12-2013

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Arthritis Care & Research
Vol. 65, No. 12, December 2013, pp 1969–1975
DOI 10.1002/acr.22088

ORIGINAL ARTICLE

Clinical and Laboratory Features Distinguishing Juvenile Polymyositis and Muscular Dystrophy

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Objective. **To differentiate juvenile polymyositis (PM) and muscular dystrophy, both of which may present with chronic muscle weakness and inflammation.**

Methods. **We studied 39 patients with probable or definite juvenile PM and 9 patients with muscular dystrophies who were initially misdiagnosed as having juvenile PM. Differences in demographic, clinical, and laboratory results; outcomes; and treatment responses were evaluated by Fisher's exact and rank sum tests. Random forests classification analysis and logistic regression were performed to examine significant differences in multivariable models.**

Results. **Clinical features and serum muscle enzyme levels were similar between juvenile PM and dystrophy patients, except 89% of dystrophy patients had muscle atrophy compared with 46% of juvenile PM patients. Dystrophy patients had a longer delay to diagnosis (median 12 versus 4 months) and were less frequently hospitalized than juvenile PM patients (22% versus 74%). No dystrophy patients, but 54% of juvenile PM patients, had a myositis autoantibody. Dystrophy patients more frequently had myopathic features on muscle biopsy, including diffuse variation of myofiber size, fiber hypertrophy, and myofiber fibrosis (44–100% versus 8–53%). Juvenile PM patients more frequently had complex repetitive discharges on electromyography and a complete response to treatment with prednisone or other immunosuppressive agents than dystrophy patients (44% versus 0%). Random forests analysis revealed that the most important features in distinguishing juvenile PM from dystrophies were myositis autoantibodies, clinical muscle atrophy, and myofiber size variation on biopsy. Logistic regression confirmed muscle atrophy, myofiber fibrosis, and hospitalization as significant predictors.**

Conclusion. **Muscular dystrophy can present similarly to juvenile PM. Selected clinical and laboratory features are helpful in combination in distinguishing these conditions.**

INTRODUCTION

The juvenile idiopathic inflammatory myopathies (IIMs) are a rare group of systemic autoimmune disorders characterized by chronic skeletal muscle inflammation of unknown causes, with onset at age <18 years (1). Although juvenile dermatomyositis is the primary clinical subgroup of juvenile IIMs, juvenile polymyositis (PM) has a prevalence of 2–8% of all juvenile IIMs (2,3). Juvenile PM can be more difficult to diagnose because it lacks the characteristic cutaneous manifestations of juvenile dermatomyositis and has a different distribution of muscle weakness and myopathologic features (4,5).

Some forms of muscular dystrophies in children can

Supported in part by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences (project ES101074). Dr. Mamyrova's work was supported by the Cure JM Foundation.

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Submitted for publication February 23, 2013; accepted in revised form July 26, 2013.

Significance & Innovations

- Muscular dystrophy can present similarly to juvenile polymyositis (PM).
- Certain clinical and laboratory features can be helpful in distinguishing juvenile PM and muscular dystrophy, including myositis autoantibodies, as well as less frequent clinical muscle atrophy and myofiber size variation on muscle biopsy.

mimic juvenile PM. However, juvenile PM and dystrophies have different biopsy characteristics, including immunopathologic features, but share some common clinical manifestations (6). The histopathologic hallmark of juvenile PM is the presence of endomysial lymphocytic infiltration, but muscle inflammation has been reported in some dystrophies, including Duchenne's muscular dystrophy, facioscapulohumeral muscular dystrophy, limb-girdle muscular dystrophy type 2B, and congenital muscular dystrophy with primary merosin deficiency (4,6).

Several patients were referred to our studies and clinics as having juvenile PM. However, upon detailed examination of their clinical features and review of their muscle biopsy specimens, followed by immunohistochemical or genetic testing, they were determined to have muscular dystrophies. We systematically examined demographic, clinical, and laboratory results; outcomes; and responses to therapy of patients with juvenile PM and those misdiagnosed with muscular dystrophy to better understand the distinguishing characteristics of these diseases.

