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CASE REPORT

The effect of COVID-19 and COVID-19 vaccines on chronic spontaneous urticaria: single center experience

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ABSTRACT

Chronic spontaneous urticaria (CSU) is known by spontaneous urticarial lesions and/or angioedema resisting ≥ 6 weeks. It is reported that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters the body and triggers urticaria and angioedema, and even might cause CSU. Although coronavirus disease 2019 (COVID-19) vaccines do not generally affect CSU patients, it has been observed that they occasionally exacerbate the disease. Here, we studied COVID-19, COVID-19 vaccines, and their effects on CSU cases. The records of 16 cases who mostly took omalizumab due to being resistant CSU cases were retrospectively reviewed. There was no problem with an inactivated (Sinovac®) vaccine. After mRNA (BioNTech®) vaccination, 2 of our patients had an exacerbation and even one had to switch to omalizumab. In 2 patients, CSU developed despite the absence of an urticaria-angioedema history and they were also unresponsive to standard antihistamine therapy and therefore had to be started on omalizumab. As a result, omalizumab had to be started in 3/8 patients after mRNA vaccination due to CSU exacerbation or treatment failure. It should be also kept in mind that SARS-CoV-2 infection and vaccination against it may exacerbate or trigger the disease in some patients.

KEY WORDS

chronic spontaneous urticaria, COVID-19, SARS-CoV-2, vaccination.

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INTRODUCTION

Chronic spontaneous urticaria (CSU) is known by spontaneous urticarial lesions and/or angioedema resisting ≥ 6 weeks [1]. It is reported in the literature that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters the body and can trigger urticaria and angioedema, and even might cause new-onset CSU [2]. Although coronavirus disease 2019 (COVID-19) vaccines do not generally affect patients with CSU, it has been observed that they occasionally exacerbate the disease [3, 4].

AIM

In this study, we investigated the effects of COVID-19 and COVID-19 vaccines on our CSU cases.

CASE REPORT

The files of 16 CSU cases of the Department of Pediatric Allergy and Immunology at a University Training and Research Hospital were retrospectively evaluated. (Non-interventional ethics committee approval number: E-71522473-050.01.04-259122-292.) Five of the cases were male and 11 were female. The mean age was 17.9 ±3.2 (min.–max.: 13–25) years. Of 16 cases, 9 cases (1 case – inactive Sinovac®, 8 cases – mRNA Pfizer-BioNTech®) were administered the vaccine.

14 out of 16 patients did not get SARS-CoV-2 infection (until 1 year after vaccination). Two people were infected and urticaria did not develop in one of them, but she was using omalizumab at the same time (Table 1). In the other patient, urticaria and Raynaud's phenom-

TABLE 1. Chronic spontaneous urticaria patients followed-up in our center during SARS-CoV-2 infection and vaccination

Case #	Gender	Age	Type and dose number of COVID-19 vaccine	Postvaccine U-A	SARS-CoV-2	U-A during COVID-19
1	F	18	No vaccine application	–	Not caught	–
2	F	19	2 doses of BioNTech	None	Not caught	–
3	M	23	2 doses of BioNTech	None	Not caught	–
4	M	19	3 doses of BioNTech	None	Not caught	–
5	F	19	No vaccine application	–	Not caught	–
6	F	18	No vaccine application	–	Not caught	–
7	F	19	2 doses of Sinovac	None	Not caught	–
8	F	20	2 doses of BioNTech	In both doses, mild itching and wheal occurred on the vaccinated arm and trunk 1 h after the vaccine	Caught	No U-A (received omalizumab during COVID-19)
9	F	15	No vaccine application	–	Not caught	–
10	M	14	2 doses of BioNTech	There was no U-A on the vaccination day but urticaria increased nearly 2 months later	Not caught	–
11	M	19	2 doses of BioNTech	There was no U-A on the vaccination day, but urticaria started 2 months later	Not caught	–
12	F	18	2 doses of BioNTech	None	Not caught	–
13	F	14	No vaccine application	–	Not caught	–
14	F	15	No vaccine application	–	Not caught	–
15	F	15	No vaccine application	–	Caught	Raynaud's phenomenon and urticaria started after COVID-19
16	M	25	2 doses of BioNTech	There was no U-A on the vaccination day, but urticaria started 2 months later	Not caught	–

M – male, F – female, U-A – urticaria and angioedema.

enon developed. She also had Hashimoto's thyroiditis before.

