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Frequency of relapse and persistent cutaneous symptoms after a first episode of chilblain-like lesion during the COVID-19 pandemic

Dear Editor,

Chilblain-like lesions (CLL) have been extensively reported during coronavirus disease-19 (COVID-19) pandemic in March–April 2020.¹ While the link between these lesions and severe acute respiratory coronavirus 2 (SARS-CoV-2) is still unclear,² emerging evidence of ‘long COVID’, with extra-cutaneous COVID-19 symptoms persisting over 60 days, is reported.³ The aim of this study was to assess the evolution of the CLL overtime. We performed a retrospective study to evaluate the frequency and the characteristics of CLL relapses and the persistence of other cutaneous symptoms. In January 2021, a survey was sent to 132 patients who were addressed to the dermatology department of Saint-Louis hospital, Paris between 1 March and 30 April 2020 for CLL lesions. Ninety-five answers were obtained.

Features of the initial CLL episode are presented in Table 1. It involved the feet in 85 cases (89%), with a median severity of 6

and a median duration of 20 days. Fifty-two patients (55%) had at least one relapse, of which 46 (89%) relapsed after 1 October 2020 (Fig. 1a). Among them, 37 (71%) had one new relapse, 12 (23%) had two and 3 (6%) had more than three. Global duration and severity of the relapses were stable (Fig. 1b).

The first CLL relapse appeared after a median remission duration of 7.2 months (IQR 6–8), 11 patients (21%) had a contact with COVID-19-positive patients or suggestive general symptoms and one patient had a positive nasopharyngeal RT-PCR out of 13 (8%). Only eleven patients (21%) changed their lifestyle before the CLL relapse (eight lockdowns, two increased physical activity and one hallux valgus surgery). During the 2nd, 3rd and 4th relapses, respectively, 2/15 (13%), 1/3 and 1/3 patients had suggestive general symptoms, and all the RT-PCRs were negative ($n = 4$).

In January 2021, 27 patients (28%) had persistent extra-cutaneous symptoms (mainly asthenia, joint pain, myalgia, anxiety, concentration disorder, shortening of the breath) and 64 (67%) had persistent cutaneous symptoms other than CLL (acral paraesthesia, acrocyanosis, erythralgia, Raynaud phenomenon, livedo). There was a significant association between persistent COVID-19 extra-cutaneous symptoms and persistent cutaneous symptoms ($P < 0.05$).

Table 1 Demographic and clinical characteristics of patients and COVID-19 documentation during the initial CLL episode in March 2020.

	Total (N = 95)
Demography	
Age (median, IQR)	33 (27–48.8)
Female (n, %)	60 (63%)
Symptoms (n, %)[†]	
CLL feet	85/95 (89%)
CLL hands	20/95 (21%)
Urticarial lesions	8/95 (8%)
Vesicular eruptions	7/95 (7%)
Livedo	18/95 (19%)
Morbiform eruption	9/95 (9%)
Duration (days) (median, IQR)	20 (10–30)
Severity (numeric scale) (median, IQR)	6 (4–7)
Treatment (n, %)[†]	
Topical steroids	13/95 (14%)
Systemic steroids	2/95 (2%)
Colchicine	2/95 (2%)
Others (antihistamines, antibiotics, anticoagulants, topical tacrolimus, ketoprofen)	14/95 (14%)
SARS-CoV-2 documentation (n, %)	
Suggestive general symptoms	23/95 (24%)
Contact with COVID-positive patients	21/95 (22%)
Positive RT-PCR	1/59 (2%)
Positive serological test	4/75 (5%)

[†]Patients can have more than one manifestation or treatment.

