Case Report
Acute cerebral infarction after spontaneous recanalization of extracranial internal carotid artery atherosclerotic occlusion: two case reports and literature review

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Abstract: Spontaneous recanalization of extracranial internal carotid artery atherosclerotic occlusion is rare in clinical practice. Herein, we reported two cases of acute cerebral infarction after spontaneous recanalization of extracranial internal carotid artery atherosclerotic occlusion. The patients were confirmed as extracranial internal carotid artery with chronic occlusion by imaging. One month after the diagnosis of occlusion, recanalization of symptomatic internal carotid artery occurred, which was confirmed by CT angiography, leading to ipsilateral hemiplegia. The patients underwent conservative medical treatment. Ipsilateral stroke or transient ischemic attack did not occur during long-term follow-up (≥2 years). Additionally, a literature review was conducted based on the incidence, possible mechanisms, treatment and prognosis in order to increase the awareness of this rare clinical phenomenon.

Keywords: Internal carotid artery, arterial occlusion, artery recanalization, atherosclerosis, stroke

Introduction

Spontaneous recanalization of extracranial internal carotid artery atherosclerotic occlusion is rarely seen in clinical practice, and the vast majority of cases involve recanalization after occlusion due to traumatic or spontaneous arterial dissection [1]. Although atherosclerosis is a common cause of extracranial carotid artery occlusion, spontaneous recanalization of atherosclerotic occlusion is rare, and the vast majority of cases are asymptomatic; with only few reported cases of symptomatic recanalization [2]. The short-term recanalization of occluded extracranial carotid arteries (within hours to 2 weeks after onset) may be related to vasospasm relief, absorption of hematoma from atherosclerotic plaque and shifting of internal carotid artery thrombus to the distal branch of the artery [3]. Long-term recanalization is related to collateral circulation compensation, use of antiplatelet drugs, anticoagulant drugs, and statin drug therapy [4]. Since spontaneous recanalization of extracranial carotid artery atherosclerotic occlusion is usually asymptomatic, it is considered a benign process. Since very few cases are seen in clinical practice, the incidence, mechanism, natural course and long-term prognosis of spontaneous recanalization of atherosclerotic internal carotid artery occlusion remain unclear, and the treatment plan is also controversial. Herein, we reported two cases of acute cerebral infarction after spontaneous recanalization of extracranial internal carotid artery atherosclerotic occlusion and conducted a literature review, in order to increase the awareness of this rare clinical phenomenon.

Case report

Case 1

A 62-year-old male patient had a 10-year history of hypertension and 8-year history of hyperlipidemia, without any history of smoking and
diabetes mellitus, and did not undergo any formal treatment. On July 8, 2014, the patient was admitted to a local hospital for sudden onset of left limb weakness. After admission, cerebral infarction in right basal ganglia region was diagnosed by emergency cranial CT scan. Additionally, color Doppler ultrasound of carotid arteries showed severe stenosis at the origin of right internal carotid artery and left internal carotid artery occlusion. During hospitalization, the patient was given aspirin tablet (100 mg) for antiplatelet aggregation therapy, atorvastatin tablet (10 mg) for reducing blood lipids and stabilizing plaques, blood-pressure control and other symptomatic treatment daily. After 15 days, the patient was discharged from the hospital in stable condition. The patient underwent right internal carotid artery stenting on the third day after admission. Intraoperative DSA angiography confirmed severe stenosis of the right internal carotid artery (Figure 1C), and occlusion of the left internal carotid artery (Figure 1D). The right internal carotid artery stenting was successful, and 4500 U of unfractionated heparin was used for whole systemic heparinization during the operation. Three days before the operation, as well as after the operation, the patient was given aspirin tablet (100 mg), clopidogrel tablet (75 mg) for antiplatelet aggregation therapy, atorvastatin tablet (10 mg) for stabilizing plaques, as well as irbesartan tablet (150 mg) for antihypertensive treatment daily; and the postoperative blood pressure was maintained at about 120/80 mmHg. On the third day after CAS, the patient experienced sudden onset of right limb weakness. The right upper arm muscle strength was grade II, the right lower limb muscle strength was grade III, and the left limb muscle strength did not significantly change as compared to that before operation. Repeat carotid CTA showed that the original right internal carotid artery stent was in proper position, and the lumen was patent (Figure 2A). The left internal carotid artery was recanalized; the lumen showed severe stenosis, and the stenosis rate was...
Acute cerebral infarction after recanalization of ICA occlusion

Figure 2. A. Carotid CTA after right internal carotid artery stent implantation; B. Carotid CTA showed spontaneous recanalization of the left internal carotid artery, and severe stenosis of local lumen; C. Before carotid artery stenting, the head MRI diffusion weighted image (DWI) of the same patient showed no infarction at the same level; D. The white arrow shows multiple new infarcts in the left frontal lobe in the head MRI-DWI.

