Potential pitfalls in the differential diagnosis of myositis *versus* hereditary myopathies

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Abstract

Objective

Hereditary myopathies and myositis share similar clinical features, making diagnosis challenging. The 2017 EULAR/ACR classification criteria for idiopathic inflammatory myopathies (myositis) provide a probability score for myositis and its subtypes. This study aims to test the accuracy of these criteria in distinguishing myositis from hereditary myopathies and to identify diagnostic pitfalls.

Methods

This retrospective study examined data from 105 patients diagnosed with genetically confirmed myotonic dystrophy type 1 and 2 (DM1 and DM2), facioscapulohumeral muscular dystrophy (FSHD), limb girdle muscular dystrophy (LGMD) and Duchenne and Becker muscular dystrophy (DMD and BMD). The performance of the 2017 EULAR/ACR criteria for myositis was tested on patient data to identify variables leading to misdiagnosis.

Results

Of the 105 patients with hereditary myopathy, 50% of DM1, 47.8% of DM2, 25% of FSHD, 35.3% of LGMD, 0% of BMD, and 36.4% of DMD patients were misclassified according to the 2017 EULAR/ACR criteria as having 'possible', 'probable' or 'definite' myositis, resulting in an overall specificity of 63.8%. The most frequently proposed myositis subtype in misclassified cases was inclusion body myositis. Analysis of the individual criteria items revealed that proximal muscle weakness, increased CK, perifascicular atrophy and endomysial infiltration in the muscle biopsy were particularly misleading factors.

Conclusion

The diagnostic challenge of differentiating between inflammatory and hereditary myopathies is reflected by the relatively low specificity of the classification criteria in this study. Relevant factors leading to misdiagnosis include similarities in clinical presentation and diagnostic findings, as well as late-onset disease manifestations, e.g. in LGMD, DM1, DM2.

Key words

classification criteria, myositis, hereditary myopathies

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Introduction

Differentiating the cause of a myopathic condition can be challenging due to a wide range of possible aetiologies and overlapping clinical features. While myositis syndromes are a clinically significant group of acquired myopathies, hereditary myopathies due to a genetic cause constitute another large group of muscle disorders, including myotonic dystrophies, muscular dystrophies, and myofibrillar myopathies. The most common hereditary myopathies in adults are myotonic dystrophy type 1 and type 2 (DM1 and DM2), which are autosomal inherited multisystem diseases. Typical symptoms include myotonic phenomena, muscle weakness, cataracts, cardiac involvements and endocrine disorders (1).

Facioscapulohumeral muscular dystrophy (FSHD) is caused predominantly by an autosomal dominant inheritance, and its clinical phenotype is usually characterised by pathognomonic involvement of the facial and shoulder girdle muscles, but can also show large variability, most likely due to genetic and epigenetic factors (2, 3). Limb-girdle muscular dystrophy (LGMD) evolves in childhood or adulthood and is inherited in an autosomal dominant or an autosomal recessive trait depending on the affected gene. The causative mutations affect various proteins of the cell membrane, cell nucleus and cytosol. The resulting diseases show variable age of onsets and clinical phenotypes, but mostly have a progressive muscle weakness and atrophy of the proximal muscles of the shoulder and pelvic girdle in common (4). Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) represent the most common hereditary myopathies in childhood and are the result of a spontaneous or inherited pathogenic variant of the DMD gene, which is localised on the X chromosome (5). DMD usually develops in early childhood and shows a more severe, rapidly progressive course of disease with involvement of the respiratory muscles and cardiomyopathy (6, 7), whereas BMD appears in adolescence and is associated with a milder phenotype (8).

Despite the availability of genetic testing, the large phenotypic variability of hereditary myopathies may complicate and delay the diagnostic process. The most important differential diagnosis in adulthood is myositis. Historically, the earliest known myositis subtypes were dermatomyositis (DM), clinical amyopathic DM (CADM), juvenile myositis (JM), juvenile dermatomyositis (JDM), polymyositis (PM), and inclusion body myositis (IBM). In recent years, new subtypes have emerged due to improvement in pathophysiological understanding and diagnostic methods, including immune-mediated necrotising myopathy (IMNM), antisynthetase syndrome (ASyS), overlap myositis (OM) and non-specific myositis (9). Diagnosis is not possible by a single marker but requires the combined evaluation of clinical, biochemical and histological markers.

