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Original Article

Characterization of the biomarkers related to the clinical course and outcomes of juvenile dermatomyositis

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KEYWORDS
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Abstract *Objective:* This study aimed to evaluate the clinical characteristics of children diagnosed with juvenile dermatomyositis (JDM) in a tertiary medical centre in Taiwan and to identify important biomarkers for predicting the disease course and outcomes of JDM.
Methods: We retrospectively reviewed patients with JDM diagnosed at the National Taiwan University Hospital between 1 January 2001 and 31 December 2021. The endpoints for disease assessment included complete clinical response or remission. The JDM courses were divided into monocyclic, polycyclic, and chronic continuous statuses. The significant relationship between the predictors and outcomes was further analysed.
Results: A total of 47 patients were included in this study. The mean age at disease onset was 7.5 years. The female-to-male ratio was 1.35. The most common initial presentations were Gottron's sign (74%), followed by muscle weakness (66%) and facial rash (66%). Among all included patients, 35 (74.5%) patients achieved complete clinical remission, 15 (31.9%) had a monocyclic course, six (12.7%) had a polycyclic course, and 24 (51.1%) had a chronic continuous course. Negative facial rash and arthralgia were favourable factors for achieving complete clinical remission. Muscle weakness, higher lactate dehydrogenase (LDH), and higher erythrocyte sedimentation rate (ESR) at disease onset were related to the chronic continuous course. The most common long-term complication was calcinosis (29.8%).
Conclusion: Juvenile dermatomyositis is a rare disease, and only a few studies have been conducted in Asia. Our results identified the important predictors of the disease course and outcomes. The chronic continuous course requires more attention and aggressive treatment.

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Introduction

Juvenile dermatomyositis (JDM) is a rare and often chronic systemic autoimmune disease. The annual incidence is estimated to range between 0.8 and 4.1 per million children. It accounts for approximately 85% of all children with idiopathic inflammatory myopathy.[1]

Clinically, JDM typically affects the skin and muscles. It is characterised by symmetrical proximal muscle weakness, elevated serum muscle enzymes, and pathognomonic cutaneous manifestations, including heliotrope rash over the eyelids, malar or facial erythema, Gottron's papules over the extensor joint surfaces, nailfold capillary changes, and calcinosis.[2] The diagnosis of JDM is based on the Bohan and Peter criteria published in 1975. The diagnosis requires symmetrical proximal muscle weakness, muscle biopsy evidence of myositis, elevation in serum skeletal muscle enzymes, characteristic electromyographic changes in chronic inflammatory myositis, and the pathognomonic rash of dermatomyositis.[3,4] The definite diagnosis of JDM requires the presence of a typical rash and three of the other four criteria. The disease courses were divided into three groups according to the features of the active and inactive disease: monocyclic, polycyclic, and chronic continuous.[5]

The treatment goals are to control inflammation, prevent long-term disease sequelae, and improve quality of life. However, the disease course in JDM varies. Only one-third of the patients have a monocyclic course; in contrast, between 3% and 30% of patients have a polycyclic course, and 30%—60% of patients continue to have an active disease without remission despite treatment.[6,7] The heterogeneous disease course and difficulty predicting the disease course in the early stages are major challenges in JDM. There is a lack of statistical data describing this issue, and few studies have focused on paediatric patients.

There have only been a few studies describing the characteristics of JDM and the factors affecting clinical outcomes.[6,8,9] In addition, no data are available to outline biomarkers characterisation for predicting the clinical course of JDM in Taiwan. By identifying the predictors of the disease outcome and course earlier, we hope to optimise treatment and minimise medication toxicity. Therefore, we conducted this large retrospective study to include patients diagnosed with JDM aged less than 18 years to clarify this issue.

