Case Report

Generalized morphea profunda following COVID-19 messenger ribonucleic acid vaccination

Gillian C McPherson, MD[1], Silas M Money, MD[2a], Adeline J Johnson, MD[2,3], Loretta S Davis, MD[2]

[1] Medical College of Georgia at Augusta University, Augusta, Georgia, United States, [2] Department of Dermatology, Medical College of Georgia at Augusta University, Augusta, Georgia, United States, [3] Division of Dermatology, Charlie Norwood VA Medical Center, Augusta, Georgia, United States

Keywords: covid-19, morphea, sars-cov-2, vaccination, vaccine

Dermatology Online Journal

Vol. 31, Issue 4, 2025

Abstract

Morphea is an uncommon inflammatory disorder characterized by progressive sclerosis of the skin and soft tissues. We describe the novel occurrence of generalized morphea profunda arising in close temporal association with the COVID-19 messenger ribonucleic acid vaccination series. An 80-year-old man presented with numerous areas of firm, tight skin across his trunk and extremities with associated itching and burning. He denied characteristic symptoms of systemic sclerosis. Physical examination revealed numerous indurated plaques, some with porcelain-white or sclerotic yellow centers, on the bilateral dorsal forearms, anterior waistline, and bilateral legs. There was no evidence of sclerodactyly or inflammatory arthritis. Punch biopsies showed thickened collagen bundles in the reticular dermis, diminished periadnexal fat, and a perivascular and interstitial mononuclear cell infiltrate. The hyalinizing fibrosing reaction extended into the fat and was manifested by notable expansion of the interlobular septa of the fat by dense collagen. He started on oral methotrexate with significant improvement in symptoms and lesion induration at 14-month follow-up. This case report provides further insight into the potential dermatologic adverse events associated with COVID-19 messenger ribonucleic acid vaccination. Further investigation is needed to determine any predisposing patient-specific intrinsic factors, unrecognized pathophysiologic mechanisms, and approximate incidence of such adverse events.

Introduction

Morphea is an uncommon inflammatory disorder characterized by progressive sclerosis of the skin and soft tissues, often leading to significant morbidity. Various local and systemic triggers have been reported to include both infection and vaccination. This manuscript describes a case of generalized morphea profunda arising in close temporal association with the COVID-19 messenger ribonucleic acid (mRNA) vaccination series.

Case Synopsis

An 80-year-old man with coronary artery disease and insulin-dependent type II diabetes mellitus presented with numerous areas of firm, tight skin across his trunk and extremities with associated itching and burning. His first lesion developed on his left forearm approximately one month after completing the Pfizer-BioNTech COVID-19 mRNA vaccination series (Pfizer Inc, New York, NY). The lesions then spread to both upper extremities, both lower extremities, and across his waistline. As the plaques enlarged and thickened, he reported significant nocturnal pruritus and feelings of stiffness with movement. He denied any preceding illnesses, including COVID-19, and denied any other recent vaccinations. He also denied symptoms of systemic sclerosis including stiffness of his fingers, shortness of breath, Raynaud phenomenon, and joint pain/swelling. Of note, the patient was previously seen by an outside dermatologist who biopsied the patient and histopathology from his right forearm was read as septal panniculitis consistent with erythema nodosum; he sought a second opinion prior to receiving any treatment.

Physical examination revealed indurated, hyperpigmented plaques on the bilateral dorsal forearms, symmetric, indurated plaques with central areas of porcelain-white color change on the anterior waistline, and

a Corresponding Author: Silas M Money MD, 1004 Chafee Avenue, Augusta, GA 30904, Tel: 706-721-6228, Email: silasmoney7@gmail.com

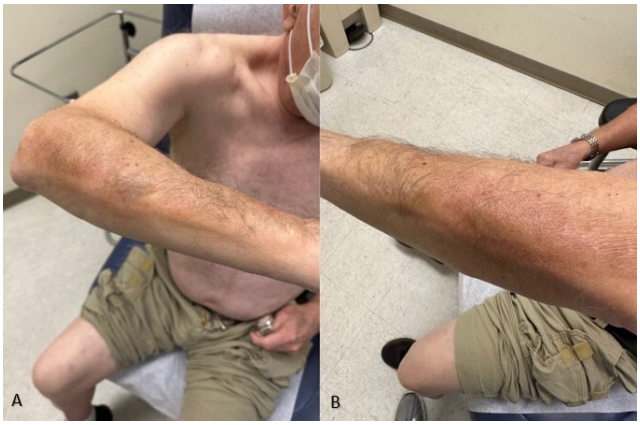

Figure 1. *Indurated, hyperpigmented plaques of the **A)** right and **B)** left dorsal forearms.*

