LETTER TO THE EDITOR

Association between COVID-19 vaccination and autoimmune bullous diseases: a random coincidence or rare event

Editor

An association between COVID-19 vaccination and autoimmune bullous diseases (AIBDs) has been suspected, but evidence-based data from larger cohorts of patients required for improved decision-making were lacking until recently.[1,2] Birabaharan *et al.*[1] determined the risk of bullous pemphigoid, the most frequent AIBD, in a large federated health research network involving over 1.5 million people with mRNA COVID-19 vaccination. No difference in risk of new-onset bullous pemphigoid was observed among persons receiving the mRNA COVID-19 vaccine within 6 months compared to non-vaccinated, matched control cohorts.[1] The results of our recent systematic review on the association between COVID-19 vaccination and AIBDs support this finding to some extent, showing that the hypothesized relationship is, if at all, at least a rather rare event.[2] Out of 932 published post-SARS-CoV-2-vaccinal cases (mostly mRNA vaccines), only about 6% presented clinically with *de novo* AIBDs and 10% had a flare or worsening of pre-existing AIBDs being usually well controlled with standard immunosuppressive treatment, whereas vaccination did not negatively influence the clinical course in all remaining patients.[2] Likewise, the validity of supposed induction or triggering of AIBDs by COVID-19 vaccines is limited, taking into account that the summarized data are generally based on single case reports with a low level of evidence and a cross-sectional study biased by subjective patient self-reports.[2,3] In addition, our previous investigation with healthy individuals who received the mRNA COVID-19 vaccine revealed that circulating anti-SARS-CoV-2 antibodies do not cross-react with pemphigus or pemphigoid autoantigens including desmoglein 1, desmoglein 3, envoplakin, BP180, BP230 and type VII collagen.[4] This argues against a link between SARS-CoV-2 vaccines and AIBDs with respect to disease-triggering antibody cross-reactivity.

In conclusion, although further observational studies on that controversial topic are needed, current epidemiological and mechanistic data basically encourage COVID-19 vaccination in patients with AIBDs since benefits of vaccination far outweigh these reported uncommon, questionable, and otherwise manageable risks. This is of particular relevance in terms of patient counselling and physician endorsement, considering that SARS-CoV-2 vaccine hesitancy is prevalent across the AIBD population (approximately one third), with concern regarding immunobullous exacerbation representing a major factor contributing to hesitancy.[3]

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