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COMMENTS

Leukocytoclastic vasculitis in possible relation to the BNT162b2 mRNA COVID-19 vaccine

Mr. Editor:

Older people have been the most affected by the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) being the first ones to be vaccinated. In Spain, the vaccines used in the older population were the mRNA BNT162b2 (Pfizer/BioNTech) and the mRNA-1273 (Moderna).[1] By the end of October 2021, a total of 46,573 vaccine-related adverse events had been reported by the Spanish Pharmacovigilance System for Medicinal Products for Human Use. Of these adverse events, 9430 were considered serious, and 4574 occurred in people older than 65 years old.[2] The most reported adverse events after administration of the mRNA BNT162b2 SARS-CoV-2 vaccine were fever (35%), headache (25%), myalgia (18%), injection site pain (12%), weakness (12%), fatigue (8%), nausea (7%), shivering (7%), lymphadenopathy (7%), and asthenia (7%).

We present the case of a 91-year-old woman, who was admitted to the hospital for the study of palpable purpuric lesions, predominantly on the lower limbs (Figure 1A). She had a relevant pathological history of moderate dementia, hypertension, and diabetes mellitus. No previous history of autoimmune diseases or introduction of new drugs for chronic use was found. He had received two doses of BNT162b2 mRNA COVID-19 vaccine (Pfizer/BioNTech). The appearance of the lesions began 4 days after the last inoculation of the vaccine. The lesions were biopsied and found to be compatible with leukocytoclastic vasculitis. Accordingly, management with oral prednisone at a dose of 0.5 mg/kg/day, for 1 month, was indicated, with subsequent resolution of the lesions, and no recurrences until today (Figure 1B,C,D).

To make a differential diagnosis, autoimmunity tests were performed with negative results (notably negative rheumatoid factor and negative antinuclear antibodies). In regards to malignancy, she did not have constitutional symptoms or signs of hematological disease. A chest and abdominal computed tomography was performed, which ruled out lesions. In regards to infection, the patient did not have fever during the hospital stay, and normal liver function tests, negative blood culture, negative urine culture, and echocardiography without evidence of vegetations were found. Other diagnostic possibilities such as idiopathic thrombocytopenic purpura and disseminated intravascular coagulation were also ruled out.

In particular, the Spanish pharmacovigilance system[3] uses several items in the process of assessing the possible causal relationship of the vaccine to adverse events reported postimmunization. Some of these items are: the time sequence of the occurrence of the adverse reaction, the previous description of the adverse effect in the drug label, the evolution of the adverse effect after administration of the vaccine, the effect of reexposure to the drug, the presence of alternative causes that could explain it, or the existence of coadjutant factors that support the causal relationship. Thus, depending on the score obtained, the possible causal relationship is classified into five categories: unrelated (< 0 points), conditional (1–3), possible (4–5), probable (6–7), or definite (8). According to this algorithm, and in line with our clinical suspicion, the causal relationship of the vaccine to vasculitis is classified as possible.

In regards to dermal lesions, several articles highlight the appearance of lesions, within the clinical spectrum of COVID-19, which can be divided into four main clinical patterns: exanthematous, vascular, urticariform, and acro-papular rash.[4,5] In the case of the patient, no evidence of acute SARS-CoV-2 infection was found.

Thus, having reasonably ruled out the most frequent causes of this type of vasculitis, exposure to the vaccine could have been a potential trigger as it meets the criterion of temporal association.

In effect, some cases of postimmunization vasculitis have been reported in the literature, most often associated with influenza and hepatitis B virus (HBV) vaccines.[6,7] Most recently, a similar case has recently been reported in a younger patient[8] after mRNA BNT162b2 SARS-CoV-2 vaccine. Despite this, no irrefutable causal association has been found for either.

Given the development of several types of vaccines to deal with COVID-19 and due to the reported cases of immunization-associated vasculitis, there is a *possibility* that the spectrum of autoimmune reactions with the new vaccines may go beyond thromboembolic disease. This text is written with the aim of motivating research and pharmacovigilance of this type of immune response and to encourage surveillance of its presentation in the older

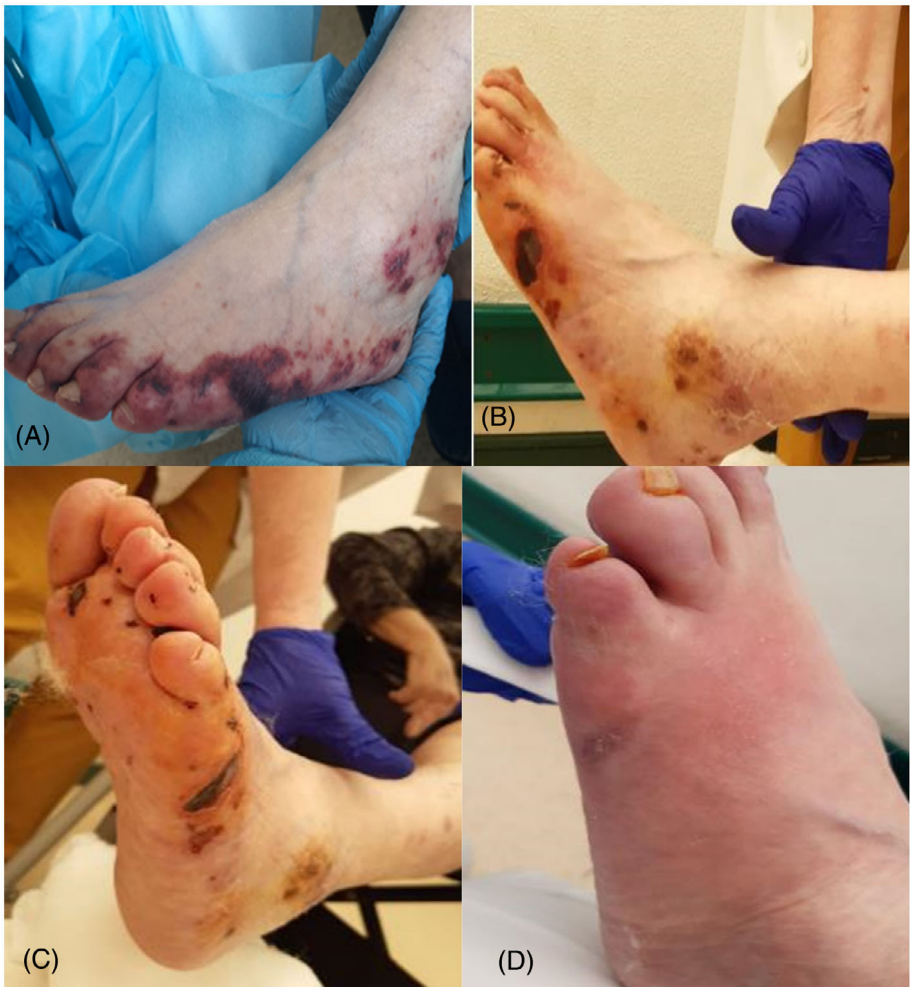

FIGURE 1 (A) Palpable purpuric lesions on the lower limbs. (B), (C), (D) Resolution of the lesions over time

population, as this is one of the groups that will benefit most from immunization and especially with the evolution of the epidemic, they will require subsequent exposure to other doses.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

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