Prolonged Low-Dose Intravenous Thrombolysis in a Stroke Patient With Distal Basilar Thrombus

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Background and Purpose—Patients with high-grade basilar artery stenosis secondary to thromboembolism are at high risk of developing subsequent vessel occlusion. Optimal medical management of this condition is unclear.

Summary of Case—We present a patient with a small subacute brain stem infarction and filiform distal basilar residual lumen attributable to arterioarterial or cardiogenic embolism. Beginning 3 days after symptom onset, low-dose intravenous thrombolysis with 0.125 mg/kg recombinant tissue plasminogen activator was continuously infused for 48 hours. Follow-up magnetic resonance angiography revealed complete resolution of the embolus. No further cerebral ischemic episodes occurred during 3-month follow-up, and the basilar artery remained patent.

Conclusion—Our observation suggests a potential for prolonged low-dose intravenous thrombolysis in basilar artery embolism, but further data are needed to judge the effectiveness and risk of this intervention. (Stroke. 2006;37:e9-e11.)

Key Words: ischemia ■ magnetic resonance imaging ■ reperfusion ■ thrombolysis

Patients presenting with a subacute ischemic stroke and with thrombi lodging within major stenotic cervicocerebral arteries are at high risk of developing subsequent thromboembolism or local vessel occlusion. In this setting, neuroradiologic angioplasty is frequently postponed because catheter-induced embolism is a concern. Although rapid dissolution of the clot appears desirable, interim medical management usually is limited to antiplatelet or anticoagulatory therapy.

Intravenous thrombolysis with 0.9 mg/kg body weight of recombinant tissue plasminogen activator (rt-PA) is an established therapy in acute ischemic stroke within 3 hours after symptom onset. Moreover, several studies suggest a benefit of this intravenous thrombolysis protocol for selected patients treated within a 6-hour time window. In contrast, its efficacy in subacute ischemic stroke with stenosing thrombi has not been examined although several studies have applied low-dose continuous thrombolysis in arterial and venous thrombi elsewhere in the body with some success.

Herein we report a patient in whom prolonged low-dose intravenous thrombolysis resulted in dissolution of a basilar thrombus within 48 hours without any complications.

Case Reports

A 70-year-old white male with a past medical history of recurrent angina attributable to 3-vessel coronary artery disease reported of weakness of his right leg, numbness of his tongue, double vision, vertigo, and nausea that had started 15 minutes after awakening. When presenting in the emergency room 9 hours later, symptoms had partially regressed. Physical examination revealed vertical gaze palsy, spontaneous nystagmus, and a gait ataxia. Cranial computed tomography (CT) was normal, but neurovascular ultrasound and CT angiography, respectively, revealed occlusion of the right vertebral artery and high-grade stenosis of the mid-to-distal basilar segment. Stroke MRI the following day showed small acute infarctions of the right midcerebellar peduncle and right mesencephalic tegmentum (Figure, A). Magnetic resonance (MR) angiography and conventional angiography demonstrated a distal basilar thrombus with a minimal residual lumen (Figure, B through D). The top of the basilar was supplied by bilateral posterior communicating arteries. Because occlusion of the vessel was feared, continuous low-dose intravenous thrombolysis was started 69 hours after symptom onset with a dose of 0.125 mg/kg body weight (ie, 10 mg per day) after informed consent was obtained from the patient. Standard coagulation parameters and blood count remained within normal limits, but plasma D-dimer antigen was slightly elevated during therapy. Forty-eight hours after initiation of thrombolytic therapy, repeated ultrasound and MRI revealed complete dissolution of the thrombus (Figure, E). No new infarcts were seen on diffusion-weighted MRI (DWI). Cardiac workup revealed a ventricular thrombus of 10-mm diameter adherent to the akinetic anteroseptal wall. Anticoagulatory therapy initially with intravenous heparin and later with coumadine was started. At 3-month follow-up, clinical status was stable, with only transient dizziness on extension of the neck. Cerebrovascular ultrasound showed persistent occlusion of the right vertebral but normal flow in the basilar artery.
Discussion

Prolonged intravenous infusion of low-dose thrombolytic therapy has been used in various conditions including hepatic veno-occlusive disease in adults and venous and arterial thrombosis in children.\textsuperscript{4–7} To our knowledge, our case report represents the first successful administration of such a low-dose rt-PA protocol to a patient with a subacute ischemic stroke associated with a basilar thrombus.

Several aspects have to be taken into consideration when considering this therapeutic option for future patients. First of all, we cannot rule out that dissolution of the thrombus occurred spontaneously. However, the thrombus, which had been stable for the initial 60 hours, resolved within the 48-hour time period of thrombolytic therapy between MR angiograms, suggesting at least a beneficial role of rt-PA. Because arteriosclerotic and cardiologic embolic sources of the basilar thrombus were identified, the angiographically proven thrombus possibly represented an embolus that favors subsequent dissolution of the clot compared with a locally developing arteriosclerotic thrombus. A particular concern with prolonged low-dose thrombolysis is a thrombolysis-induced procoagulatory state. Indeed, we observed a modest increase of D-dimer antigen, an indicator of the formation of factor XIIIa cross-linked fibrin. Fassbender et al\textsuperscript{8} reported that fibrin monomers and D-dimer antigen were substantially elevated for 72 hours after standard thrombolytic therapy in stroke patients. Similar findings were reported for thrombolysis in myocardial infarction.\textsuperscript{9} However, the clinical significance of these findings is unknown. Finally, secondary intracerebral hemorrhage is a major concern after thrombolytic therapy in ischemic stroke. The risk of secondary hemorrhage after stroke partially depends on lesion size and interval between

Pretherapeutic DWI (A), MR angiography (MRA; B), digital subtraction angiography (DSA; C and D) and post-therapeutic MRA (E). On DWI (A), only a few diffusion-restricted areas were detected in the pons and the cerebellum. MRA (B) as well as DSA (C and D) before intravenous therapy with rt-PA show the thrombus lodging in the distal basilar artery (arrow). After 48 hours of low-dose systemic thrombolytic treatment, complete recanalization of the basilar artery was seen in the MRA (E).
symptom onset and treatment initiation. Because our patient had only 2 small brain stem infarcts on DWI, the risk of hemorrhage appeared justifiable.

In conclusion, our case suggests that low-dose prolonged thrombolytic therapy with rt-PA is a therapeutic option in patients with embolic high-grade stenosis of intracranial vessels, but further data are needed to judge the effectiveness and risk of this intervention.

References

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