PATIENTS AND METHODS

Patients. Thirty-nine patients with probable or definite juvenile PM by the Bohan and Peter criteria, defined as the absence of characteristic skin rashes of dermatomyositis, including Gottron's papules and heliotrope rash (7,8), and 9 patients with muscular dystrophies eventually diagnosed by standard clinical/genetic criteria (9,10) were included. Patients were enrolled in Institutional Review Board–approved natural history protocols at the National Institutes of Health Clinical Center, Food and Drug Administration, or George Washington University. The research was performed in accordance with the ethical standards of the Declaration of Helsinki. Patients with juvenile PM were diagnosed between 1987 and 2006 and patients with muscular dystrophy were diagnosed between 1994 and 2009; all were diagnosed before age 18 years. A standardized questionnaire that included demographic, clinical, and laboratory test results (including electromyography [EMG], magnetic resonance imaging [MRI], and muscle biopsy data); treatment responses; and outcome information was completed by each patient's

Table 1. Demographic and outcome features of patients with juvenile PM versus muscular dystrophy*

	Juvenile PM (n = 39)	Dystrophy (n = 9)
Age at diagnosis, median (IQR) years	12.0 (1.7–18.0)	9.1 (4.4–16.9)
Age at onset, median (IQR) years	11.7 (2.0–16.9)	9.0 (3.0–16.8)
Delay in diagnosis, median (IQR) months	4.0 (1.0–108.0)†	12.0 (0.0–72.0)†
Female sex	30 (76.9)	5 (55.6)
Race		
White	19 (48.7)	7 (77.8)
Nonwhite	20 (51.3)	2 (22.2)
Illness onset speed		
Insidious (>6 months)	15 (38.5)	7 (77.8)
Slow (3–6 months)	11 (28.2)	1 (11.1)
Subacute (1–3 months)	9 (23.1)	0 (0.0)
Acute (<1.0 month)	4 (10.3)	1 (11.1)
Disease severity at onset		
Mild or moderate	18 (46.2)	6 (66.7)
Severe or very severe	21 (53.8)	3 (33.3)
Family history of autoimmune disease	21 (55.3)	2 (22.2)
Outcome features		
Hospitalization	28 (73.7)‡	2 (22.2)‡
Wheelchair use	8 (20.5)	2 (22.2)
Death	4 (10.5)	0 (0.0)

* Values are the number (percentage) unless indicated otherwise. Percentages may not reflect the number divided by the total number of subjects when data are missing. PM = polymyositis; IQR = interquartile range.
† $P = 0.01$.
‡ $P = 0.007$.

treating physician, with details of the questionnaire and its definitions explained previously (2,11). Progression of the first symptoms of illness to full disease presentation was characterized as acute if it occurred in <1 month, subacute if it occurred in 1–3 months, slow if it occurred over 3–6 months, and insidious if the time to full illness presentation was >6 months. Severity of illness at onset, up to the time of diagnosis, was determined by the enrolling physician and was graded on a 4-point Likert scale from mild to extremely severe disease activity. Family history of autoimmune disease was recorded for first- and second-degree relatives. Muscle enzyme values were adjusted to a common upper limit of normal, with the highest value recorded. Mortality status was established using the Social Security Death Index, which was last examined in March 2011 (2). Responses to therapy were categorized as complete clinical response if there was no remaining disease activity after an adequate treatment trial, as defined in the study by Joffe et al (12), partial clinical response if there was improvement but not remission, and no clinical response if there was no clinical improvement despite an adequate treatment trial (12).

Thirty-one patients were diagnosed with juvenile PM only and 8 patients were classified as having juvenile PM overlapping with a second autoimmune disease; the majority of patients have been previously reported (2). Among the 8 patients with overlap myositis, 4 had juvenile PM overlapping with systemic lupus erythematosus, and 1 each had juvenile PM overlapping with ulcerative colitis, Sjögren's syndrome, eosinophilic fasciitis, and juvenile idiopathic arthritis in combination with Sjögren's syndrome. All juvenile IIM patients had a muscle biopsy sample consistent with an inflammatory myopathy; the majority of biopsy specimens were reviewed by 2 myositis researchers (LGR, FWM), often with pathologists from the Department of Neuropathology of the Armed Forces Institute of Pathology, Washington, DC, or by a muscle pathologist from the Department of Pathology at George Washington University (RVJ).

