



## Case report

## Recurrent in-stent thrombosis following V4 segment of vertebral artery stenting: A case report

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## ABSTRACT

**Introduction and importance:** We report a rare case of subacute recurrent in-stent thrombosis after vertebral artery stenting of the left intracranial segment.

**Case presentation:** A 56-year-old man presented with V4 segment severe stenosis of the left vertebral artery. Stent (Apollo, 2.5 mm × 8 mm) implantation was performed for severe stenosis of the left vertebral artery. Approximately 48 h after operation, the patient developed dizziness and drowsiness. DSA showed stent thrombosis, which was treated by PTAS (Apollo, 2.5 mm × 13 mm), and the preoperative symptoms resolved. Two days later, symptoms of posterior circulation ischemia reappeared, DSA showed recurrence of stent thrombosis and CYP2C19 genotypic analysis showed intermediate metabolizers. Revision PTAS (Enterprise, 4.5 mm × 28 mm) was performed followed by administration of Ticagrelor instead of tirofiban. The patient showed good neurological outcomes. CTA performed both one week and four months after the operation showed that the blood flow of the left vertebral artery was unobstructed.

**Clinical discussion:** Endovascular therapy is an alternative treatment for severe intracranial vascular stenosis, and reocclusion is one of the serious complications.

**Conclusion:** our case report highlights that recurrent in-stent thrombosis maybe be caused by inadequate pre-operative assessment and unsuitable therapeutic drug selection for the stents.

### 1. Introduction

Intracranial atherosclerotic stenosis (ICAS) is one of the most common causes of ischemic stroke and accounts for up to 30 to 50% of ischemic stroke cases in Asia [1]. Although the data of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) and the Vitesse Intracranial Stent Study for Ischemic Therapy (VISSIT) trials suggested that medical management alone was better than endovascular treatments for ICAS [2,3], some prospective and retrospective studies from Europe and Asia reported results supporting endovascular treatment [4–9] in patients with intracranial atherosclerotic disease in whom dual-antiplatelet medical therapy failed. The major complication associated with endovascular treatment for ICAS is in-stent thrombosis (ISR). Previous

studies from the USA and Asia showed an incidence rate of symptomatic ISR ranging from 0 to 13.8% [4,10–13]. Moreover, ISR can lead to serious adverse outcomes. However, the optimal management of patients with symptomatic ISR is still unclear [13]. Here, we reported a case of recurrent ISR possibly caused by inadequate preoperative assessment and unsuitable therapeutic drug selection for the stent. This work is reported in accordance with SCARE Criteria [14].

### 2. Case presentation

A 56-year-old man presented with dizziness and walking instability for two weeks with a 10-year history of hypertension. Blood pressure was controlled at about 150/90 mmHg with nifedipine sustained-release tablets 20 mg and Irbesartan tablets 0.15 g daily. No history of

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psychosocial, diabetes or coronary heart disease, denied drug, food and other allergies. Ten days before, the patient experienced paroxysmal dizziness and walking instability accompanied by binocular vision in severe episodes. Each attack lasted for 10 min to half an hour. Digital subtraction angiography (DSA) showed V4 segment occlusion (Fig. 1A) of the right vertebral artery and a limited 80% stenosis (stenosis ratio was evaluated by the North American Symptomatic Carotid Endarterectomy Trial method (DSA-NASCET)) of the left vertebral artery V4 segment of approximately 6 mm length (Fig. 1B). The patient was diagnosed with atherothrombotic brain infarction and transient ischemic attack (TIA) of posterior circulation. After treatment with aspirin, clopidogrel, and a statin, no significant improvement in neurological symptoms was noted. The patient was treated by stenting. In order to accurately locate and maximize the radial support force, an Apollo stent (Shanghai Minimally Invasive Medical Devices (Group) Co., Ltd., China), measuring 2.5 mm × 8 mm, was placed. DSA performed after stent placement showed good distal blood flow, and no in-stent thrombosis was observed, although there was a residual localized 40% stenosis at the distal end of the lesion (Fig. 1C). Postoperative cranial CT showed no haemorrhage (Fig. 1D). The patient's symptoms improved markedly when treated with continuous infusion of tirofiban at 6 ml per hour.

