Chronic spontaneous urticaria and dermographism following COVID-19 booster vaccination: a case series

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June 14, 2022

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To the Editor,

To date, more than 3.6 million persons in Denmark have received booster doses of COVID-vaccine, of which the majority have been the Pfizer-BioNTech's "Comirnaty" (86.5%) and Moderna's "Spikevax" (13.5%) vaccines (1). While adverse events following vaccination with the first two doses of COVID-vaccine have been reported, only a handful of cases documenting adverse events after receiving a booster vaccination have been published (2-5). In private dermatology practice, we have noticed an increasing number of patients with chronic spontaneous urticaria and dermographism.

This case series is based on 15 consecutive patients cared for in a single private dermatology practice having a catchment area of 90000 patients. Clinical and demographic data are presented in Table 1. Twelve patients had no previous medical history of urticaria and developed inducible urticaria post vaccination (Figure 1) and seven of these patients also had coexisting spontaneous urticaria. The remaining three patients developed an exacerbation of their preexisting urticaria with newly developed dermographism in two patients. All patients developed symptoms within one day to three weeks following vaccination with a median time of 14 days. Most patients had severe symptoms with six requiring acute doctor visits and two being admitted to the emergency department. All patients were treated with high-dose antihistamines, and three patients received oral prednisolone. Three patients received further treatment with omalizumab due to lack of response to high dose antihistamines/oral steroids. In all cases the most likely provoking factor of the chronic spontaneous urticaria and dermographism was believed to be the COVID-vaccine, as no other plausible cause was found, despite a thorough medical history and routine blood tests following international EAACI/GA^{2}LEN/EUROGuiDerm/APAAACI guideline.

We performed a literature research and found four other case studies reporting chronic spontaneous urticaria or dermographism following booster vaccination with COVID mRNA-vaccines (2-5). The mechanism is not elucidated, but it does not appear to be consistent with a true type I allergic reaction. We hypothesize that the generation of interleukins or other factors, in addition to T-cell activation, may lead to a non-IgE-mediated mast cell degranulation. A delayed hypersensitivity reaction against vaccine excipients or the mRNA component has already been suggested as the cause of localized injection-site reactions to the Spikevax vaccine (6). Most of our patients (73.3%) received a booster vaccination with Spikevax. Out of a total of 3.629.799 Danes who have received booster vaccinations, only 489.037 (13.5%) were vaccinated with Spikevax (1). It may be possible that Spikevax is more likely to stimulate an immunologic response leading to urticaria. Due to different booster dosages of Comirnaty (0.3 mL containing 30 micrograms of mRNA)

and Spikevax (0.25 mL containing 50 micrograms of mRNA), Spikevax contains more mRNA, which could support this hypothesis, but more research is needed.

It is important to identify and distinguish between different hypersensitivity reactions, which can include anaphylaxis, angioedema or acute urticaria, and delayed reactions, which consists of delayed urticarial reactions, late local reactions, and injection site reactions ("COVID-arm"). The Centers for Disease Control and Prevention recommends that patients who experience immediate hypersensitivity reactions within 4 hours of receiving a COVID vaccine postpone the subsequent dose until after consulting with a specialist (6).

This study describes booster vaccinations with COVID mRNA-vaccine leading to the development of chronic spontaneous urticaria and dermographism, which is a distinct clinical picture. These symptoms can be treated similar to chronic spontaneous urticaria and are not a contraindication to future vaccination. As many countries now are administrating a third or even fourth dose of COVID-vaccine, we hope this letter makes clinicians aware of this potential adverse effect, especially following booster vaccination with Spikevax.

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Ethical approval

Oral and written informed consent for publication has been obtained from all patients.

This study did not require an ethics approval being a non-intervention project, because it only uses data from patients and no biological material.

Funding information

The authors have not received any funding sources, nor were they paid to write this case series.

Conflict of interest

Jakob Lillemoen Drivenes has been involved in clinical studies supported by Takeda.

Aleena Banerji has received a research grant from Takeda and Kalvista, and has been involved in consulting supported by Biocryst, Takeda, Kalvista, Pharvaris and Ionis.

Anette Bygum has been involved in clinical studies and teaching supported by Biocryst, CSL Behring, and Takeda (former Shire).

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`Allergy LTTE Table 1 Final version.docx` available at https://authorea.com/users/488932/articles/572887-chronic-spontaneous-urticaria-and-dermographism-following-covid-19-booster-vaccination-a-case-series