COVID-19 SPECIAL FORUM

Non-acral skin manifestations during the COVID-19 epidemic: COVIDSKIN study by the French Society of Dermatology

Dear Editor,

A variety of skin manifestations occurring during the COVID-19 pandemic have been reported since March 2020.[1] The most reported were chilblain-like lesions, widespread urticaria, maculopapular eruptions, vesicular eruptions and vascular lesions such as livedo or necrosis.[1–3] Cutaneous manifestations are rare with a frequency estimated around 2% of patients with a biologically confirmed COVID-19.[4–7] A national survey, COVIDSKIN study of the French Society of Dermatology, was carried out from March 30 to June 11, 2020, asking hospital and private physicians to report, using a standardized questionnaire, cases of skin manifestations in patients with COVID-19 clinically suspected. We report skin manifestations excluding acral manifestations, described separately.[3] We aimed to describe the characteristics, the skin manifestations and the biological diagnostic tests' results of suspected COVID-19 patients.

Among the 492 collected cases, after excluding 311 patients with acral manifestations and 65 for whom no COVID-19 tests were performed, we included 116 patients: 52 had positive COVID-19 tests (45 positive RT-PCR, eight positive serology; including one patient positive for both) and were then considered as 'confirmed COVID-19 group' and 64 who had negative tests (15 with negative RT-PCR and 49 with negative results for both RT-PCR and serology) but who were clinically suspected, then considered as 'unconfirmed COVID-19 group'. The available photographed manifestations were classified by four dermatologists according to Galván Casas *et al.*[1] (maculopapular eruptions, urticaria, vesicular rash, necrosis/livedo and other eruptions).

The overall median age was 38 [interquartile range (IQR) 28–52]. All the hospitalized patients were in the confirmed group (25/52) except for two patients with negative RT-PCR. Four patients were died, all from the COVID-19-confirmed group. Median time between the first infectious symptoms when present (n = 86) and RT-PCR was 6 days (IQR 3–13) and median time to serology was 26.5 days (IQR 13–33.3). Median time between the first infectious symptoms and cutaneous manifestations was 7 days (IQR 3–16). Patients' and characteristics and biological tests' are summarized in Table 1.

Pictures of the lesions were available for 71 patients (Fig. 1). The most common manifestation was maculopapular eruption. The frequency and distribution of the types of skin manifestations did not significantly differ between the confirmed and unconfirmed COVID-19 patients (P = 0.199), as summarized in

Table 1 Dermatologic manifestations in patients with confirmed and unconfirmed COVID-19

Overall population, *n* = 116	**Confirmed COVID-19 patients, *n* = 52 *n* (%)**	**Unconfirmed COVID-19 patients, *n* = 64 *n* (%)**
Age in year, median (IQR)	44.5 (30.3–63.5)	36 (25–44.5)
Male patient	31 (60)	40 (62)
Anosmia/ageusia	21 (41)	10 (16)
At least one symptom	46 (88)	40 (62)
Time between date of first infectious symptoms and:		
RT-PCR in days, median (IQR)	5 (2.25–9)	7.50 (4–26)
Serology in days, median (IQR)	28 (26.5–31)	25 (10–33)
Cutaneous manifestations in days, median (IQR)	7 (4.75–13.8)	8 (0–23)
Deaths	4 (8)	0
Patients with available pictures, *n* = 71	**Confirmed COVID-19 patients, *n* = 38 *n* (%)**	**Unconfirmed COVID-19 patients, *n* = 33 *n* (%)**
Maculopapular rash	20 (53)‡	21 (64)
Facial	2 (5)	4 (12)
Diffuse	12 (32)	16 (48)
Thoracic plaque	4 (10)	0
Erythema multiforme	1 (3)	1 (3)†
Pityriasis rosea	1 (3)	0
Vesicular rash	1 (3)	2 (6)
Urticaria	8 (21)‡	1 (3)
Purpura/livedo	3 (8)‡	2 (6)
Other	6 (16)	7(21)
Asymmetric periflexural exanthem of childhood	1	0
Erythema nodosum	0	2†
Eczema	1	3†
Impetigo	1†	0
Tongue angiomatosis	1	0
Grover's disease	1†	0
Lipodermatosclerosis	1†	0
Pityriasis lichenoides	0	2†

Data are presented as *n* (%) unless otherwise indicated.
†Histologically confirmed diagnosis. ‡Deceased patients: maculopapular rashes, n = 2; urticaria, n = 1; purpura/livedo, n = 1.