No adverse effect was detected in the case who took 2 doses of inactive vaccines, and he was using omalizumab at the time of administration. In 4 cases who took 2 doses of mRNA vaccines, there was also no adverse effect after vaccination (Table 1).

One case was given 2 doses of mRNA vaccines while getting omalizumab therapy. After both doses of vaccine, mild itching and wheals manifested on her arm and trunk within 1 h, accepted as an exacerbation of the disease. In the other patient with CSU, 2 doses of the mRNA vaccines were given while he was using an antihistamine, an intensification in the occurrence of urticaria (exacerbation) was detected after the vaccine, and the case was put on omalizumab management.

Two cases, without preceding urticaria, manifested urticarial plaques roughly 8 weeks after taking 2 doses of mRNA vaccines. Despite antihistamine use, urticarial plaques continued for ≥ 6 weeks, recognized as new-onset CSU cases. Since these cases did not react even to high-dose antihistamines, omalizumab was prescribed.

As a result, there was no problem with an inactivated/dead vaccine application. After mRNA vaccinations, 2 of our patients had an exacerbation of the disease and even one's therapy had to switch to omalizumab. In 2 patients, CSU developed despite the absence of an urticaria-angioedema history (new-onset CSU) and they were also unresponsive to standard antihistamine therapy and therefore had to be started on omalizumab as well. As a result, omalizumab had to be started in 3/8 patients after mRNA vaccinations due to CSU exacerbation and/or treatment failure.

DISCUSSION

The development of skin findings such as urticaria-angioedema during various viral infections is known as the manifestation of the disease [1, 2, 5]. The precise etiology of CSU is mainly unidentified, but it is supposed that reiterated stimulation of the dermal mast cell results in the discharge of vasoactive chemical substances [1]. The development of urticaria and Raynaud's phenomenon was observed in one of our patients after being infected with SARS-CoV-2. Conversion to systemic sclerosis has also been previously reported in some cases that developed Raynaud's phenomenon in the literature [6].

A study by Lascialfari *et al.* used telemedicine for the follow-up of CSU patients. 4/26 (19.2%) cases who had COVID-19 manifested with CSU recurrence, while 1 (3.8%) had a CSU worsening/deterioration. Meanwhile, 1/26 (3.8%) vaccinated patient had a recurrence of CSU, and 1 (3.8%) had a deterioration of CSU course [7].

The CSU case series after COVID-19 vaccination was earlier defined in the literature [3, 4, 8]. For instance, Magen *et al.* proposed that the mRNA vaccine triggered or caused CSU to exacerbate in cases with allergic disorders and/or pre-existing autoimmunity [9]. In our study, the mRNA vaccine application resulted in new-onset CSU in 2 cases and exacerbation/relapse in 2 cases.

Anti-SARS-CoV-2 vaccine-mediated CSU has been mostly demonstrated in several single-case reports [10, 11]. Similar to the South African case series [12], Ben-Fredj *et al.* described a retrospective series of 10 cases who developed CSU after SARS-CoV-2 vaccination. The improvement of the eruption was seen at least 2 months afterwards, despite the regular use of a high dose of first-generation H1 antihistamine in 9 cases. Among the included patients, 6 mRNA+2 inactive/dead + 2 vector vaccines were received, and 9 patients presented with a new-onset skin reaction; nevertheless, it was a reactivation of preexisting urticaria in one of them [13]. Similar to the literature data, the mRNA vaccine was the most blamed COVID-19 vaccine, followed by the vector and inactivated vaccines [10–13]. In a Turkish study, 181 (77 inactive, 104 mRNA) patients were vaccinated. Urticarial exacerbation occurred in 25/181 (13.8%) patients [14].

It is known that omalizumab can be used in the treatment of these CSU patients and that this treatment is safe [15–18]. Even long-term "real-life" omalizumab therapy in children seems to be well tolerated. Its safety and efficacy profile makes omalizumab a superb substitute in severe asthma and CSU patients during childhood [19].

CONCLUSIONS

It is good to see that it is mostly safe to administer inactivated and/or mRNA vaccines in CSU patients. In addition, we have also observed that catching SARS-CoV-2 infection and vaccination does not always lead to disease exacerbation or activation. It should be kept in mind that in some patients, COVID-19 vaccination may exacerbate or trigger the new onset disease as well.

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ETHICAL APPROVAL

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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