

Risk factors for anaphylaxis in patients with mastocytosis

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KEY WORDS

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ABSTRACT

INTRODUCTION Symptoms resulting from the activation and release of mediators from the mast cells are observed in about 30% of the patients with mastocytosis.

OBJECTIVES The aim of the study was to assess the prevalence of anaphylactic reactions and to identify the risk factors for anaphylaxis in patients with mastocytosis depending on the type of the disease. Furthermore, we analyzed a response to treatment of mediator-related symptoms in this patient group.

PATIENTS AND METHODS The study group included 152 adult patients with mastocytosis. The diagnostic workup included a histopathological examination, flow cytometry, *KIT* mutation analysis, and measurement of tryptase levels. The diagnosis of allergy was confirmed by the skin prick test and serum immunoglobulin E levels.

RESULTS The prevalence of anaphylactic reactions in the study group was 50% and was higher in patients with systemic mastocytosis ($P = 0.007$), specifically in its indolent variant ($P = 0.026$), than in patients with cutaneous mastocytosis. The most frequent triggers of anaphylaxis were food (29%), insect stings (22%), and drugs (15%). Tryptase levels were higher in patients with a history of anaphylaxis ($P = 0.029$) as well as in those with symptoms provoked by physical factors ($P = 0.002$). Such symptoms were reported in 112 patients (74%) and were more common in patients with systemic mastocytosis compared with those with cutaneous mastocytosis ($P = 0.026$). The treatment was ineffective in 8 patients (10.5%) and resulted only in partial remission in 14 patients (18.4%).

CONCLUSIONS The study showed a significant incidence of symptoms related to physical factors in patients with mastocytosis and anaphylaxis in history. Risk factors for anaphylaxis included increased serum tryptase levels and indolent variant of systemic mastocytosis. Standard pharmacological treatment was ineffective in 10% of the patients, who may require biological treatment.

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INTRODUCTION Mastocytosis is a group of disorders characterized by an abnormal proliferation and accumulation of atypical mast cells in various organs and tissues including the bone marrow, skin, liver, spleen, lymph nodes, and gastrointestinal tract.¹ Symptoms of mastocytosis are caused by mast cell-derived mediators and, less frequently, by destructive infiltration of the mast cells in tissues. Patients with mastocytosis often suffer from symptoms caused by the activation

and release of mediators from the mast cells, such as generalized itching, redness, headache, abdominal cramps, diarrhea, bone pain or arthritis, hypotension, and shock.² Mast cell mediators released during activation include histamine, proteases (eg, tryptase, chymase, and carboxypeptidase), lipid-derived mediators (eg, cysteinyl leukotrienes, prostaglandin D2).³ The activation of the mast cells might result from an immune response (eg, allergy to food, insect venom, drugs,

latex) or nonallergic mechanisms of hypersensitivity after activation of nonspecific stimuli such as heat, exercise, and stress. Some patients may be diagnosed with idiopathic anaphylaxis or exercise-induced anaphylaxis. Thus, in this group of patients, the presence of clonal proliferation markers of the mast cells should be determined.⁴ It is believed that mast cells in mastocytosis patients may have an intrinsic defect lowering the threshold for activation and/or increasing its sensitivity to allergens.³

Anaphylactic reactions occur in 30% of all patients with mastocytosis and in 50% of patients with systemic mastocytosis (SM).^{3,5,6} Although the incidence of anaphylactic reactions (both immunoglobulin E [IgE]-dependent and IgE-independent) in patients with mastocytosis is significantly higher than in the general population, the frequency of atopy is similar in both populations.⁷ Insect stings are considered a major cause of mast cell activation in patients with mastocytosis. It is estimated that 30% of patients with mastocytosis have anaphylactic reactions due to insect sting,⁶ which are more frequent and more severe than in the general population with insect venom allergies (IVA) (1%–3%).⁸ Non-IgE-mediated IVA are rather rare⁹ although specific IgE and skin tests are more often negative than in the general population with IVA. It was suggested that this phenomenon results from the adsorption of circulating IgE on the surface of numerous mast cells clustered in the tissues.¹⁰

Furthermore, the more severe anaphylaxis may result from the activation of a cascade of intracellular tyrosine kinases: Kit, Lyn, Syk, and Fyn in abnormal mast cells. However, the presence of *KIT* gene mutations, notably D816V, detectable in more than 90% of patients with SM resulting in an increased activation of the mast cells, does not correlate with the severity or the prevalence of anaphylaxis.¹¹ The simultaneous presence of allergy and myeloproliferative disorders is observed also in hypereosinophilic syndromes.¹²

There are scarce data on the frequency of anaphylactic reactions and their risk factors in patients with mastocytosis. The aim of this study was to analyze the prevalence of mast cell activation symptoms ranging from mild symptoms to anaphylaxis and to identify the risk factors in patients with mastocytosis in relation to the type of the disease. Furthermore, we assessed a response to the preventive treatment of mediator-related symptoms in this patient group.