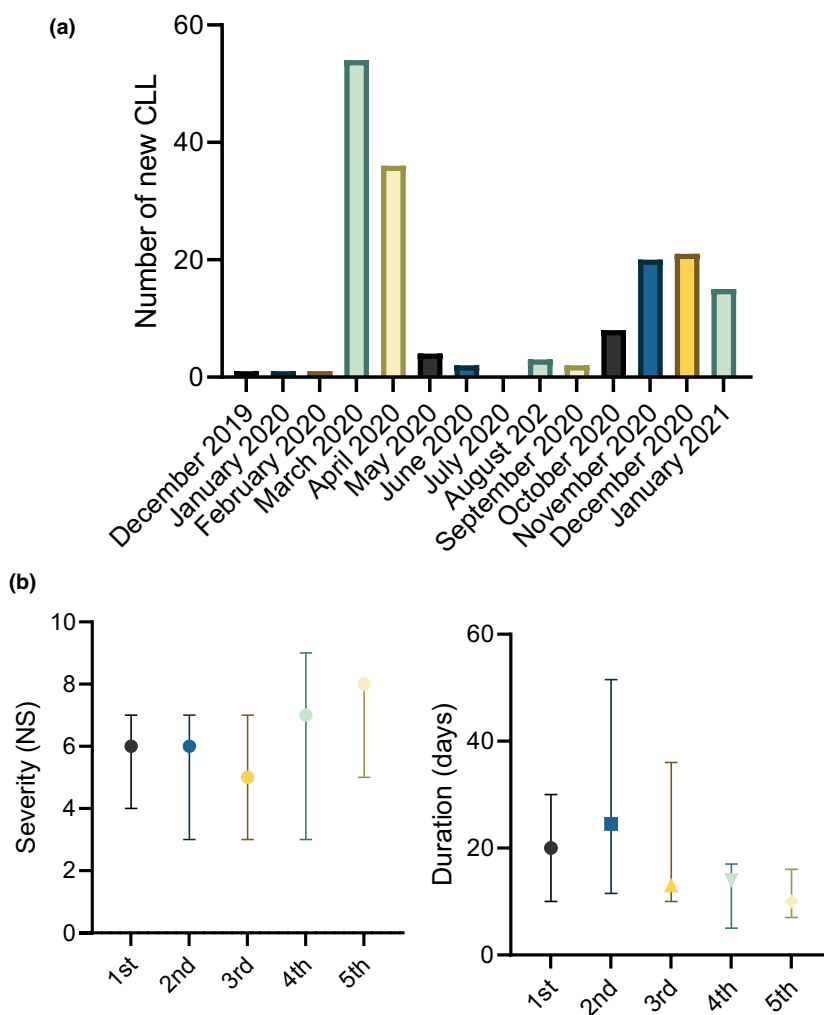


Figure 1 Duration and severity of episodes and number of chilblain-like lesions over 10 months following the initial episode. (a) Graphical representation of number of CLL cases by month. (b) Severity (numeric scale) and duration (days) of CLL episodes, expressed as median and IQR.

The association of CLL outbreak with SARS-CoV-2 is supported by growing evidence.^{4,5} The positivity of RT-PCR and serological tests in our cohort is low and comparable with published data.⁶ This can be explained by an insufficient test material during the initial peak of COVID-19, a different immune response not involving antibodies or a too early serological testing.^{7,8}

First, assuming that our patients were infected by SARS-CoV-2, we demonstrate a high prevalence of disabling persistent extra-cutaneous and cutaneous symptoms, classifying them as 'extra-cutaneous long COVID' in 28% and 'cutaneous long COVID' in 67% of cases.

Then, we illustrate that 55% of patients who experienced CLL during the first COVID-19 wave relapsed during follow-up.

Most patients relapsed during the second wave. We cannot exclude new viral exposure although the majority had neither COVID-19 symptoms nor viral contact. The role of sedentary lifestyle recently discussed is also unlikely as 79% of the patients did not change their lifestyle before the first relapse and the second lockdown in Paris (started on 30 October 2020), was much less limiting than the first lockdown (started on 17 March 2020).⁹ Vascular damages which have been reported during COVID-19¹⁰ may repeatedly flare with external factors such as cold weather, explaining the persistent cutaneous symptoms and the relapses. Our study has some limitations related to its self-reporting and retrospective nature.

