Paradoxical association of symptomatic cerebral edema with local hypoperfusion caused by the 'watershed shift' after revascularization surgery for adult moyamoya disease: a case report

Jin Yu, Miao Hu, Lei Yi, Keyao Zhou, Jianjian Zhang and Jincao Chen iD

Abstract: Superficial temporal artery–middle cerebral artery anastomosis is generally considered as an effective method in improving damage associated with intracerebral occlusions in moyamoya disease. Hemodynamic changes caused by revascularization are the cause of many postoperative complications. Of the 186 consecutive surgeries for moyamoya disease at our hospital from 2015, we herein presented one case of adult-onset moyamoya disease that manifested symptomatic local cerebral edema and local hypoperfusion caused by the 'watershed shift'. A 67-year-old woman presented with limb numbness on the right side and underwent superficial temporal artery–middle cerebral artery anastomosis, resulting in neurological dysfunction and the formation of a reversible high-signal lesion at left frontotemporal lobes on T2-weighted images along with a decrease in perfusion values on [123]I N-isopropyl-p-iodoamphetamine single-photon emission computed tomography, while the anastomotic vessel was patent on magnetic resonance angiography. This phenomenon of hypoperfusion area (left frontotemporal lobe) remote to anastomotic site (left temporal lobe area) led to the diagnosis of the 'watershed shift' phenomenon. In light of the hypoperfusion induced by 'watershed shift', the patient was treated with fluid replacement. With the gradual recovery of perfusion, the patient presented significantly improvement both on the magnetic resonance imaging findings and neurological symptoms. In conclusion, regional cerebral edema with hypoperfusion, possibly due to cerebral ischemia and the 'watershed shift' phenomenon, may be another novel entity that needs to be considered as a potential complication after extracranial–intracranial bypass for moyamoya disease.

Keywords: cerebral edema, moyamoya disease, revascularization surgery, watershed shift

Background and importance

Moyamoya disease (MMD) is a chronic occlusive cerebrovascular disease characterized by progressive stenosis at the terminal portion of the internal carotid artery (ICA) and an abnormal vascular network at the base of the brain.[1] Superficial temporal artery–middle cerebral artery (STA-MCA) bypass surgery is an effective method in improving damage associated with intracerebral occlusions.[2] Although the long-term effect of surgical revascularization is favorable, the early postoperative period is considered to be a vulnerable period for complications. Cerebral edema has been believed to originate from local cerebral hyperperfusion after revascularization for MMD.[3] Another potential complication, the so-called 'watershed shift' phenomenon caused by alteration in flow patterns and local hypoperfusion,[4] led to neurological deterioration and

Correspondence to:
Jincao Chen and Jianjian Zhang
Department of Neurosurgery, Zhongnan Hospital of Wuhan University, Donghu Road 169, Wuhan 430071, China
chenjincao2012@hotmail.com
zj57470@126.com

Jin Yu
Miao Hu
Lei Yi
Keyao Zhou
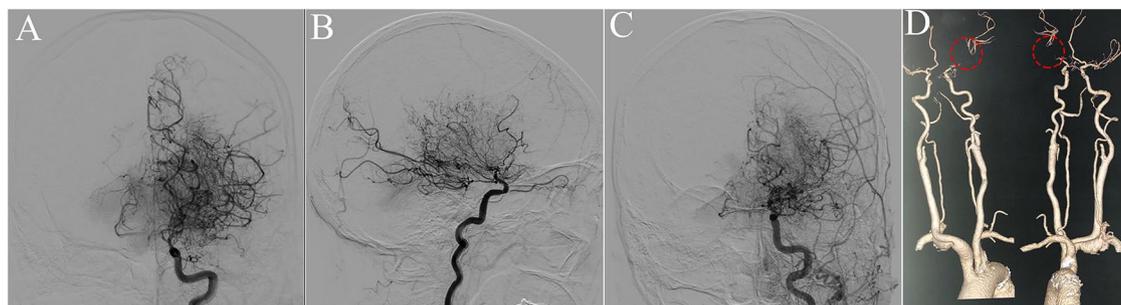Department of Neurosurgery, Zhongnan Hospital of Wuhan University, Wuhan, China

