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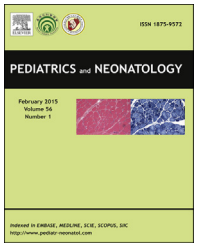

ORIGINAL ARTICLE

Juvenile Dermatomyositis: A 20-year Retrospective Analysis of Treatment and Clinical Outcomes

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Key words
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covariate-adjusted survival curve;
death;
Gowers' sign;
photosensitivity;
sex

Background: Juvenile dermatomyositis is a rare childhood multisystem autoimmune disease involving primarily the skin and muscles, and it may lead to long-term disability. This study aimed to describe the clinical course of juvenile dermatomyositis and determine if any early clinical or laboratory features could predict outcome.

Methods: Medical charts of patients aged ≤18 years and diagnosed with juvenile dermatomyositis (according to the criteria of Bohan and Peter) at the Pediatric Department, National Taiwan University Hospital, between 1989 and 2009 were reviewed. The endpoints for disease assessment were complete clinical response and complete clinical remission. Cox's proportional hazards model was fitted to identify important predictors of complete clinical remission.

Results: A total of 39 patients with juvenile dermatomyositis were reviewed. Two-thirds were females, and the mean age at disease onset was 81.97 ± 46.63 months. The most common initial presentations were Gottron's papule (82.1%) and muscle weakness (82.1%). After excluding one patient with an incomplete record, the remaining 31 patients who had muscle weakness were analyzed; among them, 22 (70.97%) achieved complete clinical response, but only six (19.4%) achieved complete clinical remission. Multivariate analysis showed that female sex, negative Gowers' sign at disease onset, and positive photosensitivity at disease onset were favorable factors to achieve complete clinical remission. Moreover, covariate-adjusted survival curves were drawn for making predictions of complete clinical remission. Only 13 (33.33%) patients were symptom free at the end of follow up, whereas the other 26 suffered from different kinds of complications. None of them developed malignancy, but two (5.13%) patients died during the follow-up period.

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Conclusion: Factors such as male sex and Gowers' sign were unlikely to favor the achievement of complete clinical remission in juvenile dermatomyositis. Certain complications cannot be avoided, and thus more effective treatments and monitoring strategies are needed for better control of juvenile dermatomyositis.

1. Introduction

Juvenile dermatomyositis (JDM) is a rare idiopathic chronic disease that accounts for 85% of idiopathic inflammatory myopathies in children.[1] It is characterized by typical skin rash and proximal muscle weakness, but it may further affect other organs, including the heart, lungs, and gastrointestinal tract. Long-term complications such as joint contracture and muscle wasting may result in childhood disability. Fatal cases have also been reported, especially when it affects the cardiopulmonary system. Its pathogenesis remains unclear. Some evidence suggests that JDM may be caused by environmental triggers, immune dysfunction, and specific tissue responses (particularly those of muscles, skin, and small vessel endothelium) in genetically susceptible individuls.[2]

There is no standard treatment for JDM to date. Bitnum et al[3] reported that prior to the steroid era of 1960s, one-third of affected children recovered completely, one-third died, and those remaining had significant disability. However, clinical and functional prognosis has been improved significantly after the introduction of corticosteroids,[4] which remain the mainstay of treatment today, with or without other immunosuppressive agents or intravenous immunoglobulin (IVIG).

This study aimed to explore important prognostic factors of JDM in children for predicting clinical outcomes of such patients.

2. Materials and methods

2.1. Patients

This clinical epidemiologic study was approved by the Institutional Review Board in advance. The medical charts of JDM patients $\leq$18 years of age who were treated at the Department of Pediatrics, National Taiwan University Hospital, between June 1989 and December 2009 were reviewed, which included patients' clinical presentations, initial laboratory data, complications, and clinical outcomes. JDM was diagnosed based on the criteria of Bohan and Peter published in 1975,[5] which included typical skin rash and two or more of the following symptoms and signs: (1) symmetric proximal muscle weakness; (2) biopsy-proven myositis; (3) elevated serum muscle enzyme levels; and (4) electromyographic changes of myositis. Muscle weakness was described mostly as difficulty in climbing stairs or getting up from squatting position, and less frequently as difficulty in combing hair or getting dressed by patients themselves. Patients with typical skin rash without evidence of muscle weakness or inflammation were defined as amyopathic dermatomyositis (DM). Patients who had evidence of mixed connective tissue disease, systemic lupus erythematosus (SLE), scleroderma, or overlapping connective tissue syndromes were excluded from this study.

