Magnetic Resonance Imaging of Muscular Dystrophies and Neuropathies

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Abstract

Discrimination between myopathy and neuropathy may be difficult especially in the early stages of the disease. Therefore it is reasonable to study the possibility of assessment of these disorders by means of magnetic resonance imaging. Children with a myopathy and children with a neurodegenerative disorder were selected for the study and compared to healthy volunteers. Measurements were performed on a small Bruker imaging system operating at 2.35 T, and T1 weighed images on the lower extremities were recorded. Images obtained on the diseased extremities were clearly distinguished from the images from healthy children. Furthermore, in myopathies a selective degeneration of muscles is definitely different from the nonselective involvement of all muscles in the spinal muscular atrophy.

Key words: Myopathy, Neuropathy, Duchenne muscular dystrophy, spinal muscular atrophy, Magnetic Resonance Imaging.

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Neuromuscular diseases are relatively difficult to diagnose, especially in the early stages. In a myopathy or muscular dystrophy the primary site of the disease is in the muscle itself while in the case of a neuropathy it is in the nervous tissue. Muscular dystrophies represent a group of genetically determined disorders characterized by progressive degenerative changes in muscle fibres which are not caused by a primary degeneration of the lower motor neurone. Duchenne muscular dystrophy (DMD), which is one of the most serious genetic diseases with a relatively high incidence (approximately 1 in 3000 male births [16]) is a representative of muscular dystrophy. It can be reliably discriminated from neurodegenerative disorder represented by a juvenile spinal muscular atrophy by use of magnetic resonance (MR) imaging, although the differential diagnosis of these two conditions may remain uncertain even after thorough clinical examination and biochemical tests of blood samples. Examination of bioptic material from muscle gives a correct diagnosis provided that a large enough sample of material is taken from the affected portion of the muscle. The discovery of dystrophin has greatly enhanced the accuracy of diagnosis based on bioptic samples, but less aggressive methods would be of great benefit in other neuromuscular diseases as well. Although electromyography (EMG) gives information on the condition of the investigated muscle and neuromuscular junctions it permits determination of the correct diagnosis only when the diseased portion of a muscle is being examined. In the early stages of these diseases it is often quite possible that, like in biopsy, the affected portion of the muscle may be missed. For those reasons various imaging techniques such as CT and MR imaging [11, 12, 13, 17, 20] have been employed in the assessment of neuromuscular disorders in addition to the previously mentioned techniques. In some countries CT has been completely replaced by MR imaging due to safety reasons and its superior diagnostic abilities. Together with the magnetic resonance spectroscopy (MRS) it seems to be a very promising, and to our present knowledge, harmless means of establishing a painless, fast, and accurate diagnosis [3, 6, 7, 10, 11, 12, 15, 19, 22, 23]. In all types of muscular dystrophies and neuropathies the muscle is gradually replaced by fibrous and fatty tissue. Therefore it is important to provide an accurate method which would enable determination of the extent of fatty infiltration of the affected musculature.

This study represents an attempt to use MR imaging as a diagnostic tool in discrimination between patients with neuropathies (e.g. Kugelberg - Welander type of SMA), where the muscle degenerates due to loss of innervation,

and a group of patients with muscular dystrophies, where the muscular system is originally affected.

Methods

A group of 7 children with clinical diagnosis of DMD and a second group of 8 children with clinically determined juvenile form of SMA was compared to a group of 8 healthy children. All of the diseased children showed typical clinical signs and symptoms. Only children in the same stage of the disease were considered for the detailed study. In addition to the clinical investigation, the diagnoses were confirmed by measurement of serum enzymes, EMG, and microscopic investigations of bioptic samples of muscle. Three qualified investigators read blindly the images from all patients and compared them to images from normal children. Children and/or their parents were informed about the nature of the investigation and consent was obtained. Measurements were performed on a small 2.35 T Bruker tomograph. A spin echo sequence with T_1 weighted images (TR = 600 ms, TE = 34 ms) was used. A field of view was 15-20 cm with data acquisition matrix 256 x 256. Slice thickness ranged between 5 and 10 mm. Images of adequate quality were obtained within 10 to 15 minutes.

Results

Fig. 1 represents a cross section of the lower limb of a healthy 11 year old boy. Major individual muscles can be identified, and there is not much fatty tissue present between the muscles and muscle groups. Subcutaneous fat is limited to a narrow band surrounding the muscles. Muscles are of homogenous dark gray color.

