

Dermatomyositis Flare After a COVID-19 Infection Successfully Treated with Rituximab: A Case Report and Literature Review

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Introduction: Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, there has been a sudden surge in the incidence of several immune-mediated diseases, including dermatomyositis. The reported cases of COVID-19-related dermatomyositis are heterogeneous in their clinical presentation and implemented therapies.

Case Study: We report a 23-year-old female patient diagnosed with a 3-year history of dermatomyositis. She has been well-controlled on maintenance therapy. However, 6 weeks after a mild COVID-19 infection, she developed a dermatomyositis flare. She improved only after aggressive treatment with pulse steroids, intravenous immunoglobulin, and rituximab.

Conclusion: Exacerbation of dermatomyositis can be encountered following a COVID-19 infection, even if the infection is mild. Aggressive therapy should be considered in such cases. The prognosis, however, is generally favorable.

Keywords: COVID-19 infection, dermatomyositis, Rituximab

Introduction

Dermatomyositis (DM) is a rare immune-mediated disease characterized by distinct dermatological features and proximal inflammatory myopathy.¹ The disease results from an amalgam of genetic predisposition and environmental factors that trigger an incompletely understood immune disturbance.^{2,3} To date, it remains controversial whether the inflammatory cascade is initiated by complement fixation or antibody-dependent activation of interferon pathway.^{3,4}

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, a sudden surge in the incidence of DM was noted.⁵⁻⁷ For instance, the rate of new cases of juvenile DM admitted in a tertiary care center in Iran from February 2020 to February 2021 was almost four times the rate of cases during the past full decade.⁶ Moreover, patients with DM were reported to have frequent relapses during the COVID-19 pandemic.⁸ In a large Italian cohort of 1641 patients with COVID-19-related autoimmune diseases, polymyositis and DM constituted approximately 1.2% of all the cases.⁹ Of 608 patients with COVID-19-related myositis reported via an online survey, DM was the most common type, occurring in 40.6% of the participants.¹⁰

The etiopathogenesis of the co-occurrence of DM and COVID-19 infection remains elusive. Clinical, laboratory and pathological similarities between the two diseases have been recognized.¹¹ Some cases of DM were reported to present with symptoms closely similar to that of COVID-19 pneumonia, such as the case reported by Mengke et al,¹² but the COVID-19 polymerase chain reaction (PCR) tests were repeatedly negative. A similar case of anti-malondialdehyde antibody-5 (MDA-5) DM was reported to present with interstitial lung disease (ILD) mimicking COVID pneumonia.^{11,13} Both DM and COVID-19 infection have similar lab profiles (such as elevated C-reactive protein (CRP) and elevated ferritin) and similar lung radiological features (ie, ground glass opacifications and bronchovascular consolidation).¹¹ Evidence exists that suggests the presence of antibodies against immunogenic muscle epitopes in patients with COVID-19 infection.^{7,14}

The described cases of DM occurring in the context of COVID-19 infection are rare in the literature and heterogeneous. Their clinical features, laboratory findings, and treatments are inconsistent. Given the incomplete current understanding of the overall theme of co-occurrence of DM and COVID-19 infection, we aimed in this article to contribute to the literature with a new rare case of DM exacerbation after a COVID-19 infection.

Case Presentation

We report a 23-year-old female patient diagnosed with DM 3 years before her current presentation. The diagnosis was based on the clinical presentation of Gottron's papules, heliotrope rash, inability to comb her hair, walk up the stairs, or stand from a sitting position (proximal myopathy), elevated creatinine kinase, and muscle biopsy. She has been well-controlled on maintenance therapy of methotrexate and oral prednisolone 5 mg daily. On July 15th, 2021, she presented with rhinorrhea, fever, and dry cough and was diagnosed with a COVID-19 mild infection. Her prednisolone dose was increased to 20 mg daily and then tapered over 4 weeks. The COVID-19 infection ultimately resolved on July 30, 2021.

Six weeks later, she presented with an exacerbation of DM symptoms in the form of re-appearance of Gottron's papules on both hands, heliotrope rash, and generalized muscle weakness, Medical Research Council's scale (MRC scale) grade 4/5, that impaired her activity of daily living (ADL). Her lab profile revealed aspartate aminotransferase (AST): 91 U/L, alanine aminotransferase (ALT): 255 U/L, elevated creatinine phosphokinase (CPK): 9052 U/L, leucocytosis: 12.04 cells/cc³, and elevated CRP: 4.45 mg/d. The patient received a dose of IVIG 1g/kg daily for 2 days, the prednisolone dose was increased to 10 mg daily, and methotrexate was continued. Nevertheless, the patient's condition got worse in terms of the progression of her weakness and persistence of the heliotrope rash. She became bedbound with an overall MRC grade 2/5 of the muscles of the proximal upper and lower limbs. She reported no fever, weight loss, dyspnea, chest pain, or bulbar dysfunction. The CPK level increased to 24,135 U/L, and the AST and ALT increased to 883 and 201 U/L, respectively. The septic and malignancy workup was unremarkable.

