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COVID-19 Reinfection in a Patient Receiving Immunosuppression for ANCA-associated Vasculitis

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Conflicts:

There are no conflicts of interest

Dear Editor,

A 61-year-old South Asian woman presented in early April 2020, during the first peak of the COVID-19 pandemic, with acute onset dry cough, dyspnea, fever, and myalgia. Initial laboratory tests were suggestive of COVID-19 (neutrophil:lymphocyte ratio 10.3, platelets 517x10^9/L, CRP 236mg/L, D-dimer 5794µg/L, ferritin 528µg/L, troponin 881ng/L), and infection was confirmed by SARS-CoV-2 PCR testing of a nasopharyngeal swab. She received supportive care for COVID-19 and had gradual resolution of fever and myalgia over the following 14 days.

During this period, she developed progressive kidney dysfunction with urinary abnormalities (serum creatinine rising to 210µmol/L [2.38mg/dL]; urinary protein:creatinine ratio [uPCR] 132mg/mmol), prompting immunological testing. This revealed PR3-ANCA at a titre of 141iu/ml (normal <3). Further assessment elicited a history of ENT symptoms (nasal discharge, hearing loss) and weight loss over the preceding six months. Cross-sectional imaging identified erosive sinusitis and bilateral pulmonary nodules. Kidney biopsy revealed a severe pauci-immune necrotizing glomerulonephritis, compatible with a diagnosis of granulomatosis with polyangiitis (GPA) that likely predated her acute presentation with COVID-19.

Twenty-three days after the initial positive test, repeat PCR testing for SARS-CoV-2 was negative on three occasions, and seroconversion was confirmed by detection of IgM and IgG antibodies to the viral S-protein. Consequently, she received treatment for GPA with rituximab (2g total dose over two weeks), pulsed intravenous cyclophosphamide (750mg total dose over two weeks) and oral glucocorticoids (commencing at 30mg per day). She responded rapidly, with improvements in symptoms, inflammatory markers (CRP 5mg/L), renal function (creatinine 110µmol/L [1.14mg/dL], uPCR <50mg/mmol), and negative ANCA testing by July 2020. Serial PCR tests for SARS-CoV-2 during this period were negative, but antibodies to viral proteins were not detectable. She received maintenance therapy with prednisolone 5mg daily, with a plan for rituximab re-dosing at six months.

She re-presented following contact with a family member with proven COVID-19 in October 2020 with fever, myalgia, dyspnea, and new pulmonary infiltrates. At this time, SARS-CoV-2 PCR testing was positive on two occasions (three viral targets identified) and laboratory tests were

compatible with acute infection (CRP 74mg/L, D-dimer 1714μg/L, ferritin 864μg/L). Her kidney function was stable, with no urinary abnormalities, and ANCA remained negative, suggesting that her vasculitis was in remission. She received supplemental oxygen, dexamethasone, prophylactic anticoagulation, and was discharged after 10 days. Repeat PCR and antibody testing to SARS-CoV-2 were both negative one month following the second COVID-19 illness. Of note, she remained peripherally B-cell deplete (CD19 <2/μL) following rituximab therapy in April, although total immunoglobulin G levels are preserved (5.8g/L).

The six-month interval between symptomatic COVID-19 illnesses, with repeated negative PCR testing between episodes, suggests reinfection with SARS-CoV-2 in this patient; however, we cannot definitively exclude persistent viral replication in this immunocompromised patient. The case highlights that those receiving immunosuppression may develop viral reinfection or persistence[1,2]. This is important as previous reports in immunocompetent individuals suggest that reinfection may have a more severe disease course[3,4]. Our experience also suggests that immunosuppression may impact the longevity of protective immune responses to SARS-CoV-2 infection. This may have important implications for vaccine efficacy in these at-risk patients, who are likely to be prioritized for immunisation programmes in the near future. We plan to delay further maintenance immunosuppression to provide an opportunity for vaccination in this case.

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