PATIENTS AND METHODS The study group included 152 adult patients (106 women and 46 men aged from 18 to 78 years) treated by the Polish Center of Excellence of the European Competence Network on Mastocytosis in the Department of Allergology, Medical University of Gdańsk, Gdańsk, Poland, between 2004 and 2011. Mastocytosis was diagnosed in accordance with the World Health Organization guidelines, including a pathological examination of the bone

marrow biopsy, examination of the bone marrow aspirate: cytology, immunophenotyping of mast cell expression of CD2 and CD25, activating point mutation of *KIT*, and serum tryptase levels.¹ In subjects without skin lesions who experienced anaphylactic reactions but who met only 1 or 2 minor criteria for SM (excluding increased serum tryptase levels at baseline), monoclonal mast cell activation syndrome (MCAS) was diagnosed.¹³ The differentiation between the subtypes of mastocytosis was performed according to the presence of clinical symptoms caused by tissue or organ infiltration of the mast cell. Cutaneous mastocytosis (CM) was recognized on the basis of typical morphology of skin lesions, positive Darier sign, and histopathology of skin biopsy after exclusion of SM. To evaluate the extent and intensity of cutaneous symptoms, the SCORMA index was used in accordance with a previously described method.¹⁴

Patients were asked by a study physician about any anaphylactic symptoms in their medical history during a medical interview. According to the European Academy of Allergy and Clinical Immunology (EAACI) guidelines, the symptoms of hypersensitivity were grouped into nonallergic and allergic reactions.¹⁵ Anaphylaxis was defined by a sudden onset of a generalized or systemic reaction in accordance with EAACI definitions.¹⁶ The severity of anaphylactic reaction was assessed by the Ring and Messmer scale.¹⁷ Grade I was defined as mild anaphylactic reaction with cutaneous–mucous signs (pruritus, urticaria, angioedema). Grade II was characterized by cutaneous–mucous signs, cardiovascular signs (tachycardia, a decrease in blood pressure by >20 mmHg), respiratory signs (rhinorrhea, hoarseness, dyspnea), alimentary tract signs (nausea, abdominal cramps, diarrhea). Grade III was characterized by cardiovascular collapse, bronchospasm, swelling of the glottis, and cyanosis (severe anaphylactic reactions). Grade IV was characterized by cardiac and respiratory arrest. The anaphylactic reactions were divided into nonimmune and immune reactions, which were subsequently divided into IgE-mediated or mediated by other immunological reactions. The basis of clinical diagnosis in IgE-mediated allergy were well-known diagnostic skin prick tests and allergen-specific IgE levels evaluated together with allergen exposure data.¹⁸ Insect venom allergy was diagnosed in accordance with the EAACI guidelines and included a specific IgE evaluation and both skin and intracutaneous tests in all patients in accordance with the symptoms of insect venom allergy in medical history. Drug hypersensitivity (nonsteroidal anti-inflammatory drugs [NSAIDs], antibiotics, local anesthetics) was diagnosed in accordance with the EAACI/European Network on Drug Allergy guidelines and was confirmed by the skin prick test or intracutaneous test (or both) followed by a drug provocation test (DPT) in a selected group of patients. Before the DPT, an individual risk-to-benefit ratio was estimated. DPTs

