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

INTRODUCTION
Observational data suggest there may be an association between rituximab and severe COVID-19 outcomes.1–3 Anti-CD20 therapies impair humoral response, theoretically increasing the risk of prolonged SARS-CoV-2 infection and shedding, as well as subsequent reinfection. Here, we report a patient with granulomatosis with polyangiitis (GPA) being treated with rituximab who appears to have developed recurrent SARS-CoV-2 infections in the setting of high-risk employment and on recovery ultimately had no detectable SARS-CoV-2 IgG antibodies. This case highlights a potential risk of rituximab in patients with rheumatic disease, which will become especially relevant as rituximab may impair the immunogenicity of SARS-CoV-2 vaccines.

CASE
A woman in her 30s with a history of limited GPA on rituximab developed COVID-19 twice (figure 1). GPA manifestations have included erosive sinusitis, otitis, saddle nose deformity and orbital pseudotumour. She started rituximab in February 2019. The most recent dose of rituximab 1000mg was given on 28 September 2020. On 14 August, a disease flare was treated with a 3-week prednisone taper, which completed approximately 4 weeks before COVID-19 infection. She works in an assisted living facility with ongoing staff and resident COVID-19 cases.

On 6 October, she developed pharyngitis, myalgia, fatigue, anosmia, dysgeusia and a mild cough. She was afebrile and her oxygenation was 99% on room air. A rapid SARS-CoV-2 antigen immunoassay on 8 October was positive. Over the next 2 weeks, she fully recovered except for residual fatigue. After a 2-week quarantine, she returned to work.

On 17 November, she developed severe cough, deep lung pain, fever of 40.5°C and shortness of breath. Respiratory symptoms were significantly more severe than her initial infection. On 22 November, a rapid SARS-CoV-2 test (Abbott ID NOW) was negative. A chest X-ray showed bilateral groundglass opacities. Symptoms progressively worsened, and on 27 November a rapid SARS-CoV-2 test (BioFire FilmArray) was positive. Her oxygen saturation was 94% on room air. She was treated with a single infusion of bamlanivimab ( monoclonal antibody targeting SARS-CoV-2). Over the next several weeks, her symptoms gradually improved. COVID-19 IgG levels checked on 6 January 2021 (>1 month after bamlanivimab) were negative.

DISCUSSION
Her near-complete recovery after her initial infection, time course, ongoing high-risk employment, negative rapid test at the beginning of her second symptom onset and the ultimate lack of COVID-19 IgG led us to suspect that these were two separate infections, in which she developed insufficient immune response due to rituximab. However, it is also possible this represented a single prolonged infection with a period of asymptomatic disease. To our knowledge, only one case has previously reported a rituximab-treated patient developing a second SARS-CoV-2 infection; that patient also received cytarabine and dasatinib for acute lymphoblastic leukaemia, and the authors suspected reactivation.

Limitations in our report include the lack of sequencing data (samples had been discarded) and the reliance on rapid SARS-CoV-2 testing. However, rapid tests are typically highly specific.1 GPA flare was considered as a cause of her illness; however, the positive SARS-CoV-2 tests and improvement without immunosuppression argue against this. Corticosteroids are a known risk factor for severe COVID-19; however, she had not taken prednisone in the approximately 4 weeks preceding initial infection. It is not known whether bamlanivimab impacts SARS-CoV-2 IgG development.

Anti-CD20 therapies prevent the formation of protective antibodies, leading to increased risk of reinfection or reactivation with SARS-CoV-2. This has implications for SARS-CoV-2 vaccination, which may not be as effective in rituximab-treated patients. Clinicians using rituximab may consider delaying rituximab to allow for vaccination,7 although in life-threatening diseases this is not always possible. Finally, further studies are necessary to determine the exact effect of anti-CD20 therapies on SARS-CoV-2 vaccines and whether delayed dosing improves vaccine immunogenicity.

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