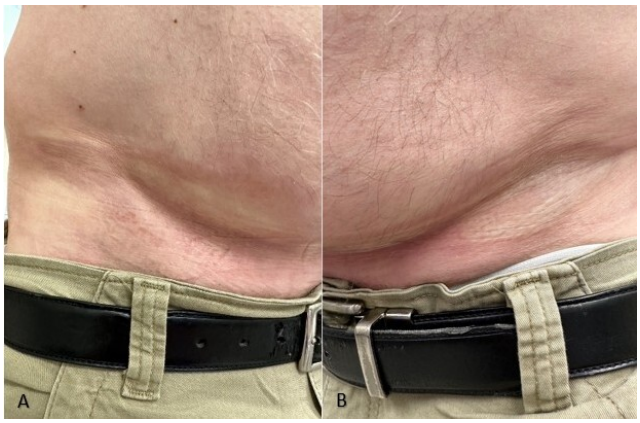

Figure 2. *Symmetric, indurated plaques of the **A)** right and **B)** left waist underlying the patient's beltline with central areas of porcelain-white color change suggesting a possible overlying component of lichen sclerosus.*

indurated plaques with sclerotic yellow centers and erythematous borders on the bilateral legs (Figures 1-3). There was no evidence of sclerodactyly or inflammatory arthritis. Punch biopsies of the left anterior leg and calf showed thickened collagen bundles in the reticular dermis, diminished periadnexal fat, and a perivascular and interstitial mononuclear cell infiltrate (Figure 4A). The hyalinizing fibrosing reaction extended into the fat and was manifested by a striking pattern of expansion of the interlobular septa of the fat by dense collagen. (Figure 4B). Complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, and antinuclear antibody were within normal limits. Based on clinical presentation, histopathology, and laboratory testing, the patient was diagnosed with generalized morphea profunda and started on methotrexate 10mg weekly, titrated to 15mg weekly within 8 weeks. Prednisone was avoided owing to concerns for hyperglycemia in the setting of diabetes mellitus. After four weeks of treatment, the patient's symptoms of pruritus and burning were improved. At 14-month follow-up, the involved sites were softer, less indurated, and nearly asymptomatic.

Discussion

COVID-19 infection-associated morphea and COVID-19 mRNA vaccine-associated morphea have been previously reported.[1-10] Although generalized morphea profunda has been reported following COVID-19 infection, the current case demonstrates its novel occurrence following the COVID-19 mRNA vaccination series.[10] Reported cases of morphea following COVID-19 vaccination are summarized (**Table 1**). Lesion onset was typically within 7 to 20 days of inoculation, with affected areas including the abdomen, back, chest, limbs, breasts, and axillae. All but one case involved morphea distant to the vaccination site, with only the case described by Veraldi et al having morphea confined to the site of inoculation.[3-9] Treatment regimens varied, with common interventions including methotrexate, topical corticosteroids, topical tacrolimus, and topical calcipotriol. Notably, a favorable treatment response was observed in all cases in which treatment response was mentioned. This collection of cases highlights the association between COVID-19 vaccination and the development of morphea, contributing to the growing body of evidence on vaccine-associated autoimmune responses.[3-9]

A variety of vaccinations, other injections, cutaneous trauma, radiation, and herpes zoster infection have been reported to trigger morphea.[11,12] Documented triggers are primarily localized cutaneous events. In contrast, systemic sclerosis has been attributed to systemic events, including chemical and/or pollutant exposures, systemic infections, and oral medications.[13] Evidence suggests that these observations are an oversimplification of the complex immunologic processes underlying the development of these conditions. Reported cases of vaccine-associated morphea often describe initial lesions at the vaccination site with eventual spread to distant sites, indicating that a local trigger may cause a systemic immunologic change.[14] In the current case, the patient never developed lesions of morphea at his sites of vaccination, but rather only at distant sites. This observation supports the potential role of a systemic immunologic trigger for morphea.

The immune response associated with both COVID-19 infection and vaccination is believed to be primarily driven by the SARS-CoV-2 spike glycoprotein 1. Immunohistochemical analysis of morphea lesions following COVID-19 vaccination demonstrated positive staining for antispike protein antibodies in vascular structures, inflammatory cells, and the cytoplasm of epithelial cells within eccrine sweat glands.[4] It is hypothesized that antigenic cross-reactivity between the spike protein and human tissue may trigger immune-mediated conditions such as morphea.[11] This proposed mechanism offers a potential explanation for the occurrence of morphea in association with both COVID-19 infection and COVID-19 vaccination, as both are associated with the spike protein as a primary immunogenic target.