Accumulation of a larger quantity of white fatty tissue in the subcutis as well as between and within individual muscles, is typical of all investigated neuromuscular diseases. The pattern of involvement of individual muscles is definitely different in the case of DMD (Fig. 2) compared to the juvenile form of SMA (Fig 3).

Fig. 2 shows a cross section of the calf of a 10 year old. boy with DMD. The diagnosis of DMD was based on the family history and confirmed by clinical picture and abnormal values of serum enzymes at the age of 5 years. EMG and biopsy proved the diagnosis. As stated before an increase of subcutaneous fat is observed. The image gives the feeling that the fatty tissue diffusely substitutes for the muscular mass in degenerated muscles, and also accumulates in the subcutis. Individual muscles or muscle groups can easily be identified. The fast muscles seem to be affected most severely whilst the soleus muscle is much better preserved. The diseased muscles can easily be identified, and the pattern of involvement of individual muscles is typical of DMD. The primary degeneration of fast muscles reconfirms earlier findings that in the case of a muscular dystrophy the fast muscles are initially affected [4, 5, 21].

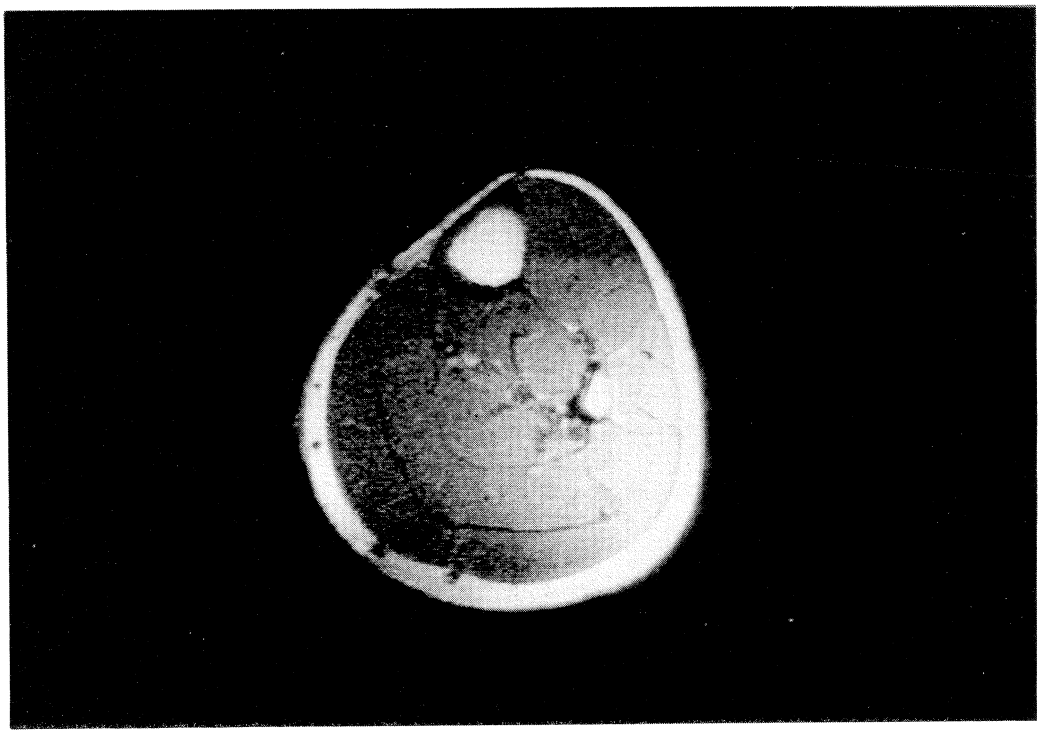

Figure 1. MR image of a calf from an 11 year old healthy boy. Note the homogeneous gray color of muscles and the absence of fatty tissue between individual muscles.

