

TOOLKIT GUIDE

Skin lesions in the context of prolonged COVID-19 symptoms

Validated by the HAS Board on 10 November 2021

The sources of the data presented below are i) data collected during the consultation process conducted at Hôtel Dieu, AP-HP, Paris, within the scope of the PERSICOR cohort, ii) patient-reported data from the association Après j20, and iii) based on the data reported in the literature.

Pseudo-chilblains

Clinical presentation

Pseudo-chilblains are predominantly observed on the feet, but can also affect the hands 1,2. They are presented in the form of red or purple inflammatory papules; in some cases, they are annular, bullous, or purpuric. They can be associated with pruritus or with neuropathic impairment (pains, dysaesthesia).

Course of symptoms

Patients presenting with pseudo-chilblains during the different COVID waves may have a single episode, or persistent lesions, with no regression, or recurrent lesions. Depending on the publications, the median time of progression of pseudo-chilblains varies from 12 to 20 days with intervals of up to 70 days.^{3–6}

More than half of patients can experience recurrences, with the duration of episodes seeming to decrease over time. ³

The majority of these patients also have persistent skin symptoms other than pseudo-chilblains (acrocyanosis, erythermalgia, Raynaud's phenomenon, livedo and/or acral paraesthesia, haematoma and petechiae).

Additional investigations

The recommended first-line additional investigations are: FBC and antinuclear antibody testing (titration and specificity).

Treatment

The first-line treatment approach is based on i) implementing measures to prevent cold and moisture and avoiding tight shoes), and ii) applying a very potent topical occlusive corticosteroid treatment based on clobetasol propionate once daily, until symptoms resolve.

When to refer to a dermatologist?

- If symptoms persist despite correctly administered topical treatment
- If symptoms recur

- If associated symptoms included in the systematic screening process are observed (potentially suggesting connective tissue disease: Raynaud's, arthralgia, photosensitivity, mucosal lesions, alopecia, etc.)



Figure 1. Photos of chilblains

Urticaria

Clinical presentation

COVID-related urticaria presents similarly to conventional urticaria: transient, migratory, pruritic, erythematous and oedematous papules. The entire integument may be affected. The palmoplantar site may have an atypical, sometimes deep, presentation.

Course of symptoms

Most urticaria rashes resolve quickly with a median duration varying between 4 and 7 days depending on the publications.

Cases of chronic urticaria (lasting more than 6 weeks) have been described by patients after SARS-CoV-2 infection, but no cases have been reported in the literature. SARS-CoV-2 infection has worsened the symptoms of one-third of patients with chronic urticaria.

Additional investigations

None as first-line approach

Before referring to a specialist, test the following: FBC, SR, CRP, antithyroid peroxidase antibody screening test (and, if result is positive, TSH assay)

Treatment

Treatment is based on the use of antihistamines, 1 to 4 tablets per day if there are no contraindications, as for any case of chronic urticaria (SFD chronic urticaria recommendations).

When to refer to a dermatologist?

- If urticaria episodes persist despite a 4-week treatment with 4 tablets of second-generation anti-H1 antihistamine per day.
- If lesions are fixed or associated symptoms suggesting systemic disease (fever, joint, digestive tract, or eye impairment, and associated skin symptoms) are observed.

Other dermatological symptoms have been described (eczematoid lesions, etc.), but the link with COVID has not been demonstrated.

Eczema

Clinical presentation

The majority of eczematoid lesions described initially appear at the extremities and primarily on the hands. A classic presentation is observed: pruritic, erythematous and ill-defined lesions, which are frequently seeping.

These lesions have been described by patients, but have not been reported in the literature, apart from cases of hand contact eczema.

Course of symptoms

The course of symptoms is highly variable.

Additional investigations

None

Treatment

Treatment is based on:

- Avoidance of aggravating factors and contact (repeated hand washing, application of irritant caustic substances, etc.)
- Use of topical emollients and high-potency dermocorticosteroids.

When to refer to a dermatologist?

- If lesions spread over 10% of body surface
- If lesions persist despite topical corticosteroid treatment

Vascular lesions

Clinical presentation

The vascular symptoms described in prolonged forms of COVID are very diverse. They include: acrocyanosis, Raynaud's phenomenon, livedo (see figures 2, 3 and 4).

A classic clinical presentation is observed: red/purple colouring of the extremities for acrocyanosis, paroxystic acrosyndrome for Raynaud's phenomenon, and net-like erythematous macules or papules for livedo.

The clinical assessment must include screening for associated symptoms: detection of pulse and vascular murmur and Allen's test, screening for trophic disorders of the extremities, screening for signs of associated connective tissue disease, characterisation of livedo to screen for pathological livedo (infiltrated livedo with large open net-like patterns).

Course of symptoms

- Acrocyanosis: this symptom is continuous and not subject to episodes
- Raynaud's phenomenon: episodes triggered by cold and moisture are observed
- Livedo: episodes are more frequently observed, interspersed by phases of partial or complete remission.

