

investigate further. First, the analysis did not include patients with similar clinical symptoms, i.e. cough or fever, but were tested negative. Since COVID-19 negative patients, likely with other viral infections, may also have similar skin manifestation as COVID-19 positive patients do, the difference in the prevalence and morphology of skin rash between COVID-19 positive and negative patients warrants comparisons. This would address whether the skin rashes of the three patterns described in the study (erythematous, urticarial and varicelliform) are specific to the COVID-19. Second, it is crucial to measure the viral load in different time points before, during and after the skin rashes in future studies. Viraemia and the skin exanthem may have different time kinetics in different viral infections. For example, viraemia of the measles peaks at the onset of skin rash,⁷ whereas viraemia of the parvovirus B19 ends before the onset of skin rash.⁸ Hence, the dynamic viral load and its reference to skin rash can become a vital clinical clue for the clinicians to determine the optimal timing (before, during or after the skin rash) to collect the samples for molecular identification.

As we have observed the heavy burden of triage and shortage of essential medical goods posed by the outspread of COVID-19, the introduction of an easy clinical assessment tool like classic COVID-19 skin manifestation is a novel path to cope with the challenge that we are facing during the pandemic. However, this will take more studies to build up the validity and reliability. Dermatology's outlook in the COVID-19 is multidimensional, starting from the pathogenesis, public health issues to applying new technologies in clinical practice, the opportunities are infinite. Most importantly, we dermatologists as part of the medical community should contribute our unique perspective in the battle against this formidable pandemic.

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Commentary to S. Recalcati, Cutaneous manifestations in COVID-19: a first perspective. *J. Eur. Acad. Dermatol. Venereol.* 10.1111/jdv.16387 (2020).

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Comment on: Cutaneous manifestations in COVID-19: a first perspective. Safety concerns of clinical images and skin biopsies

Dear Editor

We have read with great interest the article: Cutaneous manifestations in COVID-19: a first perspective by Recalcati S.¹ This article is the first report of the cutaneous manifestations in Coronavirus Disease 2019 (COVID-19) patients during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in Lombardy, Italy. From a total of 88 included patients that were evaluated by dermatologists, 18 developed skin involvement, namely erythematous rash ($n = 14$), widespread urticaria ($n = 3$) and chickenpox-like vesicles ($n = 1$). However, no clinical images are available in the article because of the risk involved in infecting other people.

We would like to report our current experience in the Ramon y Cajal Hospital, Madrid, Spain. As it occurred in Italy, dermatologists are currently involved in the first line due to staff shortages.² Because of the elevated number of COVID-19 inpatients in our hospital, a 'MACRO-COVID' unit was created on March 18, three days after a state of emergency was declared. Every medical and surgical specialty was integrated in this unit to provide assistance in the medical wards, overcrowded with COVID-19 patients.

To evaluate skin alterations in COVID-19 inpatients, we are currently performing a simple and easily reproducible method. Dermatologists and non-dermatologists who are in charge of patients with COVID-19 and skin signs, are using zip lock transparent bags to transport their mobile phones or other photographic devices (Fig. 1). These disposable bags are made of low-density polyethylene, allowing high-quality pictures through their transparent material and permitting glove interaction with current smartphones. After the evaluation, these sealed bags are dipped in a container with a 70% ethanol solution,³ thus being completely disinfected. This is a safe method to avoid unnecessary visits,⁴ attempting to reduce person-to-person spread.

We are also performing biopsies in these patients when indicated. The same plastic bags are used to introduce disposable



Figure 1 Zip lock transparent bags are used to transport photographic devices and biopsy dispensable tools. From left to right: liquid petrolatum jelly, povidone-iodine solution, silver nitrate sticks, surgical blade and 25G subcutaneous needle, local anaesthetic, syringe, 5-mm punch and formaldehyde container.

instruments (Fig. 1), in order to avoid sterilization. After local anaesthesia, we use a 4 or 5-mm biopsy punch to cut the skin. The skin sample is lifted with a 25G subcutaneous needle and then cut with the scalpel blade. A silver nitrate stick is used for haemostasis (optional) and the skin is covered with liquid petroleum jelly. The biopsy recipient is also sterilized in a 70% ethanol solution.

We present an example of an urticariform rash in a 32-years-old woman with COVID-19 (Fig. 2). It appeared 6 days after the onset of symptoms. Hydroxychloroquine and azithromycin had been administered for 4 days. Histologic examination revealed a perivascular infiltrate of lymphocytes, some eosinophils and upper dermal oedema. Oral antihistamines were added to her treatment, with clinical and symptomatic improvement in a 5-days period.