Figure 1. Preoperative diagnosis of MMD.
(A–C) Preoperative DSA showing occlusion of the terminal portions of left ICA and the occurrence of abundant moyamoya vessels in the brain base unilaterally. (D) Preoperative CTA revealing occlusion change (*dotted circles*) at the terminal portions of left ICA.
CTA, computed tomography angiography; DSA, digital subtraction angiography; ICA, internal carotid artery; MMD, moyamoya disease.
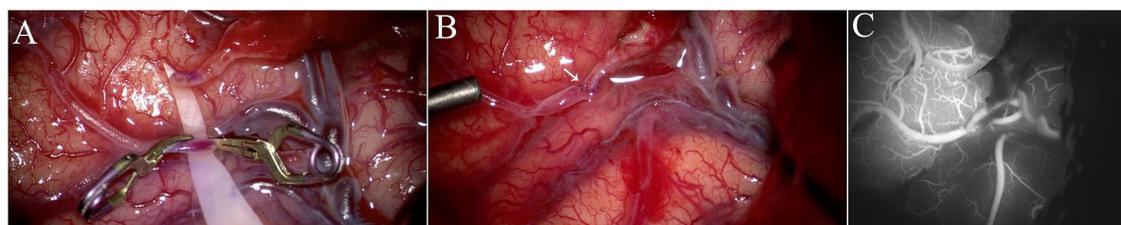

Figure 2. Surgical view of left STA-MCA anastomosis.
STA-MCA anastomosis with EDMS in the left hemisphere (the temporal lobe area) was performed. The MCA (M4 segment) was temporarily occluded (A) to perform left STA-MCA anastomosis (*arrow* in B). (C) Indocyanine green video-angiography demonstrated apparent patent bypass with the favorable distribution of bypass flow.
EDMS, encephalo-duro-myo-synangiosis; STA-MCA, superficial temporal artery–middle cerebral artery.

cerebral ischemia.[5] These opposite phenomena associated with hemodynamics changes make the postoperative management of MMD complicated.

We herein present a case of adult-onset MMD, which manifested symptomatic local cerebral edema and hypoperfusion caused by the 'watershed shift'. This rare complication may indicate a more complicated hemodynamic changes during the early perioperative period of revascularization surgery for MMD.

Clinical presentation

Medical history and examination
A 67-year-old female patient was admitted to our hospital referred by family physician on 13 December 2018 owing to limb numbness on the right side for 20 days. A physical examination revealed that the patient was conscious and able to answer questions accurately. The patient has not suffered other past medical, surgical history or other histories.

Following admission, a digital subtraction angiography (DSA) examination revealed the occlusion change at the end of left ICA with abundant moyamoya vessels, compensatory collateral formed between intracranial and extracranial vessels (Figure 1A–C), associated with computed tomography angiography (CTA) results (Figure 1D), suggested unilateral MMD.

Operation
STA-MCA anastomosis with encephalo-duro-myo-synangiosis (EDMS) in the left hemisphere (the temporal lobe area) was performed by a chief physician with 10 years' of specialized training followed the standard specification.[6] Briefly, the patient underwent general anesthesia, during the temporary occlusion time (29 min) (Figure 2A), the stump of the frontal branch of STA was anastomosed to MCA (M4 segment) (arrow in Figure 2B). The patency of the bypass was promptly confirmed by indocyanine green video-angiography (Figure 2C).
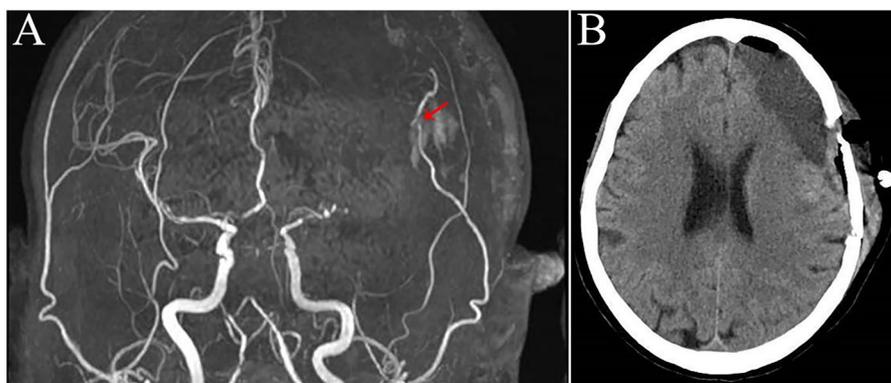
Figure 3. (A) MRA showing the patency of left STA-MCA bypass 2 days after surgery (*arrow*). (B) CT 2 days after surgery showing low-density lesion at left frontotemporal lobes without subdural hematoma.
CT, computerized tomography; MRA, magnetic resonance angiography; STA-MCA, superficial temporal artery–middle cerebral artery.

