Revascularization of Acute Stent Thrombosis after Carotid Artery Stenting in Clopidogrel Resistance Patient

Pian Wang (✉ pianpian0903@126.com)

Chengdu fifth people's hospital <https://orcid.org/0000-0001-6175-8091>

Wei Wei

Chengdu second people's hospital

Yan Wang

Chengdu fifth people's hospital

Zheng Li

Chengdu fifth people's hospital

Qingbin Zhang

Chengdu fifth people's hospital

Case report

Keywords: Acute Stent Thrombosis, Carotid Artery Stenting, revascularization, clopidogrel resistance

Posted Date: April 5th, 2019

DOI: <https://doi.org/10.21203/rs.2.1850/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Carotid Artery Stenting (CAS) is an alternative strategy to prevent ischemic stroke in patients who are at high-risk of surgery compared with carotid endarterectomy (CEA). Acute carotid stent thrombosis (ACST) was extremely rare, but devastating complication after CAS. Academically, it occurred within 30 days after CAS. There are several reasons causing ACST, such as inadequate antiplatelet therapy, early discontinuation of antiplatelet therapy, clopidogrel resistance, hypercoagulable state, local vessel dissection, vasospasm, intimal injury, and so on. Although successful recanalization cases were reported, however, there is still a lack of experience in the choice of treatment methods and the timing of ACST treatment, especially when the patient has clopidogrel resistance. We are here to provide a case that successfully revascularization after ACST in patient with evidenced clopidogrel resistance, which was further confirmed by genetic testing. In our case, both thrombus aspiration and platelet glycoprotein IIb/IIIa antagonist (GPIs) were used for recanalization. Also, we review the literature and discuss appropriate treatment strategies for this deadly and rare event.

Background

Carotid artery stenting (CAS) is an alternative strategy to prevent primary or secondary ischemic stroke in selected patients compared with carotid endarterectomy (CEA) ¹. It is well-known that acute carotid stent thrombosis (ACST) is an extremely rare event, while that accompanies with devastating complication ², and its incidence rate was accounted for 0.5%-0.8% ². Although successful recanalization cases were reported ^{3 4}, however, there is still a lack of experience in the choice of treatment methods and the timing of ACST treatment, especially when the patient has clopidogrel resistance. Here, for the first time, we aimed to report a successful revascularization of ACST in a patient with clopidogrel resistance, which was further confirmed by genetic testing. We attempted to review the literature and discuss appropriate treatment strategies for this rare event.

Case Presentation

The study protocol was approved by the Ethics Committees of the the Fifth People's Hospital of Chengdu, Chengdu, and all participants provided written informed consent.

A 69-year-old man was admitted to the Fifth People's Hospital of Chengdu, Chengdu, China for the weakness of right limb, right central facial paralysis, and hemianalgesia for 2 days. The weakness of his right limb aggravated and barylalia was detected for a half of day. He had a history of hypertension for four years due to the poor blood pressure control. After hospitalization, the magnetic resonance imaging (MRI) showed multiple internal border zone infarcts in a rosary-like pattern along the left centrum semiovale. Computed tomography (CT) angiography showed severe stenosis at the beginning of left internal carotid artery (LICA) (Figure 1). His platelet count was $107 \times 10^9/L$ and his coagulation function was normal as well. After discussion, we attempted to perform the left carotid stenting to prevent cerebral infarction. Before the surgery, the patient used aspirin (100 mg) and clopidogrel (75 mg) for 5 days, and

atorvastatin (20 mg) was routinely administered for 5 days. The National Institute of Health Stroke Scale (NIHSS) score of patient was 5 as well.

Carotid artery stenting (CAS) was performed under local anesthesia. Heparin was administered intravenously at a dose of 5,000 U (100 U/kg) bolus immediately after femoral artery puncture and at a dose of 1,000 U/h during the procedure. Angiography revealed 90% stenosis in left carotid artery by The North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. Firstly, we positioned a cerebral protection (spider FX; eV3 Inc., Plymouth, MN, USA). Then, the stenosis of the left internal carotid artery was predilated with a 5 × 30 mm balloon (Viatrac 14 Plus; Abbott Vascular, Temecula, CA, USA). Eventually, a 7 × 40 mm self-expandable carotid stent (Wallstent; Boston Scientific, Marlborough, MA, USA) was placed by a 0.014-inch guidewire and a 8-F guide catheter. Besides, the CAS was performed without any complication (Figure 2).

