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CASE REPORTS

Regression of in-stent restenosis after using a Wingspan stent to treat intracranial atherosclerotic stenosis: A case report and 5-year follow-up

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Abstract

In-stent restenosis occurs in approximately 30% of patients after receiving a Wingspan stent to treat symptomatic intracranial atherosclerosis. This report describes a 55-year-old man with intracranial atherosclerotic internal carotid artery terminus stenosis who developed significant in-stent restenosis. Follow-up angiogram 5 years later demonstrated the regression of restenosis without invasive intervention.

Keywords: In-stent restenosis, Wingspan stent, intracranial atherosclerotic stenosis

INTRODUCTION

There are significant concerns regarding in-stent restenosis after stenting for intracranial atherosclerotic disease. Late regression of in-stent restenosis has been reported in stent-assisted coiling for the treatment of intracranial aneurysm.[1,2] Literature suggests that after the initial 3-month to 6-month post-stenting period, tissue ingrowth along the stent stabilizes, and in some cases, tissue ingrowth undergoes a process of reorganization to become more compact, resulting in the regression of in-stent restenosis.[3] However, to our knowledge, late regression of Wingspan in-stent restenosis has not been well-reported in the literature.

We describe a patient with intracranial atherosclerotic stenosis who received a Wingspan stent, developed significant in-stent restenosis, and had regression of recurrent in-stent stenosis 5 years later, after conservative management.

CASE REPORT

A 55-year-old man presented to the emergency department with a sudden onset of dysarthria since 2 hours earlier. His history was significant for hypertension, and he smoked 5 packs of cigarettes per day for 20 years. A diffusion-weighted magnetic resonance (MR) imaging scan showed a small, acute infarction in the left frontal cortex. An MR angiogram showed severe stenosis of the left internal carotid artery (ICA) terminus.

A diagnostic cerebral angiogram confirmed severe stenosis in the left ICA terminus that extended into the proximal anterior cerebral artery and proximal middle cerebral artery (MCA), and decreased flow velocity to the distal segment (Figure 1A)

The patient was first treated with medication consisting of aspirin (325 mg per day) and clopidogrel (*75* mg per day). Platelet function analysis was performed using the Multiplate® platelet analyzer (Dynabyte, Munich, Germany). He was considered to be a good responder to aspirin and clopidogrel. However, despite treatment with dual antiplatelet drugs, his neurological signs of dysarthria and right-sided weakness worsened. After the patient had given the informed consent, he underwent endovascular treatment.

Endovascular treatment was performed under local anesthesia with systemic heparinization. A 6-French guiding catheter was placed in the left ICA through the right common femoral artery. A 1.5 × 9-mm Gateway balloon (Boston Scientific) was located within the stenotic segment and inflated to 6 atm. After angioplasty was performed, a 3.5 × 20-mm Wingspan stent was deployed in

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the stenotic segment. The angiogram after stent placement showed an ICA terminus and MCA with normal diameters without significant residual stenosis (Figure 1B). He was discharged home without neurological symptoms, and his condition was maintained with daily doses of 100 mg of aspirin and 75 mg of clopidogrel.

Although he did not complain of any neurologic symptoms, a follow-up angiogram performed 6 months later showed that the left ICA had high-grade (>70%), diffuse in-stent restenosis (Figure 1C). The technetium-99m hexamethylpropyleneamine oxime brain single-photon emission computed tomogram confirmed mild hypoperfusion in the left MCA territory. At that time, the patient was advised to consider interventional retreatment, but he declined and opted to continue medical therapy with dual antiplatelet therapy and atorvastatin (20 mg).

After 5 years of conservative treatment, he complained of a mild headache. A diffusion-weighted MR imaging showed no acute infarction. It was difficult to interpret patency of the stented artery on MR angiogram because of susceptibility artifact of stent. Thus, he underwent follow-up angiography. To our surprise, a repeat angiogram demonstrated nearly complete regression of the in-stent restenosis (Figure 1D).