Our data emphasize that a majority of patients, who experienced CLL during the first wave of COVID-19 pandemic,

developed relapsing CLL with or without other persistent cutaneous manifestations.

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The study was performed in accordance with the principles outlined in the Declaration of Helsinki and all patients have given their informed consent to participate in this study.

Saint-Louis CORE (COvid REsearch) group (alphabetic order): G Archer, A Benattia, A Bergeron, L Bondeelle, J.D. Bouaziz, D Bouda, D Boutboul, I Berthon, E Bugnet, S Caillat Zucman, S Cassonnet, K Celli Lebras, J Chabert, S Chevre, M Clément, C Davoine, N De Castro, E De Kerviler, C De Margerie-Mellon, C Delaugerre, F Depret, B Denis, L Djaghout, C Dupin, D Farge-Bancel, C Fauvaux, E Feredj, D Feyeux, J.P. Fontaine, V Fremeaux-Bacchi, L Galicier, S Harel, A.L. Jegu, E Kozakiewicz, M Lebel, A Baye, J Le Goff, P Le Guen, E Lengline, G Liegeon, G Lorillon, I Madelaine Chambrin, G Martin de Frémont, M. Meunier, J.M. Molina, F Morin, E Oksenhendler, R Peffault de la Tour, O Peyrony, B Plaud, M Salmona, J Sausseureau and J Soret.

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Conflict of interest

Authors state no conflict of interest involving the work under consideration for publication. Adèle De Masson reports grant support from Recordati Rare Diseases, Kyowa Kirin and Janssen. Hervé Bachelez has paid consulting activities for AbbVie, Ammiral, Biocad, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Kyowa-Kirin, Leo Pharma, Novartis and UCB, Xion; pharmaceuticals and grant support from Boehringer-Ingelheim, Janssen, Leo Pharma, Novartis and Pfizer. Martine Bagot reports scientific advisory boards for Galderma, Helsinn/Recordati, Innate Pharma, Kyowa Kirin and Takeda.

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P. Moghadam,¹ L. Frumholtz,¹ L. Jaume,¹
A. De Masson,^{1,2} M. Jachiet,¹ E. Begon,^{1,3}
L. Sulimovic,^{1,4} A. Petit,¹ H. Bachelez,^{1,5} M. Bagot,^{1,2}
J.-D. Bouaziz,^{1,2} C. Cassius,^{1,2,*}
Saint-Louis CORE (COvid REsearch)[†]

¹Dermatology Department, AP-HP, Saint-Louis Hospital, Paris, France,

²Université de Paris, Human immunology Pathophysiology Immunotherapy, INSERM U976, Institut de Recherche Saint-Louis, Paris, France, ³Dermatology Department, Renée Dubos Hospital, Pontoise, France, ⁴On behalf of the SNDV (syndicat national des dermatologues-vénérologues) /Corona group, Paris, France, ⁵Université de Paris,

Laboratory of Genetics of Skin Diseases, INSERM U1163, Imagine Institute, Paris, France

*Correspondence: C. Cassius. E-mail: charles.cassius@aphp.fr

[†]See Acknowledgements section.

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Dapsone-induced methaemoglobinaemia in leprosy: a close mimic of 'happy hypoxia' in the COVID-19 pandemic

Dear Editor,

A 24-year-old man, native of Bihar, India presented with a numb, ring like reddish patch over the left foot since 14 months (Fig. 1).

Dermatological examination revealed a solitary, well-defined, hypotrichic, hypohidrotic, annular plaque, 7 cm in diameter over the dorsum of the left foot which was hypoaesthetic to pain, touch and temperature. No satellite lesions or nerve to patch was present. Left posterior tibial nerve and superficial peroneal nerve were thickened and non-tender.