Vulnerability of patients on immunosuppressive therapy to SARS-CoV-2 reinfection

To the Editor,

The catastrophe by the novel COVID-19 has still not come to a halt in the world. There is an upsurge of COVID-19 cases and also SARS-CoV-2 reinfections or reactivations. Protective immunity following SARS-CoV-2 infection is uncertain. There are incidences of SARS-CoV-2 reinfection in patients who were on immunosuppressive therapy for other diseases. Immunosuppression in COVID-19 is a double-edged sword. It may be detrimental in the initial course of COVID-19, but may be life-saving with regard to alleviating the cytokine storm in the later course of the disease. However, it has resulted in a surge of cases of SARS-CoV-2 reinfection throughout the world.

Few viral infections provide lifelong immunity after the first infection, but seasonal coronaviruses provide short-lived protective immunity. Reinfections are expected to occur once antibody titres decrease. Gulati *et al*[1] have reported SARS-CoV-2 reinfection in a patient with antineutrophil cytoplasmic antibody-associated vasculitis after immunosuppressive therapy. It has been demonstrated in a study by Gudbjartsson *et al*[2] that antibodies to SARS-CoV-2 did not decrease within 4 months after infection. However, recurrences of COVID-19 have been documented in the literature. A systematic review of 1350 patients found COVID-19 reinfection after a mean of 34.5 days from first positive real-time PCR sample.[3] Immune suppression either reduces the clearance of SARS-CoV-2 or reduces the development of protective antibodies. COVID-19 reinfection should be differentiated from secondary complications such as superinfection. There may be persistence of viral RNA in the respiratory samples up to 6 weeks in a clinically cured patient and therefore it should be differentiated from reinfection. Immunosuppressive agents such as long-term corticosteroids, methotrexate, azathioprine, mycophenolate mofetil and biological agents (rituximab, adalimumab, infliximab) used in patients for other disease indications within 2–3 weeks of SARS-CoV-2 infection may be responsible for blunting the immune response and the inadequate production of protective antibodies. Among the immunosuppressive agents, rituximab, a monoclonal anti-CD20 antibody, is responsible for long-lasting B cell depletion. It may be highly responsible for blunting protective antibody production and thus SARS-CoV-2 reactivation. There are mixed recommendations for use of rituximab during the pandemic. However, a cohort study by Avouac *et al*[4] found patients with inflammatory rheumatic and musculoskeletal diseases had more severe COVID-19 outcomes after rituximab therapy. Therefore, intravenous immunoglobulin (IVIG) may be a potential alternative in the treatment of autoimmune diseases during the present scenario of COVID-19. There are reports of patients with severe COVID-19 who improved satisfactorily with high-dose IVIG.[5] It may prove to be beneficial in both autoimmune diseases and COVID-19.

The current evidence of short-lived acquired protective immunity needs to be elucidated with large studies. Patients may be reinfected by SARS-CoV-2 due to long-term effects of immunosuppressive drugs or a long-lasting virus carriage, and this needs to be validated by studies in the future to curb the menace of COVID-19 resurgence. Various guidelines have been formulated for the use of immunosuppressive agents during COVID-19, but these are derived from case reports and case series with low level of evidence. Although there is a high degree of suspicion for SARS-CoV-2 reactivation or reinfection in patients on immunosuppressive agents, indispensable or short-term use of these agents should be judiciously undertaken and priority for safer alternatives should be preferred.

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