Postoperative course

Accompanied by the administration of minocycline hydrochloride (200 mg/day),[7] systolic blood pressure was strictly maintained at <130 mmHg starting immediately after surgery.[8] The patient did not display any additional neurological deterioration during or immediately after surgery.

The patient developed transient aphasia and muscle strength 0 grade at right limbs 2 days after surgery. Magnetic resonance angiography (MRA) showed an apparently patent bypass (arrow in Figure 3A), while postoperative computerized tomography (CT) revealed a newly developed low-density region at left frontotemporal lobes (Figure 3B), as well as a hyperintensity area on T2-weighted magnetic resonance imaging (MRI) (Figure 4A, B), which led to the diagnosis of cerebral edema. Postoperative ^{123}I N-isopropyl-p-iodoamphetamine single-photon emission computed tomography (^{123}I-IMP-SPECT) showed relevant improvement of perfusion status at left parietal and occipital lobes [cerebral blood flow (CBF) value of 57.64 ml/min/100 g and 54.53 ml/min/100 g] than preoperative (39.76 ml/min/100 g and 35.41 ml/min/100 g), while a lower CBF at left frontotemporal lobes (14.88 ml/min/100 g) than preoperative (48.14 ml/min/100 g) (Figure 4C, D). This phenomenon of hypoperfusion area (left frontotemporal lobe) remote to anastomotic site (left temporal lobe area) led to the diagnosis of the 'watershed shift' phenomenon. The patient did not suffer from postoperative seizure and the mechanical compression by extra-axial lesion (such as subdural hematoma and compression by temporal muscle used for indirect bypass) have

also been ruled out by CT (Figure 3B) and MRA scanning (Figure 4D, E, F). Thus, we adjusted therapeutic strategies to fluid replacement by dextran (250 ml, twice per day).

The patient was ameliorated to simply talk and muscle strength 4 grade at right limbs in a few days and MRI 15 days after surgery revealed a significant improvement in the high-intensity area on T2-weighted images (dotted circles in Figure 4E). ^{123}I-IMP-SPECT showed improved local cerebral perfusion (23.91 ml/min/100 g) (Figure 4F).

Those symptoms were relieved by rehabilitation within 1 month of surgery, and there were no further cerebrovascular events during the follow-up period of 3 months.

Discussion

Hemodynamic changes caused by bypass grafting induced various complications such as cerebral hyperperfusion syndrome (CHS), infraction and hemorrhagic stroke.[9–12] Cerebral edema was associated to CHS due to increased regional CBF,[13,14] while cerebral edema with hypoperfusion has rarely been reported. In present study, the patient showed symptomatic cerebral edema with contradictory local hypoperfusion status, which was apparently unique.

