

In-stent stenosis in the patient with internal carotid aneurysm after treated by the Willis covered stent

Two case reports and literature review

Lun-Xin Liu, MS^a, Meng-Yuan Song, MB^b, Xiao-Dong Xie, MS^{a,*}

Abstract

In-stent stenosis after treated by Willis covered stent—case reports.

Background: Advancements in minimally invasive technology have allowed endovascular reconstruction of internal carotid aneurysm. However, in-stent stenosis is an important and well-characterized complication of stenting after the treatment of internal carotid aneurysm.

Case description: We would present 2 patients who were diagnosed with in-stent stenosis after the treatment of Willis covered stent. Case 1: A 57-year-old female with 2-week history of headache and vomiting before admission, whose digital subtraction angiography (DSA) demonstrated left internal carotid C6 aneurysm and showed about 20% stenosis 3 months later since operation in the position where Willis covered stent was deployed. Case 2: A 23-year-old male with skull base fracture, subarachnoid hemorrhage, right femoral fracture for 14 days and epistaxis for 9 hours caused by a car accident, whose DSA demonstrated left internal carotid paraclinoid pseudoaneurysm. One year later, the patient went to our center again because he had headache and dizziness for 6 months after the interventional operation. His DSA demonstrated about 80% stenosis in the position where Willis covered stent was deployed. The clinical and radiologic characteristics and the experience in dealing with the stenosis are presented.

Conclusions: In-stent stenosis after treated with Willis covered is uncommon, but not rare. Operators should pay more attention to the in-stent stenosis during the period of follow-up observation and monitor P2Y12 Reaction Unit (PRU) in the antiplatelet period, especially for the Willis covered stent. What is more, the treatment for stenosis ought to be carefully considered.

Abbreviations: CT = computed tomography, DSA = digital subtraction angiography, GCS = Glasgow Coma Scale, ICA = internal carotid artery, MRI = magnetic resonance imaging, PRU = P2Y12 Reaction Unit.

Keywords: covered stent, endovascular treatment, internal carotid artery aneurysm, stenosis

1. Introduction

However, the International Subarachnoid Aneurysm Trial (ISAT) has proven that the endovascular treatment of cerebral aneurysms with detachable coils is a superior alternative to open microsurgery in terms of survival free of disability at 1 year, the recanalization rate of endovascular treatment is higher than the open microsurgery which is still a serious problem to be solved.^[1,2] What is more, aneurysm located in internal carotid

artery (ICA) is difficult to deal with open microsurgery due to the bony obstacles and difficulty in proximal control.^[3–5] So that we should find a better endovascular technique to treat the aneurysm, especially the large or giant, complicated aneurysm or pseudoaneurysm, located in the ICA.

A novel stent was deployed in the parent artery to exclude the ICA aneurysm from circulation. Willis covered stent (MicroPort, Shanghai, China), a specifically designed balloon-expanded stent used in the intracranial vasculature, consists of 3 parts: a bare stent, an expandable polytetrafluoroethylene (ePTFE) membrane, and a balloon catheter.^[6–9] However, in-stent stenosis is not rare, as covered stents are more thrombogenic than others. In our center, 20 patients with ICA aneurysm received the treatment of Willis covered stent from August 6, 2014 to December 23, 2015 and only 2 were diagnosed with in-stent stenosis. One was asymptomatic with about 20% stenosis who received conservative treatment and the other was about 80% stenosis after digital subtraction angiography (DSA) diagnosis who used stent to resolve this problem. Written informed consent was obtained from both patients for the publication of their case reports and relevant images.

2. Case report

2.1. Case 1

A 57-year-old female with 2-week history of headache and vomiting before admission. Her physical examination showed

Editor: Bernhard Schaller.

Funding: This work was supported by the Scientific Research Foundation of the Scientific & Technology Department of Sichuan Province (no. 2012SZ0127).

L-XL and M-Ys contributed equally to this work.

The authors have no conflicts of interest to disclose.

^a Department of Neurosurgery, West China Hospital, ^b School of Basic Science and Forensic Medicine, Sichuan University, Chengdu, Sichuan, People's Republic of China.

