Severe cerebral edema induced by watershed shift after bypass in a patient with chronic steno-occlusive disease: a case report and short literature review

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Abstract

Background: Carotid occlusive disease is a type of progressive disease resulting in ischemic stroke. Extracranial-intracranial bypass surgery represents a valid therapeutic option when medical treatment does not make effects. The appearance of cerebral edema following bypass is common during acute stage. Additionally, there are many causes of mild cerebral edema, such as hemodynamic changes, venous congestion and others. However, severe edema involving large brain tissue, which presents as reversible aphasia and hemiplegia, remains to be elucidated.

Case presentation: A 55-year-old man was admitted to the neurosurgery department for repeated dizziness for over a year and sudden onset of syncope 1 month prior, and he was diagnosed with carotid occlusive disease. After surgical contraindications were excluded, dual bypass and encephalo-duro-myo-synangiosis were performed. Although blood pressure and fluid management were strictly under control promptly after surgery, massive cerebral edema involving the left anterior cerebral artery and middle cerebral artery territories occurred from the 6th day after surgery. Additionally, no discernible cerebral infarction or hemorrhage occurred. Moreover, the cerebral blood flow of the middle cerebral artery displayed an early decrease followed by delayed elevation on the left side. Without restricting the spreading of cerebral edema, life-threatening cerebral herniation could develop at any time. Mannitol and furosemide were administered for impending cerebral herniation. The amelioration of symptoms was noticed on the 16th day after surgery. The patient felt relief on the 21st day after surgery. Digital subtraction angiography performed on the 180th day after surgery demonstrated the patency of dual anastomosed vessels, and the patient recovered without any permanent neurological deficit.

Conclusion: Based on changes in cerebral blood flow and reversible symptoms, the “watershed shift” phenomenon could explain such a severe deficit. However, this deficit was not the same as the classical presentation of the “watershed shift”, which involves a moderate amount of brain tissue and presents significant increases in cerebral blood flow. In addition to the “watershed shift”, a swollen temporal muscle may also participate in the progression of focal edema.

Keywords: Cerebral edema, Bypass, Watershed shift, Magnetic resonance imaging 3D–arterial spin labeling (MRI 3D-ASL), Swollen temporal muscle

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Background
Carotid occlusive disease is a chronic cerebrovascular disease accompanied by decreased cerebral blood flow. In addition to optimal medical therapy to eliminate the poor effect of atherosclerotic plaques, surgical treatments to improve cerebral perfusion on the affected side have been performed in patients with steno-occlusive carotid artery. For patients with symptomatic nonmoyamoya cerebrovascular diseases, especially those caused by steno-occlusive carotid artery, extracranial-intracranial (EC-IC) bypass has offered no more benefits over medical therapy in the international randomized EC-IC study [1] and the Carotid Occlusion Surgery Study [2]. However, EC-IC bypass still works in certain symptomatic cerebrovascular diseases [3, 4], and neither of the two trials evaluated the effectiveness of EC-IC bypass in patients with multiple segmental stenosis, especially for those with stenotic extracranial segment of the carotid artery combined with intracranial arterial stenosis. Cerebral hyperperfusion syndrome (CHS) is a relatively rare but devastating complication of EC-IC bypass, which involves postoperative transient neurological deficits related to excessive increase in regional cerebral blood flow [5]. CHS following carotid endarterectomy (CEA) and carotid artery stenting (CAS) in patients with carotid occlusive disease has been widely reported with the evidence of hyperperfusion increasing >100% from baseline [5], but the incidence of CHS caused by EC-IC bypass remains low [6]. “Watershed shift”, a special hemodynamic change of CHS, occurs after dual anastomosis. And the phenomenon presents more often in pediatric moyamoya disease (MMD) than in adult MMDs [7]. Here, we describe a male patient with chronic occlusion of internal carotid artery (ICA) and middle cerebral artery (MCA) who developed severe massive cerebral edema after left dual EC-IC bypass and encephalo-duro-myo-synangiosis (EDMS).

