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Safety of BNT162b2 mRNA COVID-19 vaccine in patients with mast cell disorders

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Clinical Implications

- The BNT162b2 mRNA COVID-19 vaccine is safe and well-tolerated in patients with mast cell disorders. These patients can be immunized with this vaccine with no need for specific measures.

Mast cell (MC) disorders (MCDs) are characterized by the proliferation and accumulation of MCs in different tissues, including skin and bone marrow, and/or the inappropriate release of MC mediators, creating symptoms in multiple organ systems. The clinical presentation of MCD is heterogeneous, ranging from a typical rash (urticaria pigmentosa) to a more aggressive systemic variant.[1] All MCD patients can experience symptoms of anaphylaxis owing to massive MC activation and the release of mediators. This reaction progresses rapidly and might lead to death. It requires prompt recognition and treatment with epinephrine. In anaphylaxis, serum tryptase level (STL) is typically elevated above normal levels (above 1.2 times baseline plus 2 ng/mL), a feature that identifies MCs as the sources of inflammatory mediators.

Patients with MCD have increased risk for anaphylaxis owing to various triggers including hymenoptera sting, alcoholic beverages, contrast media, latex, and drugs.[1] Vaccines have also been reported to cause an immediate reaction in patients with MCD.[2]

The first vaccine to receive authorization for emergency use in humans for prevention of the coronavirus was the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech, PBTV). Because of some early reports of allergic reactions to the vaccine in the United Kingdom and United States,[3,4] concern has been raised regarding the safety of this vaccine for patients with risk for immediate allergic reactions in general, and specifically for patients with MCD.[5,6] To date, consistent data are lacking on the need and type of preventive measures in patients with MCD receiving COVID-19 vaccines.

The objective of this study was to evaluate the safety of the PBTV in patients with MCD.

This was a retrospective study, including all patients with a diagnosis of MCD observed by our team who had received the PBTV.

Systemic mastocytosis, monoclonal MC activation syndrome, and mast cell activation syndrome were diagnosed according to World Health Organization criteria.[1]

All participants received two 30-μg injections of PBTV (0.3 mL volume per dose) delivered into the deltoid muscle, 21 days apart.

Vaccination was performed at the Allergy and Clinical Immunology Unit at Meir Medical Center. Serum tryptase levels were measured before and 90 minutes after vaccination by the ImmunoCAP method (Phadia 100 system, Phadia-Thermo Scientific, Waltham, Mass). Patients remained under observation for 4 hours after injection and were discharged after an immediate allergic reaction was ruled out by an allergy specialist.

Data were entered and tabulated using Excel 2007 (Microsoft Corporation, Redmond, WA). Data are presented as means and standard errors for continuous variables. Comparisons among groups were performed with Student t test. All tests of hypotheses were considered significant when two-sided probability values were P less than .05.

Twenty-six adult patients with MCD who were vaccinated with the PBTV were included in our study. Table I lists demographic and clinical data.

The vaccine was well-tolerated by all patients (Table II). Two patients had mild symptoms after the first injection (7.7%). Both patients were observed and no specific treatment was delivered besides paracetamol. All patients received the second dose with no adverse events. Serum tryptase levels before and 90 minutes after the injection were available in 14 patients (54%). No significant difference was found between STL before and after the first (39.9 ± 56.3 vs 39.6 ± 55.5; $P = 1$) or second (39.1 ± 55.4 vs 38 ± 55.2; $P = 1$) injection. Of 14 patients, three (had a nonsignificant increase in STL after both injections (21.4%), with no clinical signs or symptoms of MC mediator release.