* Correspondence: Xiao-Dong Xie, West China Hospital, Chengdu, Sichuan, People's Republic of China (e-mail: xiaodong_1962@163.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Medicine (2017) 96:7(e6101)

Received: 30 May 2016 / Received in final form: 3 January 2017 / Accepted: 20 January 2017

<http://dx.doi.org/10.1097/MD.00000000000006101>

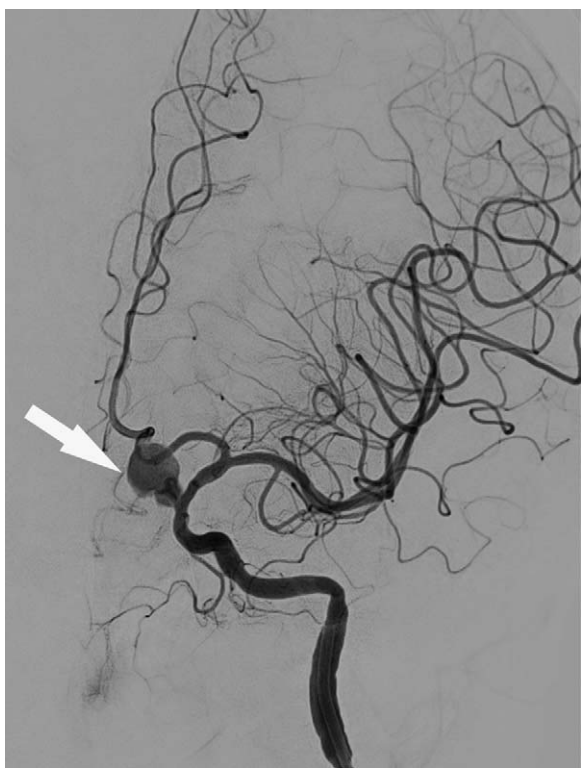


Figure 1. The white arrow demonstrated the aneurysm located at internal carotid artery C6.

neck stiffness, Glasgow Coma Scale (GCS) score was 15 points, head computed tomography (CT) revealed subarachnoid hemorrhage and DSA demonstrated left internal carotid C6 aneurysm (Fig. 1).

An endovascular reconstruction with Willis covered stent was scheduled. A Willis covered stent (3.5 mm × 10.0 mm, MicroPort) was deployed in the left internal carotid C6 segment. Intraoperative angiography demonstrated the collapse of the aneurysm and satisfactory stent positioning (Fig. 2).

Three months later since operation, her DSA showed about 20% stenosis in the position where Willis stent was deployed (Fig. 3). As she was asymptomatic, we did not deal with it. Now she is still under our observation.

2.2. Case 2

A 23-year-old male with skull base fracture, subarachnoid hemorrhage, right femoral fracture for 14 days and epistaxis for 9 hours caused by a car accident. Gauze packing and blood transfusion were used to prevent epistaxis. His physical examination revealed right leg movement restriction due to binding up his leg, his GCS score was 15 points, head CT demonstrated skull base fracture and subarachnoid hemorrhage, and X-ray showed right femoral fracture. After his admission to our center, his DSA demonstrated left internal carotid paraclinoid pseudoaneurysm (Fig. 4).

Before surgery, we gave him 225 mg clopidogrel and 300 mg aspirin for oral administration. Under the condition of general anesthesia and full heparinization, a Willis covered stent (3.5 mm × 13 mm) was deployed in the left internal carotid paraclinoid segment. Intraoperative angiography showed the collapse

