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Attenuation of antibody response to SARS-CoV-2 in a patient on ocrelizumab with hypogammaglobulinemia

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As the world faces the spread and aftermath of the novel coronavirus disease (COVID-19), we are expectantly looking forward to a vaccine. Ocrelizumab, which is a monoclonal antibody directed against peripheral CD20+ *B* cells, is approved in multiple countries for both RRMS and PPMS (Montalban et al., 2017; Hauser et al., 2017). There has been concern about differential effects on immunoglobulin production for ocrelizumab based on the rituximab literature. Rituximab decreased serum antibody levels compared to methotrexate in the pivotal trial for rheumatoid arthritis (Edwards et al., 2004; Van Vollenhoven et al., 2010). In the VELOCE trial for ocrelizumab, humoral responses were attenuated but patients were still able to mount an immune response to vaccines (Stokmaier et al., 2018).

A 48-year-old female on ocrelizumab (last dose 1/24/2020) presented to a drive up COVID-19 testing site with two days of fever, upper respiratory symptoms, and malaise on March 30, 2020. She tested positive for SARS-CoV-2 RNA by PCR. She was prescribed hydroxychloroquine and azithromycin by her primary care physician, but withheld the hydroxychloroquine due to concern about side effects. Due to worsening shortness of breath, one week later she presented to the emergency room and was admitted for supportive care. Chest x-ray showed left upper lobe and left lung base pneumonia. She was started on ceftriaxone and hydroxychloroquine. Lymphocytes were normal at 1000/ul, IgG was low at 538 mg/dl (normal range 700–1,600 mg/dl), IgM was low at <25 mg/dl (normal range 40–230 mg/dl), and IgA was normal at 161 mg/dl (normal range 70-400 mg/dl). She did not require oxygen and was discharged 3 days later after clinical improvement. She had a prolonged symptomatic period, requiring over 3 weeks from onset to recover from her shortness of breath and fever and 7 weeks to recover from her malaise. In early June 2020, she sought antibody testing and tested negative for SARS-CoV-2 IgG with the Abbott immunoassay. She had a second specimen tested several days later and it also tested negative with the same immunoassay.

This patient illustrates a growing concern about the immunogenicity of SARS-CoV-2 in patients on ocrelizumab. On the one hand, one could argue that perhaps she had a false negative result. However, a study found the Abbott IgG immunoassay to be 100% sensitive and 99.9% specific (Bryan et al., 2020). On the other hand, this could represent an example of an attenuation of humoral response in response to ocrelizumab, especially in the context of hypogammaglobulinemia. The question is whether exposure to a future vaccine will also result in an attenuation of humoral response. However, as seen in the VELOCE trial, patients were still able to mount an immune response to vaccines despite the attenuated humoral response. Further studies should be conducted and a database should be formed regarding the humoral response to SARS-CoV-2.

Conflicts of interests

Honorarium from: Allergan, Alexion, Bayer, Biogen, EMD Serono, Genentech, Novartis, Sanofi Genzyme.

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