In this case, the patient developed broad lesions of morphea across his entire waist, likely representing an

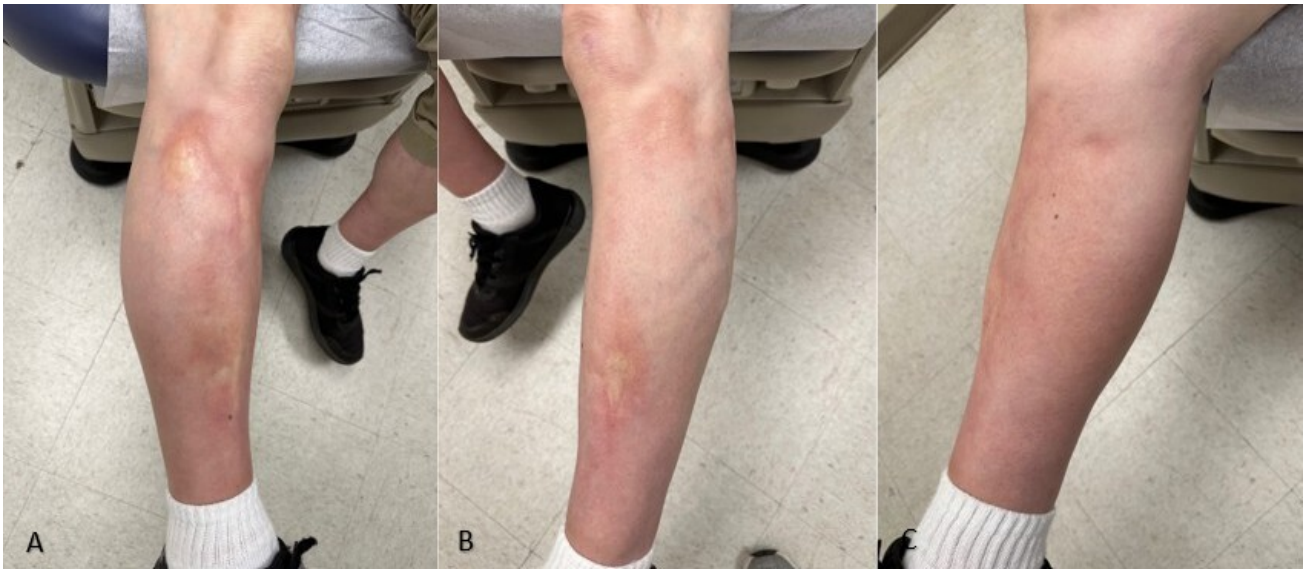

Figure 3. *Indurated plaques, some with erythematous borders and sclerotic yellow centers, of the **A)** right and **B)** left legs. **C)** Right medial leg with a dimpled, tethered-down appearance characteristic of morphea profunda.*