2.2. Data

The demographic and clinical parameters were recorded, which included the following: sex, onset age, initial symptoms and signs, duration of untreated disease, initial laboratory data, reports of electromyography and muscle biopsy, concurrent medications, duration of corticosteroid treatment, occurrence of flares, complications during treatment, and the final disease status during the follow-up period. The date of disease onset was defined as the earliest date the patient reported symptoms that were consistent with JDM. The duration of untreated disease was the time period from disease onset to the start of medical treatment. According to the definitions of the International Myositis Assessment and Clinical Studies Group,[6] complete clinical response was defined as no evidence of active myositis for $\geq$6 months while receiving medications, and complete clinical remission was defined as no evidence of active myositis for $\geq$6 months without receiving any medications. Absence of active myositis was defined as normal muscle strength and normal muscle enzyme levels during follow-up. Patients with clinical or laboratory evidence of increasing skin or muscular symptoms requiring adjustment of medications during follow-up were considered to experience juvenile DM flare.

2.3. Statistical analysis

Statistical analysis was performed using the R 3.0.2 software (R Foundation for Statistical Computing, Vienna, Austria). In statistical testing, a two-sided p value of $\leq$0.1 was considered statistically significant due to the relatively small sample size. Distributional properties of continuous variables were expressed as mean $\pm$ standard deviation (SD) and range, categorical variables were presented in terms of frequency and percentage, and the survival curve of time to complete clinical remission was plotted using the Kaplan–Meier estimates. In univariate analysis, Wilcoxon rank-sum test, Chi-square test, and Fisher's exact test were used to examine the differences in the distributions of continuous and categorical variables between patients with and without complete clinical remission. Similarly, log-rank test was used to examine the effects of continuous

variables or categorical variables on time to complete clinical remission. Next, multivariate analysis was conducted by fitting Cox's proportional hazards model to estimate the effects of prognostic factors simultaneously on time to complete clinical remission. The goodness-of-fit measures, including concordance and adjusted generalized R^2, were examined to assess the goodness-of-fit of fitted Cox's proportional hazards models. The concordance is equivalent to the estimated area under the receiver operating characteristic curve, and thus concordance value $\geq$0.7 suggests an acceptable level of discrimination power. The values of adjusted generalized R^2 ($0 \leq R^2 \leq 1$) are usually low for Cox's proportional hazards model—in our experience, adjusted generalized $R^2 \geq 0.15$ indicates an acceptable fit for Cox's proportional hazards model. If a separation (or monotone likelihood) problem occurs, the likelihood ratio test is used to replace Wald's test for computing the p value in Cox's proportional hazards model. The statistical tools of regression diagnostics for the verification of proportional hazards assumption, residual analysis, detection of influential cases, and check of multicollinearity were applied to discover any model or data problems. Finally, based on the well-fitted final Cox's proportional hazards model, covariate-adjusted survival curves for time to complete clinical remission were drawn in different scenarios for predicting complete clinical remission.

3. Results

Demographics, clinical symptoms and signs, and initial laboratory data at disease onset of the 39 patients with JDM are summarized in Table 1. No one had a family history of JDM. The ratio of females ($n = 26$) to males ($n = 13$) was 2:1, and the mean age at disease onset was 81.97 $\pm$ 46.63 months. The most common initial presentations were Gottron's papule (82.1%) and muscle weakness (82.1%).

Medications used by the patients were reviewed. The most frequently used medications were oral corticosteroids (92.3%), followed by azathioprine (85.6%), hydroxychloroquine (76.95%), nonsteroidal anti-inflammatory drugs (61.5%), cyclosporin A (56.4%), IVIG (41.0%), and etanercept (10.3%). In this study, 16 (41%) patients received IVIG therapy monthly for a total of nine courses on average within a mean follow-up period of 79 months. Indications for IVIG therapy included disease exacerbation, inability to reduce the dose of steroid, replacement of cytotoxic agents because of complications, and severe initial manifestations. Most patients showed improved muscular condition after the first three courses of IVIG. Other therapies such as methylprednisolone pulse therapy, methotrexate, cyclophosphamide, and sulfasalazine were also used concurrently for disease control.

Among 39 patients, seven with typical skin rashes but without clinical muscle weakness were classified as patients with amyopathic DM. The mean muscle enzyme levels were almost nine times higher in patients with muscle weakness than in those without muscle weakness, although some patients in the former group had normal levels. No statistical difference was found between these two groups in terms of mean age at disease onset, concurrent therapy, duration of oral prednisolone treatment, need for IVIG treatment, and incidence of calcinosis during the follow-up period. Nevertheless, four (12.9%) patients with muscle weakness had disability that required rehabilitation or surgical intervention, but no patient in the amyopathic DM group ended up with disability.

