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Relapse of chilblain-like lesions during the second wave of the COVID-19 pandemic: a cohort follow-up

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Dear Editor, Chilblain-like lesions have been reported during the COVID-19 pandemic. Studies based on serology and RT-PCR (reverse-transcriptase polymerase chain reaction) exploring the causal link between chilblains and COVID-19 infection have reported conflicting results.[1–3] However, a significant proportion of patients who developed chilblains reported they had contact with suspected cases of COVID-19.[4] Europe has faced a second wave of the pandemic since October 2020. As we had observed in our area, a new outbreak of chilblains was also reported in Italy concomitantly with the second wave.[5] Recently, the first relapses in patients who experienced chilblains during the first wave were reported.[5] The aim of this study was to explore, in our cohort of chilblain-like lesions,[4] the occurrence of relapses and exposure to COVID-19 in households during the second wave.

The 40 patients in the cohort (NCT04344119) were systematically contacted by phone between 5 and 10 February 2021. When needed, a teleconsultation was also performed. Thirty-two of the 40 patients responded to the survey (response rate of 80%). Clinical and virological information relative to the second-wave period since October 2020 were registered on a standardized form. Twenty patients (63%) among the 32 who responded to the survey reported relapses (Table 1). Patients experiencing relapses had similar clinical presentation to the first episode observed during the first wave. No severe complications were reported. Thirteen patients with relapse had undergone COVID-19 RT-PCR since October 2020, along with four in the group without relapse. These tests had been done for several reasons (travel, tests required by their jobs, positive contacts in household or at work). The median delay between the onset of chilblains and the RT-PCR test was 0 days (range −34 to +105, interquartile range 46). Only one patient had a positive RT-PCR. He was in the group who reported chilblain-like lesions. However, the test was performed 63 days before the chilblains occurred. He was asymptomatic and was tested because symptomatic COVID-19 infection was diagnosed in his father and mother.

Table 1 Epidemiological and clinical characteristics of patients and related households in the chilblain-like lesion cohort during the second wave of the COVID-19 pandemic

	Relapse	No relapse	OR for relapse[d]
Patient characteristics			
Number of patients	20 (63)	12 (37)	
Age (years), median (range)	23 (12–67)	22 (12–45)	1·04 (0·98–1·10)
Sex			
Female	10 (50)	6 (50)	–
Male	10 (50)	6 (50)	1·0 (0·24–4·18)
Patients tested for COVID-19 (RT-PCR)	13 (65)	4 (33)	
Patients with criteria for possible COVID-19 infection[a]			
Criteria absent	15	11	–
Criteria present	5	1	3·67 (0·37–36·0)
Positive RT-PCR	1 (5)[c]	0 (0)	
Household characteristics			
Number of households	19	11	
Households with COVID-19 symptoms	6 (32)	0 (0)	NA[e]
Persons in households with criteria for possible COVID-19 infection[a,b]	8	0	
Persons tested for COVID-19 (RT-PCR)	7	0	
Positive RT-PCR	5	NA	

The data are presented as n or n (%) unless stated otherwise. NA, not available; OR, odds ratio; RT-PCR, reverse-transcriptase polymerase chain reaction. [a]Possible COVID-19 infection was defined following the criteria of the European Centre for Disease Prevention and Control. [b]Not including the index patients. [c]8% of tested patients. [d]Univariate logistic regression to model risk of relapse. [e]Model did not converge, results not available.

Among the 19 households with the 20 cases of relapse, a possible COVID-19 infection was reported in six (32%). This was confirmed by PCR in four households (total of five members) of patients with relapsed chilblains. In households where patients had chilblains in the past but did not have relapses, no household members or family members had suspected COVID-19. COVID-19 household infections were reported within 2 months of the relapse of the related chilblains, with 75% occurring within 2 weeks (median 3·5 days, range −9 to +63, interquartile range 0). Simultaneous occurrence of chilblains was observed in one other member of four

households of patients who experienced relapse, suggesting that they were exposed to the same trigger event.

We observed a relatively high frequency of relapses in our chilblain-like cohort. These relapses were contemporary with the second wave of the COVID-19 pandemic in our region. Recent data suggested that recurrent pernio could be linked to exposure to cold temperature.[6] In our area, the mean minimum and maximum temperatures ranged from 12·7 °C and 19·6 °C in October 2020 to 5·3 °C and 14·6 °C in January 2021. We cannot exclude that those relapses were caused by the return of the cold season triggering relapse on a previously altered microcirculation. Recurrent pernio occurs after cold exposure in genetic interferonopathies, supporting a seasonal explanation for the relapses. However, one-third of the patients who had relapses were exposed to possible or proven cases of COVID-19 within the household, and infections in the household were observed in 75% of cases within 2 weeks of the relapse of chilblain-like lesions. Conversely, COVID-19 infection was not reported in any patients or their households in the no-relapse group. Only one patient with relapse had a positive PCR test. Despite proven circulation of the virus in the household, virological confirmation of infection is lacking in most patients.

Chilblain-like lesions associated with the COVID-19 pandemic have been suggested as interferon type I-related skin manifestations due to an efficient antiviral response in those patients.[4,7] Efficient antiviral immune response has been proposed to explain the absence of virological confirmation in children exposed to COVID-19 within households.[8] This probably explains the difficulties in proving a causal link based on a positive RT-PCR and/or serology between chilblain-like lesions and COVID-19.

Taken together, our results suggest an eventual high risk of relapses in patients who have had a previous episode of chilblains in the context of COVID-19 infection. Our data suggest that re-exposure to SARS-CoV-2 infection might trigger a relapse in chilblain-like lesions, although we cannot exclude that an initial insult from SARS-CoV-2, followed by subsequent cold exposure, could trigger these relapses in some cases.

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Kawasaki-like multisystem inflammatory syndrome associated with COVID-19 in an adult: a case report

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Dear Editor, As the COVID-19 pandemic continues to surge, the varied spectrum of clinical presentations keeps growing. The US Centers for Disease Control and Prevention (CDC) has recently described COVID-19-associated multisystem inflammatory syndrome in adults (MIS-A), which presents as an amalgam of Kawasaki disease (KD) and toxic shock syndrome (TSS).[1,2] We report a 22-year-old Indian man with 5 days of fever, headache, myalgia and skin rash, and a one day history of lower-extremity and upper-abdominal pain, and vomiting.

COVID-19 reverse-transcriptase polymerase chain reaction (RT-PCR) at admission was negative. He was febrile (104·6 °F), tachypnoeic (36 breaths per min) and tachycardic (122 beats per min), but was maintaining blood pressure (104/62 mmHg) and SpO_2 (98% room air). Dermatological examination revealed bilateral nonexudative conjunctival injection; hyperpigmented fissured lips; generalized erythema with multiple well-defined, discrete-to-coalescing, hyperpigmented macules involving the face, trunk and all extremities; and oedema of both hands and feet (Figure 1a–c). These findings were suggestive of KD as per the American Heart Association (AHA) criteria, although cervical lymphadenopathy was absent.

Investigations (normal levels in brackets) revealed haemoglobin 9·2 g dL^{-1}; total leucocyte count 11 820 cells μL^{-1} with 81% neutrophils, 10% lymphocytes and 5% eosinophils; bilirubin 1·2 mg dL^{-1}; aspartate transaminase 162 IU L^{-1} (5–40);