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LETTER TO THE EDITOR

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Reducing immunosuppressant use in patients with chronic inflammation during the COVID-19 pandemic: Risks versus benefits

Dear Editor,

The pandemic of coronavirus disease 2019 (COVID-19), a novel and potentially severe infection, has raised important questions: Should we try to reduce immunosuppressant doses during the pandemic?

The international rheumatology community (IRC) has influential databases of global research. One particularly important such database is that of the COVID-19 Global Rheumatology Alliance (C19-GRA) (http://rheum-covid.org/). This database shows that for the 1146 patients with rheumatic diseases complicated by COVID-19, the hospitalization rate was 41.97% and the mortality rate was 8.38% as of June 23, 2020. The hospitalization rate is surprisingly high, but the mortality rate does not seem to differ significantly from the COVID-19 mortality rates for all patients worldwide (mortality rates in the top three countries for patients registered in IRC database: UK 14.3%, Italy 14.1%, and Spain 11.9%).[1]

Given that rheumatic disease is frequently complicated with chronic lung disease, diabetes mellitus, or hypertension, or with coronary artery disease, this mortality rate is surprisingly low. The great gap between the hospitalization and the mortality rate might arise from the effects of immunosuppressants, including their side effects. Immunosuppressant use weakens resistance to viral invasion, resulting in high rates of infection and prolonged systemic infection, but their use might also suppress immune hyper-reactions such as acute respiratory disease syndrome (ARDS), which is well known as a cause of mortality for this novel viral infection.[2]

So, what might happen when patients with untreated chronic autoinflammatory conditions become infected with COVID-19? Unfortunately, no reports have directly addressed this question, but one interesting report notes that three out of five patients with common variable immune deficiencies (CVIDs) and COVID-19 were critically ill from the COVID-19 infection, whereas the other two patients, (X-linked agammaglobulinemia [XLA] and autosomal recessive agammaglobulinemia [ARA]), showed only mild COVID-19 symptoms.[3] Unlike XLA and ARA patients, CVID patients show autoimmune manifestations, which are among the most common noninfectious complications (20.3%–33.2%) of CVIDs.[4] This may suggest that untreated autoinflammatory conditions which are not, themselves, life-threatening could lead to serious results in patients infected with COVID-19. There is also the possibility that organ-specific untreated chronic inflammation could be a crucial factor for mortality in COVID-19 infection. Cancer produces chronic inflammation in the cancer microenvironment by inducing antitumor immune reactions. There is a report that cancer existence is an independent mortality risk factor in COVID-19 infection and that cancer poses a higher risk than diabetes or hypertension.[5] Another report in New York found that as many as 28% (61/218) of cancer patients died from COVID-19. This study found that active chemotherapy and radiation therapy were not associated with increased case fatality. Mortality rates seem to be high in hematologic malignancies (37%) and lung cancer (55%).[6] In light of this study, what seems important for mortality from this viral infection is not the immunosuppressed condition but chronic organ inflammation.

The use of immunosuppressants may cause COVID-19 to become more severe or to persist for longer, yet their use seems to have the beneficial effect of mitigating the ARDS-like hyper-inflammatory condition.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Journal of Cutaneous Immunology and Allergy —WILEY— 121

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