Approximately 48 h after the operation, pre-admission symptoms recurred, and the patient developed lethargy. DSA showed ISR (Fig. 2A). In order to pass through the narrow section smoothly and cover the lesion as much as possible, an Apollo stent (Shanghai Minimally Invasive Medical Devices (Group) Co., Ltd. China), measuring 2.5 mm × 13 mm, was chosen and placed (Fig. 2D) after transluminal balloon angioplasty (TBA) with a 2.25-mm diameter balloon (Fig. 2B, C). After this procedure, symptoms of transient ischemia disappeared, and postoperative cranial CT did not show haemorrhage (Fig. 3H). Tirofiban was initiated.

Unfortunately nearly 48 h after the second operation, symptoms of posterior circulation ischemia reappeared. DSA showed ISR (Fig. 3A, B) in the basilar artery. We treated the patient with transcatheter infusion of tirofiban 10 ml (Fig. 3C); however, the stent thrombosis persisted. TBA was performed with a 2.0-mm diameter balloon (Fig. 3E), but stent thrombosis persisted. Then, urokinase 50,000 U was given through the catheter (Fig. 3F) and in-stent thrombosis decreased slightly. TBA was then repeated with a 2.0-mm diameter balloon (Fig. 3H), and in-stent stenosis significantly improved compared with that before stenting. In order to cover the lesion as much as possible, an Enterprise stent (Johnson & Johnson Co., Miami, FL, USA), measuring 4.5 mm × 28 mm, was chosen and placed (Fig. 3I). The patient showed good neurological outcome. Postoperative cranial CT did not show haemorrhage (Fig. 3J). CYP2C19 genotypic analysis showed intermediate metabolizers. After this procedure, the patient was treated with Ticagrelor. CTA was performed at one week and four months after the operation; the vertebral artery stent and basilar artery were unremarkable (Fig. 3K, L). All three operations were performed by Xuan Sun and Zhongrong Miao.

### 3. Discussion

ICAS is one of the most common causes of ischemic stroke. To date, endovascular treatment, including balloon angioplasty alone, balloon-mounted stent placement, or self-expandable stent placement, is recommended as an alternative for the prevention and treatment of recurrent TIA or ischemic stroke caused by ICAS [15]. Symptomatic ISR is a significant consequence of endovascular treatment for ICAS that could lead to serious outcomes. Several risk factors related to ISR have been reported in previous studies such as young age, lesion at anterior circulation, rapid balloon inflation, residual stenosis, and longer lesion lengths [16]. However, there are few reported cases of subacute recurrent ISR after ICAS stenting.

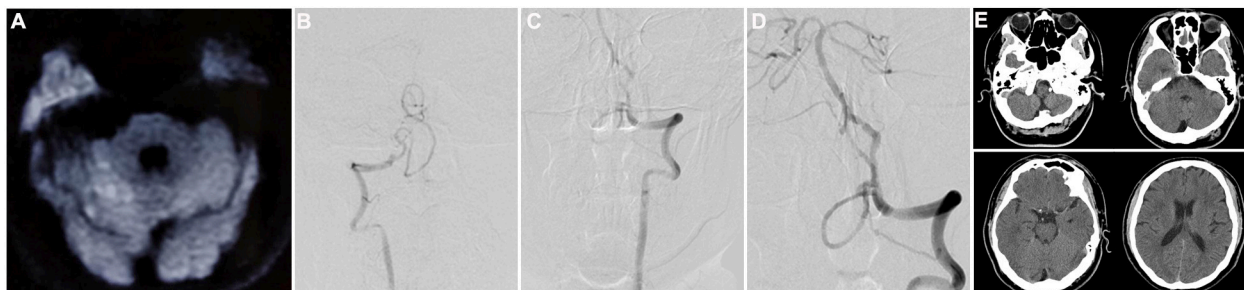
CYP2C19 genotypic analysis showed intermediate metabolizers. Previously, we showed that subacute stent thrombosis was significantly related with resistance to the treatment effects of aspirin or/and clopidogrel [17]. In this case, tirofiban was administered twice after stent implantation, but it failed to inhibit stent thrombosis. After the third stent implantation, according to the CYP2C19 genotypic analysis, we treated the patient with Ticagrelor instead of tirofiban, there was no recurrence of ISR. Therefore, for patients with aspirin or/and clopidogrel resistance, intracranial stent implantation should be cautiously performed.