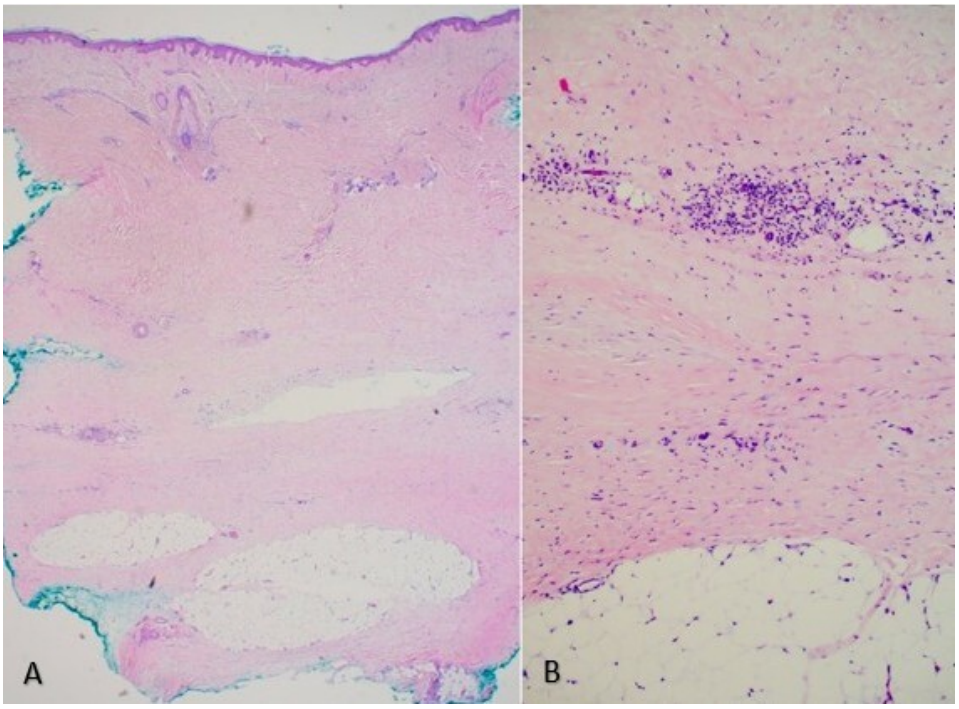

Figure 4. *Histopathology findings from a punch biopsy from the left anterior leg. **A)** Square biopsy specimen with thickened collagen bundles, diminished periadnexal fat, and a perivascular and interstitial mononuclear cell infiltrate (hematoxylin & eosin, x4). **B)** The hyalinizing fibrosing reaction extends into fat with dense collagen expanding the interlobular septa (hematoxylin & eosin, x20).*

isomorphic response, ie, koebnerization to chronic friction and pressure from his waistband and belt. A cross-sectional survey by Grabell et al found evidence for skin trauma or friction in the clinical distribution of morphea at the onset of disease in 16% of patients surveyed.[11] This observation suggests that patients with morphea should avoid unnecessary skin trauma from chronic friction, pressure, or even elective procedures because of a potentially heightened risk for disease progression via an isomorphic response.[11]

This patient initially presented with a presumed diagnosis of erythema nodosum based on a prior biopsy demonstrating septal panniculitis. In morphea profunda, the classic fibrosing reaction that typically prevails in the deep and mid-reticular dermis in classic morphea involves the interlobular septa of the fat. Other causes of hyalinizing expansion of the fat include eosinophilic fasci-

Table 1. *Comparison of Cases of COVID-19 Vaccination-Induced Morphea.*

Authors	Year of Publication	Patient Gender	Patient Age	Area Affected	COVID-19 vaccine	Time from COVID Vaccine	Treatment/ Response
Paolino G et al	2022	F	61	Abdomen, back, lower limbs	Comirnaty©	15 days after 1st dose and 15 days after 2nd dose	Clobetasol cream and MTX 7.5mg/week; MTX later replaced with MMF due to hepatotoxicity. Good improvement.
Paolino G et al	2022	F	52	Abdomen, chest, upper limbs	Comirnaty©	7 days after 2nd dose	MTX 7.5mg/ week Good improvement.
Paolino G et al	2022	M	64	Upper limbs, abdomen	Vaxzevria ©	20 days after 1st dose	Topical tacrolimus 0.1%. Improvement.
Paolino G et al	2022	F	73	Lower limbs, abdomen	Comirnaty©	20 days after 2nd dose	Topical tacrolimus 0.1%. Good improvement.
Metin Z Celepli P	2022	F	55	Left breast and axilla	Comirnaty©	4 weeks after 2nd dose	Clobetasol pomade and calcipotriol pomade. Regression of lesions.
Alhayaza et al	2023	F	63	Right shoulder, trunk, extremities	Comirnaty©	2 weeks after 2nd dose	Clobetasol and MTX 15mg/ week for three months. No mention of treatment response.
Antoñanzas et al	2022	F	45	Back	Spikevax ©	14 days after 1st dose	Betamethasone and topical calcipotriol. Great improvement.
Antoñanzas et al	2022	F	52	Abdomen and thighs	Comirnaty ©	6 weeks after 2nd dose	Topical corticosteroids and MTX 15mg/m^2/week. Lesions regressed following initiation of MTX.
Aryanian et al	2022	F	70	Arms with extension to all body surface areas after a diffuse	Vaxzevria ©	2 days after 1st dose	MTX and topical corticosteroids. No mention of treatment results.

Authors	Year of Publication	Patient Gender	Patient Age	Area Affected	COVID-19 vaccine	Time from COVID Vaccine	Treatment/ Response
				maculo-papular eruption			
Shakoei et al	2022	F	25	Generalized	Vaxzevria ©	10 days after 1st dose	Prednisone and MTX. Mild improvement.
Veraldi S et al	2022	F	79	At vaccination site: lateral surface of the right arm	Comirnaty©	1 month after 1st dose	No mention of treatment.