The EULAR/ACR classification criteria (10), published in 2017, are currently the standard for classification of adult and adolescent myositis in daily care and for clinical trials. In addition to distinguishing the major subgroups of myositis, another purpose of the 2017 criteria is to differentiate myositis from mimicking diseases. A scoping review has recently been published which analyses the performance of the EULAR/ACR classification criteria in previous publications of different patient groups worldwide (11). The sensitivity of the criteria for myositis exhibited a range of 80 to 100%. Upon examination, the specificity was found to be notably high, reaching a level of 90%. However, the control groups consisted mostly of autoimmune diseases without definite myositis and fewer metabolic myopathies or neuropathies, while hereditary myopathies were scarcely represented despite being an important disease mimic in clinical practice (12-16). Therefore, the goal of this study was to test the accuracy of the EULAR/ACR classification criteria for differentiating myositis from hereditary myopathies in order to identify possible pitfalls in the diagnosis.

Methods

This retrospective study included patients diagnosed with hereditary myo-

pathies from a single neuromuscular centre (Department of Neurology, University Medical Centre, Göttingen, Germany) until July 2024. Approval was granted by the Ethics Committee of the University Medical Centre Göttingen on 7th July 2024 (ethics number: 9/8/24). The hereditary myopathies studied include FSHD, DM1, DM2, DMD, BMD and several subgroups of LGMD.

The survey used a retrospective methodology, incorporating patients' electronic and paper medical records, including examination findings, laboratory tests, progress reports, and medical letters.

A comprehensive evaluation required access to data on age at disease onset, strength testing of extremities and trunk muscles, dysphagia, skin findings, antibody diagnostics, laboratory features (creatine kinase (CK), alanine aminotransferase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH)), muscle histology, and electron microscopy findings.

Skin findings were categorised as absent if not documented in the physical exam. The absence of a muscle biopsy or antibody finding was not an exclusion criterion.

The EULAR/ACR criteria were applied using the online calculator available at http://www.imm.ki.se/biostatistics/calculators/iim/. The calculator was used to categorise the probability of the presence of myositis based on the respondents' answers to a total of 17 items. The calculator provides the diagnostic certainties termed 'definite', 'probable', or 'possible' myositis. When the calculator failed to identify myositis, the case was classified as 'undefined' and a probability value was provided by the calculator. In some cases, the calculator also provides a categorisation for the subgroup of myositis. The subgroups that are currently differentiated using the EULAR/ACR criteria are IBM, DM, PM, JM and JDM. It should be noted that the aforementioned criteria were developed for suspected cases of myositis. The patients who were retrospectively examined in the present study did usually not have a suspected diagnosis of myositis.

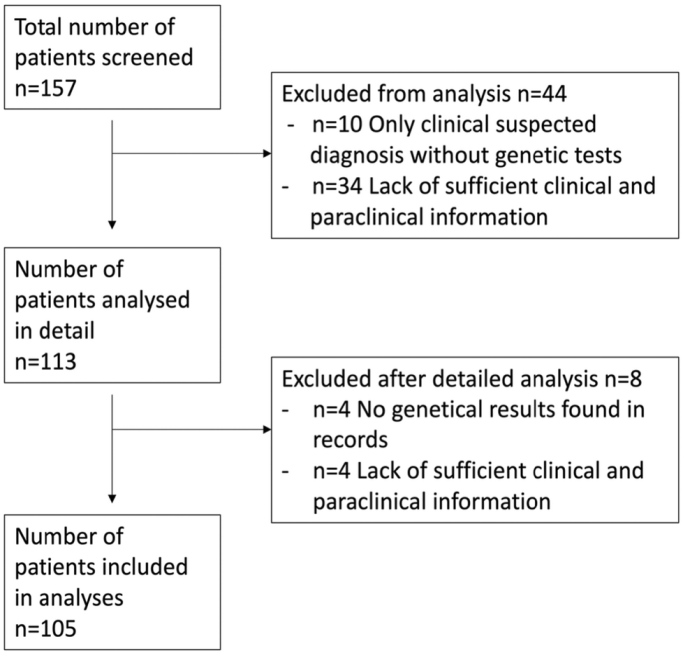


Fig. 1. Flow chart of recruitment.

