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COVID-19 and HHV8 first spotted together: an affair under electron microscopy

Dear Editor

Despite the publication of articles about dermatopathology of COVID-related skin lesions,¹ only a few among these investigate

patients with SARS-CoV-2 and other viral co-infections showing cutaneous manifestations.

According to the growing attention dedicated by your journal to the topic of novel human coronavirus SARS-Cov-2, we decided to share the rather interesting case of a woman with previous history of Kaposi sarcoma without active skin lesions, who was recently hospitalized for COVID-19 infection. The patient's newly emerging and evident skin manifestation consisted in bluish-red maculopapules (Fig. 1a) that have been biopsied revealed a dermal plaque made of spindle cells arranged in short fascicles lining irregularly shaped vascular slits and vascular structures surrounded by endothelial cells with plum nuclei. The spindle cells displayed mild atypia and rare mitotic figures, and the underlying epidermis was atrophic with a basal hyperpigmentation (Fig. 1b,c). As dermatopathologists, we performed an immunohistochemical analysis to further investigate the histological picture. The analysis results provided that all the spindle cells showed nuclear positivity for HHV8 (Clone 13B1) and cytoplasmatic reactivity for Podoplanin (Clone D2-40) (Fig. 1d, e).

These findings confirm our suspect of Kaposi's sarcoma in plaque phase. Even though we could be satisfied with the diagnosis, we could not ignore the concurrent COVID-19 infection that seemed to correlate with skin rash development, so we decided to perform transmission electron microscope (TEM) analysis and with our surprise we observed not one, but two different viral families:

