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Disease course and therapeutic approach in dermatomyositis: A four-center retrospective study of 100 patients

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Abstract

Dermatomyositis is a life-altering inflammatory disorder of skin and muscle. Details regarding the natural course of this disorder, the effects of specific therapies on its progression, and the optimal therapeutic dosage and duration of prednisone are limited. We performed a retrospective medical record review of dermatomyositis patients at four medical centers. All patients were over the age of 21 and had a clinical diagnosis of dermatomyositis with pathological confirmation. We reviewed average muscle strength, corticosteroid use, creatine kinase levels, and supplemental immunosuppressant use during the 36-month period following each patient's initial assessment. One hundred patients participated with an average age of 50.1 years. Average muscle strength improved and prednisone requirements lessened six months after initial assessment. There was no difference in the mean change in muscle strength or cumulative corticosteroid use over 36 months among those initially treated with methotrexate, mycophenolate mofetil, pulse IVIG, or azathioprine. There was a 5% mortality rate in dermatomyositis patients due to infections. Treated dermatomyositis patients demonstrate the most significant improvement in strength during the first six-to-twelve months following their initial clinical assessment. Additional prospective studies are needed to determine the relative benefit of select immunosuppressant agents in preserving strength and reducing corticosteroid use in dermatomyositis.

Keywords: Dermatomyositis; Comparative effectiveness; Immunosuppression; Inflammatory myopathies

1. Introduction

Dermatomyositis is a rare inflammatory myopathy that affects the skin, muscle, and connective tissue. The estimated prevalence of dermatomyositis is 21.4 per 100,000 persons with an overall incidence of 9.6 per 1 million persons-years [1–3].

Clinically, patients frequently present with proximal muscle weakness and a characteristic skin rash [4]. The low prevalence of dermatomyositis in the general population has limited the implementation of large-scale prospective studies of disease progression. While some studies have retrospectively evaluated the relapse rate in juvenile and adult forms of dermatomyositis, these studies have not extensively detailed overall disease progression in either of these populations [5,6]. To date, it is unknown how dermatomyositis symptoms change over extended periods of time and in response to corticosteroids. In addition, while several immunotherapies have been proposed as therapy in dermatomyositis, it is not known which agent (if any) provides the greatest long term gain of function [7–12]. Furthermore, while corticosteroids are frequently used as a first-line treatment for dermatomyositis, the optimal daily dosages of these medications are not known.

The current study retrospectively evaluates the disease course of dermatomyositis patients over time in the context of treatment with corticosteroids and other immunosuppressant agents at four tertiary centers.

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2. Methods

2.1. Patients

Dermatomyositis patients were identified from the clinical and research neuromuscular databases at the University of Rochester, The Ohio State University, University of Kansas Medical Center, and Brigham and Women's Hospital between the years 1990 and 2011. All aspects of this study were conducted with institutional review board approval.

All patients had a pathological diagnosis of either inflammatory myopathy or dermatomyositis based on skin or muscle biopsy [5]. In addition, all participants were required to: 1) be 21 years or older at the time of initial assessment; 2) have both muscle weakness and a skin rash characteristic of dermatomyositis; and 3) have had at least two subsequent clinical visits after the baseline visit performed by a specialist with either neurology or rheumatology training.

2.2. Data collection

Baseline clinical data were recorded for each participant using outpatient records. The baseline visit was defined as the first outpatient visit for dermatomyositis at the tertiary center. Subsequent clinical data for each participant were recorded at 6–12 months, 12–18 months, 18–24 months, 24–30 months, and 30–36 months after the baseline assessment. Clinical data from the first outpatient visit during each interval were utilized.

2.3. Outcome variables

At each outpatient assessment we documented: 1) the patient's corticosteroid dosage and use of secondary immunosuppressants; 2) strength as determined by manual muscle testing (MMT); 3) creatine kinase (CK) levels; and 4) any adverse reactions attributed to immunosuppressant use. For each visit, the patient's corticosteroid dosage was recorded in daily prednisone-equivalent mg dosing.