Case presentation
A 55-year-old man who had a history of hypertension was admitted to the neurosurgery department due to dizziness repeatedly for over a year and a sudden onset of syncope 1 month prior. Additionally, he once accepted medical therapy in the neurological department without alleviation. Neurological examination revealed no abnormal signs. Diffusion-weighted imaging (DWI) showed no obvious infarct in the bilateral cerebral cortex. Ultrasound examination of the carotid artery confirmed chronic bilateral stenosis of the carotid artery bifurcation caused by stable fibrous-calcific plaques. In contrast to the normal side, left stenotic anterior cerebral arteries (ACA), middle cerebral artery (MCA) and ICA were hardly detected on preoperative DSA (Fig. 1a). The left frontal and parietal lobes were supplied by the left posterior cerebral artery derived from the extracranial artery combined with intracranial arterial stenosis. Dual anastomosis between the superficial temporal artery (STA) and MCA combined with EDMS on the left side was performed. The patency of the anastomotic stoma was immediately confirmed by indocyanine green video-angiography. Accompanied by nicardipine hydrochloride, systolic blood pressure was strictly controlled at 120–140 mmHg promptly after surgery. During the first few days, the patient presented no additional neurological deterioration. Computed tomography angiography after surgery confirmed no stenosis in recipient vessels. Additionally, T2-weighed MRI and 3D-ASL on the 3rd day after surgery showed a more significantly increased CBF at the anastomotic sites than at the preoperative stage (Fig. 2b and c), indicating the effectiveness of revascularization. Nevertheless, this patient developed aphasia and right hemiplegia on the 6th day after surgery with continuous execution of the strict program of blood pressure control. Computed tomography on the same day found that the middle line

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**Fig. 1** Digital subtraction angiography (DSA) results of the patient. a. Steno-occlusive changes at the bifurcation of the left carotid artery and abnormal development of the left ACA and MCA with a normal right ICA on preoperative DSA. b. Left frontal and partial lobes mainly supplied by the left posterior cerebral artery on preoperative DSA. c. Distribution of the superficial temporal artery before bypass surgery. The black arrows indicate the frontal and parietal branches of STA. d. The superficial temporal artery grew well and participated in supplying the left temporal and partial lobes in DSA examined at 6 months after surgery.
migrated to the right side and a local low-density lesion in the left frontal lobe near the operative area. Following the application of mannitol and furosemide, the symptoms began to ameliorate on the 16th day after surgery. Nevertheless, MRI 3D-ASL on the 21st day after surgery showed more decreased CBF than at the site of anastomosis on the 3rd day after surgery (Fig. 2d). T2-weighted MRI showed a massive hyperintensity lesion around the operation area, while DWI revealed no cerebral infarction, indicating massive cerebral edema in the operative area (Fig. 3a and b). Ultimately, this patient recovered after 40 days of surgery without any neurologic deficits. MRI 3D-ASL on the 166th day showed bilateral well-developed CBF (Fig. 2e) and DSA on the 180th day presented well-developed revascularization (Fig. 1d).

**Discussion and conclusions**

Although the effectiveness of revascularization surgery for ischemic stroke has remained controversial in previous research [9], STA-MCA bypass is still a potential method for chronic occlusive cerebrovascular diseases, especially when medical therapy fails or neurological symptoms persist due to low cerebral perfusion. Additionally, potential postoperative complications should be addressed urgently, such as intracerebral hemorrhage, cerebral ischemic lesion or infarction resulting from “watershed shift” [10] and other deleterious complications.