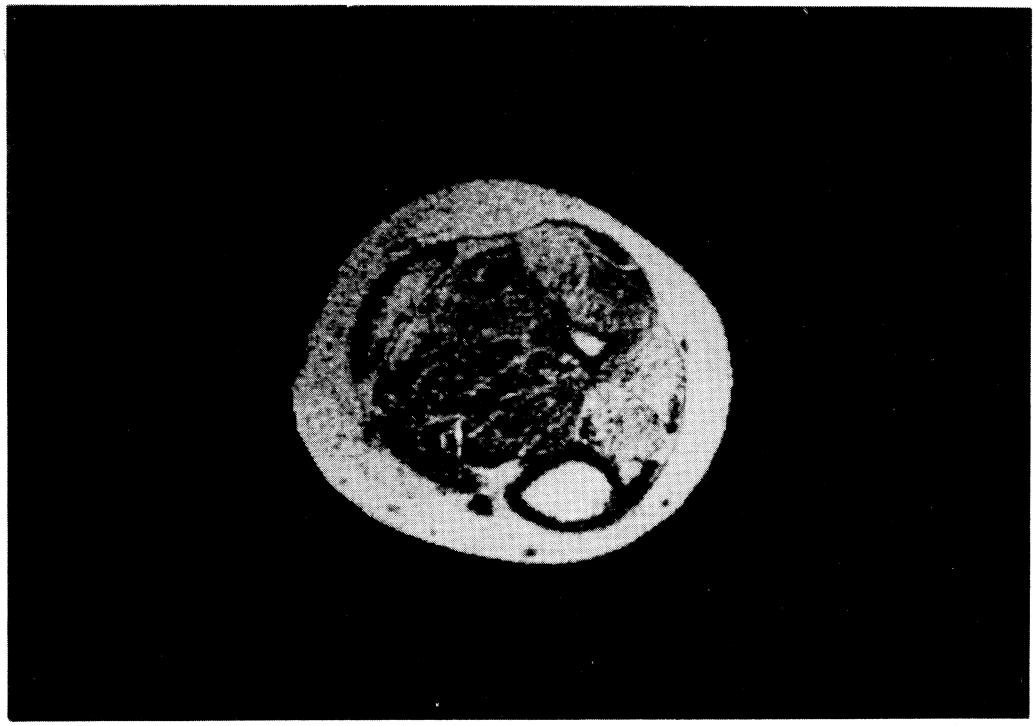

Figure 2. Cross section of a calf from a 10 year old patient with Duchenne muscular dystrophy. All muscles display higher signal intensity as compared to Fig. 1 from normal subject. Individual muscles and groups of muscles are easily identified.

The cross sections of the leg of a 10 year old boy shown in Fig. 3 represents a typical finding in patients with the juvenile form of the SMA. All the musculature is severely and equally affected. Individual muscles can hardly be distinguished from each other and there is no difference in the destruction of fast versus slow muscles. Each muscle is affected; but less uniformly as in patients with DMD. In all patients the diagnoses were determined on the basis of the clinical picture, EMG data and normal values of serum enzymes at the early childhood (age 3-5 years), and were later reconfirmed by histopathologic examination of bioptic material.

Comparison of Figs. 1-3 reveals that the discrimination between normal and diseased muscle is easy. Healthy muscles can be distinguished from the diseased muscle by the darker and homogeneous gray color. Discrimination between the DMD patients and patient with the juvenile form of SMA is based on selective involvement of fast muscles in patients with DMD which is in great contrast to the widespread and unselective involvement of all muscle groups in patients with the SMA. Additionally the affected muscles in the DMD patients are more homogeneously infiltrated by the fatty tissue than the muscles in the SMA patients.

Discussion

Neuromuscular diseases of genetic origin are the most frequent and devastating of all genetic diseases. Therefore it is important to establish the diagnosis in early childhood and to give a correct genetic counseling to the parents. In the case of Duchenne muscular dystrophy it has been shown that dystrophin is absent from muscles, while patients with the milder Becker type of muscular dystrophy (BMD) produce abnormal dystrophin [1, 8, 9]. Dystrophin can be identified in a small bioptic sample of muscles, which greatly improves the reliability of diagnoses. It has been estimated that diagnostic procedures based on determination of dystrophin in a tissue sample are capable of identifying at least 98% of DMD patients, while determination of deletions in the DMD/BMD gene provides accurate diagnosis in not more than 70% of cases [8,18]. The absence of recognizable mutations in the dystrophyn gene does rule out the DMD/BMD, but SMA and other neuropathies remain as alternatives. The juvenile type of SMA has been studied comparatively to DMD in our work, since it can mimic the DMD clinically. It is one of the neuromuscular diseases where determination of possible dystrophin abnormalities cannot contribute to the final diagnosis. MR imaging might become an important supplementary diagnostic tool for the discrimination of these two conditions. MR imaging proves to be of high diagnostic value because it can sample a whole muscle and it can also detect changes

