Perniosis in the COVID-19 era

Ishan Shah MBBS, Stephen K Stacey DO, Nandita Ganne DO, John Merfeld MD

Affiliations: Family Medicine Residency Program, Mayo Clinic Health System, La Crosse, Wisconsin, USA

Corresponding Author: Ishan Shah, Mayo Clinic Health System, 700 West Avenue S, La Crosse, WI 54601, Email: shah.ishan@mayo.edu

Abstract

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and the most common symptoms include fever, dry cough, dyspnea, fatigue, anorexia, ageusia, and anosmia. Cutaneous manifestations are less common and we share our experience with an otherwise healthy and asymptomatic young man. The patient presented with painless acrocyanosis of the left toes which progressed to desquamation by day 16 of disease onset. Disease progression is documented via multiple photographs that portray progression of disease and subsequent resolution over approximately six weeks. Symptomatic treatment included non-steroidal anti-inflammatory medications, leg elevation, and warm compresses.

Keywords: chilblains, COVID-19, pernio, perniosis, SARS CoV-2, toe

Introduction

Coronavirus disease 19 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and was first reported in December 2019 in Wuhan (Hubei province, People's Republic of China), [1]. The first reported case in the United States was on January 21, 2020. As of August 15, 2020 there have been almost 5.3 million positive cases and 167,000 deaths in the country [2]. The most common symptoms include fever, dry cough, dyspnea, fatigue, anorexia, ageusia, and anosmia [3]. As the worldwide incidence has increased, other less-common manifestations have been observed, including various skin changes. We share our experience with a healthy young man who presented with skin changes and SARS CoV-2-positive serology. The case highlights challenges with diagnosing this ever-changing disease and the subtleties it can present. It also emphasizes gaps in knowledge that exist with understanding the pathophysiology of SARS CoV-2 and the importance of frequent follow-up and monitoring of disease progression and resolution.

Case Synopsis

A 19-year-old otherwise healthy man presented with discoloration of his left toes that started three days prior to presentation (**Figure 1**). He complained of blistering, tightness, pain, and tenderness that was initially limited to the second toe but then progressed to the third, fourth and great toes by the

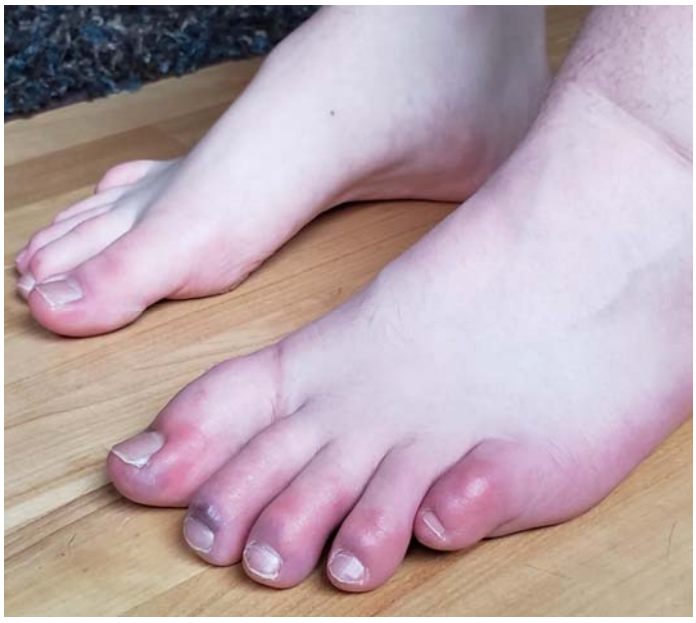

Figure 1. *Day of presentation, day three of illness. Faint cyanosis of the distal digits of the left foot associated with erythema and mild tenderness.*

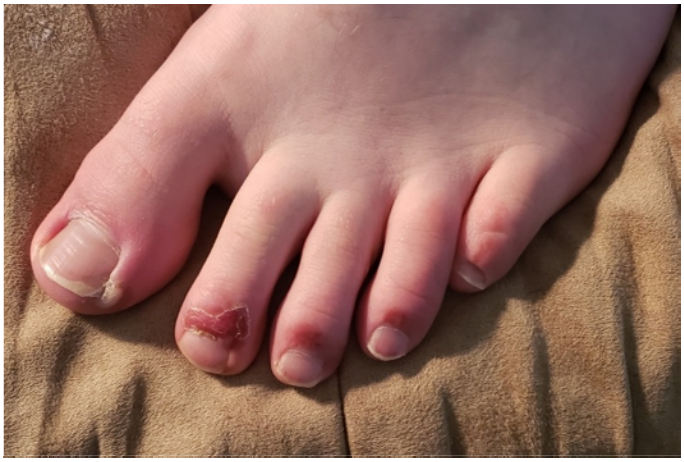

Figure 2. *Day 16 of illness. New desquamation of the second toe, with stable cyanosis in the other toes.*

time he came to clinic for evaluation. He denied fever or other systemic symptoms. He had no history of trauma or exposure to extreme temperatures or irritants. He denied paresthesia, anesthesia, or pulselessness. His past medical and surgical history only included tonsillectomy with adenoidectomy as a child. On examination, there was ecchymosis of the left foot with mild tenderness over areas of bruising. Superficial ulceration without desquamation was noted on the second toe. All toes had full range of motion, though the patient complained of tightness with flexion. Both feet were cool to palpation. As there were no concerning symptoms, he was asked to monitor for progression and look for any evidence of neurovascular compromise or infection. Owing to restrictions at the time regarding in-person visits, subsequent communication was conducted via telemedicine. At follow-up 13 days later, he shared an image which showed new desquamation on the second toe, though the degree of cyanosis was stable (**Figure 2**). By day 26 of illness, the desquamation had progressed to his remaining toes and his second toe had developed crusting (**Figure 3**). On day 27 of illness he tested positive for SARS-CoV-2 IgG antibody. He continued to share images which revealed gradual improvement in the lesions over the following weeks. By day 40 of illness, the lesions had resolved to faint cyanosis of the left toes with no scarring or pigment change (**Figure 4**). Throughout the course of his illness, the patient only had symptomatic treatment which included non-steroidal anti-inflammatory medications, leg elevation, and warm compresses.