After the surgery, the patient continued to use aspirin 100 (mg), clopidogrel (75 mg), and atorvastatin (20 mg). One day after surgery, we assayed his platelet count and coagulation function as a routine procedure. His platelet count and coagulation function were both in the normal range. Additionally, the patient did not complain about any discomfort. After that, 5 days after surgery, the patient got lethargy, gaze to the left-side, motor aphasia, and right hemiplegia, and the patient's NIHSS score was 18. CT angiography showed acute stent thrombosis of the left internal carotid artery immediately (Figure 3).

We performed the thrombus aspiration via right percutaneous transfemoral access under local anesthesia. After the 8F guiding catheter (Boston Scientific, Marlborough, MA, USA) was placed, the angiography showed acute thrombosis at the proximal end of the stent without forward blood flow. Synchro2 Micro-wire (Stryker, Kalamazoo, MI, USA) with Rebar 18 microcatheter (ev3 Inc., Irvine, CA, USA) showed thrombosis in the M1 segment. Considering that the patient's sudden aggravation of symptoms is closely associated with endovascular coil embolization of middle cerebral artery (MCA), preferentially opening the MCA blood vessel was conducted through a 4 × 20 mm Solitaire FR (ev3 Inc., Irvine, CA, USA) stent, with accompanying a thrombus about 2-3 cm long. Then, 6F Navien (ev3 Inc., Irvine, CA, USA) was used to enter the stent thrombus for thrombus aspiration, and a thrombus of about 4 cm in length was aspirated as well. After the angiography, the blood flow in the stent was partially restored, however, the forward blood flow was still very slow. A Spider distal protection device was positioned (ev3 Inc., Irvine, CA, USA), and a 5 × 30 mm balloon (Boston Scientific, Marlborough, MA, USA) was expanded twice by 12 atm. The angiography showed a significant improvement in the anterior blood flow, while there were some thrombus in the stent. Tirofiban (10 ml) was given through Rebar 18 microcatheter (ev3 Inc., Irvine, CA, USA). After that, the angiography showed complete disappearance of the thrombus and complete recovery of the forward blood flow (Figure 4). After surgery, the patient's NIHSS score was 12.

Postoperative CT showed severe cerebral edema and contrast agent leakage without hemorrhage. Then, 2 days after thrombus aspiration, CT angiography showed complete recanalization of the stent, and most of contrast agents were absorbed. However, 4 days after the second surgery, CT showed a slight hemorrhage in basal ganglia and cerebral edema around the hemorrhage area. Regarding stent

thrombosis, the patient continued to use aspirin, clopidogrel, and atorvastatin. Next, 2 weeks after thrombus aspiration, CT showed hemorrhage absorption. The patient discharged from hospital when he was consuming aspirin, clopidogrel, and atorvastatin. The patient's NIHSS score was 8 during discharge. Three months after the dual-antiplatelet, the patient switched to a single-antiplatelet. After 6 months of follow-up, the patient's NIHSS score was 3 and modified Rankin scale (mRS) score was 1. Besides, there was no stent restenosis in CT angiography at that time-period as well (Figure 5).

Discussion

It has been confirmed that CAS is an alternative strategy to prevent ischemic stroke in patients who are at high-risk of surgery compared with carotid endarterectomy (CEA) ¹. It was reported that the incidence of in-stent restenosis after CAS ranged from 3%-16.6%, and the majority of patients were asymptomatic ⁵. Acute carotid stent thrombosis (ACST) was extremely rare, while the complication was devastating, and it occurred within 30 days after CAS ². We reviewed articles related to ACST which were published in English, and their details have listed in Table 1.

