The Utility of Magnetic Resonance Imaging in Inflammatory Myopathy

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Objective. The idiopathic inflammatory myopathies (IIMs) are chronic systemic connective tissue diseases. The muscle biopsy is a definitive diagnostic tool but blind biopsy sometimes produces to negative results. Magnetic resonance imaging (MRI) as a tool for early diagnosis, guidance for biopsy, assessing extent of lesions and monitoring therapy in IIMs has been reported. The aim of this study is to assess the association of thigh inflammation through MRI and biopsy specimens with clinical findings.
Methods. Sixty patients diagnosed with dermatomyositis (DM) or polymyositis (PM) from 2004 to 2011 in one center of rheumatology were enrolled. We reviewed clinical, laboratory, histopathologic and MRI of thigh data at initial diagnosis. The inflammation grades by MRI and histopathology of muscles were evaluated through 4-point scoring systems.
Results. The laboratory findings for aldolase and CK differed significantly between DM patients (68.3%) and PM patients (31.7%). Fasciitis was detected by MRI in 43.3% of patients, of whom 88.5% had DM (p<0.05). The fasciitis was also associated with myalgia (p<0.05). Almost all MRI findings were symmetric except for two patients. The mean of total signal intensity was higher in patients with decreased muscle power. The signal intensity of affected muscle was slightly associated with muscle enzymes and histopathologic grading.
Conclusion. Fasciitis was observed more in DM patients. MRI findings were associated with muscle enzymes and histopathologic grading. Signal intensity on MRI may be useful for measurement of disease activity in acute IIMs. The noninvasive nature and high sensitivity of muscle inflammation suggest that MRI images should be considered prior to muscle biopsy and treatment of IIMs.
Key Words. Inflammatory myopathy, MRI

Introduction

The idiopathic inflammatory myopathies (IIMs) are rare, chronic systemic connective tissue diseases characterized by infiltration of inflammatory cells at skeletal muscles and progressive muscle weakness. IIMs are heterogeneous group of disease known as dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM) (1,2). The muscle biopsy is an essential and definitive diagnostic modality for IIMs. The hallmark of the histological pathology is infiltration with inflammatory cells in the muscles. However, the inflammation of muscle may be unevenly distributed and not all of the muscles are affected at the same time. Even though persistent muscle weakness exists in some cases, the inflammatory infiltrate is only minimal or can no longer be found (3,4). Therefore, the selection technique for obtaining the appropriate sample should be used to guide for biopsy. And imaging tools can be particularly useful in identifying biopsy site (5,6).

The principal sources of the magnetic resonance imaging (MRI) signal are fat and water. Owing to the method of MRI image, edema and fat are distinguished. In general, muscular edema, atrophy and fatty infiltration of muscles are seen in MRI. Muscles with inflammatory edema have high signals on T2-weighted with fat suppression (T2W/FS) or short tau inversion recovery (STIR) images, whereas low signals in those less affect of non-affected. T1-weighted images (T1W), when fat has high signal and muscles have medium signal intensity,
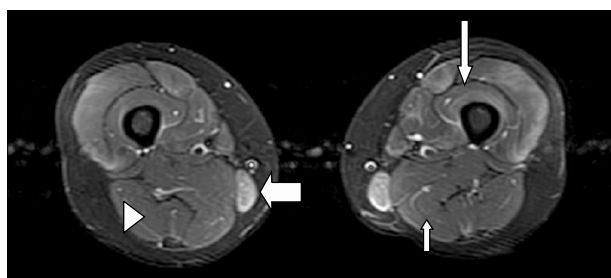
are helpful to detect fatty degeneration of affected muscles (6,7). MRI can be used as guidance for biopsy in an area of active disease and thus may decrease the false-negative rate of 10-25% without imaging guidance (4,8). It can also assess the extent of lesions and monitoring therapeutic response in patients with IIMs has been reported previously (9-11). Especially, signal intensity (SI) in MRI is associated with disease activity in the acute presentation and after treatment of PM and DM. However, the use of MRI is not a standard practice.

In this study, we focused on the utility of MRI in the assessment of IIMs. The MRI findings were compared with other findings such as histopathologic, laboratory and clinical findings.

Materials and Methods

Patients

Seventy-one patients were diagnosed of PM or DM compatible with Peter and Bohan criteria (2) from January 2004 to July 2011 in one center of rheumatology. Among them, 41 patients (68.3%) with DM 19 patients (31.7%) with PM who had both biopsied muscle specimens and MRI image of thigh at initial diagnosis were enrolled in this study. We retrospectively collected data such as demographic, laboratory and clinical findings including muscle power through electronic medical records at initial diagnosis. Muscle power was assessed by Medical Research Council scale (MRC) (12). As grade of power, 6-point scores were matched from 0 (MRC grade 0) to 5 (MRC grade V). This study was approved by Insititute Review Board of Hanyang University Hospital.

