Correspondence

COVID-19 and *Mycoplasma pneumoniae*: SARS-CoV-2 false positive or coinfection?

Dear Editor,

Several skin lesions have been associated with COVID-19, some of them classically related to other microbiological agents, making a thorough differential diagnosis essential. The detection of nucleic acid from SARS-CoV-2 is the direct evidence for a COVID-19 diagnosis, but nasopharyngeal swabs may not always reveal the SARS-CoV-2 infection. Using enzyme-linked immunosorbent assay (ELISA) to detect SARS-CoV-2 IgM can identify or screen SARS-CoV-2 infection in suspicious and close-contact populations. False-positive results from a serological test for SARS-CoV-2 have recently been described in patients with middle-high level of rheumatoid factor-IgM.[1] We report two patients who showed skin lesions associated with COVID-19 and false-positive compatible results using ELISA to detect SARS-CoV-2 IgM, who were later confirmed to have acute *Mycoplasma pneumoniae* infection.

The first case is a 48-year-old man with no significant past medical history who came to the emergency department presenting with a 5-day history of widespread urticarial, nonevanescent eruption and fever (Fig. 1). He also had a nonproductive cough and headache. No new drugs were given. A chest radiography was performed, and no radiological signs consistent with pneumonia were found. Treatment with H1-antihistamines and oral corticosteroids (prednisone 0.4 mg/kg/day) was prescribed, observing the resolution of the lesions 2 weeks later. The histopathology of the skin biopsy revealed findings compatible with urticarial vasculitis. Nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 was carried out, which was negative. Laboratory tests revealed IgE 1090 IU/ml without other significant alterations. Serological tests for Epstein-Barr virus, herpes simplex, varicella zoster, cytomegalovirus, parvovirus B19, HIV, and hepatitis B and C were carried out, as well as PCR for enterovirus, which all came back negative. The results of the SARS-CoV-2-specific IgA + IgM and *Mycoplasma pneumoniae* IgM antibody serologies were both positive, without IgG antibodies for SARS-CoV-2. Two weeks later, the serological tests were repeated, and IgM increased levels for *Mycoplasma pneumoniae* were observed (absolute increase in IgM antibody titers: 0.08) with the presence of positive IgG antibodies. However, the levels of SARS-CoV-2-specific IgM antibodies decreased (absolute decrease in IgM antibody titers: 0.43), without IgG seroconversion.

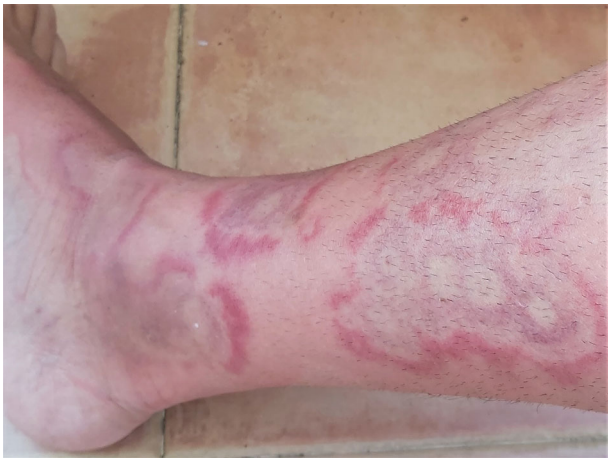

Figure 1 Clinical presentation of urticarial vasculitis in patient 1. Widespread annular, erythematous-purpuric rash on right lower limb

The second case is an 8-year-old boy with no relevant past medical history who presented to a pediatric hospital with 7 days of cough and rhinitis. On examination, he showed nonpalpable purpuric maculopapules on the pretibial region of both legs (Fig. 2). He did not report recent local trauma. His mother was a nurse who remained under home isolation with COVID-19 (positive SARS-CoV-2 RT-PCR) when the skin lesions appeared. Blood tests did not show any alterations. He was negative for SARS-CoV-2 by RT-PCR from nasopharyngeal swab, as was the PCR for other respiratory viruses (Respiratory Syncytial Virus, influenza A and B viruses). A week after, in dermatology consultation, the lesions had disappeared, so skin biopsy was not performed. At this time, the serologies for parvovirus B19, Epstein–Barr virus, cytomegalovirus, and hepatitis B and C were all negative, except for SARS-CoV-2 (IgM + IgA) and *Mycoplasma pneumoniae* (IgM), which were positive. Two weeks later, repeated serological tests showed IgM and IgG positivity for *Mycoplasma pneumoniae* (absolute increase in IgM antibody titers: 0.01) while IgM and IgG for SARS-CoV-2 were both negatives (absolute decrease in IgM antibody titers: 0.2). The patient was reevaluated 1 month later, and neither skin lesions nor respiratory symptoms were found. In both patients, rheumatoid factor levels were within the normal range.

Many cutaneous findings of COVID-19 are nonspecific. Further eruptions have also been observed in patients with *Mycoplasma pneumoniae* infection, such as Fuchs' syndrome, vasculitis (Henoch-Schönlein syndrome, urticarial vasculitis), erythema nodosum, and varicella-like eruptions.[2] The skin lesions we present have been described in patients with

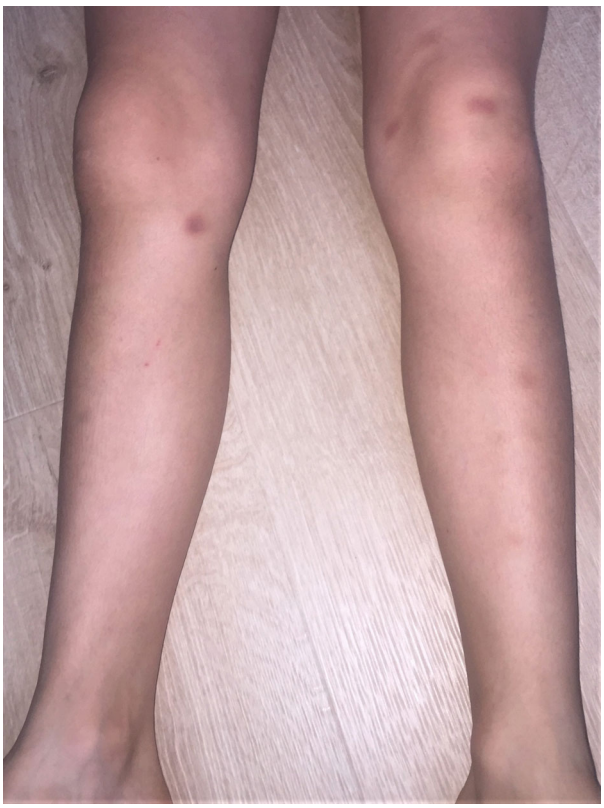

Figure 2 Clinical presentation of purpuric skin lesions in patient 2. Maculopapular purpuric, nonpalpable, nonevanescent rash on lower limbs

COVID-19 and also in patients with *Mycoplasma pneumonie* respiratory infection, making additional microbiological studies necessary for the etiological diagnosis. Generally, with an IgM serological response to microorganism, in the absence of an IgG response that is maintained over time, the results are classified as false positive. However, with SARS-CoV-2 infection, given the abnormal antibody response with low antibody development in nonsevere COVID-19 forms, we cannot affirm that these results are false positives.[3] SARS-CoV-2 coinfection with other common respiratory pathogens such as influenza virus and *Mycoplasma pneumoniae* has been reported.[4,5] Future works with PCR techniques, immunohistochemistry, and electron microscopy will be necessary to detect the viral presence in skin biopsies and to conclude whether the results are false positives or a coinfection.

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

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