European Union: a systematic review of the literature. *Patient Prefer Adherence* 2016; **10**: 2357–2367.
3 Arnold T, Schaarschmidt ML, Herr R, Fischer JE, Goerdt S, Peitsch WK. Drug survival rates and reasons for drug discontinuation in psoriasis. *J Dtsch Dermatol Ges* 2016; **14**: 1089–1099.
4 Zhu L, Xu X, Ma K *et al*. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. *Am J Transplant* 2020; **20**: 1859–1863.
5 D'Antiga L. Coronaviruses and immunosuppressed patients: the facts during the third epidemic. *Liver Transpl* 2020; **26**: 832–834.
6 Vangeli E, Bakhshi S, Baker A *et al*. A systematic review of factors associated with non-adherence to treatment for immune-mediated inflammatory diseases. *Adv Ther* 2015; **32**: 983–1028.
7 Amerio P, Prignano F, Giuliani F Gualdi G. COVID-19 and psoriasis: should we fear for patients treated with biologics? *Dermatol Ther* 2020; **e13434**.
8 Gendelman O, Weitzman D, Rosenberg V, Shalev V, Chodick G, Amital H. Characterization of adherence and persistence profile in a real-life population of patients treated with adalimumab. *Br J Clin Pharmacol* 2018; **84**: 786–795.

DOI: 10.1111/jdv.16759

An unusual case of bullous haemorrhagic vasculitis in a COVID-19 patient

Dear Editor

A novel Coronavirus strain, named 'Severe Acute Respiratory Syndrome Coronavirus 2' (SARS-CoV-2) was recently identified as the etiological agent of the COronaVIrus Disease 2019 (COVID-19). Interestingly, a consistent number of COVID-19-associated skin manifestations seem to share a certain degree of vascular damage as common pathogenetic mechanism.[1] Vascular injury may be due to the direct damage of endothelial cells by the virus or may represents an epiphenomenon of a dysregulated host inflammatory responses triggered by the infection.[2] Here, we describe an unprecedented case of leukocytoclastic vasculitis presenting with a haemorrhagic bullous eruption in a patient affected by COVID-19.

A 79-year-old man with a history of hypertension, myocardial infarction and chronic obstructive pulmonary disease has been hospitalized for acute heart failure. The patient was tested for COVID-19 (RT-PCR on nasopharyngeal swab sample) and resulted negative. Medical treatment for heart failure was started and patient's conditions progressively improved. On day 15 of the hospitalization, he rapidly developed fever and dyspnea. Chest radiograph and CT scan revealed a radiologic pattern suggestive for COVID-19 pneumonia and nasopharyngeal swab RT-PCR confirmed SARS-CoV-2 infection. Treatment with hydroxychloroquine (400 mg bid), prophylactic anticoagulation (enoxaparin 4000 IU qd), empiric antibiotics (ceftaroline 600 mg bid) and intravenous corticosteroids (methylprednisolone 80 mg qd) was started. Concomitantly, oxygen therapy was initiated at 8 liters/minute (approximately 40% FiO_2) via a non-rebreathe mask. After ten days, the patient developed multiple non-itching vesiculobullous lesions on neck and dorsal areas of hands (Fig. 1a,b). Laboratory tests including whole blood count, biochemical and coagulation parameters were within normal limits. Antinuclear antibody, antineutrophil cytoplasmic antibody and cryoglobulins resulted negative and serum protein electrophoresis as well as complement levels were normal. Moreover, the patient tested negative for enzyme-linked immunosorbent assay (ELISA) for detecting BP180 and BP230 antibodies. A punch skin biopsy was performed. Histopathologic examination demonstrated irregular hyperplasia of the epidermis and abundant erythrocytes extravasation with formation of intraepithelial haemorrhagic bullae. The epidermis was partly necrotic with keratinocytes focally showing nuclear hyperchromasia and cytoplasmic eosinophilia (Fig. 1c). Within the superficial dermis, there were marked erythrocytes extravasation and severe neutrophilic infiltrate within the wall of small vessels and in their proximity with scant leukocytoclasia (acute vasculitis). Endothelial cells were activated showing nuclear enlargement and hyperchromasia (Fig. 1d). Eosinophils and lymphocytic infiltration were not observed. Fibrinoid vascular changes and thrombi were absent as well as no viral cytopathic changes were observed. The histopathologic findings demonstrated a typical picture of leukocytoclastic vasculitis. Unfortunately, in the following days patient's respiratory conditions deteriorated and, despite intensive care support, he died of respiratory insufficiency.