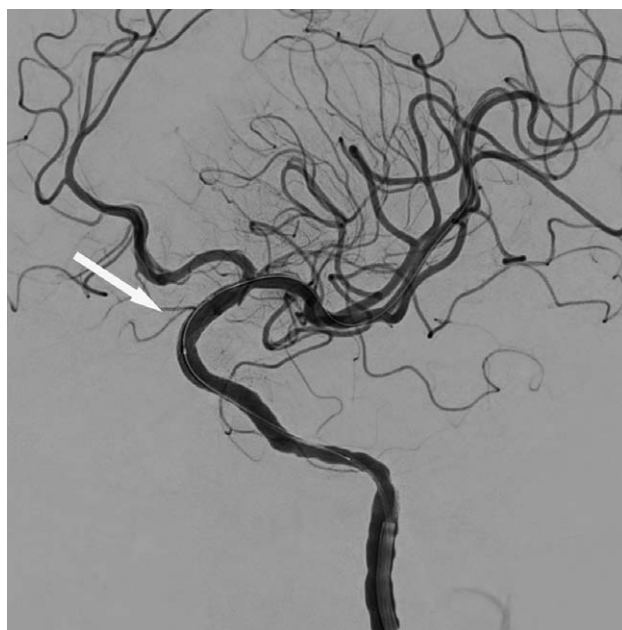


Figure 2. The white arrow showed the collapse of the aneurysm and satisfactory stent (a 3.5 mm × 10.0 mm Willis covered stent, MicroPort, Shanghai, China) positioning.

of the pseudoaneurysm and a satisfactory stent positioning (Fig. 5). Three days later, this patient discharged.

One year later, he went to our center again as he had headache and dizziness for 6 months. His physical examination showed no abnormality and DSA diagnosis found about 80% stenosis in the position where Willis covered stent was deployed (Fig. 6). Everolimus-Eluting Coronary stent (4.0 mm × 12 mm, Boston

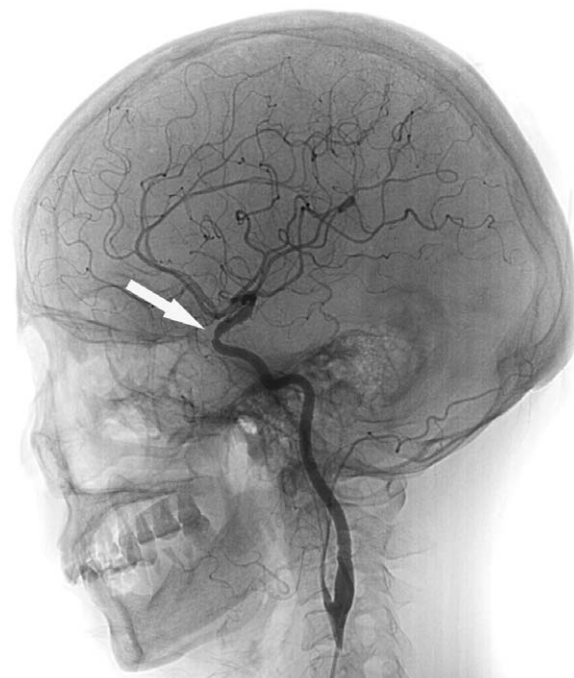


Figure 3. About 20% of stenosis in the site where deployed the Willis covered stent (white arrow) 3 months ago.

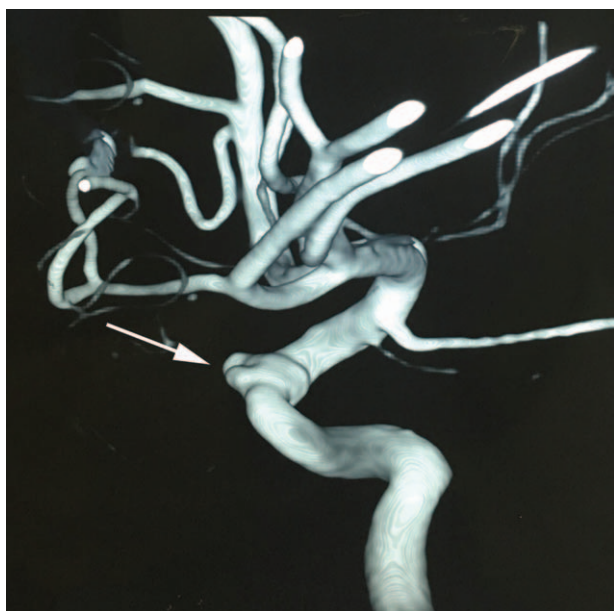


Figure 4. The white arrow showed the left internal carotid paraclinoid pseudoaneurysm.

Scientific, Marlborough, Massachusetts) was used to solve this problem. Intraoperative angiography demonstrated the stenosis disappeared and the left ICA kept patency (Fig. 7).

