Drug-induced dermatomyositis following COVID-19 vaccination

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Abstract

Dermatomyositis (DM) is a multi-organ idiopathic inflammatory myopathy that presents with proximal symmetric muscle weakness accompanied by characteristic cutaneous findings. Most individuals present with skin manifestations prior to muscle involvement and its course can involve the blood vessels, joints, esophagus, and lungs and can be paraneoplastic, making a malignancy assessment imperative. Although its etiology is unknown, type I interferon appears to be a component in evoking the characteristic inflammatory response and patients with DM often have an increase in type I inducible genes. Suspected triggers for DM are environmental factors, drugs, viral infections, and vaccines. The association of DM with vaccination poses a new conundrum within the medical community as people continue to get vaccinated and boosted with SARS-CoV2 vaccines, though it is worth noting that the most common challenges arose as type I hypersensitivity reactions and new onset autoimmune disorders are rare. Presented here is a 53-year-old man who was diagnosed with DM after receiving the second dose of the Pfizer vaccine. His case highlights the importance of the potential onset of autoimmune diseases following the COVID-19 vaccine, a phenomenon that clinicians should be aware of as the discourse concerning the pandemic continues.

Keywords: COVID-19, dermatomyositis, drug induced, SARS-CoV-2, vaccine induced dermatomyositis

Introduction

During the pandemic, new onset cutaneous eruptions following contraction of COVID-19 and inoculation with the COVID-19 vaccine posed challenges to practitioners. Although the majority of challenges arose as type I hypersensitivity reactions such as urticaria, angioedema, anaphylaxis, type IV hypersensitivity reactions, and less commonly, autoimmune disorders after COVID-19 have been reported [1-3]. Both infections and vaccines trigger or flare autoimmune diseases such as leukocytoclastic vasculitis, lupus erythematosus, immune thrombocytopenia, and dermatomyositis [2-4]. Dermatomyositis (DM), a multi-organ idiopathic inflammatory myopathy, presents with proximal symmetric muscle weakness accompanied by characteristic cutaneous findings, such as Gottron papules and heliotrope rash. Dermatomyositis has been reported following hepatitis B, influenza, tetanus toxoid, H1N1 influenza, and BCG vaccines [2-5]. Histopathology of the skin is characterized by vacuolar interface dermatitis, basement membrane thickening, epidermal atrophy, hyperkeratosis, dermal edema, mucin deposits, and perivascular infiltrate composed of CD4+ lymphocytes [5]. Dermatomyositis may also be paraneoplastic, with clinical signs of DM preceding or arising concurrently with a cancer diagnosis [6]. The association with the mRNA COVID vaccines to dermatomyositis is not clear, especially with dermatomyositis itself being poorly understood, though it is predominantly found in people over the age of 40 [2-4,7]. Presented here is a 53-year-old man who was diagnosed with DM after receiving the second dose of the Pfizer vaccine. His case highlights the importance of the potential onset of autoimmune diseases following the COVID-19 vaccine.

Case Synopsis

A 53-year-old previously healthy man presented to clinic in May 2022 with an extensive and progressing cutaneous eruption not improving with previous therapy. The eruption started at an inoculation site two days after receiving his second Pfizer vaccine in December 2021, then spread over time throughout his body. The patient had contracted Covid-19 in November 2021 and received the first Pfizer vaccine two weeks after having the virus with no significant reactions.

At initial exam, the patient had a pruritic scaly erythematous eruption on his arms, trunk, and legs in addition to diffuse erythema on his scalp, face, and neck. In addition to the cutaneous involvement, the patient also complained of muscle weakness, characterized by difficulty going up the stairs and weakness in his arms. Treatments prior to his initial visit consisted of triamcinolone, clobetasol, prednisone, crisaborole, and omalizumab, which were all deemed ineffective. Initial biopsy showed a perivascular lymphocytic infiltrate, a presumptive diagnosis of dermatitis was made, and treatment with cyclosporine was initiated. At the one month follow up visit, the patient stated his skin worsened and pruritus persisted. Upon follow up examination, the patient was found to be erythrodermic with heavy burden on his chest, shoulders, dorsal hands, arms, and legs. He had extensive salmon-colored patches on his trunk and extremities (**Figure 1**). At this time, the presence of purple discoloration on his eyelids raised concern for dermatomyositis. A punch biopsy was performed on the right upper shoulder and tested for routine histology and direct immunofluorescence. Pathology findings were significant for vacuolar change with occasional Civatte bodies, keratinocyte enlargement, thickened basement membrane, hypereosinophilia, perivascular lymphocytes, and an increase mucin present in the reticular dermis. Direct immunofluorescence was negative for IgG, IgG4, C3 and fibrinogen (**Figure 2**). Focal IgM and IgA cystoids were present along the basement membrane zone. Dermatomyositis autoantibody panel was negative for nuclear helicase protein (Mi2) antibody, TIF-gamma (P155/140) antibody, small ubiquitin-like modifier1-activating enzyme (SAE1) antibody, anti-140 kDa peptide/melanoma differentiation-associated gene5 (CADM-140/MDA5) antibody, and nuclear matrix protein 2 (NXP2) antibody. A clinical and pathologic diagnosis of dermatomyositis was made.

A malignancy workup consisting of a physician exam, a CT scan of the chest, abdomen, and pelvis, and prostate-specific antigen were unremarkable. He had had a recent colonoscopy as well that was unremarkable so this was not repeated. Laboratory tests were drawn for complete blood count, comprehensive metabolic panel, hepatitis B and C, creatinine kinase, aldolase, IgA immunoglobulin and hemoglobin A1C. Serum aldolase was slightly elevated at 7.8U/l (normal 1.0-7.5U/l) in addition to his hemoglobin A1C at 6.7% (normal below 5.7%); other laboratory tests were within normal reference range. Pulmonary function tests were also normal.

