Recalcitrant verruca vulgaris regression following severe SARS-CoV-2 infection

Devin Barzallo, BA,[a,b] Ayan Kusari, MD,[a] and Kieron S. Leslie, MBBS[a]

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INTRODUCTION

Verruca vulgaris is commonly associated with human papillomavirus (HPV) subtypes 2 and 4 and affects approximately 10% of the population.[1] In adults, warts are less likely to resolve spontaneously and are more resistant to treatment. Moreover, immunosuppressed individuals as those posttransplant[2] or those diagnosed with HIV[3] have an increased burden of warts compared with immunocompetent patients. The first-line treatment for warts includes salicylic acid and cryotherapy; however, their efficacy rates range from 0% to 80% and 14% to 90%, respectively.[4] Intralesional immunotherapies with skin test antigens, commonly *Candida*, have been shown to be 60% effective in the complete resolution of the injected wart.[5,6] It is believed that the injection of antigens leads to regression of warts by an induction of a strong, local, nonspecific immune response in treatment-resistant verruca vulgaris. The mechanism behind this response is that the skin antigen is taken up by Langerhans cells, migrates to the lymph nodes, and leads to the sensitization of the T lymphocytes. After repeated stimulation of the antigen, the $CD4^+$ T cells recognize antigens on the antigen-presenting cells and, subsequently, release inflammatory cytokines such as IFN-γ, interleukin (IL) 2, and IL-12. These cytokines activate macrophages, resulting in phagocytosis of target cells in immunocompetent patients with normal-ranged $CD4^+$ counts. Further, $CD8^+$ T cells recognize antigens on somatic cells and lead to cell-mediated cytotoxicity and direct cell destruction, including that of HPV-infected tissues.[7] Similarly, recalcitrant warts have been treated using contact therapy of contact allergens such as dinitrochlorobenzene, diphencyprone, and squaric acid dibutylester, which induce a delayed type-4 hypersensitivity reaction that enhances the response of the immune system.

Herein, we present a patient with febrile illness because of SARS-CoV-2 pneumonia who had significant improvement in wart number and size.

Abbreviations used:

HPV: human papillomavirus
IL: interleukin

CASE REPORT

A 45-year-old man with a past medical history of extensive, recalcitrant verruca vulgaris was treated by dermatology with in-office liquid nitrogen cryotherapy, topical salicylic acid—containing products, and topical 5-fluorouracil with minimal improvement. He presented to the emergency department with hypertensive nephrosclerosis in the setting of immunosuppression status after kidney transplantation in April 2016. He was on chronic daily cyclosporin A, mycophenolate mofetil, and low-dose prednisone. He had fever, cough, and dyspnea for 10 days and was found to have severe SARS-CoV-2 pneumonia and an acute kidney injury. The patient had received his third dose of the SARS-CoV-2 vaccine 5 months earlier. On evaluation, he had 79% oxygen on room air and received supplemental oxygen via a high-flow nasal cannula, but given his oxygen requirement, he was given dexamethasone 6 mg/d and baricitinib 1 mg/d. The chest X-ray confirmed bilateral infiltrates consistent with severe SARS-CoV-2 pneumonia. Elevated D-dimer level of 0.89 μg (fibrinogen equivalent units)/mL (<0.50 μg

From the Department of Dermatology, University of California, San Francisco, San Francisco, California[a]; and School of Medicine, Case Western Reserve University, Cleveland, Ohio.[b]

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Correspondence to: Devin Barzallo, BA, School of Medicine, Case Western Reserve University, 9501 Euclid Ave, Cleveland, OH 44106. E-mail: Dkb67@case.edu.

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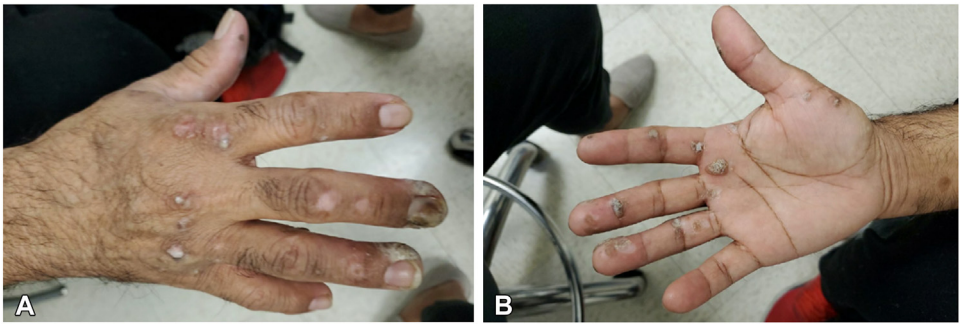

Fig 1. A and **B,** Verruca vulgaris on the dorsal and plantar aspects of the patient's hands (2 months before febrile illness).

