

Correspondence on 'Second COVID-19 infection in a patient with granulomatosis with polyangiitis on rituximab'

We read with great interest the recent article by Fiedman and Winthrop reporting a patient with granulomatosis with polyangiitis (GPA) being treated with rituximab (RTX), recurrent SARS-CoV-2 disease 2019 (COVID-19) and no detectable SARS-CoV-2 seroresponse after recovery.¹ Anti-CD20 therapy impairs humoral response, theoretically increasing the risk of prolonged SARS-CoV-2 infection and shedding as well as subsequent reinfection.¹⁻³ We have recently reported a patient with GPA under maintenance therapy with RTX and SARS-CoV-2 infection.⁴ Here, we report further details on anti-CD20 therapy with RTX, serological response to SARS-CoV-2 infection, virus elimination and corresponding B cell numbers. This case highlights that B cell numbers in patients with rheumatic diseases treated with RTX could associate with serological response to SARS-CoV-2 infection, which is particularly relevant as RTX may also impair the immunogenicity of SARS-CoV-2 vaccines.

An 80-year-old man had received a diagnosis of GPA in 2014 with biopsy-confirmed renal vasculitis and no history of pulmonary manifestation. After remission induction therapy, he received RTX at a dose of 500 mg every 6 months as maintenance therapy. The last infusion was in March 2019 with persistent B cell depletion: 0% CD19⁺ B cells in September 2019, 0,13% CD19⁺ B cells in December 2019, 2,7% CD19⁺ B cells in February 2020 (normal range 6%–19%). In March 2020, the patient presented to the emergency department with a 2-week history of productive cough and his oxygenation was 85% on room air (figure 1A). An initial nasopharyngeal swab was negative for SARS-CoV-2 RNA but positive for influenza A RNA. Because of worsening respiratory failure, the patient required mechanical ventilation. A tracheal aspirate was tested positive for SARS-CoV-2 RNA. Subsequently, the patient expired due to multiorgan failure. Serological response to SARS-CoV-2 infection was confirmed

at day 29 after admission revealing serum levels of 2.16 for IgA and 8.21 for IgG (reference ratios <0.8, EUROIMMUN, Lübeck, Germany), associated with tracheal aspirate tested negative for SARS-CoV-2 RNA (figure 1A). Urinary measurements of SARS-CoV-2 nucleocapsid protein (SARS-CoV-2 N, KIT40588, Sino Biological, Beijing, China) confirmed systemic viral infection with decreasing levels during course of disease (figure 1B).⁵ Serological response to confirmed SARS-CoV-2 infection and attenuated systemic viral spread correlated with B cell reconstitution (17.73% CD19⁺ B cells, figure 1C). These observations indicate that B cell numbers in patients with rheumatic diseases treated with RTX could associate with SARS-CoV-2 serological response and virus elimination.

To our knowledge, this is the first report of a relationship between B cell numbers, SARS-CoV-2 serological response and virus elimination in a patient with GPA on anti-CD20 therapy with RTX. It remains unclear why initial nasopharyngeal swabs for SARS-CoV-2 RNA were negative in our case, possibly attributed to the patient's immunocompromised state. However, COVID-19 was confirmed in the tracheal aspirate. Anti-CD20 therapies prevent the formation of protective antibodies, leading to an increased risk of prolonged SARS-CoV-2 infection or even reinfection.¹² This has implications for SARS-CoV-2 vaccination, which may not be effective in RTX-treated patients. Therefore, clinicians using RTX may consider delaying RTX application or testing for reconstitution of B cells to allow for vaccination, although both may not always be feasible.⁶ Finally, further studies are necessary to determine the exact effect of anti-CD20 therapy on SARS-CoV-2 vaccines and whether delayed dosing improves vaccine immunogenicity. Our observation that seroresponse to SARS-CoV-2 infection correlated with the reconstitution of B cells is of importance and implicates that assessment of B cell numbers in patients with rheumatic diseases treated with RTX could further improve the timing of SARS-CoV-2 vaccination. This underscores the need for further studies to investigate the effects of specific rheumatic diseases and anti-CD20 therapy on the efficacy and durability of the antibody response to SARS-CoV-2.

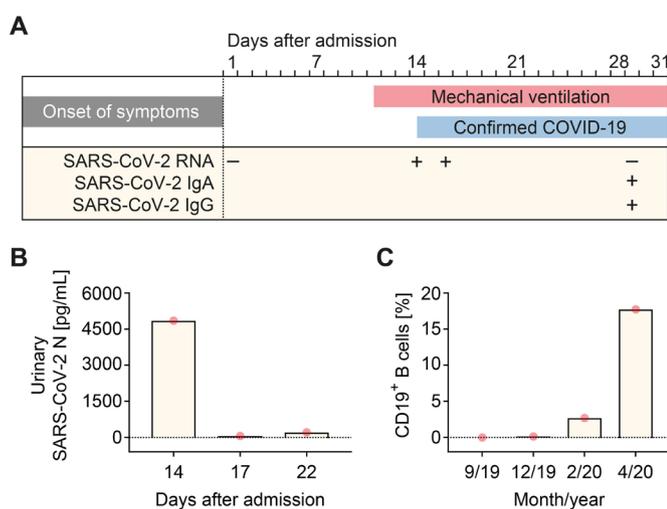


Figure 1 (A) Timeline of COVID-19 clinical course, SARS-CoV-2 RNA testing and serological response. (B) ELISA measurements of urinary SARS-CoV-2 N during disease course of COVID-19 (measurements were done in triplicates, mean values are shown). (C) Timeline of corresponding B cell numbers (normal range: 6%–19%) in September 2019, December 2019, February 2020 and April 2020 (day 25 after admission). SARS-CoV-2 N, SARS-CoV-2 nucleocapsid protein.

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