In consideration of the advantages of intracranial balloon-mounted stents such as simple operation, accurate orientation, and large radial force [18], we used an Apollo stent measuring 2.5 mm × 8 mm. DSA after the operation showed residual 40% stenosis at the distal end of the stent. It is suggested that the stent did not cover the lesion completely, which indicated that the preoperatively evaluated length of the lesion was shorter than its true length. Such miscalculations can cause plaque rupture and promote new thrombosis [1]. Forty-eight hours later, a repeat DSA showed ISR, and a longer Apollo stent was placed in order to pass through the narrow section smoothly and cover the lesion as much as possible. However, the lesion was much longer than indicated by our assessment. After 48 h, ISR recurred, and this time an Enterprise stent was chosen. CTA performed both one week and four months after the operation showed that the blood flow of left vertebral artery was unobstructed. It would be helpful to evaluate the lesions precisely for ICAS before recommending endovascular treatments. High-resolution vessel wall MRI can be used to detect the properties of the plaque, which would be useful for the selection of stents.

Based on our findings, we suggest the following: first, for patients with aspirin or/and clopidogrel resistance, intracranial stent implantation should be cautiously performed; secondly, before performing endovascular treatments, the properties of the plaques should be accurately assessed using various methodologies; and thirdly, intracranial stents should be selected to cover lesions as much as possible.

### 4. Conclusions

Our case report highlights that recurrent in-stent thrombosis maybe



**Fig. 1.** A, B: DSA showed V4 segment occlusion of the right vertebral artery and a limited 80% stenosis of the left vertebral artery V4 segment of approximately 6 mm length; C: An Apollo stent was placed; D: Postoperative cranial CT.

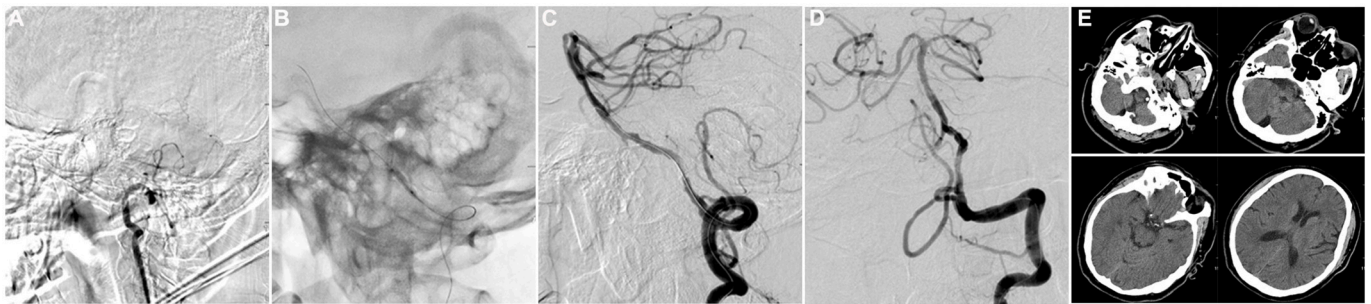


Fig. 2. A: DSA showed stent thrombosis; B,C: TBA with a balloon; D: An Apollo stent was placed; E: cranial CT.