After excluding one with an incomplete record, the remaining 31 patients with muscle weakness were further analyzed. Twenty-two (70.97%) achieved complete clinical response. According to the Kaplan—Meier estimate of survival curve for time to complete clinical response (not shown in figures), the estimated median time to complete clinical response decreased at 18 months. However, after complete clinical response was achieved, 16 (72.7%) had at least one disease flare (range: 1—8 times) during follow-up. There was no statistical difference in age of disease onset, sex, mean duration to achieve complete clinical response, and medical treatments between the patients achieving

Table 1 Demographics, clinical features, and initial laboratory data at disease onset in 39 patients with juvenile dermatomyositis.

Variable	Mean $\pm$ SD (range) or frequency (%)
Male	13 (33.3)
Age at disease onset (mo)	81.97 $\pm$ 46.63 (25—216)
Age at diagnosis (mo)	87.97 $\pm$ 45.90 (28—213)
Duration of untreated disease (mo)	6.08 $\pm$ 6.59 (0—24)
Symptoms at disease onset	
Malar rash	22 (56.4)
Gottron's papule	32 (82.1)
Heliotroph sign	29 (74.4)
Skin ulcer	1 (2.6)
Vasculitis	1 (2.6)
Muscle weakness	32 (82.1)
Gowers' sign	23 (59.0)
Myalgia	7 (18.0)
Arthralgia	7 (18.0)
Arthritis	5 (12.8)
GI symptoms	3 (7.7)
Swallowing difficulty	4 (10.3)
Calcinosis	1 (2.6)
Oral ulcer	1 (2.6)
Photosensitivity	3 (7.7)
Muscle enzymes at disease onset	
CK (U/L)*	1404.38 $\pm$ 3202.98 (40.0—17669.0)
LDH (U/L)†	1040.86 $\pm$ 684.89 (71.0—3000.0)
AST (U/L)‡	126.22 $\pm$ 167.04 (14.0—648.0)

AST = aspartate aminotransferase; CK = creatine kinase; GI = gastrointestinal; LDH = lactate dehydrogenase; SD = standard deviation.

* One record was missing, CK normal range: 38—160 U/L.

† Four records were missing, LDH normal range: 230—460 U/L.

‡ Two records were missing, AST normal range: male <37 U/L, female <31 U/L.

complete clinical response ($n = 22$) with ($n = 16$) and without ($n = 6$) disease flares.

As listed in Table 2, among the 31 patients with muscle weakness, six (19.4%) finally achieved complete clinical remission and 25 (80.6%) did not. Univariate analysis found that female ($p = 0.0712$) patients, patients without Gowers' sign ($p = 0.0101$), or patients with photosensitivity ($p = 0.0323$) had higher probabilities to achieve complete clinical remission, among which sex and photosensitivity completely separated the outcome (i.e., a 0 in one of the 4 cells). No patients who received antitumor necrosis factor (anti-TNF) treatment achieved complete clinical remission. Calcinosis was found in both groups. The Kaplan–Meier estimate of survival curve in Figure 1A showed that the estimated median time to complete clinical remission was about 101 months.

Multivariate analysis was conducted by fitting Cox's proportional hazards model to identify important predictors of time to complete clinical remission. As shown in Table 3, female sex, negative Gowers' sign at disease onset, and positive photosensitivity at disease onset were favorable factors to achieve complete clinical remission. Moreover, based on the fitted final Cox's proportional hazards model (Table 3), covariate-adjusted survival curves were drawn in Figure 1B and C for making predictions for complete clinical remission.

Table 2 Comparison between 31 patients with and without complete clinical remission.*