Recorded manual muscle tests included shoulder abduction, elbow flexion, elbow extension, wrist flexion, wrist extension, hip flexion, knee flexion, knee extension, ankle dorsiflexion, and ankle plantar flexion. Individual MMT grades were converted to numerical scores using a 13-point scale (grade 0 = 0, 1 = 1, 2− = 1.67, 2 = 2, 2+ = 2.33, 3− = 2.67, 3 = 3, 3+ = 3.33, 4− = 3.67, 4 = 4, 4+ = 4.33, 5− = 4.67, 5 = 5) and then averaged across muscles to form a composite score [13]. Given the proximal nature of dermatomyositis weakness, a proximal MMT score was calculated that included only proximal muscles (shoulder abduction, elbow flexion, elbow extension, hip flexion, knee flexion, and knee extension).

Adverse events were extracted from the progress notes in the chart. Events were included if the physician attributed symptoms or events (e.g., infections) to the medication on record. If multiple steroid-sparing agents were used, then the event was attributed to all listed agents.

2.4. Statistical methods

Composite MMT scores, proximal MMT scores, corticosteroid dosages, and treatment regimens were summarized descriptively over time. For subject-visits that had an MMT score recorded for at least one muscle but fewer than 10 muscles, multiple imputation was used to accommodate missing data [14,15]. Specifically, a Markov chain Monte Carlo procedure [16] was used to impute the missing MMT values. The imputations were performed 100 times, resulting in 100 complete data sets. All analyses (descriptive and inferential) were performed separately for each of the 100 complete data sets, and the results were combined across data sets using standard combining rules [15,17]. This method of imputation appropriately reflects the uncertainty associated with the imputed values and is valid under the standard missing at random assumption.

A formal analysis was performed to compare the mean change in composite MMT and proximal MMT scores from the visit immediately preceding the introduction of immunosuppressive treatment (other than prednisone) to the 6–12 month and 12–18 month visits among the following initial treatments: methotrexate, azathioprine, mycophenolate mofetil, and IVIG. A standard analysis of variance model was used in conjunction with multiple imputation as described above to accommodate missing data. Pairwise comparisons among the four groups were performed, with results reported as group differences in mean response along with associated 95% confidence intervals (CIs) and p-values. Paired t-tests were performed to evaluate the significance of the mean changes in composite MMT and proximal MMT scores from baseline to 6–12 months as well as from 18–24 to 24–30 months. Associated 95% CIs and p-values were also reported.

Additionally, a quadratic regression analysis was performed to relate the change in muscle strength over all combined 6–12 month intervals to prednisone dosage (that the patient was taking coming into their interval visit), irrespective of a patient's immunosuppressant use. An overall F-test was used to evaluate the significance of this association.

3. Results

One hundred dermatomyositis patients were identified for this study. Characteristics of the sample are provided in Table 1. Of the 100 patients, the last visit was in the 6–12 month assessment for 10% of patients, in the 12–18 month assessment for 9% of patients, in the 18–24 month visit for 5% of patients, in the 24–30 month visit for 13% of patients, in the 30–36 month visit for 8% of patients, and was greater than 36 months for 54% of patients. The average increase in the composite MMT score between baseline and the 6–12 month assessment was 0.22 (95% confidence interval −0.34–0.78), although this change was not statistically significant (p = 0.44, Supplementary Fig. S1a). For the proximal MMT score, the average increase between baseline and the 6–12 month assessment was 0.30 (95% CI −0.62–1.22, p = 0.52) (Fig. 1a). This increase in strength remained stable throughout subsequent visits. Over the same period of time, the average prednisone dosage declined (Fig. 1b).

The initial prednisone dosage varied substantially among patients (Table 1). By the 6–12 month follow-up period, all groups (regardless of initial prednisone dose) demonstrated