In the past year, the coronavirus pandemic had a huge impact on the world. MicroRNA-based vaccines are considered to be a major measure aimed at controlling the pandemic. Although these vaccines are considered to be safe, concern has been raised regarding their potential to induce anaphylactic reactions.[7] Since the initial report from the United Kingdom regarding anaphylaxis after the PBTV, several more cases have been reported.[4] In the real-world setting, the incidence of anaphylaxis associated with the PBTV appears to be 10 times higher than that reported with all previous vaccines.[4] It has been suggested that the underlying mechanism for allergic reactions caused by mRNA vaccines might be IgE-mediated hypersensitivity to polyethylene glycol, a rare but increasingly recognized cause of anaphylaxis.[7,8]

Patients with MCD are considered to have an increased risk for anaphylactic reactions in general, specifically those induced by drugs including vaccines. Hence, some groups have advised caution when administrating mRNA vaccines to patients with MCD. The American College of Allergy, Asthma, and Immunology statement regarding mRNA vaccines stated that data related to risk in individuals with mast cell activation syndrome are extremely limited and evolving. Excluding an encouraging case report, no data exist regarding the actual risk for immediate allergic reactions to this vaccine in patients with MCD.

In this work, we have demonstrated for the first time that the PBTV is safe and tolerable in patients with MCD, regardless of the specific MCD or documented past anaphylactic reactions. Although available in only half of the current patients, that STL was not increased after vaccination suggests that MCs are not activated by the vaccine. That this population can be safely treated with PBTV is especially important considering the potential for more severe COVID-19 respiratory disease in these patients.[9]

Most patients in our study were regularly treated with antihistamine (AH). Treatment was continued as usual before the

TABLE I. Demographics, epidemiology, and clinical characteristics

				Clinical signs			Laboratory findings					
Patient num.	Sex	Age, y	Chronic medical conditions	Presenting sign	History of anaphylaxis	Other clinical signs	High basal tryptase level (<20 ng/mL)	cKit D816V mutation	Mast cell aggregates in bone marrow	Mast cell positive to CD25	Diagnosis	Treatment
1	F	52	Hypertension	Flushing	N	None	Y	N	N	N	MMCAS	AH
2	F	31	FMF	Anaphylaxis	Y; idiopathic	None	N	N	N	N	MCAS	AH
3	F	47	None	Anaphylaxis	Y; idiopathic	Flushing, abdominal pain	Y	N	N	N	MMCAS	AH
4	F	40	None	UP	Y; NSAID	Flushing	Y	Y	Y	N	ISM	AH
5	F	66	None	Flushing	N	None	Y	Y	N	N	MMCAS	AH
6	M	43	None	UP	Y; bee sting	Abdominal pain	Y	Y	Y	Y	ISM	AH, S
7	F	34	None	Bee sting anaphylaxis	Y; bee sting, NSAID	Flushing	Y	Y	N	N	MMCAS	AH
8	F	36	None	UP	N	Abdominal pain	Y	Y	N	Y	ISM	AH
9	F	55	Asthma	Anaphylaxis	Y; idiopathic	Flushing, abdominal pain	Y	Y	Y	Y	ISM	AH, X
10	M	55	None	Bee sting anaphylaxis	Y; bee sting	None	Y	Y	N	N	MMCAS	AH
11	M	49	None	UP	N	Flushing	Y	Y	Y	Y	ISM	None
12	F	32	None	UP	N	Abdominal pain	N	Y	Y	Y	ISM	AH
13	F	44	None	Flushing	Y; NSAID	UP, abdominal pain	Y	Y	Y	N	ISM	None
14	F	73	None	Bee sting anaphylaxis	Y; bee sting	None	Y	Y	Y	N	ISM	AH
15	M	34	None	UP	N	None	Y	N/A	N/A	N/A	ISM	None
16	M	66	None	Anaphylaxis	Y; bee sting, idiopathic	Osteoporosis	Y	Y	Y	Y	ISM	AH, TKI
17	F	77	Multiple myeloma	UP	Y; radiocontrast	None	Y	Y	N	N	ISM	AH, steroids
18	M	36	None	UP	N	Anemia	Y	N	Y	Y	ISM	None
19	M	64	None	Bee sting anaphylaxis	Y; bee sting	CU, osteoporosis	Y	Y	N	N	MMCAS	AH, X
20	M	32	Polycythemia vera	UP	N	Diarrhea	Y	Y	Y	Y	ASM	AH
21	M	66	None	Osteoporosis	N	Abdominal pain, anemia	Y	Y	Y	Y	ASM	TKI
22	M	44	None	Anaphylaxis	Y; idiopathic	Flushing, abdominal pain	N	N	N	N	MCAS	AH
23	F	71	CML	UP	Y; Idiopathic	Flushing, abdominal pain	Y	N	Y	N	ISM	AH
24	M	63	None	UP	N	Pruritus, abdominal pain	Y	N	Y	NA	ISM	AH
25	M	52	None	Anaphylaxis	Y; idiopathic	None	N	N	N	N	MCAS	AH, S, X
26	F	48	None	Anaphylaxis	Y; idiopathic	None	N	N	N	N	MCAS	AH