Methods

Study design and enrolment criteria

We retrospectively reviewed consecutive patients newly diagnosed with JDM at the National Taiwan University Hospital between 1 January 2001 and 31 December 2021 and whose diagnostic codes were ICD-9-CM 710.3 or ICD-10-CM M33.0. The follow-up period continued until 31 August 2022. Patients were recruited if they fulfilled the Bohan and Peter criteria for definite and probable JDM.[3,4] In addition, the included patients had to have been managed at the National Taiwan University Hospital (NTUH) throughout the course of their illness and had at least 6 months of follow-up.

Data collection was performed by reviewing medical records. Clinical characteristics, including age, sex, symptoms at disease onset, laboratory parameters, including serum creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), antinuclear antibody (ANA), von Willebrand factor (VWF), erythrocyte sedimentation rate (ESR), and reports of electromyography and muscle biopsy, were recorded at diagnosis. Complications, including calcinosis, during the follow-up periods, were also recorded.

As for the description of disease outcomes, complete clinical remission was defined as the absence of both rash and active myositis for a minimum of 6 months off immunosuppressive medications, and complete clinical response was described as the absence of both rash and active myositis for 6 months while receiving immunosuppressive medications.[10] Patients without active myositis were defined as those with normal muscle enzyme levels and normal muscle strength. The disease course was divided into three categories: (1) monocyclic, if the patient experienced one episode of the disease and then achieved remission without relapse within 2 years of diagnosis; (2) polycyclic, if the patient had more than one remission and relapse within 2 years; and (3) chronic continuous, if disease activity continued for more than 2 years without remission despite treatment.[5] When the length of follow-up of patients was less than 2 years, the course of the disease was unspecified.

The National Taiwan University Hospital Research Ethics Committee has approved the study (NTUH-REC No. 202004069RINB).

Statistical analyses

Patients' clinical and demographic characteristics are presented as the total number (n), proportion (%), mean with standard deviation for data close to a normal distribution, or median with quartile range for skewed data. Chi-square tests were used to compare between-group categorical variables. Nonparametric Mann-Whitney-U tests and Kruskal—Wallis tests were used to compare between-group continuous variables. Multiple logistic regression model was used while adjusting for possible independent confounding factors. All risk factors with $p < 0.1$ in the univariate model were further entered into the multiple analysis. Data management and all statistical analyses were performed using SPSS Statistics software (version 26; IBM Corporation, Armonk, NY, USA). All tests were two-sided, and a value of $p < 0.05$ was considered statistically significant.

Results

Clinical characteristics of the study population

A total of 66 patients who were newly diagnosed with JDM between 1 January 2001 and 31 December 2021 at NTUH were identified. All patients fulfilled the Boahn and Peter criteria of definite or probable JDM. Patients who were initially managed at other hospitals without sufficient clinical information (n = 2) or had a follow-up period of less than 6 months (n = 17) were excluded. Finally, 47

patients with JDM were enrolled in the study. A flowchart of the patient selection is shown in Fig. 1.

The demographics, laboratory data, and treatment of the 47 enrolled patients with JDM are summarised in Table 1. The ratio of girls (n = 27) and boys (n = 20) was 1.35. The mean age at symptom onset was 7.5 ± 4.0 years, and the mean age at diagnosis was 7.8 ± 4.1 years. The mean age at symptom onset and disease diagnosis was younger in boy than in girl. The most common initial presentations were Gottron's sign (74%), followed by muscle weakness (66%), malar or facial rash (66%), and Gowers' sign (60%).

As shown in Table 1, elevated levels of CK (median, 165 U/L; range, 84—668 U/L), LDH (median, 627 U/L; range 410—1024 U/L), and vWF (median, 172%; range, 132%—242%) were found. Elevated serum muscle enzymes indicated muscle damage, and increased plasma vWF levels were compatible with active JDM in previous studies.[11] The most frequently used medications included steroids (85%), hydroxychloroquine (83%), and cyclosporine (72%). The mean duration of steroid treatment before complete remission was 23 months in patients who achieved complete clinical remission (n = 35). There was no significant difference between male and female patients for the demographic and clinical features.

