Correspondence

COVID-19, from infection to cancer

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To the Editor,

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is one of the most transmittable viruses worldwide, and the disease caused by this virus, coronavirus disease 2019 (COVID-19) has affected millions of people from 2019 until now (1). Since the COVID-19 pandemic outbreak, the unexpected news about its complications encouraged the researchers to study more about the different aspects of this disease (2). Complications such as cardiovascular (3) and neurological (4) have become more apparent over time after the pandemic onset. Fortunately, there is no specific case of cancer reported in patients after SARS-CoV-2 infection, or at least it was not discovered (5). Based on the former research, infection with viruses can lead to malignancy. Kaposi sarcoma is one of the malignancies caused by the Human Herpesvirus 8 (HHV-8), especially in patients with HIV/AIDS (6). Also, in patients infected with high risk types of HPV, including types 16 and 18, there is an increased risk of cervical cancer (7). Recent studies concerning the changes in tumor marker levels in COVID-19 patients have demonstrated that there is a significant increase in tumor marker levels, including alpha-fetoprotein and carcinoembryonic antigen particularly in severe forms of the disease (8). The epigenetic investigations on microRNAs (miRNAs) expression in COVID-19 patients have elucidated that some miRNAs involving miR-21, as an onco-miR, are upregulated in critically ill patients (9). It is also shown that COVID-19 can enforce the factors involved in cancer cell reactivation, including neutrophil extracellular traps (NETs). NETs are enrolled in inflammatory pathways which can therefore lead to the elevation of cell migration, metastasis, and invasion. Proto-oncogene protein p21 (RAS) is an oncogene protein which is dysregulated in COVID-19 patients. RAS increases the expression of TGF-β and proinflammatory cytokines which leads to pulmonary neoplasms (10). An *in silico* study implys that, Angiotensin-converting enzyme 2 (ACE2) is associated with infiltration in immune cells, and acts as a prognostic factor for uterine corpus endometrial carcinoma (UCEC) and kidney renal papillary cell carcinoma (KIRP). The expression of ACE2 was substantially enhanced in UCEC and KIRP. Increased ACE2 expression is associated with immune infiltration and poor prognoses in UCEC and KIRP. Additionally, tumor tissues in COVID-19 patients with UCEC and KIRP were more vulnerable to SARS-CoV-2 infection. Finally, it was demonstrated that malignant cells infected with SARS-CoV-2 may experience a reduction in ACE2, and decreased ACE2 levels may result in decreased immune infiltration in the tumor microenvironment, potentially compromising the prognosis of COVID-19 patients with UCEC

and KIRP (. According to these data, there might be a probable link between COVID-19, inflammation, and immune mediated cancer cell re-activation. The correlation between COVID-19 and cancer is still not clear, but if proved in the future, it might require special implications for patient management. As a result, it could be concluded that neoplastic changes in COVID-19 patients, specially in seriously ill patients, should be considered along with other complications. It is recommended that the clinicians notice the tumor and inflammatory biomarker changes in the patient follow-up schedule, and in case of any suspicious changes in these factors, refer them to the oncologists for further investigations.

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