SERIAL DIFFUSION-WEIGHTED MR IMAGING IN DELAYED POSTANOXIC ENCEPHALOPATHY

A case study


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SUMMARY

We report a case of delayed postanoxic encephalopathy (DPE) studied with serial diffusion weighted imaging five times in a one-year period along with apparent diffusion coefficient (ADC) map as well as ADC values of periventricular white matter. Compared to the normal value, the ADC values of the white matter were initially low on the three (0.68 ± 0.08 × 10⁻³ mm²/s) and seven-week images (0.67 ± 0.08 × 10⁻³ mm²/s) but gradually recovered to the normal range on the four, six, and twelve-month images (0.78 ± 0.05, 0.80 ± 0.05 and 0.87 ± 0.11 × 10⁻³ mm²/s, respectively). Among the several pathogenetic mechanisms associated with DPE, these serial changes may be consistent with cytotoxic edema, from apoptosis, trigged by hypoxia.

Key words: delayed postanoxic encephalopathy, apparent diffusion coefficient, magnetic resonance imaging, diffusion weighted image, apoptosis.

RÉSUMÉ

Étude en imagerie de diffusion de façon sériée d'une encéphalopathie post-anoxique retardée

Nous rapportons l'observation d'une encéphalopathie post-anoxique retardée, étudiée en imagerie de diffusion de façon sériée, à cinq reprises sur une période d'un an. L'examen a comporté l'étude du coefficient apparent de diffusion (ADC) dans la substance blanche pérvinectrielle. Par rapport aux valeurs normales, les valeurs de l'ADC dans la substance blanche ont été basses sur les examens faits à 3 semaines (0.68 ± 0.08 × 10⁻³ mm²/s) et à 7 semaines (0.67 ± 0.08 × 10⁻³ mm²/s). Progressivement ces valeurs sont redevenues normales sur les images effectuées à 4 et 12 mois (0.78 ± 0.05, 0.80 ± 0.05 et 0.87 ± 0.11 × 10⁻³ mm²/s). Les anomalies observées sur les examens sériés sont en faveur de l'existence d'un œdème cytotoxique, lié à une apoptose, déclenchée par l'hypoxie.

Mots-clés : encéphalopathie post-anoxique retardée, coefficient apparent de diffusion, imagerie par résonance magnétique, imagerie de diffusion, apoptose.

INTRODUCTION

Delayed postanoxic encephalopathy (DPE) is a demyelinating disorder in which cognitive, movement and behavioral deteriorations relapse several days to several weeks after an initial recovery from a hypoxic injury [2, 5]. Magnetic resonance imaging (MRI) studies of DPE, in acute carbon monoxide intoxication, often show a high signal in the periventricular white matter on T2-weighted MRI (T2WI) [1, 17, 21]. Previous reports on diffusion weighted MRI (DWI) changes have been mostly in acute anoxic encephalopathy [9, 16]. Herein, we report a patient with DPE who was followed with serial DWIs, and discuss the possible underlying mechanism.

PATIENT AND METHODS

A 67-year-old man was admitted with recent behavior change. Three weeks prior to this change he went fishing and slept in a closed tent with a butane gas stove on. The next morning he was found unconscious. The blood carboxyhemoglobin level was 25.1 % on arrival and 11.2 % two hours later. With supplemental
oxygen via facial mask, he regained consciousness several hours later. He recovered over the next several days and returned to his job. Five days prior to admission he started to show abnormal behavior and impaired judgment that were followed by bradykinesia and mutism.

On examination the patient was alert but mute. When asked to write his name and draw simple figures, he responded correctly but showed marked perseveration. He scored 0 on the MMSE. Parkinsonian features including bradykinesia, masked face, rigidity, stooped posture, and short step gait were seen. Deep tendon reflexes and plantar response were normal but grasp reflex was bilaterally present.

Routine blood tests, chest radiograph, and ECG were normal. Over the ensuing three months, the patient recovered with his cognitive and motor functions becoming self-sufficient (Barthel index 20/20). Ten months later he scored 28 out of 30 on the MMSE and again returned to his job.

Serial brain MRIs with DWI was performed using a 1.5 T MRI scanner (Signa Horizon Echospeed, GE medical system, Milwaukee, USA) a three and seven weeks, four, six, and twelve months after the hypoxic event. T2WI (TR/TE = 3,417/96 msec) and DWI (TR/TE = 6,500/96.8 msec, field of view 280 mm × 280 mm, matrix 128 × 128, section thickness 5 mm, intersection space 2 mm) were obtained during the same session and at the same orientation (parallel to the AC-PC line) and slice position. To evaluate the temporal change of the diffuse periventricular white matter lesion, ADC map and ADC values of regions of interest (ROIs) were calculated based on Stejskal and Tanner’s equation (b value = 0 and 1,000 s/mm²) [19]. In order to obtain the mean ADC value, we used the same axial T2WI and DWI slices showing symmetric and diffuse periventricular white matter changes. As illustrated in figure 1, we chose ROIs from the periventricular white matter that consisted of eight small circles of 50 mm² arranged linearly along the lateral ventricle.

RESULTS

T2WI and DWI revealed diffuse high signal intensity in the periventricular white matter that remained largely unchanged on follow-up MRIs (figures 2a et 2b). ADC map demonstrated transient low signal areas in both periventricular white matter of the third and seventh week images (figure 2c). ADC values from 8 ROIs on the initial and follow-up MRIs are presented in Table I. Compared to previously reported normal ADC values of the white matter [3, 8, 10], the mean ADC values initially remained significantly low on the third and seventh week images but returned to the normal range subsequently (figure 3).