Features of complete clinical remission

In this study, 35 (74.5%) patients with JDM achieved complete clinical remission during the follow-up period, and 12 (25.5%) patients did not. In the latter group, 10 (21.3%) patients achieved complete clinical response, and two (4.3%) did not achieve either complete clinical remission or response.

Compared with the patients who did not achieve complete remission, patients with complete remission had a higher probability of negative malar or facial rash (odds ratio [OR] 0.18; 95% confidence interval [CI] 0.04—0.82) and negative arthralgia (OR 0.12; 95% CI 0.02—0.65) as the initial presentation. Age at disease onset and diagnosis seemed to be younger in the complete clinical remission group than in the group of patients who did not achieve complete remission. In the latter group, a high portion of patients received methotrexate (58%), intravenous immunoglobulin (50%), and mycophenolate mofetil (33%). There was no significant difference in sex and laboratory data at diagnosis. The results are presented in Table 2.

Risk factors of chronic continuous course

Regarding the disease course, 15 (3%) patients had a monocyclic course, six (12.7%) had a polycyclic course, and 24 (51.1%) had a chronic continuous course. Two patients were followed up for less than 2 years and could not be categorised as having a disease course.

Among the chronic continuous group, 17 (71%) patients achieved complete clinical remission during the follow-up period, and 7 (29%) patients did not. The former group's median duration from diagnosis to complete clinical remission is 3.9 (IQR 2.7—5.8) years. The female-to-male ratio was higher in the complete remission group (2.4 and 0.4, respectively).

According to the definition of the disease course, the patients of monocyclic and polycyclic course shared a similarity, both of whom achieved remission within 2 years of diagnosis. By contrast, the patient with chronic continuous course had a longer disease course and required more attention. As the polycyclic group has a small case number and shared the clinical similarity with the monocyclic group, patients of both groups were merged into one group for further analysis.

As shown in Table 3, compared to the monocyclic and polycyclic group, the chronic continuous group had a higher probability of muscle weakness (OR 5.5; 95% CI 1.5—18.2). Serum LDH and ESR levels were significantly higher in the chronic continuous group. All clinical presentations and laboratory data at diagnosis and treatments with $p < 0.1$ in

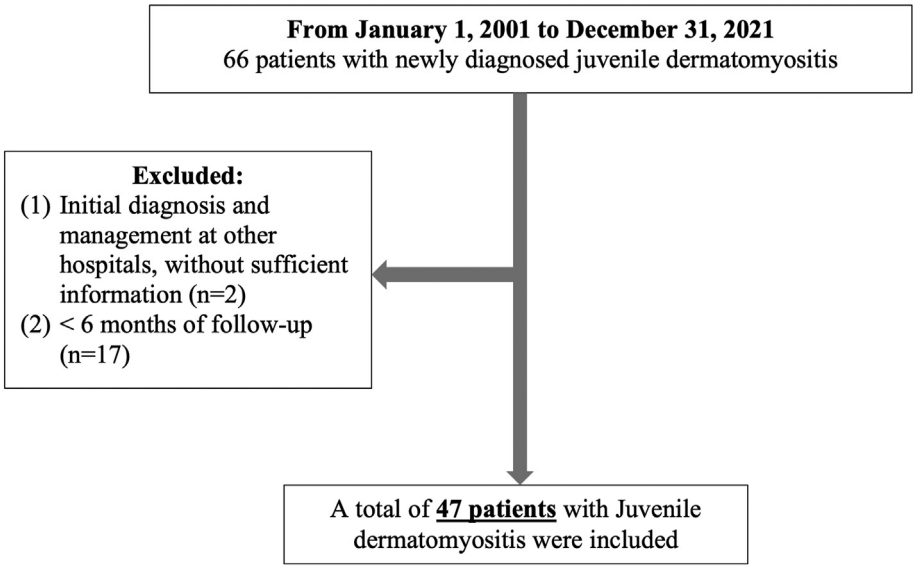

Figure 1. The flow chart of patient enrollment in the study.

