Resolution of prolonged SARS-CoV-2 infection in secondary immunodeficiency after convalescent plasma but not remdesivir

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COVID-19 creates significant clinical challenges in patients with primary and secondary immunodeficiencies. Hospitalisation and fatality rates are greater in these cohorts and, in the absence of robust immunity, chronic SARS-CoV-2 infection can occur. The frequency and determinates of chronic infection are unknown and medical and public health management strategies remains unclear. Herein, we present our experience of managing chronic SARS-CoV-2 infection in an individual with rituximab-induced B cell aplasia.

A 57-year-old lady presented to hospital on 16/4/2020 with a two-week history of dry cough shortness of breath, pyrexia (38.4^{o}C) and raised inflammatory markers. Chest x-ray demonstrated bilateral, lower-zone peripheral air space opacities. She had a thirteen-year history of anti-CCP seropositive rheumatoid arthritis, previously treated with glucocorticoids, disease-modifying anti-rheumatic drugs, etanercept and most recently, rituximab, last infused 3 weeks prior to symptom onset.

A diagnosis of likely COVID-19 was made and the patient was discharged with oral antibiotics. The patient re-represented eight days later with persistent pyrexia, cough and new gastrointestinal symptoms. Radiological progression suggested ongoing viral pneumonia and SARS-CoV-2 RNA was detected in a sputum sample on day 25. Between May and July 2020, she was re-admitted on four occasions with similar symptoms, increasing oxygen requirements and progressive radiological changes. During these admissions, she received three courses of dexamethasone and one 10-day course of remdesivir. Monotherapy with dexamethasone achieved little objective change but treatment with remdesivir was associated with symptomatic improvement, a dramatic reduction in CRP and two successive negative PCR tests. However, 24 hours after the cessation of remdesivir, recrudescence of PCR positive, symptomatic COVID-19 occurred, suggesting remdesivir monotherapy suppresses viral replication, but is unable to facilitate complete viral clearance.

Despite prolonged PCR positivity, serum anti- spike and anti-nucleocapsid SARS-CoV-2 antibodies were undetectable in mid-July 2020 due to complete, rituximab-induced B cell aplasia. On day 99, the patient received two units of convalescent plasma leading to rapid defeverscence and improvement in inflammatory markers. High titre anti-SARS-CoV-2 spike glycloprotein IgG antibodies remained detectable in the serum for 7 days after treatment and demonstrated 100% neutralising capacity in an *ex vivo* plaque reduction microneutralisation assay at a 1:100 titre. PCR remained persistently negative following plasma treatment.

We provide evidence that humoral immunity is non-redundant for SARS-CoV-2 clearance and passive transfer of high-titre neutralising antibodies is a rationale treatment strategy for individuals with humoral immunodeficiencies. However, dual treatment with remdesivir may be necessary to suppress viral replication and prevent the generation of viral escape variants in more severely immunocompromised individuals. Urgent protocols are necessary to identify and manage chronic SARS-CoV-2 infections in individuals with immune deficiencies.