Table 3 Treatments and outcomes

Patients	Effect of immunotherapy on neuropathy			Therapy for lymphoma		Effect of chemotherapy on neuropathy	mRS			Follow up duration (months)
	IVIg	Steroid	PE	Before neuropathy	After neuropathy		At admission	Afer treatment	Long-term outcome	
Neurolymphomatosis*										
1	ND	1+	ND		CHOP	1+	3	3	Dead	14
2	–	1+	ND	CHOP	Rituximab CHOP MTX** CHASE	–	3	3	Dead	7
3	2+	2+	ND		R-CHOP CODOX-M MTX	2+	5	4	4	75
4	ND	ND	ND	MTX R-CHOP	MTX AraC PSL Radiation	2+	3	2	Dead	65
5	–	ND	ND		AraC** MTX** PSL**	ND	4	4	Dead	30
6	ND	ND	ND		CHOP R-DeVIC THP-COP	2+	3	1	1	108
7	–	1+	1+		VP16	2+	4	3	Dead	91
8	ND	ND	ND	CVAD	MTX** AraC** Rituximab CPM Dexamethasone**	–	3	3	Dead	7
9	–	ND	ND	R-CHOP	IMVP-16/CBDCA CHASER	–	4	4	Dead	36
10	ND	ND	ND	R-CHOP	Rituximab DeVIC	2+	3	2	2	84
11	ND	ND	ND	R-CHOP	R-DeVIC MTX** PSL**	2+	3	2	1	69
12	ND	ND	ND	EPOCH rituximab	MTX*	–	4	4	Dead	12
13	ND	2+	ND		MTX** AraC** Dexamethasone** Radiation	–	3	2	Dead	9
14	–	2+	ND		R-CHOP	2+	3	2	2	29
15	–	–	ND		R-CHP CHASER MTX DeVIC	–	3	4	Dead	33
Paraneoplastic neuropathy CIDP type										
16	ND	ND	ND	CHOP VP16 MST16 PCZ	MST16 VP16 PSL L-PAM	–	4	5	Dead	80
17	2+	ND	ND		Rituximab CPM PSL	2+	4	3	3	46
18	ND	2+	ND	INFγ PUVA Vorinostat		ND	4	3	Dead	132
Sensory ganglionopathy										
19	2+	2+	2+			ND	5	3	Dead	92

(continued)

Table 3 Continued

Patients	Effect of immunotherapy on neuropathy			Therapy for lymphoma		Effect of chemotherapy on neuropathy	mRS			Follow up duration (months)
	IVIg	Steroid	PE	Before neuropathy	After neuropathy		At admission	Afer treatment	Long-term outcome	
Vasculitic neuropathy										
20	ND	ND	ND	CHOP		ND	4	ND	ND	24
Unclassified										
Multiple mononeuropathy										
21	1+	1+	ND		CODOX-M/IVAC R-CHOP CHASER PBSCT	–	2	2	Dead	39
22	2+	ND	ND			ND	5	4	Dead	11
23	–	ND	ND			ND	3	4	Dead	3
24	ND	1+	ND		MTX** AraC** Dexamethasone** R-CHOP	1+	3	3	Dead	41
25	–	–	ND	Rituximab THP-COP	Rituximab	ND	4	4	4	68
26	ND	ND	ND	R-CHOP F-ara-A MIT		ND	4	ND	ND	58
27	ND	–	ND	CHOP		ND	4	4	5	70
28	ND	ND	ND			ND	3	5	Dead	7
29	–	–	ND			ND	4	5	Dead	5
30	ND	ND	ND		CHOP	1+	ND	ND	ND	2
Polyneuropathy										
31	2+	2+	ND		MTX PCZ VCR AraC CHOP PBSCT	2+	3	2	2	129
32	1+	1+	ND		MTX** AraC** PSL** R-CHOP BMT	2+	2	1	1	120