Variable	Remission ($n = 6$)	No remission ($n = 25$)	p
Age at disease onset (mo)	93.00 ± 41.67 (40–144)	85.12 ± 50.35 (25–216)	0.5995
Sex†			0.0712
Female	6 (28.6%)	15 (71.4%)	
Male	0 (0%)	10 (100%)	
Duration of untreated disease (mo)	9.17 ± 8.80 (1–24)	5.40 ± 6.65 (0–24)	0.2062
Symptoms present at disease onset			
Gowers' sign‡			0.0101
No	3 (37.5%)	5 (62.5%)	
Yes	3 (13.0%)	20 (87.0%)	
Photosensitivity§			0.0323
No	4 (13.8%)	25 (86.2%)	
Yes	2 (100%)	0 (0%)	
Initial laboratory data at disease onset			
CPK (U/L)	1880.33 ± 2312.46 (62–6000)	1571.48 ± 3788.14 (47–17,669)	0.4383
LDH (U/L)	1374.60 ± 1002.60 (71–2449)	1076.57 ± 682.17 (344–3000)	0.6001
AST (U/L)	161.20 ± 163.61 (19–412)	146.40 ± 184.25 (14–648)	0.9556
Amount of concurrent therapy	4.33 ± 2.25 (2–8)	5.52 ± 1.98 (3–10)	0.1790
Duration of prednisolone treatment (mo)	81.00 ± 69.78 (11–207)	33.16 ± 35.36 (1–138)	0.0511
Patients received IVIG			0.1848
No	5 (29.4%)	12 (70.6%)	
Yes	1 (7.1%)	13 (92.9%)	
Patients ever received anti-TNFα			0.5614
No	6 (22.2%)	21 (77.8%)	
Yes	0 (0%)	4 (100%)	
Calcinosis during follow-up			0.6526
No	3 (15.8%)	16 (84.2%)	
Yes	3 (25.0%)	9 (75.0%)	

* Eight patients were excluded from this analysis, among whom seven were of amyopathic type and one had an incomplete record. Sample statistics presented in this table are mean ± SD and range for continuous variables, and frequency (percentage) for categorical variables. The listed p values of statistical tests were calculated using the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.

† Univariate analysis of complete clinical remission (yes vs. no) yielded Fisher's test: $p = 0.1411$. Univariate survival analysis of time to complete clinical remission yielded the following: (1) the likelihood ratio test: $\chi = 3.25$, degrees of freedom $= 1$, $p = 0.0712 < 0.1$; (2) Wald test: $\chi = 0$, degrees of freedom $= 1$, $p = 0.9992 > 0.1$; and (3) the score (log-rank) test: $\chi = 1.93$, degrees of freedom $= 1$, $p = 0.1649 > 0.1$.

‡ Univariate analysis of complete clinical remission (yes vs. no) yielded Fisher's test: $p = 0.1605$. Univariate survival analysis of time to complete clinical remission yielded the following: (1) the likelihood ratio test: $\chi = 4.71$, degrees of freedom $= 1$, $p = 0.0300 < 0.1$; (2) Wald test: $\chi = 4.82$, degrees of freedom $= 1$, $p = 0.0282 < 0.1$; and (3) the score (log-rank) test: $\chi = 6.62$, degrees of freedom $= 1$, $p = 0.0101 < 0.1$.

§ Univariate analysis of complete clinical remission (yes vs. no) yielded Fisher's test: $p = 0.0323$. Univariate survival analysis of time to complete clinical remission yielded the following: (1) the likelihood ratio test: $\chi = 0$, degrees of freedom $= 1$, $p = 0.9598 > 0.1$; (2) Wald test: $\chi = 0$, degrees of freedom $= 1$, $p = 0.9600 > 0.1$; and (3) the score (log-rank) test: $\chi = 0$, degrees of freedom $= 1$, $p = 0.9600 > 0.1$.

AST = aspartate aminotransferase; CPK = creatine phosphokinase; IVIG = intravenous immunoglobulin; LDH = lactate dehydrogenase; SD = standard deviation; TNFα = tumor necrosis factor α.

Finally, major complications and clinical outcomes of the 39 patients assessed at the end of follow-up are reported in Table 4. Only 13 (33.33%) patients were symptom free at the end of follow-up, whereas the remaining 26 suffered from different complications. None of them developed malignancy, but two (5.13%) died during the follow-up period.

4. Discussion

JDM is a rare, often chronic, autoimmune disease of childhood. Clinical features are associated with systemic vasculopathy and are central to the diagnosis. Demographic statistics in the current study are similar to those of a previous study conducted in America, in which the mean age of disease onset was 7.54 years, mean duration of untreated disease 0.07—98 months (median, 4.04 months), and female-to-male ratio about 1.9:1.[7] Compared with the domestic data in Taiwan, the female-to-male ratio in our study is slightly lower; however, most frequently found cutaneous features at disease onset such as Gottron's papule, malar rash, and heliotroph sign are similar.

