Early Changes in Tissue Perfusion After Tissue Plasminogen Activator Administration in Hyperacute Ischemic Stroke: Initial Experiences With Arterial Spin Labeling Perfusion Magnetic Resonance Imaging

—Two Case Reports—

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Abstract

Cerebral perfusion monitoring is an important component of hyperacute stroke treatment. Arterial spin labeling (ASL) perfusion magnetic resonance (MR) imaging provides a noninvasive method of cerebral perfusion observation. Rapid changes in cerebral perfusion were demonstrated in two patients admitted one hour after onset of hyperacute stroke who underwent recombinant tissue plasminogen activator (rt-PA) treatment. Serial MR images and ASL images were taken on admission and after rt-PA administration. Cerebral blood flow (CBF) values were obtained using the CBF workstation and analysis software. Interpretable ASL images were taken in both patients. Perfusion deficits were consistent with symptoms and/or MR angiography imaging abnormalities. Delayed arterial transit effect was present in one patient; serial imaging showed improvement of CBF after rt-PA treatment in both patients. ASL perfusion MR imaging can provide rapid noninvasive multislice imaging in hyperacute ischemic stroke, and can depict early perfusion deficit and quantify regional CBF concomitantly.

Key words: recombinant tissue plasminogen activator,
arterial spin labeling magnetic resonance imaging,   brain perfusion,   ischemic stroke

Introduction

Thrombolytic therapy is effective in acute stroke by dissolving the arterial occlusion and reestablishing tissue perfusion,[9] and intravenous recombinant tissue plasminogen activator (rt-PA) is widely used for its efficacy.[9,20] However, the narrow therapeutic window limits usage, and requires close observation during delivery.[1,7] Reocclusion, new hypoperfusion, and failure of treatment are some of the most important aspects of observation.[19] Single photon emission computed tomography (SPECT) is still the standard procedure for examining brain perfusion, but arterial spin labeling (ASL) perfusion magnetic resonance (MR) imaging is a promising, non-contrast medium-based, brain perfusion technique that offers the possibility of obtaining cerebral blood flow (CBF) maps that cover the entire brain. ASL is still being developed and is gaining popularity for clinical use in both normal and ischemic populations because of its noninvasiveness.[11,15,17,21]

In this study, we describe our early experiences with two patients with hyperacute ischemic stroke who underwent rt-PA treatment and were evaluated using ASL perfusion MR imaging.

Case Reports

Two patients with hyperacute ischemic stroke underwent ASL perfusion MR imaging as part of brain MR imaging examination at the time of admission to Seguchi Neurosurgical Hospital. Acute ischemic stroke is defined as acute focal neurological deficit with evidence of acute cerebral ischemia in the arterial distribution on brain imaging regardless of the duration of clinical symptoms. The diagnosis of acute ischemic stroke was determined by the neurosurgeon on duty during the admission period based on the results of standard clinical neurological assessment and neuroimaging according to the stroke protocol. Patients underwent ASL examination on admission (before rt-PA treatment) and after rt-PA treatment. rt-PA
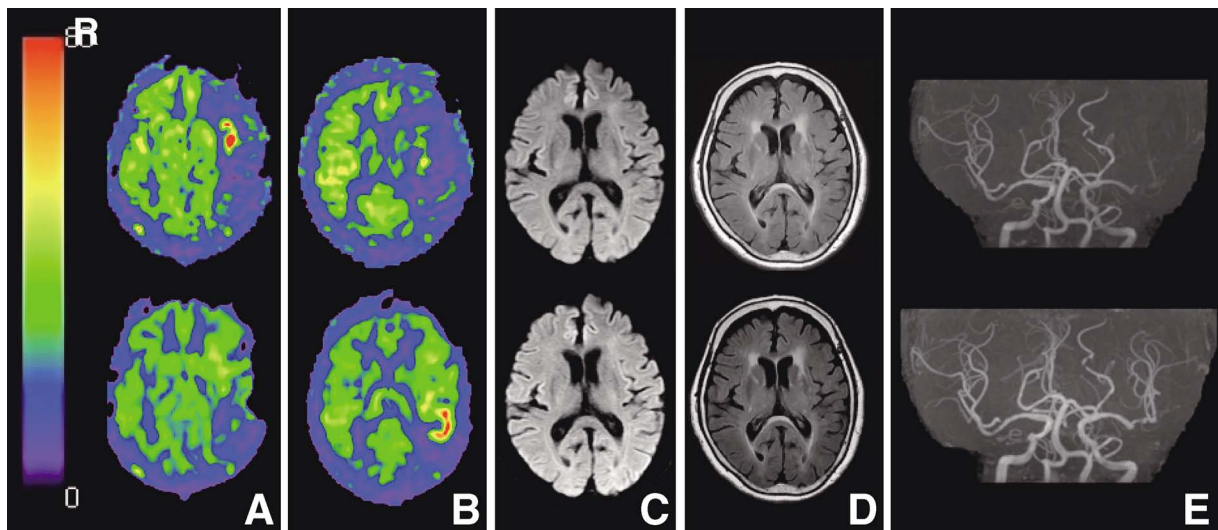
Fig. 1 Arterial spin labeling (A, B), diffusion-weighted (C), and fluid-attenuation inversion recovery (FLAIR) (D) magnetic resonance (MR) images, and MR angiograms (E) of a hyperacute stroke patient (Case 1). *Upper row*: Initial cerebral blood flow (CBF) map showing a left middle cerebral artery (MCA)-related hypoperfused area without lesion on diffusion-weighted or FLAIR images. Delayed arterial transit (hyperperfused region) is seen in the proximal portion of the left MCA. MR angiograms showing occlusion of the left MCA. *Lower row*: CBF map after 2 hours showing improved perfusion in the left MCA area, and a coma-like delayed arterial transit in the distal portion of the left MCA. All other images do not disclose any abnormalities.