AraC = Cytarabine; BMT = bone marrow transplantation; CDOX-M = Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate; CDOX-M/IVAC = CDOX-M + Etoposide, Ifosfamide, Cytarabine; CHASE = Cyclophosphamide, Cytarabine, Etoposide, Dexamethasone; CHASER = CHASE + Rituximab; CHOP = Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone; CPM = Cyclophosphamide; CVAD = Cyclophosphamide, Vincristine, Doxorubicin, Dexamethasone; DeVIC = Dexamethasone, Etoposide, Ifosfamide, Carboplatin; EPOCH = Etoposide, Prednisolone, Vincristine, Cyclophosphamide, Doxorubicin; F-ara-A = Fludarabine; INFγ = Interferon γ; IMVP-16/ CBDCA = Ifosfamide, Methotrexate, Etoposide, Carboplatin; L-PAM = Melphalan; PE = plasma exchange; MIT = Mitoxantrone; MST16 = Perazolin; MTX = Methotrexate; ND = not done; PBSCT = peripheral blood stem cell transplantation; PCZ = Procarbazine; PUVA = psoralen + ultraviolet A; PSL = Prednisolone; R-CHOP = Rituximab + CHOP; R-CHP = Rituximab, Cyclophosphamide, Doxorubicin, Prednisolone; R-DeVIC = Rituximab + DeVIC; THP-COP = Pirarubicin, Cyclophosphamide, Vincristine, Prednisolone; VCR = Vincristine; VP16 = Etoposide.

1+ and 2+ represent slight and good response to treatment, respectively.

*Patients 1 to 9 were pathologically-proven neurolymphomatosis, whereas Patients 10 to 15 were FDG-PET assessed neurolymphomatosis.

**Therapy was done intrathecally.

two of the nine cases manifesting symmetrical polyneuropathy. Therefore, patients who showed asymmetrical features in the early phase might develop the symmetrical polyneuropathy type as the disease advances. In this context, neurolymphomatosis might play a more important role in neuropathy associated with lymphoma than previously suggested. Sural nerve biopsy is limited for the diagnosis of neuropathy associated with lymphoma, as biopsy assesses only a distal portion of the PNS (van den Bent *et al.*, 1999). Notably, only one patient with sensory ganglionopathy, which is the most common form of paraneoplastic neuropathy (Oki *et al.*, 2007; Koike *et al.*, 2011a), was included among five patients with pathologically-proven paraneoplastic neuropathy. However, because this is a retrospective study and only patients who were referred to the neurological department of our institute were included, there was a sample bias.

The characteristic findings that explain the cause of neuropathy in most patients included lymphoma cell invasion-associated demyelination and axonal degeneration of the distal portion of the nerve trunk. The invasion of lymphomatous cells into the nerve trunk has been designated as neurolymphomatosis and is reported as a characteristic feature of neuropathy associated with lymphoma (Guberman *et al.*, 1978). In our cases, lymphomatous cells invaded in and around the perineurium, particularly the subperineurium. Because the lymphatic flow is preferentially present in the subperineurial space, this area has an affinity for lymphomatous cells. In addition, the lymphomatous cell invasion continued into the endoneurium. Demyelination was observed at the site of lymphoma cell invasion, and axonal degeneration occurred distal from the site of lymphoma cell invasion. Therefore, demyelination at the site of neurolymphomatosis might be the primary lesion, with axonal degeneration occurring secondarily in most patients with lymphoma-associated neuropathy. This view is supported through electrophysiological findings showing a mixture of demyelinating and axonal changes and sural nerve biopsy findings showing predominant axonal degeneration in the distal portion of the nerves. The demyelination observed in the present study was different from that in acute inflammatory demyelinating polyneuropathy or CIDP, as macrophage-mediated demyelination was not observed in our patients (Prineas and McLeod, 1976). Because lymphomatous cells do not directly contact myelinated fibres or Schwann cells, humoral factors produced by the lymphoma cells close to the myelinated fibres likely play an important role. Future studies are needed to identify the humoral factors that mediate this demyelination. In addition to the reduction of the myelinated fibres, a reduction of unmyelinated fibres was observed. Therefore, primary axonal changes might also occur, to some extent, even in patients with neurolymphomatosis. Considering the fairly well-preserved nerve fibres at the site of demyelination, most axonal changes might secondarily occur distally from the site of the lymphomatous cell invasion. Interestingly, proximal demyelination with distal axonal changes, which is considered as the most common pathogenesis of neuropathy associated with lymphoma, was observed in both B cell and T cell types of lymphoma, although most of the patients had B cell lymphoma. It is also interesting that even patients with diffuse large B cell lymphoma, which was the most common type of lymphoma in the present study, showed a diverse neuropathic presentation, including neurolymphomatosis as well as paraneoplastic demyelination and vasculitis.