TABLE 1 Clinical characteristics of patients with mastocytosis

Characteristics	All	CM	ISM	SSM	ASM	MAS	
male sex	46 (30)	23 (34.8)	21 (27.6)	1 (33.3)	0	1 (25)	
female sex	106 (70)	43 (65.2)	55 (72.4)	2 (66.7)	3 (100)	3 (75)	
age, y	41 (18–78)	37 (18–63)	43 (18–78)	51 (45–57)	59 (52–73)	51 (40–66)	
skin involvement	141 (92.7)	66 (100)	70 (92.1)	3 (100)	3 (100)	0	
tryptase levels	40.8 (1.7–296)	13 (1.7–102)	57.4 (6.6–194)	178 (101–296)	104.7 (101–112)	27 (18.9–33.8)	
<i>KIT</i> mutation	56	32	81	100	100	0	
triggering factors	physical factors	112 (74)	43 (65.1)	62 (81.6)	2 (66.7)	2 (66.7)	3 (75)
	food allergens	44 (29)	15 (22.7)	25 (32.9)	0	1 (33.3)	3 (75)
	insect stings	34 (22)	13 (19.7)	19 (25)	0	0	2 (50)
	drugs	28 (18.4)	10 (15.1)	14 (18.4)	0	1 (33.3)	3 (75)
severity of reactions	grade I	19 (12.5)	9 (13.6)	9 (11.8)	0	0	1 (25)
	grade II	18 (11.8)	5 (7.6)	12 (15.8)	0	0	1 (25)
	grade III	39 (25.7)	11 (16.7)	25 (32.9)	0	0	2 (50)

Data are presented as number (percentage) of patients, percentage of patients, or mean (interquartile range).

Abbreviations: ASM, aggressive systemic mastocytosis; CM, cutaneous mastocytosis; ISM, indolent systemic mastocytosis; MAS, mast cell-activation symptoms; SSM, smouldering systemic mastocytosis

TABLE 2 Characteristics of patients depending on the presence of anaphylaxis

Characteristics	Patients		<i>P</i> value	
	with anaphylaxis	without anaphylaxis		
men	22	24	NS	
women	54	52	NS	
age, y	41.4 (18–73)	40.5 (18–78)	NS	
type of mastocytosis	CM	25 (38)	41 (62)	
	ISM	46 (61)	30 (39)	0.007 ^a
	MAS	4 (100)	0	
	SSM	0	0	
	ASM	0	0	
skin involvement	67 (48)	74 (52)	0.028 ^b	
tryptase levels (mean, range)	43.6 (1.7–192)	38 (2–296)	0.029 ^b	

Data are presented as number (percentage) of patients, percentage of patients, or mean (interquartile range).

- a** incidence of anaphylaxis in patients with ISM compared with patients with CM
b patients with CM, ISM, and MAS

Abbreviations: NS, nonsignificant; others, see **TABLE 1**

were performed with all precaution measures at a hospital clinic. DPT results were positive if they reproduced the original symptoms or objective symptoms of intolerance as urticaria or a drop of at least 20% in forced expiratory volume in 1 second on spirometry.

A response to treatment was assessed by response criteria in accordance with the European Competence Network on Mastocytosis standards.¹

A statistical analysis was performed using the Statistica 10 software (Tulsa, Oklahoma, United States). The χ^2 test, Pearson correlation, Mann–Whitney test, and *t* test were used. The study was approved by the Ethical Committee of the Medical University of Gdansk. Written informed consent was obtained from all study participants.

RESULTS Risk of mast cell mediator-related symptoms: anaphylaxis and physical factor-related symptoms in relation to the types of mastocytosis The study group included 152 prospectively recruited patients with all types of mastocytosis as shown in **TABLE 1**.

SM was diagnosed in 82 patients (54%): indolent systemic mastocytosis (ISM) in 76 (50%), smouldering systemic mastocytosis (SSM), and aggressive systemic mastocytosis (ASM) in 6 (4%). CM was diagnosed in 66 patients (43%) and MCAS, in 4 (3%). There were no grade IV anaphylactic reactions according to the Ring scale in the study group, whereas 19 patients (12.5%) had grade I reaction; 18 (11.8%), grade II; and 39 (25.7%), grade III reaction. The prevalence of anaphylactic reactions in the whole study group was 50%, and in the SM group, 73%. There were no anaphylactic reactions in patients with ASM.

The frequency of reactions was significantly higher in the group of patients with SM (46 patients, 60.5%) compared with those with CM (25 patients, 37.8%) (*P* = 0.007). There was also a difference in the number of anaphylactic reactions between patients with ISM and those with CM (*P* = 0.026). The frequency of anaphylactic reactions was also significantly higher in patients with skin involvement (67 patients, 48%; *P* = 0.028). The characteristics of patients depending on the presence of anaphylaxis are shown in **TABLE 2**.

