



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.



Published Online
March 8, 2021

[http://dx.doi.org/10.1016/S1473-3099\(21\)00133-X](http://dx.doi.org/10.1016/S1473-3099(21)00133-X)

Chilblain-like acral lesions in long COVID-19: management and implications for understanding microangiopathy

We read with interest the Comment by Devon E McMahon and colleagues¹ describing the range of cutaneous manifestations of COVID-19. We agree that most acral chilblain-like or pernio-like lesions (commonly referred to as COVID toes) occur in young, previously healthy patients with relatively mild COVID-19 and frequently negative tests for SARS-CoV-2. Most resolve spontaneously without any treatment approximately 2 weeks from onset, particularly in children and adolescent patients. However, in our multidisciplinary post-COVID-19 follow-up clinic of adult patients and specialist tertiary referral centre for paediatric and adolescent rheumatology, we have observed a subgroup of patients with persistent chilblain lesions, similar to McMahon and colleagues' report. Clinically these chilblain-like lesions resemble the digital vasculopathy of connective tissue disease. If the lesions do not resolve within 30 days of onset, we recommend screening for other underlying causes (which might have been triggered by COVID-19) and therapeutic options including aspirin, topical corticosteroids (with oral prednisolone in severe cases), hydroxychloroquine and vasodilators, and prostacyclin analogues (eg, iloprost) if refractory (appendix). Our recommended management framework is based on the UK and British Society for Rheumatology guidelines for the management of Raynaud's phenomenon and digital ischaemia in systemic sclerosis.^{2,3} The optimal management, including treatment duration, of chilblain-like lesions in patients with long COVID is currently unclear and will

probably evolve as clinical experience and data accumulate for this new disease.

As the COVID-19 pandemic continues unabated, attention is now turning to the considerable proportion of patients with multiorgan morbidity, including unexplained symptoms such as dyspnoea and fatigue, that persist well beyond the initial viraemic phase, exerting pressure on already strained health-care resources. Endothelial cell dysfunction, hypercoagulability, and inflammation are considered central to the aetiopathogenesis in acute COVID-19, but there is a growing need to characterise the clinical course of symptoms and disease mechanisms of long COVID to facilitate prognostication and targeted interventions.

Nailfold capillaroscopy enables identification of microcirculatory morphological alterations and is widely used in rheumatological practice. There is emerging evidence to support the utility of nailfold capillaroscopy to detect and quantify endothelial alteration in COVID-19.⁴ Microvascular abnormalities have been observed on nailfold capillaroscopy in both fingers and toes of patients with COVID-19, even when lesions are confined to the toes, suggesting that chilblains might be an overt manifestation of a systemic process.⁵ We propose that nailfold microangiopathy, as assessed by capillaroscopy, might represent a peripheral measure of central pathology. Nailfold capillaroscopy might provide a surrogate, non-invasive digital window to the lung to investigate unexplained dyspnoea.

We call for further research to investigate microangiopathy in long COVID and advocate prospective, longitudinal data capture for patients with persistent chilblain-like lesions in COVID-19, including nailfold capillaroscopy where available, to better understand pathomechanisms

and inform evidence-based guidelines.

PM is an MRC-GSK EMINENT clinical training fellow with project funding outside the submitted work. PM has served on an advisory board for SOBI and receives co-funding by the NIHR University College London Hospitals Biomedical Research Centre (UCLH BRC). RCC reports grants from UKRI MRC, GlaxoSmithKline, and NIHR ULCH BRC, during the conduct of the study. CPD reports grants and personal fees from GlaxoSmithKline, Roche, CSL Behring, and Arxx Therapeutics, and personal fees from Galapagos, Boehringer Ingelheim, Corbus, and Horizon, outside the submitted work. All other authors declare no competing interests.

Puja Mehta, Christopher B Bunker, Coziana Ciurtin, Joanna C Porter, Rachel C Chambers, Charalampia Papadopoulou, Helen Garthwaite, Toby Hillman, Melissa Heightman, Kevin J Howell, Despina Eleftheriou, *Christopher P Denton
c.denton@ucl.ac.uk

Centre for Inflammation and Tissue Repair, University College London (UCL) Respiratory, Division of Medicine, UCL, London, UK (PM, JCP, RCC); Department of Rheumatology (PM), Department of Dermatology (CBB), and Department of Respiratory Medicine (JCP, HG, TH, MH), UCL Hospital, London, UK; UCL Centre for Adolescent Rheumatology, London, UK (CC, DE); Infection, Inflammation and Rheumatology Section, UCL Great Ormond Street Institute of Child Health, and Great Ormond Street Hospital NHS Foundation Trust, London, UK (CP); Microvascular Diagnostics (KJH) and Department of Rheumatology (KJH, CPD), Royal Free Hospital, London NW3 2QG, UK

- 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; published online Jan 15. [https://doi.org/10.1016/S1473-3099\(20\)30986-5](https://doi.org/10.1016/S1473-3099(20)30986-5).
- Denton CP, Hughes M, Gak N, et al. BSR and BHRP guideline for the treatment of systemic sclerosis. *Rheumatology (Oxford)* 2016; **55**: 1906–10.
- Hughes M, Ong VH, Anderson ME, et al. Consensus best practice pathway of the UK Scleroderma Study Group: digital vasculopathy in systemic sclerosis. *Rheumatology (Oxford)* 2015; **54**: 2015–24.
- Natalello G, De Luca G, Gigante L, et al. Nailfold capillaroscopy findings in patients with coronavirus disease 2019: broadening the spectrum of COVID-19 microvascular involvement. *Microvasc Res* 2021; **133**: 104071.
- El Hachem M, Diociaiuti A, Concato C, et al. A clinical, histopathological and laboratory study of 19 consecutive Italian paediatric patients with chilblain-like lesions: lights and shadows on the relationship with COVID-19 infection. *J Eur Acad Dermatol Venereol* 2020; **34**: 2620–29.

See Online for appendix