The difficulty of the diagnosis of lymphoma-associated neuropathy deserves attention. Neuropathy can occur at any stage of lymphoma, and neuropathic symptoms preceded the detection of lymphoma in approximately half of our patients. Therefore, elucidating the characteristics of neuropathy associated with lymphoma is important because it will enable the early detection of lymphoma and the immediate initiation of therapy for both the lymphoma and the neuropathy itself. The diagnostic pitfalls elucidated in this study include the scarcity of laboratory evidence suggestive of the presence of lymphoma, demyelinating features in the electrophysiological study, and the possible response to immunomodulatory therapies. These features resulted in the physicians recalling the diagnosis of Guillain-Barré syndrome or CIDP in some of the patients, as described in the case presentation (Supplementary material). Indeed, 11 patients in the present study fulfilled the EFNS/PNS electrodiagnostic criteria of definite CIDP (Joint Task Force of the EFNS and the PNS, 2010). However, patients with neurolymphomatosis in our study were characterized by a focality of neuropathic involvement even though the electrophysiological features fulfilled the EFNS/PNS criteria for CIDP, which is considered atypical (Joint Task Force of the EFNS and the PNS, 2010). In addition, the frequent presence of spontaneous pain in our patients would be suggestive of diseases other than CIDP, as pain is not common in CIDP (Nasu *et al.*, 2012). Pain has also been frequently reported in patients with neurolymphomatosis (Grisariu *et al.*, 2010; Baehring and Batchelor, 2012).

Currently, FDG-PET is the most sensitive and specific imaging technique available for patients with lymphoma (Cheson, 2011). In our study, a whole-body FDG-PET was useful for the detection of lymphoma in five of the six patients with lymphoma not observed through conventional means. With respect to patients previously diagnosed as having lymphoma, five of the six patients were positive in the FDG-PET study. Therefore, we should consider that FDG-PET does not necessarily reveal lymphoma in all patients. Case reports suggested the usefulness of this technique in the detection of neurolymphomatosis even in patients with negative MRI, CSF, or bone marrow analysis findings (Salm *et al.*, 2012). However, the specificity of FDG-PET study in the diagnosis of neurolymphomatosis (e.g. differentiation from neurolymphomatosis to CIDP) has not yet been established. In our study, FDG-PET was performed in a patient with paraneoplastic CIDP-type neuropathy (Patient 17). In this patient, no accumulation of FDG was observed in the PNS, although the presence of lymphoma was detected in the iliopsoas muscle.

Serum-soluble interleukin-2 receptor levels offer a rapid, reliable and non-invasive measure of disease activity and response to therapy in a broad spectrum of conditions associated with B or T cell immune activation, including lymphoma (Rubin and Nelson, 1990). Therefore, interleukin-2 receptor is used as an indicator for lymphoma in clinical practice, although it is not specific. Seventeen of the 24 examined patients (71%) showed elevated levels of serum soluble interleukin-2 receptor. Therefore, a high level of serum-soluble interleukin-2 receptor might lead to a suspicion of the concomitance of lymphoma in a patient with

neuropathy, although a normal level does not exclude the possibility of lymphoma.

Immunomodulatory treatment was more or less effective, particularly in the early phase of neuropathy, even in patients with neurolymphomatosis, potentially leading to the misdiagnosis of the cause of neuropathy. Because antineoplastic therapy is essential for the treatment of lymphoma, early diagnosis is necessary for neuropathy associated with lymphoma. The presence of the high degree of axonal loss irrespective of the type of neuropathy might also support this view. However, the response to the immunomodulatory treatments appeared to be better in patients with paraneoplastic neuropathies than in those with neurolymphomatosis; thus, immunomodulatory treatment before, during, or after antineoplastic therapy might also be beneficial for paraneoplastic neuropathy. The outcome determined by the 5-year survival rate in patients with non-Hodgkin's lymphoma with CNS involvement is generally poor, ranging from 14–20% (Hollender *et al.*, 2000; Kridel and Dietrich, 2011). In contrast, the outcome of neuropathy associated with lymphoma was better in our study, although the outcome was poorer than that for lymphoma overall (The Non-Hodgkin's Lymphoma Classification Project, 1997; Feugier *et al.*, 2005).

