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Clinical characteristics of pediatric cutaneous mastocytosis and the association with allergic comorbidities and inborn errors of immunity

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Abstract

Objective: Cutaneous mastocytosis (CM) is the most common form of mastocytosis in childhood; however, data on its clinical course and associated allergic and immunologic features remain limited. This study aimed to characterize the clinical phenotype of pediatric CM and to evaluate the frequency of concomitant allergic diseases and inborn errors of immunity (IEI).

Methods: This retrospective study included 17 pediatric patients diagnosed with CM between 2007 and 2025. Demographic characteristics, clinical findings, laboratory parameters, allergic sensitization, immunologic evaluation, and follow-up outcomes were systematically analyzed.

Results: The cohort showed a male predominance (64.7%), with a median age at symptom onset of 14.2 months. Maculopapular cutaneous mastocytosis was the most frequent subtype (82.3%), followed by diffuse CM and solitary mastocytoma. During a median follow-up of 4.5 years, 11.2% of patients achieved complete regression, 47.0% showed partial regression, 35.2% remained stable, and 5.8% exhibited progression. No cases of systemic mastocytosis, anaphylaxis, or mortality were observed.

Eosinophilia was present in 23.5% and hepatosplenomegaly in 11.7% of patients, without evidence of organ dysfunction. Serum immunoglobulin levels and vaccine responses were within normal ranges in all evaluated patients, and no IEI was identified. Elevated IgE levels were detected in 17.6%, while allergic sensitization was documented in 29.4%. Allergic comorbidities were observed in 41.1% of patients, most commonly allergic rhinitis.

Conclusion: Pediatric CM predominantly presents as an early-onset, skin-limited disease with a favorable and often regressive clinical course. The frequency of allergic diseases and sensitization does not appear to be increased compared to the general population, and humoral immune function remains preserved. These findings support a selective, clinically driven approach to immunologic evaluation rather than routine screening in children with CM.

Keywords: Cutaneous Mastocytosis, Inborn Errors of Immunity, Allergic Diseases, Urticaria Pigmentosa, Comorbidity, Pediatric, Primary Immunodeficiency

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Pediatrik Kutanöz Mastositozun Klinik Özellikleri ve Alerjik Komorbiditeler ile Doğuştan Bağışıklık Kusurları Arasındaki İlişki

Öz

Amaç: Kutanöz mastositoz (KM), çocukluk çağında mastositozun en sık görülen formudur; ancak klinik seyri ile ilişkili alerjik ve immünolojik özelliklere dair veriler sınırlıdır. Bu çalışmada pediatrik KM hastalarının klinik fenotipinin tanımlanması ve eşlik eden alerjik hastalıklar ile doğuştan bağışıklık yetmezliklerinin (IEI) sıklığının değerlendirilmesi amaçlanmıştır.

Yöntemler: Bu retrospektif çalışmaya 2007–2025 yılları arasında KM tanısı alan 17 pediatrik hasta dahil edildi. Demografik özellikler, klinik bulgular, laboratuvar parametreleri, alerjik duyarlanma, immünolojik değerlendirme ve izlem sonuçları sistematik olarak analiz edildi.

Bulgular: Olguların %64,7'si erkek olup, semptom başlangıç yaşı medyan 14,2 ay idi. En sık görülen alt tip makülopapüler kutanöz mastositoz (%82,3) olup, bunu diffüz KM ve soliter mastositom izledi. Medyan 4,5 yıllık izlem süresinde hastaların %11,2'sinde tam regresyon, %47,0'sinde parsiyel regresyon gözlenirken, %35,2'si stabil seyretmiş ve %5,8'inde progresyon saptanmıştır. Sistemik mastositoz, anafilaksi veya mortalite izlenmemiştir.

Eozinofili hastaların %23,5'inde, hepatosplenomegali ise %11,7'sinde saptanmış olup organ disfonksiyonu gözlenmemiştir. Tüm hastalarda immünoglobulin düzeyleri ve aşı yanıtları normal sınırlarda bulunmuş, hiçbir hastada IEI saptanmamıştır. Yüksek IgE düzeyi %17,6 oranında görülürken, alerjik duyarlanma %29,4 olarak belirlenmiştir. Hastaların %41,1'inde eşlik eden alerjik hastalık bulunmuş olup en sık alerjik rinit saptanmıştır.