Cerebral edema is defined as an increase in brain volume due to abnormal accumulation of fluid within the brain parenchyma [11], and it is classified as vasogenic,
cytotoxic, hydrocephalic and osmotic edema, despite the acknowledgment that multiple types of cerebral edema are involved in most clinical situations. Regarding the mechanism, vasogenic edema is associated with micro destructions that allow increased plasma proteins and water across the blood-brain-barrier, while cytotoxic edema is accompanied by abnormal water uptake into injured brain cells [12]. Diagnostically, unlike cytotoxic edema associated with hyperintensity in DWI and decline in Apparent Diffusion Coefficient, vasogenic edema presents a variable weak change in DWI and a relative increase in water diffusion [13]. The existence of hyperintensity on T2-weighted MRI accompanied by the lack of typical hyperintensity lesions in DWI indicates that this area mainly refers to vasogenic edema (Fig. 3a and b). Postoperative cerebral edema mostly occur in MMD or those with CEA or CAS [6, 14, 15]. This condition is rare after surgery for the patients with carotid occlusive disease. The region of edema resulting from CHS is often limited to the territories near the surgical area, and hyperintensity lesions can be found in perfusion images. Among MMDs with combined bypass, retrospective analysis found that hyperperfusion-related symptoms generally occur in the first week and are entirely ameliorated during the second postoperative week [15]. Presenting neurological deficits 6 days after bypass, this patient began improving on the 17th day and completely recovered on the 40th day after surgery. The procedure to alleviate symptoms does not exactly conform to the course of postoperative CHS among MMDs. However, the dual branches of STA were anastomosed to M4 segments, making “watershed shift” possible structurally. Normalized CBF (nCBF) calculated by MRI 3D-ASL near the operative area showed an early decrease and delayed increase (Table 1) by manually choosing the region of interest in MRI 3D-ASL [16]. Meanwhile, T2-weighted MRI on the 3rd day after surgery showed early focal cerebral edema at the sites of anastomosis (Fig. 2b). In addition to transient asphasia and hemiplegia, cerebral edema and changes in perioperative nCBF can be explained by the “watershed shift”. Nevertheless, a classical “watershed shift” is defined basis on CHS, which requires ≥50% increase in the CBF at the site of anastomosis [17]. However, the absolute values of CBF on the 3rd or 21st day after surgery were both decreased below the preoperative level, even on the normal side. T1-weighted MRI on the 21st day presented mild migration of the middle line to the right side (Fig. 3c), indicating increased intracranial pressure likely still played a role in affecting cerebral perfusion in the whole brain. The steal phenomenon was thought to result in hypoperfusion on the right side. The dual bypass associated with EDMS changed the previous hemodynamics balance between the stenotic side and right side. It reduced the vascular resistance on the left side and released blood flowing into the left rather than the right hemisphere. In contrast to contralateral nCBF, we found that nCBF on the affected side increased to different degrees. Among them, the most significant difference was 1.374 vs. 0.987, which presented on the 21st day after surgery (Table 1). Different from the classical “watershed shift”, a large amount of brain tissues were involved in cerebral edema. Thus, other mechanisms may explain the progression of cerebral edema. In addition to the “watershed shift”, a swollen temporal muscle was also considered to induce focal edema. During the acute stage, a relatively narrow free bone flap could magnify the compression of the swollen temporal muscle, influencing regional cerebral circulation and resulting in local brain edema [18]. The swollen temporal muscle found on the postoperative T2-weighted MRI may exacerbate the situation. However, its effect was temporary and limited because the temporal muscle had already shrunken to normal size when the patient began to recover on the 17th day after surgery. Venous congestion was once considered as the primary cause because such massive cerebral edema associated with CHS has not been reported previously. However, venous congestion is generally related to cerebral hypoperfusion, and it seems impossible for venous congestion to be involved. Additionally, epilepsy was unrelated to severe cerebral edema in the patient in the lack of obvious symptoms of epilepsy, which has been reported as a possible cause of vasogenic edema [19]. It remains a mystery why reversible cerebral edema could