AH, antihistamines (second-generation H1 blockers); *ASM*, aggressive systemic mastocytosis; *CML*, chronic myeloid leukemia; *CU*, chronic urticaria; *ISM*, indolent systemic mastocytosis; *MCAS*, mast cell activation syndrome; *MMCAS*, monoclonal mast cell activation syndrome; *NA*, not available; *NSAID*, nonsteroidal anti-inflammatory drug; *S*, Singulair (Montelukast); *TKI*, tyrosin kinas inhibitors; *UP*, urticaria pigmentosa; *X*, Xolair (Omalizumab; Novartis, Switzerland).

TABLE II. COVID-19 vaccination

	First injection					Second injection				
Patient num.	Immediate reaction	Late reaction	Need for treatment	Tryptase before (ng/mL)	Tryptase after (ng/mL)	Immediate reaction	Late reaction	Need for treatment	Tryptase before (ng/mL)	Tryptase after (ng/mL)
1	N	N	N	20.3	20.1	N	N	N	18.6	17.6
2	N	N	N	4.1	4	N	N	N	3.7	4.1
3	N	N	N	11.4	11	N	N	N	11.7	11.2
4	N	N	N	23.2	26.7	N	N	N	25.5	24.9
5	N	N	N	15	14.7	N	N	N	14.8	13.7
6	N	N	N	16.8	18.1	N	N	N	19.1	18
7	Y; headache	N	Paracetamol	17.1	16.5	N	N	N	14.7	12.9
8	N	N	N	74.2	80.9	N	N	N	81.7	67.6
9	N	N	N	34.6	32.5	N	N	N	31.3	29.7
10	N	N	N	NA	NA	N	N	N	NA	NA
11	N	N	N	NA	NA	N	N	N	NA	NA
12	N	N	N	NA	NA	N	N	N	NA	NA
13	Y; shortness of breath	N	N	NA	NA	N	N	N	NA	NA
14	N	N	N	NA	NA	N	N	N	NA	NA
15	N	N	N	NA	NA	N	N	N	NA	NA
16	N	N	N	NA	NA	N	N	N	NA	NA
17	N	N	N	NA	NA	N	N	N	NA	NA
18	N	N	N	NA	NA	N	N	N	NA	NA
19	N	N	N	NA	NA	N	N	N	NA	NA
20	N	N	N	NA	NA	N	N	N	NA	NA
21	N	N	N	NA	NA	N	N	N	NA	NA
22	N	N	N	6.6	5.9	N	N	N	5.5	8.5
23	N	N	N	200	200	N	N	N	200	200
24	N	N	N	122	111	N	N	N	108	112
25	N	N	N	8.3	8.3	N	N	N	8.7	7.7
26	N	N	N	5.2	4.6	N	N	N	4.77	4.62

NA, not available.

injection. We do not know whether the use of preventive AH lowered the risk for anaphylaxis, but the minority of patients who were not receiving regular AH treatment received the PBTV uneventfully as well.

The small cohort limits this study. However, MCDs are rare; thus, uneventful vaccination in 26 patients is significant. The patients in this study were observed by an allergy specialist throughout the vaccination, and we tested the change in STL after injection in more than half of the subjects, reducing the risk for misdiagnosis.

The PBTV is safe and well-tolerated in patients with MCD and can be administered to them with no need for specific measures.

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