All patients with muscular dystrophies were initially enrolled by the treating physician as having juvenile PM, and their diagnosis was revised after review of their questionnaire data and muscle biopsy sample, followed by specialized immunohistochemical and/or genetic testing to confirm the specific diagnosis. Through genetic testing and/or immunohistochemical staining of the muscle biopsy specimen, 1 patient was found to have Duchenne's muscular dystrophy, 1 was a carrier for Duchenne's muscular dystrophy, 2 had facioscapulohumeral muscular dystrophy, 2 had Emery-Dreifuss dystrophy, 1 had dysferlin dystrophy, 1 had calpain deficiency, and 1 had limb-girdle dystrophy. Sera were tested for myositis-specific autoantibodies and myositis-associated autoantibodies by using validated immunoprecipitation and immunoblotting methods (13,14).

Statistical analysis. GraphPad Instat for Windows, version 3.06 (www.graphpad.com) was used for basic statistical analyses. Summary data were expressed as medians and interquartile ranges (IQRs), and *P* values for differences between patient groups were obtained by the Mann-Whitney rank sum test. Fisher's exact test was used to compare proportions between groups. A *P* value of 0.05 or less was considered significant. Because the analyses were exploratory, correction for multiple comparisons was not performed. Random forests classification analysis was performed to further evaluate significant univariate differences between patients with juvenile PM and those with dystrophies (15). The random forests classification algorithm was performed using the statistical language R (version 2.13.1, 2011; http://stat-www.berkeley.edu/users/breiman/RandomForests/). Due to the difference in sample size between the groups, the data were resampled to ensure balance, using the method of undersampling from the larger group (15). The statistical model had 500 forests and 20,000 trees per run, and the mean decrease in accuracy (MDA) was calculated. The mean out-of-bag error rate for the model was 6.7%. Backward stepwise logistic regres-

Table 2. Clinical features of patients with juvenile PM versus muscular dystrophy*

	Juvenile PM (n = 39)	Dystrophy (n = 9)
Musculoskeletal system		
Proximal muscle weakness	39 (100.0)	9 (100.0)
Distal muscle weakness	16 (44.4)	7 (77.8)
Myalgias	25 (64.1)	6 (66.7)
Falling	23 (60.5)	5 (62.5)
Muscle atrophy	17 (45.9)†	8 (88.9)†
Asymmetric weakness	7 (18.4)	3 (33.3)
Arthralgia or arthritis	27 (69.2)	5 (55.6)
Contractures	16 (41.0)	5 (55.6)
Constitutional signs or symptoms		
Fatigue	32 (82.1)	5 (55.6)
Weight loss	21 (53.8)	2 (22.2)
Fever	18 (47.4)	1 (11.1)
Cardiac system		
Cardiac abnormalities on EKG or echocardiogram	14 (36.8)	5 (62.5)
Palpitations	9 (23.1)	1 (11.1)
Gastrointestinal system		
Dysphagia	16 (41.0)	1 (11.1)
Abdominal pain	12 (30.8)	3 (33.3)
Regurgitation	6 (15.4)	1 (11.1)
Constipation	3 (7.7)	1 (11.1)
Pulmonary system		
Dysphonia	9 (23.7)	1 (11.1)
Interstitial lung disease	7 (17.9)	1 (12.5)
Cutaneous system		
Periungual capillary changes	12 (30.8)	0 (0.0)
Raynaud's phenomenon	11 (28.2)	1 (11.1)
Photosensitivity	2 (5.1)	1 (11.1)
Mechanic's hands	1 (2.6)	0 (0.0)
Lipodystrophy	0 (0.0)	1 (11.1)

* Values are the number (percentage). Percentages may not reflect the number divided by the total number of subjects when data are missing. PM = polymyositis; EKG = electrocardiogram.
† $P = 0.027$.