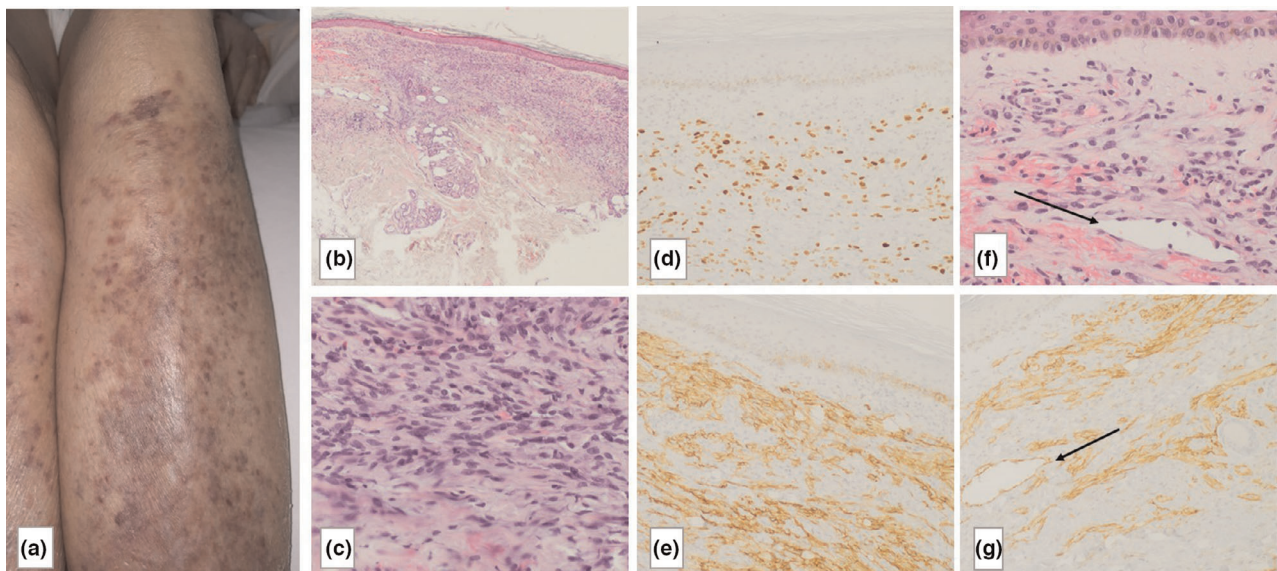


Figure 1 (a) Clinical picture at the admission in the COVID Hub from our patient affected by quiescent Kaposi sarcoma. (b, c) Haematoxylin and eosin staining of a Kaposi sarcoma in plaque stage. Compared with an early patch phase, here the spindle cell proliferation is easy to identify. Immunohistochemical analysis to confirm Kaposi sarcoma: HHV8-specific stain (d) shows nuclear positivity in the spindle cells; the same cellular population is highlighted by Podoplanin (D2–40) showing membrane and cytoplasmatic positivity (e). (f, g) Vascular slit-like spaces in haematoxylin and eosin section and with immunohistochemical stain CD31 that allows to highlight vascular structure.

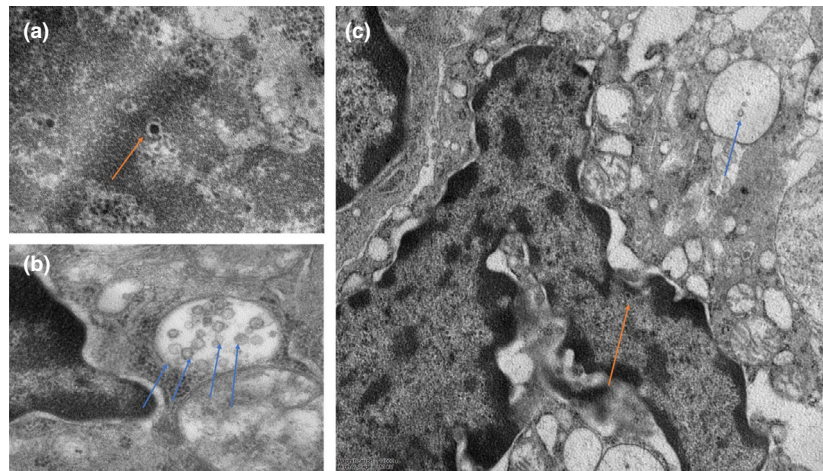


Figure 2 In these pictures, we can observe the HHV8 virus (a, orange arrow) and a macro vesicle containing numerous viral particles with the morphological features of corona virus particles (b, blue arrow). In figure c, instead, we can observe both viruses together.

- Smaller nuclear viral particles (80 nm) consisting of central round black core surrounded by a brighter halo that we interpreted as HHV8 virus (Fig. 2a,c orange arrow).
- Large cytoplasmic vesicles containing spherical particles with crown-like spikes ranging from 80 to 100 nm in diameter that we identify as SARS-CoV-2 (Fig. 2b,c blue arrow).

Considering the well-known influence of the HIV virus on some form of Kaposi sarcoma,² we wonder, if there could be any similar relation between SARS-CoV-2 virus and HHV8. Finding both COVID-19 and HHV8 viruses in a patient's specimen observed under TEM³ led us to speculate the mechanisms of co-infection of these pathogens. It also suggested a significant role of IL-6 in the process, which was already established during the trials using anti-IL-6 drugs in the hyperinflammatory phase of COVID-19 infection.⁴

Moreover, we assume there is an interaction between the SARS-CoV-2 and the Kaposi sarcoma virus, where the first actor contributes to stimulate a hyperinflammatory status leading to proliferation of the HHV8 resulting in recurrence of Kaposi Sarcoma.


Lastly, we suggest the use of TEM to confirm the presence of the virus in skin specimens in laboratory environments, where specific antibodies versus SARS-CoV-2 are not available.

Acknowledgements

The patient has given written informed consent to the publication of her case details.

Conflicts of interest

Dr. E. Leoni, Dr. M. Cerati, Dr. G. Finzi, Dr. M. Lombardo and Dr. F. Sessa have nothing to disclose.

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COVID-19 and immune checkpoint inhibitors

Editor,

SARS-CoV-2 confronts physicians with critical questions, including the use of anticancer therapies in the context of a possible COVID-19 infection. Based on a case report of a patient with metastatic melanoma, the course of a COVID-19 infection