SARS-CoV-2 antibody response after COVID-19 in patients with rheumatic disease

The impacts of rheumatic disease and immunosuppression on the development of antibodies to SARS-CoV-2 are unknown. A study of healthcare workers showed that detectable SARS-CoV-2 antibodies were associated with reduced risk of SARS-CoV-2 reinfection, and the robustness of this neutralisation antibody response has implications for seroprevalence studies and vaccine efficacy. While disease-modifying antirheumatic drugs (DMARDs) generally blunt the immune response to pathogens, immunosuppressive medications such as dexamethasone and baricitinib have efficacy in reducing the severity of COVID-19. Additionally, tumour necrosis factor inhibition has been proposed as a potential mechanism for enhancing germinal centre formation and antibody production in severe COVID-19. Understanding the SARS-CoV-2 antibody response after COVID-19 among rheumatic disease patients is therefore of particular interest.

We examined the SARS-CoV-2 antibody response among patients with rheumatic diseases and past COVID-19 at the Mass General Brigham (MGB) health system in Boston, Massachusetts, USA. Patients with COVID-19 confirmed by positive PCR testing and rheumatic disease confirmed by electronic health record (EHR) review were identified as previously described. We extracted clinically obtained SARS-CoV-2 antibody results and other relevant variables from the EHR. This study was considered exempt by the MGB Institutional Review Board.

Out of 188 patients with PCR-confirmed COVID-19 and rheumatic disease, 13 patients had subsequent SARS-CoV-2 antibody testing (table 1). Of these, 2 had undetectable antibodies, 1 had variable results and 10 had positive antibodies. Of the two patients with negative antibodies, one patient had psoriatic arthritis treated with lefunomide and prednisone and had an uncomplicated COVID-19 course. The other patient had antineutrophil cytoplasmic antibody-associated vasculitis on rituximab, azathioprine and prednisone. This patient had negative SARS-CoV-2 antibodies between 28 and 216 days after COVID-19 and had a complicated course requiring intensive care admission. One patient with antiphospholipid syndrome on prednisone, cyclophosphamide, rituximab and eculizumab had initial positive antibodies 28 to 87 days after COVID-19. However, he had a negative antibody response by

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<th>Table 1 SARS-CoV-2 antibody test results in rheumatic disease patients with COVID-19 confirmed by PCR</th>
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*Measured with the Roche Elecsys assay, which reports the positivity of total SARS-CoV-2 antibody (IgM and IgG) and has 99.5% sensitivity at 14 days after COVID-19 infection.
†T=time zero, defined as the date of the first positive COVID-19 PCR test.
‡Measured with the Viracor Eurofins assay, which reports IgM and IgG antibody positivity to SARS-CoV-2. The sensitivity of the assay is unknown.
ANCA, antineutrophil cytoplasmic antibody; ICU, intensive care unit; PCR, polymerase chain reaction; T, time zero; TTP, thrombotic thrombocytopenic purpura.
107 days despite persistently positive PCR testing, phylogenetic analysis suggestive of persistent infection and viral evolution, and clinical concern for recurrent COVID-19, and he died from respiratory failure, as reported elsewhere.5

The remaining 10 patients had detectable SARS-CoV-2 antibodies despite the presence of rheumatic diseases and/or the use of immunosuppressive medications, including prednisone, methotrexate, azathioprine, etanercept, rituximab and belimumab. The median time between SARS-CoV-2 PCR and antibody testing was 91 days (IQR: 60–146 days). Of these 10 patients, 8 patients had full recovery, 1 patient had persistent fatigue, and 1 patient with systemic lupus erythematosus (without prior haematologic involvement) had a complicated course with recurrent episodes of thrombotic thrombocytopenic purpura.

This case series of rheumatic disease patients with PCR-confirmed COVID-19 and clinically obtained SARS-CoV-2 antibody testing indicates that the majority of patients (10, 77%) developed detectable SARS-CoV-2 antibodies, which is reassuring. Three patients had negative or variable SARS-CoV-2 antibodies, and two of these patients had severe COVID-19. Three patients were on rituximab; two patients on rituximab for many years had undetectable circulating CD19+ B cells and undetectable or variable SARS-CoV-2 antibodies, while one patient who had recently started rituximab (flow cytometry not available) had detectable SARS-CoV-2 antibodies. As tests were obtained as part of routine clinical care at a tertiary care centre, generalisability may be limited, antibody titers and tests for neutralising antibodies are not available, and the timing of antibody testing relative to SARS-CoV-2 infection is variable. Further studies are needed to investigate the effects of specific rheumatic diseases and DMARDs on the efficacy and durability of the antibody response to SARS-CoV-2.

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