Muscle inflammations

All patients had at least one of the T2W/FS or STIR images at initial diagnosis. Total thirty muscles including tensor fascia lata, gluteal muscles and three compartments of thigh at MRI image were re-evaluated by one radiologist. The evaluated muscles of anterior compartment were Sartorius, Rectus femoris, Vastus lateralis, Vastus medialis and Vastus intermedialis. The muscles of medial compartment included Gracilis, Pectineus, Adductor longus, Adductor brevis and Adductor magnus. Lastly, the muscles of posterior compartment were Biceps femoris, Semitendinosus and Semimebranosus. The affected and non-affected muscles were differentiated according to presence of edema identified on T2W/FS or STIR images. The inflammations of muscles were assessed by 4-point scoring systems: 0; no signal intensity, +1; subtle intensity, +2; focal signal intensity (total affected area in each muscle $<50\%$), +3; diffuse signal intensity (total affected area in each muscle $>50\%$) (Figure 1). These inflammations were represented by scores; total affected muscles (TAM) $0\sim60$, total sum of signal intensity at affected muscles (TSI) $0\sim180$. Symmetrical nature of involved muscles, presence of muscle atrophy and fasciitis (Figure 2) were also assessed.

The biopsied muscles were obtained within a week after femur MRI examination through gun biopsy or open biopsy at initial diagnosis. One pathologist re-assessed the grades of inflammation at biopsied muscle specimens stained hematoxylin-eosin (H-E), semi-quantitatively by using 4-point scoring: 0; no inflammatory cells present, +1; slight inflammatory cells present, +2; moderate inflammatory cells present, +3; marked inflammatory cells present.
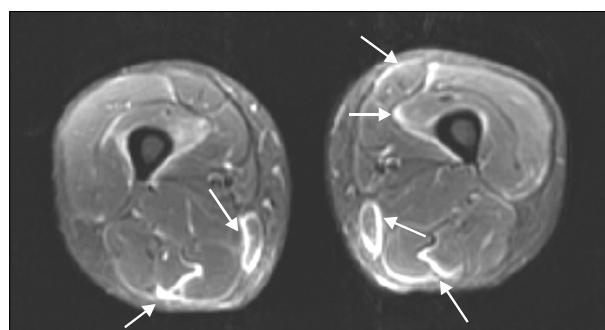

Figure 1. The signal intensity at STIR magnetic resonance imaging (MRI) of transaxial section. No signal intensity (arrowhead on Biceps femoris), subtle signal intensity (short narrow arrow on Semimembranous) were represented for score 0 and 1, respectively. Focal signal intensity (long narrow arrow on Vastus intermedialis) in each muscle which was affected less than 50% of area was represented for score 2. Diffuse signal intensity (wide arrow on Gracilis) was represented for score 3.

Figure 2. Fasciitis on STIR magnetic resonance imaging of transaxial section in a dermatomyositis patient with myalgia symptom for 5 months until diagnosis. Areas of high signal intensity (arrows) observed in the fascias surrounding the Sartorius, Vastus intermedialis, Gracilis, Semimembranosus and Semitendinosus muscles.

Statistics

We used SPSS network version 20.0 (Chicago, Illinois, USA). T-test and Spearman's rank correlation were used for statistical analysis as appropriate. p-values <0.05 were considered statistically significant.

Results

Clinical findings of patients

Total 11 patients (18.3%) were males and 49 patients (81.7%) were females. The mean age was 45.1 years and the mean duration of follow-up was 34.4 months from initial diagnosis. The laboratory findings at initial diagnosis were: aspartate aminotransferase (AST) 89.0±86.3 U/L, alanine aminotransferase (ALT) 73.4±71.3 U/L, creatine kinase (CK) 1,465.2±2,404.1 U/L, lactate dehydrogenase (LDH) 449.7±410.8 U/L, aldolase 22.5±24.1 IU/L, C-reactive protein (CRP) 0.6±0.9 mg/dL, erythrocyte sedimentation rate (ESR) 33.6±30.3 mm/hour. The means of TAM and TSI were 22.4±7.1 and 43.2±22.3, respectively. There were no statistically difference between PM and DM except mean level of CK and aldolase. The means level of CK and aldolase were increased in PM patients on the contrary (Table 1). Some DM patients did not have increased muscle enzymes; CK in 39.0%, LDH in 22.0% and aldolase in 22.0% of DM patients. Among them, total 5 DM patients (12.2%) had all 3 muscle enzymes with normal ranges though they had skin lesion and proximal muscle weakness and/or myalgia at the point of MRI evaluation. They were all referred patients with examination results. Three patients had positive EMG findings compatible with myositis such as short duration, small and low-amplitude polyphasic motor unit potentials from other hospital. Three patients had positive biopsy findings such as perifascicular mononuclear cell infiltration with muscle fiber atrophy and degeneration, one patient showed only atrophic change in biopsy specimen and the other patient showed none-made biopsy result. However, they had been identified elevated level of LDH or aldolase before referral.