The most common triggers of mast cell-activation symptoms were physical factors (112 patients, 74%), food allergens (44 patients, 29%), insect stings (34 patients, 22%), and drugs (22 patients, 15%).

The most common risk factors for severe anaphylactic reactions (grades II and III) were *Hymenoptera* stings (34 patients, 22%), followed by food (26 patients, 17%) and drug intake (17 patients, 11%). The most common triggers of mild

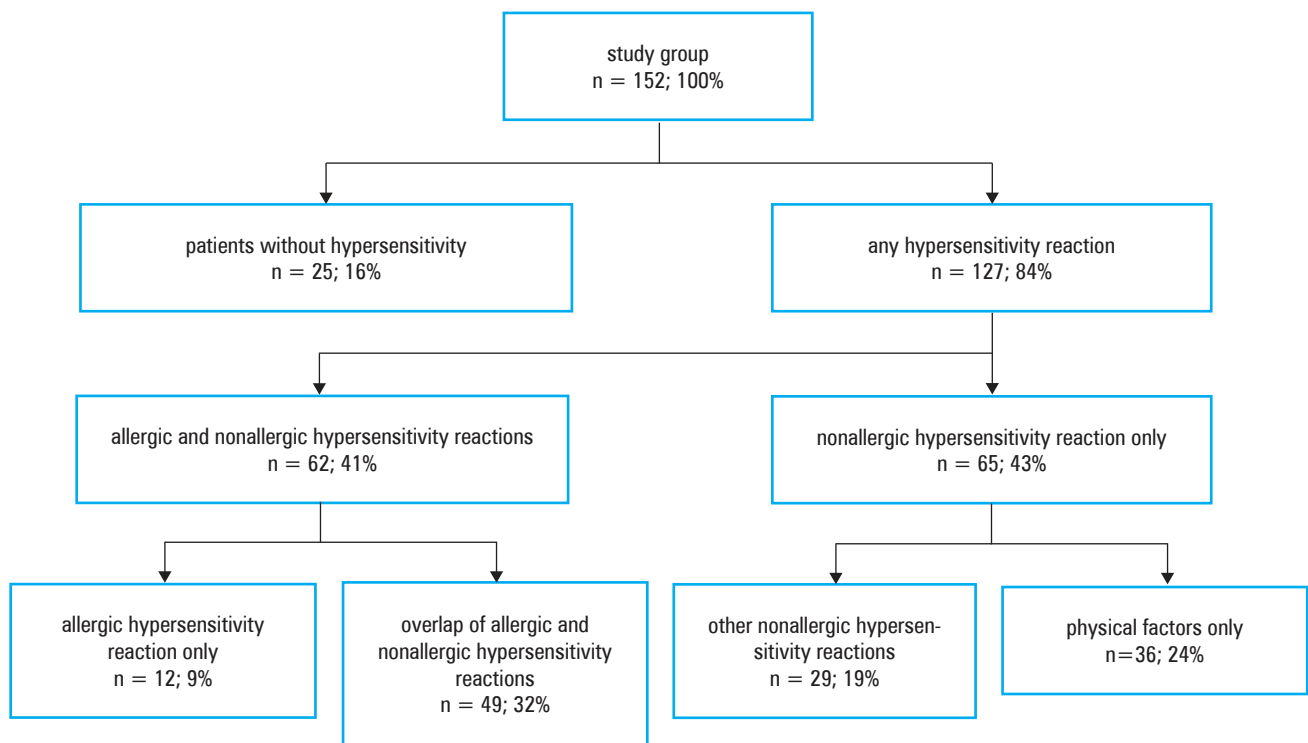


FIGURE 1 Mechanism of hypersensitivity reaction

anaphylactic reactions (grade I) were food (18 patients, 12%) and drugs (5 patients, 3%).

Mechanism of the reaction Hypersensitivity reactions were observed in 127 patients (84%), and allergic hypersensitivity reactions, in 62 cases (41%). The overlap of allergic and nonallergic reactions was found in 49 patients (32%); other factors related to nonallergic hypersensitivity such as food or drug intolerance and physical factors were found in 29 cases (19%). However, the physical factors were the only trigger of symptoms in 36 cases (24%) (FIGURE 1).

