A case of generalized morphea profunda following SARS-CoV-2 infection

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INTRODUCTION

Morphea is an immune-mediated fibrosing skin disorder of the dermis and subcutaneous fat with unclear pathogenesis and triggers. Combinations of genetic and environmental factors leading to immune dysregulation are likely involved. Here, we describe a case of generalized morphea profunda occurring after SARS-CoV-2 infection, and we discuss possible causality and pathogenesis.

CASE REPORT

A 61-year-old woman with a history of hypertension, chronic obstructive pulmonary disease, and hypothyroidism presented to our clinic with diffuse skin thickening 6 months following a two-week illness consisting of fever, body aches, shortness of breath, and cough with a positive COVID-19 nasopharyngeal swab test. While her symptoms from infection were severe, the patient elected not to be hospitalized. Her cutaneous symptoms started approximately 1 to 2 months after recovering from infection and began as pain and thickening of the skin at the base of the thumbs. It subsequently spread to involve her fingers, arms, chest, back, and legs with development of inability to bend her left index finger and a left elbow contracture. The patient reported gastroesophageal reflux disease and a remote history of the Raynaud phenomenon; she denied shortness of breath and joint swelling.

Examination was notable for diffuse and patchy skin thickening over her trunk and extremities, including hands and feet with decreased range of motion across metacarpophalangeal and proximal interphalangeal joints, a groove sign on the forearm, and inflammatory arthritis (Fig 1, *A-D*). A wedge biopsy of the left forearm was performed and revealed epidermal atrophy with superficial and deep dermal sclerosis, atrophic eccrine glands, loss of periadnexal fat, and a dermal-subcutaneous junction perivascular lymphoplasmacytic infiltrate extending to the subcutis, consistent with morphea profunda (Fig 2). Laboratory results were notable for a positive antinuclear antibody assay with titer of 1:160 and homogeneous staining and negative anti-U1-ribonucleoprotein, anti-Scl-70, and RNA polymerase III antibodies. Magnetic resonance imaging of her left arm showed mild edema and enhancement surrounding several flexor and extensor muscle groups and along the musculotendinous junctions within the anterior and posterior compartments throughout the left forearm. Her clinical presentation, biopsy results, laboratory evaluation, and imaging were supportive of a diagnosis of morphea profunda. The patient did have eosinophilia; however, this was chronic. The differential diagnosis included eosinophilic fasciitis, but this was not favored based on clinical appearance and lack of fascial thickening on biopsy. The patient was initially started on prednisone, which she stopped after a few days due to concern for side effects. She also declined treatment with methotrexate and mycophenolate

Abbreviation used:

