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CASE REPORT

WILEY

Clearance of longstanding treatment-resistant warts during COVID-19 in a transplant recipient

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Abstract

Human papillomavirus (HPV), a DNA virus, infects basal keratinocytes and causes common warts and as well as malignancies of skin and mucous membranes. Although many treatment options are available, persistent HPV infections are common among transplant recipients. Herein, we present a patient with a 15-year history of treatment-resistant warts that regressed during COVID-19 (Coronavirus disease 2019) treatment.

KEYWORDS

COVID-19, favipiravir, human papillomavirus, solid organ transplant, warts

1 | CASE

A 49-year-old man, who had a history of renal transplantation 18 years ago, was admitted to our clinic with numerous treatment-resistant warts that started 3 years after the transplantation. Clinical examination revealed numerous verrucous papules and nodules on his hands and fingers (Figure 1A). He was on methylprednisolone, mycophenolate mofetil, and cyclosporine as immunosuppressive therapy. During several years of follow-up, many treatment modalities had been used, including cryotherapy, electrocautery, imiquimod, trichloroacetic acid, and acitretin without any satisfactory response. During the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pandemic, the patient could not be followed clinically. In September 2020, he presented to the emergency department with a cough and shortness of breath. SARS-COV-2 PCR was negative but multiple focal ground-glass opacities suggesting viral pneumonia due to COVID-19 were detected on chest tomography. After 1 week of treatment at home, he had needed hospitalization due to hypoxia requiring nasal oxygen support. Laboratory investigations revealed elevated levels of C-reactive protein (95.96 mg/L), ferritin (579.5 ng/mL), creatinine (1.78 mg/dL), lymphopaenia (0.53 10^3/μL), and normal levels of d-dimer. Favipiravir, azithromycin, low molecular-weight heparin, and dexamethasone were commenced and methylprednisolone was discontinued. During COVID-19 treatment, the patient noticed that some verrucae had shrunk and disappeared without any specific treatment for them. He stated that the improvement of verrucae has continued for 2-3 weeks. The patient denied any newly developed skin lesion or rash during COVID-19. Physical examination showed a significant decrease in the number and size of the lesions on his hands compared to the previous ones (Figure 1B). Two months later, partial regrowth of the warts was detected (Figure 1C).

2 | DISCUSSION

HPV does not cause viraemia so it can escape the host immune response. However, spontaneous regression can be seen in up to two-thirds of children within 2 years.[1] In adults, it may take up to several years. Moreover, HPV infection in patients with suppressed cell-mediated immunity, such as transplant recipients, can be more widespread and resistant to treatment.[2]

The coronavirus SARS-CoV-2 generally affects the respiratory tract. COVID-19 can show a different course from asymptomatic to severe respiratory failure. Excessive release of pro-inflammatory cytokines (cytokine storm) in severe patients can lead to lung, heart, kidney, and, liver injury.[3] Endothelial damage and microthrombi caused by the vasotropic effect of the virus and circulating antigen-antibody complexes are also involved in the pathogenesis.[4]

There are increasing amounts of reports on different cutaneous presentation in patients with COVID-19 that are classified under