There are several reasons causing ACST, such as inadequate antiplatelet therapy, early discontinuation of antiplatelet therapy, clopidogrel resistance, hypercoagulable state, soft plaque and its protrusion, local vessel dissection, vasospasm, intimal injury, and so on ⁶⁻⁸. In one hand, a number of reasons, including cause of CAS (i.e., stent underexpansion, in which stent does not fully adhere to the blood vessel ⁶, balloon burst ⁹, etc.), plaque protrusion ⁴, and vasospasm that might immediately lead to ACST. Also, they can be timely resolved without any defect in the nervous system. On the other hand, other reasons, such as inadequate antiplatelet therapy ¹⁰⁻¹², early discontinuation of antiplatelet therapy ¹³, clopidogrel resistance, and hypercoagulable state ⁷, could cause ACST a few days after CAS procedure. Eventually, these may cause patient's death or severe paralysis ¹⁰.

According to the review of 32 cases, 10 cases were found without reporting the relevant reasons caused disease ^{10, 12-19}, 11 cases due to CAS procedure ^{6, 9, 19-22}, 2 cases due to antiplatelet resistance ^{18, 23}, 3 cases due to hypercoagulable state ^{4, 7, 22}, 4 cases due to discontinuation of antiplatelet ^{11, 13, 24, 25}, 1 case due to cardiac multiple embolism ¹³, and 1 case remained unclear ²⁶. As we mentioned previously, the ACST caused by CAS is often timely resolved and patients may have a good prognosis, and that may be the most common reason as well. However, for antiplatelet resistance, it is a particularly rare cause for ACST, and lack of experience in the treatment and prognosis of such patients is still a main challenge. After affecting by ACST, we tested the CYP2C19 of our patient, and found CYP2C19 *1/*2, which is one of the genetic polymorphism causing clopidogrel resistance. In absence of hypercoagulable and also antiplatelet therapy is adequate in patient, we speculate that clopidogrel resistance may be an important cause of ACST. Since an effective antiplatelet therapy is very important in treatment of CAS, some scholars recommended that the antiplatelet resistance tests should routinely be performed ³.

We carried out the thrombus aspiration immediately after affecting by ACST. However, because of slow forward blood and existence of stent thrombus in the stent, Tirofiban (10 ml) was given by Rebar 18 microcatheter. After that, we performed a successful recanalization. The solution for ACST maybe multiplex. Drugs uses, such as thrombolysis or platelet glycoprotein IIb/IIIa antagonist (GPIs), surgical therapy including thromboendarterectomy, mechanical thrombolysis and thrombus aspiration or use these two methods flexibly, these purpose is to recanalization as soon as possible.

It has been reported that Abciximab was successfully used in treatment of ACST patients^{4,14}. However, regarding Tirofiban, we herein presented the first case report including its application in treatment of symptomatic ACST patient accompanying with evidenced clopidogrel resistance. After Tirofibanf was given, the thrombus immediately shrank. As Tirofiban is a non-peptide tyrosin derivative that mimics the Arg-Gly-Asp (RGD) integrin recognition sequence, it has a very short platelet-bound half-life and relatively long plasma half-life. Therefore, it possesses an advantage when we need to rapidly reversal antiplatelet such as in combination with thrombolysis or thromboaspiration. In an ACST patient, especially after thrombus aspiration, Tirofiban plays a more significant role¹⁷.

It was revealed that 4 days after the second surgery, hemorrhage was detected without any clear cause. Regarding stent thrombosis, dual-antiplatelet therapy was continuously performed. We did not analyze the causes in-depth and did not treat cerebral hemorrhage actively as well. In other cases, cerebral hemorrhage was not reported after recanalization. We found that our patient had an appropriate progress after 6 months of follow up.

Conclusions

ACST is an extremely rare event, however, fetal complication after CAS and clopidogrel resistance are probably the reasons leading to ACST. The treatment of ACST after CAS must be undertaken urgently and immediately in order to cause restoration of blood flow and avoid major neurological adverse events. Thrombus aspiration with GPIs would be effective in treatment of ACST. The presented case report can only assist to illuminate the available treatment strategies rather than providing general therapeutic recommendations.

Abbreviations

Carotid Artery Stenting ,CAS Carotid endarterectomy ,CEA Acute carotid stent thrombosis ,ACSTGlycoprotein IIb/IIIa antagonist ,GPIs Magnetic resonance imaging ,MRI Computed tomography ,CT Left internal carotid artery ,LICA National Institute of Health Stroke Scale ,NIHSS North American Symptomatic Carotid Endarterectomy Trial ,NASCET Middle cerebral artery ,MCA Modified Rankin scale ,Mrs Arg-Gly-Asp ,RGD; Good prognosis: GP; Paresis: P; Death: D.

