Recurrence of chilblains during a second contact with SARS-CoV-2: a case report

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Dear Editor, Chilblains are among the most prevalent skin manifestations of COVID-19. However, the clinical presentation is atypical because most patients do not have a history of long cold exposure or chilblains. These chilblains occur mostly in young adults with no or few COVID-19 symptoms and who are negative for SARS-CoV-2 in reverse-transcription polymerase chain reaction (RT-PCR) and/or serological tests. Indeed, the association between chilblains and COVID-19 has been challenged because of the small proportion of patients with positive RT-PCR and/or serological tests. Community containment and lockdown measures have been suggested as possible explanations. However, it has also been hypothesized that chilblains reflect a strong antiviral response, with upregulation of interferon (IFN)-1. Here, we report on the recurrence of chilblains in a young adult following a second contact with a SARS-CoV-2-positive close relative.

A 20-year-old male patient with an unremarkable medical history (and notably the absence of chilblains or Raynaud symptoms) and no smoking history, whose body mass index was 18 kg m\(^{-2}\), developed painful acral lesions on the toes in April 2020. The only other symptoms of note were a slight cough and rhinitis. Clinical examination showed purple, infiltrated lesions on each toe. Some of the lesions were centred around a vesicle (Figure 1a). The rest of the dermatological examination (notably the hands) was normal. We diagnosed chilblains, even though there had not be a prolonged spell of cold weather in April. The blood cell counts, kidney function and haemostasis assays were normal. No antinuclear or antiphospholipid antibodies were detected.

One of the patient’s close relatives had tested positive (RT-PCR) for SARS-CoV-2, but the patient’s RT-PCR and serological tests were negative. We nevertheless diagnosed chilblains as a result of COVID-19. We initiated symptomatic treatment, and the lesions disappeared after a few weeks. Seven months later (during the second wave of epidemic COVID-19 cases), the patient developed the same lesions at the same sites (i.e. the toes, Figure 1b). Once again, the patient did not have any other symptoms and the clinical examination was completely normal. His blood samples and nasopharyngeal swabs were negative for SARS-CoV-2, although both of his parents had tested positive in a SARS-CoV-2 RT-PCR a few weeks before.

Blood cell count and kidney function were normal and there was no sign of inflammation in the blood tests. The complement parameters C3, C4 and CH50 were normal, and antinuclear antibodies, antineutrophil cytoplasmic antibodies, antiphospholipid antibodies, anti-B2GP1 and anticardiolipin were all negative. No skin biopsy was performed as the skin lesions were located on the tip of the toes, which is a painful location for a skin biopsy. The lesions lasted at least 3 months. Based on the sequence of events, we diagnosed the recurrence of chilblains following contact with a SARS-CoV-2-positive close relative.

In the literature, an electron microscopy study found COVID-19 particles in the cytoplasm of endothelial cells in skin biopsies of patients who had chilblains and whose nasopharyngeal and oropharyngeal swabs were negative in a SARS-CoV-2 PCR test. COVID-19 chilblains might result from the intense production of IFN-1, as seen in interferonopathies like lupus erythematosus. The study of Battesti and Descamps highlighted strong expression of the gene
cording for the IFN-induced Mx protein in skin biopsies from patients with chilblains. The Mx protein sequesters viral factors required for viral replication. Furthermore, an IFN-induced transmembrane protein may inhibit coronavirus replication. This could explain why PCR tests are mostly negative in patients with suspected COVID-19 chilblains. Battesti and Descamps reported that patients with moderately severe COVID-19 had high circulating levels of IFN-1. We hypothesize that in young adults with efficient innate immune responses, the IFN-1 pathway inhibits the replication of SARS-CoV-2 and damps the symptoms of COVID-19. In parallel, activation of the IFN-1 pathway might lead to manifestations that have been already described in interferonopathies like lupus (i.e. chilblains). The inhibition of viral replication might explain the negative RT-PCR and serological test results in the present case.

To conclude, we report on a case of recurrent chilblains, the appearances of which coincided with the epidemic peaks in France and contact with a SARS-CoV-2-positive close relative. Our observation reinforces the hypothesis of a causal relationship between SARS-CoV-2 infection and chilblains. It also raises the question of whether this manifestation is likely to occur or recur during contact with SARS-CoV-2 components (e.g. during a mass vaccination campaign).

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Most rare subtypes of cutaneous lymphoma display variable CD30 expression: analysis of the German Cutaneous Lymphoma Network

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Dear Editor, CD30, also known as tumour necrosis factor receptor 8 (TNF-R 8), was initially called Ki-1 and is a cell-surface molecule that was first described by a group of pathologists from Kiel in 1982. CD30 can be targeted with the drug brentuximab vedotin (BV), which is approved for relapsed or refractory CD30+ cutaneous T-cell lymphoma (CTCL) including primary cutaneous anaplastic large-cell lymphoma and CD30+ mycosis fungoides and Sézary syndrome. Treatment for rare cutaneous lymphoma (CL) subtypes such as primary cutaneous diffuse large B-cell lymphoma (PCDLBCL) may be challenging, and clinical trials in these indications are scarce. Detection of CD30 expression in the rare subtypes could provide the rationale for treatment with targeted therapy.

In the present study, 105 biopsies of 101 patients with rare CL from 10 centres (Berlin-Neukölln, Göttingen, Karlsruhe, Kiel, Krefeld, Ludwigshafen, Mannheim, Minden, Würzburg and Zurich) were collected. All patients were diagnosed with a rare CL and staged according to the current classification of the European Organization for the Research and Treatment of Cancer and International Society for Cutaneous Lymphomas:

(i) 47 CTCLs: 18 CD4+ small/medium-sized lymphoproliferations (SMTCL), nine subcutaneous panniculitis-like T-cell lymphomas (SPTCLs), six peripheral TCLs (not otherwise specified), six CD8+ aggressive epidermotropic cytotoxic TCLs, four γ/δ TCLs, four natural-killer (NK)-TCLs;
(ii) 39 B-cell lymphomas: 38 PCDLBCL leg-type and one Epstein–Barr virus-positive DLBCL;
(iii) 14 blastoid plasmacytoid dendritic cell neoplasms (BPDCN).

In total, 100 rare CL cases were evaluable for CD30 expression study; CD30 stains were performed in one centre and evaluated by six dermatologists/dermatopathologists.

Overall, a third of patients died due to the lymphoma itself, illustrating the aggressiveness of many of the rare skin lymphoma subtypes. In more than two-thirds of the cases, CD30 expression was detectable (71 of 100; 71%) (see Table 1). The expression in most cases was low [< 1–5% (59 of 71; 83.1%)] and limited to the dermal area. None of the cases displayed an epidermal expression of CD30. Only 11-3% (eight of 71) cases revealed an expression of CD30 in more than 10% of the lymphocytic infiltrate. Two of these cases had NK-TCL (10% and 14%). Staining intensity was regarded mainly as weak or moderate (61 of 71; 85.9%). Expression was detected predominantly in the cytoplasm with or without combined membrane and/or Golgi-reactivity (64 of 71; 90.1%). Eight representative cases (two PCDLBCLs, one NK-