studies are needed to establish the real risk of severe illness and death due to COVID-19 in leprosy patients.

Acknowledgments

We thank the Health Bureau of Aracaju, Sergipe, for making the databases available.

Conflicts of interest

None.

Funding source

None.

Author contributions

Dr Santos and Dr Martins-Filho had full access to all of the data in the study, take responsibility for the integrity of the data and their accuracy, involved in concept and design, and contributed to drafting of the manuscript. Santos, Martins-Filho and Barboza contributed to acquisition, analysis or interpretation of data. Barboza, Quintans-Júnior and Araújo contributed to administrative, technical or material support. Quintans-Júnior, Araújo and Martins-Filho contributed to critical revision of the manuscript for important intellectual content.

Ethical consideration

This study was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE No. 33095120.4.0000.5546) and following the Helsinki Declaration.

V. S. Santos,[1,*] L. J. Quintans-Júnior,[2] W. S. Barboza,[3] A. A. de S. Araújo,[2] P. R. Martins-Filho[2,4]

[1]Centre for Epidemiology and Public Health, Federal University of Alagoas, Arapiraca, Brazil, [2]Graduate Program in Health Science. Federal University of Sergipe, Aracaju, Brazil, [3]Health Bureau of Aracaju, Aracaju, Brazil, [4]Investigative Pathology Laboratory, Federal University of Sergipe, Aracaju, Brazil

*Correspondence: V. S. Santos. E-mail: santosvictor19@gmail.com

References

1 Zhou F, Yu T, Du R *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–1062.

2 Martins-Filho PR, Tavares CSS, Santos VS. Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data. *Eur J Intern Med* 2020; **76**: 97–99.

3 Secretaria de Vigilância em Saúde – Ministério da Saúde. Boletim Epidemiológico de Hanseníase. Brasília, DF; 2020. Retrieved from https://www.saude.gov.br/images/pdf/2020/May/22/boletim-hanseniase-2020-web.pdf

4 Martins-Filho PR, Santos VS, Quintans Júnior LJ, de Jesus MJM, Araújo AAS. Evolução Dos Óbitos Por COVID-19 No Município de Aracaju, Sergipe. Parte II: 17 a 30 de Junho de 2020. Aracaju, SE; 2020. https://doi.org/10.13140/RG.2.2.18276.40323

5 Tan L, Wang Q, Zhang D *et al.* Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther* 2020; **5**: 33.

6 de Sousa JR, Sotto MN, Simões Quaresma JA. Leprosy as a complex infection: breakdown of the Th1 and Th2 immune paradigm in the immunopathogenesis of the disease. *Front Immunol* 2017; **8**: 1635. https://doi.org/10.3389/fimmu.2017.01635

DOI: 10.1111/jdv.16899

Chilblains and COVID-19: further evidence against a causal association

Editor

Acro-ischaemic lesions have been observed both in adults with severe forms of COVID-19 and in younger patients with no or mild symptoms of COVID-19.[1–3] In severe COVID-19, peripheral cyanotic lesions are secondary to thrombotic vasculopathy and systemic procoagulant state.[4] The pathophysiology of chilblains in asymptomatic or mildly symptomatic patients is widely debated. Reports have suggested a possible link between COVID-19 and chilblains observed during the pandemic; however, only few patients were tested for SARS-CoV-2 by RT-PCR and serologic tests.[1–3,5,6] Conflicting evidence highlights that testing needs to occur in larger numbers and also at different stages of evolution of the disease and that follow-up data are important.[7]

In a recent case series of patients with chilblains, we showed not only that RT-PCRs SARS-CoV-2 in nasopharyngeal swabs was negative but also the absence of anti-SARS-CoV-2-specific IgM and IgG antibodies. These findings suggest that these patients had not been infected with SARS-CoV-2.[8] However, in order to make validated clinical data promptly available, our sample size was small and possibly not representative. We now report update data in an additional 23 patients with these lesions of the toes and/or fingers (Fig. 1), bringing the total series to 54 patients. Of these, 47 patients underwent RT-PCR and 54 serology testing. Although more than half of the patients reported flu-like symptoms a few days before the skin lesions, only one patient had low positive RT-PCR and two others had positive serum anti-SARS-CoV-2 IgG antibodies (12.75 and 135.5 AU/mL), reinforcing our previous conclusion that these lesions are neither an early nor a late sign of COVID-19. Negative RT-PCR could suggest that chilblains are a late manifestation of COVID-19. The negativity of serologic tests in all but two patients reasonably excludes this hypothesis.[9] Moreover, repeat serologic testing 3 weeks after the first (39 patients) ruled out late seroconversion. Like in our first series, other systemic causes of chilblains were excluded in these additional 23 patients. We confirmed that the body mass index (BMI) of the patients included was relatively low (23 patients < 20 kg/m^2). Sedentary lifestyle and prolonged barefoot exposure to cool indoors