The most common causative factors for mast cell-activation symptoms were physical factors reported in 112 patients (74%), while in all 34 patients with clinical symptoms of IVA, the diagnosis of allergy was confirmed. The incidence of reactions to physical factors was higher in patients with anaphylactic reactions in history (66 patients [86%]) in comparison with patients without anaphylaxis (10 patients, 13%) ($P = 0.0002$).

Symptoms of food intolerance were reported in 44 patients (29%), including food allergy diagnosed in 14 patients (9%). However, in the majority of patients (39, 26%) nonimmune hypersensitivity was diagnosed. Most potent food allergens, such as alcoholic beverages (red wine, beer, whisky, brandy), fish, chocolate, fruits (strawberries, citrus fruits), and raw vegetables (carrots, celery, parsley) were negative in both skin prick tests and specific IgE (sIgE) measurement. Thus, we assumed that the reaction was caused by food products rich in histamine rather than allergens. Food allergy was confirmed by the skin prick test and/or sIgE positive results for hazelnut ($n = 4$), meat ($n = 1$), spices ($n = 4$), tomato ($n = 5$), milk

($n = 2$), egg ($n = 2$), and mixed food allergens (assessed by sIgE) ($n = 12$).

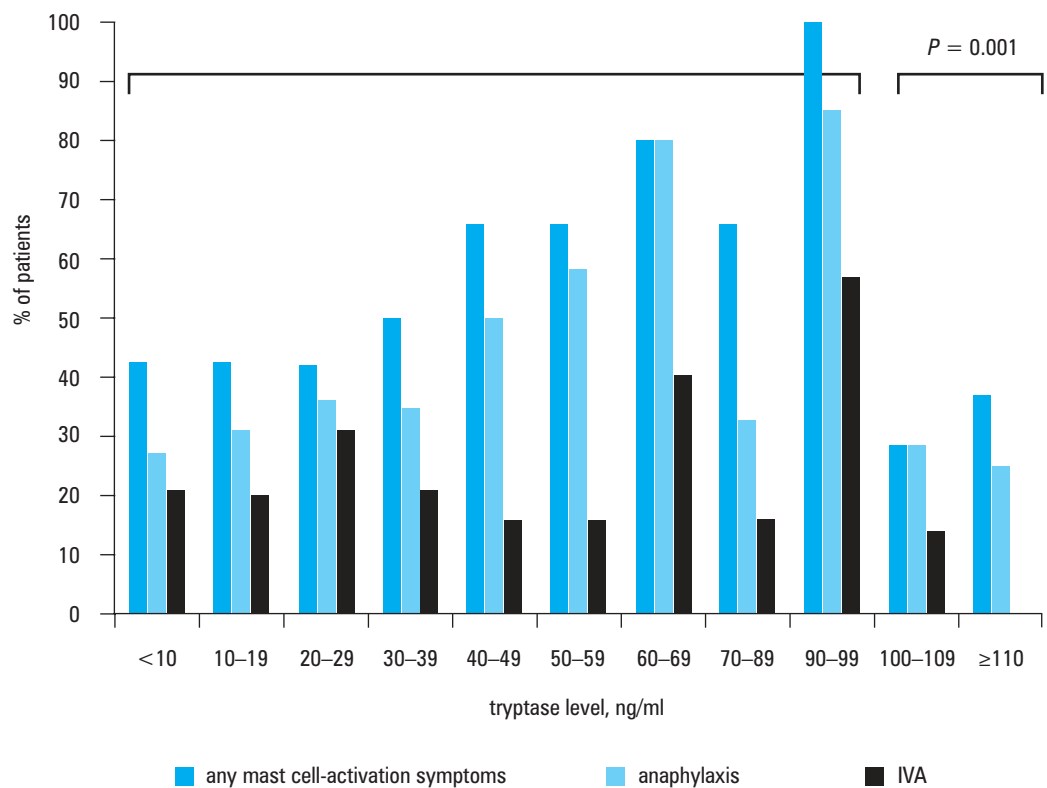
Drug hypersensitivity was diagnosed in 28 patients (18.4%). Drugs causing allergic reactions included NSAIDs ($n = 17$), antibiotics ($n = 9$), local anesthetics ($n = 5$), low-molecular-weight heparin ($n = 2$), and contrast media ($n = 1$).

No differences were found between the type of mastocytosis and the incidence of IgE-mediated anaphylaxis, ie, IVA, food allergy symptoms, food intolerance, and confirmed food allergy.

