Duchenne muscular dystrophy carriers

Proton spin-lattice relaxation times of skeletal muscles on magnetic resonance imaging

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Summary. By means of magnetic resonance imaging (MRI), the proton spin-lattice relaxation times (T₁ values) of the skeletal muscles were measured in Duchenne muscular dystrophy (DMD) carriers and normal controls. The bound water fraction (BWF) was calculated from the T₁ values obtained, according to the fast proton diffusion model. In the DMD carriers, T₁ values of the gluteus maximus and quadriceps femoris muscles were significantly higher, and BWFs of these muscles were significantly lower, than in normal control. Degenerative muscular changes accompanied by interstitial edema were presumed responsible for this abnormality. No correlation was observed between the muscle T₁ and serum creatine kinase values. The present study showed that MRI could be a useful method for studying the dynamic state of water in both normal and pathological skeletal muscles. Its possible utility for DMD carrier detection was discussed briefly.

Key words: Proton MRI - T₁ value - Duchenne muscular dystrophy carrier - Creatine kinase

Duchenne muscular dystrophy (DMD) is an X-linked recessive muscular disease, with an onset of muscular weakness around the age of 3 years and a relentless progression until the loss of ambulation around the age of 10 years and the eventual death of the victims from respiratory or cardiac failure in the mid-twenties. It is relatively common, with an incidence of approximately 1 in 3,300 male births. Although the cause of this disease has been found recently and shown to be the deficiency of the membrane-associated cytoskeletal protein called dystrophin, the precise mechanism how its deficiency leads to the clinical phenotype remains to be worked out [1-6]. Because of the lack of effective therapies and the magnitude of the disaster to both the patients and their families, genetic counselling based on both reliable and convenient means of carrier detection still remains an important theme in this disease.

Proton nuclear magnetic resonance imaging (MRI) provides not only excellent morphologic images but also allows the elucidation of specific in vivo physico-chemical characteristics of the tissues under analysis. Recently, we have demonstrated by MRI that, in the early stage of DMD, the T₁ value (spin-lattice relaxation time) of the skeletal muscles was higher than normal, while it became progressively lower than normal in the advanced stage [7]. This progression was not uniform for all skeletal muscles, being most prominent in the gluteus maximus muscle (GLU) and least so in the sartorius and gracilis muscles [7]. In the present study, we compared the T₁ values of the skeletal muscles of DMD carriers with normal control, and found a small but still significant difference between the two groups. The significance of this finding and the possible utility of MRI for DMD carrier detection are discussed in this report.

Materials and methods

The study was performed on 19 mothers of DMD patients (mean age, 42 ± 6 years) and 10 normal female volunteers (mean age, 39 ± 12 years). The former comprised 4 definite, 4 probable and 11 possible carriers (Refer to paper 8 for the classification of DMD carriers). Informed consent was obtained from all of the subjects.

An Asahi Mark J-NMR-CT (magnetic field strength, 1056 gauss; resonance frequency, 4.5 MHz) was used. For the pulse sequence, saturation recovery (SR) with a repetition time of 1000 ms, and inversion recovery with a repetition time of 1000 ms,
and an inversion time of 300 ms were performed alternately 256 times each. The calculated T1 images were produced on a 256 x 256 matrix and interpolated to a 512 x 512 matrix for display.

Scans perpendicular to the body axis were carried out at three different levels in each case: at 2.5 cm above the symphysis pubis, mid-thigh level and the level of the largest diameter of the lower leg. For the identification of muscles, SR images were also referred to. The T1 values were determined for the medial portion of GLU, the vastus lateralis of the quadriceps femoris (QUAD) and the gastrocnemius (GAS) muscles. The mean pixel value and its standard deviation for the region of interest, 10 x 10-30 x 30 pixels, were determined for each muscle. The data for the right and left muscles were averaged for each muscle. All the scans were performed between 2 and 4 pm.

The bound water fraction (BWF) was calculated from the T1 value obtained, according to the fast proton diffusion (FPD) model [7, 9].

The serum creatine kinase level (CK; upper limit of normal range, 170 U/l) was measured in all the DMD carriers. They were divided into the following groups: definite or probable carriers (8 cases), possible carriers (11 cases), carriers with abnormally high CK values (8 cases) and those with normal CK values (11 cases). The data for each group were compared with those for the normal females.

The relationship between the muscle T1 and serum CK values was examined in all the DMD carriers.

Results

Figure 1 shows the MRI T1 images of a normal female and DMD carriers. The GLU, QUAD and GAS muscles can be clearly identified in these pictures.

The muscle T1 values for the normal controls and the DMD carriers are shown in Table 1. The mean

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Age (yr)</th>
<th>GLU</th>
<th>QUAD</th>
<th>GAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal females</td>
<td>10</td>
<td>39 ± 12</td>
<td>262 ± 12</td>
<td>274 ± 8^a</td>
</tr>
<tr>
<td>Definite or probable carriers</td>
<td>8</td>
<td>42 ± 7</td>
<td>273 ± 12^d</td>
<td>280 ± 9</td>
</tr>
<tr>
<td>Possible carriers</td>
<td>11</td>
<td>42 ± 5</td>
<td>273 ± 14^e</td>
<td>282 ± 8^f</td>
</tr>
<tr>
<td>Carriers with high CK values</td>
<td>8</td>
<td>44 ± 7</td>
<td>274 ± 10^e</td>
<td>284 ± 8^g</td>
</tr>
<tr>
<td>Carriers with normal CK values</td>
<td>11</td>
<td>41 ± 5</td>
<td>272 ± 15^d</td>
<td>297 ± 7</td>
</tr>
</tbody>
</table>

Abbreviations: DMD = Duchenne muscular dystrophy; GLU = gluteus maximus; QUAD = quadriceps femoris; GAS = gastrocnemius; CK = creatine kinase (normal range ≤ 170 U/l).

All values are expressed as means ± SD

Statistical significance by Wilcoxon test: ^aP<0.05, ^bP<0.005 compared to GLU of the normal females; ^dP<0.05 compared to QUAD of the normal females; ^eP<0.05, ^fP<0.025 compared to GLU of the normal females; ^gP<0.025, ^hP<0.01 compared to QUAD of the normal females