International Journal of Advances in Medicine
Athul H et al. Int J Adv Med. 2024 Sep;11(5):542-544
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20242324

Case Report

Challenges and insights: a case report on refractory dermatomyositis

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Received: 17 June 2024
Revised: 16 July 2024
Accepted: 17 July 2024

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ABSTRACT

Dermatomyositis is a rare inflammatory myopathy known for its unique skin symptoms and muscle inflammation leading to proximal muscle weakness. It can be classified as idiopathic, juvenile dermatomyositis, or amyopathic dermatomyositis in adults, and may be associated with solid organ tumors. The pathophysiology of the disease is most likely influenced by immune-related variables, but genetic and environmental factors may also play a significant role. The majority of patients who receive immunosuppressive medication treatment report success, but there are chances of relapse. We report a case of dermatomyositis relapse that is refractory to pulse therapy and methotrexate.

Keywords: Dermatomyositis, Rituximab, IVIG, Refractory disease

INTRODUCTION

Idiopathic inflammatory myopathies (IIM), also known as myositis, represents a diverse range of autoimmune conditions characterised by distinct clinical presentations, responses to treatment, and prognostic outcomes. While muscle weakness commonly presents as a hallmark symptom, other organs, including the skin, joints, lungs, heart, and gastrointestinal tract, may also be affected, indicating the systemic inflammatory nature of IIM. Various myositis-specific autoantibodies have been identified, allowing for the classification of IIM into subgroups such as dermatomyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy, inclusion body myositis, polymyositis, and overlap myositis based on clinical, histopathological, and serological characteristics. The prognosis, response to treatment, and organ involvement differ among these subgroups, suggesting distinct underlying pathophysiological mechanisms for each subtype.[1]

Dermatomyositis is an IIM characterised by muscle inflammation and damage in association with the distinctive cutaneous signs such as the scaly alopecia, heliotrope rash, periungual telangiectasia, Gottron's papules, and poikiloderma or photodistributed erythema.[2] It has traditionally been seen as a humorally mediated vasculopathic disease given the findings of autoantibodies and complement deposition in vessels.[3,4] The proposed mechanism is that the binding of antibodies targeting the endothelium of the endomysial capillaries leads to activation of the complement system with subsequent MAC deposition. This in turn may lead to endothelial swelling, capillary necrosis, perivascular inflammation, and muscle ischemia.[5]

The management of myositis involves various immunosuppressive, immunomodulatory, and biologic agents. Typically, the firstline therapy consists of glucocorticoids along with either methotrexate or azathioprine. Second Line treatments may incorporate tacrolimus, mycophenolate mofetil (MMF) or cyclosporine, or a combination like azathioprine and methotrexate. The third line therapy includes cyclophosphamide, rituximab, repository corticotropin injection (RCI), or other experimental biologic agents especially in the event of a major organ involvement. Intravenous immunoglobulin (IVIG) may serve as a

standalone first, second, or third-line treatment or as an adjunct alongside any medication based on clinical presentation or disease refractoriness.[6]

Here we present a case of relapsed dermatomyositis that is refractory to steroid pulse therapy and methotrexate.

CASE REPORT

A 52-year-old female patient was referred from a local clinic to the rheumatology department BCMCH due to complaints of myalgia for 3 weeks. Her symptoms started as fever which was followed by pain in the upper thigh along with difficulty in squatting. She developed associated rashes over both eyelids, upper chest and shoulders and also complained of weight loss. She gives a history of hardening of both hands with crackling in the past. Her initial elevation showed elevated creatine kinase (CPK 1455) with normal C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Patient was started on oral steroids and was referred to our centre for further evaluation. Subsequently creatine kinase worsened (1504.8), LDH (570), mild transaminitis (SGPT/OT: 65/67). Initially a working diagnosis of viral myositis was made. However, in view of heliotropic rashes, V-sign, she was diagnosed with dermatomyositis and was planned for steroid pulse therapy. Accordingly, she was administered Inj Methylprednisolone 500 mg for 3 consecutive days. In the meanwhile, her autoimmune along with malignancy work-up turned unremarkable (ANA IFA, profile, RF, myositis panel, CEA, AFP, Ca 125). She developed steroid induced hyperglycemia and was managed. The patient was clinically better after 3 days of intravenous infusion along with CPK, LFT showing a decreasing trend (CPK-922, SGPT/OT-51/49).

Hence, she was discharged on oral steroids at 0.5 mg/kg/day and methotrexate. Two weeks later, she presented with complaints of progressive weakness which led to quadriparesis and neck muscles weakness. She also had weakness in bilateral intrinsic muscles along with wasting suggestive of peripheral neuropathy. She did not have any pharyngeal muscle involvement or respiratory distress. Her manual muscle testing (MMT) showed no activity in bilateral lower limbs and neck muscles and trace activity in bilateral upper limbs. Her labs substantiated a disease flare and the CPK value was found to be 39925.3 U/l and she had no signs of infection. There was no recent history of fever, difficulty in swallowing, keratoconjuctivital sicca, oral ulcers, altered mental status or other constitutional symptoms. Since she was having rapid deterioration, she was started on IVIG rescue therapy at 2 gm/kg (total 120 gm given) along with a repeat dose of pulse MP. After which her MMT improved to grade 2. Magnetic resonance imaging (MRI) thigh was suggestive of dermatomyositis (Figure 1).

