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COVID-19 vaccination in the setting of mastocytosis—Pfizer-BioNTech mRNA vaccine is safe and well tolerated

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Clinical Implications

Here, we report our experience with coronavirus disease 2019 (COVID-19) vaccination in a series of 73 fully vaccinated patients with mastocytosis. Pfizer-BioNTech vaccine was safe under antihistamine premedication and an extended observation of 45 minutes because only 2.7% reacted with mild, immediate symptoms.

Mastocytosis refers to a heterogeneous group of disorders characterized by accumulation and activation of mast cells (MCs) in the skin and/or internal organs.[1] Patients with clonal MCs limited to the skin are classified as having cutaneous mastocytosis, whereas in systemic mastocytosis (SM), at least 1 extracutaneous organ is involved.[1] Furthermore, monoclonal mast cell activation syndrome (MMAS) is a rare variant of this disorder in which patients have clonal MCs but do not meet criteria for SM.[1]

Patients with mastocytosis typically present with a range of recurrent MC mediator–related local or systemic clinical symptoms including pruritus, flushing and life-threatening anaphylaxis.[2] Elicitors of anaphylaxis include in most mastocytosis patients *Hymenoptera*-venom stings, but rarely drugs and foods.[2] Nevertheless, data related to the tolerance of vaccinations in adult mastocytosis patients are scanty.[3] Recent development of coronavirus disease 2019 (COVID-19) vaccines has actualized this issue and the question has been raised whether mastocytosis patients will safely tolerate COVID-19 vaccines because most of these patients are prone to anaphylaxis and these vaccines have been initially linked to an increased risk for allergic reactions in patients with previous allergies.[4] Although some previous studies reported that COVID-19 vaccines were well tolerated in mastocytosis,[5,6] the paucity of the enrolled subjects in the studies makes generalizability difficult. Hence, this retrospective study was conducted to evaluate safety and prevalence of COVID-19 mRNA vaccine–related immediate reactions in a series of 73 fully vaccinated (2 doses) mastocytosis patients.

Between January 2006 and May 2021, 512 consecutive adult patients have been referred to the Mastocytosis Centre Karolinska owing to clinically suspected MC disorders including patients with mastocytosis in the skin, patients with severe anaphylaxis, or patients with elevated serum baseline tryptase levels of unknown origin. The final diagnoses of SM or MMAS were obtained in a total of 255 patients following World Health Organization (WHO) criteria.[1] Moreover, serum baseline tryptase and total immunoglobulin E levels were measured, and patients underwent a comprehensive allergy workup to confirm atopic status and history of anaphylaxis.

Of 255 patients, 73 were identified for COVID-19 vaccination. Patients either made contact with the clinic themselves due to vaccine-related anxiety or were undergoing regular follow-up in the clinic for venom immunotherapy (VIT) or treatment with biologic drugs. Of 73 enrolled patients, 62 were diagnosed with SM (60 patients had indolent SM, 1 patient had SM with hematological neoplasm, and 1 had aggressive SM); 2 patients obtained a diagnosis of mastocytosis in the skin because they refused to undergo bone marrow investigation. In addition, 9 patients had a diagnosis of MMAS (Table I). Informed consent was obtained according to the guidelines of the Stockholm's Ethics Review Board (Dnr: 2011/1750/31/3 and Dnr: 2018/2621-31).

All vaccinations were performed in our allergy outpatient clinic using a special protocol, which is derived from our VIT setting for patients with mastocytosis.[7] Accordingly, all patients received premedication with antihistamine (AH) (2 tablets of desloratadine 5 mg) 30 to 60 minutes prior to vaccination (51 patients were on scheduled AHs and took 2 additional tablets). Subsequently, 30 μg (0.3 mL) of Pfizer-BioNTech (Comirnaty) vaccine (which was the only available vaccine at that time) was given. Afterward, patients remained for a 45-minute observation. The second doses were administered 3 to 4 weeks after the first dose. The vaccine was administered at least 7 days after or before in those who were treated with VIT or biologic drugs (eg, omalizumab).

In our series, 2 of 73 patients (2.7%) developed mild, immediate (within 20–40 min after vaccination) reactions in 3 of 146 injections. Both patients were females and experienced facial flushing, tingling in mouth and/or tongue, or a sense of general discomfort; however, cardiorespiratory parameters were stable. Patients responded well to 2 extra AH tablets (desloratadine 5 mg) and were observed for an additional 2 hours without further progress of their reactions. Both patients had diagnosis of indolent SM and had no history of anaphylaxis or atopies. Interestingly, 1 patient reacted to both doses (more recently, even reacted with the third dose) with same reaction pattern, whereas the second patient only reacted to first dose. Moreover, none of the patients in our cohort developed severe, immediate allergic reactions requiring epinephrine. In a recent study on highly allergic nonmastocytosis patients,[8] immediate reaction rate was 2%, which is comparable with 2.7% found in this study. Furthermore, the rate of delayed hypersensitivity reactions (including skin eruption, itching, or urticaria) was 14.7% in this highly allergic cohort.[8] Interestingly, however, none reported delayed hypersensitivity reactions in our cohort, as documented prior to the second dose of immunization (ie, ≥3 wk after the first dose). Nevertheless, nonallergic adverse reactions including injection-site pain or tenderness, myalgia, malaise, or chills were common among our patients.