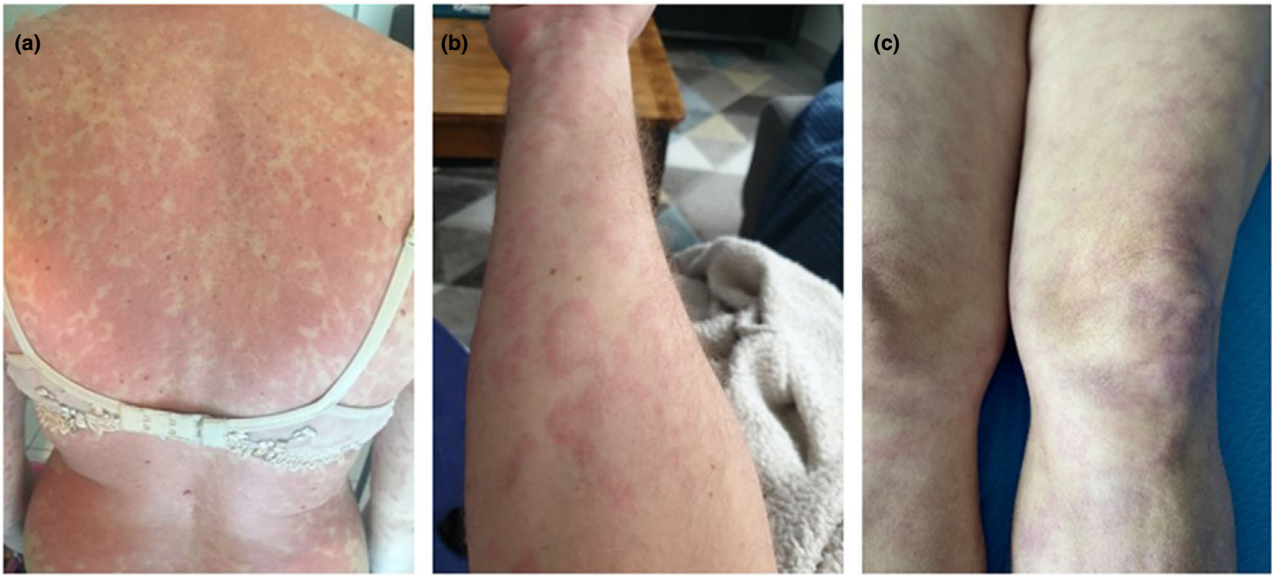

Figure 1 Photographs of dermatologic manifestations. (a) Diffuse maculopapular rash, (b) urticaria, (c) livedo.

Table 1, although urticarial eruptions seemed more frequent among confirmed patients. In the confirmed group, the frequency and distribution of the types of manifestations did not differ between hospitalized and non-hospitalized patients.

Previously, two large retrospective series classified respectively 304 COVID-19 and 126 cases found the following types of non-acral manifestations' frequencies: 58–61% maculopapular eruptions; 21–24% urticaria; 11–14% vesicular eruptions; and 7–9% livedo/necrosis.[1,2] We observed these manifestations in similar proportions, especially among patients with confirmed COVID-19 (Table 1). We could not exclude the possibility of false negative for some patients, specifically for those who reported anosmia/ageusia and when RT-PCR was not followed by serological testing, while this probability was low for RT-PCR and seronegative patients. Indeed, asymptomatic COVID-19 patients have a similar rate of seroconversion than symptomatic patients and the 58 serologies performed had a sensitivity and specificity above 98% in the timeframe they were performed.[8]

As previously stated, given the dermatological manifestations' heterogeneity, possible differential diagnoses, classification bias and the absence of gold-standard test to exclude COVID-19, it was not possible to determine which cutaneous manifestations are directly related or not to the infection.[9,10] Further prospective studies with systematic dermatological examination of patients with proven COVID-19 are needed to establish a formal association between infection and specific cutaneous manifestations.