Figure 1 Clinical aspect of the chilblains observed, with purplish erythematous macules and vesiculo-bullous lesions located on the toes.

associated with quarantine remain possible explanations for these lesions especially considering that the follow-up of patients confirmed improvement of symptoms when warming measures were adopted and with relaxation of lockdown restrictions. Moreover, this hypothesis, also put forwards by other authors,[10] seems to be further endorsed by the fact that we have observed no new cases of chilblains since the lifting of the containment measures in Belgium and despite new infections, especially among young people, in recent weeks.

In conclusion, these update data give further evidence against a causal relationship between chilblains and COVID-19. Our data illustrate that all clinicians should interpret clinical symptoms observed in the course of the COVID-19 pandemic with caution and that reliable RT-PCR and serological testing are essential to confirm an association with COVID-19.

Acknowledgements

The patients in this manuscript have given written informed consent to publication of their case details.

Conflicts of interest

The authors have no conflict of interest.

Funding source

The authors disclosed no financial association, funding source.

Ethical approval

Approvals of the hospital and faculty institutional review boards were obtained for the study and data collection.

Author contributions

Marie Baeck, Anne Herman and Caroline Peeters realized the literature search, and reviewed and approved the manuscript. Marie Baeck prepared the manuscript. Marie Baeck and Anne Herman decided to submit the manuscript for publication.

M. Baeck*, C. Peeters, A. Herman
Division of Dermatology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain (UCLouvain), Brussels, Belgium
*Correspondence: M. Baeck. E-mail: marie.baeck@uclouvain.be

References

1 Piccolo V, Neri I, Filippeschi C *et al*. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol* 2020; **34**: e291–e293.
2 Recalcati S, Barbagallo T, Frasin LA *et al*. Acral cutaneous lesions in the time of COVID-19. *J Eur Acad Dermatol Venereol* 2020; **34**: e346–e347.
3 Galván Casas C, Català A, Carretero Hernández 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; **183**: 71–77.
4 Zhang Y, Cao W, Xiao M *et al*. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and Acro-ischemia. *Zhonghua Xue Ye Xue Za Zhi* 2020; **41**: E006.
5 Freeman EE, McMahon DE, Lipoff JB *et al*. Pernio-like skin lesions associated with COVID-19: a case series of 318 patients from 8 countries. *J Am Acad Dermatol* 2020; **83**: 486–492.
6 Le Cleach L, Dousset L, Assier H *et al*. Most chilblains observed during the COVID-19 outbreak occur in patients who are negative for COVID-19 on PCR and serology testing. *Br J Dermatol* 2020; **183**: 866–874.
7 Hernandez C, Bruckner AL. Focus on "COVID Toes". *JAMA Dermatol* 2020; **156**: 1003. https://doi.org/10.1001/jamadermatol.2020.2062
8 Herman A, Peeters C, Verroken A *et al*. Evaluation of chilblains as a manifestation of the COVID-19 pandemic. *JAMA Dermatol* 2020; **156**: 998–1003. https://doi.org/10.1001/jamadermatol.2020.2368
9 Long QX, Liu BZ, Deng H-J, Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med* 2020; **26**: 845–848.
10 Neri I, Virdi A, Corsini I *et al*. Major cluster of paediatric 'true' primary chilblains during the COVID-19 pandemic: a consequence of lifestyle changes due to lockdown [published online ahead of print, 2020 Jun 13]. *J Eur Acad Dermatol Venereol* 2020; **34**: 2630–2635.

DOI: 10.1111/jdv.16901

Skin manifestations in COVID-19 provide a clue for disease's pathophysiology understanding

Dear Editor,

The most common symptoms of COVID-19 are fever, malaise, headache, muscle pain, dry cough and pneumonia, which showed the disease as an upper respiratory tract viral infection. The first observation about COVID-19 patients who develop cutaneous manifestations was done by Recalcati.[1] In numerous French,[2] Belgian[3] Spanish[4] and Italian[5] studies, the diversity of inflammatory and vascular skin lesions in COVID-19 was described. In sum,