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Successful seroconversion following mild COVID-19 contraction in a double-vaccinated B-cell-depleted person with multiple sclerosis: A hint towards booster efficacy?

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ABSTRACT

Background: While early booster administration has been started in many regions to tackle failure of seroconversion among people with multiple sclerosis (pwMS) on anti-CD20 therapies (aCD20), its efficacy is still doubted in presence of B-cell depletion.

Case presentation: We report the case of a rituximab-treated person with MS who contracted COVID-19 after being double-vaccinated. While hypothesizing that COVID-19 contraction itself could mimic a vaccination booster, we investigated anti-SARS-CoV-2-Spike serology and B-cell counts in this case. The results showed successful seroconversion despite low relative counts of CD19+ and CD20+ cells.

Conclusion: Until further population-based data becomes available, further administration of early boosters among pwMS on aCD20 is highly encouraged.

Background

To date, multiple studies documented that most people with multiple sclerosis (pwMS) on anti-CD20 therapies (aCD20) fail to elicit antibody responses both to COVID-19 contraction and vaccination, unless after delayed aCD20 infusions/repopulation of B cells (Sormani et al., 2021b; Etemadifar et al., 2021; Apostolidis et al., 2021). Although adequate cellular responses are observed among them (Apostolidis et al., 2021; Sabatino et al., 2021), it is unclear whether these people are protected against COVID-19 and its unfavorable outcomes after being vaccinated. Many argue that even early booster administration may not be enough to elicit humoral immunization among the B-cell-depleted, which can neither be approved nor disapproved until further population-based data becomes available. Meanwhile, considering that COVID-19 contraction itself can mimic a vaccination booster, we investigated anti-SARS-CoV-2-Spike serology and B cell counts in an adult with MS on rituximab therapy, after contracting COVID-19 despite being fully-vaccinated with BBIBP-CorV COVID-19 vaccine.

Case presentation

The present man with MS in his late 20s,[1] presented to our clinic on October 2nd 2021, for a neurological checkup after contracting and recovering from COVID-19 nearly a week before. He was diagnosed with relapsing-remitting MS since 2017, when presented with recurrent episodes of extremity weaknesses and ataxia. He received interferon-beta and dimethyl fumarate until July 2020 when he was put on low-dose aCD20 therapy (Rituximab 500 mg every 6 months). He received his last rituximab infusion in July 1st, 2021, nearly a month before receiving his first dose of BBIBP-CorV COVID-19 vaccine on July 28th. Less than three weeks after receiving his second dose on August 25th, he started to show symptoms of fever and anosmia. Diagnosis of COVID-19 was later confirmed with RT-PCR on September 14th. He was closely observed while being provided with supportive indoor care and recovered without complications without any requirement of supplementary oxygenation or hospitalization, after a week. After presenting to our clinic, he was consensually referred for screening of anti-SARS-CoV-2-Spike IgG – performed using enzyme-linked immunosorbent assay (ELISA) with a seropositivity cut-off index of 8 relative units (RU)/ml – and CD19+, CD20+ B cell counts – performed using flowcytometry. His sample, obtained by a mobile phlebotomist at home on October 4th,

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[1] The exact value was not reported to prevent de-anonymization of the patient.

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interestingly showed an anti-SARS-CoV-2-Spike IgG measure of more than 50 RU/ml,[2] while relative and absolute counts of CD19+ and CD20+ cells were both 0.3% (reference [%]: CD19, 4.6–21.2; CD20, 5–22), and 8/μL (reference [count/μL]: CD19, 57–417; CD20, 74–441) respectively, indicating a successful seroconversion despite B cell depletion. He later provided written informed consent for anonymized publication of his case, and was advised to continue fulfilling the preventive measures considering his state of B cell depletion.