The possibility of infarction of the high signal intensity region on T2 should be excluded, since the patency of anastomotic vessels has been confirmed by postoperative MRA. On the other hand, infarction often led to permanent damage to the brain
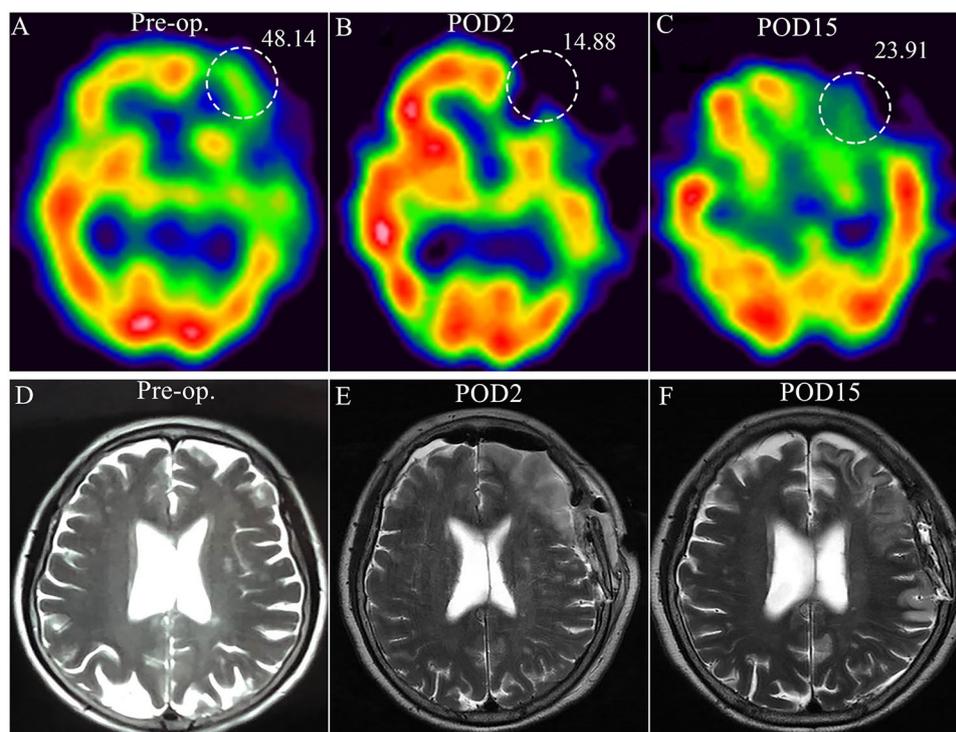
Figure 4. Temporal profile of ^{123}I-IMP-SPECT images and MRI.
Quantitative local CBF values (*dotted circles*) (A) before surgery, (B) 2 days after surgery, and (C) 15 days after surgery. Preoperative SPECT showing decreased CBF in left frontal, temporal, parietal and occipital lobes; combined bypass surgery resulted in prominent hypoperfusion at left frontotemporal lobes 2 days after surgery, which improved 15 days after surgery. High-signal-intensity lesion on T2-weighted magnetic resonance images (D) before surgery, (E) 2 days after surgery, and (F) 15 days after surgery. Preoperative MRI showing no abnormal lesion at left frontotemporal lobes; combined bypass surgery resulted in prominent high-signal-intensity lesion on T2 left frontotemporal lobes 2 days after surgery, which improved 15 days after surgery. The low signal on T2 images of the sticking temporal muscle suggesting that there was no edema in temporal muscle and no obvious compression of brain tissue in the hypoperfusion area.
CBF, cerebral blood flow; MRI, magnetic resonance imaging; Pre-op, preoperative; POD, postoperative day; SPECT, single-photon emission computed tomography; STA-MCA, superficial temporal artery–middle cerebral artery.

parenchyma and would not result in imaging improvements so quickly,[15] which led to the consideration of cerebral edema. Sakata *et al.* has reported cerebral edema without hyperperfusion status after direct revascularization surgery.[16] In this case, however, postoperative cerebral edema caused by hypoperfusion was rare, especially due to regional hypoperfusion caused by 'watershed shift'.

The 'watershed shift' phenomenon is a special hemodynamic change after MMD revascularization. The incidence of the 'watershed shift' phenomenon was as high as 10.9% after STA-MCA anastomosis for adult MMD.[17] Since the reconstructed bypass contradicted the blood flow of MCA, the remote distribution area of MCA and its branches became the so-called 'watershed area', which shows hypoperfusion on SPECT.[4] In this case, although the patency of anastomotic

vessels was confirmed by MRA after revascularization, the perfusion value of the left frontotemporal lobes was lower than that before operation (while the perfusion at the left parietal and occipital lobes were significantly improved), and the hypoperfusion area (left frontotemporal lobe) is different from the anastomotic site (left temporal lobe area), which presented characteristics of the 'watershed shift' phenomenon and resulted in an ischemic area in the left frontotemporal lobe.