Table 3. Laboratory test abnormalities in patients with juvenile PM versus muscular dystrophy*

	Juvenile PM (n = 39)	Dystrophy (n = 9)
Autoantibodies		
Antinuclear antibodies	24 (61.5)	3 (33.3)
Any myositis autoantibody	21 (53.8)†	0 (0.0)†
Myositis-specific autoantibodies		
Anti–Jo-1	4 (10.3)	0 (0.0)
Anti-SRP	6 (15.4)	0 (0.0)
Myositis-associated autoantibodies‡		
Anti–U1 RNP	7 (17.9)	0 (0.0)
Anti-Ro	4 (10.3)	0 (0.0)
Anti-La	2 (5.1)	0 (0.0)
Anti–PM-Scl	2 (5.1)	0 (0.0)
Anti–U2 RNP, anti–TMG cap, anti-Sm (1 each)	3 (7.7)	0 (0.0)
Magnetic resonance imaging		
Muscle edema	16 (76.2)	2 (33.3)
Myofasciitis	11 (52.4)	1 (16.7)
Subcutaneous edema	4 (19.0)	1 (16.7)
Muscle atrophy	4 (19.0)§	5 (83.3)§
Fatty replacement of muscles	5 (23.8)	4 (66.7)
Electromyography		
Increased insertional and spontaneous activity in the form of fibrillation potentials	20 (87.0)	5 (55.6)
Short duration, small amplitude polyphasic motor unit action potentials	17 (73.9)	7 (77.8)
Complex repetitive discharge	16 (69.6)¶	2 (22.2)¶
Positive sharp waves	4 (60.9)	3 (33.3)

* Values are the number (percentage). Percentages may not reflect the number divided by the total number of subjects when data are missing. One patient with anti–Jo-1 also had anti-Ro and anti-La autoantibodies and another Jo-1–positive patient also had anti–U1 RNP and anti-Sm autoantibodies. Of the myositis-associated autoantibodies, 1 patient had both anti-Ro and anti-La autoantibodies, 1 patient had anti–U1 RNP and anti-Sm autoantibodies, and 1 patient had anti–U1 RNP, anti–U2 RNP, anti-Ro, anti-La, and anti–TMG cap autoantibodies. PM = polymyositis; anti-SRP = anti–signal recognition particle; anti-TMG = anti-trimethylguanosine.
† $P = 0.003$.
‡ Some patients had >1 myositis-associated autoantibody.
§ $P = 0.008$.
¶ $P = 0.02$.

sion analysis was also performed with significant variables from the univariable analysis using Stata, version 12.1. Variables significant in the univariable analysis with missing data could not be examined in the random forests analysis or by logistic regression modeling. Sensitivity, specificity, and positive and negative predictive values for juvenile PM versus dystrophy were calculated using the variables in the final logistic regression model using the prevalence of juvenile PM in the full sample (0.8).

RESULTS

Patients with muscular dystrophy had a longer delay to diagnosis (median 12.0 months) than patients with juvenile PM (median 4.0 months) (Table 1). There was no difference in the age at diagnosis or racial distribution between patients with juvenile PM and muscular dystrophy. The female:male ratio was 3.3:1 in the juvenile PM group compared to 1.3:1 in the dystrophy group. Patients with dystrophies tended to have a more insidious disease onset (78% versus 38% in juvenile PM patients; $P = 0.06$) (Table 1). There was no difference in the frequency of a family history of autoimmune disease. Hospitalization was more frequent in patients with juvenile PM compared to patients with dystrophies (74% versus 22%; $P = 0.007$). The number of patients reporting use of a wheelchair was similar. Mortality did not differ between the 2 groups.

Regarding the clinical features of juvenile PM and muscular dystrophy (Table 2), muscle atrophy was more frequent in patients with muscular dystrophy (89%) compared to those with juvenile PM (46%; $P = 0.027$). Fever occurred more often in juvenile PM patients who had overlap myositis (62%) than in patients with muscular dystrophy (11%; $P = 0.05$), but was not significantly different between the total juvenile PM group (47%) compared to those with dystrophies. The other reported clinical features did not differ between the 2 groups of patients.