We are currently performing a prospective study to describe the clinical and histological characteristics of cutaneous manifestations in COVID-19. In our preliminary experience, we have also found some cases of unspecific maculopapular rash (some of them with a purpuric component) and urticaria. As stated by Recalcati S,¹ it appears that the SARS-CoV-2 may produce similar skin alterations to other common viruses.

First clinical descriptions of COVID-19 in China are scarce regarding skin involvement. From a 1099 cohort of confirmed COVID-19 patients, only 2 presented 'skin rash' without any further description.⁵ Dermatologists have a unique opportunity to make our contribution during this pandemic and adequately describe skin manifestations of COVID-19. Time is of the essence. Our method is easily replicable, preventing possible transmissions, and providing a correct dermatological evaluation.



Figure 2 Picture of an urticariform rash in a 32-years-old woman inpatient with COVID-19. Evanescent hives were present for 5 days, predominantly on the lower trunk and thighs.

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SARS-CoV-2 infection in a psoriatic patient treated with IL-23 inhibitor

Editor

Since December 2019, an outbreak of 2019 novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading worldwide. This has risen concern among patients undergoing biologics and physicians who administer them, as far as the possible increase of incidence and severity of COVID-19 in this delicate population concerns.¹

We describe the case of a 32-year-old woman, affected by psoriasis and psoriatic arthritis since 18 years, previously treated with several conventional and biologic drugs, including cyclosporine, methotrexate, infliximab, etanercept, adalimumab, secukinumab and ixekizumab. She had no other medical conditions.

In April 2019, she developed a severe Crohn's disease while taking ixekizumab. Therefore, she switched to ustekinumab, with improvement of Crohn's disease but a worsening of both psoriasis and psoriatic arthritis. On 6th November, we added methotrexate 10 mg/week, which was further increased to 25 mg/week after 4 weeks because of an unsatisfactory response. On 23rd December, since psoriasis was still worsening, we switched ustekinumab to guselkumab, while maintaining methotrexate at 25 mg/week.

On February 26, after two injections of guselkumab the patient showed a marked improvement of psoriasis and arthritis.

On February 29, she went out for dinner with some friends and, 2 days later, one of them was discovered to be affected by COVID-19. On March 4, she had mild rhinorrhea and fever (37.4°C), and the next day, she was tested positive for SARS-CoV-2.

The day after the body temperature lowered to 36.3°C, and the rhinorrhea was still mild. We advised her to interrupt methotrexate and to postpone the next guselkumab injection, which was originally scheduled for March 16.

In the following days, the body temperature never rose above 36.5°C and she never developed sore throat, cough, shortness of breath or other symptoms of the infection. Her blood tests revealed increased erythrocyte sedimentation rate (120 mm/h),

C-reactive protein (4.76 mg/dL), D-dimer (381 µg/L) and fibrinogen (701 mg/dL). All the other parameters were normal.

On March 13, the rhinorrhea subsided. On March 20, RT-PCR was still positive for SARS-CoV-2. On March 28 and March 30, the tests resulted negative, meeting the criteria to be considered successfully healed.

In COVID-19, inflammatory cytokines assume a double role: firstly, they stimulate the activation of an effective immune response, while later they can mediate the development of an exaggerated systemic inflammation. This 'cytokine storm' is both ineffective towards the pathogen and detrimental for the body, eventually leading to acute respiratory distress syndrome and potentially to death.²

Available data suggest that the adaptive response towards SARS-CoV-2 develops mainly in a Th1-polarized fashion, being CD8+ cytotoxic cells the main effectors of the antiviral response.² With the progression of the disease, the worsening of clinical conditions is associated to a marked increase in proinflammatory cytokines, such as IL-1, IL-6 and TNF-α.^{2,3}

Interestingly, the IL-23/IL-17 axis does not seem to be pivotal in an effective immune response. On the contrary, observations carried on both coronavirus and non-coronavirus pneumonia patients show that an aberrant Th17 polarization may correlate with a worse outcome.^{4,5}

Based on these observations, a clinical trial investigating the use of ixekizumab associated with antiviral therapy is currently ongoing in China as a possible treatment for COVID-19 infection.⁶

In conclusion, we reported the first case of COVID-19 infection in a psoriatic patient treated with a biologic. The outcome of this case and data from currently available literature suggest that IL-23/IL-17 axis inhibition might not be detrimental in the setting of COVID-19 infection. Further data are needed to support this hypothesis.

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The patient in this manuscript has given written informed consent to publication of her case details.

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