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Muscle MRI in myotonic dystrophy type 1 with foot drop

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Abstract

The purpose of this study was to investigate the relationship of muscle MRI findings and gait disturbance in myotonic dystrophy type 1 (DM1) patients. Thirteen patients with DM1 were evaluated by manual muscle strength test and muscle MRI of the lower limb. All DM1 patients presenting with foot drop showed high intensity signals in the tibialis anterior muscles on T1-weighted imaging ($p < 0.001$). The patients presenting with gait disturbance showed high intensity signals in the semimembranosus, vastus intermedius and gastrocnemius medialis muscles, too. Disturbance of the gastrocnemius lateralis muscles was mild in all DM1 patients. The patients without gait disturbance showed no abnormalities, especially in tibialis anterior muscles on muscle MRI. Muscle MRI is useful for the detection of pathological muscles in DM1 patients with gait disturbance.

Introduction

Myotonic dystrophy type 1(DM1) is the most common form of inherited myopathy in adults, presenting with myotonia, muscle weakness in the distal portion of the upper and lower limbs. DM1 patients also show general symptoms, including cataract, frontal baldness, endocrinological abnormalities such as hypogonadism, and hyperinsulinemia associated with insulin resistance, and dementia, or mental retardation [1, 2, 3]. By the weakness of the distal portion of lower limbs, some patients show walking difficulties, and experience repeated falls [4]. Foot drop is the term commonly used to describe weakness or contracture of the muscles around the ankle joint [5]. Foot drop may be one of the causes of falls and ankle fracture in these patients [1, 3, 5]. Therefore, management of foot drop or steppage gait is important to maintain the patients' activities of daily living. In this study, we evaluated the relationship between foot drop and muscle MRI findings of lower limb in DM1 patients.

Patients and Methods

Patients

Thirteen DM1 patients were enrolled in this study (Table 1). All patients exhibited degenerative myopathy on clinical and/or myopathological examination as well as a myotonia observed by clinical and/or electromyographic examination. All patients gave fully informed consent prior to participation. Neurologically, they were examined and evaluated by at least three neurologists. Muscle strength was graded according to the Modified Medical Research Council (MRC) scale classifying muscle weakness in ten degrees from normal strength (10) to no voluntary movement (0) [6]. The definition of foot drop in this study is as follows: Patient who showed severe weakness of tibialis anterior (TA) muscles, and during walking, advancing foot is lifted higher than usual so that it can be clear the ground.

Genetic studies

Genetic study of the expansion of CTG repeat length in the 3' untranslated lesion of myotonin protein kinase was performed using DNA separated from leukocytes. Digestion with EcoRI and Bgl I restriction enzyme, separation of DNA fragment by gel electrophoresis, transfer on the nylon membrane by Southern blotting, hybridization with radiolabeled DM1 specific probe and finally visualized by autoradiography [7].

Muscle MRI

T1-weighted muscle MRI (GE-Signa, 1.5 Tesla) of the lower extremity was carried out in all DM1 patients [8]-[10]. Muscle MRI findings were evaluated by a neurologist (TH) and radiologist (YK).

Statistical analysis

Statistical analysis was performed with the aid of Stat view J version 4.5 (Abacus Concepts, Inc, Berkeley, CA) to see the correlation of clinical symptoms and muscle MRI findings or CGT repeat length by Spearman's rank correlation coefficient. Significance was estimated by $p < 0.05$.

Results

Fig. 1a shows typical findings of muscle MRI in a severe patient and a mild patient. Table 1 shows the distribution of affected muscles detected by muscle MRI in all patients. It was proven that all DM1 patient presenting with foot drop showed high intensity signals in the TA muscle (<0.001). Patients with severe leg weakness showed that high intensity signals expanded in the vastus intermedius, semitendinosus (ST), and gastrocnemius medialis (GM) muscles (fig. 1a A). However, the posterior tibial muscles were relatively spared even in patients in the advanced stage (table 1).

Statistically, the duration of illness and foot drop were positively correlated (<0.05). However, CTG repeat length, steppage gait, and muscle MRI findings were not positively correlated. There was a tendency for patients with a prolonged duration of illness to show a higher prevalence of foot drop, or severe leg weakness. However, there was a correlation between the duration of illness and foot drop only. There was no correlation with CTG repeat length, drop foot or weakness of the lower limbs. Patients with severe weakness showed high intensity signals not only in the distal part but also in the thigh, including the vastus intermdius, semimembranosus, and semitendinosus muscles. In the calf muscles, especially in the TA, GM, and soleus muscles showed high intensity signals. However, the gastrocnemius lateralis was not severely involved. Tibialis posterior (TP) muscles were affected only in two patients (table 1). The correlation between muscle MRI findings and muscle pathology using autopsied sample was examined in patient 7 (table 1, fig. 1b). TA muscle presented high intensity signals in muscle MRI showed characteristic typical pathological findings including the central nucleus, variable range of fiber size, and fatty degeneration (fig. 1b). The distribution of affected muscles is listed in table 1. In general, the vastus

intermedius, TA and gastrocnemius muscles were severely affected, but the adductor magnus and TP muscles were mildly affected.

