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CASE REPORT

Refractory dermatomyositis in a young female

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ABSTRACT

Background: Dermatomyositis is an idiopathic autoimmune connective tissue disease. It is typically characterized by proximal muscle weakness and skin rashes, but is known to have a spectrum of cutaneous and muscle involvement.

Methods: We present the case of a 37-year-old female, smoker, with breast implants in 2019, with no other significant medical history, who presented for important pain and muscle weakness with functional impairment. Taking into consideration the clinical presentation (characteristic skin rash, proximal and symmetrical muscle weakness), the serological tests (positivity of anti-Mi-2 antibody), the suggestive electromyographic aspect, the diagnosis of dermatomyiositis was established.

Results: The present case illustrates a refractory dermatomyositis with highly increased muscle enzymes.The patient required multiple treatment regimens including high dose glucocorticoids, methotrexate, azathioprine, mycophenolate mofetil without significant clinical improvement. Thus, the intravenous imunoglobulines therapy was initiated which achieved control of both clinical and biological features of the disease activity.

Conclusion: Treatments for refractory dermatomyositis requires effective immunosupressive therapy. The selection of specific agents depends on patient's disease activity, comorbidities, and tolerance. Thus, severe refractory idiopathic inflammatory myopathy represents a challenge for the clinician.

Keywords: dermatomyositis, anti-Mi-2 antibody, methotrexate, mycophenolate mofetil.

Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathy that most commonly presents with progressive, symmetric, proximal muscle weakness and a group of characteristic cutaneous findings.

The management of patients with refractory dermatomyositis is very difficult because often they fail to respond to corticosteroids or methotrexate, or they relapse during therapy with these agents. Usually, it requires a more aggressive immunosuppressive or immunomodulatory therapy.

Case report

We present the case of a 37-year-old female, smoker, with breast implants in 2019, with no other significant medical history, who presented to emergency room in April 2022 for important pain and weakness of the scapular and pelvic girdle, with functional impairment. Physical examination confirmed muscle weakness, heliotrope rash, fingertips telangiectasias (Figure 1A, 1B) and red macules on the skin on the dorsal surface of finger joints. Upon admission, she was under no chronic medication, no new food ingestion and no significant history regarding allergies was mentioned.

Figure 1 – Heliotrope rash (A), fingertips telangiectasias (B).

Initial blood tests showed normal inflammatory markers, elevation of serum levels of muscle-associated enzymes (creatine kinase – CK 6421 u/l, creatine kinase muscle brain – CKMB 395 u/l, lactate dehydrogenase – LDH 734 u/l, aspartate aminotransferase – AST 502 u/l, alanine aminotranferase–ALT 433 u/l). Other tests were negative: rheumatoid factor, anti-citrullinated protein antibodies (ACPA). Complement fractions C3 and C4 were normal. The immunological tests showed positivity for anti-Mi-2 antibodies. At the same time, extensive screening for infectious diseases was performed. Viral hepatitis, HIV infection, syphilis, toxoplasma and toxocara were excluded. In addition, thyroid function was assessed and thyroid hormone levels were optimal and anti-TPO and antithyroglobulin antibodies were negative. Further imagistic assessment including abdominal ultrasound and chest X-rays showed no particular features. Findings on electromyography (EMG) included short, small, low-amplitude polyphasic motor unit potentials.

Taking into consideration the clinical presentation (characteristic skin rash, proximal and symmetrical muscle weakness in the shoulders and hip s), the serological tests (positivity of anti-Mi-2 antibody), the suggestive electromyographic aspect, in the absence of other diseases, the diagnosis of dermatomyiositis was established according to 2017 ACR/ EULAR classification criteria having 100% probability for a diagnosis of DM.

Once the diagnosis was established, pulse therapy with corticosteroids was initiated (500 mg daily intravenous methylprednisolone 3 consecutive days), followed by 0.75 mg/kg/day corticotherapy. In the next weeks, the patient complained of persistant muscle weakness that led to initiation of methotrexate up to 20mg/week [3]. For almost 2 years, patient was continuously treated with methotrexate and 5 mg folic acid weekly. The subsequent clinical and biological evolution was favorable, except for some flares when it was necessary to increase the dose of oral cortisone. Corticosteroids were prescribed in varied doses (20-30 mg/day) and tapered down in between flare-ups.