All patients started steroid treatment including high dose steroid pulse (5%) immediately after diagnosis. The mean dose of initial steroid (prednisolone equivalent dose) was 49.6±62.0 mg. Other medications as steroid sparing agents were used: methotrexate (MTX, 56.7%) 11.2±2.8 mg, cyclosporine (CsA, 23.3%) 114.3±30.6 mg and azathioprine (AZA, 8.3%) 70.0±27.4 mg. Total 13.3% of patients needed intravenous immunoglobulin therapy for disease control. The combination of medications were steroid with MTX (53.3%), steroid with CsA (20.0%), steroid with AZA (8.3%), steroid with MTX and CsA (3.3%) and steroid with tacrolimus (1.7%) in descending order.

Total 47 patients were identified location of biopsied muscle. The most compartment of biopsy was anterior portion (78.7%), especially. Vastus lateralis was the dominant site for muscle biopsy among muscles of anterior compartment (n=30). In addition to muscle biopsies were taken at medial compartment (8.5%), gluteal muscles (8.5%), posterior compartment (2.1%) and tensor fascia lata (2.1%).

MRI findings and correlation with clinical findings and histopathologic scorings

Although two patients with DM asymmetrically affected in thigh MRI, almost patients showed symmetrically involved

Table 1. Demographic and clinical findings between patients with DM and PM

	DM (n=41)	PM (n=19)	Total (n=60)
Age (years) at diagnosis	41.9±13.0	40.2±14.6	41.4±13.4
Female (%)	80.5	84.2	81.7
Duration[†] (months)	5.2±5.2	9.7±13.1	6.6±8.7
Muscle power scale	4.0±0.8	3.9±0.6	3.9±0.8
Myalgia (%)	43.9	26.3	38.3
AST (IU/L)	79.1±70.0	110.5±113.7	89.0±86.3
ALT (IU/L)	64.2±64.5	93.37±82.42	73.4±71.3
LDH (mg/dL)	391.3±343.2	575.6±516.7	449.7±410.8
CK (U/L)*	976.0±1,547.2	2,520.7±3,450.2	1,465.2±2,404.1
Aldolase (IU/mL)*	17.6±16.5	33.2±33.4	22.5±24.1
ESR (mm/hour)	31.8±25.8	37.5±38.9	33.6±30.3
CRP (mg/dL)	0.7±1.0	0.5±0.5	0.6±0.9
Anti-Jo1 positivity (%)	7.3	6.3	7.0
Malignancy (%)	4.9	5.3	5.1
Interstitial lung disease (%)	70.3	53.8	66.0

DM: dermatomyositis, PM: polymyositis, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CK: creatine kinase, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein. [†]Durations from symptoms to diagnosis, *p<0.05.

muscles of thigh. Among two asymmetrical affected patients, one patient involved at posterior compartment of right side and the other patient involved at medial compartment of right side. The dominant compartment of TSI by compartments was anterior compartment, and the TSI by compartments were decreased medial, posterior compartment and gluteal muscles in order. This order was similar with the order of biopsy sites.

Total 38.3% of patients had myalgia (Table 1) and 78.3% of patients with myalgia were DM. And total 43.3% of patients had fasciitis in MRI (Table 2). Total 88.5% of patients noted fasciitis were DM patients (p<0.05). Fasciitis was identified in 60.9% of patients with myalgia (p<0.05). Although the durations from symptom to diagnosis were not statistically different between patients with and without fasciitis, the patients with fasciitis had short duration to diagnosis (4.5±4.1 months vs. 8.2±10.7 months).

Although there were 12.2% of DM patients who had normal levels of all 3 muscle enzymes, the means of TAM and TSI of those patients were 26.2±4.4 (21-30) and 49.6±28.0 (26-88), respectively. In 60 patients, laboratory findings showed modest correlations with TSI (Table 3). TSI was significantly increased in patients with decreased muscle power (46.9±22.8) than patients with normal power (29.8±24.6) (Figure 3). The mean of MRI SIs and histopathologic scorings at biopsied muscles were 2.1±0.9 and 1.2±0.8, respectively. The histopathologic scores showed modest correlations with SI of biopsied muscles (r=0.339, p<0.05), edema (r=0.381, p<0.05) and atrophy (r=−0.311, p<0.05) (Figure 4).