Accordingly, she was admitted to our hospital and administered pulse methylprednisolone 1g/day for 3 days, followed by oral prednisolone 1mg/kg/day and IVIG 1g/kg daily for 2 days. Methotrexate was stopped and was replaced with rituximab. In about 10 days, the patient improved, ie, the power of the upper extremity muscles became MRC grade 5/5, the lower extremity muscles became 4/5, the CPK was reduced to 12,108 U/L, and the rash disappeared. The patient was discharged from the hospital on oral prednisolone 40 mg daily to be tapered gradually (5 mg every week) along with rituximab as maintenance therapy. Since then, her DM remained in remission.

Discussion

Our patient presented with a DM flare in the context of COVID-19 infection. The case, despite having a mild COVID-19 infection, developed a flare-up in the form of cutaneous manifestations and muscle weakness that was only responsive to pulse methylprednisolone, IVIG, and rituximab.

Reference to Relevant Literature

In the literature, several cases have been reported to occur in the context of COVID-19 infection or vaccination.^{5,10,12,15–22} Table 1 summarizes the clinical characteristics, laboratory and investigational findings, treatment received, outcome, and temporal relation of DM to the COVID-19 infection. Table 2 outlines the same in relation to DM flare post-COVID vaccination. Of the 13 cases reported, two patients had DM following COVID-19 vaccination.^{20,21} Most of the reported cases had DM either during, shortly after, or up to 2 months following COVID-19.^{5,10,12,15–22} The case series reported by Gokhale et al⁵ were diagnosed with DM before COVID-19 infection, similar to the case we present in this review, and their disease was exacerbated shortly before or during the COVID-19 infection.⁵ The weakness in the 13 reported cases ranged from severe weakness MRC grade 1/5 to mild weakness MRC grade 4/5.^{5,10,12,15–22} Systemic manifestations included ILD,^{19,22} polyarthritis,¹⁶ and cardiomyopathy.^{16,21,22} In the vast majority of reported cases, pulse intravenous methylprednisolone and/or IVIG were used to treat DM exacerbation. In a few cases, the DM exacerbation improved on oral prednisolone along with immunosuppressants.^{5,16,19,21} Similar to the case of our patient, the outcome of all reported cases in the literature was favorable.

Table 1 Summary of Case Reports in Literature: Dermatomyositis Flare in Relation to COVID-19 Infection

Author	Year	Age - Sex	Clinical Manifestations	Dermatomyositis Diagnosis [New Versus Flare]	Temporal Relation to COVID-19	Findings on Investigations	Treatments Received	DM Outcome
Gokhale et al ⁵	2020	64 Yr Male	Heliotrope rash Shawl's sign Proximal weakness grade 3/5 Bulbar weakness	New	During COVID-19 infection	ANA: +ve CPK 990 IU/L Myositis panel: -ve [Anti Mi-2, Jo-1, PM-SCL 75, PM SCL 100 and Anti MDA-5]	Prednisolone 1mg/kg IVIG 5 days MMF 1.5 gm daily	Improved
Gokhale et al ⁵	2020	50 Yr Female	Erythema Proximal quadriparesis grade 4/5	Flare	Before COVID-onset	ANA: -ve MDA-5 and SAE-I: +ve CPK: 150 IU/L	IV MP IV Cyc 1gm MTX 15mg/ week	Died
Gokhale et al ⁵	2020	26 Yr Female	Erythematous skin rash Proximal weakness grades 3/5 and 4/5	Flare	Suspected COVID during DM, test not done	ANA: +ve Anti-Mi2: +ve CPK: 8439 IU/L	Prednisolone MTX Hydroxychloroquine	Improved
Gokhale et al ⁵	2020	46 Yr Male	Erythematous rash Proximal weakness grade 4/5	Flare	Suspected COVID during DM	ANA: +ve Anti-SAE: +ve CPK: 570 IU/L Skin biopsy: Interface dermatitis	Hydroxychloroquine MMF MTX	Improved
Gokhale et al ⁵	2020	50 Yr Male	Erythematous rash Severe proximal weakness grade 1/5	Flare	Diagnosed prior to COVID, exacerbated during COVID infection	Mi-2 and PM-SCL: +veCPK: 1169 IU/L	Prednisolone IVIG MTX	Improved
Sacchi et al ¹⁹	2020	77 yr Female	Myositis only ILD	New	After 15 days	ANA: +ve Anti-Mi2 and anti-Ku: Positive	Steroids 1mg/Kg/day	Improved
Borges et al ¹⁵	2021	36 yr Female	Gotttron's papules Erythema Raynaud's phenomenon Proximal quadriparesis grade 4/5	New	After 15 days	ANA +ve Anti-Mi2 +ve CPK 3518 U/L Skin biopsy: lamellar keratosis with foci of vascular changes in the epidermal layer and dilated vessels with a thickened wall and perivascular lymphocytic infiltrate.	Pulse MP 5 days	Improved

