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LETTERS

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Factors influencing severe COVID-19 in systemic vasculitis patients: comment on the article by Rutherford et al

To the Editor:

We read with great interest the article by Dr. Rutherford and colleagues on the risk factors for severe COVID-19 in patients with systemic vasculitis (1). This has been the first report to describe the features of COVID-19 among a vasculitis-specific cohort. We would like to address several points of interest.

First, 9% of patients with COVID-19 in this study had a negative SARS–CoV-2 polymerase chain reaction test result. Viral (including influenza) (2,3) and bacterial (4) coinfections and various opportunistic superinfections (5) have been reported in the literature. Were these cases investigated for other causes of respiratory infections?

Second, vasculitis disease activity was determined using the physician's global assessment of disease activity. Given that the majority (85%) of the COVID-19 cases were among patients with antineutrophil cytoplasmic antibody–associated vasculitis, validated scoring systems such as the Birmingham Vasculitis Activity Score (6) and its modification for granulomatosis with polyangiitis (7) could have been used to denote the level of disease activity.

Finally, no further information regarding the patients who died was provided in the report. For instance, given that the rate of active disease was high among these patients, did any of them die due to the complications of active vasculitis (rather than COVID-19)?

Author disclosures are available at https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fart.42022&file=art42022-sup-0001-Disclosureform.pdf.

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Reply

To the Editor:

We are grateful to Drs. Kardaş and Küçük for the interest shown in our article and for their comments. We are happy to supply additional information to address the questions posed.

First, we would like to provide clarification on the comment "9% of patients with COVID-19 in this study had a negative SARS–CoV-2 polymerase chain reaction result." Of the patients in our study population, 9% (6 of 65 patients) were reported as having clinical or radiologic evidence supporting the diagnosis of COVID-19, but information regarding whether a polymerase chain reaction (PCR) test was undertaken for these patients was not available to us except in the case of 1 patient who did have a negative test result at the time of case report form submission. However, the reporting physicians were confident in the diagnosis based on relevant features identified by clinical examination and computed tomography scan.

Regarding whether cases were investigated for other causes of respiratory infections, reporting physicians were asked about the presence of concomitant respiratory tract infection. In the 28% of patients (18 of 65) who did not have a definite PCR-confirmed diagnosis, no other specific respiratory pathogens were reported. Of those patients, 4 of 18 had secondary, presumed bacterial pneumonia. However, data in this section of the case report form were missing for approximately one-half of the patient population.

The Birmingham Vasculitis Activity Score (BVAS) instrument (1) was available for the reporting physician to complete, but it was an optional component of the case report form due to the

clinical pressures of the pandemic. Of the 65 patients included in the cohort, BVAS data were provided for 28 (43%), but this was not included in the analysis as the proportion of missing data was deemed too high.

Of the patients who died, 11 of 18 were deemed to be in remission by the treating clinician at the time of COVID-19 diagnosis, 5 of 18 had moderate disease activity, and 2 of 18 had minimal disease activity. The cause of death in all patients was deemed likely, or highly likely, to be attributable to COVID-19. Clinical information was incomplete for 1 patient; this patient's death was presumed to be attributable to COVID-19, and there was no mention of active vasculitis at any point in the case report form. In 1 other patient, active vasculitis was considered to be the possible cause of death, but on balance, COVID-19 was deemed the more likely cause.

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Rapid attenuation of anti–SARS–CoV-2 antibodies in patients with musculoskeletal diseases in whom intensive immunosuppressive therapies were reinitiated after COVID-19: comment on the article by Curtis et al

To the Editor:

We read with great interest the recently published, updated guidance from the American College of Rheumatology on COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases (RMDs) (1). Because the expected response to vaccination was deemed likely to be blunted in many RMD patients receiving treatment with certain systemic immunomodulatory therapies (2–4), interrupting or otherwise optimizing the timing of some immunomodulatory therapies was recommended. However, the impairment of long-term immunologic memory of SARS–CoV-2 (5) remains a concern in RMD patients requiring continuous immunomodulatory therapies after infection.

We recently assessed the longitudinal antibody response in patients with RMDs who experienced natural SARS–CoV-2 infection, and we report the results herein. Patients were infected with SARS–CoV-2 during a COVID-19 outbreak in the Daini Osaka Police Hospital in Japan. A post–COVID-19 monthly follow-up serosurvey was conducted using an anti–SARS–CoV-2 spike S1 protein and nucleocapsid protein immunoassay (Elecsys; Roche) 2–11 months postinfection in 10 patients with RMDs (Table 1). The patients were receiving intensive immunomodulatory therapies prior to SARS–CoV-2 infection, and immunosuppressive therapy was reinitiated after recovery from the infection. The severity of COVID-19 was determined based on the World Health Organization Clinical Progression Scale (6). All patients exhibited a sufficient antibody response to SARS–CoV-2 at 2–3 months postinfection. The initial antibody response to the spike S1 protein was maintained until 9–11 months in most patients. Antibody retention in these patients was comparable to that reported in healthy individuals in previous studies (7,8).

However, the initial favorable spike S1 protein antibody titer decreased in 2 patients in whom intensive immunosuppressive therapies were reinitiated after COVID-19 (Table 1). One of the patients resumed cyclosporin A (CSA) therapy (Supplementary Figure 1A, available on the *Arthritis & Rheumatology* website at https://onlinelibrary.wiley.com/doi/10.1002/art.42003), and the other patient, who had thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly (TAFRO; a variant of multicentric Castleman's disease [8]), resumed weekly treatment with subcutaneous tocilizumab with CSA (Supplementary Figure 1B). Intensive immunosuppressive therapy, such as treatment with CSA, may alter immunologic memory that contributes to long-term protective immunity. Conversely, the spike S1 protein antibody response remained stable in a patient in whom intensive immunosuppressive therapy was suspended after COVID-19 infection (Supplementary Figure 1C).

This report presents the findings from a longitudinal serosurvey of natural SARS–CoV-2 infection in patients with RMDs who were receiving immunomodulatory therapies. In all patients, treatment with immunomodulatory therapy was withheld during infection and resumed after the patients recovered. At 9 months after infection with SARS–CoV-2, the serum retained <40% of the neutralizing antibodies arising from infection among those patients who continued to receive aggressive immunosuppressive therapy following the onset of COVID-19. The shorter-duration immunity conferred by natural SARS–CoV-2 infection in patients with RMDs receiving immunomodulatory therapies suggests that the estimated duration of vaccine-induced protection against COVID-19 might be shorter in these patients than in the general population, potentially necessitating reimmunization. A third dose of a COVID-19 vaccine is being considered for solid organ transplant recipients who are receiving immunosuppressive therapy (9,10). Further large-scale studies are warranted to confirm the influence of immunomodulatory therapies on the maintenance of immunity against COVID-19.