


## COMMENTARY

# Chilblains in children in the time of COVID-19: New evidence with serology assay

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## 1 | INTRODUCTION

In a previous report in *Pediatric Dermatology*,<sup>1</sup> we described chilblains-like lesions in four pediatric patients. From April 18, 2020, to May 10, 2020, 45 children presented to our Pediatric Dermatology department with similar acral lesions. The clinical appearance ranged from red to violaceous macules and dusky, purpuric plaques on the heels, soles and lateral margin of the feet, often accompanied by painful edema, consistent with chilblains. A personal or familiar history of low-grade fever and systemic symptoms (cough and gastrointestinal disorders) were frequently reported before the cutaneous eruption. These findings were consistent with the features observed in the first patients we described in our original report.<sup>1</sup> All patients tested negative for SARS-CoV-2 with nasopharyngeal swab and aspirate. Respiratory specimens were tested for SARS-CoV-2 infection with a commercial RT-PCR method, Seegene Allplex<sup>TM</sup>2019-nCoV Assay (Seegene). Automated RNA extraction and PCR setup were carried out using Seenege NIMBUS, a liquid-handling workstation. Real-time PCR was run on a CFX96TMDx platform (Bio-Rad Laboratories, Inc.).

The recent introduction of validated serology tests (IgG) allowed us to further explore the correlation between chilblains-like lesions and COVID-19 infection. Eight pediatric patients, including the four we reported in the previous paper, underwent serologic testing for COVID-19. Measurement of anti-SARS-CoV-2 IgG was performed with LIAISON<sup>®</sup> SARS-CoV-2 S1/S2 IgG test kit automated

on LIAISON<sup>®</sup> XL (Diasorin) that detects antibodies anti-Spike 1 and 2 proteins with a sensitivity of 97.4% (95% CI 86.8%-99.5%) and a specificity of 98.5% (95% CI 97.5%-99.2%). Seven patients tested negative and one, previously negative to nasopharyngeal swab and aspirate for SARS-CoV-2, turned out tested positive with a high level of IgG (64.50 AU/mL, normal range < 3.8 AU/mL). Two patients had an elevation of D-dimer and fibrinogen degradation products.<sup>2</sup> To date, it has not been possible to definitively confirm the relationship between chilblains-like lesions and COVID-19 infection because of lack of positive testing in patients with the acral clinical findings. However, considering the number of cases reported worldwide and the timing of the pandemic, we agree with Cordoro et al<sup>3</sup> who suggested that these lesions may represent a response to subclinical infection or a convalescent-phase reaction. We recommend that patients presenting with these cutaneous manifestations should undergo clinical observation and a comprehensive laboratory evaluation, including coagulation panels (D-dimer, fibrinogen, INR, PT and PTT) and viral serology (CMV, parvovirus B19, EBV, and coxsackievirus) to exclude underlying viral infections. Severe acral ischemic lesions associated with procoagulant disorders are described in patients with acute COVID-19 infection. According to the current literature, changes observed are probably due to the inflammatory response to SARS-CoV-2. An evaluation of coagulation panels could be carried out to further support diagnosis and investigate systemic involvement.<sup>4</sup>

In conclusion, given the still uncertain relationship between chilblains-like lesions and COVID-19, we highly recommend testing patients presenting with acral chilblains-like lesions with nasopharyngeal swab-aspirate and serology for SARS-CoV-2 in order to fully investigate the elusive relationship between the clinical presentation and the historic viral infection, COVID-19.

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