Table 1 The demographics and clinical features of the enrolled patients.

	All patient (n = 47)		Male gender (n = 20)		Female gender (n = 27)		*p* value
Age at symptoms onset, year, mean	7.5	(±4.0)	6.2	(±4.2)	8.4	(±3.7)	0.09
Age at diagnosis, year, mean	7.8	(±4.1)	6.6	(±4.3)	8.7	(±3.7)	0.07
Follow-up period, year, mean	8.7	(±5.2)	8.7	(±5.1)	8.6	(±5.5)	0.85
Clinical presentations at diagnosis, n(%)							
Gottron's papule	35	(74%)	17	(85%)	18	(67%)	0.15
Muscle weakness	31	(66%)	12	(60%)	19	(70%)	0.46
Malar rash/facial rash	31	(66%)	12	(60%)	19	(70%)	0.46
Gowers' sign	28	(60%)	12	(60%)	16	(59%)	0.96
Heliotrope sign	17	(36%)	9	(45%)	8	(30%)	0.28
Myalgia	13	(28%)	4	(20%)	9	(33%)	0.31
Fever	6	(13%)	3	(15%)	3	(11%)	0.69
Arthralgia	6	(13%)	2	(10%)	4	(15%)	0.62
Laboratory data at diagnosis, median (IQR)							
CK (U/L)	165	(84–668)	185	(106–666)	111	(75–868)	0.61
LDH (U/L)	627	(410–1024)	670	(348–1024)	594	(426–1013)	0.83
AST (U/L)	51	(32–120)	56	(46–117)	45	(26–140)	0.14
vWF: Ag (%)	172	(132–242)	201	(125–222)	162	(131–323)	0.90
Treatments, n (%)							
Steroid	40	(85%)	–		–		–
Plaquenil	39	(83%)	–		–		–
Cyclosporin	34	(72%)	–		–		–
Azathioprine	28	(60%)	–		–		–
Methotrexate	13	(28%)	–		–		–
Intravenous immunoglobulin	10	(21%)	–		–		–
Mycophenolate mofetil	5	(11%)	–		–		–

CK = creatine kinase, LDH = lactate dehydrogenase.
AST = aspartate aminotransferase, vWF:Ag = von Willebrand factor Ag.

the univariate model were further entered into the multiple logistic regression model. There was no significant difference between the chronic continuous group and the others.

For sensitivity analysis, we used Chi-square tests (for categorical variables) and Kruskal–Wallis test (for continuous variables) for monocyclic, polycyclic and chronic continuous courses. The univariate analysis showed that muscle weakness, higher serum LDH and ESR were significant variables between the three disease courses.

As for the treatment, compared to the monocyclic and polycyclic group, the chronic continuous group had a higher percentage of patients receiving steroids and a lower percentage of patients receiving cyclosporin treatment. The results are presented in Table 3.

Complications

The most common long-term complication was calcinosis (14 patients, 29.8%). Calcinosis was independent of sex, age, or laboratory data at disease onset in our population. Heliotrope sign at disease onset was associated with calcinosis during the follow-up period (OR 5.6; 95% CI 1.5–21.9). Calcinosis was not associated with the disease outcome or disease course. The results are presented in Table 4.

Discussion

In this single-centre retrospective study, we characterised the biomarkers for predicting the outcome and clinical course of JDM. By identifying these predictive biomarkers earlier, we hope to optimise treatment in the future management of patients. The diagnosis was confirmed by a comprehensive review of all medical records, and thorough information on disease characterisation and clinical course of the recruited patients was obtained.

In our cohort, JDM affected girls 1.35 times more frequently than boys, similar to the studies in the previous literature. The female-to-male ratio was reported to be 1.7:1 in a 16 patient-included study from the USA,[12] 1.4:1 in 39 patients included in an Iranian cohort,[9] and 1.4:1 in a European multicentre study.[13] The peak incidence of JDM ranged from 5 to 10 years of age.[14] The mean age at disease onset was defined as 7.5 ± 4.0 years in our study, which is in accordance with previous studies from the USA, the UK, and Turkey.[1,6,14] Moreover, the mean age at symptom onset and disease diagnosis was younger in boy than in girl.