DISCUSSION

In-stent restenosis occurs in approximately 30% of patients after receiving a Wingspan stent, and small intracranial artery restenosis is most

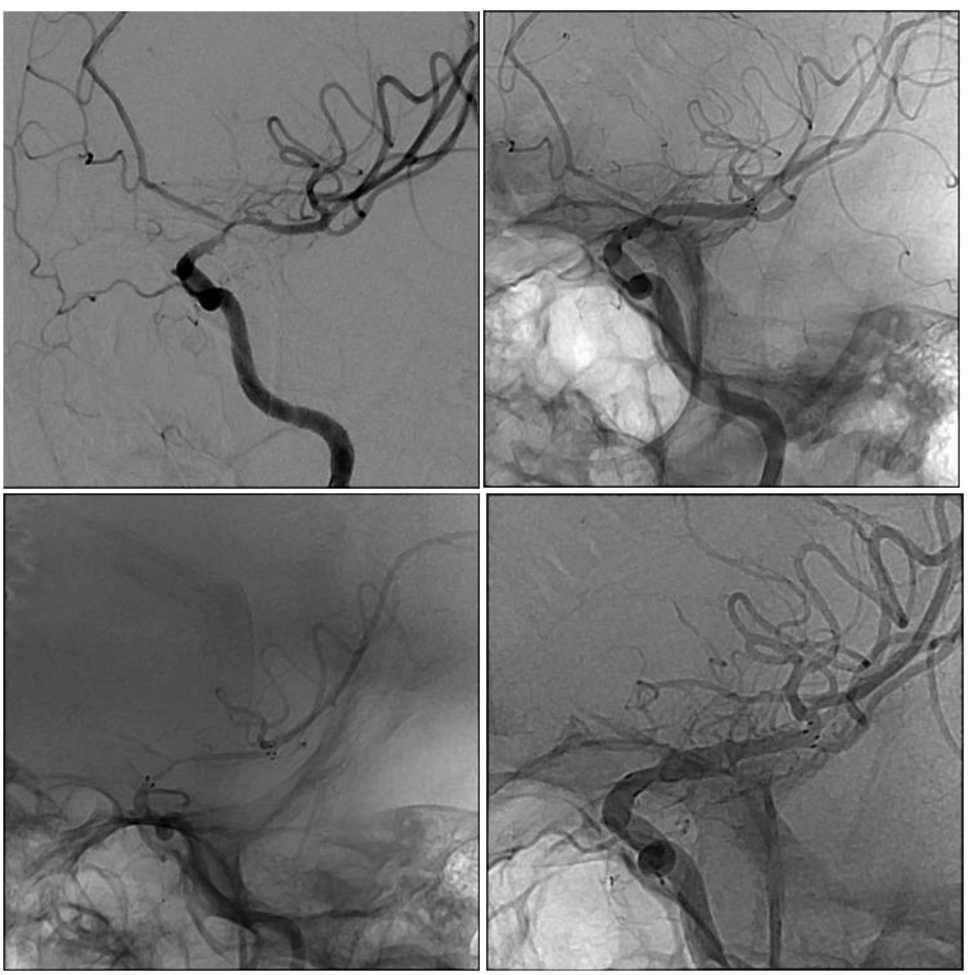

Figure 1. (A) Diagnostic angiogram showing severe stenosis of the internal carotid artery (ICA) terminus, extending to the proximal anterior cerebral artery and middle cerebral artery (MCA). (B) After the Wingspan stent is deployed, the diameters of the ICA terminus and proximal MCA are normal. (C) The 6-month follow-up subtracted image showing diffuse, severe (>70%) stenosis within the stent. (D) The subtracted image 5 years after stenting showing spontaneous regression of in-stent stenosis

common.[4,5] In-stent restenosis is usually related to excessive neointimal hyperplasia. When deployed, the self-expanding Wingspan stent exerts a continuous outward radial force on the vessel wall.[6] An oversized stent significantly increases intramural stress, which can cause acute vessel dissection, and it can chronically stimulate smooth muscle proliferation and initiate an inflammatory response.[6] In our case, the Wingspan stent was oversized, measuring 1.5 mm larger than the diameter of the reference artery. It is possible that vessel wall stress from the self-expanding Wingspan stent caused more damage to the vessel wall and subsequent excessive repair, resulting in in-stent restenosis.