Discussion

It is unclear in the present case whether humoral immunization was obtained after vaccination, still, this is highly doubtful, as previous studies showed very low rates – if any – of seroconversion among the vaccinated pwMS who received their last aCD20 infusion within two months of their first vaccine dose (Etemadifar et al., 2021; Sormani et al., 2021a; Tallantyre et al., 2021), not to mention the contraction of COVID-19 after vaccination which would have probably been prevented in case of an adequate humoral immunization against SARS-CoV-2. Likewise, based on the previous studies, attribution of the observed humoral response solely to the contraction of COVID-19 might not sound realistic (Sormani et al., 2021b). Hence, in this case, it can be concluded that the COVID-19 contraction might have acted as an early successful vaccination booster, resulting in successful seroconversion despite the documented state of B cell depletion. For this reason, although it is doubted if the available COVID-19 vaccines could provide as much immunogenicity as the actual infection – as seen in cases of pwMS on sphingosine 1-phosphate receptor modulators, who seem to obtain immunization after infection but not after vaccination (Rommer et al., 2021) – early administration of booster doses among pwMS on aCD20 is highly encouraged, until further population-based data pertaining to the real-world immunogenicity of the boosters become available.

Declaration of Competing Interests

The authors declare that they have no conflict of interest and received no funding.

References

APOSTOLIDIS, S.A., KAKARA, M., PAINTER, M.M., GOEL, R.R., MATHEW, D., LENZI, K., REZK, A., PATTERSON, K.R., ESPINOZA, D.A., KADRI, J.C, 2021. Cellular and humoral immune responses following SARS-CoV-2 mRNA vaccination in patients with multiple sclerosis on anti-CD20 therapy. Nat. Med. 1–12.

ETEMADIFAR, M., SEDAGHAT, N., NOURI, H., LOTFI, N., CHITSAZ, A., KHORVASH, R., ZOLFAGHARI, H., GHASEMI MOVAGHAR, A., MOHAMMAD, P. & SALARI, M. 2021. SARS-CoV-2 serology among people with multiple sclerosis on disease-modifying therapies after BBIBP-CorV (Sinopharm) inactivated virus vaccination: same story, different vaccine. Multiple Sclerosis and Related Disorders. *DOI:10.1016/j.msard.2021.103417*.

ROMMER, P.S., BSTEH, G., BERGER, T., ZETTL, U.K, 2021. SARS-CoV-2 antibodies in multiple sclerosis patients depending on the vaccine mode of action? Multiple Scler. J. 13524585211039128.

SABATINO, J.J., MITTL, K., ROWLES, W., MCPOLIN, K., RAJAN, J.V., ZAMECNIK, C.R., DANDEKAR, R., ALVARENGA, B.D., LOUDERMILK, R.P., GERUNGAN, C., SPENCER, C.M., SAGAN, S.A., AUGUSTO, D.G., ALEXANDER, J., HOLLENBACH, J.A., WILSON, M.R., ZAMVIL, S.S., BOVE, R., 2021. Impact of multiple sclerosis disease–modifying therapies on SARS-CoV-2 vaccine-induced antibody and T cell immunity. medRxiv : Preprint Server Health Sci. 2021.09.10.21262933.

SORMANI, M.P., INGLESE, M., SCHIAVETTI, I., CARMISCIANO, L., LARONI, A., LAPUCCI, C., DA RIN, G., SERRATI, C., GANDOGLIA, I., TASSINARI, T., 2021a. Effect of SARS-CoV-2 mRNA vaccination in MS patients treated with disease modifying therapies. EBioMedicine, 103581.

SORMANI, M.P., SCHIAVETTI, I., LANDI, D., CARMISCIANO, L., DE ROSSI, N., CORDIOLI, C., MOIOLA, L., RADAELLI, M., IMMOVILLI, P., CAPOBIANCO, M., 2021b. SARS–CoV-2 serology after COVID-19 in multiple sclerosis: an international cohort study. Multiple Scler. J. 13524585211035318.

TALLANTYRE, E.C., VICKARYOUS, N., ANDERSON, V., ASARDAG, A.N., BAKER, D., BESTWICK, J., BRAMHALL, K., CHANCE, R., EVANGELOU, N., GEORGE, K., 2021. COVID-19 vaccine response in people with multiple sclerosis. medRxiv.

[2] The exact value was not reported to prevent de-anonymization of the patient.