IL: interleukin

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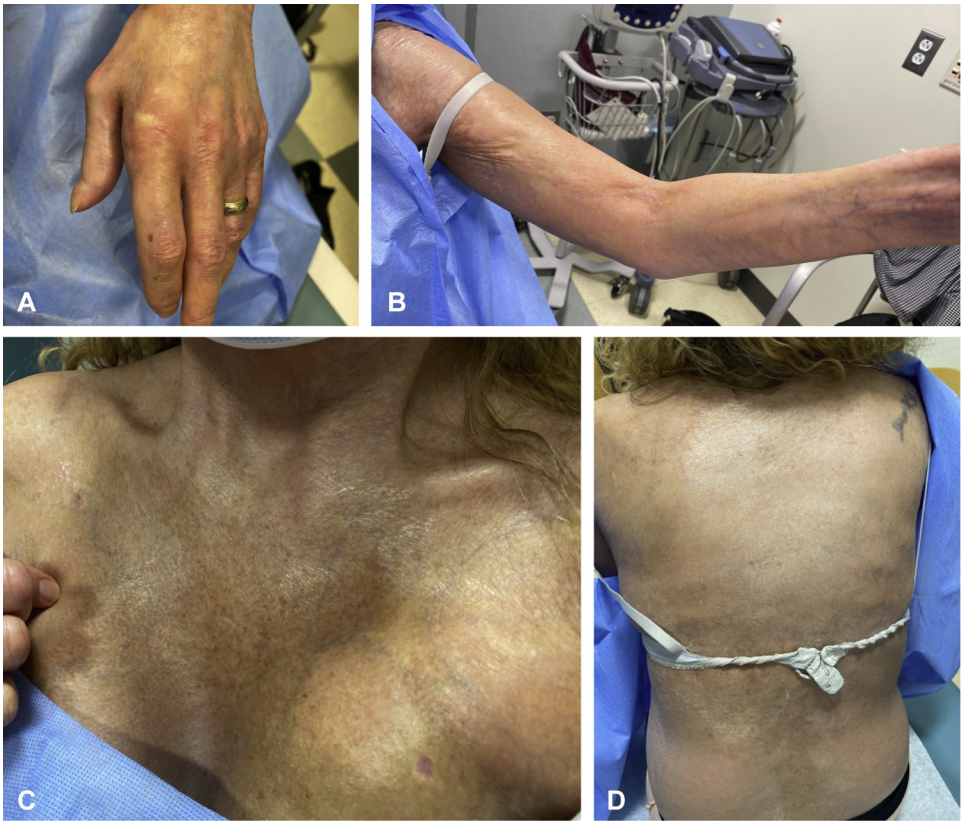

Fig 1. Clinical images of indurated plaques on the hand (**A**), arm (*with groove sign*) (**B**), chest (**C**), and back (**D**).

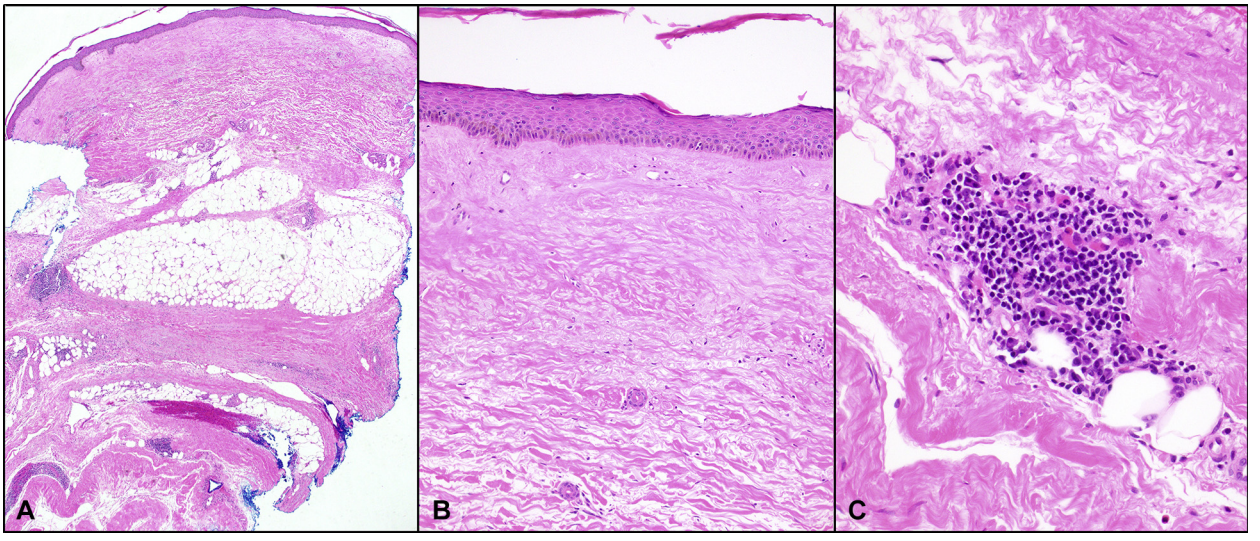

Fig 2. Pathology findings from a wedge biopsy of the left forearm. **A,** Epidermal atrophy and superficial and deep dermal sclerosis with scattered perivascular infiltrate. **B,** Atrophic eccrine glands with loss of periadnexal fat. **C,** Perivascular lymphoplasmacytic infiltrate with scattered eosinophils involving the subcutis. (**A**-**C** Hematoxylin-eosin stain; original magnifications: **A,** ×4; **B,** ×20; **C,** ×40.)

mofetil due to potential side effects. She was eventually started on mycophenolic acid (for better tolerability), but has not yet returned for follow-up.

