Diffusion-weighted Imaging Reversibility In Stroke After Successful Mechanical Recanalization. Case report
Reversión De La Difusión En El Stroke Luego De Una Exitosa Recanalización Mmecánica.
A propósito de un caso

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ABSTRACT

Increased use of Diffusion-weighted imaging (DWI) in acute stroke has led to observations of early diffusion normalization in lesions that initially show diffusion slowing. The “renormalization” of DWI may be spontaneous or the result of thrombolytic therapy, thus, acute slowing of diffusion is not necessarily an indicator of irreversible tissue damage. The perfusion-diffusion mismatch concept is attractive as it assumes that DWI lesion size reflects the infarct core whilst the mismatch area reflects the penumbra. However, this concept may be an oversimplification. This paper shows a case with Diffusion Lesion Reversal after successful neuroendovascular treatment and excellent clinical outcome, and discuss the imaging characteristics associated with this phenomenon.

Keywords: Stroke; Mechanical recanalization; Diffusion-weighted imaging reversibility

RESUMEN

El mayor uso de la secuencia de Diffusion-weighted imaging (DWI) en el accidente cerebrovascular isquémico agudo ha conducido a observaciones de la normalización de la difusión temprana en las lesiones que inicialmente muestran una restricción de la difusión. La “renormalización” de DWI puede ser espontánea o puede ser el resultado de una terapia trombolítica, por lo tanto, la restricción de la difusión no es necesariamente un indicador de daño irreversible en los tejidos. El concepto mismatch perfusión-difusión es atractivo ya que asume que el tamaño de la lesión DWI refleja el núcleo del infarto, mientras que el área de la falta de coincidencia refleja la penumbra. Sin embargo, este concepto puede ser una simplificación excesiva. Este trabajo muestra un caso con reversión de la restricción en difusión después de un tratamiento neuroendovascular exitoso y un resultado clínico excelente, y analizamos las características de imagen asociadas con este fenómeno.

Palabras-clave: Stroke; Recanalización mecánica; Reversibilidad de imagenes de difusión

INTRODUCTION

Magnetic resonance imaging (MRI) is an invaluable tool used in the diagnosis of ischemic stroke, specially useful in those beyond the 6 hour window or unknown onset time. Increased use of DWI in acute stroke has led to observations of early diffusion normalization in lesions that initially show diffusion slowing. Such ‘renormalization’ may be spontaneous but most of them are after revascularization. We show 2 cases with Diffusion Lesion Reversal after successful neuroendovascular treatment and excellent clinical outcome, and discus the imaging characteristics associated with this phenomenon.

CASE PRESENTATION

Female patient, 82 year-old, with a history of hypertension and dyslipidemia woke up with a right middle cerebral artery (MCA) stroke syndrome with left-sided facial palsy, right gaze deviation and left-sided weakness; a National Institutes of Health Stroke Scale (NIHSS) score of 12. Brain MR imaging (Signa 1.5T) initiated 75 minutes after the patient woke up. A mild hyperintensity in the right deep middle cerebral artery (MCA) territory was shown on diffusion-weighted imaging (DWI) with a decreased apparent diffusion coefficient. Fluid-attenuated inversion recovery (FLAIR) and T2-weighted...
imaging showed no parenchymal signal-intensity changes. 3D time-of-flight MR angiography showed a proximal occlusion of the right MCA. The lack of signal-intensity changes on FLAIR indicated that the patient may still have potentially salvageable brain tissue.

Mechanical thrombectomy was performed. Control angiography showed complete recanalization of the branch with normal antegrade flow, TICI 3.

**OUTCOME AND FOLLOW-UP**

NIHSS score at 72 h was 0. 18 days later a control MR was performed. The mild hyperintensity area in the right deep middle cerebral artery (MCA) territory was normal on diffusion-weighted imaging (DWI) with no decreased apparent diffusion coefficient.

