

were taken only in hospitalized patients; serological tests are currently still limited to regional regulations.

Seven patients with PV (23%) experienced suspected symptoms of COVID-19. Four patients with PV (suspected or asymptomatic) reported contact with patients with suspected ($n = 3$) or known ($n = 1$) COVID-19. Six patients with PV (19%) experienced 'mild-to-moderate' symptoms (as described above) and one patient with PV (3%) experienced 'severe' symptoms that needed hospitalization. This patient (69 years old, comorbidity of previous breast cancer), confirmed with a positive COVID-19 nasal swab, has now recovered.

For all those taking systemic steroid therapy, the current dosage was not considered immunosuppressive (> 20 mg per day).⁵ No patient independently discontinued the current therapy for fear of recurrence of bullous lesions. Ongoing steroid or immunosuppressive therapy has been stopped for hospitalized patients. All patients with pemphigoid and pemphigus were in remission, even 10 newly diagnosed patients (duration of disease < 6 months). One patient with pemphigus had been treated with rituximab 6 months earlier; he reports no COVID-19 symptoms.

Observation of these data shows that the main risk factor for developing suspected COVID-19 symptoms was contact between the patient and an individual with known or suspected COVID-19. Furthermore, we have seen that longer disease duration is more frequently associated with patients with suspected COVID-19 symptoms. A longer duration of therapy, although not at immunosuppressive dosages, probably creates a condition of infectious risk predisposition. Contact with COVID-19 is probably the most important factor: in patients with BP we found statistical significance, while in patients with PV we found no significance but a consistent trend. It must be considered that, given that many tests were performed, it is possible that some lower P-values arose by chance. Observations of a larger number of patients will be required to evaluate whether these trends can be confirmed.

It is therefore important to create a communication channel with these patients to give clinical and human support and to help in managing therapies. We found it essential to advise and empower patients on activities that limit the risk of infection (hand hygiene, social distancing, use of protective devices), especially the most fragile, elderly and comorbid patients.

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Thrombotic occlusive vasculopathy in a skin biopsy from a livedoid lesion of a patient with COVID-19

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DEAR EDITOR, Some authors have reported the presence of cutaneous lesions related to the new coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, in up to 20–4% of cases. However, these lesions are not well characterized either clinically or histopathologically.¹ A recently highlighted finding is congested and oedematous blood vessels along with hyaline thrombi in the alveolar septum, and also in the heart, liver and kidney of three autopsied patients who died due to severe infection by SARS-CoV-2.² Thus, anticoagulant treatment has been proposed to decrease mortality in certain cases of severe COVID-19 disease.³ We report a case of livedoid purple lesions along with acrocyanosis in a patient with confirmed SARS-CoV-2 infection with positive nasopharyngeal swab, showing an underlying obstructive cutaneous vasculopathy

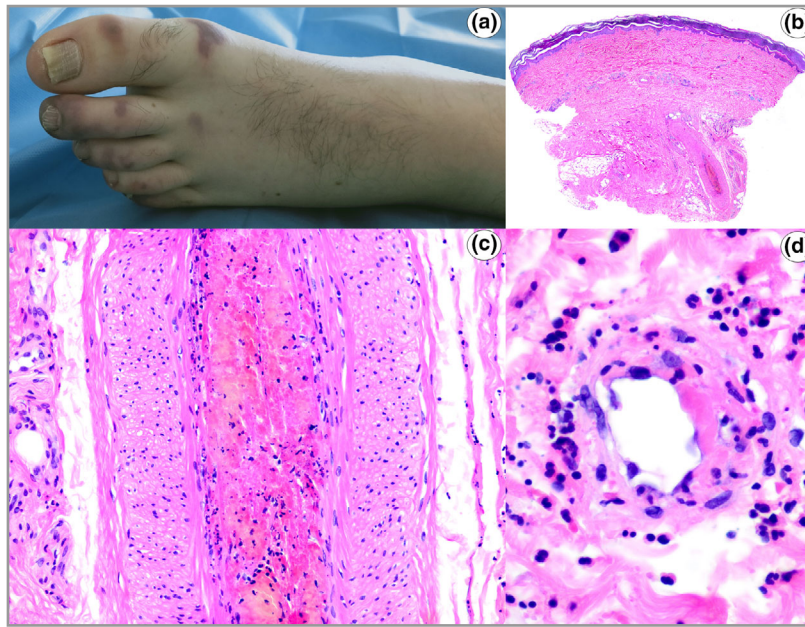


Figure 1 (a) Purplish retiform and roundish patches (livedoid lesions) on the dorsal areas of the left foot. The contralateral foot presented similar, milder lesions. Some of them presented angled edges. No other cutaneous or mucosal lesions in other areas were observed. (b) Panoramic picture from a skin biopsy showing upper-epidermal necrosis and intravascular thrombi in a larger muscular dermo-hypodermal artery. (c) Detail of the thrombi in the larger muscular vessel. (d) Detail of fibrinoid necrosis and leucocytoclasia surrounding some of the vessels in the reticular dermis. Endotheliitis is present. (b–d) Haematoxylin and eosin stain, original magnification (b) $\times 2$, (c) $\times 20$, (d) $\times 40$.

and sweat gland necrosis, both previously undescribed in this disease.