Patient recruitment

The selection of patient cases for further analysis was based on internal documentation of neuromuscular patients' diagnoses, with a focus on conditions such as DM1, DM2, FSHD, DMD, BMD, and LGMD. Cases were excluded from the study if the diagnosis was merely suspected or if the genetic findings were not present in the patient files. In a subsequent step, the patient's medical records and findings available in the hospital system were examined for comprehensive information regarding the age of the disease manifestations, the clinical distribution pattern of muscle paresis and the possible presence of a muscle biopsy. Cases were excluded if the available information regarding the clinical appearance or manifestation of the disease was considered insufficient.

The first analysis included a total of 157 patients. In 10 of them, the clinical diagnosis of hereditary myopathy was only suspected but not genetically confirmed, and in 34 patients, the distribution pattern of paresis was not documented in the patient files. Subsequently, 113 patients were analysed in detail based on medical reports and genetic findings. As a result of this precise analysis, eight patients were excluded. In four cases, the information on the clinical presentation was insufficient, while in four other cases the information on the confirmed genetic findings was missing. 105 patients were subsequently subjected to analysis (Fig. 1).

Statistical methods

The specificity was determined by calculating the rate of false positive cases with hereditary myopathies that were misclassified as 'probable', 'possible' or 'definite' myositis based on the 2017 EULAR/ACR web-based calculator. Data compilation and calculations were performed using Microsoft Excel.

Results

Baseline characteristics of patient cohort with hereditary myopathies

The most prevalent diagnosis was DM1 (n=24), followed by DM2 (n=23) and FSHD (n=20). Seventeen patients were diagnosed with LGMD, while those with DMD and BMD were represented in the analysis with 11 and 10 patients, respectively.

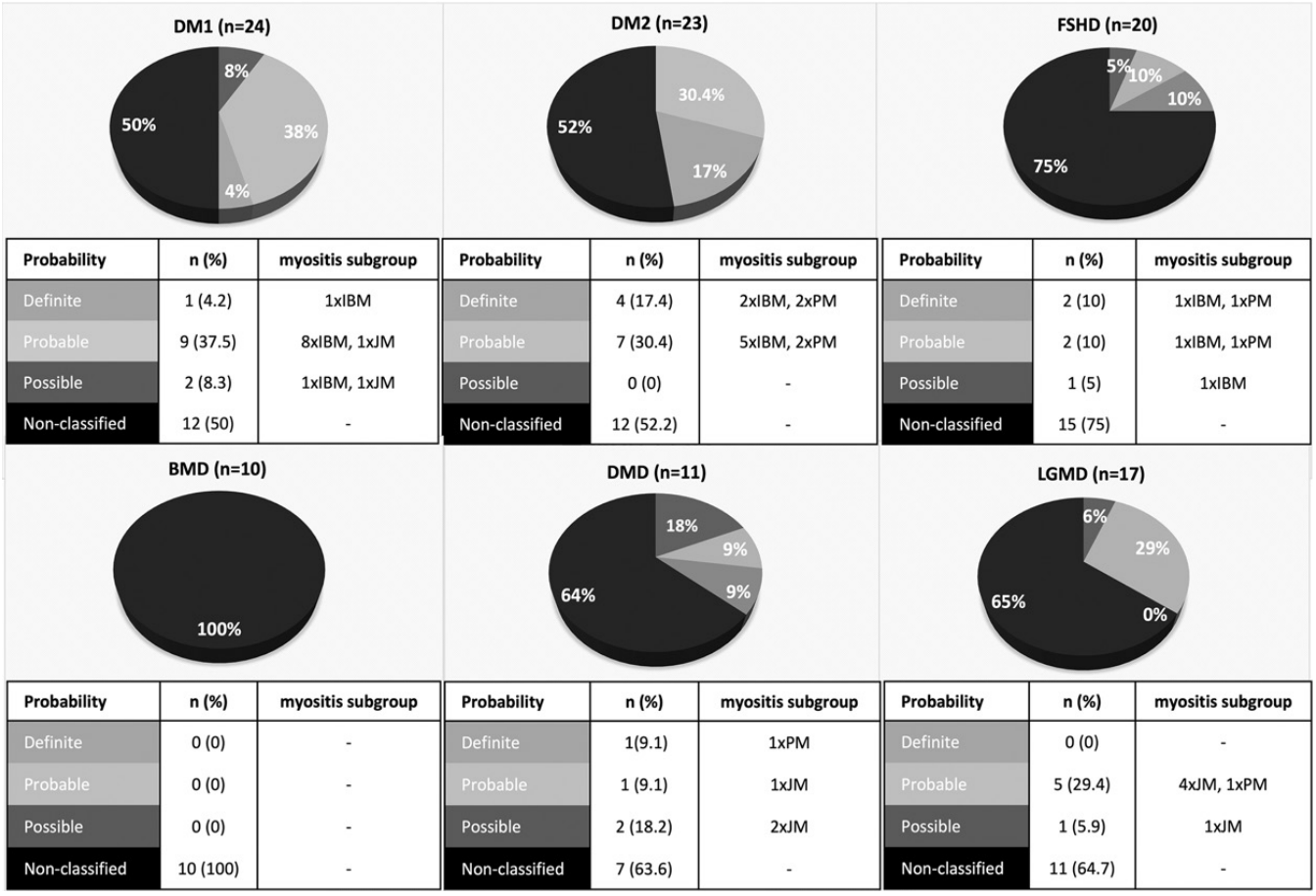
The mean age of all patients was 50.5 years (SD=16.8), with the majority of patients being male (54.3%). The largest proportion of women was observed in the DM2 group (69.6%).