In the current study, seven patients (17.9%) had cutaneous manifestations but without muscle weakness. Three had elevated muscle enzymes and were considered to have hypomyopathic DM,[8] whereas the other four were classified as patients with amyopathic DM. In the literature, amyopathic DM accounts for 5—10% of all cases of DM, with a higher prevalence among Asians.[9—11] Most amyopathic DM cases do not progress to clinically evident myositis, especially among juvenile-onset patients. In three case series of patients with amyopathic DM who received no systemic therapy, two of 28 adults (7%) and none of the 20 juvenile patients progressed to symptomatic muscle disease in a mean follow-up period of 5 years.[11—13]

Predictive factors for the progression of amyopathic DM to classical DM have not been identified clearly. Calcinosis, skin ulcerations, and muscle weakness may develop several years later during follow-up, since aggressive treatment is suggested by some clinicians.[14,15] However, some cases have been reported to have true amyopathic DM that resolved spontaneously.[16,17] Thus, there is still considerable controversy about the treatment strategy for amyopathic DM.

In the current study, seven patients remained clinically without muscle weakness after a mean follow-up of 10 years. However, most still required systemic prednisolone treatment for an average of 32 months, which was similar to those with muscle weakness (mean, 39.81 months). Three patients (42.86%) without muscle weakness eventually developed calcinosis even under prednisolone treatment. The prognosis of amyopathic DM, unlike in adult groups with increasing risks for interstitial lung disease and malignancy,[18,19] is generally excellent among pediatric patients.

It is well recognized that a proportion of patients with muscle weakness has normal muscle enzyme levels at the time of diagnosis.[20] Furthermore, levels of creatine kinase and other muscle enzymes (i.e., aspartate aminotransferase and lactate dehydrogenase) do not correlate well with the improvement of muscle strength.[21] It is suggested that the inconsistency between laboratory data and clinical presentation is partially due to the fact that muscle enzymes often improve weeks before improvement in muscle strength, while the rise is more than 1 month prior to clinical relapse.[22] This finding is consistent with that of the current study, making it difficult to monitor the disease. To better determine occult disease activity, a number of immunological biomarkers, including interferon α, downstream targets of interferon α, or interleukin-17 and interferon-regulated genes, appear to be promising. These are now under investigation and may be proved to be sensitive markers of disease activity.[2,23]

Since the 1970s, the standard treatment of JDM has been administration of high-dose oral corticosteroid daily, which is continued until clinical and laboratory improvements are evident, and then slowly reduced over at least a 2-year period.[24] However, most patients experience side effects from corticosteroid treatment, including avascular hip joints necrosis, osteoporosis, and retarded growth velocity. Steroid-sparing therapies have been introduced to reduce the cumulative doses of corticosteroid use. Previous studies suggest that children who receive methotrexate at disease onset have half of the cumulative corticosteroid dose, less weight gain, and improved height velocity, while achieving the same disease control as those who are treated with corticosteroid only.[25]

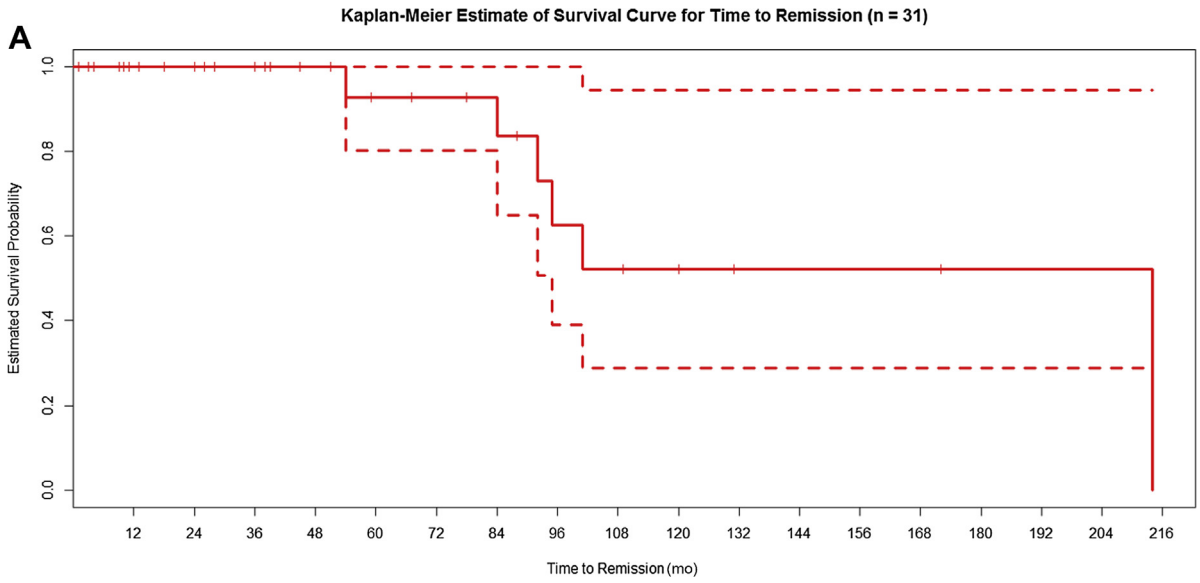
IVIG was efficacious in a controlled trial for adult DM.[26] Several case series have shown the effectiveness of IVIG for treating JDM.[27—29] The proposed mechanism for the beneficial effect is intercepting the assembly and deposition of C5b—C9 membranolytic attack complex on the endomysial capillaries through the formation of complexes between the infused immunoglobulin and C3b, thereby preventing the incorporation of activated C3 molecules into C5 convertase.[28,30]

