Chilblain-like lesions with prominent bullae in a patient with COVID-19

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SUMMARY
A 27-year-old patient presented with acral chilblain-like lesions atypical of dermatological presentations appearing in current reports of COVID-19. Prominent bullae had formed on the dorsa of her toes and became haemorrhagic 2 days after the initial presentation. The patient had no underlying medical conditions, including any history of collagen vascular disease, Raynaud’s phenomenon, chilblains or cold exposure, and was not taking any medications. The patient reported 10 days of ageusia and anosmia 6 weeks prior to the manifestation of her toe lesions, with no other symptoms. A nasopharyngeal swab test for SARS-CoV-2 RNA was positive. It is important that physicians recognise the myriad of cutaneous lesions associated with COVID-19 in this ongoing pandemic.

BACKGROUND
Chilblain-like lesions are one of many cutaneous manifestations associated with the novel coronavirus, SARS-CoV-2. Chilblains may be idiopathic or secondary to rheumatological conditions, malignancy or other diseases including viral infections. The clinical presentation and histopathology of chilblains, including cases of chilblain-like lesions associated with COVID-19, are similar.1 Herein, we present a patient with COVID-19 whose chilblain-like lesions exhibited prominent bullae that may confound the initial diagnosis.

CASE PRESENTATION
Some of the more commonly reported dermatological manifestations associated with COVID-19 disease include erythematous rashes, maculopapular and urticarial eruptions, and chilblain-like (also called pernio-like) lesions.2 This case report illustrates an atypical presentation of a cutaneous lesion associated with COVID-19 and reviews the potential pathophysiology and clinical relevance.

A 27-year-old woman requested a teledermatology consult concerning a 2-day history of bilateral, progressively oedematous and pruritic toes that were painful when confined by shoes. The patient had no underlying medical conditions, including any history of collagen vascular disease, Raynaud’s phenomenon, chilblains and cold exposure, and was not taking any medications. However, 6 weeks prior to her toe manifestation, she experienced 10 days of ageusia and anosmia with no other symptoms. On examination, multiple bilateral non-haemorrhagic bullae of various sizes up to approximately 1.5 cm in diameter were present on the dorsa of her toes (figure 1). Her toes were oedematous with widespread erythema. Acrocyanosis and livedo reticularis were not present. Two days following her initial presentation, the bullae appeared haemorrhagic (figure 2A,B). No other clinical changes were noted and there were no petechiae or signs of bruising or bleeding elsewhere. The patient was advised to self-isolate and subsequent test results for SARS-CoV2 were positive.

OUTCOME AND FOLLOW-UP
At a 3-month follow-up, acral oedema and pruritus had completely resolved. The bullous lesions on the dorsa of the toes healed with residual scaling and cutaneous violaceous hyperpigmentation. The patient remained otherwise asymptomatic.

DISCUSSION
SARS-CoV-2, the RNA coronavirus virus that causes COVID-19, results in widely disparate clinical manifestations among infected individuals. Skin lesions associated with COVID-19 are similarly varied in appearance, and generally do not reflect the course of disease with a few notable exceptions, chilblain-like lesions being one such example.1 Although this patient’s lesions displayed the characteristic oedematous, erythematous macules associated with pain and pruritus in an acral distribution, the prominent bullae were atypical for chilblains.3 4 However, the diagnosis of COVID-19 was suspected given the presence of these skin lesions coupled with the patient’s recent history of anosmia and ageusia, and subsequently confirmed by a nasopharyngeal swab positive by PCR for SARS-CoV-2. Thus, it is important to maintain a high degree of vigilance for atypical presentations associated with SARS-CoV-2 in potentially contagious individuals during this pandemic.

Chilblains is a cold-induced inflammatory vasculopathy that may be hereditary, idiopathic or associated with diseases including leukaemia, viral hepatitis, HIV infection, rheumatoid arthritis and connective tissue disorders including lupus erythematosus. Although the diagnosis of chilblains is established clinically, the histopathology of chilblains, including cases of chilblain-like lesions associated with COVID-19, is similar and includes papillary dermal oedema, a superficial and deep, perivascular and eccrine associated lymphocytic infiltrate and lymphocytic vasculitis, and occasional necrotic keratinocytes and vacuolisation of the basal layer.5 6

Tissue injury of various severities associated with COVID-19 is generally ascribed to one of the following non-mutually exclusive mechanisms:
Case report

Figure 1  Patient presented with non-haemorrhagic bullae, along with oedema and widespread erythema on the dorsa of her toes.

Figure 2 (A, B) Acral bullae appeared haemorrhagic 2 days following the initial presentation.

direct viral infection, coagulopathy and cytokine-induced injury. Arterial and venous endothelial cells express the ACE2 viral receptor, and SARS-CoV-2 has recently been identified by electron microscopy in dermal endothelial cells of patients with chilblain-like lesions. Coagulopathy is not causally associated with chilblain-like lesions. However, the upregulation of interferon and other cytokine signalling pathways is associated with clinical conditions that produce chilblains, and early type 1 interferon (IFN-1) upregulation can effectively limit SARS-CoV-2 infection. An IFN-1 response is also associated with a familial form of chilblains caused by heterozygous mutations in TREX1, a gene encoding the 3' to 5' repair exonuclease 1, leading to the accumulation of nucleic acids, which activate innate immune sensors. It is also possible that specific cytokines may be associated with the prominent bullae seen in this case, as reported in patients with autoimmune bullosal disorders.

As exemplified by the patient, chilblain-like lesions are observed in healthy children and young adults who exhibit otherwise minimal COVID-19 signs and symptoms, and typically occur in the convalescent phase of COVID-19 infection. It remains to be elucidated why the majority of these lesions occur in acral areas. Although the nasopharyngeal swab tested positive for SARS-CoV-2 RNA by PCR, recent studies suggest these results may not necessarily indicate a replication-competent virus, although patients should still be instructed to self-quarantine given the uncertainty. In summary, this case report of a patient with atypical chilblain-like lesions with prominent haemorrhagic bullae extends the diversity of cutaneous signs associated with COVID-19.

Learning points

- Chilblain-like lesions are one of the numerous skin manifestations associated with COVID-19. They tend to occur in younger patients who exhibit otherwise minimal COVID-19 signs and symptoms, and typically in the convalescent phase of the infection.
- Upregulation of interferon and other cytokine signalling pathways is associated with clinical conditions that produce chilblains. Cytokine production may follow the infection of dermal endothelial cells by SARS-CoV-2 recently identified by electron microscopy in patients with chilblain-like lesions.
- Clinicians should be alert to atypical presentations of cutaneous lesions associated with COVID-19 such as the presence of acral haemorrhagic bullae.

Contributors AR and MA conceived the idea of the case report and conducted a review of literature. AR additionally wrote the manuscript and MA conducted final editing of the manuscript. BKR provided commentary on the clinical course of the case and interpreted lab findings. JR acquired case data necessary to produce manuscript content.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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