At the time of data collection, patients with DMD were the youngest cohort, followed by those with BMD. Patients

Table I. Overview of the patient cohort.

	All hereditary myopathies n=105	DM1 n=24	DM2 n=23	FSHD n=20	DMD n=11	BMD n=10	LGMD n=17
Age (in years) mean (SD)	50.5 (16.8)	48.8 (15.2)	61.6 (12.6)	60.2 (16.0)	34.0 (9.0)	39.7 (17.0)	43.4 (12.6)
Gender Female (in %)	45.7	58.3	69.6	35	9.1	0	58.8

DM1: myotonic dystrophy type 1; DM2: myotonic dystrophy type 2; FSHD: facioscapulohumeral muscular dystrophy; DMD: Duchenne muscular dystrophy; BMD: Becker muscular dystrophy; LGMD: limb-girdle muscular dystrophy.



Probability	n (%)	myositis subgroup
Definite	1 (4.2)	1xIBM
Probable	9 (37.5)	8xIBM, 1xJM
Possible	2 (8.3)	1xIBM, 1xJM
Non-classified	12 (50)	-

Probability	n (%)	myositis subgroup
Definite	4 (17.4)	2xIBM, 2xPM
Probable	7 (30.4)	5xIBM, 2xPM
Possible	0 (0)	-
Non-classified	12 (52.2)	-

Probability	n (%)	myositis subgroup
Definite	2 (10)	1xIBM, 1xPM
Probable	2 (10)	1xIBM, 1xPM
Possible	1 (5)	1xIBM
Non-classified	15 (75)	-

Probability	n (%)	myositis subgroup
Definite	0 (0)	-
Probable	0 (0)	-
Possible	0 (0)	-
Non-classified	10 (100)	-

Probability	n (%)	myositis subgroup
Definite	1(9.1)	1xPM
Probable	1 (9.1)	1xJM
Possible	2 (18.2)	2xJM
Non-classified	7 (63.6)	-

Probability	n (%)	myositis subgroup
Definite	0 (0)	-
Probable	5 (29.4)	4xJM, 1xPM
Possible	1 (5.9)	1xJM
Non-classified	11 (64.7)	-

Fig. 2. Misclassification of patients with hereditary myopathies based on the 2017 EULAR/ACR criteria for myositis.
DM1: myotonic dystrophy type 1; DM2: myotonic dystrophy type 2; FSHD: facioscapulohumeral muscular dystrophy; DMD: Duchenne muscular dystrophy; BMD: Becker muscular dystrophy; LGMD: limb-girdle muscular dystrophy; IBM: inclusion body myositis (IBM); PM: polymyositis; JM: juvenile myositis.

with DM2 were the oldest group. In BMD, the cohort was 100% male, consistent with the x-linked inheritance of the disease. The DMD cohort included one female conductor (n=1). Table I provides an overview of the age and gender distribution.

Specificity of the EULAR/ACR classification criteria in different hereditary myopathies

A total of 38 patients (36.2%) were incorrectly classified as 'possible', 'probable', or 'definite' myositis, indicating an overall specificity of 63.8%. 19 patients (18.1%) were misclassified as having IBM, followed by 11 patients (10.4%) being misclassified as JM, and 8 patients (7.6%) as PM. A definitive diagnosis of myositis was made in a total of 8 patients, followed by a probable diagnosis in 24 patients, and a possible diagnosis in 6 patients.

The disease with the lowest degree of specificity was DM1. In total, 50% of patients were incorrectly categorised as 'possible', 'probable' or 'definite' myositis. The majority were misdiagnosed as IBM, followed by JM.