Complete clinical remission (CR) is an important outcome. However, there is no standard definition for remission or disease inactivity in JDM. We decided to use the absence of active cutaneous rash, absence of muscle weakness on muscle strength testing, absence of arthritis,

Table 2 The comparison between juvenile dermatomyositis patients with complete clinical remission and those with non-achieved complete clinical remission.

	Complete clinical remission (n = 35)		Non-achieve complete CR (n = 12)		*p* value
Male gender, n (%)	14	(40%)	6	(50%)	0.54
Age at onset, year, mean	7.1	(±4.1)	8.5	(±3.8)	0.26
Age at diagnosis, year, mean	7.5	(±4.2)	8.6	(±3.9)	0.36
Follow-up period, year, mean	8.6	(±4.8)	8.8	(±6.6)	0.9
Clinical presentations at diagnosis, n(%)					
Gottron's papule	27	(77%)	8	(67%)	0.47
Muscle weakness	23	(66%)	8	(67%)	0.95
Malar rash/facial rash	21	(60%)	10	(83%)	0.02* (odds ratio: 0.18, 95% CI:0.04—0.82)
Gowers' sign	21	(60%)	7	(58%)	0.92
Heliotrope sign	12	(34%)	5	(42%)	0.65
Myalgia	8	(23%)	5	(42%)	0.21
Fever	5	(14%)	1	(8%)	0.59
Arthralgia	2	(6%)	4	(33%)	0.01* (odds ratio: 0.12, 95% CI:0.02—0.65)
Laboratory data at diagnosis, median (IQR)					
CK (U/L)	162	(88—868)	185	(50—327)	0.21
LDH (U/L)	627	(387—1038)	644	(438—1000)	0.98
AST (U/L)	53	(31—133)	50	(34—116)	0.81
vWF: Ag (%)	172	(140—233)	167	(121—281)	0.75
Treatments at any time, n(%)					
Steroid	28	(80%)	12	(100%)	0.09
Plaquenil	30	(86%)	9	(75%)	0.39
Cyclosporin	23	(66%)	11	(92%)	0.08
Azathioprine	20	(57%)	8	(67%)	0.56
Methotrexate	6	(17%)	7	(58%)	0.01*
Intravenous immunoglobulin	4	(11%)	6	(50%)	0.01*
Mycophenolate mofetil	1	(3%)	4	(33%)	0.01*

CR = clinical remission, CK = creatine kinase, LDH = lactate dehydrogenase.
AST = aspartate aminotransferase, vWF:Ag = von Willebrand factor Ag.
* A value of $P < 0.05$ was considered statically significant.

and normal muscle enzyme levels off treatment for 6 months as the definition of complete clinical remission of JDM.[10,15] A few studies have mentioned the predictive factors for complete clinical remission. Stringer et al. demonstrated that the persistence of Gottron's papules and nailfold abnormalities early in the disease course was associated with a longer time of remission.[15] Sun et al. reported that female sex, negative Gowers' sign at disease onset, and positive photosensitivity at the onset have been favourable factors for remission.[8] In our study, negative malar or facial rash (OR 0.18, 95% CI 0.04—0.82) and negative arthralgia (OR 0.12; 95% CI 0.02—0.65) at disease onset was positive factor for complete clinical remission. As shown in a previous study, arthralgia and arthritis were seen in the early course of JDM.[16] Although arthralgia and arthritis respond to treatment, they may recur while tapering medication. Intractability makes complete clinical remission difficult.

The disease course of JDM appears to vary, and little is known about the predictors of the clinical course. Because of our study's small case number, no significant predictors were identified in the multiple logistic regression model. Nevertheless, in the univariate analysis, our study identified that muscle weakness, higher LDH levels, and higher ESR levels at disease onset were significant predictors and potential biomarkers for the chronic continuous course in JDM patients.

