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The Peruvian Association of Patients with Hereditary Angioedema and COVID-19 vaccination

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Hereditary angioedema (HAE) is a rare, potentially life-threatening disorder characterized by cutaneous and submucosal swelling attacks.[1] The coronavirus disease 2019 (COVID-19) pandemic has spread rapidly worldwide, and it can lead to death from respiratory failure or multi-organ compromise. [2] Vaccines against COVID-19 could cause adverse reactions or trigger HAE attacks in patients. The main objective of this study was to describe the features of adverse reactions following COVID-19 vaccination in patients with HAE.

We included 16 patients of the Peruvian Association of Patients with HAE, of whom 14 were women and 2 were men. Participants signed an informed consent form and completed a questionnaire about HAE history, COVID-19 infection, and COVID-19 vaccination. Mean patient age was 26.3 years (age range: 18-64 years). Eleven participants had HAE type I, and 5 had HAE with normal C1 inhibitor (HAE-nC1-INH). Genetic diagnosis was positive in 11 patients (2 FXII and 9 SERPING1) and unknown in 5. Patients with unknown mutations were only included in the study if they met the following criteria: clinical symptoms consistent with HAE with C1 inhibitor (HAE-C1-INH); presence of hormonal, trauma, and/or stress triggers; normal levels of C1-INH and C4; good response to tranexamic acid or danazol prophylaxis; and absence of mutations in FXII, plasminogen (PLG), angiopoietin-1 (ANGPT1), kininogen (KNG1), and SERPING1.

Before receiving the COVID-19 vaccine, 10 of 16 patients reported having mild to moderate attacks once a month, and 13 of 16 patients reported the abdomen as the most frequent region. Five had COVID-19 infection without worsening HAE crisis.

Fourteen patients received Pfizer®, 1 patient received Astrazeneca®, and 1 patient received Sinopharm®. After the first (11/16) and second (7/16) doses, patients had general discomfort, fatigue, headache, fever, and pain at the site of administration; some patients took acetaminophen, with good symptom control. There were 14 HAE crisis in total, 9 of which (65%) began after 24 hours of vaccine administration. The most frequent attacks were facial and upper airway angioedema, followed by abdominal crisis. Three patients had attacks only after the first dose; these patients received pre-treatment and did not have any attacks after the second dose. Four patients had a crisis only after the second dose; none were taking prophylaxis. Three patients had attacks after both doses and had not received any medication for prophylaxis.

Regarding the first dose, 3 of 16 patients had received short-term prophylaxis (2 tranexamic acid and 1 danazol), and 2 of them did not have attacks (1 with tranexamic acid and the other with danazol). Seven of 16 patients had a HAE crisis, of whom 6 were women and 1 was a man. Five of these 6 women had attacks during their menstrual period (range: 1 day before to 4 days after the beginning of menstruation). They reported worsening HAE crises during their periods. Three of 7 patients with mild/moderate HAE attacks did not received treatment, and the crisis lasted from 48 to 72 hours. The remaining 4 patients, all women with moderate/severe attacks, received specific treatments: 1 received icatibant (facial and tongue edema; attack remission in 24 h); 2 received high doses of tranexamic acid (facial and hand edema; attack remission in 72 h); and 1 received ecallantide (pharynx edema and difficulty to swallow; attack remission in 24 h).

Regarding the second dose, 9 of 16 patients received short-term prophylaxis (500 mg tranexamic acid, 3 times a day, 5 days pre- and post-vaccination), and none of them had a crisis. Seven patients without prophylaxis had moderate/severe angioedema attacks, which began 3 to 48 hours after vaccine administration. Only 1 patient had severe abdominal crisis, 5 days after receiving the vaccine. Five of 7 patients received treatment: 1 received icatibant (facial and tongue edema; attack remission in 24 h), and 4 were treated with high doses of tranexamic

acid (abdominal crisis and hands edema; attack remission in 96 h on average).

We conclude the following:

- Patients with HAE-C1-INH deficiency or HAE-nC1-INH may experience angioedema attacks after COVID-19 vaccination.
- The administration of COVID-19 vaccines during the menstrual period may induce HAE attacks. A possible recommendation would be to not administer COVID-19 vaccination immediately before or during the menstrual period.
- Patients with HAE included in this study had a positive response to prophylaxis with tranexamic acid.
- Specific treatments should be available to treat angioedema attacks after COVID-19 vaccination.
- The benefits of COVID-19 vaccination outweigh the risks of possible adverse events.
- To our knowledge, the present study has new findings. Further studies assessing COVID-19 vaccination in patients with HAE are needed.

References

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