In conclusion, patients with lymphoma can manifest various neuropathic patterns, and neurolymphomatosis is the major cause of neuropathy. Demyelination unrelated to macrophages at the site of lymphomatous cell invasion and axonal degeneration distal from the site of the lymphomatous cell invasion were the most prominent pathologies of this type of neuropathy. The misdiagnosis of neurolymphomatosis as CIDP is frequent due to the presence of a demyelinating pattern and the initial response to immunomodulatory treatments in patients with neurolymphomatosis. The possibility of the concomitance of lymphoma should be actively considered in various types of neuropathy even if the neuropathy meets the diagnostic criteria of CIDP, particularly in patients complaining of pain.

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Supplementary material

Supplementary material is available at *Brain* online.

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Contrasting echogenicity in FDP-FCU: a diagnostic ultrasound pattern in sporadic inclusion body myositis

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AUTHOR CONTRIBUTIONS

Dr. Noto: design of the study, analysis of data, and drafting of the manuscript. Dr. Shiga and Tsuji: design of the study and revision of the manuscript. Drs. Kondo, Tokuda and Mizuno: interpretation and acquisition of data. Dr. Nakagawa: revision of the manuscript.

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Abstract

Introduction: We aimed to clarify whether muscle ultrasound (US) of the forearm can be used to differentiate between patients with sporadic inclusion body myositis (s-IBM) and those with s-IBM-mimicking diseases.

Methods: We compared the echo intensity (EI) of the flexor digitorum profundus (FDP) muscle and the flexor carpi ulnaris (FCU) muscles in patients with s-IBM (n = 6), polymyositis/dermatomyositis (PM/DM) (n = 6), and amyotrophic lateral sclerosis (ALS) (n = 6).

Results: We identified EI abnormalities in 100% of patients with s-IBM, 33% of those with PM/DM, and 33% of those with ALS. An "FDP-FCU echogenicity contrast", a US pattern involving a higher EI in the FDP than in the FCU, was observed in all patients with s-IBM, but in none of those with PM/DM or ALS.

Conclusions: "FDP-FCU echogenicity contrast" in muscle US is a sensitive diagnostic indicator of s-IBM.

Key words: ultrasound, muscle, diagnosis, inclusion body myositis, amyotrophic lateral sclerosis.

Introduction

Sporadic inclusion body myositis (s-IBM), one of the most common myopathies in older adults, is characterized by slowly progressive muscle weakness with a predilection for the quadriceps femoris and flexor digitorum profundus (FDP) muscles.[1,2] In needle electromyography (EMG), s-IBM can be confused with amyotrophic lateral sclerosis (ALS) because of the presence of so-called "neurogenic changes" such as high amplitude and long-duration motor unit potentials. These findings may be indicative of motor units with hypertrophied myofibers in chronic myopathy.[3] Hokkoku et al. reported that examination of the FDP muscle in EMG can reduce the risk of making a misdiagnosis of ALS in patients with s-IBM.[4] In addition, magnetic resonance imaging (MRI) of the forearm was also reported as useful for the diagnosis of s-IBM.[2] Selective involvement of the FDP has thus drawn attention in the clinical diagnosis of s-IBM.

Over the past few decades, high-frequency US of muscles and peripheral nerves has emerged as a non-invasive and simple tool to assist in the diagnosis of neuromuscular disorders. Therefore, we employed US of the FDP to accurately differentiate between patients with s-IBM and those with other s-IBM-mimicking diseases.

Materials and Methods

Subjects. Consecutive Japanese patients who presented with s-IBM (n = 6), polymyositis (PM) or dermatomyositis (DM) (PM: n = 2, DM: n = 4), or ALS (n = 6) at our hospital were enrolled. Informed consent was provided by all patients. The diagnosis of s-IBM or PM/DM was confirmed by muscle biopsy according to previously established criteria.[5,6] All ALS patients fulfilled Awaji criteria for probable/definite ALS, or showed progressive muscle weakness compatible with ALS.

Ultrasound. US imaging for all patients was performed by the same physician (Y.N.) using a GE LOGIQ P5 system with a 10-MHz linear array probe (GE healthcare Japan, Tokyo, Japan). Each subject lay in the supine position with the right elbow bent. The transducer was placed at 5 cm distal to the right olecranon, as shown in **Figure 1A**. The FDP could be identified as a triangular compartment adjacent to the ulna. The ulnar nerve is a landmark for identification of the 3 muscles [flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), and flexor carpi ulnaris (FCU)], because the nerve is encircled by those muscles. This transducer placement provides a favorable cross-sectional view of the FDP and FCU muscles at the same depth to enable effective comparison of echo intensity (EI) between them. Machine settings for image acquisition were preset and constant for all images without adjusting the focal point, gain, or time gain compensation settings.