According to recent consensus guidelines, muscle enzymes are considered an important monitoring tool for JDM.[17,18] Increased LDH, which leaks from inflamed or damaged muscles, reflects muscle damage and disease severity in JDM.[18,19] Lactate dehydrogenase has previously been reported to correlate better with disease activity than CK in JDM.[20,21] Moreover, LDH is utilised as one of the variables in the Pediatric Rheumatology International Trials Organization, the criteria for disease activity of the clinically inactive disease in JDM.[22] ESR is a nonspecific measure of the acute phase response, which may be elevated during the active disease and reflects the extent of systemic inflammation.[23] In addition, ESR served as a serum indicator of disease activiy in dermatomyositis.[24] Elevated ESR correlates with pulmonary impairment and overall mortality in dermatomyositis.[25] In our study, higher LDH and ESR levels are associated chronic continuous course. Thus, monitoring LDH and ESR should be an essential part of the clinical care of JDM patients.

Table 3 The comparison between monocyclic, polycyclic, and chronic continuous disease course in patients with juvenile dermatomyositis.

					Univariate analysis	Multiple analysis[#]
	Monocyclic or polycyclic (n = 21)		Chronic continuous (n = 24)		*p* value	*p* value
Male gender, n (%)	9	(43%)	10	(42%)	0.94	–
Age at onset, year, mean	6.5	(±3.8)	8.0	(±4.3)	0.23	–
Age at diagnosis, year, mean	7.0	(±3.8)	8.4	(±4.5)	0.36	–
Clinical presentations at diagnosis, n(%)						
Gottron's papule	18	(86%)	16	(67%)	0.14	–
Muscle weakness	10	(48%)	20	(83%)	0.01* (odds ratio: 0.18, 95% CI:0.06–0.67)	0.62
Malar rash/facial rash	15	(71%)	14	(58%)	0.36	–
Gowers' sign	10	(48%)	18	(75%)	0.06	0.54
Heliotrope sign	7	(33%)	9	(38%)	0.77	–
Myalgia	4	(19%)	9	(38%)	0.17	–
Fever	2	(10%)	4	(17%)	0.48	–
Arthralgia	2	(10%)	4	(17%)	0.48	–
Laboratory data at diagnosis, median (IQR)						
CK (U/L)	140	(74–487)	233	(91–867)	0.43	–
LDH (U/L)	489	(342–688)	849	(501–1285)	0.01*	0.70
AST (U/L)	49	(30–80)	60	(40–194)	0.19	–
vWF: Ag (%)	157	(116–182)	202	(133–244)	0.40	–
C3 (mg/dL)	110	(97–120)	100	(89–116)	0.23	–
C4 (mg/dL)	20	(16–25)	19	(17–23)	0.77	–
ESR (mm/hr)	10	(3–14)	17	(10–27)	0.01*	0.06
ANA (+)	12	(57%)	11	(46%)	0.45	–
Treatments at any time, n(%)						
Steroid	14	(67%)	24	(100%)	0.01*	0.99
Plaquenil	19	(90%)	19	(79%)	0.30	–
Cyclosporin	13	(62%)	4	(17%)	0.01*	0.97
Azathioprine	11	(52%)	16	(67%)	0.33	–
Methotrexate	6	(29%)	6	(25%)	0.79	–
Intravenous immunoglobulin	5	(24%)	5	(21%)	0.81	–
Mycophenolate mofetil	1	(5%)	4	(17%)	0.20	–

CK = creatine kinase, LDH = lactate dehydrogenase, AST = aspartate aminotransferase, vWF:Ag = von Willebrand factor Ag, ESR = erythrocyte sedimentation rate, ANA = antinuclear antibody.

[#] All clinical presentations and laboratory data at diagnosis and treatments with $p < 0.1$ in the univariate model were further entered into the multiple logistic regression model.

* A value of $P < 0.05$ was considered statically significant.

