

Rescue Treatment with Intra-arterial Tirofiban Infusion and Emergent Carotid Stenting

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Rapid arterial rethrombosis is associated with high-grade residual stenosis and usually occurs at the site of the initial occlusion, resulting in reocclusion of the recanalized artery. Platelets may play an active role in such rethrombosis after thrombolytic-induced clot lysis. Given that glycoprotein IIb/IIIa receptor blockers, like tirofiban, prevent thrombus formation by inhibiting the final common pathway of platelet aggregation, they may be helpful for treating rethrombosis after thrombolysis. A 64-year-old man presented with an acute ischemic stroke due to internal carotid artery (ICA) occlusion. The ICA was recanalized by intravenous thrombolysis but reoccluded shortly after recanalization. The reoccluded ICA was successfully recanalized using intra-arterial tirofiban. A carotid stent was subsequently inserted to relieve severe stenosis and to prevent recurrent stroke. Here, we report a case of rescue treatment of a successfully recanalized ICA by intra-arterial tirofiban. We suggest that rescue use of intra-arterial tirofiban may be effective and safe, especially in hemorrhage prone situations, due to the relatively lower dose of tirofiban compared with intravenous doses.

Key Words: Carotid stent, glycoprotein IIb/IIIa receptor blocker, tissue plasminogen activator

INTRODUCTION

Reocclusion after successful arterial recanalization occurs commonly in acute ischemic stroke.^{1,2} Rapid rethrombosis is associated with high-grade residual stenosis and usually occurs at the site of the initial occlusion, resulting in reocclusion of the recanalized artery.³ Platelets may play an active

role in such rethrombosis following thrombolytic-induced clot lysis.

Glycoprotein (GP) IIb/IIIa receptor blockers prevent thrombus formation by inhibiting the final common pathway of platelet aggregation. There are three GP IIb/IIIa receptor blockers (abciximab, tirofiban, eptifibatide) available for clinical use. There are significant differences in the biological and plasma half-lives of abciximab and the small molecule agents (tirofiban and eptifibatide). Tirofiban is a small, non-peptide molecule that has been used intravenously, in combination with recombinant tissue plasminogen activator (rt-PA), to treat patients with acute coronary artery disease. Some promising pilot results using intravenous tirofiban combined with thrombolytics for acute ischemic stroke have been demonstrated.^{4,5}

CASE REPORT

A 64-year-old man was admitted to the hospital due to left-sided weakness and drowsiness. His initial National Institutes of Health Stroke Scale (NIHSS) score was 16. Brain CT showed no low-density lesions, but bilateral cervical internal carotid artery (ICA) occlusions were observed on CT angiography (Fig. 1). Intravenous rt-PA was administered 160 minutes after the initial onset of symptoms. Because there was no improvement at the end of the intravenous rt-PA infusion, we proceeded to cerebral angiography to perform intra-arterial thrombolysis. Cerebral angiography showed complete occlusion of the left cervical ICA and severe stenosis of the right cervical ICA (Fig. 2A) with delayed filling of the right middle

Received March 22, 2007

Accepted May 8, 2007

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cerebral artery and both anterior cerebral arteries. The left ICA territory was supplied by an ophthalmic collateral from the left external carotid artery and pial collateral flow from the left posterior cerebral artery. Due to the severe stenosis of the right ICA and delayed intracranial perfusion, plans were made to insert a carotid stent to prevent recurrent ischemic stroke. However, the right ICA was reoccluded approximately 20 minutes after the initial angiography (Fig. 2B). Tirofiban was administered through the microcatheter by hand injection. After injection of

200 μ g of tirofiban over five minutes, the occluded ICA was recanalized with the remaining stenosis as severe as that seen on initial angiography (Fig. 2C). We inserted a self-expandable carotid stent (SMART, 7 \times 80 mm Cordis, Warren, NJ, USA), and subsequent angiography showed no remaining stenosis (Fig. 2D). A brain MRI performed 10 days after thrombolysis showed acute cerebral infarctions involving the right fronto-parietal and medial frontal cortex. Four weeks following thrombolysis, the patient's NIHSS score had improved to six.

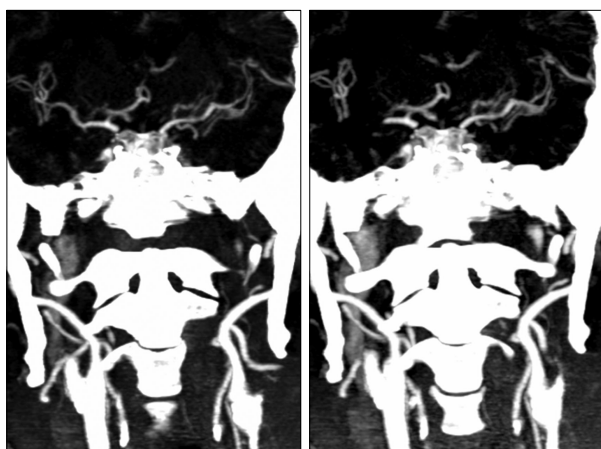


Fig. 1. Initial brain CT angiography shows bilateral internal carotid artery occlusions.

