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Reversal of Large Ischemic Injury on Hyper-Acute Diffusion MRI

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Key Words
Diffusion-weighted MRI · Ischemic stroke · Reversal · Thrombolysis

Abstract
Reversal of early ischemic injury on diffusion-weighted MRI (DWI) occurs rarely. In a stroke patient who abruptly developed stupor and left hemiparesis, DWI scanned 78 min after onset demonstrated a large ischemic injury in the right hemisphere with a DWI-ASPECTS (Albert Stroke Program Early Computed Tomography Score) of 5 points, although baseline brain CT was perfectly normal. MR angiography (MRA) showed an occlusion of the right middle cerebral artery trunk, and the patient received intravenous thrombolysis 105 min after onset. A second MRA 30 h later showed complete vessel recanalization, and DWI demonstrated a perfect reversal of the initial large ischemic injury, associated with very small thrombus-fragmented cortical surface infarctions. Outcome at 3 months was a modified Rankin Scale score of 0, and the fluid-attenuated inversion recovery image showed only a small final infarction at the cortical surface. Hyper-acute DWI-defined large ischemic injury may very rarely represent a nearly perfect reversible area, and it may be a therapeutic target.

Introduction

Reversal or shrinkage of early ischemic injury demonstrated by diffusion-weighted MRI (DWI) is clinically uncommon, even after early thrombolytic reperfusion therapy [1–5]. The DWI-defined early ischemic injury physiologically represents an irreversible ischemic core and a potentially reversible surrounding area [2]. Recently, we experienced the case of a nearly complete reversal of a hyper-acute large ischemic injury on DWI.

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Case Report

A 67-year-old previously healthy woman suddenly developed stupor and left hemiparesis, and arrived at our hospital 45 min after symptom onset. Upon presentation, the National Institute of Heath Stroke Scale (NIHSS) score was 12 points, and baseline brain CT was perfectly normal. DWI (single-shot echo-planar, b = 1,000 s/mm^2, TR = 8,000 ms, TE = 80.8 ms, slice thickness = 6 mm) performed on the 1.5T MR scanner (Signa 1.5T; General Electric, USA) imaged 78 min after onset demonstrated a large high-signal intensity area in the right hemisphere with a DWI-ASPECTS (Albert Stroke Program Early Computed Tomography Score [6]) of 5 points, and MR angiography (MRA) showed an occlusion of the right middle cerebral artery trunk (**fig. 1**). Perfusion MRI was not performed. On the apparent diffusion coefficient (ADC) map, the mean ratio of the ADC value of ischemic to unaffected hemispheres was 0.86 (range 0.78–0.92) within the five DWI-ASPECTS-negative ischemic areas, and the mean ADC ratio was 0.99 (0.98–1.00) within the remaining five DWI-ASPECTS-positive non-ischemic areas. Accordingly, the patient received intravenous thrombolysis with tissue plasminogen activator at a lower dose of 0.6 mg/kg alteplase on the Japanese guideline [7]. The state of health of the patient was improved, and the NIHSS score 24 h later was of 0 points with minor left-sided numbness. The second DWI (b = 1,000 s/mm^2, TR = 5,000 ms, TE = 55 ms, slice thickness = 5 mm) performed on the 3T MR scanner (Achieva 3T; Phillips, the Netherlands) imaged 30 h later showed a nearly complete reversal of the large high-signal intensity area demonstrated by initial DWI, and there were very small high-signal intensity spots at the cortical surface (fig. 1). MRA showed complete recanalization of the middle cerebral artery trunk. The mean ADC ratio was 1.00 (0.99–1.02) within the five areas of the initial DWI-ASPECTS-negative ischemic territory and 0.97 (0.88–1.01) within the remaining five initial DWI-ASPECTS-positive non-ischemic areas. The systemic work-up including cardiac and hematological profiles revealed the presence of patent foramen ovale and venous thrombus in her leg, suggesting a paradoxical brain embolism as an etiological mechanism for this stroke. The patient received anticoagulation with warfarin for secondary prevention. At 3 months, clinical outcome was a modified Rankin Scale score of 0, and only minor final infarction was localized at the cortical surface on the fluid-attenuated inversion recovery (FLAIR) image (TR = 11,000 ms, TE = 125 ms, slice thickness = 5 mm) (fig. 1).

Discussion

In this patient, after early thrombolytic reperfusion therapy, the initial DWI-defined large hemispheric ischemic injury showed nearly complete reversal on the follow-up DWI, and very small thrombus-fragmented ischemic areas after complete vessel recanalization were localized at the cortical surface of the terminal zone of the initially occluded middle cerebral artery.