Discussion

Previously, the usefulness of muscle MRI has been reported for various neurogenic and myogenic disorders. For example, typical muscle MRI findings were reported for neurogenic disorders; benign monomelic amyotrophy of lower limb [8], HTLV-1-associated myelopathy [9], spinobulbar muscular atrophy [10], and Charcot Marie-Tooth disease type IV. Furthermore, myogenic disorders also showed typical muscle MRI findings in inclusion body myositis [11], polymyositis [12], and Duchenne muscular dystrophy [13].

In this study, it was proven that all patients presenting with foot drop showed high intensity signals in the TA muscles. Patients with severe leg weakness, moreover, showed high intensity signals in the vastus lateralis, semitendinosus, and GM muscles. Duration of illness and foot drop was positively correlated (<0.005), which may reflect the chronic progressive nature of DM1.

It was previously reported that in DM1 patients, medial gastrocnemius muscles were involved in the early phase, and the posterior tibial muscles were relatively spared. In the thigh muscles, the vastus muscles were damaged most often and rectus femoris least [2, 14, 15]. On the other hand, in Duchenne type muscular dystrophy, sartorius, gracilis (G), and ST muscles are preserved. Hypertrophy of G muscle is sometimes observed. Fatty infiltration of calf muscles are considerably mild and anterior compartment is relatively mildly disturbed [13].

There is no satisfactory explanation for the distribution of muscular changes showing the different dystrophic processes. One possible factor would be based on the distribution of the two histopathological types, type 1 and type 2, of muscular fibers [16], and the selective alteration of these fiber types in some diseases, such as atrophy

of type I fibers in DM1. Another author suggested that anatomical characteristics such as shape, length, or extension over one or two joints may be contributing factors affecting the muscle strength [17].

Wiles et al. reported that DM1 patients stumble or fall about 10 times more often than healthy volunteers, and found that muscle strength of ankle flexion and ankle plantar flexion were significantly impaired in DM1 patients [3]. Ray et al. reported that adult-type DM1 patients develop a foot drop or steppage gait with increasing age, frequently utilized ankle-foot-orthoses, and occasionally required wheelchairs.

In conclusion, muscle MRI findings, especially TA muscle findings are useful for estimating muscle functions and anticipating drop foot in DM1 patients. Therefore, information obtained by muscle MRI contributes to the estimation of prognosis.

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Figure legends

Fig. 1a. Muscle MRI findings of myotonic dystrophy type 1 patients.

A, B. Muscle MRI findings with severe leg weakness. Vastus intermedius, adductor magnus, and semimembranosus muscles showed high intensity signals. Gastrocnemius medialis and soleus muscles showed high intensity signals.

C, D. Muscle MRI findings with mild leg weakness.

RF: rectus femoris, VI: vastus intermedius, VL: vastus lateralis, AM: adductor magnus, ST: semitendinosus, SM: semitendinosus, BL: biceps femoris longus

G: gracilis, TA: tibialis anterior, TP: tibialis posterior, PE: peronei, GM: gastrocnemius medialis, GL: gastrocnemius lateralis, S: soleus

Fig. 1b. Correlation of muscle MRI findings and muscle pathology (Patient 7, in table

1). Left tibialis anterior muscle pathology obtained at autopsy showed fatty degeneration, and central nucleus. Muscle MRI showed high intensity signal in tibialis anterior muscles.

Figure 1.a

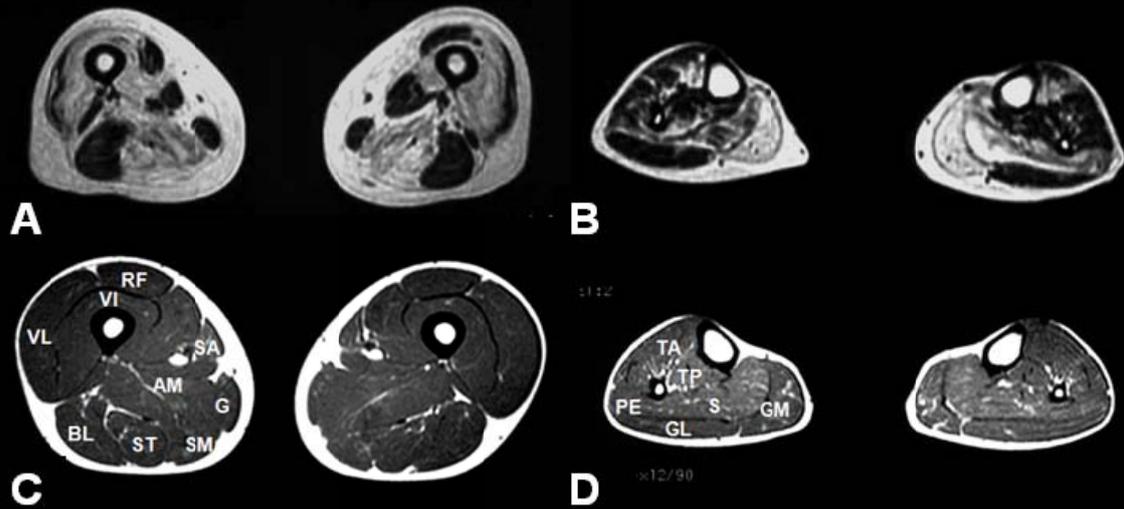


Figure 1.b

