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Chronic spontaneous urticaria after COVID-19 mRNA vaccination

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Introduction

A range of adverse events has been reported in response to SARS-CoV-2 vaccination. New onset of cutaneous reactions and flares of preexisting dermatoses (mainly psoriasis, atopic dermatitis, urticarial) as well as reactivations of herpes infection were observed (1). Urticaria/Angioedema events following COVID-19 vaccines are commonly reported. In most cases, they are delayed in onset, have a harmless course and are transient.
During the last 2 years, several cases of new onset chronic spontaneous (CSU) have been described after COVID19 Vaccination. Since there is a general recommendation for booster vaccination, more cases of urticaria (both acute and chronic) have been reported in Switzerland (Swissmedic update "Suspected adverse reactions to Covid-19 vaccinations in Switzerland" on 06.05.2022).
To our knowledge, only 3 cases of new-onset CSU after Booster vaccination have been published to date (all after vaccination with mRNA-1273 (Moderna)) (Table 2).

Aim

To characterize 26 cases of new-onset CSU after vaccination with mRNA-1273 (Moderna) including 23 cases of booster-induced CSU.

Methods

This was a cross-sectional study in which all patients with a new onset of CSU (symptoms for at least 6 weeks, with wheals occurring at least twice weekly) within 2-3 weeks of mRNA Co19Vac were analysed. All data were collected from medical records.

Results

We included 26 CSU patients with a mean age of 40 years (SD ±12.1), 16 were female (62%). In all but 3 cases, CSU was induced by booster vaccination. All of our patients received mRNA-1273 vaccine. The mean latency from vaccination to disease onset was 11 days (SD±3.9). No major laboratory abnormalities occurred in any of the cases. One patient had an elevated basal serum tryptase (bST) level (17.5 µg/l). The mean bST of the remaining patients was 3.8 µg/l (SD±1.1). In 4 out of 23 patients (17%) we observed low total IgE levels (<10 kUL). Six patients (26%) had values higher than 100 kUL (SD±443). Seven Patients (27 %) had atopy.
The clinical course of urticaria was favorable in most cases. The majority of patients showed remarkable urticaria facticia. Treatment with omalizumab was initiated in 2 patient with antihistamine-resistant CSU (Table 1).

Table 1. Characteristic of Patients with new-onset CSU after vaccination with mRNA-1273 (Moderna)

Sub.	Sex	Age	Vaccine used	Dosis Nr	Latency	IgE	Atopie	Tryptase	Cours	Therapy	Urticaria factitia
1	M	19	Moderna	Booster	14	38	-	4.7	mild	AH	+
2	M	26	Moderna	Booster	7	n.d.	-	3.3	mild	AH	-
3	F	32	Moderna	Booster	10	69	+	4.8	moderate	AH	+
4	F	43	Moderna	Booster	10	3	-	3.8	mild	AH	+
5	F	51	Moderna	Booster	14	41	-	4.9	mild	AH	+
6	F	58	Moderna	Booster	6	34	-	17.5	mild	AH	-
7	F	38	Moderna	Booster	14	95	-	5.1	mild	AH	+
8	F	50	Moderna	Booster	4	59	+	5.9	sever	AH/Omalizumab	-
9	M	36	Moderna	Booster	7	149		2.7	mild	AH	-
10	F	52	Moderna	Booster	14	5	-	2.8	mild	AH	-
11	F	42	Moderna	Booster	10	n.d	+	n.d.	mild	AH	+
12	M	33	Moderna	Booster	10	82	+	4	mild	AH	-
13	F	39	Moderna	Booster	10	n.d.		3	mild	AH	-
14	M	46	Moderna	Booster	10	26	+	4.2	moderate	AH	-
15	F	38	Moderna	Booster	7	73	-	3.6	mild	AH	+
16	F	32	Moderna	Booster	14	9	-	3.5	severe	AH/Omalizumab	+
17	F	38	Moderna	Booster	6	1235	+	2.8	mild	AH	+
18	F	31	Moderna	Booster	14	34	-	1.3	mild	AH	-
19	M	75	Moderna	Booster	21	290	-	4.6	mild	AH	+
20	M	19	Moderna	Booster	10	63	-	3.3	mild	AH	-
21	F	30	Moderna	Booster	14	144	-	5.4	mild	AH	-
22	M	40	Moderna	Booster	10	18	-	3.2	mild	AH	-
23	M	37	Moderna	Booster	8	115	-	4.9	mild	AH	+
24	F	36	Moderna	2nd Vaccine	17	19	-	n.d.	mild	AH	+
25	F	40	Moderna	1st Vaccine	14	9	-	2.3	mild	AH	-
26	M	56	Moderna	2nd Vaccime	14	108	+	3.3	mild	AH	+

F: female, M: male, nd: not done, AH: antihistamines

Table 2. Summary table of published data of new-onset chronic spontaneous urticaria after COVID19 vaccination

Ref.	No. of Cases	Alter	Sex	Onset-Vaccine Interval (days)	Type of Vaccine (n. Individuals)	Urticaria onset after: dose number (n. Individuals)
2	8	56 ± 19.7	6F/2M	8.6 ±6.5	Moderna (1) Pfizer (3) AstraZeneca (4)	First (6) Second (2)
3	1	20	M	7	Pfizer (1)	Second
4	1	60	M	5	AstraZeneca (1)	First
5	1	39	M	14	AstraZeneca (1)	Second
6	32	41.2 ± 11.5	21 F/11 M	within 3 Months	Pfizer (32)	First oder Second
7	3	41 ± 23.6	2F/1M	11±4.6	Pfizer (1) Moderna (2)	First (1) Booster (2)
8	1	12	F	12	Moderna (1)	Booster

F: female, M: male

Conclusions

In the WHO pharmacovigilance database, a total of 3,880,081 cases of ADRs are currently found in associations with Covid-19 vaccination, of which 807 cases are chronic spontaneous urticaria (IC0251 2.2), resulting in a positive dysproportionality signal for these reactions (Data from 13.06.2022).
The literature search revealed in total: 37 cases of CSU within 3 months after BNT162b2 (Pfizer) vaccination (first or second Dose) and 1 case with onset 2 days after the first vaccination with mRNA-1273 (Moderna). In Addition overall 6 cases with onset 1-15 days after the first or second dose of vector-based COVID19 vaccine ChAdOx1-S (AstraZeneca) were published (Table 2). In our study, the short time interval between vaccinations and first urticaria symptoms (11±3.9 days) suggests that mRNA COVID19 vaccine (especially the booster vaccination) with mRNA-1273 (Moderna) may act as a CSU trigger in patients without a history of urticaria. There is no reason to believe that vaccine-induced urticaria differs from classical CSU. Accordingly, apart from a pronounced urticaria facticia, we could not find any relevant clinical features or laboratory analytical findings among the affected patients in our study group.
Further studies are needed to understand the exact mechanisms of COVID19 vaccine-induced CSU. Whether some preparations have more potential for triggering urticaria than others needs to be further investigated. Proper education of patients with vaccine-induced urticaria is essential to avoid general immunoscepticism.

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