A limitation of this case study was the subtle low imaging quality of the hyper-acute DWI, due probably to body motion in acute confusion and to the simple acute stroke MRI protocol to minimize scan time in the emergency setting. To assess the ischemic injury more accurately, an advanced 3-tesla MR scanner was utilized at the later scans, although a difference of MRI scanner between hyper-acute and the later phases may affect the precise comparison of ischemic injury. Since a recent study reported that standard 1.5-tesla MR scanner, rather than 3-tesla MR scanner, provided a lower false-positive and false-negative rate for detecting DWI-defined early ischemic injury within 6 h after stroke [8], hyper-acute DWI imaged on a 1.5-tesla MR scanner might have been an optimal selection as acute stroke MRI protocol in this case study.

The latest meta-analysis reported that the rate of complete or partial reversal of ischemic DWI lesions was surprisingly high by an average of 24%, varying from 0 to 83% probably due to the variable definition of the DWI reversibility [9]. Time of acute DWI scan from stroke onset, as well as time and type of sub-acute to chronic scans such

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as DWI, T2- or FLAIR image to assess the final infarct area, may affect frequency and size of the DWI reversibility [9]. A recent study reported that 'true reversal' of a DWI abnormality, defined by eliminating the false-positive reversal effect, was uncommon at only 7% in patients receiving early intravenous thrombolysis [1]. In this patient, nearly complete reversal of the initial DWI-defined large ischemic injury persisted on the 3-month follow-up FLAIR image.

A previous study quantitatively measured severity or depth of ischemic injury by ADC values to define the threshold of the infarct process [10]. In the DWI-defined ischemic area, an ADC value below 80% of the unaffected area and no reperfusion were the factors of DWI irreversibility, but the exact threshold of the ADC value could not be determined [10]. In this patient, an ADC decline with an average of 86% in the DWI-defined ischemic area and early successful reperfusion may largely account for complete and sustained reversal, associated with a favorable clinical outcome.

In conclusion, hyper-acute large ischemic injury demonstrated by DWI may very rarely represent a nearly perfect reversible area, and it may be a therapeutic target.

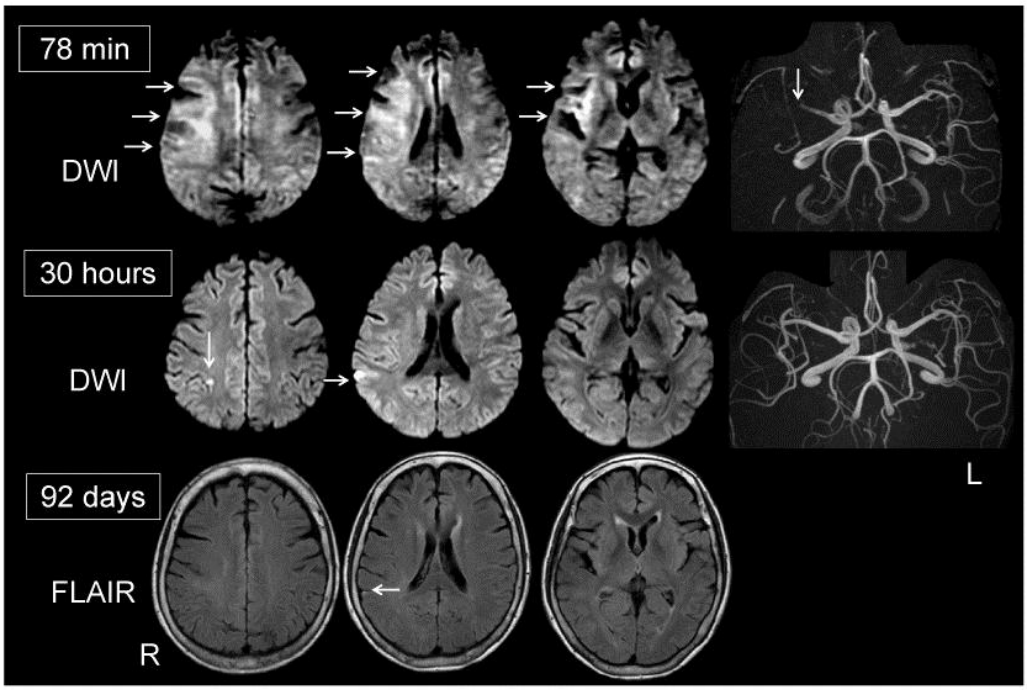

Fig. 1. Top row: initial DWI performed on a 1.5T MR scanner before thrombolysis demonstrates a large high-signal intensity area in the right hemisphere, and MRA shows an occlusion of the right middle cerebral artery trunk. Middle row: second DWI performed on a 3.0T MR scanner 30 h later shows perfect reversal of the initial large ischemic injury associated with small new cortical surface high-signal spots, and MRA displays complete vessel recanalization, suggesting scattered fragmentation of the initially occluded thrombus of the middle cerebral artery trunk. Bottom row: FLAIR image taken at 3 months shows only a small final infarction at the cortical surface.

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