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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 chilblain-like lesions as possible manifestations of SARS-CoV-2 infection.1,2

To test this hypothesis, we performed serologic and stool/rectal polymerase chain reaction tests in a cohort of children who developed chilblain-like 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 chilblain-like 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 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 chilblain-like 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 chilblain-like 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.3 As confirmed by other studies,4 the low...
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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Table I. Comparison between pediatric cohorts with chilblainlike lesions and severe acute respiratory syndrome coronavirus 2 infection

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

The differences between groups were analyzed with Mann-Whitney U test for continuous data and Fisher’s exact test for categoric 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.

REFERENCES


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