

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at

ScienceDirect www.sciencedirect.com Elsevier Masson France



www.em-consulte.com/en

LETTER TO THE EDITOR

Chilblains and COVID19 infection: Causality or coincidence? How to proceed?



KEYWORDS Chilblains; COVID19

At the beginning of April 2020, several cases of chilblainlike lesions limited to toes and fingers have been seen in France. The potential link with a COVID 19 infection was immediately evoked. The information has been broadcasted across media and "social" networks. Very quickly, the message 'chilblains = COVID 19 infection' circulated. Nevertheless, there is no data to affirm that COVID 19 virus is the cause of these chilblain-like lesions even if many details could be in favour of this hypothesis. It is perhaps only a coincidence. These chilblains can also be an indirect consequence of containment with lifestyle changes (patient remaining barefoot at home ...). Many viruses (Human Immunodeficiency Virus (HIV), cytomegalovirus (CMV), human T-cell lymphotropic virus type 1 (HTLV-1), Hepatitis B and C virus, Epstein-Barr-Virus (EBV), parvovirus B19...) are able to induce vasculitis either cutaneous leucocytoclastic vasculitis, either systemic vasculitis [1].

The aim of this article is to give a short synthesis of known data and to propose standardised guidelines to follow in case of apparition of a new acrosyndrome in the context of COVID 19 pandemic.

What do we know?

Currently, nothing is published about acrosyndrome and COVID 19, but some microvascular manifestations linked with COVID 19 have been published like 2 cases of transient livedo reticularis [2].

Since the beginning of the containment, many cases of acral lesions looking like chilblains have been described. The patients were often young and have had sometimes inaugural general symptoms compatible with a viral infection. These cases have been first identified by private dermatologist physicians and then shared via numeric networks and the French Society of Dermatology with the Covidskin survey. Among 114 skin manifestations, this survey has collected 84 cases of chilblain-like lesions at April 16th, 2020 [3]. Eighty per cent of the 84 patients have never had prior acrosyndrome, less than 50% have had general signs of COVID 19 infection 8-15 days before apparition of the chilblainlike lesions [3]. Some cases have been identified in hospital practice but most of cases seemed not to be severe COVID 19 cases. These cutaneous symptoms seem to be absent in hospitalised patients.



Figures 1–3 First episode of sudden painful chilblains of the toes and right hand in a 23-year-old adult, associated unusual muscle pains, no triggering factor.

https://doi.org/10.1016/j.jdmv.2020.05.002 2542-4513/© 2020 Published by Elsevier Masson SAS.



Figure 4 First episode of painful chilblains limited to the toes in a female teenager, no triggering factor.

The symptoms look like classic chilblains with sometimes a very intense associated pain but no atypical features like livedo, cyanosis, ischemia or necrosis (Figs. 1–4). The local treatment with corticosteroids doesn't seem to be efficient.

Until now, among the 18 available results of the 35 nasal PCR COVID 19 in Covidskin survey patients, none was positive [3]. This could be explained by the fact that the patients were seen after the phase of general symptoms. It is also to note that the sensitivity of this PCR test is around 56–83% with possible false negative results [4]. Serological diagnosis, which is not yet available, will be useful retrospectively in these patients.

These patients seem not to have coagulation or rheological abnormality but no tests were systematically performed.

So far, very few biopsies were done. Results of skin biopsies of Covidskin survey have not been published [3].

It is possible that the low temperatures observed about 10 days in France have led to an increase in cases of ''banal'' chilblains, thus disturbing the interpretation of a potential causal link with a viral infection. The containment with lifestyle changes (patient remaining barefoot at home with cold floor, loss of weight associated with an infectious context) could also influence the chilblains epidemiology in this season.

An unproven hypothesis could be that this aspect of chilblains could indicate an early immune reaction in young subjects who do not have severe forms of COVID 19 infection.

It is currently impossible to say if these patients are contagious. Until now, data showed no argument in favour of potential contagiousness (in Covidskin survey, chilblain-like lesions seemed to appear 8-15 days after general symptoms and performed PCR were negative) [3].

What should we tell patients and treating physicians?

At this point, we propose the following course of action:

- in all cases, it seems reasonable to us to exclude causality in patients having a history of chilblains;
- in case of a first attack of chilblains or in case of an unusual attack of chilblains:
 - there is no indication for a PCR test unless there is fever or respiratory symptom of possible COVID 19 infection,
 - it is necessary to reassure patients, and to explain to them that we have no argument in favour of potential contagiousness,
 - if patients have flu-like symptoms, the same care should be performed as for other patients suspected to have COVID 19 infection,
 - to obtain a detailed history of all symptoms (previous event of acrosyndrome, cold or humidity exposition, weight loss, evolution of acrosyndrome, possible other signs and chronology of symptoms),
 - $\circ\;$ to take pictures with patient's agreement,
 - to perform a blood test to search for an inflammatory syndrome (C-Reactiv Protein, fibrinogen, blood protein electrophoresis), signs of dysimmunity (antinuclear antibodies, anti-neutrophil cytoplasmic antibodies) and factors favouring distal vasculopathy (cryoglobulin, C3, C4, CH50, cold agglutinin, anticardiolipin and antiβ2GP1 antibodies, lupus anticoagulant),
 - if possible, to perform even a biopsy of a recent lesion for histology and immunofluorescence in order to precise the type of lesions (inflammation, thrombosis, vasculitis..),
 - to prescribe a local steroid treatment in case of recent lesions;
 - to complete systematically the blood test by a COVID 19 serology when it will be available.

This proposal is probably susceptible to change in the coming days, depending on the evolution of the knowledge. Our proposition is to collect the cases of microcirculation vascular manifestations (livedo or chilblains) suspected to be linked to COVID 19. You could send your documented cases to isabelle.dauriac@sfmv.fr with the mention ''MICROVASC-COVID''.

Disclosure of interest

The authors declare that they have no competing interest.

References

 Pagnoux C, Cohen, Guillevin L. Vasculitides secondary to infections. Clin Exp Rheumatol 2006;24:S71–81.

- [2] Manalo IF, Smith MK, Cheeley J, Jacobs R. A dermatologic manifestation of COVID-19: transient livedo reticularis. J Am Acad Dermatol 2020, http://dx.doi.org/10.1016/j.jaad.2020.04.018, pii: S0190-9622(20)30558-2.
- [3] Martin Agudelo L. https://www.larevuedupraticien.fr/article/ covid-et-pseudo-engelures-possible-mais-pas-forcementcontagieux.
- [4] Kokkinakis I, Selby K, Favrat B, Genton B, Cornuz J. Covid-19 diagnosis: clinical recommendations and performance of nasopharyngeal swab-PCR. Rev Med Suisse 2020;16:699–701.

M.A. Pistorius^{a,*} S. Blaise^b C. Le Hello^c S. Barbarot^d B. Dréno^d, for the French Society for Microcirculation ^b Department of Vascular Medicine, Grenoble University Hospital, University Grenoble Alpes, 38000 Grenoble, France

^c Department of Therapeutic and Vascular Medicine, Saint-Etienne University Hospital, inserm, U1059 Sainbiose, University de Lyon, Saint-Etienne, 42000 Saint-Etienne, France

^d Department of Dermatology, Nantes University Hospital, 44000 Nantes, France

> * Corresponding author. E-mail address: marc.pistorius@chu-nantes.fr (M.A. Pistorius)

> > Available online 11 May 2020