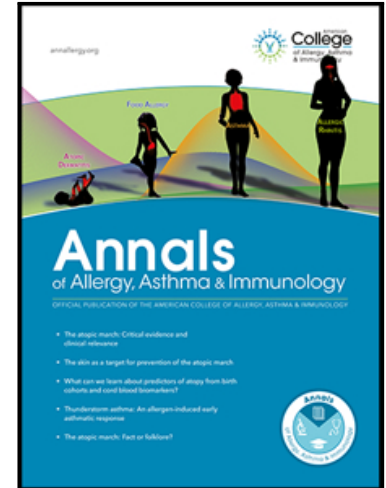


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SARS-CoV-2 vaccines are well tolerated in patients with mastocytosis

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Key words: COVID-19 vaccination, mastocytosis, SARS-CoV-2 infection, anaphylaxis

Abbreviations: COVID-19: Coronavirus Disease 2019; ECNM: European Competence Network on Mastocytosis; AIM: American Initiative in Mast Cell Diseases.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19) initially emerged in December 2019 in Wuhan, China, and its rapid spread led to a global pandemic. Vaccines are the single, most effective method of stopping the pandemic and concerns about vaccine safety have necessitated updates to the knowledge, especially in terms of allergic diseases. Patients with mastocytosis, who frequently experience recurrent anaphylaxis, constitute an important group that needs to be investigated as to whether the COVID-19 vaccines can be administered safely (1).

Mastocytosis describes a group of disorders in which pathological mast cells accumulate in tissues. Pruritus, flushing, recurrent anaphylaxis, nausea, vomiting, shortness of breath, drop in blood pressure, urticaria, angioedema, diarrhea, weakness, headache, muscle pain are the symptoms of mast cell activation in these patients. The overall risk for anaphylaxis is considerably higher than that of the general population and has been reported in up to 49% of some cohorts (1). Valent et al. recommended that anti-mediator-type drugs, venom immunotherapy, or vitamin D, should be continued and chemotherapy or immunosuppressive drugs should be carefully evaluated on a case-by-case basis during COVID-19 in patients with mastocytosis. (2). Rama et al. presented two patients with mastocytosis, who were vaccinated with the mRNA vaccine, the BNT162b2 (Biontech) vaccine (3). Both were vaccinated with premedication with H1 and H2 antihistamines, one hour before, and montelukast 10 mg, at one and 24 hours, without side-effects or a reaction but one of the patients had myalgia on the following day. Kaakati et al. reported a series of 18 patients with history of mastocytosis who underwent SARS-CoV-2 vaccination, and none had an allergic reaction or anaphylaxis after the vaccination (4). Of the 18 patients, 13 received the Pfizer, four the Moderna, and one the Janssen vaccine. Four patients took an antihistamine 30 to 60 minutes before vaccination.

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki, revised in 2013, and was approved by Hacettepe University Ethics Committee (2021/29-11). The hospital records of seven patients (four females and three males) have been reviewed retrospectively. These patients had been diagnosed with either cutaneous or systemic mastocytosis and were treated and followed up in our tertiary care center. The characteristics of six vaccinated patients are summarized in Table 1. Anaphylaxis to drugs had been reported by three patients, and one patient had had a history of anaphylaxis due to food allergy. The mean baseline tryptase level was 15.9 ng/mL (range, 3-200 ng/mL). The patients were contacted by telephone call and asked if they have received any premedication before vaccination or experienced any reaction or adverse effect after vaccination. Only one (14%) patient had swelling of the throat, cough, and shortness of breath two minutes after Sinovac

vaccination. This patient had received 45.5 mg pheniramine and 40 mg methylprednisolone intravenously (IV) one hour before the vaccine. Although the patient had received the same premedication IV one hour before the second dose of the same vaccine, the reaction has recurred, and the patient has been treated with 45.5 mg pheniramine and 40 mg methylprednisolone IV. The complaints have resolved in one hour. One patient, who had received 16 mg methylprednisolone and 22.7 mg pheniramine orally as premedication in each dose of vaccines, has not experienced any reaction after the first two doses of Sinovac and the first dose of Biontech. In addition, one patient has not been vaccinated on his will due to post-vaccine reaction concerns. A total of 15 vaccinations were administered to six patients, and one patient with cutaneous mastocytosis has experienced two non-life-threatening reactions after the vaccination. None of the patients had history of any vaccine, polyethylene glycol or polysorbate allergy. We did not recommend our patients allergy testing with PEG before Biontech vaccine.

European Competence Network on Mastocytosis (ECNM) and American Initiative in Mast Cell Diseases (AIM) recommended the use of COVID-19 vaccines in patients with mastocytosis, and by determining the individual risks of the patients, safety precautions, premedication, and post-vaccination observation should be considered in every mastocytosis patient (5). Although history of an anaphylactic reaction has been reported in up to 22% against other triggers in patients with mastocytosis, COVID-19 vaccines seemed to be well tolerated in the current study population (4). There is a consensus among experts that antihistamine premedication should be administered 30 or 60 minutes before vaccination in patients with mastocytosis at high risk of anaphylaxis, and the use of systemic corticosteroids before the vaccines has been debated due to concerns about vaccine efficacy (5). In a previous report, two patients with mastocytosis and a history of anaphylaxis were able to tolerate Biontech vaccine with premedication (3). The current cohort includes two patients who had been premedicated with antihistamine and corticosteroid. While one has had mild reactions after both doses of Sinovac, the other had no reaction after Biontech vaccines. Although there were only three patients vaccinated with Biontech in our study, all of them could be safely vaccinated. Four patients did not receive premedication and did not experience any reaction.

Limitations of this study are primarily the small sample size, and that patients had only received Biontech and Sinovac vaccines. Despite the COVID-19 pandemic continuing at full speed, the introduction of new vaccines will enrich current knowledge with new data that will emerge in large populations with mastocytosis. Further studies are needed to ensure the safety of COVID-19 vaccines, however. The strength of the study was that it provides information to

literature about possible reaction risk for the Sinovac vaccine. The findings of the current study suggest that most patients with mastocytosis can be safely vaccinated, even those with an allergy or anaphylaxis history. Our results point that the COVID-19 vaccines seem to be safe, and patients should be encouraged to get vaccinated. The role of premedication in preventing vaccine reactions was not supported by the data in this study.

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Table 1: The characteristics of the cohort

Patient No.	Age/ gender , years	Mastocytosis	SARS-CoV-2 vaccines			Premedication	Any vaccine reaction
			First dose	Second dose	Third dose		
1	26/M	Indolent systemic	Sinovac	Sinovac	-	No	No
2	50/F	Aggressive systemic	Sinovac	Sinovac	Biontech	Intravenous 45.5 mg pheniramine and 16 mg methylprednisolone one hour before each dose	No
3	47/F	Indolent systemic	Sinovac	Sinovac	-	No	No
4	46/F	Aggressive systemic	Sinovac	Biontech	Biontech	No	No
5	54/M	Indolent systemic	Sinovac	Sinovac	Sinovac	No	No
6	28/F	Cutaneous	Sinovac	Sinovac	-	Oral 22.7 mg pheniramine and 40 mg methylprednisolone one hour before each dose	Swelling of the throat, cough, and shortness of breath two minutes after each dose