Intra-arterial Tirofiban after Intravenous Thrombolysis in a Patient with Capsular warning syndrome: A case report

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Case Report

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Abstract

**Background:** Capsular warning syndrome (CWS) is a special type of transient ischemic attack syndrome with a high risk to progress into a stroke with a permanent disability. An effective and standard therapy has not yet been established.

**Case presentation:** We report a 57-year-old man who experienced 4 episodes of dysarthria and left-sided hemiplegia. He was diagnosed with CWS and treated by r-tPA intravenous thrombolysis (IVT) in the third episode. He achieved a transient remission after IVT. However, he developed more severe and persistent symptoms with a National Institute of Health Stroke Scale (NIHSS) score of 8 points at the fourth attack. Intra-arterial tiroban was administered as remedial therapy and the patient achieved a favorable outcome with a modified Rankin Scale score of 0 at the 3-month follow-up. **Conclusion:** Intra-arterial tiroban may act as an effective and safe remedial therapy for patients with CWS who failed to respond to IVT.

1. **Background**

Capsular warning syndrome (CWS), first proposed in 1993, has a high stroke risk of 60% within 7 days\(^1\), \(^2\). Though various treatments have been suggested, the best clinical management of CWS is yet to be established\(^3\). Here we reported a patient treated by bridging treatment, consisting of intravenous thrombolysis and intra-arterial tiroban followed by intravenous tiroban continually, and reached a favorable clinical outcome.

2. **Case presentation**

A 57-year-old man suddenly developed two episodes of dysarthria and left-sided hemiplegia one hour before he was admitted to our emergency department. It lasted about five minutes for each episode. He had a history of hypertension for one year and was treated with amlodipine 5mg once a day. He denied any other history of diseases. His blood pressure was 150/110 mmHg, random blood sucrose was 6.3 mmol/L, and electrocardiogram (EEG) was normal on admission.

The third episode occurred while performing urgent diffusion-weighted magnetic resonance imaging (DWI) and time-of-flight MR angiography (TOF-MRA). No significant signal change was detected in DWI (Fig. 1A\(_1\)-A\(_3\)). However, TOF-MRA (Fig. 1B\(_1\)) showed significant stenosis of the right middle cerebral artery (MCA) M1 segment. Neurological examination showed slight weakness in left-sided limbs with dysarthric speech and his National Institute of Health Stroke Scale (NIHSS) was 3 points. He was diagnosed with CWS according to the recurrent stereotyped episodes of three transient ischemic attacks during a short period of time, affecting the left-sided limbs and dysarthria, but sparring the cortical function. Intravenous thrombolysis (IVT) was administered with recombinant tissue plasminogen activator (r-tRA, 81mg, 0.9mg/Kg) after fully informed consent was obtained from the patient and his guardian. Complete remission of symptoms was seen at the end of IVT.
However, 2 hours later, he was exposed to the fourth episode presenting with an NIHSS score of 8 points. Persistent symptoms motivated the patient to accept cerebral digital subtraction angiography (DSA). The 3D angiographic reconstruction showed stenosis of the right MCA M1 segment (Fig. 1 B₂) and the axial DSA image showed the stenosis located in the origin of the lenticulostriate branches (Fig. 1 B₃). Excellent reperfusion (mTICI [modified Treatment in Cerebral Ischemia] of 3) prevented a following mechanical thrombectomy or balloon dilation. We injected tirofiban 8ml (0.05mg/ml) with an infusion rate of 1 mL/min via a 5F catheter placed in the right internal carotid artery. His symptoms improved after the intra-arterial injection, and a continuous intravenous infusion of tirofiban (0.1µg/kg/min) was administered subsequently. He achieved complete remission the next morning without any attacks again. Hypodensity, which means infarction, in the striatum was seen in computed tomography (CT) performed 24h post intravenous thrombolysis (Fig. 1C₁-C₃). What’s more, reperfusion in the area of infarction was seen in Perfusion CT (Fig. 2). After 48 hours of intravenous infusion of tirofiban, it was replaced with aspirin 100mg plus clopidogrel 75mg per day, whereaspirin and clopidogrel were administered for 4 hours in overlap with tirofiban. One week later, the follow-up CT showed lesion hypodensity reversed (Fig. 1 D₁-D₃). The patient was discharged without any stroke attacks again and the modified Rankin Scale (mRS) was 0 at the 3-month follow-up.

3. Discussion

The exact pathophysiology underlying CWS is not well elucidated. Various theories have been proposed to explain its complex pathophysiology. However, intrinsic cerebral small vessel disease and hemodynamic instability are the most widely accepted aetiologies[^4]. Concerning cerebral small vessel disease, micro-atherosclerosis at the origin of a deep perforating artery is considered to be the main associated pathological process[^5].

In our case, DSA showed stenosis of the right MCA M1 segment at the origin of the lenticulostriate branches. We speculated that micro-atherosclerosis is the pathologic mechanism for our patient. Consistent with the result of a previous study that IVT did not provide an advantage in preventing recurrences in CWS[^6], we found that IVT administered in this case did not prevent the CWS developed into an established infarct confirmed by lesion hypodensity in CT. This may likely be explained by the mechanism that IVT could activate platelet aggregation leading to the restenosis of the recanalized perforating artery by intravenous rt-PA[^7]. The restenosis of perforating artery could cause the recurrence and exacerbation of symptoms. We speculate that a treatment that can provide fast-acting and powerful anti-platelet aggregation effects may prevent restenosis and help to return to normal perfusion leading to a favorable outcome.

For the first time, we reported a patient with CWS who received intra-arterial tirofiban followed by intravenous infusion of tirofiban after IVT. Tirofiban, a platelet GP IIb/IIIa receptor inhibitor, has been confirmed to be effective and safe in stopping recurrent and fluctuating symptoms in patients with CWS[^8]. However, there still 26.7% of patients with CWS suffered new episodes during the maintenance
A recent study has confirmed that using intra-arterial tirofiban during endovascular therapy after IVT could be safe\(^8\). Accordingly, we administered intra-arterial tirofiban and followed by intravenous infusion when the patient underwent another episode after IVT. The patient achieved significant improvement of symptoms without any attacks again after intra-arterial tirofiban. Follow-up CTP showed reperfusion in the area of infarction and ischemic lesion hypodensity in CT was reversed. The possible reason may be that intra-arterial tirofiban provides fast-acting and powerful anti-platelet aggregation effects which prevent restenosis. As a result, it return to normal perfusion and the patient achieved a favorable outcome.

In conclusion, there is still no consensus on the treatment of CWS. Intra-arterial tirofiban may act as an effective remedial therapy for patients with CWS who failed to respond to IVT.

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Written consent for publication was provided from the participant.

**Availability of data and materials**

All data generated or analysed during this study are included in this published article.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

Qingqing Fu wrote the main manuscript text and prepared all the figures. Zhonghua Jiang plays a guiding role.

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**References**


**Figures**
Figure 1

A₁–A₃ DWI showed no significant signal change on admission. B₁, B₂ TOF-MRA and 3D angiographic reconstruction showed stenosis of the right MCA M1 segment. B₃ Axial DSA image showed the stenosis located in the origin of the lenticulostriate branches. C₁–C₃ CT performed 24h post intravenous thrombolysis showed hypodensity in the striatum. D₁–D₃ 1-week follow-up CT showed lesion hypodensity reversed.
Figure 2

CT showed hypodensity in the striatum. CTP showed an increase in cerebral blood volume and cerebral blood flow and a slight delay in mean transit time and time to peak.