3. Discussion

Although the Willis novel covered stent has advantages in treating the complicated, wide necked, large, or giant aneurysms in ICA, its disadvantages should also be considered. Compared with other stents, in-stent stenosis is not rare, particularly in this reconstruction treatment technique (Table 1).^[2,10,11] The

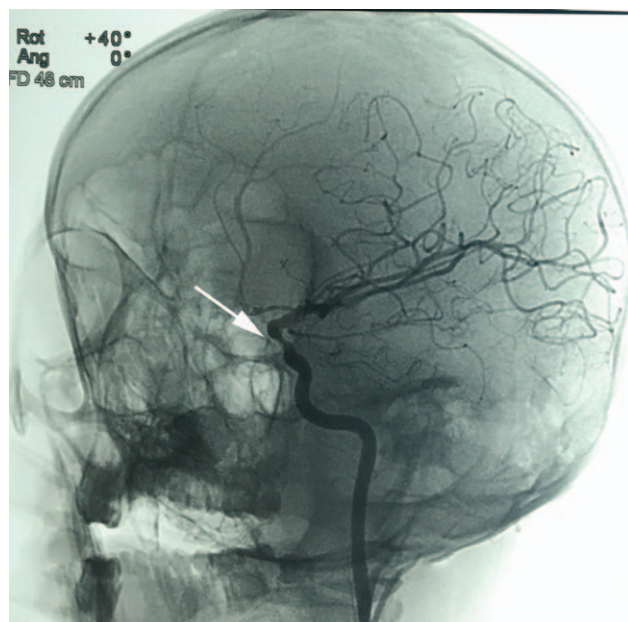


Figure 6. About 80% of stenosis in the position where deployed the Willis covered stent (white arrow).

deployment of a balloon-expanded stent will inevitably result in endothelial disruption and denudation over the treated vascular segment. There will be a proliferation and activation of regional smooth muscle cells in the disappearance of functional endothelium, which will lead to neointimal tissue formation, finally resulting in in-stent stenosis.^[11,12] One important factor for the development of stenosis might be the reendothelialization of the stent area. Stent covering may lead to a prolonged process

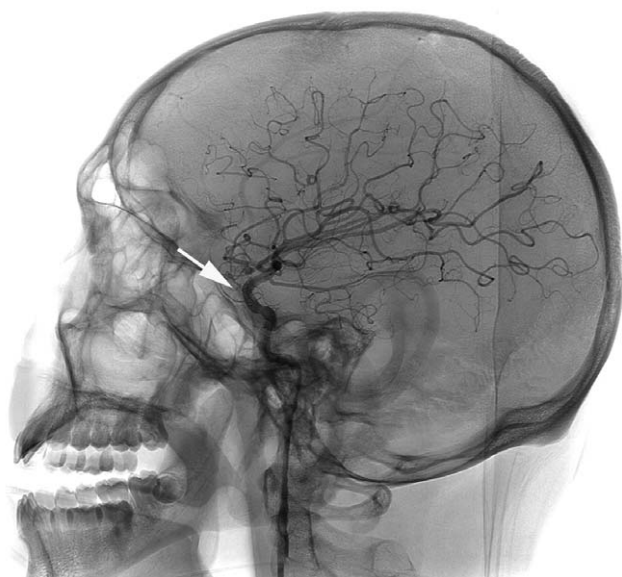


Figure 5. Intraoperative angiography showed the collapse of the pseudoaneurysm and a satisfactory stent (a 3.5mm × 13mm Willis covered stent, MicroPort, Shanghai, China) positioning (white arrow).