Identification of risk factors for anaphylaxis Owing to the lack of mast cell-activation symptoms in patients with ASM, the further analysis included 142 patients with ISM and CM only (76 and 66, respectively).

The mean baseline serum tryptase level was higher in patients with anaphylaxis (43.76 ng/ml) compared with patients without anaphylactic reactions (30.02 ng/ml) ($P = 0.029$). However, the risk of mast cell-activation symptoms and increased tryptase levels was observed only among patients with a tryptase level lower than 100 ng/ml ($P = 0.001$). There was only 1 case of anaphylaxis due to insect venom in the group of patients with the tryptase level higher than 100 ng/ml. Anaphylactic reactions were also less prevalent among subjects with a higher tryptase level and more aggressive variants of the disease (FIGURE 2). The higher incidence of anaphylactic reactions was observed in patients with SM ($n = 46$) compared with patients with CM (46 patients vs 25 patients; $P = 0.007$). Patients with SM also had higher serum tryptase levels at baseline ($P = 0.0001$). In addition, tryptase levels were significantly higher in patients with mast cell-activation symptoms

FIGURE 2 Tryptase level and prevalence of anaphylaxis
Abbreviations: IVA, insect venom allergy



provoked by physical factors compared with patients without such symptoms ($P = 0.002$).

Furthermore, the incidence of hypotension was observed more often in patients with SM than in those with CM ($P = 0.03$). The increased frequency of symptoms of mast cell activation depending on physical factors was also higher in SM patients compared with those with CM ($P = 0.026$).

The risk of reaction related to physical triggers was increased in patients with ISM (odds ratio, 2.15; confidence interval, 1.02–4.52). Serum tryptase levels at baseline were higher in patients with mast cell activation caused by physical factors compared with patients without such symptoms ($P = 0.014$). There was no difference in the prevalence of *KIT* mutations among patients with mast cell activation. We hypothesized that there might be a relation between the incidence of mast cell activation triggered by physical factors and skin involvement including the Darier sign as a marker of mast cell degranulation. However, we did not observe any significant differences.

Prevention of mast cell-mediated symptoms The prevention of anaphylaxis was administered according to the EAACI and European Competence Network on Mastocytosis standards.¹ All patients with mastocytosis were treated with antihistamines (H_1 - and H_2 -blockers). A few patients received also other drugs including corticosteroids ($n = 3$) and cromons ($n = 2$). All patients were equipped with an emergency kit. Treatment with epinephrine was prescribed for every patient with anaphylaxis in history and with SM, and patients were trained in proper techniques of self-administration. Venom immunotherapy was started in 26 patients (76.5%) with confirmed allergy to

insect venom ($n = 34$). The remaining 8 patients (24%) are due to start venom immunotherapy in the near future. The treatment was performed according to an ultrarush (wasp) or rush (bee) protocol with a maintenance dose of 100 μ g. According to the guidelines, this should be a lifelong therapy in patients with mastocytosis. To avoid side effects, a pretreatment with antihistamines at high doses (ie, 40 mg of cetirizine per day) was administered. Side effects were reported only in 1 patient, in whom the build-up phase of honeybee venom immunotherapy was complicated by a grade III reaction on the Ring scale (anaphylactic shock). The maintenance treatment was not complicated by any systemic side effects, which confirms that venom immunotherapy may be safely administered in patients with mastocytosis.^{19,20} One patient, who had finished treatment in 2000, was stung 5 years after the completion of therapy and suffered from anaphylactic shock. Once mastocytosis was diagnosed, venom immunotherapy was restarted. The overall response to treatment, which consisted of antihistamines, corticosteroids, cromons and/or venom immunotherapy, in all mastocytosis patients with anaphylaxis in history is presented in TABLE 3. Patients were treated for at least 1 year before the assessment. Our study showed no remission in 8 patients (10.5%), which indicates that they might be candidates for biological treatment (ie, omalizumab, *KIT* inhibitor). In 14 patients (18%), only partial remission was achieved. In 3 patients, responsiveness to treatment was not evaluated because the therapy had just been started.

