

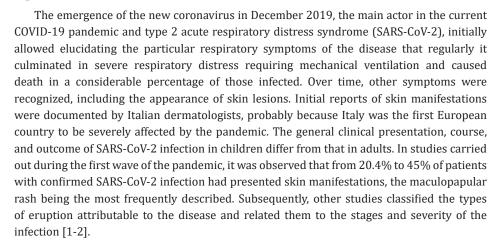


COVID-19 "A Novel Great Imitator" and Its Cause-Effect Relationship on the Skin

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Opinion



In a rather simplified way, cutaneous manifestations have been separated into two forms in terms of pathophysiology: inflammatory, as an immune response to viral nucleotides, and vascular, secondary to phenomena of vasculitis, vasculopathy, and thrombosis. Clinically, the patterns of dermatological manifestations associated with SARS-CoV-2 infection could be classified into four categories: exanthema (varicella-like, papulo-vesicular, and morbilliform eruptions), vascular (chilblain, purpuric/petechial, and livedoid-like lesions), urticarial and acropapular rash, other skin manifestations to be taken into account are skin adverse reactions to drugs prescribed for the treatment of COVID-19. Despite the multiple studies that have reported eruptions related to SARS-CoV-2 infection during the first wave, due to healthcare pressure and insufficient diagnostic tests at that time, few studies adequately documented this relationship. Most only performed PCR or serology on a percentage of the included patients, while others did not refer to the microbiological method used [3].

Regarding the mechanism of lesion production, the risk of an organ developing a SARS-CoV-2 infection is determined by the presence of functional viral receptors ACE2 (angiotensin-converting enzyme 2) and TMPRSS2 (transmembrane protease serine 2). The direct action of the virus on the skin could influence its appearance, different studies have shown that the ACE-2 receptor is present in the endothelial cells of the blood vessels located in the basal layer of the epidermis, as well as in hair follicles, they have not been found in keratinocytes or melanocytes, which means that the virus cannot penetrate and infect the skin directly and mainly. Skin involvement is indirect and is caused by infection of the endothelial cells of the dermal vessels [4].

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Viral activation of mast cells and basophils could account for lesions such as urticaria and rashes. Regarding vascular phenomena, the most studied lesions are of the pernio erythema type, it is believed that the pernio erythema associated with COVID-19 is also the product of an exaggerated immune response with type I interferon signaling, which is transcendental for viral eradication, but with a generalized highly inflammatory reaction. In critical patients with purpura, vascular thrombosis in the skin and other organs would be associated with a minimal interferon response, allowing excessive viral replication, with the release of viral proteins that are located in the extrapulmonary endothelium and trigger extensive complement activation. All of the above has been elucidated by detecting the virus using electron microscopy and PCR techniques in skin biopsies; generalized endothelial infection by SARS-CoV-2 could play a pathogenic role in severe forms of COVID-19. It has recently been suggested that SARS-CoV-2 could induce the reactivation of other latent viruses, such as HHV-6, which is actually responsible for some skin manifestations initially attributed to COVID-19, such as rashes and pityriasis rosea-like eruptions [5].

Establishing the cause-effect relationship between SARS-CoV-2 infection and skin manifestations has been difficult, and few studies have demonstrated immunolabeled SARS-CoV-2 antigens in skin biopsies under immunohistochemistry. The low availability of immunomarkers is another factor that has had a negative influence on establishing this relationship. The works that have studied immunomarkers for SARS-CoV-2 have shown positivity in endothelial cells and epithelial cells of eccrine glands, even coronavirus particles have been found in the cytoplasm of endothelial cells in electron microscopy [6].

The clinical and histopathological characteristics of the cutaneous manifestations by SARS-CoV-2 are similar to other forms of infectious eruptions, therefore this entity can be added to the list of previously known simulating diseases, such as the case of syphilis, due to its wide repertoire of skin manifestations. Cutaneous manifestations are therefore nonspecific and should be carefully evaluated and attributed to COVID-19 only after ruling out other differential diagnoses. In case of generalized urticarial and maculopapular eruptions, the differential diagnosis should be made with other infectious diseases or adverse drug reactions [7].

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