The primary aim of imaging in acute stroke is to determine the ischemic tissue at risk. This requires imaging techniques able to accurately depict tissue that can be salvaged within the narrow window available for making therapeutic interventions. The current therapeutic approach in acute ischemic stroke relies on successful recanalization of the occluded artery to establish reperfusion within the ischemic territory. Therefore, it is highly critical to identify patients that are more likely to benefit from recanalization/reperfusion therapies. The ideal patients in this regard are those with a small infarct core, large salvageable penumbra, and low risk for intracerebral hemorrhage.

A variety of imaging modalities exist for the diagnosis of stroke, however, Diffusion-weighted imaging (DWI) has been described as the more sensitive imaging technique for diagnosing acute ischemic stroke providing the earliest information about the physiology. It enables further classification of stroke and confirms the presence and location of infarcts with strong contrast and high sensitivity in comparison to Computed Tomography (CT) and other MRI techniques.

Conventional MRI sequences like T1-, T2-, and fluid-attenuated inversion recovery (FLAIR) become sensitive to ischemic changes only after a net increase in water content of the cerebral tissue and, therefore, can detect ischemia after a few hours of symptom onset. Diffusion-weighted imaging (DWI), on the other hand, is sensitive to cytotoxic edema and energy depletion — the primary pathology during the
hyperacute ischemia setting — and can, therefore, provide the opportunity to determine the extent of ischemic injury even within the initial hours of ischemia4.

Diffusion-weighted Magnetic Resonance imaging (MRI) (DWI) is an advanced MRI technique, which allows non-invasive evaluation of water diffusibility in brain tissue6. It is sensitive to the random translational motion of water molecules due to Brownian motion. Diffusion-weighted images (DW-images) are generated by adding an opposing pair of diffusion gradients to spin-echo or echo planar imaging sequences. For stationary molecules, the effects of the first (tagging) and the second (un tagging) gradient pulses cancel each other out. For mobile, diffusible molecules there is incomplete rephasing resulting in a net phase shift, which leads to a signal loss. The degree of signal loss is proportional to the exponent of the diffusion coefficient and to the duration, distance and strength of the applied diffusion gradients (so-called “B-value”)9. The diffusion coefficient measured by DWI is referred to as the “apparent” diffusion coefficient (ADC) rather than the true diffusion coefficient.

Acute cerebral ischaemia appears as a hyperintensity on DW-images and a hypointensity on ADC maps. Then, after the acute stage ADC values return to pseudonormal values and subsequently increase above baseline, which is assumed to reflect vasogenic edema and cell lysis7,8.

Advanced neuroimaging techniques estimate the volume of brain tissue in potential risk for progression to infarction (ie, ischemic penumbra) if recanalization does not occur. The volumetric difference between a surrogate for established infarction and penumbra, if present, is referred to as a “mismatch” and represents a rational biomarker for treatment selection. Some studies using diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI), and other studies using DWI and fluid attenuated inversion recovery (FLAIR) sequences of magnetic resonance have been made to identify infarcted versus at-risk tissue5,10.

Studies evaluating lesion volume dynamics by serial MRI examinations highlight that DWI lesion volume underestimates final infarct size in majority of patients and there is a growth by 144%–180%, on average, in the size of ischemic lesions on follow-up11,12,13. On the other hand, in approximately a quarter of patients, there is evidence for some degree of DWI reversal5,12. The “renormalization” of DWI may be spontaneous or may be the result of thrombolytic therapy14,15,16. Thus, acute slowing of diffusion is not necessarily an indicator of irreversible tissue damage.

All of these findings suggest the presence of factors, other than extent of cytotoxic edema, in determination of tissue fate after an ischemic insult. One of these major factors is the amount of hypoperfusion within the ischemic territory, which can be assessed by perfusion-weighted imaging (PWI) MRI. Brain tissue that appears normal on DWI but have abnormal perfusion is considered to represent regions that are viable, but at risk for conversion to infarction over the ensuing hours. Patients with large vessel occlusion evident on MRI angiography do not only have an increased probability of diffusion perfusion mismatch, but also are more prone to lesion expansion9.