Methotrexate was initiated at a dose of 15mg a week and four weeks later, the patient noted some improvement in his skin and no new areas of involvement, though he still complained of severe

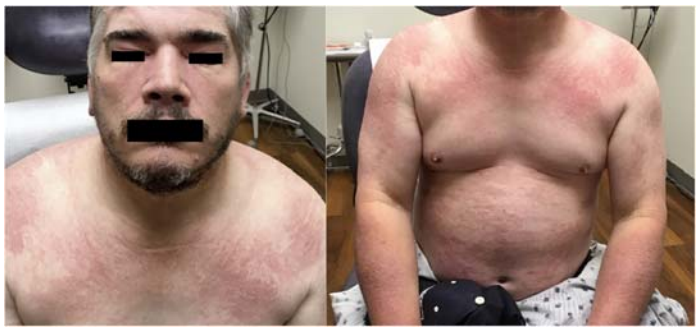

Figure 1. *Clinical findings from initial visit reveal diffuse erythema on his scalp, face and neck, and a scaly erythematous eruption with heaviest burden on the patient's arms and upper trunk.*

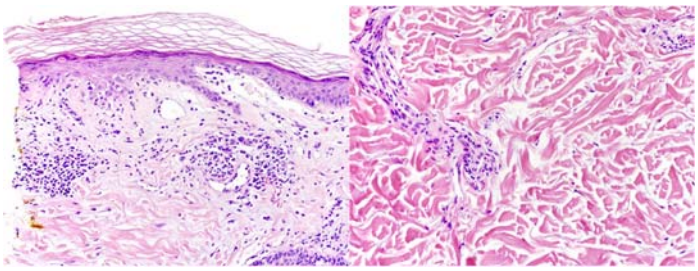

Figure 2. *Histology images using H&E are significant for vacuolar change with occasional Civatte bodies, keratinocyte enlargement, thickened basement membrane, hypereosinophilia, perivascular lymphocytes, and increased mucin in the reticular dermis, 100×.*

itching on the scalp, neck, and legs; mild muscle weakness persisted. He denied dyspnea. Physical examination revealed red, lichenoid papules on the upper trunk and diffuse erythema noted on the scalp. Upper and lower extremity neuromuscular strength assessed and found to be 5/5. As the patient was not showing satisfactory improvement, methotrexate was increased to 17.5mg weekly, which has shown partial improvement of his symptoms thus far. The patient returned for a follow up visit in February 2023 with the complaint of persistence of symptoms. He stated that the cutaneous flares have improved, but he was still experiencing muscle weakness and joint soreness and was not tolerating the methotrexate well. He denied muscle pain at the time. Additionally, aldolase levels continued to be elevated so the decision was made to stop the methotrexate and initiate hydroxychloroquine with the plan to return for follow up in 6 weeks. Improvement of symptoms on hydroxychloroquine therapy have yet to be assessed as patient was lost to follow up at this time. If the patient subsequently followed up with persistence of symptoms, performing a muscle biopsy and muscle MRI to guide properly tailored therapy would have been considered at that time.

Discussion

Dermatomyositis is an uncommon autoimmune disorder that has characteristic skin involvement along with involvement in the muscles, blood vessels, joints, esophagus, and lungs. Most individuals present with skin manifestations prior to muscle involvement [7,8]. Although its etiology is unknown, suspected triggers for DM are environmental factors, drugs, viral infections, and vaccines [3, 7, 9]. Drug-induced DM is usually diagnosed by clinical findings and biopsy confirming diagnosis, with variable serology titers of antinuclear antibody, anti-Jo-2, and anti-Ro antibodies. Serologic findings can be used to aid in characterizing drug-induced DM rather than verify the diagnosis as clinical application can be controversial [10]. The documented cases of new DM symptom onset after inoculation with the COVID-19 vaccine range from one to fourteen days and were documented to occur both after the initial and second dose of the Moderna (mRNA-1273), Pfizer BNT162b2, and Covidshield (ChAdOx1 nCoV-19) vaccines [2-4,7,9,11-13,19].

Dermatomyositis poses a therapeutic challenge [14,15]. Immunosuppressants and immunomodulators largely encompass DM treatment, ranging from systemic glucocorticosteroids, such as prednisolone and methylprednisolone, mycophenolate mofetil, methotrexate, hydroxychloroquine, tofacitinib, and high-dose intravenous immunoglobulin therapy with varying effectiveness [2-4,7,8,11-13,16,17]. As with this case, treatment failure may be encountered when treating DM [14]. In clinical practice, treatment may include a combination of systemic medications to induce remission [15]. Refractory cases have been treated with tofacitinib and rituximab [14,18].

The link between vaccines and dermatomyositis is not well understood. Theoretically, an mRNA vaccine may induce a T cell-mediated immune response to a protein translated from the mRNA and then upregulate a high level of type I interferon, thereby precipitating or flaring any number of immune-mediated diseases [4,9]. Most notably, patients with DM have an increase in type I inducible genes driven by myeloid dendritic cells in muscle fibers, endothelial cells, skin, and peripheral blood [4,19]. Although this thinking may explain flares in patients with existing DM after receiving a dose of the COVID-19 vaccine, the onset of this autoimmune disease in previously unaffected individuals remains largely unclear. The increase in morbidity associated with some subsets of DM makes further documentation of such cases paramount. Such information will help delineate the role of the SARS-CoV-2 vaccine as a trigger in autoimmune mediated diseases. Thus, clinicians should keep such diagnoses in the differential when interpreting unexplained cutaneous reactions as the worldwide vaccine campaign continues.

Potential conflicts of interest

The authors declare no conflicts of interest.

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