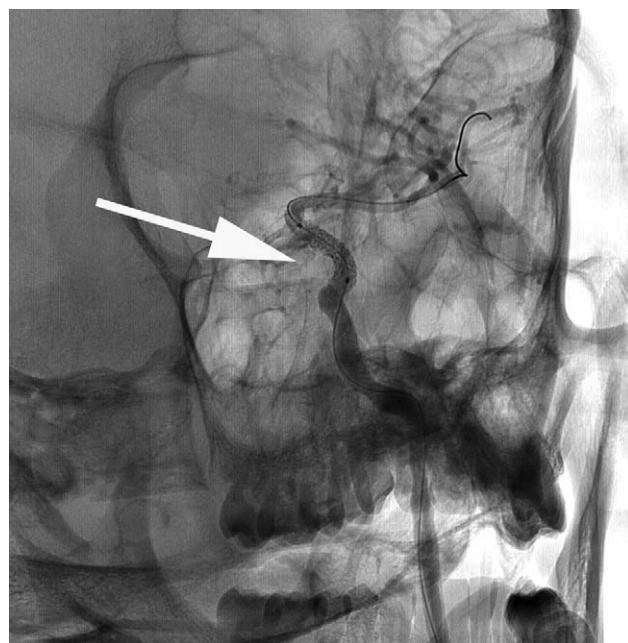


Figure 7. Intraoperative angiography demonstrated that the stenosis disappeared and that the left internal carotid artery kept patency after the stent deployed (Everolimus-Eluting Coronary stent 4.0mm × 12mm, Boston Scientific, Boston, USA).

Table 1**The stenosis rate of Willis covered stent compare with other kinds of stents.**

	Stent type	No. of stenosis patients	No. of total patients	Stenosis rate
Lai et al ^[2]	Willis*	6	46	13.0%
Fiorella et al ^[11]	Neuroform [†]	9	156	5.8%
Fargen et al ^[10]	Enterprise [‡]	8	229	3.4%

* MicroPort (Shanghai, China).

[†] Boston Scientific/Target (Fremont, CA).[‡] Codman Neurovascular (Ratham, MA).

for reendothelialization as the middle of the stents had to be reached from stent edges. This longer time needed for reendothelialization could be a stimulus for more and higher proliferation of smooth muscle cell at stent edges because this process lasts as long as the endothelial layer is incomplete.^[13,14]

As in-stent stenosis may spontaneously resolve along with the progress of natural history, the patient in the first case who had asymptomatic stenosis received conservative treatment.^[11] But the second case use an Everolimus-Eluting Coronary stent. In China, Everolimus-Eluting Coronary stent is much cheaper than Willis covered stent and pseudoaneurysm could be repaired by Willis covered stent, that is why we choose another kind of stent. In our center, the treatment is reserved for patients who develop ischemic symptoms during the follow-up observation, show new focus of asymptomatic ischemic injury on magnetic resonance imaging (MRI) within the ipsilateral vascular distribution, or appear a “steal phenomenon” on a cerebral blood flow study.^[11]

According to the literature review, it was found that postprocedure irregular antiplatelet therapy and cerebrovascular arteriosclerosis, diabetes and lesion length, multiple stents, and smaller final minimal lumen diameter are associated with increased risk of in-stent stenosis.^[2,15,16] Both patients in the literature had no history of diabetes and cerebrovascular arteriosclerosis, and they were all deployed with only 1 Willis covered stent, aneurysm is in the trunk of the ICA. But the patient in Case 2 received irregular antiplatelet therapy, and that may be the reason why he developed in-stent stenosis.

The patient in Case 1 received regular antiplatelet therapy, but she still developed in-stent stenosis. Prabhakaran et al^[17] found that aspirin resistance was relatively uncommon, whereas clopidogrel resistance occurred in half of patients undergoing cerebrovascular stent placement. And P2Y12 Reaction Unit (PRU) is changeable in the same patient during the antiplatelet procedure.^[18] Maybe the patient in Case 1 is clopidogrel resistance, she ought to be monitored the PRU in the antiplatelet period. Furthermore, cigarette smoking and use of medications (proton pump inhibitors, antifungal or antihuman immunodeficiency virus medications, and antidepressants may influence the clopidogrel resistance).^[19]

4. Conclusion

In-stent stenosis after treated with Willis covered is uncommon, but not rare. Operators should pay more attention to the in-stent stenosis in the follow-up observation period and monitor the PRU in the antiplatelet period, especially for the Willis covered

stent. What is more, the treatment of stenosis ought to be carefully considered.