DISCUSSION

Fibrinolysis by rt-PA heightens platelet activity and exposes clot-bound thrombin, facilitating rethrombosis via the cleavage of fibrinogen to fibrin.⁶ In addition, high blood flow velocity due to remaining arterial stenosis may further activate platelet aggregation. Thus, a blockade of platelet-mediated thrombotic mechanisms appeared to be a rational approach to the management of this patient, as platelets seemed to play a key role in the rethrombosis. Highly effective inhibition of platelet activity can be achieved by the introduction of potent inhibitors of the GP IIb/IIIa

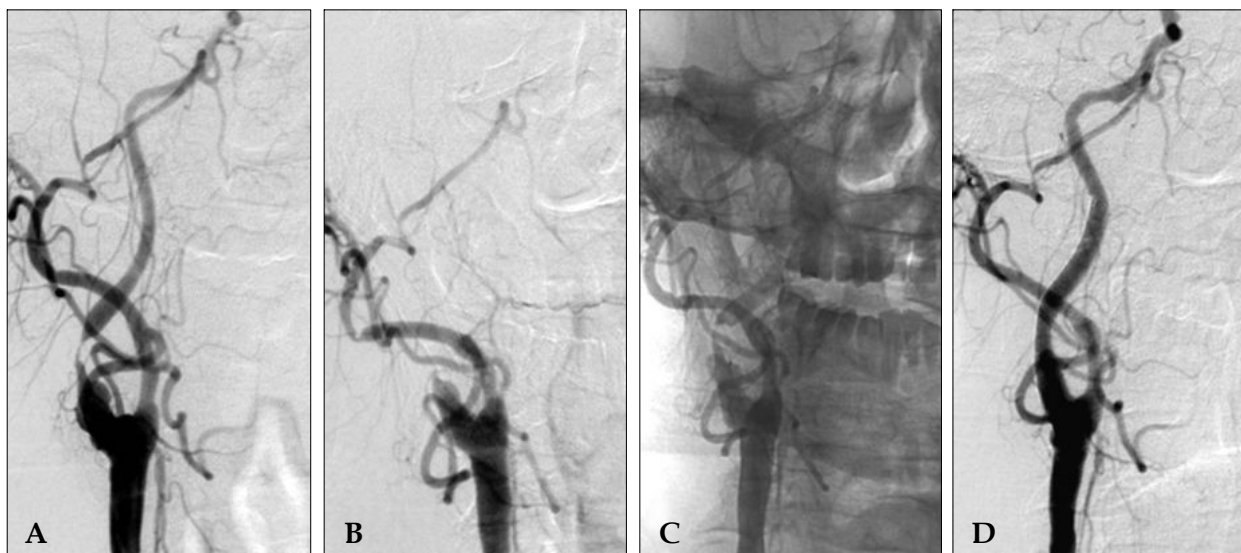


Fig. 2. Serial cerebral angiography. (A) The initial angiography reveals severe stenosis of the right cervical ICA. (B) Reocclusion of the right ICA 20 minutes after initial angiography. (C) After intra-arterial tirofiban infusion, the occluded right ICA is recanalized and severe stenosis remains. (D) Final angiography after carotid stent insertion shows no stenosis of the right ICA. ICA, internal carotid artery.

receptor.

It has been reported that GP IIb/IIIa receptor blockers can decrease the incidence of restenosis and ischemic complications after percutaneous transcatheter angioplasty.⁷ Recently, GP IIb/IIIa receptor blockers were advocated as potentially promising agents for acute stroke therapy, and there were some case studies reporting the successful rescue use of GP IIb/IIIa receptor blocker in acute ischemic stroke.^{6,8-10} Tirofiban is a non-peptide tyrosine derivative that mimics the RGD integrin recognition sequence. It has a very short platelet-bound half-life and a relatively long plasma half-life, therefore providing an advantage when the rapid reversal of antiplatelet action is required such as in cases of high-risk hemorrhage or in combined use with thrombolytics. It has been reported that tirofiban produces a dose-dependent, dethrombotic effect on thrombosis and inhibits acute *de novo* stent thrombosis under high-shear flow conditions in an *ex vivo* canine arteriovenous shunt model.¹¹ Tirofiban is generally used intravenously in coronary artery disease, with a loading dose of 0.4 µg/kg/min for 30 minutes and a subsequent infusion of 0.1 µg/kg/min. We initially planned to use the standard intravenous loading dose (900 µg) intra-arterially; however, after use of only 200 µg intra-arterial tirofiban, the ICA was successfully recanalized. We speculate that intra-arterial drug delivery may reduce the dose of tirofiban required to dissolve the thrombus.

This case demonstrates that a GP IIb/IIIa receptor blocker is effective for the recanalization of reoccluded arteries, especially in the presence of arterial stenosis. The dose of GP IIb/IIIa receptor blocker can be reduced by intra-arterial use, as compared with intravenous use and may be effective at preventing hemorrhagic complications, especially when used in combination with thrombolytics. Although this case showed promising results of intra-arterial tirofiban use, further studies are necessary to verify the effect of

intra-arterial use of tirofiban and to determine its proper dose.

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