DISCUSSION Our study showed that half of the patients with mastocytosis had anaphylactic

TABLE 3 Response to prophylactic treatment with venom immunotherapy, antihistamines, cromons, and/or steroids

Type of response	No. of patients	% of anaphylactic patients
complete remission	7	9.2
significant regression	44	57.8
partial regression	14	18.4
no regression	8	10.5

reactions in their medical history. The percentage of reactions was even higher in patients with SM (76%). The risk factors for anaphylaxis were systemic disease and higher tryptase levels. The most common triggers of anaphylactic reactions were *Hymenoptera* stings, food, and medications, similarly to data from previous reports.^{2,6,7} What is novel in our study is that we identified the underestimated triggers of mediator-related symptoms, namely, physical factors. Symptoms of mast cell activation provoked by physical factors were reported in 74% of the patients (n = 112). The prevention of anaphylactic reactions using the EAACI and ECNM guidelines was effective in the majority of patients (89.5%), indicating that biological treatment (currently in clinical studies) may be required in more than 10% of mastocytosis patients with anaphylaxis.

Our results showed that anaphylaxis is more common in patients with mastocytosis (50%) than in the general population where the prevalence ranges from 0.05% to 2%.^{19,20} It is assumed that anaphylaxis is more severe in mastocytosis patients.⁸ The frequency of all anaphylactic reactions was higher in patients with SM compared with those with CM, as reported previously by Brockow et al.⁶ The triggers for severe anaphylaxis were *Hymenoptera* stings, followed by food and drug intake, which did not differ from triggers of anaphylactic reactions in the general population of that age.^{21,22} Mild anaphylactic reactions were caused by food and drugs. However, no differences were found in the prevalence of IgE-mediated anaphylaxis in mastocytosis patients in comparison with the general population except for insect venom allergy. Most of the symptoms caused by food did not result from the IgE-dependent reaction. In a review by Vlieg-Boerstra et al.,²³ it was assumed that food containing a high level of biogenic amines and histamine-releasing components may cause the release of mast cell mediators. Symptoms resulting from mediator release may be related to high mast cell load rather than to increased susceptibility to degranulation.²³ Anaphylaxis caused by drug intake resulted mostly from hypersensitivity to NSAIDs and allergy to antibiotics and local anesthetics. Our results confirmed the data published by Moneret-Vautrin et al.²² that life-threatening anaphylaxis due to medications was triggered mostly by amoxicillin, cephalosporins, and NSAIDs.

Tryptase is a reliable marker of mast cell degranulation and can serve as a surrogate marker of anaphylaxis.²⁴ Increased tryptase levels (lower

than 100 ng/ml) were significantly associated with anaphylaxis in our study and may be considered a risk factor for severe allergic reactions. These data confirmed the previous reports on *Hymenoptera* venom anaphylaxis and increased tryptase levels.^{8,25} The anaphylactic reactions were less prevalent among subjects with a tryptase level exceeding 100 ng/ml and more aggressive forms of the disease. More aggressive forms of the disease are associated with more abnormal and disturbed function of mast cells. In the group of patients with more aggressive forms of mastocytosis, such as SSM or ASM, anaphylactic reactions were suppressed, which is in line with a study by van Anrooij et al.²⁶ Patients might be at an increased risk of a number of fatal anaphylactic reactions induced by exercise, exposure to extremes of temperature or humidity, high pollen counts, fever, or acute infection.¹⁹ Brockow et al.⁶ reported that, in some cases of anaphylaxis, elicitors remained unknown. In mastocytosis patients, clinical symptoms may result from a massive release of mast cell-derived vasoactive mediators.²⁷ In our study, we identified a trigger of allergic reactions in the majority of patients. Additionally, in most patients (74%), we found symptoms of mast cell degranulation, such as flushing, pruritus, headache, abdominal cramps, and hypotension provoked by physical factors such as exercise, rubbing of the skin, heat, cold, and sunlight. In SM, we observed hypotension more often than in CM. Interestingly, in patients with SM, we also found a higher incidence of symptoms of mast cell activation depending on physical factors. In addition, baseline serum tryptase levels were higher in patients with mast cell activation related to physical factors compared with patients without those symptoms. It is assumed that patients with SM or with increased tryptase levels are at a higher risk of anaphylactic reaction. In this study, we also reported a higher incidence of anaphylactic symptoms resulting from mast cell activation depending on physical factors in mastocytosis patients with anaphylaxis in history. In these patients, serum tryptase levels at baseline were higher and the *KIT* mutation was more common, which is in line with the available data. We assume that mast cell-activation symptoms related to physical factors could be a risk factor for anaphylaxis in mastocytosis patients, and these symptoms should be recorded in medical history in every patient with mastocytosis.

