A Case of Recanalized Cardioembolic Stroke
Possible Effect of Transcranial Color-Coded Real-time Sonography on Thrombolytic Therapy

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Thrombolytic therapy appears to be one of the most valuable treatments for acute ischemic stroke. The major objective of thrombolysis in acute ischemic stroke is to recanalize occluded arteries to reestablish brain function by saving tissue from ischemic risk. Rapid lysis of intracranial clots has been strongly associated with early neurologic improvement, reduction of infarct size, and favorable outcome.1–6 It has been reported in vitro and in animal models that the combination of the administration of tissue plasminogen activator (t-PA) and the application of ultrasound was effective for thrombolysis.7–11 Moreover, Alexandrov et al12 have recently shown that the reperfusion rate of occluded arteries by t-PA is improved by the combined therapy with the application of ultrasound. Here we report a patient with cardioembolic stroke whose occluded middle cerebral artery (MCA) was recanalized during an examination with transcranial color-coded real-time sonography (TCCS) after thrombolytic therapy by urokinase. The combined therapy of ultrasound with urokinase may also be effective in the treatment of acute ischemic stroke.

Case Report

A 64-year-old man was admitted to our hospital because of a disturbance in consciousness. He had a history of smoking and arrhythmia but did not receive medication, including warfarin. One hour after the onset, he was transferred to our hospital with severe right hemiparesis and global aphasia. Laboratory findings showed that his blood cell counts, serum cholesterol levels, and blood glucose levels were normal. Although the prothrombin time international normalized ratio, the activated partial thromboplastin time, and the levels of fibrinogen, antithrombin III, and D dimer were within the normal range, the thrombin-antithrombin III complex level was above normal (10.8 ng/mL). His electrocardiogram showed atrial fibrillation. An initial computed tomographic scan of his brain on admission showed a hyper-
dense MCA sign on the left side, indicating occlusion of the left MCA. The cortex of the left temporal lobe was obscure. The Doppler flow velocity of the internal carotid artery revealed no abnormality.

We diagnosed cardioembolic occlusion of the left MCA and planned intra-arterial thrombolytic therapy. Intra-arterial digital subtraction angiography showed an occlusion of the left MCA (Figure 1A), and urokinase (180,000 U) was administrated to the patient intra-arterially; however, recanalization of the occluded artery was not observed (Figure 1B).

After the thrombolytic therapy, we performed TCCS with a SONOS 5500 sonography system (Philips Medical Systems, Tokyo, Japan) with a 1- to 3-MHz sector transducer. The acoustic power of the pulsed wave transducer (190.2 mW/cm²) was within the range approved by the US Food and Drug Administration. At the beginning of the examination, only the proximal portion of the left MCA was observed on color Doppler imaging. Flow velocity was reduced according to the pulsed Doppler findings, suggesting the presence of occlusion of the MCA (Figure 2). One hundred three minutes after the administration of urokinase, the distal portion and even the branch of the left MCA suddenly became visible on color Doppler imaging. The flow velocity of the left MCA measured with the pulsed Doppler examination increased to the normal range, showing marked improvement compared with the initial sonographic finding (Figure 3).

The patient’s right hemiparesis disappeared completely, and his motor aphasia improved; thereafter, a computed tomographic scan of the brain showed a small infarct in the left basal ganglia and temporal lobe, with minor hemorrhagic transformation. An intracranial magnetic resonance image taken 6 days after the onset also disclosed recanalization of the left MCA.
Discussion

Because TCCS has both B-mode and color-coded Doppler facilities, vessels in the brain can be displayed more clearly by TCCS than by conventional transcranial Doppler (TCD) imaging. Moreover, the angle of insonation by TCCS can be corrected easily. Thus, the flow velocity measured by TCCS may be quite close to the true value. We have shown recently that the measurement of MCA flow velocity by TCCS is useful for identifying the existence of occlusion of the MCA and its branches; therefore, TCCS is useful for monitoring the actual hemodynamic state during thrombolytic therapy. In our patient, we clearly detected the change in the Doppler waveform and the MCA flow velocity and confirmed recanalization of the MCA occlusion during the test.

In our patient, we observed recanalization of the MCA during sonography. We speculate that application of ultrasound may have contributed to the increased efficacy of the thrombolytic therapy. It has been reported that the application of ultrasound combined with thrombolytic agents such as t-PA may improve the efficacy of thrombolytic therapy in acute ischemic stroke. Eggers et al suggested the beneficial effect of TCCS combined with t-PA on the outcome of patients with acute stroke and a higher recanal-
ization rate of the occluded MCA. Furthermore, Alexandrov et al.\textsuperscript{12} showed that the use of TCD imaging had a positive effect on t-PA–induced recanalization and clinical recovery of patients with acute ischemic stroke and that it did not increase intracranial hemorrhage; however, to our knowledge, there are no data that show the efficacy of ultrasound on thrombolytic therapy using urokinase. In previous in vitro and animal model studies, efficacy of streptokinase and urokinase as well as t-PA was reported.\textsuperscript{17–22} In our patient, we found that the occluded MCA was recanalized during the TCCS examination after thrombolytic therapy with urokinase. Thus, the combined therapy of ultrasound with urokinase may also be effective in the treatment of acute ischemic stroke. Several mechanisms have been proposed to explain the acceleration of thrombolysis by ultrasound. Ultrasound appears to change a large number of fibrin fibers into thinner fibers.\textsuperscript{23} It may also accelerate the binding of fibrinolytic agents to fibrin.\textsuperscript{24} It has also been reported that fluid motion by ultrasound-induced cavitations accelerate thrombolysis by promoting the transport of plasminogens to their target sites on fibrin.\textsuperscript{9}

The relationship between the thrombolysis and the duration of insonation is unknown. Eggers et al.\textsuperscript{16} reported that the beneficial effect was obtained with continuous monitoring of TCCS for 1 hour. On the other hand, Alexandrov et al.\textsuperscript{12} performed continuous TCD monitoring for 2 hours after administration of a t-PA bolus and showed that complete recanalization occurred more frequently with continuous TCD imaging. They also indicated that severe bleeding was not seen frequently with TCD imaging compared with controls. For our patient, recanalization of the MCA was observed 103 minutes after the administration of urokinase, and a minor hemorrhage was found; however, the patient’s neurologic findings did not worsen. The optimal setup of TCCS equipment, including the frequency and acoustic power of ultrasound, also needs to be elucidated.\textsuperscript{25} During thrombolytic therapy, the application of ultrasound may reduce the dose of thrombolytic agents and thereby may reduce the risk of hemorrhagic transformation.

In conclusion, we report a case of cardioembolic stroke in which the recanalization of the occluded MCA was obtained during TCCS after thrombolytic therapy with urokinase. We speculate that the recanalization of the occluded MCA may have been influenced by the ultrasound. Thrombolytic therapy combined with TCCS may improve the outcome of patients with acute stroke and may hasten the recanalization of the occluded MCA.

References