The perfusion-diffusion mismatch concept is attractive as it assumes that DWI lesion size reflects the infarct core whilst the mismatch area reflects the penumbra. However, this concept may be an oversimplification. DWI lesion are reversible to some degree, as, for example, in the case of early reperfusion. This observation challenges the idea that DWI lesions solely reflect the infarct core. In addition, perfusion abnormalities tend to overestimate the penumbra by including areas of benign oligohemia17.

The reported prevalence of reverse acute diffusion (RAD) varies between studies17,18, with extremes from 7%11 to 85%18. The increase in % RAD with shorter onset to treatment time suggests that the less prolonged the ischemia, the more likely the chance of DWI lesion reversibility. This finding indirectly strengthens that the ischemic penumbra extends into the acute DWI lesion17,19. Threatened but potentially salvageable tissue (tissue at risk) includes not only tissue with abnormal perfusion and normal diffusion, but also potentially some tissue with abnormal diffusion.

ADC normalization phenomenon seems to be time dependent. Jens Fiehler et al. showed in their study that ADC normalizations occurred in 11 of 31 patients (35.5%) studied 3 hours after symptom onset, but in only 3 of 37 patients (8.1%) studied within 3 to 6 hours after symptom onset. Based on their findings, the tissue at risk as target of thrombolysis therapy might be extended toward the DWI lesion at least within 3 hours after stroke onset. Consequently, at least within 3 hours, the absence of a PWI/DWI mismatch does not imply the absence of tissue at risk20.
Last, but not least, not only is there time dependence for DWI reversal but also location dependence. DWI reversal predominates in white matter (WM) after thrombolysis. It is suggested that WM is more resistant to ischemia than gray matter (GM), given their markedly different cellular constituency, vascular anatomy, and metabolic rate. Supporting this hypothesis, the percentage of RAD lesions increased with the proportion of WM present in the acute DWI lesion\textsuperscript{14,15,16}. The amount of WM in the initial DWI lesion may therefore be a significant determinant of RAD lesions, which is itself associated with early neurological improvement. In turn, acute DWI lesions predominantly or exclusively involving WM may be more prone to reversal and to respond to therapy than their GM counterparts. This may have bearing on the DWI lesion volume predictive of poor response to reperfusion therapy, which could be adjusted for its WM content for improved accuracy. Also, DWI lesions involving WM may have a longer time window for positive response to therapy. Finally, thresholds for core and penumbra may need adjustment for WM content\textsuperscript{16}.

As there are differences between WM and GM, DWI studies in posterior circulation strokes showed that there are indeed important differences to anterior circulation. Firstly, the rate of false negative DWI findings is significantly higher in posterior compared to anterior circulation strokes if DWI is performed within 24 hours of stroke onset. In particular, lesions in the medulla oblongata harbor the highest risk of being missed. Furthermore, in posterior circulation stroke, DWI lesion detection rate is significantly lower than in anterior circulation stroke\textsuperscript{17}. Thus, using DWI to exclude acute basilar artery occlusions from treatment based on extensive brainstem injury cannot be recommended because of the potential for DWI reversal.

CONCLUSION

DWI characteristics provide clinically useful information with respect to diagnosis, etiological work-up, treatment decisions, surveillance of stroke’s preventive means and outcome prediction. The observation of reversal DWI challenges the idea that DWI lesions solely reflect the infarct core. DWI reversal depends on time and location. DWI lesions involving WM may have a longer time window for positive response to therapy. Thus, thresholds for core and penumbra may need adjustment for WM content. Finally, at least within 3 hours, the absence of a PWI/DWI mismatch does not imply the absence of tissue at risk, so, using DWI to exclude artery occlusions cannot be recommended during this time.

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