Visual assessment of muscle echo intensity

The EI of the FDP muscle adjacent to the ulna was scored retrospectively by a single examiner (Y.N.), based on the Heckmatt rating scale, as follows: 1, normal; 2, slightly increased muscle EI with normal bone reflection; 3, moderately increased muscle EI with reduced bone reflection; and 4, severely increased muscle EI without bone reflection.[7] Then, the Heckmatt grade of the FCU muscle was scored by comparing it with that of the FDP muscle. A patient with increased "FDP-FCU echogenicity contrast" was defined when the EI grade of the FDP muscle was more than 1 grade higher than the FCU muscle. The proportion of patients who had increased FDP-FCU contrast was calculated in each disease group. Additionally, FDP/FCU EI ratios (EI score of the FDP muscle divided by score of the FCU muscle) by Heckmatt rating scale scoring were also calculated.

Quantitative assessment of muscle echo intensity

Quantification of muscle EI using gray scale analysis was performed to confirm the results obtained by visual assessment (i.e., Heckmatt rating scale scoring). This objective assessment was done with a standard histogram function, which was available in Adobe Photoshop (Adobe systems Inc., San Jose, CA, USA) as reported previously. [8] The mean gray values of FDP and FCU muscles were calculated respectively from the histogram, after encircling these muscles without surrounding fascia using the tracking software function. FDP/FCU EI ratios by gray scale analysis were calculated.

Assessment of muscle atrophy

At the site described above, the muscle cross-sectional areas (CSAs) of FDP and FCU were measured by continuous manual tracing of the muscle circumference excluding surrounding fascia. Measurement of the FDS muscle was omitted, because a fraction of the circumference of the FDS muscle was often out of the cross-sectional image we obtained. FDP/FCU CSA ratios were calculated.

Statistical analysis. All statistical analyses were performed using STATA software (Stata Corp., Texas, USA). Frequencies of all EI abnormalities and FDP-FCU contrast detected by US were tested with the Fisher exact test. Multiple comparisons of Heckmatt rating scale scores, mean gray values, FDP/FCU EI ratio of Heckmatt rating scale and gray scale analysis, and FDP/FCU CSA ratio between the 3 groups were tested with ANOVA and the Bonferroni procedure.

Standard protocol approvals. The local ethics committee of Kyoto Prefectural University of Medicine Graduate School of Medical science approved this study.

Results

Clinical characteristics and Echo intensity. Clinical profiles, Heckmatt rating scale scores for FDP and FCU, and detection rates of EI abnormalities and FDP-FCU contrast are shown in

Table 1. The mean Heckmatt rating scale score for the FDP and the FDP/FCU EI ratio by the Heckmatt rating scale were significantly higher in the s-IBM group than in the PM/DM or ALS groups. All s-IBM patients had EI abnormalities of the FDP muscle, whereas 2 of 6 PM/DM patients (33%) and 2 of 6 ALS patients (33%) had EI abnormalities. All EI abnormalities in the FDP muscles obtained from s-IBM arms showed a homogeneous high echoic pattern, whereas those obtained from PM/DM and ALS arms showed a rather heterogeneous high echoic pattern, as shown in **Figure 1B.** On visual assessment, none of the s-IBM patients had EI abnormality of the FCU, while 2 PM/DM patients and 2 ALS patients had increased EI in both the FCU and FDP muscles. In the PM/DM or ALS arms, no patients exhibited a higher EI in FDP than in FCU. Thus, the FDP-FCU echogenicity contrast pattern, indicating higher EI in FDP compared to the FCU muscle, was a characteristic finding in s-IBM patients (**Figure 1B**). Quantitative analysis using gray scale analysis also showed that the FDP/FCU EI ratio was significantly higher in the s-IBM group than in the PM/DM or ALS groups (P <0.01 and P <0.01, respectively). The mean FDP/FCU EI ratios of s-IBM, PM/DM, and ALS patients were 1.33, 0.88, and 1.02, respectively. No significant differences in any indices were found in comparing between the PM/DM and ALS groups.