was given at a standard protocol dose for acute stroke treatment.

MR images were obtained for clinical indications according to the institutional clinical stroke protocol, including diffusion-weighted imaging with apparent diffusion coefficient maps (repetition time [TR]/echo time [TE] 5800/78 msec, matrix 128 × 128, slice thickness 4.8 mm, b value 0 and 1000 sec/mm²), T_1-weighted imaging (magnetization-prepared rapid gradient echo, TR/inversion time [TI]/TE 2050/1050/2 msec, matrix 256 × 256, slice thickness 1 mm), T_2-weighted imaging (turbo spin echo, TR/TE 6000/108 msec, matrix 256 × 256, slice thickness 1.5 mm), fluid-attenuation inversion recovery imaging (TR/TI/TE 9000/2500/95 msec, matrix 256 × 256, slice thickness 4.8 mm), and MR angiography (TR/TE 36/3 msec, matrix 448 × 448, slice thickness 1 mm). MR imaging was obtained using a Signa HDxt 3T scanner (GE Medical Systems, Milwaukee, Wisconsin, USA). Continuous ASL perfusion images were obtained using the following parameters: gradient echo-planar images were obtained with field of view of 24 cm along the frequency-encoding direction and 15 cm along the phase direction, and acquisition matrix of 64 × 40. Acquisition bandwidth of 662.5 kHz allowed effective echo time of 22 msec and image acquisition time of 45 msec. Multislice image acquisition was performed without pausing between slices so that 8 slices could be acquired in 400 msec. Slice thickness of 8 mm was used, and interslice gap of 2 mm was used to minimize interference between slices. Slice locations were chosen to include supratentorial structures. Total scan time was 4 minutes 20 seconds.

Perfusion data were saved as raw echo amplitudes and transferred to a workstation for processing. NEURO-
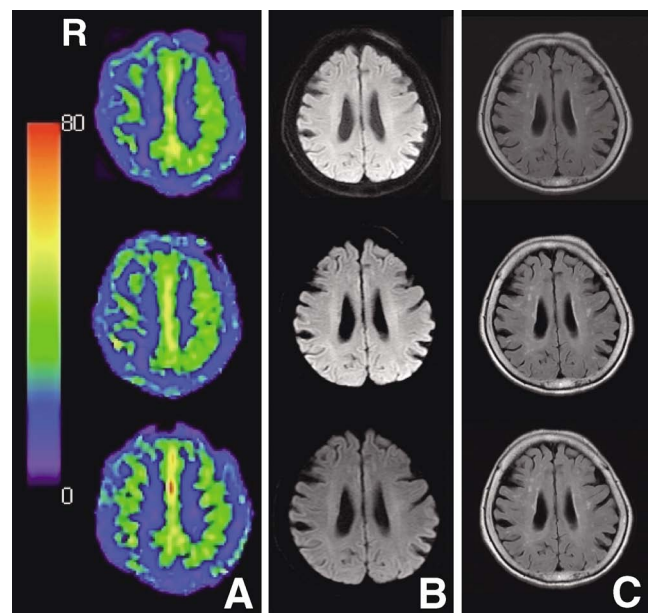

Fig. 2 Arterial spin labeling (A), diffusion-weighted (B), and fluid-attenuation inversion recovery (FLAIR) (C) magnetic resonance images of a hyperacute stroke patient (Case 2). *Upper row*: Initial cerebral blood flow (CBF) map showing a right middle cerebral artery (MCA)-related hypoperfused area without lesion on diffusion-weighted or FLAIR images. *Middle and lower rows*: Post-treatment day 1 and day 7 CBF maps, respectively, showing improved perfusion in the right MCA area compared to the normal side. All other images do not disclose any abnormalities.

FLEXER version 1.00.01 (Nihon Medi-Physics Co., Ltd., Tokyo) was used for perfusion data analysis. Template of the arterial supply-based perfusion area was automatically set up for perfusion data analysis.