Ischemic brain edema can be differentiated into two pathophysiological different types: an early cytotoxic type which initiated at flow values close to 30% of control, when stimulation of anaerobic metabolism causes an increase of brain tissue osmolality and, hence, an osmotically obliged cell swelling.[18] With the evolution of tissue necrosis and the degradation of basal lamina, the blood–brain

barrier (BBB) breaks down and a later vasogenic type occurred.[19] After 4–6h, serum proteins begin to leak from the blood into the brain, which further enhances the water content of the tissue.[20,21] Vasogenic edema reaches its peak at one to several days after the onset of ischemia and may cause an increase of tissue water by more than 100%.

We speculated that, on the one hand, as Mukerji *et al.*[22] reported, significant cerebral hypoperfusion can cause cytotoxic edema and subsequent cerebral infarction, the patient suffered cytotoxic edema which results from abnormal regional hypoperfusion caused by postoperative 'watershed shift'. On the other hand, STA-MCA caused damage to the BBB and blood vessels, further leading to increased vascular permeability. The plasma protein infiltrated into the interstitial space and the fluid gathers in the interstitial space, resulting in vasogenic cerebral edema.

Cytotoxic or vasculogenic edema can be differentiated by the diffusion weighted images (DWIs).[23] Unfortunately, lack of DWI examination hindered our judgment of the type of edema.

The clinical outcome of the 'watershed shift' phenomenon is generally favorable, but there is a potential risk for perioperative cerebral infarction. Thus, Tashiro *et al.*[17] recommend routine CBF measurement in the acute stage after revascularization surgery for adult MMD to avoid surgical complications, such as local CHS and cerebral ischemia, caused by the 'watershed shift' phenomenon. Hayashi *et al.*[4] and Tu *et al.*[5] have reported hyperperfusion near the anastomotic site along with 'watershed shift' hypoperfusion in the distal area of MCA and corresponding neurological dysfunction in MMD patients. With the gradual recovery of perfusion, the corresponding symptoms of neurological impairment were consequently improved. Indeed, along with the perfusion on left frontotemporal lobes improved after blood volume expansion, our patient presented significantly improvement both on the MRI findings and neurological symptoms.

Conclusion

We have reported an extremely rare case of adult MMD that manifested as a paradoxical symptomatic local cerebral edema and hypoperfusion caused by the 'watershed shift' after combined revascularization surgery. Although the exact mechanism of this rare association is unknown, the dysfunction of brain cells and damage to the BBB caused by hypoperfusion in MMD may explain this unique pathophysiological condition.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Ethical approval

Ethical approval was obtained from the Zhongnan Hospital Ethics Committee (approval number: Kelun-2017005).

Informed consent

The patient is aware of all the content, descriptions, images, and details presented in this article and agreed for it to published as a case report scientific research paper in any scientific research magazine.

ORCID iD

Jincao Chen [iD] https://orcid.org/0000-0001-9882-7978

References

1. Scott RM. Moyamoya syndrome: a surgically treatable cause of stroke in the pediatric patient. *Clin Neurosurg* 2000; 47: 378–384.

2. Ueki K, Meyer FB and Mellinger JF. Moyamoya disease: the disorder and surgical treatment. *Mayo Clin Proc* 1994; 69: 749–757.

3. Kokuzawa J, Kaku Y, Watarai T, *et al.* Pure vasogenic edema caused by cerebral hyperperfusion after superficial temporal artery to middle cerebral artery anastomosis–case report. *Neurol Med Chir (Tokyo)* 2010; 50: 250–253.

4. Hayashi T, Shirane R, Fujimura M, *et al.* Postoperative neurological deterioration in pediatric moyamoya disease: watershed shift and hyperperfusion. *J Neurosurg Pediatr* 2010; 6: 73–81.

5. Tu XK, Fujimura M, Rashad S, *et al.* Uneven cerebral hemodynamic change as a cause of neurological deterioration in the acute stage after direct revascularization for moyamoya disease: cerebral hyperperfusion and remote ischemia caused by the 'watershed shift'. *Neurosurg Rev* 2017; 40: 507–512.

6. Uchino H, Kim JH, Fujima N, *et al.* Synergistic interactions between direct and indirect bypasses in combined procedures: the significance of indirect bypasses in moyamoya disease. *Neurosurgery* 2017; 80: 201–209.