(Continued)

Table 1 (Continued).

Author	Year	Age - Sex	Clinical Manifestations	Dermatomyositis Diagnosis [New Versus Flare]	Temporal Relation to COVID-19	Findings on Investigations	Treatments Received	DM Outcome
Dadras et al ¹⁶	2021	58 yr Female	Pruritic malar erythema Gottron papules Ragged nail cuticles Proximal quadriparesis grade 2/5 Cardiomyopathy	New	After 2 months	ANA -ve All myositis panel -ve [anti-Mi-2, -Ku, -PM/Scl-100, -Scl-75, -SRP, -PL-7, -PL-12, -EJ, -OJ, -Jo-1, and -Ro-52] CPK 1193 U/L Skin biopsy: Suggestive of dermatomyositis lupus features	Prednisolone (60 mg daily) MTX (15 mg weekly) Hydroxychloroquine sulfate (400 mg daily)	Improved
Balaini et al ¹⁷	2021	16 yr Male	Heliotrope eruption Gottron papules Proximal quadriparesis Neck weakness	New	During COVID-19 infection	Elevated liver enzymes CK-NAC: elevated Myoglobinuria Anti-Mi2: +ve Muscle biopsy: Multiple necrotic fibers without inflammatory infiltrate.	Intravenous then oral steroids Rituximab	Recovered gradually
Vincent et al ¹⁸	2021	58 yr Male	Erythematous papules and plaques Proximal upper extremities weakness	New	Shortly after the COVID-19 infection	Elevated liver enzymes ANA: -ve CPK: 9684 U/L Myositis panel: -ve [anti-Jo-1, anti-U1-RNP, and anti-Mi-2 antibodies] Skin biopsy: vacuolar interface changes with subepidermal edema and perivascular mixed cell infiltrate. Muscle biopsy: mild perifascicular atrophy, but no evidence of necrosis, regeneration, or inflammation	IV MP 1g daily 5 days, Then oral prednisone 60 mg for 1 month and 40 mg daily for 1 month thereafter. MTX 10 mg weekly.	Improved
Derbel et al ²²	2021	61 yr Female	Gingival ulcers Proximal quadriparesis Arthritis	New	Two months after the COVID-19 infection	Elevated liver enzymes ANA: +ve Anti-Jo1: +ve CPK: 1052 U/L	Steroids high dose	Improved
Described case	2022	23 Yr Female	Gottron's papules Heliotrope rash Quadriparesis	Flare	Six weeks following the COVID-19 infection	Elevated liver enzymes CPK: 9052 U/L	IV MP IVIG Rituximab	Improved

Abbreviations: ANA, antinuclear antibody; CK-NAC, creatine kinase-N-acetyl-cysteine; CPK, creatinine phosphokinase; COVID-19, coronavirus disease 2019; Cyc, cyclophosphamide; DM, dermatomyositis; ILD, interstitial lung disease; IV, intravenous; IVIG, intravenous immunoglobulin; MDA-5, malondialdehyde antibody-5; MMF, mycophenolate mofetil; MTX, methotrexate; MP, Methylprednisolone; NRP, Nuclear ribonucleoprotein; NXP, nuclear matrix protein; PM/Scl, polymyositis/systemic scleroderma; Scl, scleroderma; SLE, systemic lupus erythematosus; SRP, signal recognition particle; Yr, year.