References

- [1] Molyneux A, Kerr RS, Yu LM, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 2002;360:1267–74.
- [2] Lai XB, Li MH, Tan HQ, et al. Predictors of in-stent stenosis and occlusion after endovascular treatment of intracranial vascular disease with the Willis covered stent. *J Clin Neurosci* 2013;20:122–7.
- [3] Roy D, Raymond J, Bouthillier A, et al. Endovascular treatment of ophthalmic segment aneurysms with Guglielmi detachable coils. *AJNR Am J Neuroradiol* 1997;18:1207–15.
- [4] Kattner KA, Bailes J, Fukushima T. Direct surgical management of large bulbous and giant aneurysms involving the paraclinoid segment of the internal carotid artery: report of 29 cases. *Surg Neurol* 1998;49:471–80.
- [5] Molyneux AJ, Kerr RS, Yu LM, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet (London, England)* 2005;366:809–17.
- [6] Saatci I, Cekirge HS, Ozturk MH, et al. Treatment of internal carotid artery aneurysms with a covered stent: experience in 24 patients with mid-term follow-up results. *AJNR Am J Neuroradiol* 2004;25:1742–9.
- [7] Zhu YQ, Li MH, Lin F, et al. Frequency and predictors of endoleaks and long-term patency after covered stent placement for the treatment of intracranial aneurysms: a prospective, non-randomised multicentre experience. *Eur Radiol* 2013;23:287–97.
- [8] Li MH, Li YD, Gao BL, et al. A new covered stent designed for intracranial vasculature: application in the management of pseudoaneurysms of the cranial internal carotid artery. *AJNR Am J Neuroradiol* 2007;28:1579–85.
- [9] Alexander MJ, Smith TP, Tucci DL. Treatment of an iatrogenic petrous carotid artery pseudoaneurysm with a Symbiot covered stent: technical case report. *Neurosurgery* 2002;50:658–62.
- [10] Fargen KM, Hoh BL, Welch BG, et al. Long-term results of enterprise stent-assisted coiling of cerebral aneurysms. *Neurosurgery* 2012;71:239–44. discussion 244.
- [11] Fiorella D, Albuquerque FC, Woo H, et al. Neuroform in-stent stenosis: incidence, natural history and treatment strategies. *Neurosurgery* 2006;59:34–42.
- [12] Kipshidze N, Dangas G, Tsapenko M, et al. Role of the endothelium in modulating neointimal formation: vasculoprotective approaches to attenuate restenosis after percutaneous coronary interventions. *J Am Coll Cardiol* 2004;44:733–9.
- [13] Sick PB, Brosteanu O, Niebauer J, et al. Neointima formation after stent implantation in an experimental model of restenosis: polytetrafluoroethylene-covered versus uncovered stainless steel stents. *Heart Dis (Hagerstown, Md)* 2002;4:18–25.
- [14] Rogers C, Edelman ER. Endovascular stent design dictates experimental restenosis and thrombosis. *Circulation* 1995;91:2995–3001.
- [15] Zhu SG, Zhang RL, Liu WH, et al. Predictive factors for in-stent restenosis after balloon-mounted stent placement for symptomatic intracranial atherosclerosis. *Eur J Vasc Endovasc Surg* 2010;40:499–506.
- [16] Kastrati A, Schomig A, Elezi S, et al. Predictive factors of restenosis after coronary stent placement. *J Am Coll Cardiol* 1997;30:1428–36.
- [17] Prabhakaran S, Wells KR, Lee VH, et al. Prevalence and risk factors for aspirin and clopidogrel resistance in cerebrovascular stenting. *AJNR Am J Neuroradiol* 2008;29:281–5.
- [18] Delgado Almandoz JE, Kadkhodayan Y, Crandall BM, et al. Variability in initial response to standard clopidogrel therapy, delayed conversion to clopidogrel hyper-response, and associated thromboembolic and hemorrhagic complications in patients undergoing endovascular treatment of unruptured cerebral aneurysms. *J Neurointerv Surg* 2014;6:767–73.
- [19] Asterios Tsimpas SJM, Fernando Gonzalez L, Gonzalez F, Albuquerque FC, McDougall CG. Pharmacology in the endovascular suite: dosages, antidotes, and point-of-care testing. *Neurointerventional Techniques Tricks of the Trade* Thieme Publishers, New York:2015;300.