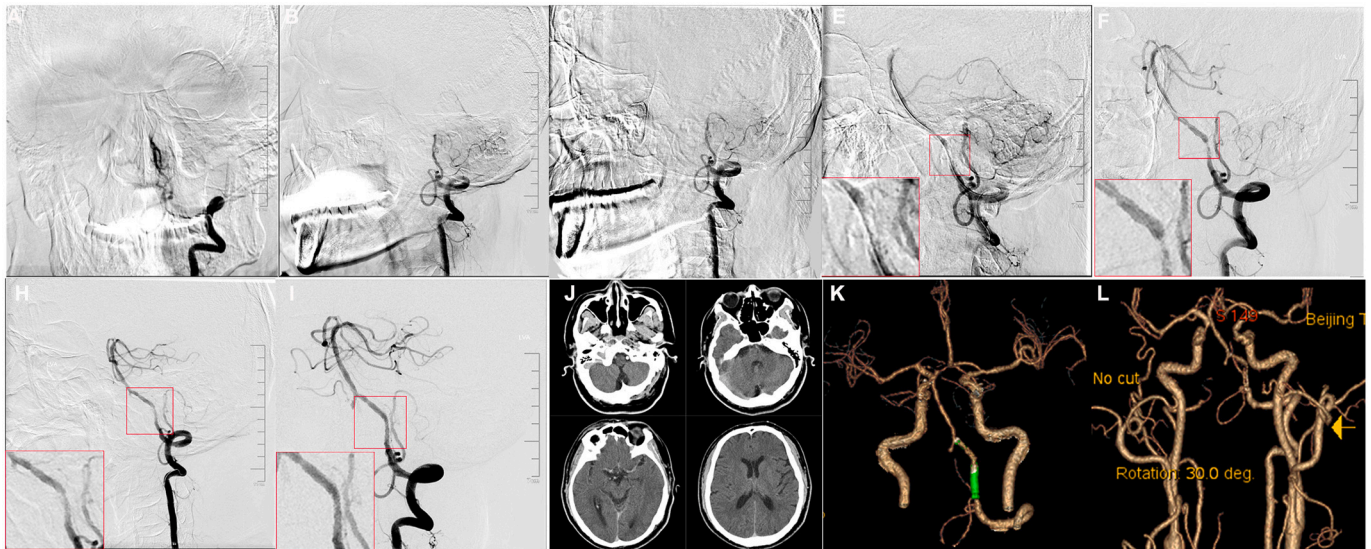


Fig. 3. A, B: DSA showed stent thrombosis; E: TBA was performed with a 2.0-mm diameter balloon; F: urokinase 50,000 U was given; H: TBA was then repeated with a 2.0-mm diameter balloon; I: an Enterprise stent was placed; J: cranial CT; K, L: CTA was performed at one week and four months after the operation.

be caused by inadequate preoperative assessment and unsuitable therapeutic drug selection for the stents.

**Abbreviations**

- ICAS intracranial atherosclerotic stenosis
- ISR subacute recurrent in-stent thrombosis
- PTAS percutaneous transarterial balloon angioplasty and stent implantation
- MRI Cranial magnetic resonance imaging
- DSA Digital subtraction angiography

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Z.M. designed research, collection, analysis, and interpretation of data.

**Ethics approval**

This case has been informed by patients and their families.

**Consent for publication**

Publication consent was obtained from the patient.

**Research registration (for case reports detailing a new surgical technique or new equipment/technology)**

This is a case report so registration was not required.

**Guarantor**

All the authors are the guarantor of the study.

**Provenance and peer review**

Not commissioned, externally peer-reviewed.

**Footnotes**

No patient or author details are included in the figures.

**Consent**

Publication consent was obtained from the patient.

**CRediT authorship contribution statement**

Study Concept: X.S., H.Z. and Z.M.  
 Data Collection: X.S., H.Z., Q.Y., W.J., H.S., Z.Z. and Y. Z.  
 Writing: X.S. and Y.Z.  
 Revising and critical review: X.S., H.Z.

**Declaration of competing interest**

The authors declare no conflict of interest.

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