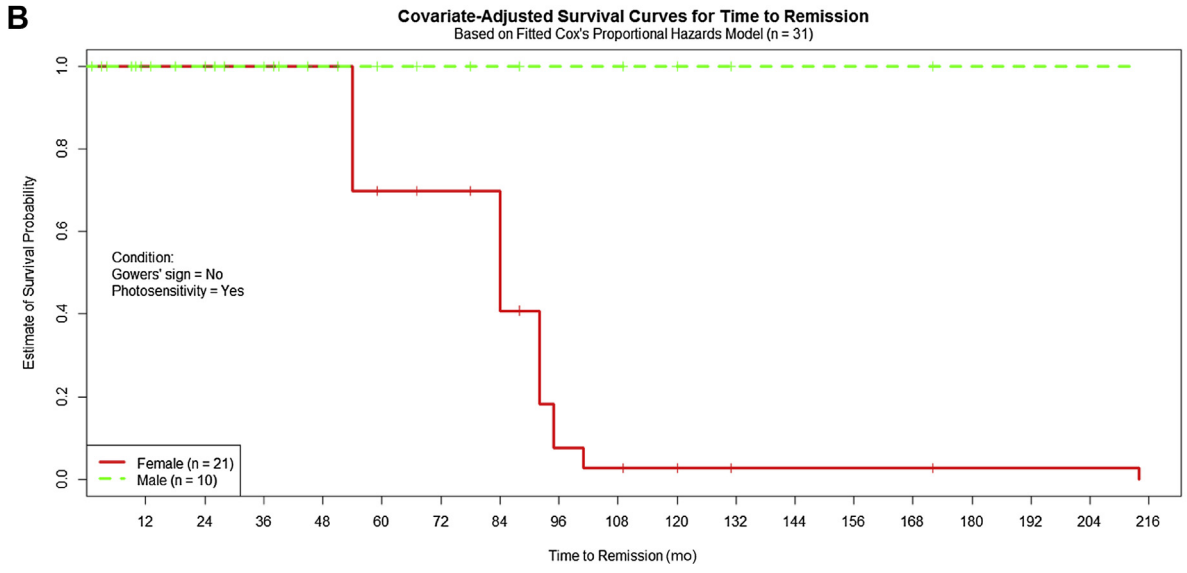
TNFα has recently been recognized as an important cytokine in the pathogenesis of DM.[2,31] Moreover, the TNFα-308A allele has been associated with a disease course that is more resistant to the immunosuppressive therapy and may be complicated by a higher frequency of pathologic calcification.[32] The use of anti-TNF agents (e.g., etanercept or infliximab) in children has only been reported in a few meeting abstracts. Reports of their effectiveness in adult myositis are conflicting.[33,34]

In the current study, four patients received anti-TNF agents (etanercept), of whim two achieved complete clinical response after 15 and 18 months of treatment (including etanercept and corticosteroid), but one had disease flares later during follow-up and required corticosteroid control. The other two patients did not improve well and were still under multiple medications. One was bedridden and the other had a refractory disease course. None achieved complete clinical remission. Treatment with an anti-TNF agent may be effective for adults with refractory DM or polymyositis, but it was not that promising in the current study.

Complete clinical remission is an important endpoint. We found that female sex and photosensitivity at disease onset are positive factors for complete clinical remission, whereas male sex and the presence of Gowers' sign at disease onset are adverse factors.

