

LETTER

Treatment of pemphigus patients in the COVID-19 era: A specific focus on rituximab

Dear Editor,

The coronavirus disease 2019 (COVID-19) outbreak poses a remarkable challenge for pemphigus treatment. High-dose corticosteroids and rituximab are recommended as first-line treatments for moderate-to-severe pemphigus. High-dose corticosteroids impair both cell-mediated and humoral immunity and may increase the complications of COVID-19. There is paucity of evidence on the impact of corticosteroids on COVID-19 course. Meanwhile, there are controversial reports about either negative or positive effect of corticosteroids on COVID-19.¹⁻³

During COVID-19 pandemic, the safety of rituximab is unclear. To reach a hypothesis, focus on the role of B cells and antibodies in the pathogenesis of COVID-19 can be helpful. Lymphopenia has been frequently reported in patients with severe COVID-19.⁴ In contrast to T cell, B cell count was not found to be a prognostic factor for the clinical outcome in COVID-19.⁴ Moreover, in a multicenter cohort study in multiple sclerosis (MS) patients, usage of disease-modifying therapies, such as rituximab, was associated with a lower risk of severe COVID-19.⁵ A retrospective study on 712 MS patients found that suspected COVID-19 cases experienced mild to moderate disease course, although using B cell depleting treatment increased the susceptibility to contracting the infection.⁶ Also, patients with agammaglobulinemia infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a mild and short course of COVID-19.⁷ Focusing on antibodies, several studies showed that high titers of anti-SARS-CoV-2 antibodies or higher numbers of antibody-secreting cells were associated with disease severity.⁸ These findings suggest that antiviral antibodies may not necessarily be needed for a successful immune response against SARS-CoV-2. On the other hand, antiviral antibodies could facilitate the entry of the virus into the phagocytic cells; a phenomenon called antibody-dependent enhancement (ADE). Although ADE has not been proved in COVID-19, it may lead to cytokine storm and COVID-19 worsening.⁹ In sum, these results suggest that B cells may not necessarily be required for the recovery of COVID-19 patients; however, most likely, they can effectively protect patients against SARS-CoV-2 reinfection.

For new and relapsing pemphigus cases, who are not infected with SARS-CoV-2, avoiding high-dose corticosteroids is recommended. At the same time, it seems that low-dose corticosteroids appear to be relatively safe.¹ Intravenous immunoglobulin (IVIg) is a safe option in severe pemphigus cases, although it is costly and mostly not available. According to a previous recommendation for rituximab, it could be better to postpone rituximab treatment due to the critical

role of B cells in the late-phase immune response against viral infections.¹⁰ On the basis of the few aforementioned reports on the possibly nonessential role of B cells and antibodies in the recovery from COVID-19, rituximab may still be considered for the management of moderate-to-severe pemphigus during the COVID-19 pandemic.

In COVID-19 patients with active pemphigus, a minimal increase in the predniso(lo)ne dose concomitant with the use of IVIg may be an efficient strategy. Although the use of high-dose systemic corticosteroids in COVID-19 patients¹⁰ was discouraged in the first few months of the pandemics, there is strong evidence that intravenous dexamethasone decreased the mortality in severe COVID-19 patients.¹ IVIg also appears to be a rational option for COVID-19 patients. Notably, in pemphigus patients infected with SARS-CoV-2, rituximab is recommended to be delayed until recovery from COVID-19.

To conclude, for the treatment of severe pemphigus patients during COVID-19 outbreak, although there is still a lack of strong evidence, we suggest that rituximab could still be considered as a treatment option for moderate-to-severe cases. More studies are required to gain a better insight into how B cell depletion may affect the response to SARS-CoV-2 in pemphigus patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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