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Conflict of interest

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References

1 Galván Casas C, Català A, Carretero Hernández G *et al.* Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol* 2020; **183**: 71–77.
2 Freeman EE, McMahon DE, Lipoff JB *et al.* The spectrum of COVID-19-associated dermatologic manifestations: an international registry of 716 patients from 31 countries. *J Am Acad Dermatol* 2020; **83**: 1118–1129.
3 Le Cleach L, Dousset L, Assier H *et al.* Most chilblains observed during the COVID-19 outbreak occur in patients who are negative for COVID-19 on polymerase chain reaction and serology testing. *Br J Dermatol* 2020; **183**: 866–874.
4 Guan W, Ni Z, Hu Y *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–1720.
5 Fernandez-Nieto D, Ortega-Quijano D, Suarez-Valle A, Jimenez-Cauhe J, Jaen-Olasolo P, Fernandez-Guarino M. Lack of skin manifestations in COVID-19 hospitalized patients during the second epidemic wave in Spain: a possible association with a novel SARS-CoV-2 variant - a cross-sectional study. *J Eur Acad Dermatol Venereol* 2021; **35**: e183–e185.
6 Guarneri C, Venanzi Rullo E, Gallizzi R *et al.* Diversity of clinical appearance of cutaneous manifestations in the course of COVID-19. *J Eur Acad Dermatol Venereol* 2020; **34**: e449–e450.
7 Matar S, Oulès B, Sohier P *et al.* Cutaneous manifestations in SARS-CoV-2 infection (COVID-19): a French experience and a systematic review of the literature. *J Eur Acad Dermatol Venereol* 2020; **34**: e686–e689.
8 Maine GN, Lao KM, Krishnan SM *et al.* Longitudinal characterization of the IgM and IgG humoral response in symptomatic COVID-19 patients using the Abbott Architect. *J Clin Virol* 2020; **133**: 104663.
9 Vesely MD, Perkins SH. Caution in the time of rashes and COVID-19. *J Am Acad Dermatol* 2020; **83**: e321–e322.
10 Long QX, Tang XJ, Shi QL *et al.* Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med* 2020; **26**: 1200–1204.

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Adamantiades-Behçet's disease (Behçet's disease) and COVID-19

Dear Editor,

The immunopathogenesis of COVID-19 remains ill-defined.[1] Through hyperstimulation of the immune system, SARS-CoV2 may cause a multi-facetted inflammatory disease and generate immune-mediated organ damage even leading to fatal consequences.[2] However, it is still unclear, whether a modified course of COVID-19 occurs in patients with autoimmune and/or autoinflammatory diseases.[3,4] Among them, Adamantiades-Behçet's disease (ABD; Behçet's disease) is a rare, multisystem, inflammatory disease characterized by variable vessel vasculitis and relapsing-remitting course, exhibiting both autoimmune and autoinflammatory signs.[5] So far, rudimentary data on COVID-19 in ABD patients and no information about the proper management of ABD patients in the pandemic period exist.

In a telematic survey of 2789 Spanish patients, 28 had uveitis due to a systemic autoimmune disease.[6] Among them, 12 were ABD patients; with six reporting clinical manifestations compatible with COVID-19. Moreover, among 2135 consecutive COVID-19 patients presented to the Hospital Clínic (Barcelona, Spain), four (0.19%) were co-diagnosed with ABD and three were hospitalized.[7] In all four patients, ABD activity during the first COVID-19 symptoms was low. No patient required intensive care unit (ICU) treatment or mechanical ventilation. Further, 51 of 54 ambulatory ABD patients of the Necmettin Erbakan University Hospital (Konya, Turkey) continued their immunological treatment during the pandemic period; none of them developed COVID-19.[8] Lastly, among 10 ABD patients of the Cerrahpasa Medical School (Istanbul, Turkey) with COVID-19, eight were hospitalized (median hospitalization length 7 days, interquartile range 5.5–10). Two patients were admitted to the ICU and a patient, not been on treatment for ABD before getting COVID-19, died.[9] COVID-19 symptoms were mild in the nine patients who survived, and three patients reported exacerbations of their ABD-associated oral ulcers or arthralgia.

In a digital conference of the International Society for Behçet's disease, which took place on 22 January 2021, ABD experts reported on the association of ABD with COVID-19 in their countries (Table 1). With exception of the Netherlands, where ABD patients presented a significantly higher – almost twofold – COVID-19 prevalence (11.55%) than the general population (6.31%), the overall prevalence of COVID-19 in ABD patients at 0.61% was significantly lower – 4.4-fold – than that in the general population (2.71%, $P < 0.00001$). Hospitalization due to COVID-19 symptoms was required in 33 of 168 COVID-19+ ABD patients (19.6%) and ICU in two patients (1.19%). Three ABD patients deceased with COVID-19 (1.79%).

The participants analysed the available data and the existing literature and based on the current evidence concluded on a list of measurements to be taken from ABD patients and their physicians during the COVID-19 pandemic:

- The prevalence of COVID-19 in patients with ABD is apparently lower than that in the general population. This may be due to ABD patients having been especially careful with social shielding.
- ABD appears not to be associated with a more severe COVID-19 course, although the number of reported cases is still low to be able to analyse the effects of disease subtypes, activity and medications on COVID-19 outcome.
- Treatment of ABD with low-dose prednisolone (<10 mg/day) and/or biologics (esp. TNF-α inhibitors) seems not to increase the risk for COVID-19 or induce a more severe course.
- Treatment initiation of ABD with high-dose prednisolone, cyclosporine A, methotrexate or cyclophosphamide should