7. Fujimura M, Niizuma K, Inoue T, *et al.* Minocycline prevents focal neurological deterioration due to cerebral hyperperfusion after extracranial-intracranial bypass for moyamoya disease. *Neurosurgery* 2014; 74: 163–170.

8. Fujimura M, Inoue T, Shimizu H, *et al.* Efficacy of prophylactic blood pressure lowering according to a standardized postoperative management protocol to prevent symptomatic cerebral hyperperfusion after direct revascularization surgery for moyamoya disease. *Cerebrovasc Dis* 2012; 33: 436–445.

9. Fujimura M, Mugikura S, Kaneta T, *et al.* Incidence and risk factors for symptomatic cerebral hyperperfusion after superficial temporal artery–middle cerebral artery anastomosis in patients with moyamoya disease. *Surg Neurol* 2009; 71: 442–447.

10. Schubert GA, Biermann P, Weiss C, *et al.* Risk profile in extracranial/intracranial bypass surgery–the role of antiplatelet agents, disease pathology, and surgical technique in 168 direct revascularization procedures. *World Neurosurg* 2014; 82: 672–677.

11. Guzman R, Lee M, Achrol A, *et al.* Clinical outcome after 450 revascularization procedures for moyamoya disease. Clinical article. *J Neurosurg* 2009; 111: 927–935.

12. Yu J, Shi L, Guo Y, *et al.* Progress on complications of direct bypass for moyamoya disease. *Int J Med Sci* 2016; 13: 578–587.

13. Fujimura M, Shimizu H, Mugikura S, *et al.* Delayed intracerebral hemorrhage after superficial temporal artery–middle cerebral artery anastomosis in a patient with moyamoya disease: possible involvement of cerebral hyperperfusion and increased vascular permeability. *Surg Neurol* 2009; 71: 223–227.

14. Fujimura M, Shimizu H, Inoue T, *et al.* Significance of focal cerebral hyperperfusion as a cause of transient neurologic deterioration after extracranial-intracranial bypass for moyamoya disease: comparative study with non-moyamoya patients using *N*-isopropyl-p-[^{123}I]iodoamphetamine single-photon emission computed tomography. *Neurosurgery* 2011; 68: 957–964.

15. Huttner HB and Schwab S. Malignant middle cerebral artery infarction: clinical characteristics, treatment strategies, and future perspectives. *Lancet Neurol* 2009; 8: 949–958.

16. Sakata H, Fujimura M, Mugikura S, *et al.* Local vasogenic edema without cerebral hyperperfusion after direct revascularization surgery for moyamoya disease. *J Stroke Cerebrovasc Dis* 2015; 24: e179–e184.

17. Tashiro R, Fujimura M, Kameyama M, *et al.* Incidence and risk factors of the watershed shift phenomenon after superficial temporal artery–middle cerebral artery anastomosis for adult moyamoya disease. *Cerebrovasc Dis* 2019; 47: 178–187.

18. Hoehn-Berlage M, Norris DG, Kohno K, *et al.* Evolution of regional changes in apparent diffusion coefficient during focal ischemia of rat brain: the relationship of quantitative diffusion NMR imaging to reduction in cerebral blood flow and metabolic disturbances. *J Cereb Blood Flow Metab* 1995; 15: 1002–1011.

19. Wang CX and Shuaib A. Critical role of microvasculature basal lamina in ischemic brain injury. *Prog Neurobiol* 2007; 83: 140–148.

20. Kniesel U and Wolburg H. Tight junctions of the blood-brain barrier. *Cell Mol Neurobiol* 2000; 20: 57–76.

21. Nielsen TH, Stahl N, Schalen W, *et al.* Recirculation usually precedes malignant edema in middle cerebral artery infarcts. *Acta Neurol Scand* 2012; 126: 404–410.

22. Mukerji N, Cook DJ and Steinberg GK. Is local hypoperfusion the reason for transient neurological deficits after STA-MCA bypass for moyamoya disease? *J Neurosurg* 2015; 122: 90–94.

23. Karapanayiotides T, Meuli R, Devuyst G, *et al.* Postcarotid endarterectomy hyperperfusion or reperfusion syndrome. *Stroke* 2005; 36: 21–26.