| Table 1 Cerebral perfusion calculated on MRI 3D-ASL |
|-----------------|--------|--------|--------|--------|
|                 | PRE    | POD3   | POD21  | POD166 |
| L MCA (mean ± SD) (a) | 40.099 ± 21.104 | 31.981 ± 22.397 | 25.802 ± 12.429 | 47.109 ± 18.265 |
| Cerebellum (mean ± SD) (a) | 29.406 ± 9.695 | 27.204 ± 9.943 | 18.782 ± 6.519 | 36.485 ± 8.837 |
| nCBF (a) | 1.394 | 1.176 | 1.374 | 1.291 |
| R MCA (mean ± SD) (a) | 44.554 ± 12.035 | 32.945 ± 20.146 | 24.473 ± 12.416 | 44.421 ± 16.137 |
| Cerebellum (mean ± SD) (a) | 39.079 ± 11.926 | 31.380 ± 8.041 | 31.380 ± 8.041 | 37.683 ± 12.200 |
| nCBF (a) | 1.140 | 1.051 | 0.987 | 1.179 |

L left, R right, MCA mean distribution of the middle cerebral artery, Cerebellum mean distribution of the cerebellum, (a) Units: ml/100 g/min, (b) nCBF means normalized CBF and nCBF = MCA (mean)/cerebellum (mean)
lead to such severe clinical symptoms, even requiring surgical intervention. To prevent such severe cerebral edema from further into brain hernia or causing subsequent hemorrhage, one possible approach is a strict perioperative strategy. As standardized management to prevent CHS, the blood pressure should be below 130 mmHg. However, extensive low blood pressure could lead to cerebral infarction [20], and so the blood pressure of this patient was controlled under 140 mmHg by nimodipine rather than 130 mmHg. Fluid intake and hydroelectrolytic equilibration should also be considered cautiously every day. We regulated fluid intake and focused on blood tests to maintain homeostasis. Additionally, the combination of mannitol and furosemide was employed to lower intracranial pressure when clinical symptoms presented and MRI-DWI confirmed focal cerebral edema. Another possible approach is the use of edaravone, which is an antioxidant to prevent reperfusion-associated hemorrhage that can be administered to reduce effects from huge changes in CBF [21]. Additionally, quantitative magnetic resonance angiography may potentially identify patients at risk for CHS by assessing mean flow differences between ICA and MCA [22]. By applying multiple strategies, the complete disappearance of focal cerebral edema was obtained without permanent neurological deficits. Therefore, further study with a larger number of patients is necessary to validate the relationship between cerebral edema and the “watershed shift”.

In conclusion, this case presents massive cerebral edema after bypass. Based on changes in cerebral blood flow and reversible symptoms, the “watershed shift” may explain this severe deficit. However, this deficit is not the same as the classical presentation resulting from the “watershed shift”, which does not involve brain tissues and presents significant increases in CBF compared with the preoperative level. In addition to the “watershed shift”, the swollen temporal muscle also participated in the progression of focal edema.

Abbreviations
ACA: Anterior cerebral artery; CAS: Carotid artery stenting; CBF: Cerebral blood flow; CEAn: Carotid endarterectomy; CHS: Cerebral hyperperfusion syndrome; DSA: Digital subtraction angiography; DWI: Diffusion-weighted imaging; EC-IC bypass: Extracranial-intracranial bypass; EDMS: Encephalo-duro-myo-synangiosis; ICA: Internal carotid artery; MCA: Middle cerebral artery; MRI 3D-ASL: Magnetic resonance imaging 3D—arterial spin labeling; STA: Superficial temporal artery

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Authors’ contributions
Study concept and design: LW and YL. Acquisition, analysis and interpretation of data: YW, YC, XL, YY. Drafting of the manuscript: YL. Study supervision: LW. All of the authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
The Institutional Review Board of Second Affiliated Hospital, School of Medicine, Zhejiang University approved this study. Informed consent for participation was obtained from the patient.

Consent for publication
Written informed consent was obtained from the patient’s daughter to publish the information related to his course in the hospital.

Competing interests
The authors declare that this article content has no competing interests.

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