Declarations

Consent to publish

All writers agreed to publish this manuscript. The patient has signed an informed consent form.

Authors Contributions

Wei Wei and Pian Wang drafted the manuscript for intellectual content, Yan Wang design and conceptualized study, Zheng Li and Qingbin Zhang analyzed the data.

Funding

No funding was obtained for this study.

Competing Interests

Non-financial competing interests.

Availability of data and materials

Access to study data is regulated by Chinese law. Data are available from the Fifth People's Hospital of Chengdu Institutional Data Access/Ethics Committee for researchers who meet the criteria.

Acknowledgments

None.

References

1. Massop D, Dave R, Metzger C, et al. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHERE Worldwide Registry first 2,001 patients. *Catheter Cardiovasc Interv* 2009;73:129-136.
2. Moulakakis KG, Mylonas SN, Lazaris A, et al. Acute Carotid Stent Thrombosis: A Comprehensive Review. *Vasc Endovascular Surg* 2016;50:511-521.
3. Arslan S. Reply to the Letter: "Acute Carotid Artery Stent Thrombosis". *Cardiovasc Intervent Radiol* 2018;41:357.
4. Steiner-Boker S, Cejna M, Nasel C, Minar E, Kopp CW. Successful revascularization of acute carotid stent thrombosis by facilitated thrombolysis. *AJNR Am J Neuroradiol* 2004;25:1411-1413.
5. Lal BK, Beach KW, Roubin GS, et al. Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial. *Lancet Neurol* 2012;11:755-763.
6. Hu W, Wang L, Wang G. Acute In-Stent Thrombosis after Carotid Angioplasty and Stenting: A Case Report and Literature Review. *Interv Neurol* 2018;7:265-270.
7. Kanemaru K, Nishiyama Y, Yoshioka H, et al. In-stent thrombosis after carotid artery stenting despite sufficient antiplatelet therapy in a bladder cancer patient. *J Stroke Cerebrovasc Dis* 2013;22:1196-

1200.

8. Okazaki T, Satomi J, Satoh K, Hirasawa M, Nagahiro S. Rescue revascularization therapy with a stent-in-stent technique for acute intracranial internal carotid artery occlusion. *Neurol Med Chir (Tokyo)* 2005;45:253-258.
9. Iancu A, Grosz C, Lazar A. Acute carotid stent thrombosis: review of the literature and long-term follow-up. *Cardiovasc Revasc Med* 2010;11:110-113.
10. Chaturvedi S, Sohrab S, Tselis A. Carotid stent thrombosis: report of 2 fatal cases. *Stroke* 2001;32:2700-2702.
11. Hamann GF, Liebetrau M, Pfefferkorn T, Heiss MM. Successful systemic thrombolysis for carotid stent thrombosis. *Eur Neurol* 2002;48:37-39.
12. Masuo O, Terada T, Matsuda Y, et al. Successful recanalization by in-stent percutaneous transluminal angioplasty with distal protection for acute carotid stent thrombosis. *Neurol Med Chir (Tokyo)* 2006;46:495-499.
13. Setacci C, de Donato G, Setacci F, et al. Surgical management of acute carotid thrombosis after carotid stenting: a report of three cases. *J Vasc Surg* 2005;42:993-996.
14. Tong FC, Cloft HJ, Joseph GJ, Samuels OB, Dion JE. Abciximab rescue in acute carotid stent thrombosis. *AJNR Am J Neuroradiol* 2000;21:1750-1752.
15. Owens EL, Kumins NH, Bergan JJ, Sparks SR. Surgical management of acute complications and critical restenosis following carotid artery stenting. *Ann Vasc Surg* 2002;16:168-175.
16. Bush RL, Bhama JK, Lin PH, Lumsden AB. Transient ischemic attack due to early carotid stent thrombosis: successful rescue with rheolytic thrombectomy and systemic abciximab. *J Endovasc Ther* 2003;10:870-874.
17. Seo KD, Lee KO, Kim DJ, Lee KY. Rescue use of tirofiban for acute carotid in-stent thrombosis. *Yonsei Med J* 2008;49:163-166.
18. Choi HJ, Kim ST, Jeong YG, Jeong HW. Superficial temporal artery-middle cerebral artery anastomosis for internal carotid artery occlusion by subacute in-stent thrombosis after carotid artery stenting. *J Korean Neurosurg Soc* 2012;52:551-554.
19. Moulakakis KG, Lazaris AM. Emergent Carotid Stent Removal after Carotid Stent Thrombosis. *Ann Vasc Surg* 2018;46:401-406.
20. Kim YW, Kang DH, Hwang JH, Park J, Hwang YH, Kim YS. Rescue strategy for acute carotid stent thrombosis during carotid stenting with distal filter protection using forced arterial suction thrombectomy with a reperfusion catheter of the Penumbra System: a technical note. *Acta Neurochir (Wien)* 2013;155:1583-1588.
21. Munich S, Moftakhar R, Lopes D. Recanalization of acute carotid stent occlusion using Penumbra 4Max aspiration catheter: technical report and review of rescue strategies for acute carotid stent occlusion. *BMJ Case Rep* 2013;2013.