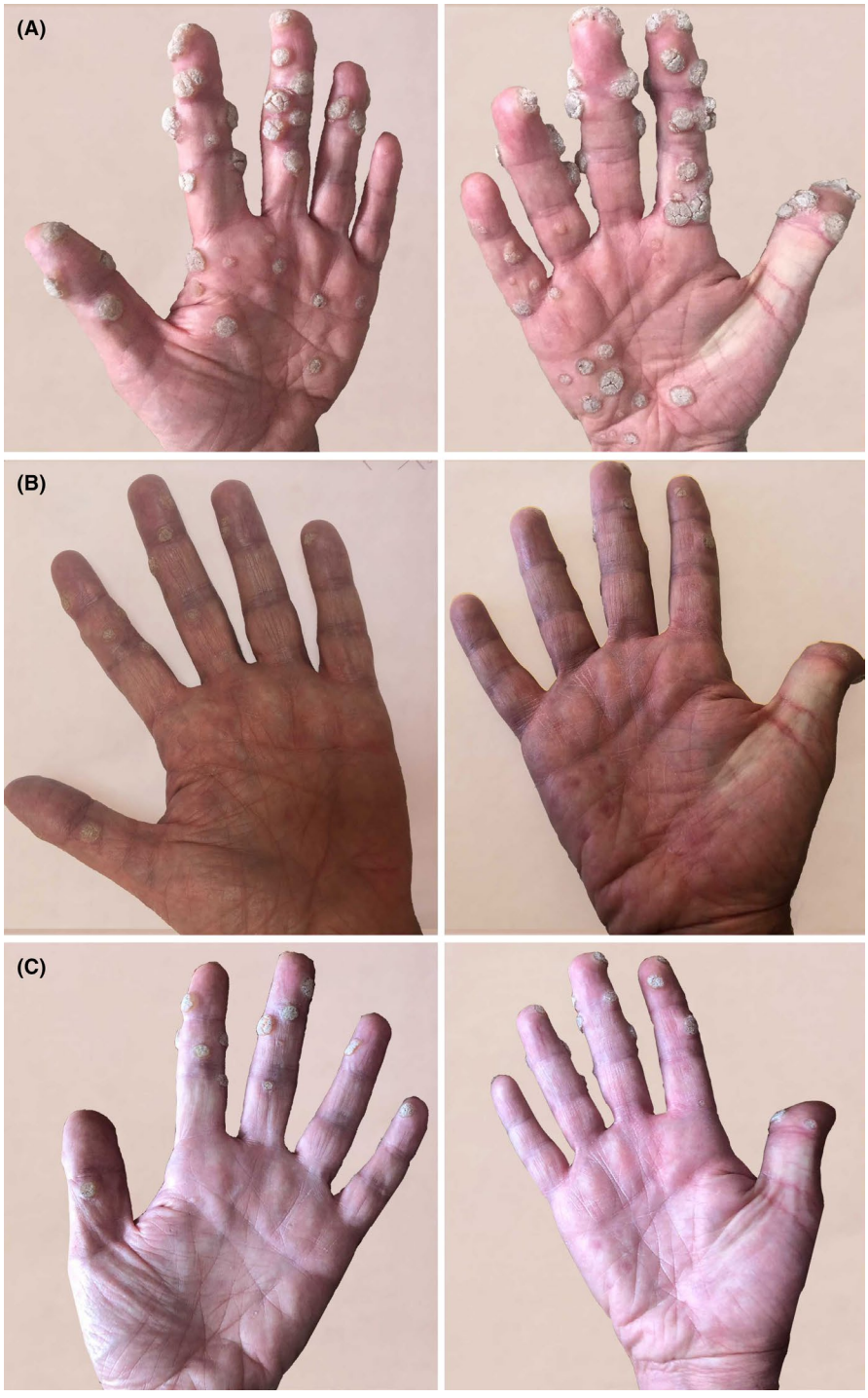

FIGURE 1 (A) Presentation 6 months before COVID-19 showing numerous warts on the hands. (B) Improvement 3 weeks after discharge. (C) Partial regrowth 3 months after hospitalization

Skin lesion	Possible pathogenic mechanisms
Maculopapular exanthem	İnitial cell-mediated response to viral antigens
Urticarial eruptions	Complement activation and serum sickness induced by viral antigens
Vesicular eruptions	Viraemia, the cytopathic effect of the virus
Vasculitis	Immunocomplex-mediated reactions to viral antigens
Chilblain-like lesions	Lymphocytic vasculitis, focal microthrombi

TABLE 1 Skin lesions associated with COVID-19 and proposed pathogenic mechanisms (based on references 3 and 4)

five main groups as maculopapular exanthema, urticarial eruptions, vasculitis, vesicular eruptions, and chilblain-like lesions.[5] Cutaneous involvement is related to the interaction between cellular and humoral immune response.[4] Proposed underlying pathogenic mechanisms for skin involvement of COVID-19 are summarized in Table 1.[3,4]

As far as we know, this is the first report about a dramatic regression of treatment-resistant warts in a patient with COVID-19. Although we cannot clearly explain the underlying mechanism, we will focus on three possibilities:

1. Antiviral effect of favipiravir: Favipiravir, an RNA-dependent RNA polymerase inhibitor, is widely used in the treatment of COVID-19.[6] Although there is no information in the literature regarding the effect of favipiravir on DNA viruses, warts may have disappeared by an unknown mechanism.
2. Discontinuation of methylprednisolone: A change in the immunosuppressive therapy regimen may be responsible for a relative improvement in cell-mediated immunity. As other immunosuppressive treatments are ongoing, switching from 4 mg/d methylprednisolone to dexamethasone may cause a minimal change in immunosuppressive status.
3. SARS-CoV-2 infection: Various skin involvement of COVID-19 is known; however, an effect on warts has not been reported yet. One of the pathogenic mechanisms suggested for the known skin involvement of COVID-19 may be valid for our patient, although no skin lesions associated with COVID-19 have been observed. The normal d-dimer level of the patient may suggest the immune response to antigen-antibody complex and cytopathic effect of the virus rather than the microthrombosis as the responsible pathogenesis. Unfortunately, since we were not able to see the patient in the acute period of SARS-CoV-2 infection, we could not take a biopsy to show histopathological changes.

SARS-CoV-2 induces both innate and adaptive immune responses. It is suggested that type 1 interferons and activation of both CD4+ Th1 and CD8+ cytotoxic T lymphocytes provide viral clearance in patients with COVID-19.[3,7] When viral spread could not be controlled, cytokine storm characterized by increased levels of IL-1, IL-6, IL-12, and TNF-α was associated with many organ damages in COVID-19.[3] Tissue damage in verrucae by the same mechanism is a possibility.

The hypoxic state of the patient due to COVID-19 may also have an impact on the regression of warts. Besides, regrowth of warts 3 months after COVID 19 also suggests an improvement may be associated with COVID-19.

Although spontaneous regression cannot be ruled out definitely, we can say that this is unlikely, given the 15-year history of the treatment-resistant disease course.

In conclusion, we observed a dramatic regression of longstanding treatment-resistant warts in a transplant recipient during the treatment of COVID-19. Certainly, this temporal association does not mean that the regression of warts is strictly COVID-19 related. Further studies involving clinical follow-up of patients with verrucae during and after SARS-CoV-2 infection may shed light on this issue.

CONFLICT OF INTEREST

No conflict of interest.

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