Sonuç: Pediatrik KM genellikle erken başlangıçlı, deri ile sınırlı ve iyi prognozlu bir hastalık olup çoğunlukla stabil veya regrese olan bir seyir göstermektedir. Alerjik hastalık ve duyarlanma sıklığı genel popülasyona kıyasla artmış görünmemekte, humoral immünite korunmuş olarak izlenmektedir. Bu bulgular, KM'li çocuklarda rutin immünolojik tarama yerine klinik bulgulara dayalı seçici bir yaklaşımın daha uygun olduğunu desteklemektedir.

Anahtar kelimeler: Kutanöz Mastositoz, Doğuştan Bağışıklık Kusurları, Alerjik Hastalıklar, Ürtikerya Pigmentoza, Komorbidite, Pediatrik, Primer İmmün Yetmezlik.

INTRODUCTION

Mastocytosis is a heterogeneous group of clonal mast cell disorders characterized by the pathological accumulation of mast cells (MCs) in the skin and/or extracutaneous organs, most notably the bone marrow, spleen, liver, lymph nodes, and gastrointestinal tract. In most cases, the disease is driven by activating mutations in the KIT gene. It is frequently accompanied by a spectrum of mast cell mediator–related symptoms resulting from the release of bioactive mediators such as histamine, tryptase, and prostaglandins[1,2].

Mastocytosis is broadly classified into three major entities: cutaneous mastocytosis (CM), systemic mastocytosis, and the rare but highly aggressive mast cell sarcoma[3]. The diagnosis of CM is primarily based on clinical findings, with the major criterion being the presence of typical skin lesions in association with a positive Darier's sign. In addition, at least one minor criterion should be fulfilled: (i) histopathological evidence of increased mast cell density in lesional skin, or (ii) molecular detection of an activating KIT mutation, most commonly at codon 816, within the affected tissue[1].

In the pediatric population, mastocytosis almost exclusively presents as CM[4]. The classification of CM is based on the morphology, distribution, and age at onset of skin lesions, and it has prognostic implications regarding disease course and symptom burden. The most widely accepted classification includes maculopapular cutaneous mastocytosis (MPCM; also known as urticaria pigmentosa), diffuse cutaneous mastocytosis (DCM), and solitary mastocytoma (SM)[3].

Although the prevalence of atopy and inborn errors of immunity (IEI) in patients with mastocytosis appears to be comparable to that of the general population, the risk of severe mediator-related events, particularly anaphylaxis, is significantly increased[5,6]. However, data regarding the allergic and immunologic profile of pediatric CM remain limited.

In this context, we hypothesized that allergic and immunologic comorbidities may be more prevalent in pediatric CM due to mast cell–driven Th2 polarization. Therefore, the present study aimed to comprehensively characterize the clinical phenotype of children with CM and to determine the prevalence of accompanying allergic and immunologic comorbidities. Furthermore, we sought to evaluate baseline humoral immune function in this population to assess whether routine immunologic screening is warranted in clinical practice.

METHODS

Between January 2007 and June 2025, a total of seventeen pediatric patients presenting with cutaneous lesions clinically compatible with CM and histopathologically confirmed diagnoses were enrolled in this retrospective study conducted at the Department of Pediatric Allergy and Immunology, Fırat University Hospital.

The study population consisted of pediatric patients (aged 0–18 years) with a diagnosis of CM. The diagnosis was confirmed based on the presence of typical skin lesions (e.g., maculopapular, plaque, or nodular) associated with a positive Darier's sign. Skin biopsy was performed in cases where clinical findings were atypical or further histopathological confirmation of mast cell infiltration was required. Exclusion criteria included patients with incomplete clinical data, those lost to follow-up within the first 6 months, and patients with evidence of systemic involvement at the time of initial diagnosis (e.g., significantly elevated basal tryptase levels >20 ng/mL or organ dysfunction). CM was classified in line with the consensus recommended by the World Health Organization (WHO), as modified by Hartmann et al.[1].

