SARS-CoV-2 Infection in Pemphigus Vulgaris Two Weeks after Rituximab Therapy with Total Recovery: A Case Report

Dear Editor,

The mortality risk factors for Corona Virus Disease-19 (COVID-19) infection (caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)) include advanced age, male sex, certain comorbidities, and immunosuppression (1).

Pemphigus vulgaris is a rare mucocutaneous autoimmune disease with autoantibodies against desmosomal desmoglein-1 and desmoglein-3, resulting in acantholysis and blister formation. This epithelial barrier defect increases susceptibility to infections, which may lead to relapses (2). Additionally, therapy-associated immunosuppression can lead to severe infections. Corticosteroids are the mainstay therapy. For moderate and severe pemphigus, rituximab is recommended in first-line treatment along with other immunosuppressants, and it may also be added in refractory cases. It is a monoclonal antibody against CD20 with long-lasting B-cell depletion potency. Recovery of B-cell function may last from one to seven years. Consequently, patients receiving rituximab cannot produce enough COVID-19 specific plasma cells, leading to a severe course of COVID-19 (2). Shashidi-Dadras et al. reported five mild COVID-19 cases among 167 patients with pemphigus who had received rituximab one to five years earlier. The authors presumed rituximab use within five years increases COVID-19 susceptibility regardless the number of courses received (3). Among 48 patients with pemphigus treated with rituximab within five years, Uzuncakmak et al. reported one mild case of COVID-19 (in a patient who had received a single course seven months earlier) (4). In another study, high titers of SARS-CoV-2 antibodies and high counts of antibody-secreting cells were associated with severe COVID-19 (5), which may be the consequence of antibody-dependent enhancement (6). Mahmoudi et al. concluded that B-cells may not be necessary for recovery in COVID-19, but they may protect from reinfection (7). Considering these data, rituximab should be postponed during the pandemic (8). In exceptional cases, it may be applied with careful consideration of the risk-benefit ratio (2,4). Patients should be monitored for signs of COVID-19 before and during treatment.

A 63-year-old woman with pemphigus vulgaris presented at our department with widespread skin lesions. Comorbidities included hypertension, hypothyroidism, and glaucoma. Diagnosis was established based on histology and direct and indirect immunofluorescent microscopy results. Both desmoglein-1 and desmoglein-3 autoantibodies were detectable by ELISA. The patient was initially treated with low-dose systemic methylprednisolone (8 mg/day), because glaucoma contraindicated a higher dose. Azathioprine was subsequently started (gradually increased from 0.6 to 2.5 mg/kg/day). Continuous mucocutaneous progression 4 weeks later led to the decision to add rituximab therapy. The patient was confirmed as SARS-CoV-2 negative and received 1000 mg 12 weeks after starting glucocorticoid treatment. Two weeks later, she developed fever and became SARS-CoV-2 positive, and therefore the second rituximab treatment had to be cancelled. The patient had fever for six weeks without any other complaints, hospitalization was not required, and immunosuppression was continued with 8 mg methylprednisolone and 2.5 mg/kg azathioprine. Two weeks after recovery, she was diagnosed with pulmonary embolism, but recovered completely. Pulmonary embolism is a relatively common complication of COVID-19 which may be triggered by inactivity, loss of body fluids due to fever, a hypercoagulable state, and direct toxic venous endothelial damage caused by the virus (9). At a follow-up 4 months later, minimal skin lesions and significantly decreased desmoglein-1 and desmoglein-3 titers were observed. Azathioprine and methylprednisolone therapy were continued, and a second dosage of rituximab was given 7 months from the first one without any side-effects.

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We conclude that rituximab is a highly effective therapy in pemphigus, but the risk-benefit ratio should be carefully considered during the COVID-19 pandemic. We have not observed irreversible or permanent consequences of its administration, but our patient had a potentially lethal complication, pulmonary embolism, which may be associated with a more severe COVID-19 course due to immunosuppression. Total recovery was observed despite COVID-19 shortly after the initiation of rituximab.

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