Muscle cross-sectional area

Muscle CSAs and FDP/FCU CSA ratios are shown in **Table 2.** No significant difference in CSA of the FDP muscle was found among the 3 groups, whereas CSAs of the FCU muscles in s-IBM were significantly larger than those in ALS patients. The FDP/FCU EI ratio was significantly lower in the s-IBM group than in the PM/DM or ALS group.

Discussion

This study revealed that patients with s-IBM show "FDP-FCU echogenicity contrast", in which the EI of the FDP muscle is higher than that of the FCU muscle. This recognizable EI pattern was not seen in any of the patients with PM/DM or those with ALS in this study. These results demonstrate that muscle US of the forearm is a non-invasive and easily accessible diagnostic tool for s-IBM.

A high EI in muscle US suggests increased fibrous tissue or fatty degeneration in interstitial components of the muscle indicating chronic myopathy. A low EI reflects interstitial edema, which is often observed in the acute stage of inflammatory myopathy. [9, 10] It remains to be elucidated whether s-IBM is caused by an inflammatory or degenerative mechanism together with a secondary inflammatory process. In general, muscle biopsy of s-IBM patients reveals abundant chronic myopathic changes, such as marked variation in fiber size, endomysial fibrosis, and fatty degeneration. In this study, a visually homogeneous high echoic pattern of the FDP muscle was found in s-IBM patients, whereas EI abnormality in muscle in ALS and PM/DM patients showed a rather heterogeneous pattern. Although we found that mean gray scale values of the FDP in s-IBM were higher than those in PM/DM and ALS patients, it is unclear what determines the increased echoic pattern (i.e., homogeneous or heterogeneous). Further study related to the correlation between the visual ultrasound pattern and the muscle pathology of s-IBM is needed.

Sekul et al. reported that muscle MRI of the forearm demonstrates selective involvement of the FDP muscle in up to 95% of s-IBM patients.[2] Furthermore, they observed marbled brightness of the FCU and FDS muscles on T1-weighted MRI in 33 and 29% of patients, respectively, and concluded that the FDS muscle was spared even in late stages of s-IBM. In addition, a quantitative motor unit potential (MUP) analysis revealed decreased amplitude, short duration, and reduced MUP size index in the FDP.[4] Both the MRI study and quantitative MUP indicate

that selective involvement of the FDP can be a unique finding to identify patients with s-IBM. In our US study, the frequencies of a high EI of the FDP and FCU muscles were comparable to the MRI study (100% in FDP and 33% in FCU muscles), indicating that US image analysis is another promising technique to identify FDP muscle pathology. This study also revealed decreased FDP/FCU CSA ratios in s-IBM patients, indicating selective atrophy of the FDP. Among the various tests, muscle US is advantageous because it is not only less invasive than EMG or muscle biopsy, but it is also far less expensive than MRI. In addition, US assessment is readily available in any hospital and can be repeated easily at the bedside.

There are a few limitations in this study. First, our findings were obtained from a small population of patients. Second, the patients with PM/DM in this study were younger than those with ALS. Muscle echo intensity increases with age due to replacement by fat or fibrous tissue.[8] This could have influenced the results of echo intensity in older patients to some extent. Finally, the US examinations in this study were done by a single examiner who was not blinded to the clinical diagnoses. A blinded design with a larger number of patients including inter- or intra-rater reliability assessment are essential to confirm the results of our study.

Abbreviation

ALS = amyotrophic lateral sclerosis

CSA = cross-sectional area

DM = dermatomyositis

EI= echo intensity

FCU = flexor carpi ulnaris

FDP = flexor digitorum profundus

FDS = flexor digitorum superficialis

PM = polymyositis

s-IBM= sporadic inclusion body myositis

US = ultrasound

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Figure legends

Figure 1. Transducer position used to visualize the flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), and flexor carpi ulnaris (FCU) muscles simultaneously (A). The ulnar nerve (*) is encircled by the FDP, FDS, and FCU muscles. Patterns of muscle ultrasound images in a normal subject, sporadic inclusion body myositis (s-IBM), polymyositis, and amyotrophic lateral sclerosis (B). Note moderately high echo intensity of the FDP and normal echo intensity of the FCU in the s-IBM patient ("FDP-FCU echogenicity contrast") (arrow in B). Slightly high echo intensities of the FDP and FCU muscles in PM and ALS patients (B).

Table 1. Demographics, clinical findings, and echo intensity abnormalities.