The frequency of abnormal values and serum muscle enzyme levels, including creatine kinase, aldolase, lactate dehydrogenase, and transaminases, and the ratio of aspartate aminotransferase to alanine aminotransferase levels did not differ between juvenile PM and muscular dystrophy patients. For example, the median creatine kinase level was 7,439 units/liter (IQR 224–53,896) in juvenile PM patients and 13,541 units/liter (IQR 551–56,941) in patients with dystrophies ($P = 0.5$). The median aldolase level was 27 units/liter (IQR 3–217) in juvenile PM patients and 59 units/liter (IQR 8–1,756) in patients with dystrophies ($P = 0.27$).

Twenty-four patients (62%) in the juvenile PM group had a positive antinuclear antibody compared with 3 patients (33%) in the dystrophy group (Table 3). Patients with juvenile PM were more frequently positive for one of the myositis autoantibodies (54%), but none of the dystrophy patients had a myositis autoantibody ($P = 0.003$) (Table 3). Muscle atrophy on MRI of the thighs was more frequent in patients with muscular dystrophy compared to patients with juvenile PM (83% versus 19%; $P = 0.008$) (Table 3). The frequency of other MRI features, including muscle edema, myofasciitis, subcutaneous edema, and fatty replacement of the muscles, did not differ between juvenile PM and dystrophy patients. Complex repetitive discharges were more often reported in the EMGs of juvenile PM patients compared with dystrophy patients (70% versus 22%; $P = 0.02$). The other EMG features (increased insertional and spontaneous activity in the form of fibrillation potentials, small amplitude polyphasic motor unit action potentials, and positive sharp waves) did not differ between the groups.

Comparing the muscle biopsy characteristics of juvenile PM and muscular dystrophy patients (Table 4), patients with dystrophies more often had diffuse variation of myofiber size (100% versus 53%; $P = 0.008$), as well as fiber hypertrophy (44% versus 8%; $P = 0.018$) and myofiber fibrosis (56% versus 10%; $P = 0.007$). Other histopathologic features on muscle biopsy, including inflammatory changes, did not differ between the 2 groups (Table 4).

In terms of therapy, 1 muscular dystrophy patient was treated with prednisone alone and 8 were treated with prednisone in combination with other immunosuppressive agents, whereas 9 juvenile PM patients were treated with prednisone alone and 30 were treated with a combination of prednisone and other immunosuppressive agents. Methotrexate alone was the most frequently used immunosuppressive agent in both juvenile PM patients (40%) and muscular dystrophy patients (56%). The absence of a clinical response to treatment was more frequent in patients with dystrophies compared to those with juvenile PM (33% versus 0.0%; $P = 0.005$). There were no differences in the frequency of partial clinical responses to treatment. None of the dystrophy patients had a complete response to therapy, whereas 43.6% of patients with juvenile PM had a complete clinical response ($P = 0.018$).

Random forests analysis was used to examine the 9 distinguishing features between juvenile PM and dystrophies that were significant on univariate analysis and for which no data were missing; 3 juvenile PM patients were excluded from this analysis due to missing variables. Random forests analysis revealed that myositis autoantibodies were best for discriminating juvenile PM from dystrophies (average MDA score 100.0), followed by clinical muscle atrophy (MDA 45.0), diffuse variation in myofiber size (MDA 35.9), and total response to immunosuppressive therapy (MDA 32.0).

Multivariate logistic regression analysis revealed that more frequent hospitalization (odds ratio [OR] 32.8, 95% confidence interval [95% CI] 2.2–478.5), less frequent myofiber fibrosis on biopsy (OR 0.06, 95% CI 0.004–0.77), and less frequent muscle atrophy on examination (OR 0.067, 95% CI 0.033–1.21) were significant predictors of juvenile PM compared to dystrophy. Because none of the dystrophy patients had a myositis autoantibody, a point estimate could not be obtained for this variable. The final multivariable model using hospitalization, myofiber fibrosis on biopsy, and clinical muscle atrophy provided a sensitivity of 91.4% and a specificity of 77.8% for detecting juvenile PM versus dystrophy, with a positive pre-

Table 4. Muscle biopsy features of patients with juvenile PM versus muscular dystrophy*

