

Tofacitinib as a Treatment for Refractory Dermatomyositis: A Case Report

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Abstract

In very scarce case reports and case series, tofacitinib has been a therapeutic alternative for dermatomyositis. To corroborate the literature, we described a refractory dermatomyositis that had a good outcome with tofacitinib. **Case Report:** An adult female patient presented with definite dermatomyositis and with refractoriness to high doses of intravenous and oral glucocorticoids, intravenous human immunoglobulin, several immunosuppressive drugs (methotrexate, azathioprine, and leflunomide) and two previous immunobiological drugs (rituximab and abatacept). However, the patient had a good outcome with tofacitinib. **Conclusions:** Tofacitinib appears to be a promising alternative therapy for refractory dermatomyositis.

Keywords

Dermatomyositis, Immunosuppressive Agents, Muscle Diseases, Myositis, Therapeutics

1. Introduction

Dermatomyositis (DM) is a rare systemic autoimmune myopathy associated with high functional disability [1]. Although skeletal striated muscle tissue is the main target in DM, its involvement is often accompanied by tissue and/or organ impairment as a result of systemic inflammatory processes [1]. The cause could be multifactorial involving interactions between genetic and environmental risk factors and, in this aspect, several trigger factors (*i.e.*, drugs, infections, hormones, occupational exposures, vaccines, among others) would act on predisposed patients, favoring changes in the immunoregulatory mechanism responsible for the DM manifestations [1].

In this sense, considering the pathogenesis of DM, scarce case reports and case

series have shown the relevance of tofacitinib—a JAK kinase inhibitor, preventing the phosphorylation and activation of signal transducer and activator [2]. It is standardized medicine in the treatment of ulcerative colitis, rheumatoid arthritis and psoriatic arthritis, and recently has been used as a therapeutic option for treating DM, especially for cutaneous and pulmonary conditions [2] [3] [4] [5] [6]. However, patients from these studies used few immunosuppressive drugs before starting the JAK kinase inhibitor [2] [3] [4] [5] [6]. Herein, we contribute with a case report in which a DM response clearly correlates to tofacitinib in a refractory disease. The case report includes glucocorticoid, intravenous human immunoglobulin, different immunosuppressive drugs, and two immunobiological drugs.

2. Case Report

The informed consent was obtained from the patient.

In September of 2016, a white, 47-year-old female patient showed symmetrical muscle weakness and proximal predominance of the four limbs (grade IV muscle strength), a 10 kg weight loss, dysphonia, and skin lesions (erythematous and/or universal ulcerations, papules, and Gottron's sign, heliotrope rash, a neckline "V" sign, a "shawl" sign, a "holster" sign, a "flagellate" sign, periungual hyperemia, cuticular hypertrophy, a "Hoster" sign, panniculitis and facial rash)—part of these cutaneous lesions is showed in **Figure 1**. Anti histamines and prednisone 80 mg/day (80 kg) were prescribed for one month for suspected allergic disease.

In February of 2017, the patient was admitted to our service. The patient retained the previous clinical condition using prednisone. During this period, neoplastic and infectious causes were ruled out.

The following complementary exams were performed: a magnetic resonance of the thighs, showing edema of pelvic and thigh muscles (adductor, gluteal, obturator, and proximal quadriceps muscles); a muscle biopsy of the vastus lateral muscle, showing evidence of inflammatory myopathy; a serum level exam muscle enzymes within a normal range; negative myositis-associated and myositis-specific autoantibodies (anti-Mi-2, -OJ, -EJ, -SRP, -PL7, -PL12, -PM/Scl, -Ro, -MDA5, -SAE, Myositis Profile, Euroimmun, Germany, according to the manufacturer's protocol); and a chest-computed tomography without any lung alteration.

With the DM hypothesis [7], we used pulse therapy with methylprednisolone (1 g, 1 x/day, for 3 consecutive days), intravenous human immunoglobulin—IVIg (2 g/kg, divided between 2 consecutive days), and subsequently maintained prednisone 1 mg/kg/day. However, due to persistent skin activity, IVIg cycles were repeated on various occasions, with or without associated pulse therapy with methylprednisolone (**Figure 2**). For glucocorticoid sparing, immunosuppressive drugs (azathioprine, methotrexate, leflunomide) were associated and suspended for ineffective and/or adverse events (clinical and/or laboratory). In addition, the patient received rituximab and abatacept.