Among 13 male patients in the current study, none achieved complete clinical remission during the follow-up


A
Kaplan-Meier Estimate of Survival Curve for Time to Remission (n = 31)
Estimated Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192 204 216
Time to Remission (mo)


B
Covariate-Adjusted Survival Curves for Time to Remission
Based on Fitted Cox's Proportional Hazards Model (n = 31)
Estimate of Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
Condition:
Gowers' sign = No
Photosensitivity = Yes
Female (n = 21)
Male (n = 10)
12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192 204 216
Time to Remission (mo)

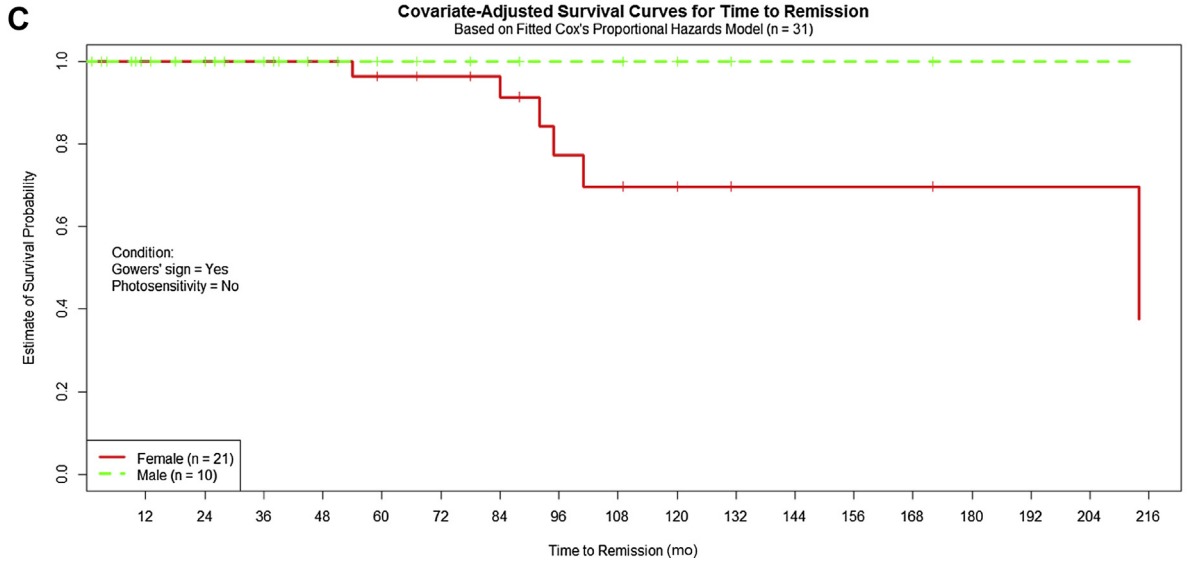

C
Covariate-Adjusted Survival Curves for Time to Remission
Based on Fitted Cox's Proportional Hazards Model (n = 31)
Estimate of Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
Condition:
Gowers' sign = Yes
Photosensitivity = No
Female (n = 21)
Male (n = 10)
12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192 204 216
Time to Remission (mo)

Table 3 Multivariate analysis of the predictors of time to complete clinical remission using Cox's proportional hazards model in 31 patients.*

Covariate†	Regression coefficient	Standard error	*z* value	*p*‡	Hazard ratio	95% confidence interval
Male versus female	−19.7825	21,936.2229	−0.0009	0.2763	2.5620×10^{-9}	0−9999+
Gowers' sign (yes vs. no)	−1.8189	1.1589	−1.5696	0.0849	0.1622	0.0167−1.5721
Photosensitivity (yes vs. no)	0.4797	1.4227	0.3372	0.7371	1.6156	0.0994−26.2651

* All covariates satisfied the proportional hazards assumption. All variance inflating factors were <1.5. Adjusted generalized $R^2 = 0.376 > 0.15$ and concordance $= 0.825 > 0.7$ indicated a good fit.

† The overall likelihood ratio test: $\chi = 6.44$, degrees of freedom $= 3$, $p = 0.0920 < 0.1$. The overall score (log-rank) test: $\chi = 7.18$, degrees of freedom $= 3$, $p = 0.0663 < 0.1$.

‡ To accommodate the separation (monotone likelihood) problem (see Table 2), the partial likelihood ratio test was used to compute the *p* value.

Table 4 Clinical outcomes and major complications of 39 patients with juvenile dermatomyositis at the end of follow-up.