	Juvenile PM (n = 39)	Dystrophy (n = 9)
Endomysial infiltration of mononuclear cells surrounding but not invading myofibers	23 (60.5)	5 (55.6)
Non-necrotic myofibers surrounded and invaded by mononuclear cells	3 (7.9)	0 (0.0)
Perimysial and/or perivascular infiltration of mononuclear cells	26 (68.4)	3 (33.3)
Phagocytosis	9 (23.7)	2 (22.2)
Presence of macrophages/ histiocytes	13 (34.2)	2 (22.2)
Myofasciitis	2 (5.3)	1 (11.1)
Myofiber degeneration/regeneration	25 (65.8)	7 (77.8)
Necrosis of type I and type II myofibers	15 (39.5)	2 (22.2)
Many necrotic muscle fibers as the predominant feature; inflammatory cells are sparse	3 (7.9)	1 (11.1)
Diffuse variation of myofiber size	20 (52.6)†	9 (100.0)†
Rounded fiber at the edge of the fascicle	6 (15.8)	1 (11.1)
Fiber hypertrophy	3 (7.9)‡	4 (44.4)‡
Hypercontracted fibers	2 (5.3)	1 (11.1)
Perifascicular atrophy	12 (31.6)	1 (11.1)
Myofiber fibrosis	4 (10.5)§	5 (55.6)§
Fiber fatty replacement	1 (2.6)	2 (22.2)

* Values are the number (percentage). Percentages may not reflect the number divided by the total number of subjects when data are missing. PM = polymyositis.
† $P = 0.008$.
‡ $P = 0.018$.
§ $P = 0.007$.

dictive value of 94.1% and a negative predictive value of 70.0%.

DISCUSSION

Distinguishing between juvenile PM and muscular dystrophies can be clinically challenging, since both conditions are characterized by the presence of chronic muscle weakness and inflammation and share a number of clinical features. As demonstrated here, 9 muscular dystrophy patients were initially misdiagnosed as having juvenile PM and were correctly diagnosed only after further careful evaluation, including eventual pathologic or genetic testing. We systematically examined many different characteristics of patients with juvenile PM or defined muscular dystrophies, including demographics, clinical findings, laboratory results, outcomes, and treatment responses, to identify distinguishing features of these conditions.

Compared to patients with juvenile PM, patients with dystrophies had more frequent muscle atrophy clinically and on MRI, did not have myositis autoantibodies, and had certain myopathic muscle biopsy findings more frequently, including the presence of diffuse variation of myofiber size, fiber hypertrophy, and myofiber fibrosis. Patients with juvenile PM, in contrast, were more often hospitalized and more frequently had a clinical response to treatment with prednisone and/or other immunosuppressive agents.

Many of the clinical and demographic features and the serum muscle enzyme levels were indistinguishable between juvenile PM and dystrophy patients. This suggests that further investigation and careful evaluation are needed for children presenting with muscle weakness and enzyme changes without the characteristic skin rashes of juvenile dermatomyositis. The level of creatine kinase elevation (16) or the presence of muscle edema on MRI (17,18) has been noted to be similar in adult patients with PM and dystrophies, as we also observed in this pediatric study. We did not have information on other inflammatory markers, such as neopterin or von Willebrand factor antigen level (1), and differences in these variables between patients with juvenile PM and dystrophies. Endomysial lymphocytic infiltrates, considered to be a hallmark of PM, are frequently present in certain dystrophies (19,20). We did not observe differences in the inflammatory features of the muscle biopsy samples of juvenile PM and dystrophy patients.

Some of the features we found that differentiate juvenile PM from muscular dystrophies have been noted individually by others in distinguishing adult PM from dystrophies, based on case reports and limited clinical experience, or based on examination of a single laboratory test, rather than from a systematic investigation such as this one. Prior distinctions between PM and dystrophies have included a slower rate of progression and lack of response to immunosuppressive therapy in dystrophy patients (17,19,20), as well as a stronger family history of autoimmune disease in patients with IIMs (21). The higher frequency of a positive antinuclear antibody test and the presence of myositis autoantibodies in patients with PM and not in patients with dystrophies also have been observed previously (17,22,23) and were confirmed here.