Another myopathy with low specificity was DM2, 11 patients from 23 DM2 patients (47.8%) were incorrectly classified as myositis. Four patients were classified as having 'definite' myositis, with a further 7 patients designated as 'probable' myositis. In these cases, the most common misclassification was IBM, followed by PM.

In the DMD group 56.4% of patients

were misclassified with one patient erroneously classified as JM and another as PM, whereas the latter was a female conductor. A total of four patients were incorrectly categorised as myositis. BMD demonstrated a specificity of 100%, with no misclassified patient in this group.

In the LGMD group, 6 patients were misclassified as 'probable' and 'possible' myositis. In particular, the patients were incorrectly categorised as juvenile myositis.

The specificity of FSHD was relatively superior with 75%. In the FSHD cohort, five patients out of a total of 20 were incorrectly categorised as myositis, with erroneous classification as IBM and PM being the most common.

The respective classification based on the EULAR/ACR criteria and the specificities with regard to the different myopathies are presented in Figure 2.

Item analysis of the EULAR/ACR classification criteria in patients with hereditary myopathies

We analysed the individual items of the 2017 EULAR/ACR criteria in order to identify the variables with the greatest impact on potential misclassification of hereditary myopathies as myositis.

Analysis of the age of onset of symptoms revealed a general tendency for earlier onset in patients with hereditary myopathies. 40 patients (38.1%) in this study cohort exhibited symptoms before the age of 18. In DMD, BMD, followed by LGMD, patients with an early onset of symptoms constitute the largest proportion overall as expected. In DMD, only the female conductor showed a delayed onset of the disease (+40 years). In the case of BMD, only one patient exhibited symptoms in the middle age group (18-40 years) and one in the older age group (40+). All others had an early onset (0-17 years) of symptoms. In the LGMD cohort no individuals with onset after the age of 40 were observed. In contrast, over 50% of patients with DM2 showed symptom onset after the age of 40, with no cases of the disease manifesting before the age of 18. In the case of FSHD and DM1, the onset of symptoms occurred after the age of 18 in at least 70% of cases respectively.

When focusing on the muscular distribution pattern of the paresis, a majority of 81 patients (77.1%) with hereditary myopathies showed symmetrical weakness of the proximal lower extremities and 70 patients (66.7%) exhibited symmetrical weakness of the proximal upper extremities. The item of the EULAR/ACR criteria, which refers to the more pronounced weakness in the neck flexors compared to the strength levels of the neck extensors, was also present in 45 patients (42.8%). In 49 patients (46.6%), the proximal leg muscles presented a relatively weaker performance than the distal muscles. Symmetrical weakness of the upper extremities was particularly evident in DMD, LGMD and FSHD, while patients with BMD did not exhibit symmetrical weakness of the upper extremities at the time of the examination. As for the lower extremities, the analysis identified symmetrical weakness as a prevalent feature in DMD (100%), LGMD (100%) and DM2 (82.6%). The pronounced involvement of the neck flexors relative to the neck extensors was most frequently observed in DM1 (83.3%). This finding was rarely observed in FSHD and BMD (25% and 10%, respectively). The weakness of the proximal muscles of the extremities relative to the distal muscles is particularly evident in cases of DM2 and LGMD.

The presence of all four clinical items from the EULAR/ACR criteria ('Objective symmetric weakness, usually progressive, of the proximal upper extremities', 'Objective symmetric weakness, usually progressive, of the proximal lower extremities', 'Neck flexors are relatively weaker than neck extensors', 'In the legs proximal muscles are relatively weaker than distal muscles'), which corresponds to typical muscle involvement in myositis, was present in a total of 15 patients with hereditary myopathies. The disease group which best fulfilled all 4 items was LGMD, with 35.3% of the disease group (n=6).

A total of 31 patients (29.5%) showed signs of dysphagia. The diseases with the highest incidence of dysphagia were DMD (n=8, 72.7) and DM1 (n=13, 54.2%).

With regard to the laboratory parameters, which are taken into account in the EULAR/ACR criteria, the muscle decay parameters were elevated in 93 patients. A total of six patients were tested for MSA and MSS with none found to be positive for anti-Jo-1 antibodies. Muscle biopsy findings were only available for 19 patients (18.1% of the total number of patients). Muscle biopsies revealed the presence of endomysial inflammatory infiltrates in four cases (DMD=2, FSHD=1, LGMD=1) and perimysial inflammatory infiltrates in three cases (DMD=1, FSHD=1, DM2=1). Rimmed vacuoles were observed in one muscle biopsy from an LGMD patient.