Table 2 Summary of Case Reports in Literature: Dermatomyositis Flare in Relation to COVID-19 Vaccination

Author	Year	Age - Sex	Clinical Manifestations	Dermatomyositis Diagnosis [New Versus Flare]	Temporal Relation to COVID-19	Findings on Investigations	Treatments Received	DM Outcome
Gouda et al ²¹	2022	43 Yr Female	Erythematous pruritic rash, Shawl's sign Proximal weakness grade 3/5 ILD Polyarthrititis	New	10 days after the COVID-9 vaccination	Elevated liver enzymes ANA: +ve Anti-RNP: +ve CPK: 3358 IU/L Skin biopsy: atrophic epidermis with flattened ridges, a marked vacuolar interface with pigment incontinence, a superficial and deep perivascular and periadnexal lymphocytic infiltrate with increased mucin	Prednisolone 60 mg/day MMF 1.5 g/day Hydroxychloroquine 200 mg/day	Improved
Lee et al ²⁰	2022	53 Yr Male	Crusted skin eruptions Proximal quadriparesis grade 4/5	New	Two weeks after the COVID-19 vaccination	Elevated liver enzymes CPK 14659IU/L Anti-NXP2: +ve Muscle biopsy: non-necrotizing myositis	Pulse IV MPThen prednisolone 1mg/kg MMF	Recurrence twice but improved.

Abbreviations: ANA, antinuclear antibody; CPK, creatinine phosphokinase; COVID-19, coronavirus disease 2019; DM, dermatomyositis; IV, intravenous; MMF, mycophenolate mofetil; MP, methylprednisolone; NXP, nuclear matrix protein; Yr, year.

Comparison to the Current Gold Standard of Care

The standard treatments of DM include oral or pulse corticosteroids with or without IVIG for acute flares and corticosteroids, methotrexate, azathioprine, cyclophosphamide, cyclosporine, and/or hydroxychloroquine as maintenance therapy.^{23–25} In patients with severe or refractory symptoms, more potent immunosuppressive drugs should be offered, such as rituximab.²⁴

Relevant Hypothesis Generation

In the literature, it has been proposed that certain proteins and receptors, such as MDA-5, play a crucial role in the innate immunity defense mechanisms against viral infections, including COVID-19.⁵ These receptors are activated by viral ribonucleic acid (RNA).⁵ Once activated, they stimulate interferon I (INF-I) and subsequent production of proinflammatory cytokines such as interleukin (IL-6), IL-1 β , IL-18, INF- γ , and tumor necrosis factor-alpha (TNF- α).²⁶ Then, the cytokine storm stimulates T helper cells and macrophages and precipitates a flare-up or initiation of several immune-mediated disorders, including dermatomyositis.⁹ For DM in specific, six distinct epitopes were found to be highly identical to the COVID-19 virus.^{7,14} This consolidates the involvement of the molecular mimicry mechanism in evaluating DM in the context of COVID-19 infection.

Implications of Clinical Practice

The patient we describe represents an addition to the few reported cases in the literature that can add to the still-growing knowledge of the association between DM and COVID-19 infection. Similar to the cases reported by Gokhale et al,⁵ our patient exacerbated following a COVID-19 infection. Treatment of exacerbation with increasing doses of oral prednisolone did not seem to be adequate in our patient, and pulse steroids were necessitated. Clinicians should inquire about any history of COVID-19 infection, even if mild, in all patients with DM presenting with a flare-up of their symptoms. If COVID-19 was suspected of triggering the flare, clinicians should consider aggressive treatment of the DM exacerbation with pulse intravenous steroids, IVIG, and/or rituximab.

Strength and Limitations

The strength of this report is being one of the rare cases of COVID-19-related DM in the literature that can help understand and draw the full but still unclear picture of the actual relationship between the two disease entities, including the clinical presentation, lab tests, treatment, and prognosis. The main limitation is the relatively short-term follow-up of the case.

Conclusion

Dermatomyositis can occur within the context of COVID-19 infection either for the first time or as an exacerbation of a previously diagnosed disease. The prognosis is generally favorable. Clinicians should consider aggressive treatment of DM exacerbations post-COVID, with pulse intravenous steroids, IVIG, and/or rituximab. The use of rituximab should be based on the physician's own clinical judgment.

Learning Points/Take-Home Messages

- A COVID-19 infection can possibly induce a dermatomyositis flare.
- The clinical presentation is heterogeneous.
- Treatment is similar to standard therapy, but aggressive treatment is required in many cases.
- The prognosis is favorable.

Ethics Approval and Consent to Participate

This article was performed in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of, our hospital, King Faisal Specialist Hospital & Research Centre, Jeddah, Saudi Arabia. The approval reference number is IRB 2021-CR-39. Written consent was obtained from the patient for the publication of her case and accompanying data.

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Disclosure

The authors report no conflicts of interest in this work.

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