There is currently no effective causative therapy for mastocytosis. It generally involves avoidance of trigger factors, targeting symptoms of mast cell-mediated release and allergen-specific immunotherapy for patients with confirmed allergy.²⁸ In a study by Brockow et al.,⁶ the therapy of mastocytosis patients involved the use of antihistamines or corticosteroids (or both) but epinephrine was prescribed only to 11% of adult patients. In other studies, similar results were reported with epinephrine administration from 10% to 16% in patients with an anaphylactic reaction in history.^{29,30}

We suggest that all patients with mastocytosis equip their safety kits with epinephrine until validated tools for predicting the risk of anaphylaxis are introduced into clinical practice.

We assessed the efficacy of the prophylactic treatment of mediator-related symptoms, which was ineffective in 8 patients (10.5%) and resulted only in partial remission in 14 patients (18%). This suggests that, at least in the first group, biological therapy (ie, with omalizumab and *KIT* inhibitor) focused on the mast cells might be considered in the future.

In conclusion, we confirmed a significantly higher incidence of anaphylactic reactions, especially in patients with SM. We also reported a significant incidence of symptoms resulting from mast cell activation related to physical factors in mastocytosis patients with anaphylaxis in history. Our results show that there is a linear correlation between tryptase levels lower than 100 ng/ml and anaphylaxis. Higher tryptase levels are a risk factor for more aggressive variants of mastocytosis and probably a lower risk of anaphylaxis.²⁶ We believe that mast cell-activation symptoms related to physical factors may be a risk factor for anaphylaxis and should be assessed in every patient with mastocytosis. Furthermore, it is possible that even every tenth patient with mastocytosis may be resistant to the currently recommended treatment and might be a candidate for novel biological therapy, which so far has been available only in clinical trials.

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Czynniki ryzyka reakcji anafilaktycznych u chorych na mastocytozę

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SŁOWA KLUCZOWE

anafilaksja, czynniki ryzyka, efektywność leczenia, mastocytoza, mediatorzy

STRESZCZENIE

WPROWADZENIE Objawy wynikające z aktywacji i uwalniania mediatorów z mastocytów są obserwowane u około 30% chorych na mastocytozę.

CELE Celem badania była analiza częstości występowania reakcji anafilaktycznych oraz identyfikacja czynników ryzyka anafilaksji u chorych na mastocytozę w zależności od postaci choroby. Ponadto oceniono odpowiedź na leczenie objawów degranulacji mastocytów u tych chorych.

PACJENCI I METODY Grupa badana obejmowała 152 dorosłych chorych na mastocytozę. Rozpoznanie ustalano na podstawie badania histopatologicznego, cytometrii przepływowej, badania mutacji KIT oraz pomiaru stężenia tryptazy. Rozpoznanie alergii potwierdzono wynikiem punktowego testu skórniego oraz poziomem immunoglobuliny E w surowicy.

WYNIKI Częstość reakcji anafilaktycznych w badanej grupie wynosiła 50% i była większa u chorych na postać układową mastocytozy ($p = 0,007$), zwłaszcza o powolnym przebiegu ($p = 0,026$), niż u chorych z postacią skórną. Najczęstszymi czynnikami wywołującymi anafilaksję były: pokarm (29%), użądlenie przez owady (22%) oraz leki (15%). Stężenia tryptazy były wyższe u chorych z reakcjami anafilaktycznymi w wywiadzie ($p = 0,029$), a także w przypadku występowania objawów spowodowanych czynnikami fizykalnymi ($p = 0,002$). Objawy te stwierdzono u 112 chorych (74%) i występowały one częściej u osób z postacią układową choroby w porównaniu z chorymi z postacią skórną ($p = 0,026$). Leczenie było nieskuteczne u 8 chorych (10,5%) i dało jedynie częściową odpowiedź na leczenie u kolejnych 14 chorych (18,4%).

WNIOSKI W badaniu stwierdzono znaczne występowanie objawów wywołanych czynnikami fizykalnymi u chorych na mastocytozę z reakcjami anafilaktycznymi w wywiadzie. Czynnikiem ryzyka reakcji było stężenie tryptazy w surowicy oraz postać układowa choroby o powolnym przebiegu. Standardowa farmakoterapia była nieskuteczna u 10% chorych, którzy prawdopodobnie wymagają leczenia biologicznego.

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