Skin changes reminiscent of dermatomyositis were not described in any of the patients with hereditary myopathies.

Table II shows the detailed analysis of the individual hereditary myopathies in relation to the items of the EULAR/ACR classification criteria.

Discussion

Hereditary myopathies represent a relevant differential diagnosis in suspected myositis cases. In this study, we demonstrate a specificity of 63.8% when applying the EULAR/ACR classification criteria for myositis to a cohort consisting only of hereditary myopathies, compared to previous studies on the specificity of the criteria using mixed disease control groups. The lowest level of specificity is demonstrated for DM1 (50%) and IBM representing the most common misdiagnosis. This misclassification correlates with the distal emphasis in the distribution of paresis in DM1 and the similarly high proportion of dysphagia in patients with DM1. The specificity for DM2 is also low with 52.2%. Here too, the misclassification to IBM is particularly noteworthy, which can be explained by the older age of the cohort analysed, the slightly higher age of manifestation of the disease and the distribution of paresis. Literature indicates that FSHD and LGMD should be considered as mimics of IBM (17,18), our data suggest DM1 and DM2 as further potential differential diagnosis when suspecting IBM in patients.

In the event of muscle weakness in chil-

Table II. EULAR/ACR classification criteria in patients with hereditary myopathies.

n (%)	All HM n=105	DM1 n=24	DM2 n=23	FSHD n=20	DMD n=11	BMD n=10	LGMD n=17
Age of onset							
0-17	40 (38.1)	6 (25)	0 (0)	6 (30)	10 (90.9)	7 (70)	11 (64.7)
18-39	37 (35.2)	13 (54.2)	10 (43.5)	7 (35)	0 (0)	1 (10)	6 (35.3)
40+	27 (25.7)	5 (20.8)	13 (56.5)	7 (35)	1 (9.1)	1 (10)	0 (0)
missing	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)
Muscle weakness							
Sym. weakness of the proximal upper extremities	70 (66.7)	15 (62.5)	16 (69.6)	15 (75)	11 (100)	0 (0)	13 (76.5)
Sym. weakness of the proximal lower extremities	81 (77.1)	15 (62.5)	19 (82.6)	14 (70)	11 (100)	5 (50)	17 (100)
Neck flexors are relatively weaker than neck extensors	45 (42.9)	20 (83.3)	9 (39.1)	5 (25)	4 (36.4)	1 (10)	6 (35.3)
In the legs proximal muscles are relatively weaker than distal muscles	49 (46.7)	4 (16.7)	18 (78.3)	6 (30)	5 (45.5)	4 (40)	12 (70.6)
Skin manifestations							
Heliotrope rash	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gottron's papules	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gottron's sign	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Dysphagia	31 (29.5)	13 (54.2)	5 (21.7)	1 (5.0)	8 (72.7)	0 (0)	4 (23.5)
Anti Jo-1 antibody available	**n=6**	**n=0**	**n=4**	**n=0**	**n=1**	**n=0**	**n=1**
positive	0 (0)	-	0 (0)	-	0 (0)	-	0 (0)
Elevated muscle enzyme levels	93 (88.6)	22 (91.7)	20 (87.0)	16 (80)	10 (90.9)	9 (90)	16 (94.1)
Muscle biopsy available	**n=19**	**n=0**	**n=7**	**n=5**	**n=2**	**n=1**	**n=4**
Endomysial infiltration of mononuclear cells	4 (21.1)	-	0 (0)	1 (20)	2 (100)	0 (0)	1 (25)
Perimysial and/or perivascular infiltrations of mononuclear cells	3 (15.8)	-	1 (14.2)	1 (20)	1 (50)	0 (0)	0 (0)
Perifascicular atrophy	11 (57.9)	-	5 (71.4)	2 (40)	1 (50)	1 (100)	2 (50)
Rimmed vacuoles	1 (5.3)	-	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)

HM. hereditary myopathies; DM1: myotonic dystrophy type 1; DM2: myotonic dystrophy type 2; FSHD: facioscapulohumeral muscular dystrophy; DMD: Duchenne muscular dystrophy; BMD: Becker muscular dystrophy; LGMD: limb-girdle muscular dystrophy.

dren, a hereditary myopathy is a more probable cause than the presence of juvenile myositis. Nevertheless, myositis should be considered as an alternative diagnosis, particularly in cases with myalgia and skin symptoms. In accordance with the early onset of DMD, three patients in this study have been misclassified as having juvenile myositis. Furthermore, LGMD exhibits an overlap with the distribution pattern of juvenile myositis, particularly in the early stages of the disease. Consequently, five LGMD patients in our cohort are misclassified as JM.