Interventional retreatment options to treat in-stent restenosis includes balloon angioplasty, restenting, implantation of a drug-eluting stent, and reangioplasty with drug-eluting balloons. Unfortunately, these methods may be complicated by in-stent dissection or require retreatment.[7] Furthermore, retreatment may either cause symptoms or lead to angiographic worsening of stenosis. Therefore, there is no consensus regarding the threshold for reintervention therapy. Similarly, very little is known regarding the long-term natural history of in-stent restenosis and treatment success rate with medical therapy. Our case may provide indirect evidence to support the belief that if patients with in-stent restenosis do not become symptomatic after the procedure and an appropriate medication regimen is maintained, it is unlikely that they will ultimately become symptomatic during follow-up.[8]

We are unsure why the in-stent restenosis regressed after 5 years. Late regression of in-stent restenosis may be related to a decrease in the extracellular matrix and fibrotic maturation of neointimal hyperplasia over time.[9] Also, since in-stent neoatherosclerosis may be an important contributing factor to late vascular complications, including late in-stent restenosis and thrombosis[10], statin therapy with its effect of decreasing neoatherosclerosis, may have played a role.[11] Positive effects of statin adherence for stent patency may be explained by the pleotropic effects of statins, which include the inhibition of neointimal hyperplasia, inhibition of vascular inflammation, and platelet inhibition.[12] However, we have no direct evidence to support this, and more research is needed to evaluate if statins can be used as a non-invasive alternative to treating in-stent restenosis.

In conclusion, this case demonstrates regression of in-stent restenosis over a 5 year follow-up in a patient with a Wingspan stent without invasive intervention. Further research is needed to study the potential of medical alternatives to endovascular treatment.

DISCLOSURE

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Conflicts of interest: None

REFERENCES

1. Fiorella D, Albuquerque FC, Woo H, Rasmussen PA, Masaryk TJ, McDougall CG. Neuroform in-stent stenosis: incidence, natural history, and treatment strategies. *Neurosurgery* 2006: 59:34-42.
2. Hasanefendioglu A, Bayrak B, Kocer N, *et al*. Regression of neointimal hyperplasia of an intracranial stent: 6 years follow-up of a wide-necked aneurysm. *Turkish Neurosurgery* 2010; 20:90-5.
3. Fiorella DJ, Turk AS, Levy EI, *et al*. U.S. Wingspan Registry: 12-month follow-up results. *Stroke* 2011; 42:1976-81.
4. Albuquerque FC, Levy EI, Turk AS, *et al*. Angiographic patterns of Wingspan in-stent restenosis. *Neurosurgery* 2008; 63:23-7.
5. Zhang L, Huang Q, Zhang Y, *et al*. Wingspan stents for the treatment of symptomatic atherosclerotic stenosis in small intracranial vessels: safety and efficacy evaluation. *Am J Neuroradiol* 2012; 33:343-7.
6. Chen HY, Hermiller J, Sinha AK, Sturek M, Zhu L, Kassab GS. Effects of stent sizing on endothelial and vessel wall stress: potential mechanisms for in-stent restenosis. *J Appl Physiol* 2009; 106:1686-91.
7. Scheller B, Hehrlein C, Bocksch W, *et al*. Treatment of coronary in-stent restenosis with a paclitaxelcoated balloon catheter. *N Engl J Med* 2006; 355:2113–24.
8. Fiorella DJ, Levy EI, Turk AS, *et al*. Target lesion revascularization after wingspan: assessment of safety and durability. *Stroke* 2009; 40:106-10.
9. Kimura T, Yokoi H, Nakagawa Y, *et al*. Three-year follow-up after implantation of metallic coronary-artery stents. *N Engl J Med* 1996; 334:561-6.
10. Otsuka F, Byrne RA, Yahagi K, *et al*. Neoatherosclerosis: overview of histopathologic findings and implications for intravascular imaging assessment. *Eur Heart J* 2015; 36:2147-59.
11. Kocas C, Abaci O, Kocas BB, *et al*. Impact of statin non-adherence on in-stent restenosis following bare-metal stent implantation. *Int J Cardiol* 2016; 203:529-31.
12. Natsuaki M, Nakagawa Y, Morimoto T, *et al*. CREDO-Kyoto PCI/CABG Registry Cohort-2 Investigators. Impact of statin therapy on late target lesion revascularization after sirolimus-eluting stent implantation (from the CREDO-Kyoto Registry Cohort-2). *Am J Cardiol* 2012; 109:1387-96.