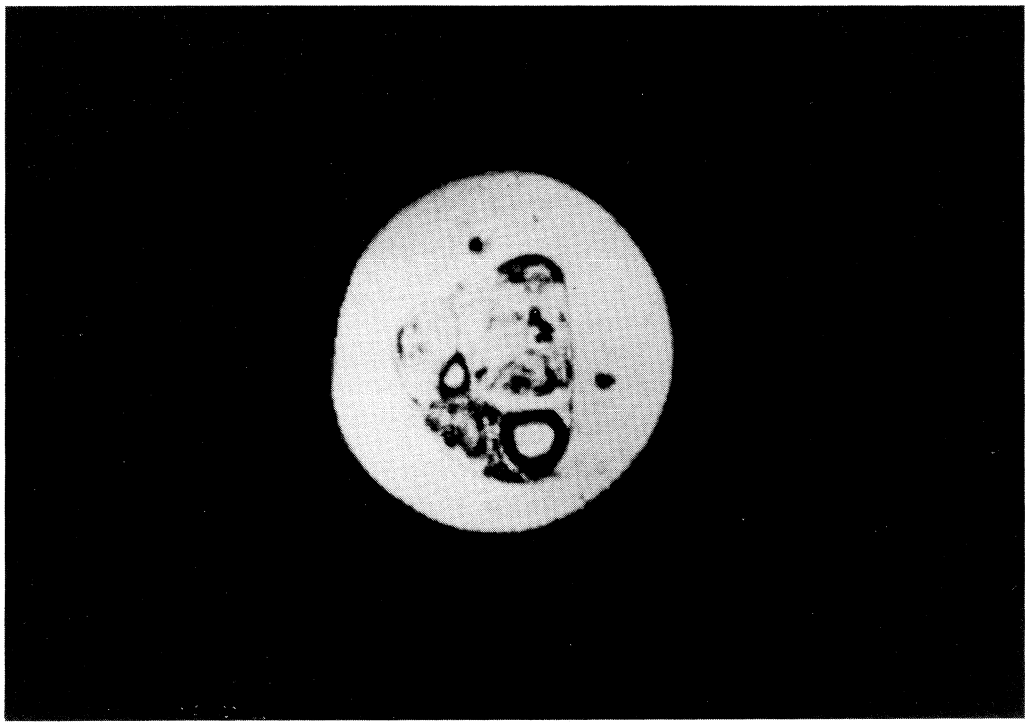

Figure 3. Axial scan from a 10 year old boy with the juvenile Kugelberg - Well-ander type of spinal muscular atrophy. Note the typical accumulation of subcutaneous fatty tissue. There is no difference in the degree of involvement of fast and slow muscles.

in deep muscles, which are not routinely accessible either to biopsy or to EMG measurements. Our study includes young children with similar clinical picture and different diagnoses. Most of them were barely ambulant or even confined to a wheelchair. Patients who developed contractures in the knee were excluded from the study because the size of the magnet prevented us from investigating such patients and patients in the very early stages of the disease. All SMA patients showed general and indiscriminate involvement of all muscles which is in great contrast to the findings on the DMD patients. Another valuable means of distinguishing between the two disorders is a regular finding that individual muscles in patients with DMD are more easily identified than muscles in normal subjects, whilst in the patients with the juvenile form of the SMA individual muscles cannot be identified at all.

Several authors have used MR imaging in assessment of musculoskeletal diseases [11, 14, 17, 20]. Their results agree with our finding that the musculature is gradually replaced by adipose tissue. This was precisely studied by means of ^{1}H MR spectroscopy [2, 10]. However no detailed study of the distribution of the fatty infiltration of individual muscles was described. Our study discloses clear differences in the degeneration of particular groups of muscles. There is no rule or differences between the destruction of slow and fast muscles in patients with the SMA while in patients with DMD the fast muscles seem to be much more affected than the slow muscles. This finding facilitates discrimination between the two disorders.

MR imaging seems to be the method of choice in assessment of neuromuscular diseases as it provides high resolution images of the musculoskeletal system without, to our present knowledge, any risk to the patient. Comparison of the images obtained on a healthy child, a patient with DMD and a patient with SMA portrays the diagnostic value of MR imaging. As MR imaging can easily be combined with MR spectroscopy they provide a morphological as well as pathophysiological insight into the condition of investigated musculature. It may become one of the most important morphological methods in the assessment of neuromuscular diseases.

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