The design of the 2017 EULAR/ACR classification criteria for myositis likely explains the inherent difficulties in accurately classifying and distinguishing between non-myositis (hereditary myopathy) and myositis. These difficulties are particularly evident in the context of the age of onset, the clinical distribution pattern, and the results of the muscle biopsy. As previously outlined, the age of onset of hereditary myopathies exhibits significant variability within a given disease. For instance, the age of onset of DM1 demonstrates considerable variation, ranging from congenital forms to manifestation in older adulthood. Late onset of disease is characteristic for DM2 (19) and has been described in FSHD (18) and LGMD (20). The clinical appearance of myositis and hereditary myopathies can also be very similar: symmetrical proximal paresis of the upper and lower extremities is common, with or without involvement of the trunk muscles, and clinical features typical of hereditary myopathies, such as myopathic facies, myotonia, or scapular winging, may be very subtle in some individuals or may become apparent only at a later stage of the disease. Myalgias are also described in both myositis and hereditary myopathies (21). The sole presence of inflammation in the muscle, detected on muscle biopsy, is not a sufficient marker for differentiaing between hereditary myopathies and myositis. Especially LGMD, DMD and FSHD frequently show inflammatory changes on muscle biopsy (2).

In DMD, inflammation is a key histological feature alongside necrosis and fibrosis, resulting from vulnerable myofibres due to the loss of dystrophin gene function (22). In FSHD and LGMD, detailed analysis of muscle histology frequently reveals inflammatory infiltrates, which poses diagnostic challenges (23).

In muscle biopsies from patients with dysferlinopathy, a subtype of LGMD (LGMD R2), evidence of inflammatory changes ranged from 34% (24) to 100% (25) of all patient samples examined (n=40 and n=10, respectively). The in-

flammatory changes in dysferlinopathy were particularly evident in the endomysium or perivascular area and consisted of CD4+ and CD8+ cells as well as macrophages (26). MHC-I-positive fibres have also been observed in dysferlinopathies (25). An initial misclassification of dysferlinopathy as polymyositis due to histopathological inflammatory infiltrates and a reportedly rapid progression of symptoms was observed in 25% of cases in a study involving 40 patients (27). Other LGMD subtypes with prominent histological inflammatory changes include calpainopathy (LGMD R1) (28) and α-dystroglycanopathy (FKRP-related, LGMD R9) (29).

FSHD often shows inflammatory infiltrates in muscle biopsies. In a study by Arachata *et al*., 72% (13/18) of patients showed more than 50 inflammatory mononuclear cells per 1,000 muscle fibres, and in 33% even more than 600 inflammatory mononuclear cells per 1,000 muscle fibres were detected (30). Importantly, infiltration of CD8+ cells into non-necrotic fibres is pathognomonic for IBM and usually not observed in FSHD or LGMD, making this feature a reliable discriminator (25, 30). Autophagic vacuoles, also known as rimmed vacuoles, are an additional hallmark of IBM, though they may not be present in all cases (31).

Apart from the items in the 2017 classification criteria, there are further factors that may challenge the clinical differentiation between myositis and hereditary myopathies. For instance, the variability of the course of the disease can be a contributing factor and is exemplified by the slow progression of hereditary myopathies and the slow progression of some inflammatory myopathies, particularly IBM. Consequently, the disease progression itself is not always a sufficient characteristic for differentiation (32). Moreover, an initial favourable outcome resulting from immunosuppressive therapy in cases of hereditary myopathies has been documented, *e.g*. in a small case series with FSDH patients demonstrating improvement in muscle strength and CK levels following glucocorticoid administration (33), or in a randomised, double-blind, parallel group study of DMD patients with a positive response to glucocorticoid therapy (34). Although the therapeutic effects of immunosuppression are not long-lasting in hereditary myopathies, an initial favourable response can be potentially misleading in finding the correct diagnosis.

