Successful BNT162b2 booster vaccinations in a patient with rheumatoid arthritis and initially negative antibody response

The COVID-19 pandemic poses unique challenges regarding the optimal care of patients with rheumatic diseases, who may have an increased risk of infection and hospitalisation. It is therefore highly important to ensure successful vaccination of these patients.[1] The messenger RNA vaccine BNT162b2 (Comirnaty by BioNTech/Pfizer) against SARS-CoV-2 strongly reduces infection, transmission, hospitalisation and death in immunocompetent patients. The development of neutralising antibodies after vaccination has been associated with protection from COVID-19.[2] However, a decreased immunogenicity of several vaccines has been described under immunosuppressive medication,[3] and first reports seem to confirm reduced antibody responses after vaccinations against SARS-CoV-2 in patients on some immunosuppressive medications (e.g. in one preprint rituximab, glucocorticoids and possibly JAK inhibitors).[4] This led rheumatologists to address the question of how to deal with patients who show insufficient immunogenicity after vaccination.

In this letter, we describe a case with an initially negative antibody response and seroconversion after repeated booster vaccinations without interruption of immunosuppressive medication. The patient is a 54-year-old man, with a body mass index of 30.7 kg/m². He suffers from seropositive rheumatoid arthritis (RA, since 2013), polycythemia vera and had a leucocytoclastic vasculitis in 2020, confirmed by skin biopsy, which was successfully treated with an initial dose of 100 mg prednisolone. The prednisolone dose was then decreased to 5 mg/day and eventually stopped five days before the first vaccination. Leucocytoclastic vasculitis and polycythemia vera were in remission throughout the vaccination periods. The RA had been highly active in 2020, but remained with low disease activity (Disease Activity Score 28-C reactive protein ≤3.2) since January 2021 and throughout the vaccinations under treatment with upadacitinib 15 mg/day and methotrexate 10 mg/week, both since January 2021. Both medications were not paused for the vaccinations because the risk of recurrence of disease activity was considered high, and methotrexate was even increased to 12.5 mg/week between the second and third vaccination. Previous medications included anti-tumour necrosis factor-α antibodies, but not rituximab.

After the first vaccination, the patient suffered from fever, nausea, weakness, tiredness and headache for 5 days. After the second vaccination, he described tiredness for 2 days. Antibody titres against SARS-CoV-2 spike protein did not show a titre increase from earlier testing in May 2020 to 14 days after the first two vaccinations with BNT162b2. The patient then received an additional cycle of two vaccinations with the same vaccine in a standard dose outside of our care, which led to IgA and IgG seroconversion and development of neutralising antibodies until 15 days after the fourth vaccination (figure 1). He reported only mild tiredness for 1 day after the third and fourth vaccination.

Of course, a delayed antibody response to the first two vaccinations or the longer interval between the first and fourth vaccination may have contributed to the response in this case. It is also possible that a significant T-cell response already existed after the first two vaccinations, given the clinical reactogenicity. However, after hepatitis B virus vaccinations, testing for antibodies and booster injections have been advised for immunocompromised patients with low titres of protective antibodies independent of T-cell responses.[5] Currently, American College of Rheumatology guidance does not recommend routine measurement of antibody titres after SARS-CoV-2 vaccination,[1] and it remains unclear how to best interpret the results. The German Rheumatology Association acknowledged in a recent statement that booster vaccinations may have to be considered in patients who do not show sufficiently high or long-lasting titres of neutralising antibodies,[6] but this remains subject to an ongoing debate. Our case demonstrates that booster vaccinations in patients with an initially negative antibody response may induce a positive antibody response even without pausing immunosuppression.

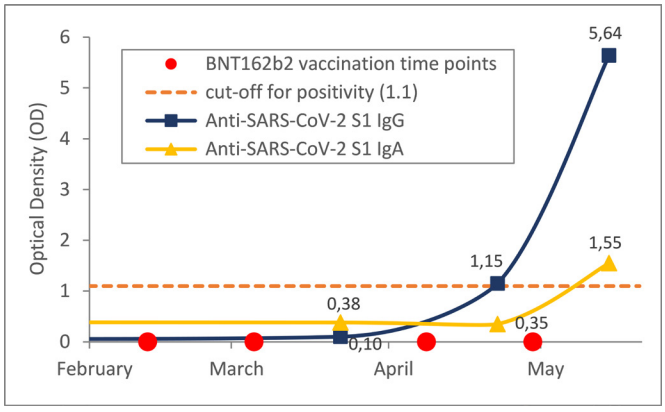

Figure 1 IgG and IgA antibody measurements against the SARS-CoV-2 spike protein (S1 domain) were performed with a semiquantitative ELISA by Euroimmun and showed a positive response after repeated vaccinations. In addition (not shown), neutralising antibodies assessed with a plaque reduction neutralization test (PRNT) were negative after the third and positive after the fourth vaccination ($PRNT_{50}$ 1:160; $PRNT_{90}$ 1:40). T-cell response against SARS-CoV-2 measured with a lymphocyte transformation test by IMD Berlin was only measured after the fourth vaccination and showed a positive result. Antibodies against SARS-CoV-2 nucleocapsid measured with an ELISA by Roche remained negative.

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