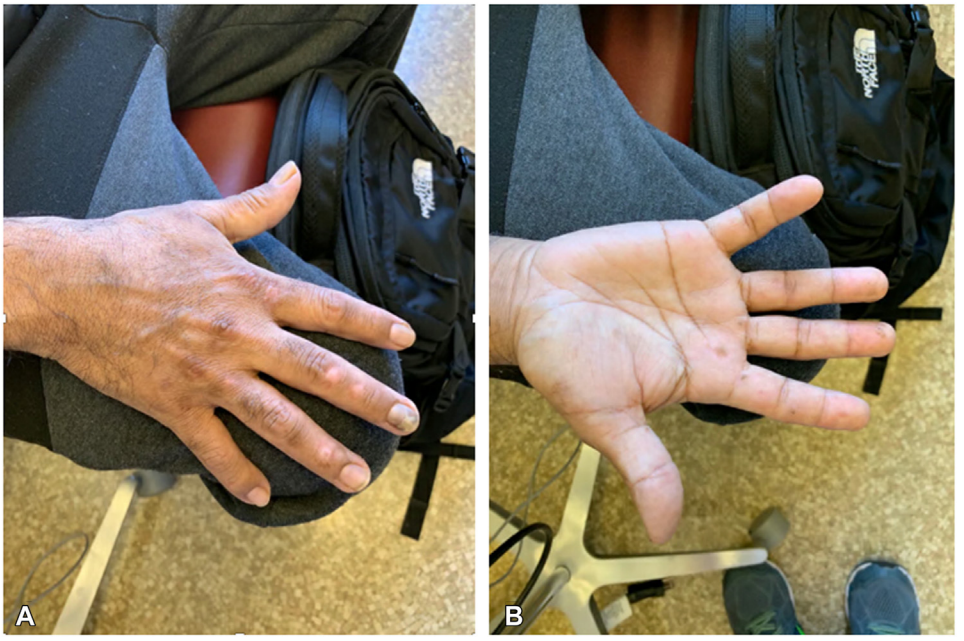

Fig 2. A and **B,** A decrease in verruca vulgaris on the dorsal and plantar aspects of the patient's hands 2 months after his febrile illness.

(fibrinogen equivalent units)/mL), erythrocyte sedimentation rate of 108 mm/h (0-15 mm/h), procalcitonin level of 0.6 ng/mL (<0.10 ng/mL), and C-reactive protein level of 142 mg/L (0-8 mg/L) indicated a severe inflammatory response. Additional work-up demonstrated evidence of kidney failure with increased creatine level from a baseline of 1.5 mg/dL to 3.7 mg/dL, as well as hyperkalemia and metabolic acidosis. On day 5 of hospitalization, the patient noted that his warts had become red and irritated and had started to peel. During this time, he was not taking any oral or topical therapies for warts and had not recently used home treatment. The patient was discharged after 7 days and completed his course of dexamethasone and baricitinib at home. The patient had dramatic improvement in reduction of warts after febrile illness and continued to improve on cryotherapy and salicylic acid–containing products (Figs 1 and 2).

DISCUSSION

Infection of SARS-CoV-2 has been shown to result in a robust immune response in a subset of patients and can lead to increased production of proinflammatory cytokines such as IL-6 and tumor necrosis factor α, which subsequently recruit macrophages, T cells, and B cells in the lung alveolar cells, resulting in acute respiratory distress and potentially multiple organ failure.[8] Infection with SARS-CoV-2 is often associated with cutaneous manifestations such as chilblain-like acral lesions, morbilliform rash, or urticarial rash, but to our knowledge, regression of warts has not been described to date. Provoking an immune response to warts is a well-established

therapeutic strategy, and some treatments (measles-mumps-rubella vaccine, *Candida* antigen) may frequently provoke a febrile response. However, improvement of verruca vulgaris after a febrile illness has not been consistently established. In the present case, it is unlikely that the regression of warts was related to the administration of dexamethasone or baricitinib. On the contrary, immunosuppressant medications are associated with extensive, refractory, and large warts.[9]

The SARS-CoV-2 vaccine is highly immunogenic without resulting in subsequent respiratory distress and end-organ failure. It has also been shown that the administration of the SARS-CoV-2 vaccine can result in the partial clearance of *Molluscum contagiosum*, a cutaneous infection secondary to poxvirus, most likely because of a strong nonspecific immune response.[10] It would be interesting to further investigate to see whether there has been a response to verruca vulgaris as well following the SARS-CoV-2 immunization, given the large-scale nature of the vaccination campaign and the efficacy of intralesional vaccine therapies on verruca vulgaris.

SARS-CoV-2 has been shown to result in worse health outcomes in patients with pre-existing conditions such as hypertension and results in a greater inflammatory response, including a cytokine storm. Our patient had a history of hypertension and end-stage renal disease, which could explain his severe pneumonia after being infected with SARS-CoV-2. In this proinflammatory state, the patient's HPV-infected tissue was likely targeted via a nonspecific immune response during his febrile illness. Moreover, during the 2-month follow-up, there was no recurrence of the verruca vulgaris.

Conflict of interest

None disclosed.

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