Intra-Arterial rtPA Treatment of Stroke Assessed by Diffusion- and Perfusion-Weighted MRI

Maarten G. Lansberg, MD; David C. Tong, MD; Alexander M. Norbash, MD; Midori A. Yenari, MD; Michael E. Moseley, PhD

Background—Diffusion-weighted MRI (DWI) and perfusion-weighted MRI (PWI) are new techniques that can be used for the evaluation of acute ischemic stroke. However, their potential role in the management of patients treated with recombinant tissue plasminogen activator (rtPA) has yet to be determined.

Case Description—The authors present the case of a 73-year-old man who was treated with intra-arterial rtPA, and they compare findings on DWI and PWI scans with angiography. PWI revealed decreased cerebral perfusion corresponding to an area that was not successfully recanalized, but revealed no abnormality in regions in which blood flow was restored. DWI was unremarkable in the region that was reperfused early (3 hours) but revealed hyperintensity in an area that was reperfused 3.5 hours after symptom onset and in the area that was not reperfused.

Conclusions—Findings on PWI correlated well with angiography, and DWI detected injured tissue in the hyperacute stage, whereas conventional MRI findings were negative. This suggests that these techniques may be useful to noninvasively evaluate the success of thrombolytic therapy. (Stroke. 1999;30:678-680.)

Key Words: angiography ■ diagnostic imaging ■ plasminogen activator, tissue type ■ stroke management

Recombinant tissue plasminogen activator (rtPA) is currently the only drug approved for treatment of acute stroke. Little is known about the effect of rtPA on cerebral perfusion and lesion size in humans; parameters that may provide prognostic information and reveal insight into the pathophysiology of tissue recovery. CT is usually the means by which patients with acute stroke are assessed. However, the sensitivity of CT for detection of hyperacute infarcts is low, and conventional CT provides no information on cerebral perfusion.

Diffusion-weighted MRI (DWI) and perfusion-weighted MRI (PWI) are rapid noninvasive techniques that have recently been used to study acute stroke. Several studies have suggested a relationship between lesion size on DWI and PWI and subsequent neurological outcome. DWI has very high sensitivity for detecting acute cerebral infarction, and PWI can provide a rapid qualitative measure of tissue perfusion, suggesting that DWI and PWI may be suitable techniques to monitor the efficacy of thrombolytic therapy. Although this has been demonstrated in animal models, few data are available on the use of DWI and PWI in patients treated with rtPA, and to the best of our knowledge there are no reports with angiographic correlation. The authors present the case of a patient who was treated with intra-arterial rtPA and who subsequently underwent DWI and PWI. They compare the DWI/PWI findings with those from angiography.

Case Report

A 76-year-old man with a history of hypertension, insulin-dependent diabetes mellitus, and triple bypass surgery underwent cardiac catheterization for unstable angina. During the procedure he developed aphasia and weakness of his right leg. Emergency cerebral angiography demonstrated occlusion of 3 arteries within the left hemisphere: the angular artery (distal branch of the middle cerebral artery [MCA]), the prefrontal artery (proximal branch of the MCA), and the callosomarginal artery (branch of the anterior cerebral artery [ACA] Figure 1A). Initially, 15 mg rtPA was infused into the origin of the angular artery. This artery was successfully recanalized 3 hours after symptom onset. The callosomarginal artery recanalized 3.5 hours after symptom onset. An additional 20 mg of rtPA was infused into the left supraclinoid internal carotid artery in an attempt to open the prefrontal artery, but this MCA branch remained occluded (Figure 1B). During the procedure the patient’s right-side weakness resolved, but some receptive and expressive aphasia persisted.

MRIs (Figure 2) were obtained 6 hours after symptom onset, using a 1.5-Tesla GE Signa Horizon EchoSpeed magnet. The T2-weighted images were acquired using a fast spin-echo pulse sequence (repetition time, 4000 msec; echo time, 96 msec). DWI and PWI images were obtained as previously described, using a single-shot spin-echo echo...
planar imaging sequence. PWIs were processed to generate maps of relative cerebral blood volume (rCBV), relative time to bolus peak (rTTP), relative mean transit time (rMTT), and relative cerebral blood flow (rCBF). The rCBF maps were calculated from the relation \( \text{rCBF} = \frac{\text{rCBV}}{\text{rMTT}} \).

Although the patient did well initially, he subsequently became obtunded, aphasic, hypertensive, and bradycardic. A CT scan revealed a large left basal ganglia, parietal, and temporal bleed with midline shift. It could not be determined exactly where the bleed had originated. The patient expired the following day.

**Discussion**

This case provided a unique opportunity to compare the DWI/PWI-determined characteristics of brain tissue that was successfully reperfused with those of tissue that was not reperfused in an angiographically proven case. This has not been previously reported. Findings on PWI correlated well with the angiographic result. Brain regions supplied by arteries that had successfully recanalized revealed no abnormalities on PWI, whereas tissue in the distribution of the occluded prefrontal artery demonstrated a clear PWI abnormality. This suggests that PWI is a suitable technique to evaluate thrombolytic therapy.

DWI hyperintensity in combination with a low ADC is believed to indicate the presence of cytotoxic edema. In stroke patients such regions typically evolve into brain infarction. The frontal MCA region that was not reperfused and a small area in the ACA distribution, which was reperfused 3.5 hours after symptom onset, demonstrated DWI hyperintensity and low ADC, whereas the region supplied by the angular artery (posterior parietal/posterior temporal region), which was reperfused after 3 hours, was normal. The duration of hypoperfusion is believed to be an important factor in the development of irreversible brain damage. Clinical trials with intravenous rtPA, for example, have shown benefit only in patients treated less than 3 hours after symptom onset. In our patient, the callosomarginal artery was recanalized after the angular artery, which may account for the ACA territory lesion on DWI. Data like these may aid in determining a suitable window for treatment with intra-arterial rtPA.

This case report has several limitations. First, because the patient expired we were unable to confirm the location of infarcts with conventional MRI. However, other studies have demonstrated a strong relationship between acute DWI lesions and subsequent infarcts on T2-weighted MRI. Second, because no MRI was performed before thrombolysis, we do not know what the DWI and PWI would have shown at that time. To clarify this issue, further studies need to be performed with DWI and PWI both before and after thrombolysis.

We conclude that in this case the perfusion abnormalities observed with PWI were consistent with angiographic findings, whereas DWI lesions reflected early tissue changes associated with ischemia. These findings substantiate the belief that DWI and PWI may prove to be useful in the evaluation of patients undergoing thrombolytic therapy.

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Figure 2. A (left-to-right), fast spin-echo T2-weighted MRI, DWI, and ADC map obtained 6 hours after symptom onset. The T2-weighted MRI was unremarkable. DWI hyperintensity and corresponding low ADC were seen in a small area of the anterior cerebral artery distribution (arrows) and in a larger area corresponding to the distribution of the occluded prefrontal artery (arrowheads). B, PWIs were obtained at the same time point. The rCBV, rTTP, and rCBF perfusion maps demonstrate abnormal perfusion in the distribution of the occluded prefrontal artery (arrowheads).

References

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