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## LETTER

## RESEARCH LETTER

**All that glisters is not COVID: Low prevalence of seroconversion against SARS-CoV-2 in a pediatric cohort of patients with chilblain-like lesions**

*To the Editor:* On January 7, 2020, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was isolated in a patient affected by interstitial pneumonia. As SARS-CoV2 infection has spread worldwide, an increasing number of authors have reported chilblainlike lesions as possible manifestations of SARS-CoV-2 infection.<sup>1,2</sup>

To test this hypothesis, we performed serologic and stool/rectal polymerase chain reaction tests in a cohort of children who developed chilblainlike lesions during the SARS-CoV-2 outbreak in Italy, between March 8 and April 30, 2020.

Enrollment criteria are described in the Supplemental material (available via Mendeley at <https://doi.org/10.17632/wzh2tyb46y.2>).

During the enrollment period, 35 cases of chilblainlike lesions were eligible for the study. Twenty-four patients agreed to serologic testing (68.6%).

All patients were white, mean age was 13 years (range, 6-17 years), and the female to male ratio was 2:1. Twenty-two patients presented with chilblains on the toes (Fig 1) and 2 lesions were located on the heels, 6 patients developed blistering lesions, 83% of lesions lasted more than 14 days, and 8% lasted less than 1 week.

Two patients had known contact with SARS-CoV-2–positive individuals, defined by positive nasal swab result. Seven more patients had close contact with someone who presented symptoms that might be SARS-CoV-2 related such as asthenia, loss of smell (anosmia), cough, and prolonged fever. In 25% of cases, at least 1 parent was a health worker. Further details are available in the Supplemental Results.

Chemiluminescence assay (Liaison SARS-CoV-2 IgG, Diasorin) was performed for all patients; 7 patients were tested with In3diagnostic ERADIKIT COVID19, and the other 17 with EDI Novel Coronavirus COVID-19.

A total of 3 patients (12.5%) tested positive via both enzyme-linked immunosorbent assay and chemiluminescence. In 1 patient (4.1%), enzyme-linked immunosorbent assay test result was positive, whereas chemiluminescence result was negative. None of the 4 patients with positive results presented



**Fig 1.** Typical chilblainlike lesions in a pediatric patient enrolled in the study.

with fever, 50% had cough, and 25% presented with transient diarrhea up to 14 days before skin lesion appearance. All 4 patients had contact with a relative who had confirmed SARS-CoV-2 infection (2 patients) or anosmia (2 patients). Fecal polymerase chain reaction was tested in 4 patients (16.6%), and no result was positive; rectal swab was performed in 17 patients (70.8%) and was positive in 1, which also was positive at both serologic tests.

Finally, patients with chilblainlike lesions were compared with a cohort of 24 SARS-CoV-2–infected children. Table I shows the comparison between the 2 groups. Chilblain patients were significantly older (13 vs 4 year;  $P < .001$ ); fever was present in a limited number of cases (16.7% vs 92%;  $P < .001$ ), and certainty of exposure to SARS-CoV-2 was limited (8% vs 56%;  $P < .001$ ).

According to our data, the hypothesis of a direct etiologic link between SARS-CoV-2 and chilblain is not confirmed by serologic tests; it is difficult to assess whether in the 4 patients with positive serology SARS-CoV-2 was involved in the pathogenesis of chilblainlike lesions. A limit of our study is the absence of tissue biopsies, so our experimental approach could not rule out the presence of virus in patients' lesions that may induce an interferon-I response.<sup>3</sup> As confirmed by other studies,<sup>4</sup> the low

**Table I.** Comparison between pediatric cohorts with chilblainlike lesions and severe acute respiratory syndrome coronavirus 2 infection

Epidemiological characteristics and symptoms	Chilblains	SARS-CoV-2 infection*	P value
No. of patients	24	25	NA
Age, y, (range)	13 (10.5–14)	3.8 (0.95–9)	<.001
Female patient, no. (%)	15 (62.5)	8 (32)	.04
Skin lesions, no. (%)	24 (100)	3 (12)	<.001
Fever, no. (%)	4 (16.7)	23 (92)	<.001
Cough, no. (%)	10 (41.7)	13 (52)	.5
Conjunctivitis, no. (%)	3 (12.5)	0	.1
GI symptoms, no. (%)	5 (20.8)	6 (24)	>.99
Certain exposure to SARS-CoV-2, no. (%)	2 (8.3)	14 (56)	<.001

The differences between groups were analyzed with Mann-Whitney *U* test for continuous data and Fisher's exact test for categorical data. All tests were 2 tailed, and the significance was set at  $P < .05$ .

GI, Gastrointestinal; NA, not available; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

\*Twenty-two patients hospitalized and 3 evaluated in the emergency department at the Regina Margherita Children's Hospital.

prevalence (12.5%) of seropositive patients suggests that other pathologic hypotheses should be considered to explain the recent outbreaks of chilblainlike lesions worldwide.

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