DISCUSSION

Our patient with DPE showed diffuse high signal intensities in the periventricular and deep white matter on T2WI as previously reported [1, 17, 21]. Previous studies with DWI that were performed during an acute phase of a monophasic postanoxic encephalopathy [9, 16] or in the state of DPE [13] all demonstrated white matter hyperintensities as in our case.

The ADC values of ROIs from the third and seventh week images were significantly lower than the normal white matter, and ADC map also revealed a low intensity area. On further follow-up images, ADC values returned to the baseline as did the ADC map. These findings replicate the results of a previous case report [13]. Based on the reports of diffusion abnormalities in acute stroke [12, 18], increased signal on DWI at the initial stage represents diffusion abnormalities due to cytotoxic edema, although pathologic correlation of diffusion abnormalities have not been fully elucidated.

Our results of serial MR study with DWI may help to understand the pathogenesis of DPE. The primary pathology of DPE has been known as demyelination [6, 20] and multiple sclerosis (MS) is one of the most representative demyelinating disorders. Although MS is an oligodendropathy whereas DPE is not an exclusive oligodendropathy, we can expect a common diffusion abnormality between DPE and MS. Many studies, however, reported that ADC values of MS plaque are higher than those of the normal white matter and suggested...
FIG. 2. — Serial MR imaging study including T2WI (A), DWI (B) and ADC map (C). On serial ADC maps, the low signal intensity area (arrows) in both periventricular white matter disappeared slowly. W : weeks ; M : months.

Fig. 2. — Étude IRM sériée. Séquences pondérée en T2 (A), pondérée en diffusion (B) et cartes de l’ADC (C). Sur les cartes d’ADC, l’hyposignal (flèche) dans la substance blanche pérventriculaire disparaît progressivement (W : semaine ; M : mois).

TABLE I. — Serial ADC values (10⁻³ mm²/s) from 8 ROIs depicted in figure 1.

<table>
<thead>
<tr>
<th>Time after hypoxic event</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 weeks</td>
<td>0.639</td>
<td>0.578</td>
<td>0.678</td>
<td>0.794</td>
<td>0.648</td>
<td>0.633</td>
<td>0.665</td>
<td>0.802</td>
<td>0.680</td>
<td>0.079</td>
</tr>
<tr>
<td>7 weeks</td>
<td>0.657</td>
<td>0.563</td>
<td>0.690</td>
<td>0.787</td>
<td>0.637</td>
<td>0.600</td>
<td>0.686</td>
<td>0.774</td>
<td>0.674</td>
<td>0.078</td>
</tr>
<tr>
<td>4 months</td>
<td>0.845</td>
<td>0.707</td>
<td>0.714</td>
<td>0.780</td>
<td>0.827</td>
<td>0.783</td>
<td>0.726</td>
<td>0.819</td>
<td>0.775</td>
<td>0.054</td>
</tr>
<tr>
<td>6 months</td>
<td>0.841</td>
<td>0.780</td>
<td>0.752</td>
<td>0.849</td>
<td>0.842</td>
<td>0.772</td>
<td>0.738</td>
<td>0.856</td>
<td>0.804</td>
<td>0.048</td>
</tr>
<tr>
<td>12 months</td>
<td>0.988</td>
<td>0.903</td>
<td>0.754</td>
<td>0.897</td>
<td>1.020</td>
<td>0.769</td>
<td>0.742</td>
<td>0.852</td>
<td>0.866</td>
<td>0.106</td>
</tr>
</tbody>
</table>
that high ADC values can be explained by increased extracellular space resulting from demyelination [7, 14]. In contrast, ADC values of our patient were low until the seventh week of follow up. Therefore the pathologic process in our patient cannot be accounted for exclusively by myelin destruction per se. Interestingly enough, more recent studies of MS reported that the ADC value obtained at the peripheral rim of acute demyelinating plaque is lower than that of chronic lesion and explained the result as a cytotoxic edema associated with oligodendrocyte dysfunction [22]. The results of Lucchinetti and their coauthors’ study may further support the heterogeneity of the underlying pathology in MS [11]. They reported four different patterns of demyelination in MS plaque: (1) T-cell mediated demyelination; (2) T-cell plus antibody-mediated demyelination; (3) primary oligodendrocyte dystrophy showing apoptosis; and (4) primary oligodendrocyte death without morphological features of apoptosis. In the third pathogenesis pattern, immunocytochemistry staining demonstrated evidence of apoptosis [11, 15].

Likewise, the demyelinating process of DPE might be an apoptosis primarily affecting oligodendrocytes. Anoxic injury might have triggered an apoptotic process in DPE just as an unknown viral infection or toxin would trigger oligodendrocyte dystrophy in MS. Our apoptotic hypothesis may explain the delayed onset of symptoms. That is, over a few weeks, accumulated apoptotic oligodendrocyte damage may become significant enough for the symptoms to appear, resulting in a DPE. In keeping with our hypothesis, recent studies suggested that apoptosis may be a possible mechanism of delayed cell death after mild cerebral ischemia [4, 23].

Our patient’s clinical symptoms began to show improvement several weeks after DPE which roughly coincided with the normalization of ADC values. Murata and their coauthors’ case [13] showed a similar temporal profile of serial DWI and ADC compared with ours, however, clinical improvement was not observed even after the normalization of ADC values. Therefore recovery from DPE appears to depend on individual differences of neuronal plasticity rather than simple normalization of ADC values.

So far, we conjectured the mechanism of DPE based on the apoptotic cell death of oligodendrocyte. However, other cells like astrocytes or perivascular microglia, and neuronal sheaths could also be affected in a global anoxic condition. Thus several pathogenetic mechanisms other than apoptosis could be associated with DPE, including necrosis and transient membrane dysfunctions without cellular death.

REFERENCES