The scope of the study was focused on the clinical characterization of pediatric CM and the evaluation of common allergic and immunologic comorbidities. Systematic evaluation included a detailed clinical history, physical examination (including Darier's sign), and baseline laboratory investigations [CBC (complete blood count), serum tryptase, and biochemistry]. A targeted immunological assessment was performed through measurement of serum immunoglobulin levels (IgG, IgA, IgM, IgE) and anti-HBs vaccine titers. Patients were clinically monitored for signs of immunodeficiency, such as recurrent or severe infections. Advanced immunological investigations were reserved only for patients with a clinical suspicion of primary immunodeficiency. CBC parameters were evaluated using the age-specific reference intervals provided in the Nelson Textbook of Pediatrics[7]. Serum immunoglobulin levels (IgG, IgA, and IgM) were interpreted according to the age-related reference ranges established for healthy Turkish children by Bayram et al.[8].

Demographic variables encompassed sex, age at symptom onset, age at diagnosis, parental consanguinity, family history, and the presence of concomitant allergic or immunologic comorbidities. Clinical parameters included the morphology, distribution, and extent of cutaneous lesions, the presence of dermographism and Darier's sign, associated clinical symptoms, and disease severity evaluated using the Scoring Index of Mastocytosis (SCORMA). Additionally, abdominal ultrasonography (USG), administered treatments, follow-up period, disease course, occurrence of anaphylaxis,

transformation to systemic mastocytosis, and mortality were recorded.

Laboratory evaluations were performed at baseline. Allergy work-up was indicated for patients presenting with clinical symptoms suggestive of IgE-mediated hypersensitivity (e.g., rhinitis, asthma, urticaria, or food-related reactions) or those with elevated total IgE levels. Skin prick testing (SPT) was performed using a standardized panel of common aeroallergens (house dust mites, pollens, molds, animal dander) and food allergens (milk, egg, wheat, nuts) where clinically relevant. A wheal diameter ≥3 mm greater than the negative control (saline) was defined as a positive result. Serum-specific IgE (sIgE) levels were measured using the ImmunoCAP system, with a positivity threshold defined as ≥0.35 kU/L. The diagnostic work-up prioritized food sensitization in children under 2 years of age, while the evaluation focused primarily on aeroallergen sensitization in children over 2 years of age, in accordance with age-related clinical relevance. Serum total tryptase levels were measured using a fluoroenzyme immunoassay (FEIA) on the Phadia™ 250 platform (Thermo Fisher Scientific, Uppsala, Sweden). Immunological assessments, including serum immunoglobulin levels (IgG, IgA, IgM), were performed using nephelometry on the BN™ II System (Siemens Healthineers, Erlangen, Germany). Specific IgE (sIgE) and total IgE measurements were conducted using the ImmunoCAP™ system (Thermo Fisher Scientific, Uppsala, Sweden). Skin prick testing (SPT) was performed on the volar aspect of the forearm using standardized allergenic extracts (Apither, Spain). Histamine dihydrochloride (10 mg/mL) and sterile saline were used as positive and negative controls, respectively. Diagnostic sensitivity was ensured by using sterile, disposable lancets for each application, and results were recorded 15 minutes after testing.

Clinical variables, including lesion morphology, distribution, and the presence of a positive Darier's sign, were assessed by a pediatric allergist at the time of initial diagnosis. For patients with a follow-up duration exceeding one year, clinical course and symptomatic control were re-evaluated during annual clinical visits. The severity of skin involvement was objectively assessed using the SCORMA at the time of initial diagnosis (baseline). The score was calculated based on three parameters: the extent of skin involvement (A, using the 'rule of nines'), the intensity of the lesions (B, including pigmentation, vesiculation, and Darier's sign), and subjective symptoms (C, such as pruritus and flushing). The final score was determined by a pediatric allergist using the standard formula SCORMA = A/5 + 5B + C. For patients with prolonged follow-up, SCORMA was periodically re-evaluated to monitor clinical progression or regression. The clinical course of the disease was categorized into four operational definitions: Complete Regression: Total disappearance of all skin lesions and a negative Darier's sign. Incomplete Regression: A significant reduction in the number, size, or pigmentation of skin lesions without total disappearance. Stable Disease: No significant change in the number or appearance of skin lesions and stability of symptomatic findings during the follow-up period. Progression: An increase in the number or extent of skin lesions, or evidence of systemic involvement (e.g., persistent organomegaly or significantly rising serum tryptase levels).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics Version 27.0. All data were primarily analyzed using descriptive statistics. Categorical variables were expressed as frequencies (n) and percentages (%), while continuous variables (e.g., age at diagnosis, SCORMA scores, and follow-up duration) were presented as median and range (minimum–

maximum). Given the descriptive nature of the study and the cohort size, formal hypothesis testing between subgroups was limited, and findings were reported as observational.

