LETTER TO THE EDITOR

Asymptomatic infection after BNT162b2 mRNA COVID-19 vaccination in multiple sclerosis patient

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To the Editor:

Since the start of coronavirus disease (COVID-2019) pandemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), there has been more than 160 million infection cases and more than 3.3 million deaths worldwide [1]. As a response to the pandemic, swift efforts towards discovery, production, and distribution of SARS-CoV-2 vaccines have been undertaken. This has resulted in approval and implementation of half a dozen vaccines including mRNA-based (BNT162b2, mRNA-1273), viral vector-based (Ad26.COV2.S, ChAdOx1 nCov-19 and Gam-COVID-Vac), and inactivated-virus vaccines (BBIBP-CorV). In particular, such vaccines are able to significantly lower the incidence of symptomatic and asymptomatic SARS-CoV-2 infections [2]. Data regarding the infectiousness of already-vaccinated people and the effectiveness of the vaccines in immunocompromised or vulnerable patients are still emerging.

Hereafter, we describe a case of asymptomatic SARS-CoV-2 infection in fully vaccinated multiple sclerosis (MS) patient, her associated serostatus and epidemiological data regarding her infectiousness. A 51-year-old Caucasian female MS patient treated with natalizumab for the past 10 years (extended interval dosing, q8 weeks) was seen by the immediate care facilities due to open wound from a human bite. The injury occurred at work as a social worker taking care of young students. She was started on oral antibiotics and screened for infectious agents, including COVID-19 antibody test which confirmed acute and first exposure to SARS-CoV-2 with increased levels of IgM antibodies and negative IgG antibodies. (Luminescence-based VITROS anti-SARS-CoV-2 IgG test, VITROS ECi/ECiQ/3600 Immunodiagnostic Systems) Additional nasal swab for polymerase chain reaction (PCR) test which was positive for SARS-CoV-2 RNA confirming current and active infection. This event occurred after 1 month since administration of the second dose of BNT162b2 mRNA vaccine. Both vaccination sessions were uneventful with minor local injection-site reactions (arm soreness). The last natalizumab infusion was administered 1 week after the first dose of the BNT162b2 mRNA vaccine. Throughout the entire time and after the positive tests, the patient felt good with no reports of COVID-19-related symptoms.

Additional epidemiological survey and SARS-CoV-2 testing of close contacts was performed. No positive tests were noted among the patient’s co-workers and close family members. Additional repeat serologic and nasopharyngeal testing was performed 2 weeks after the asymptomatic infection. The latest results demonstrated loss of the IgM antibodies and high titer of anti-spike IgG antibodies, indicating acquired immunity. The follow-up PCR test was negative for SARS-CoV-2 RNA.

Albeit anecdotal, this case report may provide a glimpse to the real-world effectiveness of SARS-CoV-2 vaccination, the measurement and clinical response of MS patients towards the vaccines, and the patient’s infectiousness after full vaccination. First, our case is corroborating the vaccine utility to prevent severe COVID-19 by reducing or fully blocking COVID-19 symptomatology. Despite the lack of detectable anti-SARS-CoV-2 antibodies, the patient had highly favorable clinical outcome and low infectiousness. Although natalizumab is not associated with systemic immunosuppression, it has been previously associated with lower vaccine response [3]. In addition to the favorable demographic factors such as young age and female sex,
MS patients treated with natalizumab commonly have good COVID-19 outcomes [4, 5]. The protective effects can be mainly attributed to T cell-based vaccine response (CD8+ T cells primed towards SARS-CoV-2 infected cells) which effectively limits the viral replication and control further spread of the virus. Therefore, evidence of anti-bodies is only one part of immune response towards the vaccine and future decisions should not be solely based on this test. Along those lines the Centers for Disease Control and Prevention (CDC) and other medical governing bodies do not recommend testing for humoral response or following-up mild COVID-19 infections in people who underwent full vaccination [6].

The findings indirectly provide encouraging data regarding the overall expectations of COVID-19 vaccination in MS patients and in particular in patients that use disease-modifying therapies (DMT) that cause B-cell depletion or immune cell sequestration [7]. While recent studies have demonstrated low SARS-CoV-2 seroconversion after vaccination, these findings were uncommon in patients with natalizumab [8]. For example, data from 35 Italian MS centers has shown that natalizumab does not affect the anti-SARS-CoV-2 antibody levels measured 4 weeks after the full vaccination course [9]. Similar results were seen in UK where 92% of natalizumab-treated MS patients had positive serostatus after the full vaccination course (56 seropositive and 5 seronegative patients) [10]. In contrast, our patient did not develop detectable IgG antibodies after her vaccination course. However, her good disease control can be attributed to sufficient and specific anti-SARS-CoV-2 immunity through T-cell activation which can be measured on IFN-γ enzyme-linked immunosorbent assay and may provide additional protective immunity [11]. Moreover, the patient could already have pre-existing T-cell immunity towards other non-snipe proteins that is based on the cross-reactivity between the SARS-CoV-2 and the common cold coronaviruses such as (HCoV)-OC43, HCoV-229E, HCoV-NL63 and HCoV-HKU1 [12, 13]. A limitation to this case report is the lack of information regarding the specific SARS-CoV-2 variant which may circumvent the vaccine immunity. In conclusion, our case report indirectly corroborates the vaccine effectiveness despite the seronegative status. MS care providers should continue recommending SARS-CoV-2 vaccination regardless on which DMT is used. The aforementioned CDC guidelines regarding the vaccine efficacy in the general population may be directly applicable to the MS population.

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