DISCUSSION

This case highlights the occurrence of morphea soon after infection with SARS-CoV-2. Reported

etiologies for morphea include antecedent trauma several months prior to the emergence of morphea, radiation, and certain medications.[1-3] Whether infections due to eg, *Borrelia burgdorferi*, precipitate this cascade remains unclear. Isolated reports, predominantly in the pediatric literature, have documented a temporal association with vaccinations; however, these cases may relate to trauma at the vaccine site rather than immunologic reaction to vaccine contents.[4]

Like other infectious diseases, COVID-19 has been linked to the development of various autoimmune conditions, including 1 case of development of autoantibodies and systemic sclerosis 3 weeks after a mild SARS-CoV-2 infection.[5] In our case, it is difficult to definitively assess causality versus a coincidental development of morphea unrelated to the SARS-CoV-2 infection. Several reports have documented development of morphea after infection with HIV and hepatitis C virus, though the time frame reported was several years after infection.[2,6]

We speculate that the viral infection triggered an aberrant inflammatory host response that may have triggered the disorder. Multiorgan tropism, extending to the skin and muscle, has been reported in the literature in autopsies of patients with COVID-19; the presence of the cutaneous virus could potentially be a part of the pathogenesis.[7] Several cytokines including interleukin (IL)-6, interferon gamma, IL-1, and tumor necrosis factor-alpha have been found to be some of the key mediators of inflammation in the viral cytokine storm in patients with COVID-19 and have also been implicated as important mediators of skin fibrosis in morphea and interstitial lung disease in systemic sclerosis.[8-10] While multiple cytokines may play a role in driving the fibrotic process in the skin, IL-6 is one cytokine that appears to be very important in this process. Tocilizumab, an inhibitor of IL-6, has proven to be helpful in reducing lung inflammation in hospitalized patients with COVID-19 and was recently approved by the Food and Drug Administration to treat interstitial lung disease in scleroderma. We do not, however, have data on the level of IL-6 or other cytokines in this patient, and while she had significant symptoms, she did not develop a severe pneumonia requiring intubation and did not receive inpatient treatment.

In the case of our patient, while there appears to be a temporal correlation between infection with SARS-Cov-2 and the subsequent development of morphea (albeit a short time frame), we ultimately cannot definitively know whether SARS-Cov-2 infection was causative of or coincidental to the development of morphea given the lack of staining for virus in the tissue and the lack of data about inflammatory markers and cytokine levels. Her clinical course is notable for diffuse disease that progressed rapidly, and, unfortunately, we were not able to start treatment immediately due to her many concerns for potential side effects of systemic medications. Patients like the one presented here would benefit from early treatment with an effective modality, such as pulsed steroids and methotrexate, mycophenolate, or anti-IL-6 therapy, such as tocilizumab.[1] Finally, this patient was not previously vaccinated. Given her comorbidities of chronic obstructive pulmonary disease and smoking and her age, we still recommended vaccination given that the benefits of vaccination in preventing more severe reinfection were deemed to outweigh the potential risk of vaccination exacerbating her cutaneous disease.

This report has implications for considering the scope of dermatologic sequelae from COVID-19 disease. Further investigation of any additional cases will be crucial to determine the incidence and pathophysiology of morphea developing after COVID-19 disease.

Conflicts of interest

None disclosed.

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