Rituximab treatment of refractory skin involvement in anti-TIF1 ϒ dermatomyositis

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Abstract

Dermatomyositis is one type among a heterogeneous group of idiopathic inflammatory myopathies. Among these anti-TIF1 ϒ dermatomyositis is characterized by specific skin lesions, often severe and refractory to conventional treatments. We report a 58-year-old woman who had fatigue associated with myalgia with proximal and bilateral muscle weakness along with a generalized lilac erythematous rash on the face with Gottron papules on the metacarpophalangeal joints and periungual erythema on both hands. She also exhibited a widespread dark-violaceous-red skin eruption on the whole trunk. She was diagnosed with anti-TIF1 ϒ dermatomyositis and received a treatment regimen of topical corticosteroids, hydroxychloroquine, oral corticosteroids, and conventional immunosuppressive drugs (methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide, and immunoglobulins) with no improvement of the skin rash. Therefore, she received rituximab, and three months later, the skin lesions improved magnificently. Rituximab is an efficient and safe option for patients with dermatomyositis-related skin disease refractory to conventional treatments.

Keywords: dermatomyositis, skin, treatment

Introduction

Dermatomyositis (DM) is one type among a heterogeneous group of idiopathic inflammatory myopathies. It includes a variety of clinical phenotypes depending on the type of specific autoantibodies. It is characterized by some pathognomonic skin lesions such as Gottron papules and sign and heliotrope rash. Skin involvement is a major aspect feature of the disease, especially in the anti-transcriptional intermediary factor 1 gamma (anti-TIF1 ϒ) group, reaching up to nearly 100% of patients [1]. Skin lesions in TIF1G can be widespread, more severe than classical DM, and treatment resistant.

Case Synopsis

A 58-year-old woman had a three-month evolving history of a generalized skin rash and fatigue associated with myalgia and arthralgia. The physical examination exhibited a generalized edematous lilac erythematous rash on the face including eyelids (**Figure 1**), with Gottron papules on the metacarpophalangeal joints (**Figure 2**) and erythema on both hands and forearms (**Figure 3**) with palpable calcinosis.

She also exhibited widespread dark violaceous-red skin rash on the whole trunk. The patient had a proximal and bilateral muscle weakness, yet no swallowing troubles. The electromyogram was normal. The creatine kinase level was increased (1280U/l [normal range, 30-200]).

A skin biopsy from the forearm found a fibrous dermis with rare inflammatory cells. The hypodermis contained numerous basophilic calcifications of variable sizes (**Figure 4**). Immunological screening found myositis specific autoantibodies of the type,

transcriptional intermediary factor 1 gamma (TIF1Y).

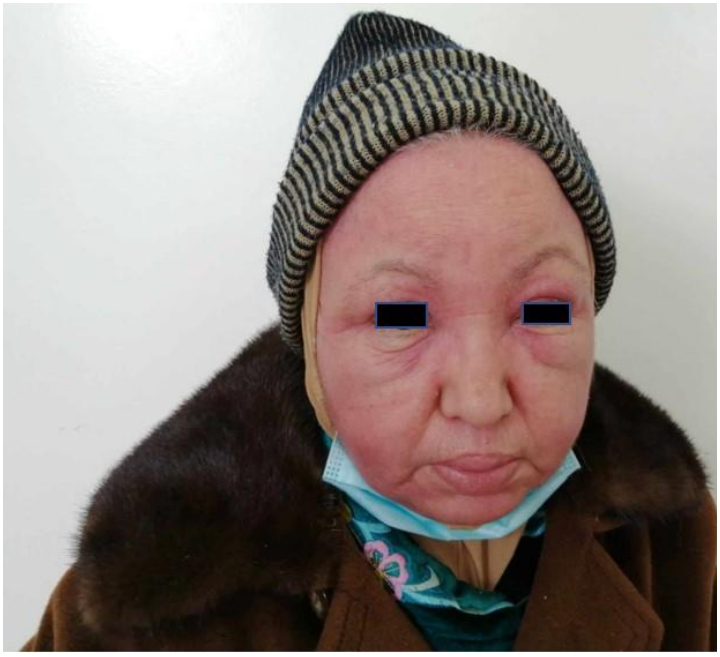

Figure 1. *Generalized lilac erythematous rash on the face with edema and periorbital involvement.*

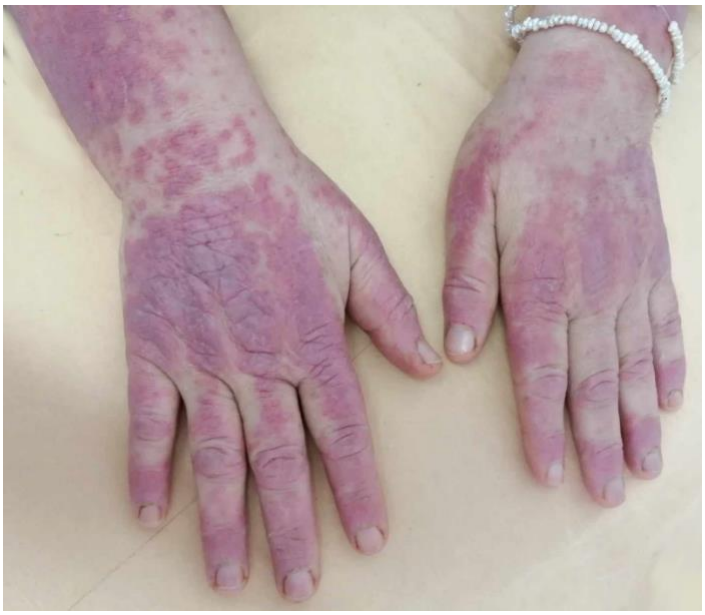

Figure 2. *Gottron papules in association with erythematous, edematous eruption.*

