Pause in immunosuppressive treatment results in improved immune response to SARS-CoV-2 vaccine in autoimmune patient: a case report

Patients on immunosuppressive drugs have been excluded from studies of SARS-CoV-2 mRNA vaccines’ (mRNA-BNT162b2 and mRNA-1273) clinical trials that resulted in their Emergency Use Authorization in the USA and Europe. Since the initiation of the global vaccination campaign, it became apparent that patients on immunosuppressive drugs may not generate optimal immune response following vaccination.1 Prednisone and mycophenolate are potent inhibitors of immune responses. Prednisone acts at many levels of immunity including the innate and adaptive responses, whereas mycophenolate mainly targets T and B cells.2 These and other immunosuppressive drugs used to treat patients with autoimmune disorders and organ transplant patients were shown to significantly curtail antibody responses following SARS-CoV-2 mRNA vaccines.3,5

We report on a 75-year-old male patient with an underlying autoimmune disorder, myasthenia gravis, which was controlled after receiving high doses of prednisone and mycophenolate for 9 months. At his first SARS-CoV-2 vaccination, he was receiving 7.5 mg prednisone on alternate days and 3 g mycophenolate daily (figure 1A). He received two doses of Moderna mRNA-1273 vaccine with a 4-week interval between doses. Neutralisation titres were measured using a pseudovirus neutralisation assay (PsVNA) as described previously.6 No SARS-CoV-2 neutralising antibodies were detected in plasma at 4 weeks after the second mRNA-1273 vaccination. In the same assay, age-matched (65–77 years old) immunocompetent individuals (healthcare workers who were not on any immunosuppressive drugs and vaccinated with two doses of mRNA-1273 SARS-CoV-2 vaccine in Maryland) generated neutralising antibody titres (PsVNA50: 50% reduction in neutralisation titres) ranging between 1:451 and 1:3293 against the WA-1 strain following mRNA-1273 vaccination.

The patient was able to receive a second series of vaccinations with the Pfizer mRNA-BNT162b2 at 42 days and 63 days (first and second dose, respectively) following the last vaccination with mRNA-1273. Three weeks prior to the first dose of mRNA-BNT162b2, the mycophenolate dose was reduced from 3 g to 2 g daily. The day prior to the second dose with mRNA-BNT162b2 and for 3 subsequent days, the patient did not take any prednisone or mycophenolate. Thereafter (3 days post-second vaccination), the maintenance dose of 7.5 mg prednisone on alternate days and 2 g mycophenolate daily was resumed (figure 1A). No change in his clinical status related to the myasthenia gravis was observed during the study. Two weeks after the second mRNA-BNT162b2 vaccination, the patient’s plasma was used to measure virus neutralisation against SARS-CoV-2 vaccine-matched WA-1 strain and multiple variants of concern. Robust virus neutralising antibody titres were measured with the highest titre against the vaccine-matched WA-1 strain and lowest against the B.1.351 SARS-CoV-2 variant strain (figure 1B).

This case study exemplifies a strategy that could lead to better immune responses following SARS-CoV-2 vaccination in patients on prolonged immunosuppressive drugs. It is possible that the additional vaccination series received by the individual in this report may have been sufficient without reducing the immunosuppressive medications. Indeed, this approach is being evaluated in ongoing trials. In this regard, Werbel et al7 reported that 24 of 30 (80%) of organ transplant recipients on multiple immunosuppressive regimens showed no receptor-binding domain (RBD) antibody binding response after the first vaccination series with mRNA vaccines. Among those, 67% were still seronegative for SARS-CoV-2 RBD antibodies following a third vaccination with no treatment modification.7

Therefore, if the virus neutralisation titres after SARS-CoV-2 vaccination are undetectable or low, it may be reasonable to consider temporary supervised reduction in the dose of immunosuppressive drugs prior and during the time of a second vaccination, to allow recovery of B and T cell function and a robust immune response to vaccination. This may be associated with risk that autoimmune diseases may relapse, or transplant rejection may occur. Careful studies need to be performed to determine whether the risk:benefit profile favours a temporary decrease in immunosuppressive drugs to allow for a successful SARS-CoV-2 vaccination-induced immune response against COVID-19.

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