

Inflammation and Vascular Injury as the Basis of COVID-19 Skin Changes: Preliminary Analysis of 23 Patients from the Literature [Letter]

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Dear editor

We read with great interest and excitement the findings published in your journal by Yue Zheng and colleagues attempting to elucidate the pathological nature of SARS-CoV-2-related dermatologic manifestations. The authors speculate on interesting and relevant information related to the pathogenesis of skin manifestations and hypothesize that direct virally mediated destruction does not play a factor in the clinical manifestations seen in this emerging pathology.¹ We believe that it is still too soon to rule out a direct viral pathogenesis for a portion of these skin lesions. Good evidence has emerged at this point in time to support the idea that the SARS-CoV-2 virus is capable of infecting human cells via the interaction between its Spike protein and the ACE2-receptors on human cells.² Outside of the heart, kidneys, lungs, and testes, ACE2-receptors are expressed by vascular endothelial cells in most organs, including those vessels found within the skin.³ It is true that as of yet no evidence exists of viral RNA within sampled skin lesions thought to be caused by SARS-CoV-2 infection, but evidence does exist that the virus is capable of infecting a variety of cells that express ACE2-receptors including the intestines and even those with a well-developed blood-tissue barrier, such as the testes. Limitations in RNA detection or sampling may limit our current ability to detect viral RNA in skin lesions, as evidenced by the initial negative results of studies done on viral RNA in semen samples that were later contradicted with further study.⁴ It is interesting to look at Zheng et al's analysis of skin manifestations that demonstrates such variation in onset, relation of severity, and pathological characteristics. It raises the possibility that some of these clinical lesions may have different pathophysiological backgrounds. We also did not see any uniformity in diagnostic methods for confirming SARS-CoV-2 in the patients of this paper, and that perhaps may lead to us seeing similar features of different etiologies manifested in these patients. As we discuss in our own paper, it is still difficult to differentiate between inflammatory skin manifestations related to medications versus those of viral etiology, as many of the apparent histopathological clues are non-specific, but recent reports of viral spike proteins in vascular endothelial cells and eccrine cells within the dermis does lend credence to the idea that the SARS-CoV-2 virus may play a direct role in the clinical

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manifestations we encounter.⁵ As such, some the vascular features showcased in Zheng et al's patient data may still be in part due to the direct cytotoxic effect of viral infection on endothelial cells within the skin and good statistical analyses as shown in Zheng et al's research may be key to helping categorize this emerging entity of SARS-CoV-2-related skin phenomena.

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