Patients with dystrophies often have weakness in other muscle groups or additional clinical manifestations, such as muscle hypertrophy, scapular winging, spinal rigidity, and macroglossia, which are absent in patients with PM, and they may have a family history of muscle disease (24,25). However, those features were not part of our questionnaire and therefore could not be assessed.

The differences in the biopsy features that we observed included the myopathic features, which were more frequent in the dystrophy group, including myofiber size variation, fiber hypertrophy, and hypercontracted fibers. In a previous study in which 13 patients were misdiagnosed with juvenile PM and had undetected dystrophies, the distinguishing biopsy features in patients with dystrophies included subsarcolemmal blebbing, isolated fiber degeneration without accompanying inflammation, and a perimysial infiltrate consisting of macrophages (6). We did not find differences in these latter biopsy features in this study and did not examine subsarcolemmal blebbing. The presence of diffuse class I major histocompatibility complex (class I MHC) antigen expression on the sarcolemma of muscle fibers is an important feature for distinguishing inflammatory from noninflammatory myopathies (26–28). However, class I MHC antigen staining of myofibers has also been described in some forms of dystrophies, including dysferlinopathies and Duchenne's muscular dystrophy (29). We did not have access to class I MHC staining. The common biopsy features of juvenile PM included not only endomysial inflammation, but also the frequent presence of perimysial and/or perivascular inflammation, myofiber degeneration/regeneration, and even perifascicular atrophy, which are thought to be characteristic of dermatomyositis (30).

A strength of our study is the simultaneous examination of many features of similar, and often misdiagnosed, muscle diseases to determine which are most strongly associated with juvenile PM versus the dystrophies. However, because not all patients had an MRI or EMG examination, we were unable to analyze these particular test results in multivariable modeling. We were also unable to examine differences in the time to treatment responses because of an absence of detailed response to therapy data over time. Due to the rarity of these conditions, the small sample sizes also limited the power of the multivariable modeling and the overall study. The population of patients studied also may have potential selection bias, in that the majority of patients were submitted by rheumatologists. Given the multiple comparisons made, the findings would be susceptible to Type I error, although this is preferred to avoid rejecting the null hypothesis too readily in exploratory analyses (31). Future studies are needed to confirm the robustness of these data when applied to a larger population.

In conclusion, muscular dystrophy can present clinically very similarly to juvenile IIM, particularly juvenile PM. Specific clinical findings, responses to immunosuppressive therapies, and laboratory test results help distinguish muscular dystrophy and juvenile PM.

ACKNOWLEDGMENTS

The authors would like to thank Drs. Rodolfo Curiel and Christine Castro for critical reading of the manuscript and Dr. Mona Shah for assistance with the random forests analysis.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Rider had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Mamyrova, Katz, Olcay Y. Jones, Miller, Rider.

Acquisition of data. Mamyrova, Katz, Robert V. Jones, Targoff, Olcay Y. Jones, Rider.

Analysis and interpretation of data. Mamyrova, Robert V. Jones, Lachenbruch, Rider.

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APPENDIX A: MEMBERS OF THE CHILDHOOD MYOSITIS HETEROGENEITY COLLABORATIVE STUDY GROUP

Members of the Childhood Myositis Heterogeneity Collaborative Study Group who contributed to this study are as follows: Richard Brackett, Sarah Campillo, Andrew H. Eichenfield, Terri H. Finkel, Ellen A. Goldmuntz, Gary V. Gordon, Brandt P. Groh, Melissa Hawkins-Holt, Michael Henrickson, Claas Hinze, Russell J. Hopp, Norman T. Ilowite, Jerry C. Jacobs (deceased), Lisa Imundo, Andrew Lasky, Katherine Madson, Ann M. Neumeyer, Judyann C. Olson, Barbara E. Ostrov, Lauren M. Pachman, Ramesh Pappu, Maria D. Perez, Karin S. Peterson, Paul H. Plotz, Marilynn G. Punaro, Charles D. Radis, Linda I. Ray, Robert M. Rennebohm, Peter D. Reuman, Deborah Rothman, Robert Sheets, David D. Sherry, Carol A. Wallace, and Patience H. White.