However, there was no statistical difference between patients with DM and PM.

Discussion

There were no significant differences of demographic and laboratory findings between DM and PM patients except level of CK and aldolase in this study. These muscle enzymes could not be helpful to distinguish IIMs and to assess of disease activity because some patients had normal level of muscle enzymes and others have persistent elevated muscle enzyme without other signs of disease activity (13). In this study, al-
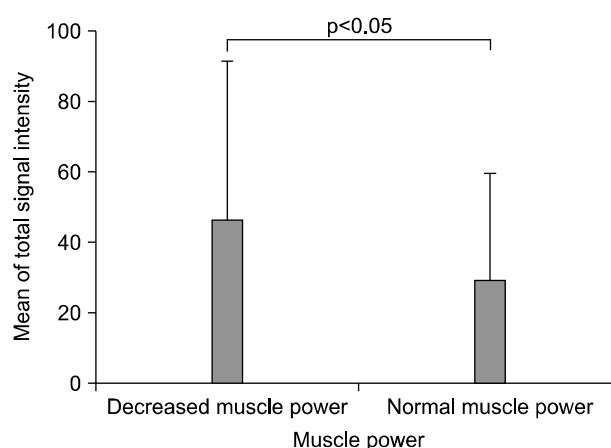
Figure 3. Difference of total signal intensity depending on muscle power. Decreased muscle power MRC grade 0-IV, Normal muscle power MRC grade V.

**Table 2.** MRI findings in patients with DM and PM

	DM (n=41)	PM (n=19)	Total (n=60)
Symmetric involvement (%)	39 (95.1)	19 (100)	58 (96.7)
TAM	22.3±7.6	22.4±6.3	22.3±7.2
TSI	42.4±22.6	44.7±22.2	43.2±22.3
Atrophy portion (%)	11.1±22.7	20.2±31.8	14.0±26.0
Fascia involvement (%)*	23 (56.1)	3 (15.8)	26 (43.3)

DM: dermatomyositis, PM: polymyositis, TAM: total affected muscles, TSI: total sum of signal intensity. *p<0.05.

Table 3. Correlation of MRI findings with laboratory findings

Laboratory findings	Total signal intensity(TSI)		Total affected muscles (TAM)	
	r (correlation coefficient)	p (two-tailed)	r (correlation coefficient)	p (two-tailed)
AST	0.313	0.015	0.178	0.173
ALT	0.361	0.005	0.284	0.028
CK	0.304	0.018	0.203	0.119
LDH	0.297	0.021	0.145	0.271
Aldolase	0.363	0.004	0.224	0.085

AST: aspartate aminotransferase, ALT: alanine aminotransferase, CK: creatine kinase, LDH: lactate dehydrogenase.
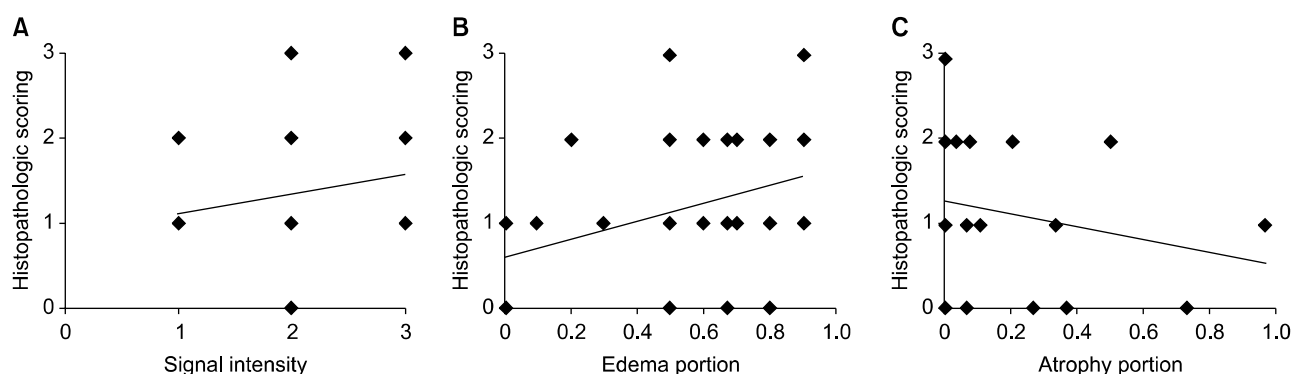
Figure 4. Scatter plots of histopathologic scoring with MRI findings at biopsied muscles. Histopathologic scoring showed slightly positive correlations with signal intensity (r=0.339, p<0.05) (A) and edema portion (r=0.381, p<0.05) (B), and slightly negative correlation with atrophy portion (r=−0.311, p<0.05) (C) at the biopsied muscles.

though all patients had positive MRI findings, there were also some DM patients with muscular manifestation and normal muscle enzymes. Therefore, MRI may be helpful to patients who have muscular manifestations without increased muscle enzymes.