Abbreviations: MMF, mycophenolate mofetil; MTX, methotrexate.

itis, necrobiosis lipoidica, and a chronic pauci-inflammatory fibrosing phase of erythema nodosum. Thus, clinicopathologic correlation to include lesion morphology, distribution, and symptoms of tightness and pain is essential to the diagnosis of morphea.

Conclusion

This case report provides further insight into the potential dermatologic adverse events associated with COVID-19 mRNA vaccination. Further investigation is needed to determine any predisposing patient-specific intrinsic factors, unrecognized pathophysiologic mechanisms, as well as an approximate incidence of such adverse events among the various commercially available COVID-19 mRNA vaccines.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Pigliacelli F, Pacifico A, Mariano M, et al. Morphea induced by SARS-CoV-2 infection: A case report. *Int J Dermatol*. 2022;61:377-378. doi:10.1111/ijd.15983. PMID:34783020

2. Saraswat N, Tripathy DM, Mishra A, et al. Tocilizumab for refractory post-COVID-19 pansclerotic morphea. *J Eur Acad Dermatol Venereol*. 2024;38:e364-e365. PMID:38078570

3. Paolino G, Campochiaro C, Di Nicola MR, et al. Generalized morphea after COVID-19 vaccines: A case series. *J Eur Acad Dermatol Venereol*. 2022;36:e680-e682. doi:10.1111/jdv.18249. PMID:35604052

4. Metin Z, Celepli P. A case of morphea following the COVID-19 mRNA vaccine: On the basis of viral spike proteins. *Int J Dermatol*. 2022;61:639-641. doi:10.1111/ijd.16062. PMID:35073411

5. Veraldi S, Benaglia C, Pisapia A, et al. Morphea at the site of anti-COVID-19 vaccination: The first reported case? *Ital J Dermatol Venerol*. 2022;157:531-532. doi:10.23736/S2784-8671.22.07324-8. PMID:36651212

6. Alhayaza R, Alhayaza G, Algarni A, Alhumidi A, AlHarithy R. Generalized morphea following COVID-19 vaccine: Case report and literature review. *Clin Case Rep*. 2023;11(4):e7133. doi:10.1002/ccr3.7133

7. Antoñanzas J, Rodríguez-Garijo N, Estenaga Á, Morelló-Vicente A, España A, Aguado L. Generalized morphea following the COVID vaccine: A series of two patients and a bibliographic review. *Dermatol Ther*. 2022;35(9):e15709. doi:10.1111/dth.15709

8. Aryanian Z, Balighi K, Hatami P, Tootoonchi NM, Goodarzi A, Mohseni Afshar Z. Morphea in two patients after being infected to and being vaccinated against SARS-CoV-2 infection. *Clin Case Rep*. 2022;10(4):e05667. doi:10.1002/ccr3.5667

9. Shakoei S, Kalantari Y, Nasimi M, et al. Cutaneous manifestations following COVID-19 vaccination: A report of 25 cases. *Dermatol Ther*. 2022;35(8):e15651. doi:10.1111/dth.15651

10. Stephens MR, Moore DF, Dau J, et al. A case of generalized morphea profunda following SARS-CoV-2 infection. *JAAD Case Rep*. 2022;23:20-23. doi:10.1016/j.jdcr.2022.02.033. PMID:35308063

11. Grabell D, Hsieh C, Andrew R, et al. The role of skin trauma in the distribution of morphea lesions: A cross-sectional survey of the Morphea in Adults and Children cohort IV. *J Am Acad Dermatol*. 2014;71:493-498. doi:10.1016/j.jaad.2014.04.009. PMID:24880663

12. Careta MF, Romiti R. Localized scleroderma: Clinical spectrum and therapeutic update. *An Bras Dermatol*. 2015;90:62-73. doi:10.1590/abd1806-4841.20152890. PMID:25672301

13. De Martinis M, Ciccarelli F, Sirufo MM, et al. An overview of environmental risk factors in systemic sclerosis. *Expert Rev Clin Immunol*. 2016;12:465-478. doi:10.1586/1744666X.2016.1125782. PMID:26610037

14. Torrelo A, Suárez J, Colmenero I, et al. Deep morphea after vaccination in two young children. *Pediatr Dermatol*. 2006;23:484-487. doi:10.1111/j.1525-1470.2006.00289.x. PMID:17014648