Letter to Editor

A Potential Role of Cytomegalovirus Reactivation in the Severity of COVID-19 in the Elderly

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Dear Editor-in-chief

In late 2019, severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was reported in Wuhan, China. This virus spread quickly worldwide, with millions of victims until now. The clinical manifestations of the novel coronavirus disease (COVID-19) are a broad spectrum, from asymptomatic and mild cases with a flu-like syndrome to severe cases requiring intensive care[1].

The severity of diseases and risk of mortality is higher in the elderly, which most authorities attribute to underlying conditions, including diabetes, hypertension, cardiovascular diseases, and respiratory diseases. However, some neglected factors, such as cytomegalovirus (CMV) reactivation, can affect patient outcomes[2].

As the age increases, the seroprevalence of CMV increases. Most adults have a latent CMV (70-90%), which may reactivate following an inflammation[1]. Besides, a previous study on critically ill patients with COVID-19 has shown that CMV infection is associated with a higher mortality rate. Also, bacterial and fungal infections were more common among COVID-19 patients with CMV infection[3]. So an issue needs to be clarified. What is the pathogenesis explaining the potential role of CMV reactivation in the severity of COVID-19 in the elderly?

CMV plays a pivotal role in immunosenescence, a gradual process of the immune system becoming ineffectual. Prolonged exposure of the immune system to CMV overproduces CMV-specific memory T cells in exchange for a decrease in naive T cells. Decreased naive T cell repository reduces the immune system's capacity to combat novel pathogens such as SARS-CoV-2. Thus, the cellular immune response against SARS-CoV-2 is impaired, and a cytokine storm occurs instead. Some proinflammatory cytokines (IL-6 and TNF-α) are elevated in the serum of COVID-19 patients, which directly trigger CMV reactivation[2,4].

COVID-19 itself leads to the impairment of cell-mediated immunity[5]. Also, systemic corticosteroid, a typical therapy among hospitalized COVID-19 patients, cause dysregulation of the inflammatory response, followed by opportunistic infections[6]. As a result, the patient becomes more susceptible to CMV reactivation and subsequent exacerbation of the cytokine storm. Inflammation caused by SARS-CoV-2 and CMV acts as a vicious cycle deteriorating patient' symptoms. Furthermore, CMV may lead to thrombotic events, which contribute to severe complications of COVID-19 (myocardial infarction, stroke, and deep vein thrombosis). The above pathogenesis probably explains why the mortality rate was higher in COVID-19 patients with CMV reactivation[2,4].

Physicians should be aware of CMV reactivation in COVID-19 patients, which is one of the factors affecting patient outcomes. So in suspected cases, early

diagnosis and initiation of antiviral drugs (mainly Ganciclovir) may reduce the inflammatory response, improve the prognosis of the disease, and reduce mortality.

Keywords: COVID-19, Cytomegalovirus, Opportunistic infections, Prognosis, SARS-CoV-2

References

1. Söderberg-Nauclér C. Does reactivation of cytomegalovirus contribute to severe COVID-19 disease? *Immunity & ageing : I & A.* Mar 12 2021;18(1):12.
2. Kadambari S, Klenerman P, Pollard AJ. Why the elderly appear to be more severely affected by COVID-19: The potential role of immunosenescence and CMV. *Reviews in medical virology.* Sep 2020;30(5):e2144.
3. Niitsu T, Shiroyama T, Hirata H, et al. Cytomegalovirus infection in critically ill patients with COVID-19. *The Journal of infection.* Oct 2021;83(4):496-522.
4. Müller L, Di Benedetto S. How Immunosenescence and Inflammaging May Contribute to Hyperinflammatory Syndrome in COVID-19. *International journal of molecular sciences.* Nov 21 2021;22(22).
5. Vigón L, García-Pérez J, Rodríguez-Mora S, et al. Impaired Antibody-Dependent Cellular Cytotoxicity in a Spanish Cohort of Patients With COVID-19 Admitted to the ICU. *Frontiers in immunology.* 2021;12:742631.
6. Yamamoto Y, Shiroyama T, Hirata H, et al. Prolonged corticosteroid therapy and cytomegalovirus infection in patients with severe COVID-19. *Journal of medical virology.* Oct 28 2021.