The fasciitis in MRI and myalgia were more manifested in patients with DM than PM in this study. And myalgia showed statistical correlation with fasciitis. This result was consistent with previous reports. Kimball et al demonstrated that the changes of fascia were very common in juvenile DM (14). Yoshida et al reported that the fasciitis was a common lesion not only in amyopathic DM but also in myopathic DM. They also described that the fasciitis was one of the causes of the muscle symptoms in DM (15). Although metabolic alterations in local tissue through a loss of functioning capillaries and phenotypic changes in the endothelial cells could contribute to muscle fatigue, fasciitis may also contribute to muscle symptoms such as myalgia (16,17). The fasciitis was histopathologically demonstrated in patients of adult onset with newly diagnosed as early as 2 months after the onset of myalgia, so the fascial microvasculature was suggested the primary target tissue of inflammatory cell infiltration in DM (15). Therefore, identification of fasciitis in MRI may be helpful for the considering DM in the absence of intramuscular inflammatory infiltrates, especially in early stage of DM.

Almost IIMs are diagnosed clinically and confirmed with biopsy. A small portion of patients have normal muscle enzyme level, and up to 10% of patients have a normal EMG (5,18). The muscle biopsy is the "gold standard" diagnostic test in most cases of IIMs. However, even the biopsy has inherent limitations such as sampling error, lowering the diagnostic yield and invasive procedure. And in their series of 150 patients with DM and PM, Bohan et al reported that blind muscle biopsy was negative in 12.5% of cases (19). To obtain

a muscle biopsy to make a definitive diagnosis, the selection of an appropriate site is important. MRI can evaluate much larger area of muscle tissue than biopsy and procedure itself is less dependent on the operator compared with ultrasonography and other imaging studies (20,21). MRI also provides a non-invasive method of demonstrating subtle or subclinical changes unlike biopsy or EMG in individual muscles that cannot be isolated on strength testing (9,11). A muscle biopsy guided by positive MRI findings was contained more inflammatory cells than a biopsy taken from non-affected sites (11). In this study, histophatological score showed positive correlation with edema and negative correlation with atrophy. Therefore, the biopsy site should be chosen in the active area without atrophic change for accurate diagnosis.

Inflammatory muscle tissue of IIMs patients is edematous, though not specific for myositis. It may also be seen in injuries, infection, infarction and rhabdomyolysis et al. However, the presence of muscle edema is not exclusive to IIMs and the increased signal intensity by edema is a typical finding in acute IIMs (22,23). In this study, TSI or SI on affected area rather than TAM showed correlations with muscle enzymes, muscle power and histopathologic grading. It could be suggested that the SI on MRI is more associated with clinical status of IIMs than affected extents. Some also reported that SI in the acute presentation of IIMs was associated with the disease activity, and improvement in MRI score could be a good parameter for short-term follow-up and clinical status assessment (11,13). Because of invasive nature, biopsy and EMG are not useful for follow-up and clinical status assessment. Therefore, SI on MRI can be used for assessment of disease activity and evaluation of effect for treatments.

There were some limitations in this study. Sample size was small and information of clinical assessments such as accurate muscle weakness, atrophy, muscle power and any other clin-

ical symptoms was lack because of its nature of retrospective study. Biopsy might not be done in targeted sites through MRI, actually. And there might be some bias in the evaluation of inflammation because MRI and biopsied specimen were re-evaluated by one radiologist and one pathologist, respectively. There was no follow up study of MRI and biopsy after treatments for evaluating disease activity.

In summary, we evaluated the utility of MRI in patients with DM and PM. MRI can be more helpful for suspicious myopathy with normal muscle enzyme. The fasciitis in MRI also can be helpful in diagnosing DM, especially in early stage of DM. The biopsy should be taken at high affected muscle in MRI. The patients with decreased muscle power showed more increased total signal intensity than patients with normal power, and the signal intensity of MRI correlated with muscle enzymes and histopathologic grading. Therefore, the noninvasive nature and high sensitivity of muscle inflammation suggest that MRI should be considered prior to muscle biopsy and it can be used for assessment of disease activity during follow-up.

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