In December 2023, after COVID-19 infection, the patient presented with elevated muscle enzymes (CK 4341 u/l, CKMB 208 u/l, LDH 475 u/l, AST 215 u/l, ALT 105 u/l). Pulse therapy with 500 mg daily intravenous methylprednisolone (3 consecutive days) was administered, with improvement of the symptoms, followed by a medium dose of oral corticotherapy. Taking into account the multiple flares under the maximum dose of methotrexate 20mg/week, we considered appropriate the switch to azathioprine 100mg daily.

Four months after, the patient present another flare, this time with CK 3692 u/l, AST 319 u/l, ALT 218 u/l, CKMB 471 u/l, LDH 818 u/l. She developed persisting low-grade fever, proximal symmetrical muscle weakness and a diffuse erythematous rash on chest, neck and upper back, as well as macules on the metacarpophalangeal and interphalangeal joints (Figure 2).

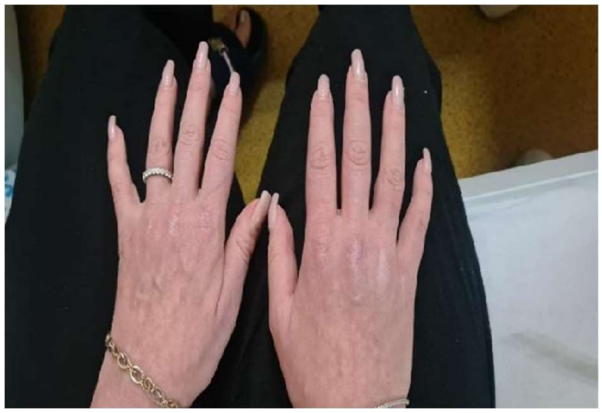

Figure 2 – ***Gottron's sign.***

We performed an ear-nose-throat (ENT) exam which revealed white papules that enlarge and coalesce to form a reticular, annular or plaque-like pattern (Figure 3), suggestive for Wickham's striae, a fine, lace-like network of white lines, specific for oral lichen planus. Pharyngeal exudate was negative [6].

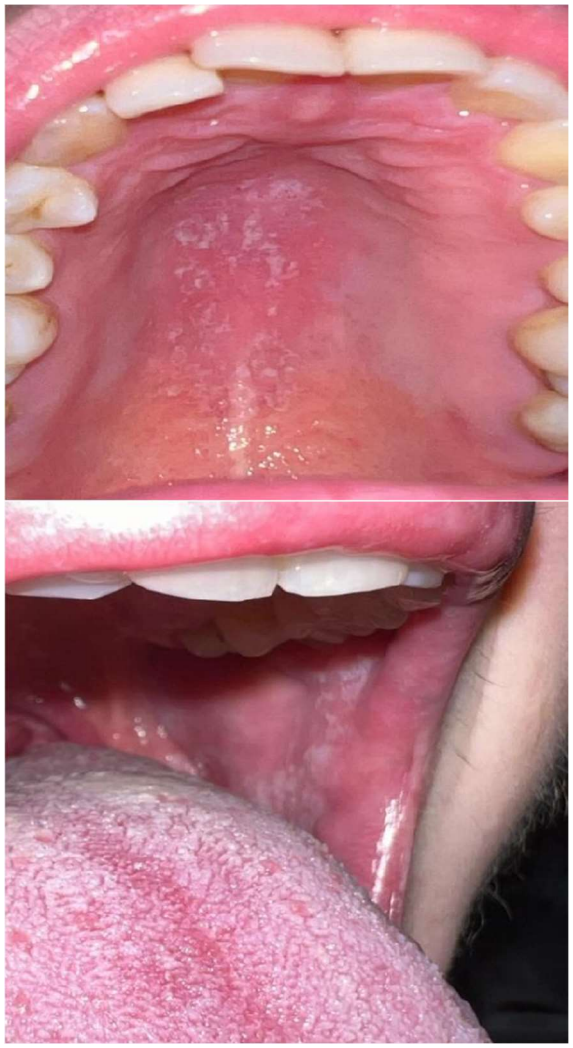

Figure 3 – ***Wickham's striae (oral lichen planus).***

Several lines of treatment failed to control the disease including steroids, methotrexate and azathioprine. This time the patient underwent muscle biopsy from the right quadriceps muscle which revealed normal findings (Figure 4). The patient started methylprednisolone 0.75 mg/kg daily to be slowly tapered, and received intravenous immunoglobulins (IVIG, 2 g/kg over 3 consecutive days). Azathioprine was substituted with mycophenolate mofetil (MMF) 2 g daily while continuing glucocorticoids. Five days after, muscle symptoms had improved, muscle enzymes decreased to CK 1910 u/l and CKMB 243 u/l.

