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Letter to the Editor

Autoimmune diseases and vaccines against COVID-19. Decision-making in uncertain scenarios☆

Enfermedades autoinmunes y vacunas contra la COVID-19. Toma de decisiones en escenarios de incertidumbre

Mr. Editor:

We have read the special article that was recently published in your journal by Cairoli and Espinosa regarding vaccines against the 2019 coronavirus disease (COVID-19) in patients with systemic autoimmune diseases (SADs)[1]. We greatly appreciate the authors' clarity in presenting such a complex situation from a clinical point of view for physicians who work with these conditions, including their contribution of responses to when, how, whom, and with what to vaccinate patients with SADs.

A key issue is to determine whether patients with SADs develop immunity against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and what factors have an impact on this response. As discussed in the paper, this problem is even more important in patients under treatment with rituximab, as this drug is linked to a decline in immunoglobulin production and, therefore, to lower post-vaccination antibody levels. Although we believe that we are all clear on this, the question is whether the risk of infection is greater as a result of this treatment. This stems from the possibility that rituximab induces a decrease in humoral response, but not in cellular response. The data available in the literature in this regard are scarce and yield inconclusive results. Ferguson et al.[2] published the case of a patient treated with rituximab who received two doses of a messenger ribonucleic acid (mRNA) vaccine and failed to produce antibodies, but did have a positive interferon-gamma release assay (IGRA) after receiving the second dose. This suggests that it could be advisable to study this group of patients with an IGRA whenever individuals with B-cell depletion have a negative serology test[2]. Bonelli et al.[3] described five cases of patients under treatment with rituximab who were vaccinated with BNT162b2 (Pfizer/BioNTech), with only two cases exhibiting a serological response concurring with a recovery of their levels of $CD19^{+}$ B-cells, although the IGRA was positive in five cases. Along these lines, Prendecki et al.[4] evaluated subjects' serological responses with an enzyme linked immunosorbent assay (ELISA) and their T-cell response with an IGRA after receiving both a first and second dose of mRNA vaccines BNT162b2 and ChAdOx1 in a cohort of 161 patients under treatment with rituximab and other immunosuppressive drugs used to treat different SADs. They included a total of 114 patients who had received treatment with rituximab at some point of the clinical evolution of their disease. Of these, 64 (56%) patients received the vaccine earlier than 6 months since the administration of rituximab and 69 (60.5%) had a B-cell count <10 cells/μl at the time of vaccination. As expected, those vaccinated over 6 months after receiving the last dose of rituximab had higher seroconversion rates (71% vs. 49%). The IGRA was positive in 38 (82.6%) of the 46 patients in which it was performed. Most significantly, 15 patients had a positive IGRA and a negative serology test, with B-cell levels <10 cells/μl.

From a clinical point of view, although the significance of potential protection against a SARS-CoV-2 infection in this subgroup of patients is unknown, it is possible that they may have some degree of protection compared with those who fail to develop any response. More studies must be carried out to answer these questions.

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Alberto E. Calvo Elías[a], Lucía Pérez Casado[b], José Luis Callejas Rubio[c]

[a] *Servicio de Medicina Interna, Hospital Clínico San Carlos, Madrid, Spain*
[b] *Servicio de Medicina Interna, Hospital Universitario de Cabueñes, Gijón, Spain*
[c] *Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna, Hospital Clínico Universitario San Cecilio, Granada, Spain*

E-mail address: ae.calvoelias@gmail.com (A.E. Calvo Elías).

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