The case described is an unusual case of bullous haemorrhagic vasculitis in a COVID-19 patient. The macroscopic characteristics of the lesions were compatible with a localized bullous pemphigoid (BP) or a heparin-induced bullous haemorrhagic dermatosis (BHD).[3,4] In our patient, absence of eosinophilic infiltrates as well as negativity of ELISA for BP180/BP230 autoantibodies reasonably rule out the hypothesis of localized BP. The second diagnostic diagnosis was BHD. Nevertheless, focally necrotic epidermis and vasculitis observed in our case have never been reported in BHD and thus we excluded this diagnosis. Histopathologic features observed in our patient are characteristic of an evolving leukocytoclastic vasculitis (LCV).[5] Interestingly, capillary injury and/or neutrophilic infiltrates have been described in lung tissues from COVID-19 and, in one recent report, also in the skin.[6,7] Nonetheless, we can expect that the number of reports concerning COVID-19-related vasculitis is likely to increase since inflammatory vascular damage is emerging as one of the main pathogenic mechanisms of SARS-CoV-2 infection, including its cutaneous manifestations. However, only further studies, novel reports including clinical images and detailed histology as well as data from international dermatology registries will be able to confirm this hypothesis.

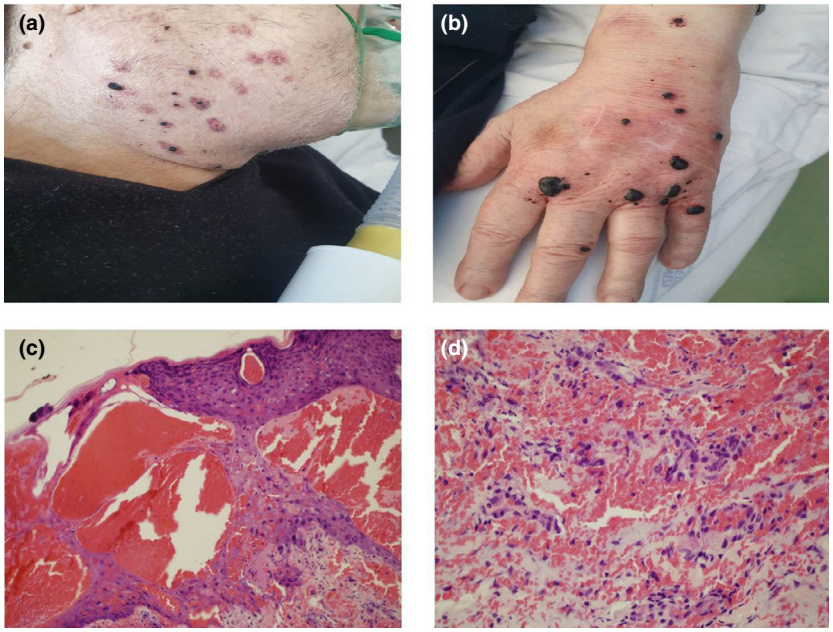

Figure 1 Clinical images of COVID-19-associated cutaneous eruption (a, b). Histopathological images of epidermis and dermis. Haematoxylin and eosin staining, original magnification: 20×, 40× (c, d).

Acknowledgement

The patient in this manuscript has given written informed consent to publication of their case details.

Conflicts of interest

All authors have nothing to disclose.

Funding sources

None reported.

S. Negrini,[1] A. Guadagno,[2,*] M. Greco,[1] A. Parodi,[3] M. Burlando[3]

[1]Department of Internal Medicine, University of Genoa and Ospedale Policlinico San Martino, Genoa, Italy, [2]Anatomic Pathology Unit, University of Genoa and Ospedale Policlinico San Martino, Genoa, Italy, [3]Di.S.Sal. Section of Dermatology, University of Genoa and Ospedale Policlinico San Martino, Genoa, Italy

*Correspondence: A. Guadagno. E-mail: antonio.guadagno@hsanmartino.it

References

1 Bouaziz JD, Duong T, Jachiet M *et al*. Vascular skin symptoms in COVID- 19: a French observational study. *J Eur Acad Dermatol Venereol* 2020. [Epub ahead of print]. https://doi.org/10.1111/jdv.16544

2 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.

3 Cozzani E, Gasparini G, Burlando M, Drago F Parodi A. Atypical presentations of bullous pemphigoid: clinical and immunopathological aspects. *Autoimmun Rev* 2015; **14**: 438–445.

4 Russo A, Curtis S, Balbuena-Merle R *et al*. Bullous hemorrhagic dermatosis is an under-recognized side effect of full dose low-molecular weight heparin: a case report and review of the literature. *Exp Hematol Oncol* 2018; **7**: 15.

5 Baigrie D, Bansal P, Goyal ACrane JS. Leukocytoclastic Vasculitis (Hypersensitivity Vasculitis). In: StatPearls. StatPearls Publishing, Treasure Island, 2020.

6 Yao XH, Li TY, He ZC *et al*. A pathological report of three COVID-19 cases by minimally invasive autopsies. *Zhonghua Bing Li Xue Za Zhi* 2020; **49**: E009.

7 Varga Z, Flammer AJ, Steiger P *et al*. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; **395**: 1417–1418.

DOI: 10.1111/jdv.16760

Systemic or biologic treatment in psoriasis patients does not increase the risk of a severe form of COVID-19

Dear Editor

Some systemic and biologic psoriasis treatments [SBT] have been associated with an increased risk of infection.[1] To date, more and more data regarding the risk of COVID-19 infection in patients receiving SBT become available.[2-5]