



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Response to: “Reply to ‘Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients’: To consider varicella-like exanthem associated with COVID-19, virus varicella zoster and virus herpes simplex must be ruled out”



To the Editor: We would like to thank Llamas-Velasco et al¹ for their interest in our research letter “Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients.”² They emphasize the need to use *Herpesviridae* family microarray polymerase chain reaction (PCR) on the vesicle fluid of patients with coronavirus disease 2019 (COVID-19) with papulovesicular eruptions to define the etiology of the exanthem by giving the example of 3 patients with laboratory-confirmed COVID-19. PCR demonstrated the presence of herpes simplex virus (HSV) 1, human herpes virus (HHV) 6, and Epstein-Barr virus (EBV) in patient 1, HSV-1 and HHV-7 in patient 2, and varicella-zoster virus (VZV) in patient 3.

We did not use vesicle fluid *Herpesviridae* family microarray PCR for logistical reasons in the case of 15 patients: 6 were in our intensive care unit, 4 in our infectious disease unit, and 5 were in isolation at home and evaluated by means of teledermatology. The remaining 7 patients were outpatients who had undergone a skin biopsy, and PCR was not used because true varicella could be ruled out on the grounds that the vesicles were not umbilicated, were scattered, and were often seen on the surface of papules; there were no pustules; and usually no itching. Furthermore, all of our patients had a previous history of varicella infection, and given the similarity of the lesions to those of varicella, we decided to use the term “varicella-like exanthem.”

Lymphopenia was detected in only 8 patients, who were affected by more severe infection with severe acute respiratory syndrome coronavirus (SARS-CoV-2) and therefore possibly more susceptible to the development of a viral infection other than COVID-19.

In relation to the patients described by Llamas-Velasco et al,¹ patient 1 can be diagnosed as having a classic Kaposi varicelliform eruption, which could be clinically excluded in our patients, and patient 3 can be diagnosed as having varicella with a purpuric component that was possibly due to alterations in the coagulation cascade or anticoagulant treatment administered to prevent COVID-19-related

thromboembolic complications. We would have liked to have been able to see photographs of patient 2 to assess whether there were any similarities to the skin condition of our patients.

The detection of different viruses (HSV-1, HSV-2, HHV-6, HHV-7, VZV, and EBV) in the patients of Llamas-Velasco et al¹ raises the question about whether they had a true viral infection other than COVID-19 or just a superinfection, because it is possible to speculate that the dysfunctional immune response associated with COVID-19 acts both systemically and locally in the skin, thus attracting viral bystanders. This can occur in patients with autoimmune bullous diseases receiving immunosuppressive treatment, as HSV-1 and HSV-2 DNA sequences have been demonstrated by means of blister fluid PCR.^{3,4}

Finally, it is important to point out that neither we nor Llamas-Velasco et al¹ assessed SARS-CoV-2 RNA, whereas SARS-CoV-2 RNA and the DNA of *Herpesviridae* family members should both be sought in COVID-19-associated skin lesions.

Angelo Valerio Marzano, MD, and Giovanni Genovese, MD

From the Dermatology Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda Ospedale Maggiore Policlinico, Milan, and the Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy.

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Angelo Valerio Marzano, MD, Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Pace 9, 20122, Milano, Italy.

E-mail: angelo.marzano@unimi.it

REFERENCES

1. Llamas-Velasco M, Rodríguez-Jiménez P, Chicharro P, De Argila D, Muñoz-Hernández P, Daudén E. Reply to “Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients.” To consider varicella-like exanthem associated with COVID-19, virus varicella zoster and virus herpes simplex must be ruled out. *J Am Acad Dermatol.* 2020;83(3):e253-e254.
2. Marzano AV, Genovese G, Fabbrocini G, et al. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients. *J Am Acad Dermatol.* 2020;83(1):280-285.

3. Marzano AV, Turlaki A, Merlo V, Spinelli D, Venegoni L, Crosti C. Herpes simplex virus infection and pemphigus. *Int J Immunopathol Pharmacol.* 2009;22(3):781-786.
4. Tufano MA, Baroni A, Buommino E, Ruocco E, Lombardi ML, Ruocco V. Detection of herpesvirus DNA in peripheral blood mononuclear cells and skin lesions of patients with

pemphigus by polymerase chain reaction. *Br J Dermatol.* 1999;141(6):1033-1039.

<https://doi.org/10.1016/j.jaad.2020.05.072>