Additional investigations

- Isolated acrocyanosis: none
- Raynaud's phenomenon: screening for antinuclear antibodies (titration and specificity, including anti-centromere and anti-Scl70 antibodies). The role of capillaroscopy has not been assessed and may be discussed in a specialist setting.
- Livedo racemosa: FBC, PT, PTT, blood electrolytes, HIV, HCV serology test, and APS screening.

Treatment

- Acrocyanosis: no treatment
- Raynaud's phenomenon: avoid triggering factors, refer if symptoms persist.
- Livedo racemosa: to be decided based on underlying cause.

When to refer to a dermatologist?

- Acrocyanosis: no indication
- Raynaud's phenomenon: in the event of an irregularity in the clinical assessment, symptoms suggestive of connective tissue disease, or an irregularity in the immunological assessment.
- Livedo racemosa: systematically

When to refer to an angiologist?

In the event of atypical vascular symptoms: atypical Raynaud's phenomenon, atypical acrocyanosis, etc.



Figure 2. Physiological livedo



Figure 3. Physiological Covid-19 livedo



Figure 4. Pathological livedo

Also note that, in prolonged forms of COVID, approximately 20% of patients describe hair loss.

Finally, cases of **spontaneous ecchymosis**, sometimes involving pain, have been described. The symptoms affect the limbs or torso with rapid spontaneous resolution. A platelet count and a haemostasis work-up must be conducted

Physiopathological hypotheses

Other than for pseudo-chilblains, there has been little study of the physiopathology of these symptoms. The physiopathology of pseudo-chilblains is reported to associate immune activation of the interferon type I pathway and vascular impairment. The immune activation is primarily local, but also systematic, and the interferon type I response might explain the lack of molecular or virological markers of SARS-CoV-2. Some authors have detected the presence of viral particles in the endothelium. but other teams have refuted this theory.

Bibliographic references

1. Galvan Casas C, Catala A, Carretero Hernandez 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; :bjd.19163.
2. de Masson A, Bouaziz J-D, Sulimovic L, et al. Chilblains are a common cutaneous finding during the COVID-19 pandemic: a retrospective nationwide study from France. *J Am Acad Dermatol* 2020. doi:10.1016/j.jaad.2020.04.161.
3. Moghadam P, Frumholtz L, Jaume L, et al. Frequency of relapse and persistent cutaneous symptoms after a first episode of chilblain-like lesion during the COVID-19 pandemic. *J Eur Acad Dermatology Venereol* 2021; 35:e566–8.
4. Giraud-Kerleroux L, Mongereau M, Cassius C, et al. Detection of a second outbreak of chilblain-like lesions during COVID-19 pandemic through tele dermatology. *J Eur Acad Dermatology Venereol* 2021; 71:2020–2.
5. Mehta P, Bunker CB, Ciurtin C, et al. Chilblain-like acral lesions in long COVID-19: management and implications for understanding microangiopathy. *Lancet Infect Dis* 2021; 21:912.
6. McMahon DE, Gallman AE, Hruza GJ, et al. Long COVID in the skin: a registry analysis of COVID-19 dermatological duration. *Lancet Infect Dis* 2021; 21:313–4.
7. Hedou M, Carsuzaa F, Chary E, et al. Comment on "Cutaneous manifestations in COVID-19: a first perspective" by Recalcati S. *J Eur Acad Dermatol Venereol* 2020; :0–2.
8. van Damme C, Berlingin E, Saussez S, Accaputo O. Acute urticaria with pyrexia as the first manifestations of a COVID-19 infection. *J Eur Acad Dermatology Venereol* 2020; :0–1.
9. Henry D, Ackerman M, Sancelme E, et al. Urticarial eruption in COVID-19 infection. *J Eur Acad Dermatology Venereol* 2020. doi:10.1111/jdv.16472.
10. Tamaro A, Adebajo GAR, Parisella FR, et al. Cutaneous manifestations in COVID-19: the experiences of Barcelona and Rome. *J Eur Acad Dermatol Venereol* 2020; :0–2.
11. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol* 2020; :0–1.
12. Miriam Morey-Olivé, Espiau M, Mercadal-Hally M, et al. Cutaneous manifestations in the current pandemic of coronavirus infection disease (COVID 2019). *An Pediatr* 2020. doi:10.1016/j.jinf.2020.02.020.
13. Molaei H, Allahyari F, Emadi SN, et al. Cutaneous manifestations related to the COVID-19 pandemic: a review article. *Cutan Ocul Toxicol* 2021; 40:168–74.
14. García-Gil MF, Monte Serrano J, Lapeña-Casado A, et al. Livedo reticularis and acrocyanosis as late manifestations of COVID-19 in two cases with familial aggregation. Potential pathogenic role of complement (C4c). *Int J Dermatol* 2020; 59:1549–51.
15. Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. *Nat Med* 2021; 27:601–15.