Figure 1. Patient's cutaneous lesions before ((a)-(e): above) and after ((a)-(e): below) tofacitinib treatment.

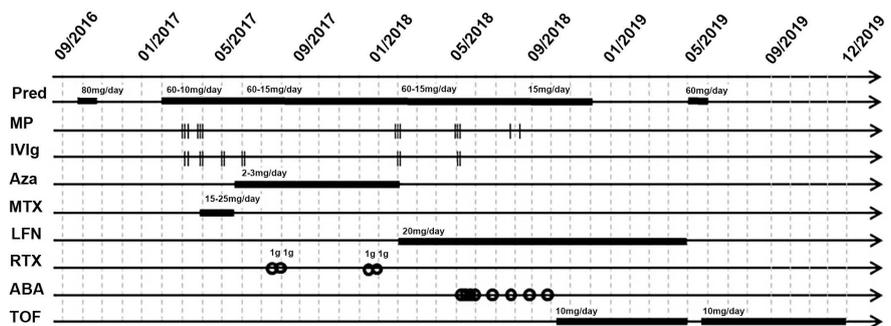


Figure 2. General treatment schedule. Legends: ABA: abatacept; Aza: azathioprine; IVIg: intravenous human immunoglobulin; LFN: leflunomide; MP: methylprednisolone pulse therapy; MTX: methotrexate; Pred: prednisone; RTX: rituximab; TOF: tofacitinib.

In October of 2018, due to persistence of the cutaneous condition, steroid dependence and the presence of leflunomide, it was decided to start tofacitinib (5

mg every 12 hours orally). The cutaneous condition significantly improved over a period of 3 to 4 weeks, allowing a complete cessation of prednisone within 2 months of tofacitinib use.

In May of 2019, she presented herpes zoster on the 5th right thoracic dermatome. Parenteral acyclovir was introduced, tofacitinib and leflunomide suspended, and prednisone was temporarily reintroduced at a dose of 60 mg/day.

After 2 - 3 weeks, there was a recurrence of skin lesions and, so tofacitinib was reintroduced. Again, the skin lesions significantly improved, even allowing a complete prednisone suspension.

The patient was reevaluated in December of 2019, the last outpatient visit, using only tofacitinib and a complete absence of skin lesions (**Figure 1**).

3. Discussion

Herein, we report a refractory DM case to high doses of intravenous and oral glucocorticoids, intravenous human immunoglobulin, immunosuppressive drugs and two previous immunobiological drugs that showed a good outcome with tofacitinib.

Although there are no controlled clinical trials, glucocorticoid drugs representing a first-line treatment of DM [8] associated or unassociated with intravenous human immunoglobulin [8] followed by a high dose of oral glucocorticoid should be considered. In clinical practice methotrexate, azathioprine and/or cyclosporine are most frequently used [8]. Alternatively, previous study showed good skin response to leflunomide use in refractory patients with DM [9]. The greatest evidence for immunobiologicals' efficacy is the use of rituximab [8]. Our described patient was actually refractory to multiple immunosuppressive drugs and high doses of immunoglobulin-associated glucocorticoid, including two immunobiological agents (rituximab and abatacept). For the cutaneous condition associated with tofacitinib, we used leflunomide, with presented a good therapeutic response thereafter.

More recent studies considered tofacitinib a possible therapeutic modality, with results regarding skin and lung involvement [2] [3] [4] [5] [6]. The most varied skin lesions, including calcifications, have responded to tofacitinib [2] [3] [4] [5] [6]. Our patient had associated muscle weakness without increased muscle enzymes and no pulmonary involvement. Moreover, the patient had several classic cutaneous manifestations of DM, including ulcerations. After using several immunosuppressive drugs, introducing tofacitinib gave a clear answer regarding refractory dermatological lesions.

An adverse effect to using a JAK kinase inhibitor in our patient was a herpes zoster (HZ) infection. In patients with rheumatoid arthritis, the HZ occurred at a rate of approximately 4% per year and doubled with glucocorticoid exposure. Concomitant methotrexate did not confer additional risk [10]. It is possible to reintroduce the drug after the infectious process when taking the necessary care [10]. Our case presented the infectious process with the correct treatment, reintroduction of tofacitinib after resolution of the condition, with a good profile of recovery after.

4. Conclusion

Tofacitinib appears to be a promising alternative therapy for refractory DM, with emphasis on severe skin manifestations and refractory to the most used immunosuppressive drugs.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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