The EULAR/ACR criteria are currently being updated and revised. In particular, the revision of the criteria aims to better separate the various new subgroups described (11, 35). In the original development of the criteria, hereditary myopathies were relatively underrepresented in the control group with 16% compared to a majority of 36.5% consisting of autoimmune diseases, while the rest of the comparators spanned a wide range including motor neuron disease/neuropathies, other myopathies, myalgias, and dermatologic diseases (10). Later external validation studies included even fewer muscle dystrophies as comparators with percentages ranging from 0-6% (12-15) and a maximum of 25% in a paediatric cohort (16). However, our data suggest that the clinical features of hereditary myopathies might be closer mimickers of myositis compared to systemic inflammatory diseases overall, as evidenced by the significantly lower spe-cificity in this study. Therefore, the inclusion of more hereditary myopathies as comparators may well be considered and discussed in the current efforts to revise the classification criteria in order to improve their accuracy.

In order to enhance the discriminatory capacity of the new criteria for distinguishing between other neurological diseases such as hereditary myopathies, it is necessary to incorporate additional criteria and modify the weighting of the items.

While the clinical appearance of myositis is undoubtedly pertinent to the diagnosis, the present study has demonstrated that the discriminatory power based on the clinical distribution pattern, including dysphagia, is not sufficient. In recent years, further diagnostic findings characteristic for myositis have emerged and may enrich the criteria. In this context, the use of a broader range of MSA and MAA is of particular importance (36). In the cohort analysed, anti-Jo-1 autoantibodies were only tested in 6 patients. This is due to the fact that the differential diagnosis of myositis was not prioritised in most cases of the present cohort.

Previous studies have shown that the presence of lung involvement, the inclusion of more dermatologic features, and a more precise description of muscle biopsy findings could lead to a higher sensitivity and specificity of the EULAR/ACR criteria (37, 38) and would also serve to differentiate from hereditary myopathies.

A current review on the performance of the 2017 EULAR/ACR criteria (11) also suggests the incorporation of additional diagnostic procedures such as muscle MRI and EMG, in order to enhance the distinction between myositis and its differential diagnoses. However, it is important to note that these diagnostic tests are not specific and may also have a potential for mimicry, especially in regard to hereditary myopathies. For example, the detection of oedema on muscle MRI is suggestive of active myositis, but may also occur in hereditary myopathies (39, 40). EMG may show a myopathic damage pattern in both hereditary myopathies and myositis, with pathological spontaneous activity more evident in myositis (41). Nevertheless, EMG may aid in the differential diagnosis, *e.g*. revealing signs of myotonia in myotonic dystrophies (42).

Limitations

There are several limitations of this study. First, the monocentric data collection results in a relatively small sample size, hindering definitive conclusions about the entire population. Secondly, the university cohort may introduce a selection bias, leading to an overrepresentation of patients with atypical presentations and more severe disease courses. The reliance on existing medical reports carries the potential for inaccuracies, such as erroneous muscle strength descriptions. Moreover, the EULAR/ACR criteria are intended for use when myositis is suspected in clinical routine (10), which only applies to a minority of cases in our cohort. Lastly, the retrospective application of the criteria is a limitation of the present study. The criteria had been applied on the ba-

sis of reports and discharge letters and not collected in a systematic and prospective manner. The retrospective usage of the criteria in this study served the academic purpose of evaluating difficulties that can arise from overlapping symptoms in different myopathies

Conclusion

Distinguishing between hereditary myopathies and myositis can be challenging. Hereditary myopathies often present with clinical features similar to myositis and inflammatory muscle biopsy findings. These potential pitfalls in distinguishing myositis from hereditary myopathies should be considered in the next revision of myositis classification criteria. In daily practice, the diagnosis of myositis in patients with a poor response to immunosuppression and a slowly progressive course should prompt re-evaluation. This includes a thorough clinical examination with attention to certain clinical patterns such as facial weakness or myotonic phenomena, inquiring about other affected individuals in the family, and a critical review of the muscle biopsy. In particular, IBM needs to be carefully differentiated from hereditary myopathies when considering clinical similarities like advanced age at onset, slow disease progression, dysphagia and lack of response to immunosuppressive treatment. While the distal predominance of paresis including involvement of the deep finger flexors might also occur in hereditary myopathies such as DM1 or myofibrillar myopathies, the histological evidence of $CD8^+$ T cells invading non-necrotic fibres is usually not observed in diseases other than IBM. Identifying the correct diagnosis may help to avoid unnecessary treatment with immunosuppressants and enable targeted therapies and inclusion in clinical trials for patients with hereditary myopathies.

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