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COVID-19 Vaccine Response in Chronic Lymphocytic Leukaemia is More Than Just Seroconversion

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Commentary on Shen et al, COVID-19 Vaccine Failure in Chronic Lymphocytic Leukaemia and Monoclonal B-Lymphocytosis; Humoral and Cellular Immunity, Brit J Haematol 2021 Dec 28. doi: 10.1111/bjh.18014. Online ahead of print. (1)

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is about to enter its third year. Patients with chronic lymphocytic leukaemia (CLL) experience worse outcomes than the general population with a case fatality rate of approximately 30% (2, 3). Significant progress has been made in the management of COVID-19, including antiviral drugs, anti-SARS-CoV-2 antibodies. Despite these advances, 2021 has seen more COVID-19-related deaths than 2020 and the emergence and dominance of more transmissible variants.

Vaccination against SARS-CoV-2 is a critical strategy to prevent severe COVID-19 and limit transmission. Among immunocompromised people, patients with CLL have some of the lowest rates of antibody response to vaccines. In this issue of the British Journal of Haematology, Shen et al. assessed antibody response to COVID-19 vaccination in 206 patients with CLL and 29 with monoclonal B-cell lymphocytosis (MBL), a precursor state of CLL (1). The rate of seroconversion was 55% in CLL and 90.5% in MBL. Among patients with detectable anti-spike antibodies, antibody levels were significantly lower in patients with CLL and MBL than healthy controls. The authors further showed that antibody level was correlated with neutralizing activity. Taken together, a significant proportion of vaccinated CLL and MBL patients with seroconversion remains vulnerable to COVID-19 due to low levels of antibody.

Shen et al. identified several factors associated with seroconversion. In line with previous reports (4), most patients treated with Bruton tyrosine kinase inhibitor or anti-CD20 monoclonal antibodies did not develop anti-spike antibodies. Interestingly, baseline IgM was found to be a strong predictor of antibody response. This finding is compatible with our own observation that the primary immune response to novel antigen is suppressed compared to the amnestic immune response in patients with CLL (5).

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Conflicts of Interest

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SARS-CoV-2-specific T cells are likely an important part of immunological memory, providing long-term protection against COVID-19 (6). To investigate the T-cell response to COVID-19 vaccination, Shen et al. evaluated the presence of IFNγ and IL-2 producing T cells after stimulation with spike protein peptide pool. While antibody and cellular immune responses are generally coordinated in healthy individuals (7), no association between spike-specific T cells, anti-S antibody, and neutralizing activity was observed in this study. Notably, more patients had detectable spike-specific T cells than anti-spike antibodies.

This study from Shen et al. is an important contribution to our understanding about COVID-19 vaccine responses in patients with CLL and MBL. It also leads to new questions that warrant further investigation. What factors drive the dissociation between antibody and T-cell immune responses? Do spike-specific T cells alone protect against COVID-19? Can the vaccine response be elicited or boosted by additional doses? Are there other interventions to improve repsonse when repeated vaccinations are insufficient? These questions and their answers will remain relevant well beyond the COVID-19 pandemic.

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