Case 1: An 81-year-old woman had a history of arterial fibrillation without medication. She experienced aphasia and was admitted to the hospital one hour later. On admission, the National Institutes of Health Stroke Scale (NIHSS) score was 7 and rt-PA therapy was started. MR angiography revealed occlusion of the left middle cerebral artery (MCA), but diffusion-weighted imaging did not reveal any hyperintense abnormality. ASL images on admission revealed a wide area of hypoperfusion in accordance with the left MCA territory. CBF value of the right MCA territory compared to the left MCA territory was 36.37:12.63 ml/100 g/min. A small circular hyperperfused area was also seen on the left side, which reflects the delayed arterial transit effect of the proximal portion of the MCA (Fig. 1). Soon after the treatment was given, aphasia improved. MR angiography revealed recanalization of the left MCA. ASL images at 2 hours following rt-PA treatment also revealed improved cerebral perfusion in the left MCA territory, and a comma-like hyperperfused area at the distal portion of the MCA. CBF value of the right MCA territory compared to the left MCA territory was 37.95:33.35 ml/100 g/min. Two weeks later she was discharged without obvious neurological deficit.

Case 2: An 81-year-old woman had a history of arterial fibrillation under warfarin medication. She experienced left hemiparesis and was admitted to the hospital one hour later. On admission, her NIHSS score was 8 and rt-PA therapy was started. MR angiography revealed occlusion of the right MCA, but diffusion-weighted imaging did not reveal any hyperintense abnormality. ASL images on admission revealed a hypoperfused area in accordance with the right MCA territory (Fig. 2). CBF value of the right MCA territory compared to the left MCA territory was 23.64:34.37 ml/100 g/min. One hour after the treatment was given, hemiparesis improved. MR angiography after 24 hours revealed recanalization of the left MCA. ASL images also revealed improved cerebral perfusion in the right MCA territory at 24 hours and on days 7 and 14 following rt-PA treatment. Two weeks later she was discharged with full recovery. CBF value of the left MCA territory compared to the right MCA territory was 28.20:31.90 ml/100 g/min.

Discussion

Tissue reperfusion is thought to be the leading mechanism underlying the efficacy of intravenous rt-PA.[7–10,18] Early reperfusion may promote survival in vulnerable tissue that would otherwise progress to infarction.[1,7] The importance of close observation during rt-PA therapy has been emphasized by several authors.[1,2,7] Changes in cerebral perfusion within 6 hours after rt-PA administration have been observed using dynamic susceptibility contrast perfusion imaging.[2]

The present study of reperfusion after rt-PA disclosed accordance between ASL imaging and MR angiography in Case 1 as a wide hypoperfused area on ASL images without abnormalities on diffusion-weighted images, which demonstrated a diffusion/perfusion mismatch commonly used as a reference in stroke treatment.[12,13] By using ASL images, information about the potential area of reperfusion can be obtained on admission, and reperfusion after rt-PA treatment can be observed even at only 2 hours after administration.

Reliability of the ASL technique has been assessed before in normal and ischemic populations.[3,11,14,15] Furthermore, the noninvasive nature of ASL is superior for routine and frequent use, especially in close monitoring of rt-PA treatment compared to the invasive standard procedures such as positron emission tomography and SPECT.[4,5,17,21,22] This superiority of the ASL technique was also shown in Case 2, in which close observation from pre-treatment to post-treatment days 1, 7, and 14 was possible without harming the patient or risking reocclusion events.[19]

The detection of delayed arterial transit time (DAT) in Case 1 was also an interesting finding. DAT results from labeled arterial blood that had not transited into the brain tissue at the time of image acquisition.[6] Proximal DAT area may be caused by partial occlusion of the artery, resulting in slower flow of the related portion of the MCA. Later on, post-administration of rt-PA showed a DAT area at the distal part of the MCA, which may be evidence of restoration of flow as well as lysis-related location changes of the thrombus. However, this early finding still needs confirmation to reach a conclusion. DAT may have a protective effect for cerebral reperfusion.[6] However, DAT might only be an artifact of ASL.

Despite the superiority of ASL, some limitations remain. ASL is noninvasive for patients, but is sensitive to even the most subtle head and respiratory movements.[17] ASL is also prone to susceptibility effects which create artifacts, for example in the paranasal sinuses, which limit its interpretation for the medial temporal lobes and skull base.[17] ASL perfusion imaging can be influenced by various cardiovascular factors such as hypertension, vascular disease, diabetes mellitus, CO_2 concentration, hydration, caffeine intake, and hormonal imbalance.[15] Several authors have attempted to standardize quantification of ASL in adults and children,[3,16] but a reference value is yet to be determined.

ASL is a promising, non-contrast medium-based, brain perfusion technique that offers the possibility of obtaining CBF maps that cover the entire brain. The present two cases clearly showed that ASL can provide information consistent with MR imaging in terms of the presence of artery occlusion. Thus, ASL can provide information on the cerebral circulation that is important when treating patients with hyperacute ischemic stroke.

Acknowledgment

Conflicts of Interest Disclosure

All authors have no financial, commercial, legal, or professional relationship with other organizations or with the people working with us that may exert an influence on this research. Therefore, we have disclosed any conflict of interest in the making of this paper. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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