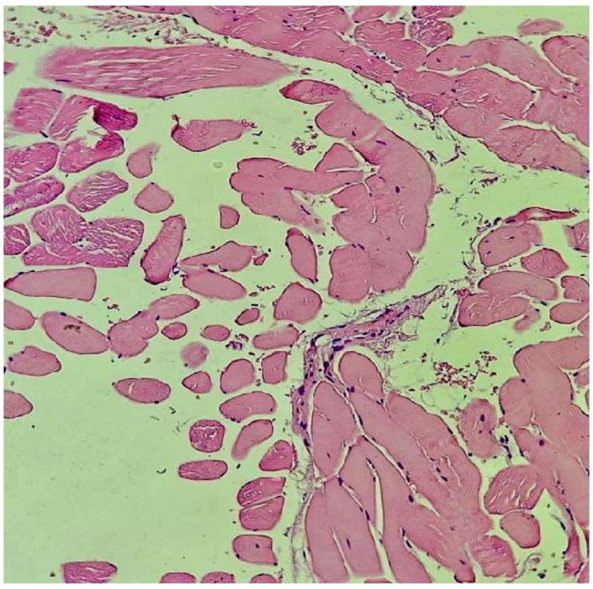

Figure 4 – Striated muscle fibers – no pathological findings of muscle biopsy from the right quadriceps muscle (HE stain x20).

Discussion

The present case illustrates a refractory dermatomyositis with highly increased muscle enzymes. It highlights therapeutic challenges raised by failure of various treatment regimens. Moreover, the presented case had negative muscle biopsy, probably because of prior corticosteroids use.

Lack of response to common first-line therapies such as glucocorticoids and methotrexate are not uncommon. Fortunately, there are second-line therapies that may be used in such refractory cases.

Severe refractory idiopathic inflammatory myopathy represents a challenge for the clinician [2]. Patients with refractory dermatomyiositis were defined as still having active cutaneous DM after being treated with at least two immunosupressive medications [4, 5].

Many studies have demonstrated that intravenous immunoglobulin (IVIG) is an effective alternative. Dalakas *et al*. performed a double-blind, placebo-controlled study of fifteen cases of resistant adult DM treated with IVIG. The study found that those treated with both prednisone and adjuvant IVIG showed clinical improvement in strength and increased muscle fiber diameter on repeated biopsies [1]. Treatment with IVIG was also associated with decreased use of systemic glucocorticoids with or without a decrease in steroid-sparing immunosuppressive medications in 80% of patients [1].

Regarding oral lichen planus in the context of dermatomyositis, we know that reports of oral mucosal involvement in DM are limited. When they are published, there is often a clinical description of "resembling lichen planus" or "leukoplakia-like" without histological evaluation. This makes it difficult to establish the definitive diagnosis of these oral lesions and formulate treatment options. It is also difficult to assess the relationship between oral lesions and oral malignancy in this patient population [6].

Anti-Mi-2 antibodies are associated with a subgroup of DM with a low frequency of interstitial lung disease and malignancy, good treatment response, and favourable outcome. Moreover, anti-Mi-2 levels correlated with disease activity. It is thought to be associated with photosensitivity in patients with DM because higher expression levels of Mi-2 antigens have been found in UV-irradiated cultured cells and also epidemiological studies have supported this association [7].

Conclusions

In conclusion, dermatomyositis is a complex and challenging autoimmune disease characterized by distinctive skin rashes and muscle weakness, often accompanied by systemic inflammation affecting various organs. Furthermore, refractory dermatomyositis presents a considerable challenge in clinical practice, requiring an innovative and holistic treatment approach. The evolving landscape of immunosupressive therapies plays a pivotal role for these difficult-to-treat cases, emphasizing the importance of ongoing research and clinical trials. Ultimately, the goal is to achieve a better quality of life for patients through a combination of advanced pharmacological treatments, supportive care, and personalized management strategies.

Conflicts of interest

The authors declare no conflict of interest.

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