about 90% (Figure 2B). However, the cranial MRI scan showed multiple new infarctions in the left frontal lobe (Figure 2D). Given the imaging findings, and since the left acute cerebral infarction was caused by spontaneous recanalization of left internal carotid artery leading to plaque abscession, the patient was suggested to undergo left carotid artery stent implantation after one month, which the patient refused. Since the patient was previously treated with antiplatelet aggregation therapy and atorvastatin tablet, no further symptomatic treatment was given. Five days later, the patient was discharged from the hospital in stable condition, and continued taking oral aspirin tablet (100 mg) and clopidogrel tablet (75 mg) for stabilizing plaques once every night, as well as irbesartan tablet (150 mg) for antihypertensive treatment once daily. The patient was followed-up, and carotid artery ultrasound and cranial MRI were conducted for >2 years after discharge. There was no recurrence of stroke and transient ischemic attack (TIA). The left internal carotid artery was patent, and the right internal carotid artery showed severe stenosis.

Case 2

A 63-year-old male patient, had a 5-year history of hypertension, without any history of smoking and diabetes mellitus. His blood pressure was maintained at about 130/80 mmHg with regular oral amlo- dipine besylate tablet (5 mg) for antihypertensive treatment daily. In October 2011, the patient was admitted to our hospital due to left acute cerebral infarction. The carotid CTA showed mild stenosis of the left internal carotid artery. The patient suffered from aphasia and right hemiplegia at discharge. After discharge, the patient was treated with oral aspirin tablet (100 mg) and atorvastatin tablet (10 mg) daily for a long time. When the patient was reexamined at a local hospital, the color Doppler ultrasound of carotid artery showed severe stenosis of the right internal carotid artery and left internal carotid artery occlusion. On March 15, 2013, the patient visited our hospital to undergo endarterectomy of the right internal carotid artery. At admission, his blood pressure was 147/95 mmHg, and the patient suffered from aphasia and right hemiplegia (upper-limb muscle strength was grade II, lower limb muscle strength was grade III). Left limb muscle strength was grade V. There was no abnormality detected in blood biochemistry and routine electrocardiogram at our hospital. The carotid CTA further demonstrated severe atherosclerotic stenosis at the origin of right internal carotid artery, with about 80% stenosis rate (Figure 3A), and occlusion at the origin of left internal carotid artery (Figure 3B, 3C). Cranial MRI scan showed old cerebral infarction in the left frontal lobe and parietal lobe, and there was no infarction in right hemisphere brain parenchyma. Before endarterec-
tomy, the DSA angiography confirmed complete occlusion of the left internal carotid artery (Figure 3D). After excluding the contraindication of operation, the patient underwent carotid endarterectomy (CEA) of the right internal carotid artery on the fifth day after admission, and the operation was successful. After the operation, the patient was given aspirin tablet (100 mg), clopidogrel tablet (75 mg) for antiplatelet aggregation therapy, atorvastatin tablet (10 mg) for stabilizing plaques once per night, as well as amlodipine besylate tablet (5 mg) for antihypertensive treatment daily. The patient was followed-up, and carotid artery ultrasound and cranial CT were conducted for more than 3 years after discharge. There was no recurrence of stroke and TIA. The right internal carotid artery was patent, and the left internal carotid artery showed moderate-severe stenosis. The right upper arm muscle strength was grade I, and the right lower limb muscle strength was grade I.

Discussion

Spontaneous recanalization of intracranial internal carotid artery occlusion due to various causes is common. The spontaneous recanalization rates at the acute phase ranged from 17-67% [1]. The proportion of spontaneous recanalization of extracranial internal carotid artery occlusion from traumatic or spontaneous aortic dissection is about 68%, and the proportion of recanalization is up to 85% in three months [2]. However, although atherosclerosis is a common cause of extracranial internal carotid artery occlusion, spontaneous recanalization of extracranial internal carotid artery atherosclerosis is rare. Lehrer [5] first reported this rare clinical phenomenon in
Acute cerebral infarction after recanalization of ICA occlusion

1958, and only few cases have been subsequently reported [4]. The spontaneous recanalization rate reported in only one long-term follow-up study of spontaneous recanalization of extracranial internal carotid artery atherosclerosis was about 2.3%, and the proportion of symptomatic spontaneous recanalization was <1% [6]. Most reported cases of spontaneous recanalization of atherosclerotic internal carotid artery occlusion are asymptomatic, and are incidentally discovered by imaging (such as color Doppler ultrasound of carotid artery, carotid CTA). However, acute severe ischemic cerebral infarction after recanalization, as seen in our two patients, has been rarely reported [7].