Clinical outcomes	Frequency (%)
Symptom free	13 (33.33)
Mild atrophy or contracture	11 (28.21)
Disability*	4 (10.26)
Calcinosis	15 (38.46)
GI perforation	1 (2.56)
Avascular necrosis of the hip joint	1 (2.56)
Pulmonary involvement†	4 (10.26)
Death‡	2 (5.13)

GI = gastrointestinal.

* Patients required rehabilitation or auxiliary supports.

† Patients had interstitial pneumonitis or restricted lungs (3 proven by lung biopsy, 1 by clinical diagnosis).

‡ One patient died of interstitial pneumonitis with respiratory failure and septic shock at the age of 5, and the other died of end-stage renal failure and intracranial hemorrhage with herniation at the age of 29.

period. It is assumed that females are more susceptible to autoimmune diseases than males. In SLE, for example, various reasons have been proposed for this sex discrepancy, including sex hormone hypothesis, sex chromosome hypothesis, and intrauterine selection hypothesis.[35] However, previous studies also suggest that, although less common in men, SLE tends to run a more severe course when it occurs.[36] The reason why men with SLE tend to have worse outcomes has yet to be determined. Whether men with JDM have similar pathogenic patterns to men with SLE warrants further investigations.

Another adverse factor for complete clinical remission is the presence of Gowers' sign. Gowers' sign generally suggests more severe muscular involvement, which may be more difficult to control and require longer treatment. However, photosensitivity was found to be a favorable factor for complete clinical remission in this study. It is believed that ultraviolet light-induced apoptotic cell in skin leads to a suprathreshold concentration of antigenic peptides. Apoptotic cells are normally cleared through noninflammatory pathways. In the presence of genetic polymorphisms that lead to over- or underexpression of proteins involved in promoting apoptosis (e.g., TNF promoter polymorphism) or impairing clearance (e.g., decreased serum mannose binding lectin), increased apoptotic cells may lead to cutaneous autoimmune conditions found in patients with SLE or JDM.[37]

Although photosensitivity is not easily reported among pediatric patients because it may be underestimated, several studies have shown that recurrent photosensitive dermatitis can be an early sign of occult JDM[38,39] that requires further attention. Speculations about the finding in this series may be that photosensitivity at disease onset may lead to an early intervention and result in better disease control. The patients may also be more sensitive to medications in some ways. However, reasons for this finding remain unclear, and more clinical experiences from other series should be investigated.

It took 18 months for half of the patients with muscle weakness to achieve complete clinical response. However, 72.7% experienced at least one disease flare during follow-up. It took 8.5 years for half of the patients to achieve complete clinical remission without disease flares. These findings suggest that JDM runs a chronic and heterogenic course that requires a long-term follow-up, even if

Figure 1 (A) Kaplan−Meier estimate (solid line) and 95% confidence interval (dashed line) of survival curve for time to complete clinical remission ($n = 31$). As shown in the figure, the estimated median time to complete clinical remission during the follow-up period was about 101 months. (B) Estimated covariate-adjusted survival curve for time to complete clinical remission, based on the fitted final Cox's proportional hazards model ($n = 31$), which represents the best scenario: as shown by the solid line, female patients without Gowers' sign and with positive photosensitivity at the onset of the disease were most likely to achieve complete clinical remission. (C) Estimated covariate-adjusted survival curve for time to complete clinical remission, based on the fitted final Cox's proportional hazards model ($n = 31$), which depicts the worst scenario: as shown by the solid line, female patients with Gowers' sign and without positive photosensitivity at the onset of the disease were least likely to achieve complete clinical remission. All male patients failed to achieve complete clinical remission by the end of follow-up.

complete clinical response is achieved. The mortality rate in this study is slightly higher than other series (5.13% vs. 4.2% in a Brazilian series[40]) but similar to domestic data in Taiwan. However, one-third of patients were symptom free after treatment at the end of follow-up.

In conclusion, JDM is a chronic and heterogenic inflammatory myopathy that requires corticosteroids and other immunosuppressive agents for disease control. The time required to achieve complete clinical remission is relatively long, but female sex and the presence of photosensitivity at disease onset may be favorable factors to achieve this endpoint. Male sex and positive Gowers' sign at disease onset are adverse factors for disease remission that may require more attention and aggressive treatment. Exact reasons for these findings require further investigations. Although one-third of patients in this series reached the symptom-free status after treatment, certain complications cannot be avoided, highlighting the need for more efficient treatment strategies and monitoring parameters for better disease control.

Conflicts of interest

All authors have no conflicts of interest to declare.

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