10 days. The low-density lesion was partly resolved 10 days after surgery (Fig 3, A) and completely disappeared at 1 month (Fig 3, B). She then underwent right STA–MCA anastomosis with encephaloduro-myo-synangiosis without complication. FLAIR MR imaging at 2 months after initial surgery confirmed the complete disappearance of the high-intensity lesion (Fig 3, C). The patient has been fine, and she did not exhibit any cerebrovascular event during the 1-year postoperative period after bilateral revascularization surgeries.

Discussion

Direct extracranial-intracranial revascularization surgery, such as STA-MCA anastomosis, is widely employed not only for ischemic-onset MMD but also for hemorrhagiconset MMD.²⁻⁴ The long-term outcome of STA-MCA anastomosis for MMD is favorable, but it is known to have the risk of potential complications, such as perioperative cerebral infarction and delayed intracerebral hemorrhage, due to cerebral hyperperfusion.^{2,3} Recent flow studies in the acute stage after direct revascularization surgery for MMD revealed that this procedure can result in a variety of postoperative hemodynamic conditions, including local cerebral hyperperfusion,5-7 remote ischemia due to watershed shift phenomenon,^{9,10} and hypoperfusion.⁸ Among them, local cerebral hyperperfusion is one of the most deleterious complications that can cause transient neurological deterioration, vasogenic edema



Figure 3. Postoperative computed tomography at 7 days (A) and 1 month (B) after left superficial temporal artery–middle cerebral artery anastomosis showing gradual disappearance of the low-density lesion in the left frontal lobe at the vascular territory supplied by the bypass. Fluid-attenuated inversion recovery magnetic resonance imaging at 2 months after initial surgery showing the complete disappearance of the local high-intensity lesion, but laminar necrosis due to the initial stroke is evident (C).

formation, and delayed intracerebral hemorrhage.⁵⁻⁷ In light of the underlying pathology of vasogenic edema, it has been believed to originate from local cerebral hyperperfusion and subsequent dis-autoregulation/bloodbrain barrier disruption after revascularization for MMD.¹¹ Therefore, the association of global cerebral hypoperfusion with exclusive local vasogenic edema, which was transiently responsible for the focal neurological deterioration in our case, was apparently unique.

Regarding the involvement of heterogeneous hemodynamic conditions in the cortical signal changes by MR imaging after surgical revascularization for MMD, Hamano et al reported that cortical FLAIR high-intensity signs can be caused by many postoperative hemodynamic conditions including hyperperfusion and hypoperfusion.¹² We also reported 2 adult patients with MMD presenting with local vasogenic edema after direct revascularization surgery without evidence of cerebral hyperperfusion.¹³ These patients in our previous report had favorable CBF improvement to the normal range after STA-MCA anastomosis, although asymptomatic local vasogenic edema was transiently evident in both. Taken together with the present case, vasogenic edema can be caused by a variety of hemodynamic conditions after direct revascularization surgery for MMD, and an accurate diagnosis of the perioperative condition by hemodynamic studies, such as SPECT, is necessary when symptomatic vasogenic edema is evident after surgery.

Although the exact mechanism of this rare association is unknown, the intrinsic vulnerability of intracranial vascular wall structures and the increased vascular permeability in MMD may partly explain this unique pathophysiological condition.^{2,14} The excessive hemodynamic stress on the fragile vessel in the acute stage after STA–MCA anastomosis may trigger increased vascular permeability in the pial artery with anatomical fragility, such as the waving of internal elastic lamina and the thin ning of the intimal layer, in patients with MMD.^{2,14} Regarding the molecular biological condition, previous studies demonstrated a higher expression of serum vascular endothelial growth factor¹⁵ and matrix metalloproteinase (MMP)-9 in MMD patients,^{16,17} both of which contribute to the increased vascular permeability by blood-brain barrier disruption and the subsequent formation of vasogenic edema after revascularization surgery.¹⁸ Alternatively, reactive oxygen species produced by reperfusion in the chronic ischemic brain may also affect vascular permeability by direct endothelial cell damage via lipid peroxidation as well as by activating MMP-9.19-21 To counteract these deleterious cascades, we used a free-radical scavenger in addition to the routine use of minocycline hydrochloride in the present case because minocycline has a potential role in inhibiting MMP-9 and therefore may ameliorate postoperative neurological deterioration after STA-MCA anastomosis for MMD.¹⁸ Indeed, our patient's symptoms gradually resolved under intensive perioperative management, and the local vasogenic edema was completely cleared within 1 month after surgery. Future studies with a larger number of patients are needed to clarify the exact mechanism of vasogenic edema formation under global hypoperfusion after revascularization surgery in patients with MMD.

Conclusion

We report an extremely rare case of adult MMD that manifested as a paradoxical formation of symptomatic local vasogenic edema with global hypoperfusion after direct revascularization surgery. Although the exact mechanism of this rare association is unknown, the intrinsic vulnerability of intracranial vascular wall structures and the increased vascular permeability in MMD may partly explain this unique pathophysiological condition.

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