

## Correspondence

### Bullous dermatosis on the hands following SARS-CoV-2 infection

Dear Editor,

The novel coronavirus SARS-CoV-2, which causes Coronavirus disease 2019 (COVID-19), can lead to heterogeneous symptoms which range from interstitial pneumonia to generalized disturbances characterized by severe immune responses and aberrant inflammation, which may be associated to various dermatologic manifestations.<sup>1,2</sup>

A 77-year-old male patient was admitted to our hospital for bilateral pneumonia and symptomatic SARS-CoV-2 infection, which was confirmed with a positive oropharyngeal swab. His personal history was positive for hypertension and atrial fibrillation. The patient was treated with dexamethasone 6 mg/day for 10 days and enoxaparin 1 mg/kg/day. On day 10 from the admission, the patient was intubated and mechanical ventilation was administered. Furthermore, continuous renal replacement therapy was started. On the 22nd day of admission, a skin eruption abruptly occurred bilaterally at the hands of our patient. On physical examination, bilateral and confluent purplish and violaceous macular and papular lesions were evident at the dorsal region of both hands. In addition, multiple tense and prominent bullae were observed in both hands, strained from 0.5 to 1 cm in diameter with hemorrhagic and necrotic content (Figs. 1 and 2). We proposed a cutaneous biopsy for the histological examination of the lesions, but the patient's family refused the exam; hence we were not able to look for BP180/230 antibodies. Blood tests for antinuclear antibody (ANA), antiphospholipid antibody, extractable nuclear antigen antibodies (ENA) panel, and cryoglobulins were within normal range. Notably, D-dimer and white blood cells were abnormally elevated. The patient died on day 27 from the admission.

To date, numerous COVID-19-related dermatologic manifestations have been described. The heterogeneity of the skin manifestations documents the complexity of the clinical and pathogenic features of the SARS-CoV-2 infection. The most frequent dermatologic pictures are macular-papular exanthemas, pernio-like lesions, papules-vesicles, urticarial lesions, and livedo reticularis. Vascular lesions encompassing chilblain-like lesions and acral necrosis have been largely associated with COVID-19.<sup>1</sup> The reported occurrence of vascular lesions supports the hypothesis that endothelial dysfunction plays a key role in organ injury.<sup>2</sup> Many hypotheses have been advanced to explain the onset of endothelial damage in COVID-19 patients: It has been considered as an immunological reaction to viral antigens deposition; also, immune activation, especially high



**Figure 1** Bullous dermatosis on the hands of the patient. Purplish and violaceous macular and papular lesions are evident at the dorsal region of both hands. Tense bullae are present as well

level of IL-6, and the stimulation of the coagulation system due to viral load have been proposed as possible triggers.<sup>3</sup>

In case of prominent vascular damage, conspicuous bullous lesions may appear; however, only few cases of extended bullous vasculitis following the novel coronavirus infections have been reported so far.<sup>3,4</sup> Importantly, the published evidence described bullous lesions which were primarily localized on the lower extremities.<sup>3,4</sup>




Compellingly, the concept that a virus may induce a blistering dermatosis has been previously hypothesized: both herpes simplex virus and Chikungunya virus have been linked to the development of prominent blistering lesions.<sup>5,6</sup> Thus, we may conjecture that SARS-CoV-2 may somehow lead to the appearance of bullous manifestations. Notwithstanding, further studies are warranted to substantiate this statement.



**Figure 2** Bullous dermatosis on the left hand of the patient. Multiple grayish bullae containing hemorrhagic and necrotic material on top of maculopapular skin changes are evident

Because a biopsy of the skin lesions could not be performed, the presence of bullous pemphigoid could not be verified. Moreover, there is published evidence describing numerous drugs, with enoxaparin being one of them, and renal replacement therapy as agents that are able to induce drug-induced bullous pemphigoid.<sup>7-9</sup>

We report this case to add a new dimension of knowledge to the understanding of the dermatologic manifestations of COVID-19.

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### References

- Tammaro A, Chello C, Sernicola A, *et al.* Necrotic acral lesions and lung failure in a fatal case of COVID-19. *Australas J Dermatol* 2020; **61**: e467–e468.
- Tammaro A, Adebajo GAR, Del Nonno F, *et al.* Cutaneous endothelial dysfunction and complement deposition in COVID-19. *Am J Dermatopathol* 2021; **43**: 237–238.
- Gouveia PADC, Cipriano IC, de Melo MAZ, *et al.* Exuberant bullous vasculitis associated with SARS-CoV-2 infection. *IDCases* 2021; **23**: e01047.
- Rubin A, Alamgir M, Rubin J, *et al.* Chilblain-like lesions with prominent bullae in a patient with COVID-19. *BMJ Case Rep* 2020; **13**: e237917.
- Lecluse AL, Buijnzeel-Koomen CA. Herpes simplex virus infection mimicking bullous disease in an immunocompromised patient. *Case Rep Dermatol* 2010; **2**: 99–102. <https://doi.org/10.1159/000315352>
- Robin S, Ramful D, Zettor J, *et al.* Severe bullous skin lesions associated with Chikungunya virus infection in small infants. *Eur J Pediatr* 2010; **169**: 67–72. <https://doi.org/10.1007/s00431-009-0986-0>
- Verheyden MJ, Bilgic A, Murrell DF. A systematic review of drug-induced pemphigoid. *Acta Derm Venereol* 2020; **100**:adv00224. <https://doi.org/10.2340/00015555-3457>
- Osipowicz K, Kalinska-Bienias A, Kowalewski C, *et al.* Development of bullous pemphigoid during the haemodialysis of a young man: case report and literature survey. *Int Wound J* 2017; **14**: 288–292. <https://doi.org/10.1111/iwj.12670>
- Suo H, Su H, Lu C, *et al.* Development of generalized bullous lesions after hemodialysis with polysulfone membrane dialyzer. *J Dermatol* 2020; **47**: e119–e120. <https://doi.org/10.1111/1346-8138.15261>