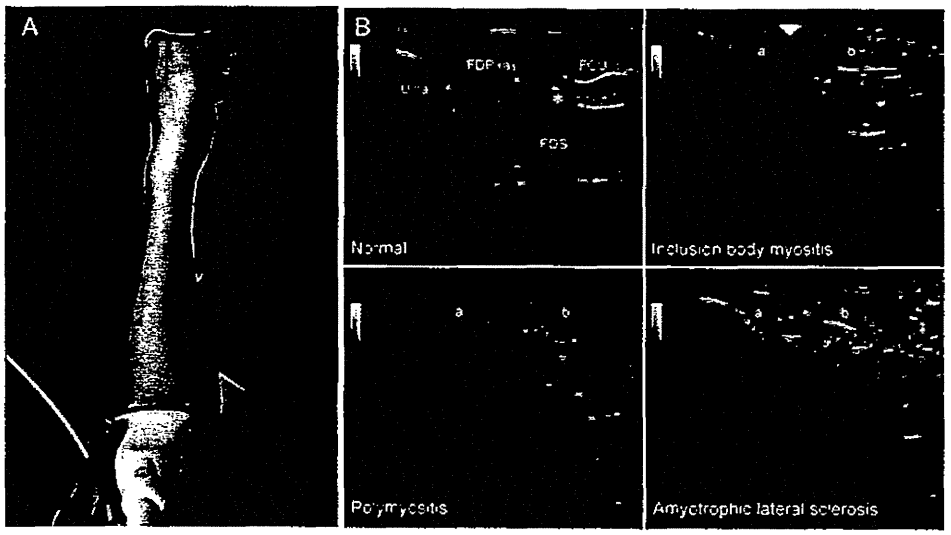
	s-IBM (n = 6)	PM/DM (n = 6)	ALS (n = 6)
Gender (M:F)	5:1	3:3	3:3
Age; mean (range)	71.5 (68-79)	56.3 (39-72)	72.2 (62-79)
Disease duration (months); mean (range)	56.7 (14-120)	49.3 (1-215)	29.8 (2-94)
Heckmatt rating scale of FDP; mean (range)	2.7 (2-3)* †	1.3 (1-2)	1.3 (1-2)
Heckmatt rating scale of FCU; mean (range)	1.3 (1-2)	1.3 (1-2)	1.3 (1-2)
FDP/FCU Heckmatt rating scale ratio; mean	2.2* †	1.0	1.0
EI abnormality of any FDP and FCU muscle; n (%)	6 (100) ** ††	2 (33)	2 (33)
FDP-FCU echogenicity contrast; n (%)	6 (100) ** ††	0 (0)	0 (0)

*P<0.05 and **P <0.01 vs. PM/DM. †P <0.05 and ††P <0.01 vs. ALS. s-IBM, sporadic inclusion body myositis; PM/DM, polymyositis/dermatomyositis; ALS, amyotrophic lateral sclerosis; EI, echo intensity; FDP, flexor digitorum profundus muscle; FCU, flexor carpi ulnaris muscle. FDP/FCU Heckmatt rating scale ratio is defined as EI score of the FDP muscle divided by EI score of the FCU muscle. EI abnormality is defined as Heckmatt ration scale ≧2. FDP-FCU echogenicity contrast is defined as an echo intensity pattern of a higher intensity in FDP than in FCU muscle.

Table 2. Comparison of muscle cross-sectional area.

	s-IBM (n = 6)	PM/DM (n = 6)	ALS (n = 6)
CSA of the FDP muscle (mm^2); mean (range)	80.5 (63.0-117.4)	165.9 (90.4-332.3)	106.3 (62.1-148.6)
CSA of the FCU muscle (mm^2); mean (range)	131.8 (100.9-149.5) †	110.3 (73.9-135.6)	86.3 (49.4-129.4)
FDP/FCU CSA ratio: mean	0.61** †	1.47	1.28

**P <0.01 vs. PM/DM. †P <0.05 vs. ALS. s-IBM, sporadic inclusion body myositis; PM/DM, polymyositis/dermatomyositis; ALS, amyotrophic lateral sclerosis; CSA, cross-sectional area; FDP, flexor digitorum profundus muscle; FCU, flexor carpi ulnaris muscle. FDP/FCU CSA ratio is defined as CSA of the FDP muscle divided by CSA of the FCU muscle.



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