Given that the chronic continuous course was the most concordant predictor of a poorer long-term outcome, namely, muscle weakness, persistent disease activity, cumulative damage, and functional impairment—these significant predictors highlight the need for optimised treatment that enables better control of disease activity over time and the minimisation of non-reversible damage.[26]

Calcinosis is the hallmark sequela of JDM, and its prevalence ranges from 10% to 70% in patients with JDM.[26,27,28] This wide variation in the prevalence of calcinosis in patients with JDM may be related to the length of follow-up, treatment strategies, and differences in frequency regionally and internationally.[26,27] In our study, calcinosis occurred in up to 29.8% of patients with JDM. Local tissue trauma, active inflammation, and dysregulation of the proteins involved in calcium metabolism have been found to affect the formation of calcinosis in JDM cohorts.[27,29] Fisler et al. and Tabarki et al. reported that higher initial levels of serum CK, prolonged elevation of muscle enzymes, and longer time to diagnosis and treatment were associated with calcinosis.[30,31] A large multicentre study demonstrated that older age at onset, polycyclic or chronic continuous disease course, and longer disease duration are risk factors for calcinosis.[26] In contrast, our study showed that patients with calcinosis had a higher probability of heliotrope signs at disease onset than those without calcinosis.

Our study has some limitations. Due to the retrospective nature of this study, selection and recall bias existed. There was incomplete documentation of findings and duration of symptoms, especially regarding the absence of less common clinical features. In addition, the bias of clinical courses and the prevalence of calcinosis in JDM cohorts may depend on the follow-up duration. Most patients in our

Table 4 The clinical features of juvenile dermatomyositis patients with and without calcinosis.

	Calcinosis (n = 14)		No calcinosis (n = 33)		*p* value
Male gender, n (%)	6	(43%)	14	(42%)	0.98
Age at onset, year, mean	5.9	(±3.0)	8.1	(±4.3)	0.12
Age at diagnosis, year, mean	6.3	(±3.1)	8.4	(±4.3)	0.14
Clinical presentations, n(%)					
Gottron's papule	10	(71%)	25	(76%)	0.76
Muscle weakness	10	(71%)	21	(64%)	0.61
Malar rash/facial rash	7	(50%)	24	(73%)	0.13
Gowers' sign	10	(71%)	18	(55%)	0.28
Heliotrope sign	9	(64%)	8	(24%)	0.01* (odds ratio: 5.6, 95% CI:1.5—21.9)
Myalgia	4	(29%)	9	(27%)	0.93
Fever	3	(21%)	3	(9%)	0.25
Arthralgia	3	(21%)	3	(9%)	0.25
Laboratory data at diagnosis, median (IQR)					
CK (U/L)	98	(71—474)	205	(100—767)	0.20
LDH (U/L)	599	(334—938)	643	(441—1089)	0.33
ALT(U/L)	25	(12—126)	34	(15—138)	0.55
AST (U/L)	42	(30—138)	54	(38—120)	0.50
vWF: Ag (%)	133	(123—179)	202	(148—323)	0.08
Disease outcome and course					
Complete clinical remission	9	(64%)	26	(79%)	0.30
Chronic continuous course	8	(57%)	16	(48%)	0.59

CK = creatine kinase, LDH = lactate dehydrogenase.
AST = aspartate aminotransferase, vWF:Ag = von Willebrand factor Ag.
* A value of $P < 0.05$ was considered statically significant.

cohort lacked myositis autoantibodies, which are associated with distinct clinical features.[32]

In conclusion, JDM is a rare and often chronic systemic autoimmune disease. The time required to achieve complete clinical remission is relatively long, but negative facial rash and negative arthralgia as an initial presentation might be favourable factors to achieve this endpoint. Muscle weakness, higher LDH levels, and higher ESR levels at disease onset were related to the chronic continuous course, which might require more attention and treatment strategies to control disease activity better. The exact reasons for these findings require further investigation.

Declaration of competing interest

The authors declare no conflicts of interest.

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