The mechanism of spontaneous recanalization of internal carotid artery occlusion remains unclear. The mechanisms underlying short-term recanalization of occluded extracranial carotid arteries (within hours to 2 weeks after onset) may include: relief of vasospasm due to original artery dissection, hematoma caused by atherosclerotic plaque hemorrhage originally leading to severe stenosis of internal carotid artery occlusion, severe stenosis of the arterial lumen and internal carotid artery thrombosis after absorption of the hematoma, and shifting of the thrombus to the distal branch of artery leading to recanalization of the internal carotid artery [2-4]. The spontaneous recanalization in our patients occurred >1 month after the diagnosis of occlusion. Thus, the above-mentioned possibilities could be eliminated. Nguyen-Huynh et al. [1] performed pathological examination of surgical specimen from a patient with spontaneous recanalization of atherosclerotic internal carotid artery occlusion who underwent endarterectomy, and found evidence of spontaneous clot lysis. Thus, they speculated that spontaneous recanalization may be related to the activation of antithrombotic system in vascular endothelial cells and self-lysis of thrombus. The collateral circulation is well compensated after occlusion of the internal carotid artery, and the use of antiplatelet drugs (such as aspirin, clopidogrel), anticoagulant drugs (heparin and warfarin) and statins may contribute to self-lysis of the thrombus. However, the length of internal carotid artery occlusion, the nature of thrombus and the time of thrombosis may affect the probability of recanalization of the internal carotid artery in the occluded section. In the perioperative period, aspirin and clopidogrel were used in our patients to enhance platelet aggregation, and atorvastatin was used to reduce blood lipids and stabilize plaques. The patients underwent stent implantations, and were given systemic heparin. Meanwhile, DSA of the two patients showed good intracranial vascular compensation, and retrograde flow filling in the distal vessels of internal carotid artery occlusion during the late arterial phase.

Figure 4. A. Carotid CTA showed that the lumen was patent after endarterectomy of the right internal carotid artery; B. Carotid CTA showed spontaneous recanalization of the left internal carotid artery, the stenosis rate was about 90%; C. Enhanced cranial CT scan showed a large infarction in the left frontal lobe, which was larger than before the operation; D. Before CEA, the head MRI-T2WI of the same patient showed an old infarction at the same level.
Therefore, we hypothesized that spontaneous recanalization may be caused by the combined effects of these factors. A previous study suggested that formation of nutrient artery of internal carotid artery may cause spontaneous recanalization [8]. However, careful observation of the carotid CTA images of our patients did not indicate any arterial wall nutrient artery formation.

Since spontaneous recanalization of extracranial atherosclerotic carotid artery occlusion is rare, its natural course is not well defined. Hence, the need for further surgical treatment (endarterectomy or stent implantation) in the arterial stenosis after recanalization remains controversial. The collaborative Group of North American Symptomatic Carotid Endarterectomy Trial indicated that endarterectomy or stent implantation can significantly reduce the risk of recurrent stroke in patients with symptomatic internal carotid stenosis >50% or asymptomatic internal carotid stenosis >70% [9]. However, this study did not include any patient with internal carotid artery stenosis after occlusion. Therefore, whether this group of patients should be aggressively intervened remains doubtful. Some patients with spontaneous recanalization reportedly underwent endarterectomy or stent implantation to prevent long-term recurrence of ischemic cerebrovascular events [7]. However, other patients with spontaneous recanalization (including the two cases in this report) underwent conservative medical treatment [2, 6] with aspirin and clopidogrel for antiplatelet aggregation therapy as well as atorvastatin for lowering blood lipids and stabilizing plaques. Long-term follow-up (>1 year) of all reported cases (including symptomatic recanalization) that underwent conservative medical treatment showed no recurrence of ischemic stroke events in the internal carotid artery after recanalization, which indicated that the long-term prognosis was good. However, a larger sample size, long-term follow-up study is needed to confirm these findings.

Previously, it was believed that once internal carotid artery was completely occluded, the risk of recurrent stroke was very low, therefore, it was considered as a benign course of disease. However, recent studies have shown that recanalizing occluded internal carotid artery is not superior to the best conservative medical treatment for patients. Therefore, follow-up of such patients have not been given due attention [1]. Although our cases and literature review showed that spontaneous recanalization of internal carotid artery occlusion is rare, the recanalization may still cause acute ischemic brain infarction. Therefore, we believe that the follow-up strategy should be more active in this group of patients. A previous study suggested that radiographic examination once every 3-6 months is necessary for patients with internal carotid artery occlusion [7]. Both color Doppler ultrasound of carotid artery and carotid CTA are accurate and noninvasive method for the diagnosis of carotid artery occlusion, false sign of occlusion recanalization and predicting the possibility of recanalization after occlusion [10]. We believe that repeat color Doppler ultrasound of the carotid artery or carotid CTA once every six months may be appropriate.

In summary, spontaneous recanalization of extracranial carotid artery atherosclerotic occlusion is a rare clinical phenomenon. Although the incidence is very low, spontaneous reperfusion may cause severe ischemic stroke. Therefore, regular follow-up of patients with internal carotid artery occlusion, especially those receiving antiplatelet drugs and anticoagulant therapy, should be conducted. A larger sample size clinical study is needed to further clarify the incidence, mechanism, natural course, and long-term prognosis of this rare clinical phenomenon.

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Disclosure of conflict of interest

None.

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Acute cerebral infarction after recanalization of ICA occlusion

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