22. Moulakakis KG, Kakisis J, Tsivgoulis G, et al. Acute Early Carotid Stent Thrombosis: A Case Series. *Ann Vasc Surg* 2017;45:69-78.
23. Koklu E, Arslan S, Yuksel IO, Bayar N, Koc P. Acute Carotid Artery Stent Thrombosis Due to Dual Antiplatelet Resistance. *Cardiovasc Intervent Radiol* 2015;38:1011-1014.
24. Buhk JH, Wellmer A, Knauth M. Late in-stent thrombosis following carotid angioplasty and stenting. *Neurology* 2006;66:1594-1596.
25. Markatis F, Petrosyan A, Abdulamit T, Bergeron P. Acute carotid stent thrombosis: a case of surgical revascularization and review of treatment options. *Vascular* 2012;20:217-220.
26. Dhall A, Malani SK, Chadha DS. Thrombosuction for procedural acute thrombosis during high-risk carotid angioplasty—a case report. *J Invasive Cardiol* 2010;22:E144-146.

Tables

Due to technical limitations, the Table 1 has been placed in the Supplementary Files section.

Figures

Figure 1

(A) The magnetic resonance imaging (MRI) showed multiple internal border zone infarcts in a rosary-like pattern along the left centrum semiovale; (B, C) The computed tomography (CT) angiography showed severe stenosis at the beginning of left internal carotid artery (LICA); (D) Doppler ultrasonography showed the formation of atherosclerotic plaque in the LICA, and the blood flow velocity was accelerated in the lumen.

Figure 2

(A) Angiography revealed 90% stenosis in left carotid artery according to The North American Symptomatic Carotid Endarterectomy Trial criteria; (B) CAS was performed without any complication, and the stenosis of LICA was fully solved. Figure 3 5 days after surgery, CT angiography showed acute stent thrombosis of the left internal carotid artery.

Figure 3

5 days after surgery, CT angiography showed acute stent thrombosis of the left internal carotid artery.

Figure 4

The thrombus aspiration was carried out for the patient with acute carotid stent thrombosis. (A) Angiography confirmed acute stent thrombosis of the left internal carotid artery, however, there was no blood flue at the distal end of the stent; (B) After thrombus aspiration, the blood flow in the stent was partially restored, while the forward blood flow was still very slow and there were some thrombus in the stent; (C) The acute carotid thrombosis was fully solved after balloon expansion, and Tirofiban (10 ml) was given through Rebar18 microcatheter.

Figure 5

A-F showed the radiographic changes in patient after thrombus aspiration. (A) Postoperative CT showed contrast agent leakage; (B,C) 2 days after thrombus aspiration, CT angiography showed complete recanalization of the stent, and most of contrast agents have been absorbed; (D) 4 days after the second surgery, CT showed a slight hemorrhage in basal ganglia and cerebral edema around the hemorrhage area; (E) 2 weeks after thrombus aspiration, CT showed hemorrhage absorption; (F) There was no stent restenosis in CT angiography after 6 months of follow-up.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplement1.docx](#)