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A Retrospective Review of Tofacitinib in the Treatment of Refractory Dermatomyositis

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INTRODUCTION

Dermatomyositis (DM) is an autoimmune myopathy with characteristic dermatologic features.[1] Tofacitinib is an immunomodulator with proven efficacy against numerous immune-mediated disorders, including rheumatoid arthritis (RA) and psoriasis.[2] Several reports have demonstrated oral tofacitinib's ability to treat the cutaneous and extracutaneous manifestations of refractory dermatomyositis (DM).[1,4,5] However, evidence for sustained improvement remains limited.[2,3] The goal of this study is to investigate the long-term response of recalcitrant DM to oral and topical tofacitinib at varied dosing regimens.

A retrospective review was conducted of all patients from May 2012 to March 2021 who were treated for DM with tofacitinib. This study was approved by the Institutional Review Board at the Medical University of South Carolina. Four patients were identified (Table I). All were white and refractory to numerous therapies. The median duration of treatment prior to initiating tofacitinib was 7.5 years (range 1-22).

Tofacitinib was used adjunctively in all patients (Table 2). The median duration of tofacitinib therapy was 23 months (range 11-42). Topical therapy was used in one patient. All patients exhibited favorable initial and sustained clinical responses. The cutaneous response to therapy was scored as mild (2), moderate (1) and significant (1) relative to pre-treatment baseline using patient-reported factors (pruritus and pain) and physical examination findings (erythema, tenderness, and affected area).

In patient 1, topical therapy was only applied to the eyebrows, and this led to hair regrowth and reduced inflammation. Remarkable improvement was observed in patients 2 and 3 (Figure 1), and these effects were enhanced when dosing was increased to three times daily after 3 and 4 months, respectively. Concurrent therapies were tapered to 5 mg of daily prednisone (patient 2) and a reduced dose of intravenous immunoglobulin (IVIG) with topical steroids (patient 3). Patient 4 initially presented with anti-synthetase syndrome and was eventually diagnosed with RA. Although his cutaneous disease and RA

TABLE 1.

Disease Course Prior to Tofacitinib Therapy

Patient Number	Sex	Age at Diagnosis (Years)	Disease Subtype	Autoantibodies	Systemic Involvement	Prior Treatment Duration (Years)	Prior Therapies
1	F	63	Classic	None	Mild cutaneous disease, alopecia, myopathy	1	HCQ, pimecrolimus cream, tacrolimus ointment, topical steroids
2	F	44	Clinically amyopathic → Classic	ANA, anti-SAE	Severe cutaneous disease, alopecia, myopathy	3	AZA, HCQ, IVIG, MTX, MMF, prednisone, rituximab, tacrolimus ointment, topical steroids
3	F	16	Juvenile	ANA	Severe cutaneous disease, myopathy	22	Cyclosporine, HCQ, IVIG, MTX, MMF, prednisone, rituximab, tacrolimus ointment, topical steroids
4	M	38	Classic	ANA, anti-Jo-1	Moderate cutaneous disease, myopathy, arthropathy, ILD	12	HCQ, MTX, MMF, prednisone, rituximab, topical steroids

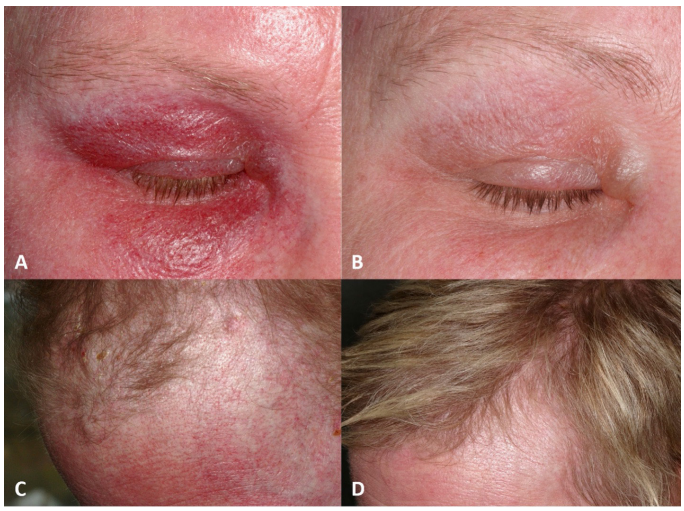
F, female; M, male.
ANA, antinuclear antibody; AZA, azathioprine; HCQ, hydroxychloroquine; ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; MTX, methotrexate; SAE, small ubiquitin-like modifier activating enzyme.

TABLE 2.

Disease Course During Tofacitinib Therapy							
Patient Number	Drug Route	Dose	Concurrent Therapies	Treatment Duration (Months)	Cutaneous Response at Month 6[1]	Longitudinal Cutaneous Response[1]	Extracutaneous Response
1	Topical	2% Cream BID	Tacrolimus ointment, topical steroids	31	+1	+1	N/A
2	Oral	5 mg QD, BID, TID	HCQ, IVIG, PTX, pimecrolimus cream, prednisone, tacrolimus ointment, topical steroids	42	+3	+2	Improved strength, alopecia, fatigue, dysphagia
3	Oral	5 mg BID, TID	IVIG, topical steroids, prednisone	18	+2	+3	Improved strength
4	Oral	11 mg QD	MTX, prednisone	11	+1	+1	Improved arthritis; stabilized strength

QD, once daily; BID, twice daily; TID, thrice daily.
HCQ, hydroxychloroquine; ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; MTX, methotrexate; N/A, not applicable; PTX, pentoxifylline.
[1]Treatment responses were graded relative to baseline disease severity: -3, much worse; -2, moderately worse; -1, mildly worse; 0, no change in disease activity; +1, mildly improved; +2, moderately improved; +3, greatly improved.

FIGURE 1. Patient 2 before (A,C) and after (B,D) 4 months of tofacitinib therapy demonstrating hair regrowth and reduced erythema.



responded well to tofacitinib, progression of his interstitial lung disease led to discontinuation of the drug.

Complete blood counts and comprehensive metabolic panels were reviewed in all patients. Abnormal liver function tests and decreased hemoglobin were transiently observed in one patient. Lipid panels were available for review in 3 patients. Elevations in cholesterol were noted in 2 patients but did not require treatment. One patient experienced shingles at month 5 of treatment and a deep venous thrombosis (DVT) with pulmonary embolus at month 9 of treatment. The DVT was attributed to concurrent IVIG therapy and did not recur after discontinuing IVIG. No other adverse events were reported.

Topical and oral formulations of tofacitinib led to positive, sustained clinical improvement in dermatologic as well as systemic symptoms of DM. Stronger responses were observed in patients receiving higher doses of tofacitinib, a finding consistent with previous studies.[4] One patient experienced a significant adverse event attributed to IVIG, but tofacitinib was otherwise well-tolerated with only minor laboratory abnormalities noted.

Limitations of this study include the small sample size, retrospective study design, adjunctive treatments, and lack of a widely accepted scoring method.[4] In conclusion, this study supports oral and topical tofacitinib for the treatment of cutaneous and extracutaneous manifestations of refractory DM.

DISCLOSURES

The authors have declared no conflicts of interest and/or support, financial interests, or patents.

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