The main strength of this single-center study was the homogeneity of the subjects enrolled and protocols applied. Patients were investigated in a standardized manner and underwent a comprehensive allergy workup in our center as well as received COVID-19 vaccination from the same manufacturer using a standard protocol. Another distinguishing feature of this study was that our vaccination cohort included high-risk patients not only because of mastocytosis but also 66% (48 of 73) had a history of anaphylaxis (some with recurrent episodes). Of 73 patients, 35

TABLE I. Demographics, epidemiology and clinical and laboratory characteristics of enrolled subjects

Characteristics	Total cohort (n = 73)	SM (n = 62)	MIS (n = 2)	MMAS (*n* = 9)
Female gender, n (%)	38/73 (52)	35/62 (56)	2/2 (100))	4/9 (44)
Age at diagnosis, (y) median (range)	54 (18−79)	54 (18−79)	n/a	47 (36−67)
Baseline tryptase (ng/mL), median (range)	19 (3.2−160)	22 (5.3−160)	n/a	8.5 (3.2−15)
Total IgE (kU/L), median (range)	16 (1−1,000)	16 (1−1,000)	n/a	28 (8.3−250)
Presence of MC aggregates in bone marrow biopsy, n (%)	29 (41) (2 NA)	29 (47)	2 NA	0 (0)
Presence of atypical morphology in bone marrow biopsy, n (%)	61 (86) (2 NA)	58 (94)	2 NA	3 (33)
Presence of CD25 in bone marrow MCs, n (%)	71 (100) (2 NA)	62 (100)	2 NA	9 (100)
Presence of D816V mutation, n (%)	59 (81)	55 (89)	2 (100)	2 (29)
Presence of mastocytosis (skin lesions), n (%)	38 (52)	36 (58)	n/a	n/a
Presence of atopy, n (%)	19 (26) (1 n/a)	16 (26)	1 (50)	2 (25) (1 n/a)
Presence of atopic diseases (rhinoconjunctivitis and/or asthma), n (%)	16 (22) (1 n/a)	13 (21)	1 (50)	2 (25) (1 n/a)
History of any kind of anaphylaxis, n (%)	48 (66)	39 (63)	None	9 (100)
History of venom-induced anaphylaxis, n (%)	35/73 (48)	28/62 (45)	None	7/9 (78)
History of food-/drug-induced anaphylaxis, *n* (%)	2/73 (2.7)	2/62 (3)	None	None
History of idiopathic anaphylaxis, n (%)	11/73 (15)	9/62 (15)	None	2/9 (22)

IgE, Immunoglobulin E; *MIS,* mastocytosis in the skin; *n/a,* not applicable; *NA,* not analyzed.

(48%) had a history of venom-induced anaphylaxis, whereas only 1 had drug-induced anaphylaxis (caused by diclofenac). However, our cohort contained no patients with a history of anaphylaxis with prior vaccinations or polyethylene glycol polysorbate.

At present, it is difficult to assess whether premedication with AH might have been lowered the risk for potential anaphylaxis. We do not routinely recommend premedication with AH in mastocytosis patients, for instance, prior to other vaccinations. Nevertheless, some mastocytosis patients are regularly on AH prophylaxis. Therefore, randomized trials are needed to assess the exact role of premedication with AH in mastocytosis patients before providing general or patient-based recommendations. Until then, the usage of AH as premedication prior to COVID-19 vaccination should be encouraged, which is also in compliance with current recommendations regarding COVID-19 vaccination in mastocytosis.[9]

In conclusion, we report that, in our settings, COVID-19 vaccination of mastocytosis patients was safe and well tolerated, even those with an anaphylactic history. Furthermore, 39 of 73 patients (53%) received a third dose of Pfizer-BioNTech vaccine and only 1 (the patient who reacted to the first 2 doses) reacted with mild symptoms. Thus, we suggest that, because anaphylaxis is more severe in mastocytosis,[2] patients should be given premedication with an AH prior to COVID-19 vaccination and should pursue their daily medications (if any). Further, we recommend an extended observation period of 45 minutes after vaccination. Moreover, COVID-19 vaccinations can be administered in vaccine sites with resuscitation equipment readily available and staff trained in recognizing and managing anaphylaxis.

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