Case Discussion

The SARS CoV-2 virus has been associated with a variety of dermatologic manifestations, including a viral exanthem, livedo reticularis, urticaria, petechial rashes, and acral pernio-like lesions [4]. Perniosis is a cold-induced inflammatory vasculopathy and is typically seen in healthy individuals and mainly associated with cold weather, but has also been noted in association with viral and bacterial infections [3]. The etiology of the perniosis-like presentation of COVID-19 is still not completely clear, though there are two primary theories. It has been

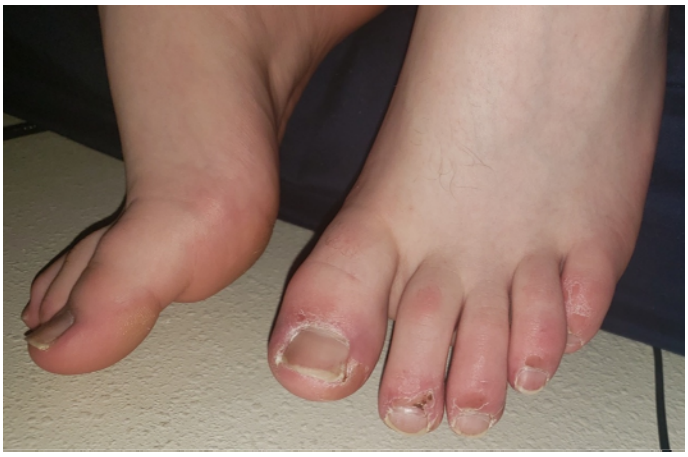

Figure 3. *Day 26 of illness. Desquamation progressed to his remaining toes and the second toe developed crusting.*

Figure 4. *Day 40 of illness. Persistence of mild cyanosis without residual scarring or pigmentation.*

theorized that endothelial vasculature injury results from the inflammatory response to the virus entering the endothelium. This may be related to injury to angiotensin converting enzyme-2 (ACE 2) expressed by the endothelial cells, which ultimately results in immune dysregulation [5]. This hypothesis is supported by histopathology showing lymphocytic infiltrate and hemorrhagic parakeratosis in the stratum corneum [6] Another proposed etiology is that it may be caused by macrovascular occlusive disease or embolism. This hypothesis is supported by the presence of microscopic intravascular thrombi which have been seen on biopsy of lesions in critically ill patients [7]. At the same time, there is not strong evidence to explain a causal relationship between SARS CoV-2 infection and the perniosis-like symptoms and this may be an epi-phenomenon. Kanitakis et al. shared their experience with 17 cases of perniosis and could not elucidate causality related to the virus [8]. With the lack of concrete evidence and pathophysiology to explain perniosis in these times, there is also the possibility that quarantine and home environments may have played a part in the onset of these symptoms.

In the case of this patient, his perniosis improved with conservative treatment, including warming and leg elevation. Topical corticosteroids and non-steroidal anti-inflammatory medications have been used in other case reports [6].

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. WHO. WHO Timeline - COVID-19. https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19. Published 2020. Accessed on May 18, 2021.
2. CDC. Cases in the U.S. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html. Published 2020. Accessed on May 18,2021.
3. Wang D HB, Hu C, Zhu F et. al, Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323:1061-1069. [PMID 32031570].
4. The profound dermatological manifestations of COVID-19: Part IV – Cutaneous features. https://www.aad.org/dw/dw-insights-and-inquiries/2020-archive/april/dermatological-manifestations-covid-19-part-4. Accessed on May 18, 2021.
5. Moore HW. COVID Toes: Dermatologic Observations and Theories. https://www.clinicaladvisor.com/home/topics/dermatology-information-center/covid-toes-dermatologic-observations-and-theories/?utm_source=newsletter&utm_medium=Email&utm_campaign=ca-update-dmd-20200521&cpn=pcp_all,latuda3561,pcp_md,breo_105221,cambia_august2018,toujeo_oct2018,toujeo_nov2018,toujeo_nov2018updated,verzenio122018,toujeo_dec2018,abilify12518,shingrix1297382019,latuda20192020,shingrix5292019,shingrixwatson5232019,shingrixwatson_920,latuda_nov201&hmSubId=&hmEmail=5zrvXEIrY5sFd1bIO4IkZpro2TpNBuuS0&NID=1578550281&Email_hash=e55df4667f6a6cca2270e4d065e51d8a&dl=0&mpweb=1323-92568-2051262. Published May 15, 2020. Accessed on May 18, 2021.
6. Cordoro KM, Reynolds SD, Wattier R, McCalmont TH. Clustered cases of acral perniosis: Clinical features, histopathology, and relationship to COVID-19. *Pediatr Dermatol*. 2020;37:419-423. [PMID: 32396999].
7. Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. *Transl Res*. 2020;220:1-13. [PMID: 32299776].
8. Kanitakis J, Lesort C, Danset M, Jullien D. Chilblain-like acral lesions during the COVID-19 pandemic ("COVID toes"): Histologic, immunofluorescence, and immunohistochemical study of 17 cases. *J Am Acad Dermatol*. 2020;83:870-875. [PMID: 32502585].