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 neutralising 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 Massachusetts 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 leflunomide 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 unit 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

### Table 1 SARS-CoV-2 antibody test results in rheumatic disease patients with COVID-19 confirmed by PCR

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Sex</th>
<th>Rheumatic disease diagnosis</th>
<th>Rheumatic disease treatment</th>
<th>Timing of SARS-CoV-2 antibody test results relative to first positive COVID-19 PCR</th>
<th>SARS-CoV-2 antibody test results</th>
<th>COVID-19 complications</th>
<th>COVID-19 pharmacologic treatment</th>
<th>COVID-19 clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>Female</td>
<td>Psoriatic arthritis</td>
<td>Leflunomide 10mg daily, prednisone 10mg daily</td>
<td>T+177 days</td>
<td>Negative total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>62</td>
<td>Female</td>
<td>ANCA-associated vasculitis</td>
<td>Rituximab 1g (started T−6 years, most recent dose T−149 days), azathioprine 100mg daily, prednisone 7.5mg daily</td>
<td>T+28 days†</td>
<td>Negative IgG, negative IgM Negative total antibody* Negative total antibody*</td>
<td>Hospitalisation with ICU admission Respiratory failure requiring oxygen therapy by high flow nasal cannula</td>
<td>Hydroxychloroquine, Remdesivir</td>
<td>Persistent cough (T+238 days) Oxygen requirement resolved by hospital discharge</td>
</tr>
<tr>
<td>45</td>
<td>Male</td>
<td>Antiphospholipid syndrome</td>
<td>Prednisone 15mg daily, cyclophosphamide 250mg daily, rituximab 1g (started T−5 years, most recent dose T−11 days), eculizumab 900mg (started and most recent dose T−9 days)</td>
<td>T+28 days†</td>
<td>Positive IgM, negative IgG‡ Positive IgM, positive IgG§ Positive IgM, positive IgG§ Negative total antibody*</td>
<td>Hospitalisation with ICU admission Respiratory failure requiring mechanical ventilation; circulatory shock</td>
<td>Remdesivir, SARS-CoV-2 antibody cocktail (regeneron) (T+145 days)</td>
<td>Death (T+154 days)</td>
</tr>
<tr>
<td>26</td>
<td>Female</td>
<td>Systemic lupus erythematosus</td>
<td>None</td>
<td>T+1 hour</td>
<td>Positive total antibody* Positive total antibody*</td>
<td>Hospitalisation with ICU admission TTP requiring plasma exchange and glucocorticoids</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>71</td>
<td>Female</td>
<td>Rheumatoid arthritis</td>
<td>None</td>
<td>T+58 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>73</td>
<td>Male</td>
<td>Psoriatic arthritis</td>
<td>Etanercept 50mg weekly</td>
<td>T+60 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>54</td>
<td>Female</td>
<td>Systemic lupus erythematosus</td>
<td>Rituximab 720mg (started T−86 days, most recent dose T−2 days)</td>
<td>T+60 days</td>
<td>IgG positive, IgM not performed†</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>63</td>
<td>Female</td>
<td>Systemic lupus erythematosus</td>
<td>Azathioprine 100mg daily, belimumab 720mg monthly (started T−336 days, most recent dose T−20 days)</td>
<td>T+88 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>55</td>
<td>Female</td>
<td>Sarcoidosis</td>
<td>None</td>
<td>T+93 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>52</td>
<td>Female</td>
<td>Rheumatoid arthritis</td>
<td>None</td>
<td>T+94 days T+210 days</td>
<td>Positive total antibody* Positive total antibody*</td>
<td>Hospitalisation without ICU admission Supplemental oxygen by nasal cannula</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>68</td>
<td>Female</td>
<td>Polymyalgia</td>
<td>Prednisone 6mg daily, methotrexate 25mg weekly</td>
<td>T+129 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>51</td>
<td>Female</td>
<td>Neurosarcoïdosis</td>
<td>Methotrexate 15mg weekly</td>
<td>T+155 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Fully recovered</td>
</tr>
<tr>
<td>72</td>
<td>Female</td>
<td>Psoriatic arthritis</td>
<td>Methotrexate 25mg weekly</td>
<td>T+203 days</td>
<td>Positive total antibody*</td>
<td>None</td>
<td>None</td>
<td>Prolonged fatigue (T+262 days)</td>
</tr>
</tbody>
</table>

*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.
‡T=time zero, reported by Viracor.-Eurofins assay.
§T=time zero, reported by Remedia assay.
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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