



Case Report

# Waning Humoral Immune Response to SARS-CoV-2 Vaccination with Symptomatic Infection after Initiation of Anti-CD20 Treatment in a Patient with Multiple Sclerosis

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**Abstract:** Waning humoral responses to SARS-CoV-2 vaccination have been reported arguing for booster vaccinations even in healthy populations. Multiple sclerosis (MS) immunotherapy with anti-CD20 monoclonal antibodies may negatively influence morbidity and mortality of COVID-19. The opportunity to treat patients at risk for a severe COVID-19 course with specific monoclonal antibodies targeting SARS-CoV-2 represents an important novel measure for patient safety. We report a patient with waning humoral vaccination response around five months after two mRNA vaccination doses upon initiation of ocrelizumab treatment. Symptomatic COVID-19 infection was treated with casirivimab/imdevimab with rapid symptom recovery.

**Keywords:** MS; COVID-19; ocrelizumab; rituximab; casirivimab/imdevimab



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## 1. Introduction

Treatment with anti-CD20 agents, such as rituximab and ocrelizumab, in patients with multiple sclerosis (MS) has been associated with both a higher risk for a severe course of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1] and reduced humoral immune responses upon vaccination against SARS-CoV-2 [2].

## 2. Case Report

We report a 34-year-old female patient with relapsing remitting MS (RRMS) who had been vaccinated against SARS-CoV-2 with Comirnaty® (BNT162b2, BioNTech Pfizer, 2nd dose given on 25 May 2021) twice with a 4-week interval between the two doses while being treated with dimethyl fumarate (Tecfidera®, Biogen, Cambridge, MA, USA). Initial vaccination response was evaluated after three months (20 August 2021) and revealed a positive result (257 AU/mL anti-spike IgG; cut-off value of  $\geq 100$  AU/mL considered as positive, internal communication of in-house infectious disease specialists). Due to MS disease activity, ocrelizumab (Ocrevus®, Roche, Basel, Switzerland) was started on 6 August 2021 (1st dose of 300 mg on 6 August 2021, 2nd dose of 300 mg on 20 August 2021), controlling MS disease activity during the short-term follow-up.

The patient developed fever and chills, fatigue, anosmia, and respiratory symptoms with cough on 16 November 2021 and performed a SARS-CoV-2 antigen self-test, which was positive. Due to anti-CD20 treatment and previous vaccination, the patient's anti-spike antibody response was retested, demonstrating a decline in the antibody level to 88.7 AU/mL (16 November 2021), and SARS-CoV2 infection was additionally confirmed by a positive PCR test (17 November 2021, nasopharyngeal swab: Ct-value 25.51, internal reference:  $\geq 34$  low, 26.01–33.99 medium,  $\leq 26$  high viral load).

Due to the high viral load, insufficient anti-spike IgG and drug-induced immunosuppression, casirivimab 1200 mg and imdevimab 1200 mg (REGEN-COV™, Roche) [3] were given intravenously on 17 November 2021. Four days later, she recovered without sequelae.

### 3. Concluding Remarks

In line with the recently published data on the gradual decline in humoral responses starting early after vaccination [4,5], our immunosuppressed, albeit young and female, patient experienced a relevant loss in anti-spike protein IgG around five months after the second vaccination followed by symptomatic SARS-CoV-2 infection. This case supports the notion that anti-spike protein IgG may serve as a proxy for protective immunity. A vaccination strategy with a total of four dosages in immunosuppressed patients as recommended by the Swiss regulatory authority might be useful in such situations. As a limitation, neutralizing antibodies and T cell responses were not measured during clinical routine in our patient.

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