A 61-year-old man, otherwise apparently healthy except for a history of diabetes, was accepted as an inpatient at the intensive care unit with a diagnosis of COVID-associated severe bilateral pneumonia complicated with diabetic ketoacidosis. He simultaneously started showing cutaneous lesions. There was no previous history of immunosuppression, new drugs or endovascular manipulation. He was treated with low-molecular-weight heparin. Physical examination showed purple ischaemic digits involving the second and fourth distal phalanges of the right hand, and milder on the second, fourth and fifth digits of the left hand. The second, third and fifth digits of the left foot were also involved. In addition, we observed livedoid purplish retiform and roundish patches on the other fingertips, and on both the volar and dorsal areas of both feet and hands, some with angled edges (Figure 1a). No cutaneous or mucosal lesions in other areas were observed.

A biopsy showed a slightly necrotic upper epidermis. In the papillary dermis, dilated blood vessels were found, most of them filled with hyaline thrombi and a few with a mild neutrophilic component surrounding them. In some areas, larger arterial vessels located in the dermo-hypodermal interface showed focal fibrinoid necrosis surrounded by a scarce neutrophilic infiltrate (Figure 1b–d). Orcein staining demonstrated that the larger vessel was an artery. Sweat gland necrosis and degeneration were present, more evident in the secretory portion of the eccrine sweat coil, with preserved eccrine ducts. Microbiological cultures from skin biopsy and

blood, and polymerase chain reaction for SARS-CoV-2 from the skin biopsy were negative.

Blood tests showed increased fibrinogen (up to 995 mg mL^{-1}) and D-dimer levels (60.8 mg L^{-1}) and leucopenia, with later progressive normalization. Coagulation tests showed a heterozygous factor V Leiden mutation with normal antithrombin III, homocysteine, protein C and protein S levels. No prothrombin G20210A mutation, cryoglobulin, anticardiolipin antibodies, anti-beta-2 glycoprotein IgG and IgM antibodies, or lupus anticoagulant were demonstrated. Follow-up after 17 days showed some improvement of the cutaneous lesions and he was extubated shortly after.




Regarding the livedoid and necrotic lesions observed in our case, a recent series described seven cases of COVID-19 with presence of finger cyanosis and skin bulla, all of them showing coagulation alterations, although none of them were studied histopathologically.⁴ Five of those patients (71%) died, within a mean time of 12 days.⁴ Very recently Kolivras *et al.* reported the first histopathology of a chilblain-like lesion showing a superficial infiltrate and deep lichenoid, perivascular and perieccrine infiltrates of lymphocytes without any thrombi.⁵

The retiform purpura and livedoid lesions in our patient could be explained as a cutaneous manifestation of an underlying systemic coagulopathy related to COVID-19, as has been previously described in other coagulopathies.⁶ Our patient's heterozygous mutation of factor V Leyden is an additional known risk factor favouring thrombosis.⁷ Our case's sweat gland necrosis was similar to that present in non-drug-related

coma-associated bulla.⁷ However, in our case, thrombi and even fibrinoid necrosis were observed not only in the upper-dermis vessels but also in all the other vessels in the biopsy, even in the dermo-hypodermal junction. This unexpected finding could be related to more extensive endothelial damage secondary to COVID-19 infection, as this has recently been reported after observation of viral inclusion bodies in electron microscopy of the kidney, small bowel and lung of severely affected patients.⁸

To our knowledge, this is the first report of a patient with COVID-19 where the presence of an occlusive vasculopathy at the cutaneous level has been demonstrated. In our case, we also observed a striking sweat gland necrosis, a finding previously reported as being associated with ketoacidosis coma but not with COVID-19 infection. Additional studies are needed to characterize completely the tissue damage associated with the virus, including within the gamut of lesions observed in the skin.

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Absence of images of skin of colour in publications of COVID-19 skin manifestations

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DEAR EDITOR, There are now over 1 million confirmed cases of COVID-19 globally, with more than 270 000 recorded deaths to date.¹ COVID-19 has been shown to impact people of colour disproportionately, both in the UK and in the USA, where black people make up 13.4% of the population but 30% of cases of COVID-19.^{2,3} Mounting evidence shows that COVID-19 impacts several organ systems, including the skin.⁴ Knowledge of cutaneous manifestations of COVID-19 and the ability to identify them in patients of all skin types is important for dermatologists and other healthcare providers who may be evaluating patients who are otherwise asymptomatic. In order to provide optimal care to all patients, it is therefore important that we are able to identify cutaneous manifestations of COVID-19 in patients with darker skin.

We completed a systematic literature review, using the PRISMA guidelines, of all articles describing cases of cutaneous manifestations associated with COVID-19. We included English-language articles published between 31 December 2019 and 3 May 2020. We extracted patient case numbers, race and ethnicity descriptors when available, photographs, and descriptions of cutaneous manifestations. In order to assess background skin colour, a board-certified dermatologist with expertise in diagnosing and treating patients with skin of colour (Fitzpatrick type IV–VI) evaluated each of the images and categorized them based on Fitzpatrick type I–VI.

We collated these images, ordered by skin type (Figure 1a). We then manually selected a pixel of background skin, unaffected by the rash, from each image. In order to adjust for lighting conditions, we then standardized the lightness portion of the hue–saturation–lightness scale of this pixel within each coded Fitzpatrick category, thus approximating true skin colour (Figure 1b).

Forty-six articles met our inclusion criteria. Of those, 36 articles included clinical photos of COVID-19-related skin lesions for a total of 130 images. We obtained permission to use 116 of these images in this publication, and they are shown in Figure 1. In total, 92% (120 of 130) showed skin types I–III, 6% (seven of 130) showed patients with type IV skin and 2% (three of 130) could not be classified because they depicted only acral skin. There were no clinical images representing Fitzpatrick type V or VI skin. Photographed eruptions among skin of Fitzpatrick phototypes I–III included chilblain-like, urticarial, maculopapular and vesicular lesions. The images among patients with Fitzpatrick phototype IV included