A USG guided muscle biopsy was taken to confirm the diagnosis and also look for evidence of any necrotizing myositis as the patient was on statin in the recent past. Subsequently injection rituximab 1 gm was given as a steroid sparing immunomodulator. She was also planned for whole body PET-CT to look for associated occult malignancy in case of worsening. A neurology consultation was sought for neuropathic symptoms and orders were carried out wherein a NCV showed demyelinating neuropathy in her lower limbs and had no involvement of the upper limb. The patient had mild improvement in upper limb weakness and hence physiotherapy was initiated. Her glycemic levels were controlled during hospital stay with intravenous short acting insulin injection and deranged electrolytes were given relative corrections. In the meantime, the patient was subjected to a second muscle biopsy as the first sample that was insufficient. However, reports were inconclusive since the patient was already pulsed with steroids and IVIG was given as part of rescue therapy. After that a second dose of injection Rituximab 1 gm was given after ruling out infections after 15 days. Patient was symptomatically better with a power improvement of zero to 3/5 and near normalised CPK levels and was discharged. Post rituximab therapy, the patient was reviewed on OP basis which revealed the normalisation of the CPK, complete recovery of muscle function (MMT-grade 4). PET-CT was done on subsequent visits and ruled out the possibility of association with malignancy.

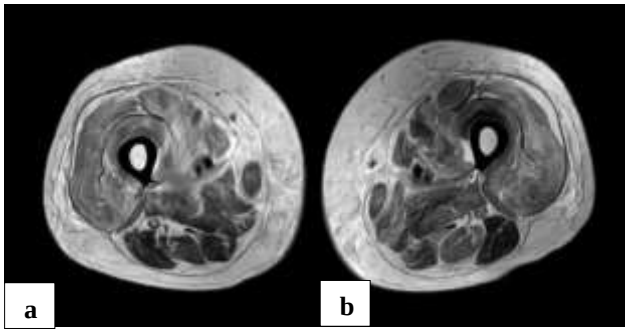

Figure 1 (a and b): Coronal view of the MRI of the bilateral thighs showing marked muscular and intermuscular oedema predominantly involving the anterior and adductor compartment muscles. Diffuse subcutaneous tissue swelling and oedema throughout.

DISCUSSION

Each patient with dermatomyositis necessitates a personalized treatment plan, considering factors such as the severity of their skin condition, the presence of concurrent muscle issues, systemic implications, other health conditions like cancer, and the overall impact on their quality of life. Specifically addressing skin problems, the objective of therapy is to effectively manage the skin condition using the safest combination of treatments available. Treating skin issues in dermatomyositis presents unique challenges, as the skin manifestations often prove stubborn to treatment compared to muscle involvement. It's widely acknowledged that glucocorticoids should serve as the primary medication for initial myositis

management. The initial dosage varies based on factors like age and specific indications.[7]

Glucocorticoids are seldom administered as standalone treatments due to their potential side effects and the likelihood of relapses being high. Systemic corticosteroids (SCS) have remained the primary approach for initiating therapy in DM patients with active muscle involvement. Corticosteroid dosages are typically kept elevated until the muscle disease becomes inactive, after which they are gradually tapered over several months. Methotrexate is frequently combined with glucocorticoids as an initial treatment for myositis and for managing disease flare-ups in patients whose corticosteroid doses have been reduced, despite the lack of clinical trials supporting its use in adults with myositis. It's worth noting that methotrexate serves as an effective agent to reduce the reliance on corticosteroids in cutaneous dermatomyositis (CDM) and may also alleviate joint symptoms in affected patients.[6,8]

In this particular case, the patient did not respond to the conventional methotrexate and steroid therapy. Instead, the patient experienced a significant flare-up, including neck muscle weakness, indicating a refractory nature of the disease. One of the critical complications in untreated or poorly managed dermatomyositis is the progression of muscle weakness, which can severely affect the neck muscles. This condition, if not promptly and adequately treated, can extend to pharyngeal weakness and eventually respiratory muscle paralysis. Such progression is a medical emergency that may necessitate intensive care unit (ICU) admission due to the risk of respiratory failure.

Given the patient's rapid disease progression and inadequate response to standard therapy, we initiated intravenous immunoglobulin (IVIG) and rituximab therapy. IVIG has been known to modulate immune responses, while rituximab, a monoclonal antibody targeting CD20 on B cells, offers a potent immunosuppressive effect.[9,10] This combination therapy resulted in significant clinical improvement, highlighting its potential efficacy in cases where conventional treatments fail.

This case underscores the need for advanced biomarkers to detect and predict rapid progression in dermatomyositis patients. Early identification of such biomarkers could facilitate timely intervention with alternative therapies, potentially improving patient outcomes and preventing severe complications like respiratory paralysis. Further research into these biomarkers is essential for developing tailored treatment strategies and improving the prognosis for patients with refractory dermatomyositis.

CONCLUSION

Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by muscle weakness and distinctive skin manifestations. The treatment for dermatomyositis requires a personalized approach, taking into account disease severity, treatment response, comorbidities, and patient preferences. Collaboration between healthcare providers and active involvement of patients in treatment decisions are critical for achieving optimal outcomes.

ACKNOWLEDGEMENTS

Authors would like to thank the Department of Rheumatology, Believers Church Medical College Hospital, Thiruvalla and the Department of Pharmacy Practice, Nazareth College of Pharmacy, Othera for helping in publishing this case report.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Athul H, Akshara KR, Sona A, Chandran VS. Challenges and insights: a case report on refractory dermatomyositis. Int J Adv Med 2024;11:542-4.