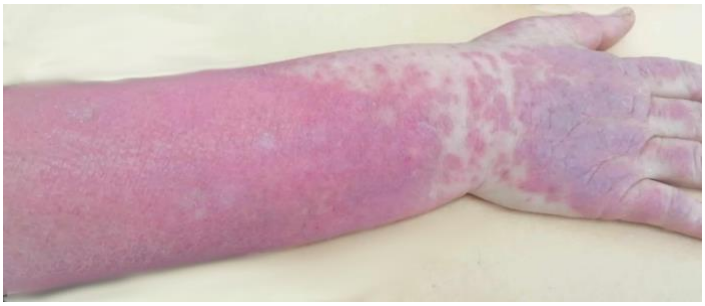

Figure 3. *Forearms/hands showing extensive eruption.*

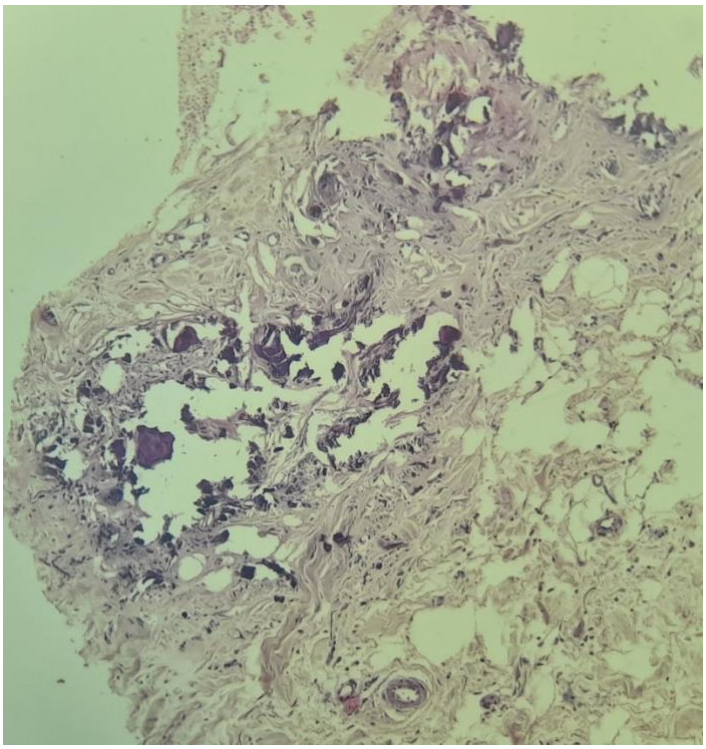

Figure 4. *Numerous basophilic calcifications of variable sizes (hematoxylin eosin stain, power of microscopic mag=100).*

The patient fulfilled the criteria for anti-TIF1Y dermatomyositis, and no muscle biopsy was needed since she had a typical case and specific antibodies. Screening for cancer was negative. The mammography and gynecological exam were normal and the colonoscopy and gastric fibroscopy were normal. Thoraco-abdominal-pelvic computed tomography showed a homogenous hepatomegaly but no other sign of malignancy.

The patient received a treatment regimen of topical corticosteroids, hydroxychloroquine 200mg twice daily, oral corticosteroids (1mg/kg/day), and methotrexate (20mg weekly) for one year. The muscle weakness improved, and the creatine kinase levels returned to normal, but the skin rash continued to worsen with unbearable pruritis resistant to topical emollients antihistaminic drugs, and maximal doses of methotrexate, which was switched to azathioprine (150mg/day). Azathioprine needed to be discontinued because of liver enzyme elevation and mycophenolate mofetil (2g/day) was substituted. Lack of response led to substitution of cyclophosphamide (1g/month for three months), again with no response. The patient also received

intravenous immunoglobulin perfusions (total dose of 2g/kg of body weight) with no improvement. At last, a rituximab perfusion regimen of 375mg/m^2 of corporal surface was given two weeks apart. Three months later the skin lesions improved magnificently. The follow-up 6 months later showed a stable improvement of the skin and no side effects.

Case Discussion

TIF1Y dermatomyositis is characterized by severe skin involvement, dysphagia, and absence of interstitial lung disease [1]. The association with malignancy is very well described in the literature, reaching up to 86%, and it is significantly higher compared to other types of DM [1].

The skin involvement in TIF1Y is characterized by extensive rash and severe lesions [2]. Our patient showcased calcinosis cutis, unlike what is generally reported in the literature regarding TIF1Y dermatomyositis. Nuclear matrix protein-related DM is strongly associated with calcinosis, however [3].

The therapeutic panel includes different immunosuppressive agents therapies and glucocorticoids are the first-line treatment [4]. Based on a better understanding of the disease pathogenesis, biologic therapies such as rituximab may offer a better treatment option [5]. Aggarwal et al [6] showed a significant improvement in the cutaneous lesions in DM after B cell depletion, supporting the role of the B cell in the pathogenesis of the cutaneous features of DM and juvenile DM. In that study, the median time to improvement of skin eruption by 40% was at week 16, which is in line with the remarkable result of skin improvement by week 12 noted in our case [6]. In the same cohort, it has been demonstrated that earlier treatment with rituximab resulted in a faster improvement of the skin [6].

The improvement of skin lesions in our patient is in line with the literature results, reported to reach 81% in a recent systematic review [7].

Conclusion

Treatment refractoriness of the skin involvement can be disturbing and frustrating for DM patients. Rituximab is an effective option for patients with DM-related skin disease refractory to conventional treatments.

Potential conflicts of interest

The authors declare no conflicts of interest.

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