Informed consent was obtained from all patients included in the study. Ethical approval was granted by the Non-Interventional Research Ethics Committee of Fırat University on September 4, 2025 (approval number: 2025/12-10).

RESULTS

General Characteristics

The patient cohort exhibited a male predominance, comprising 64.7% (n=11) males and 35.2% (n=6) females. The onset of symptoms occurred before 2 years of age in 82.3% (n=14) of the cases, with a median age of onset calculated as 14 (range: 0–48) months. One case presented with symptoms in the neonatal period. Parental consanguinity was observed in 23.5% (n=4), and a family history of mastocytosis was reported in 11.7% (n=2) of the cases (Table I).

Table I: Demographic and prognostic characteristics

Patient ID	Age Onset (months)	Sex	Consanguinity	Family History	Tryptase (µg/L)	Organomegaly	Prognosis	Treatment
P1	12	M	-	-	4.59	-	Incomplete Regression	AH
P2	0	M	-	-	2.39	-	Complete Regression	AH, TT
P3	25	M	-	-	5.09	-	Incomplete Regression	AH, TT
P4	6	F	-	-	4.1	-	Incomplete Regression	AH
P5	30	M	-	+	2.86	-	Incomplete Regression	AH, TT
P6	14	F	-	+	2.9	-	Incomplete Regression	AH
P7	8	M	-	-	16.9	-	Incomplete Regression	AH, TT, LTRA
P8	10	M	-	-	5.96	-	Stable	AH, TT, LTRA
P9	11	M	-	-	2.99	HSM	Incomplete Regression	AH, LTRA
P10	22	M	+	-	5.15	-	Stable	AH
P11	18	F	-	-	3.78	-	Stable	AH, TT
P12	7	M	-	-	6.47	-	Worsening	AH
P13	6	M	+	-	4.45	HSM	Complete Regression	AH, TT
P14	6	M	-	-	2.86	-	Stable	AH
P15	12	F	+	-	3.79	-	Stable	AH
P16	48	F	-	-	15.6	-	Incomplete Regression	AH, TT
P17	8	F	+	-	11.9	-	Stable	AH

Abbreviations: AH: Antihistamine; F: Female; HSM: Hepatosplenomegaly; LTRA: Leukotriene Receptor Antagonist, M: Male; TT: Topical Treatment; +: Yes; −: No.

MPCM was the predominant clinical form, observed in 82.3% (n=14) of patients, whereas DCM and SM were identified in two (11.7%) and one patient, respectively (Figure 1). The morphology of the lesions varied, with 76.4% (n=13) presenting as macules, papules, plaques; 17.6% (n=3) as bullous lesions (Figure 2), and 5.8% (n=1) as nodular lesions. Among MPCM cases, the lesions were polymorphic in 64.7% (n=9) and monomorphic in 35.7% (n=5) (Figure 1). The median number of lesions was 27 (range: 0–286). Darier's sign (Figure 3) was positive in 88.2% (n=15) of the patients, whereas dermatographism was absent in all. The median SCORMA score was 14.5 (range: 0–49.2). (Table II). An increased count of CD117-positive mast cells was detected in skin biopsies of 41.1% (n=7) of the patients. The clinical course was evaluated over a median follow-up period of 4.5 years (range: 1.2–18.0 years).

Table II: Skin Lesion Characteristics

Patient	WHO Classification	MPCM Lesion Morphology	Lesion Type	Lesion Darier	SCORMA
P1	MPCM	Polymorphic	MP, Plaque	2	+	5.9
P2	MPCM	Polymorphic	MP, Plaque	3	+	9.5
P3	MPCM	Monomorphic	MP, Plaque	1	+	8.6
P4	MPCM	Polymorphic	MP	3	-	9.5
P5	MPCM	Polymorphic	MP, Plaque	9	+	9.2
P6	MPCM	Monomorphic	MP, Plaque	0	+	1
P7	MPCM	Monomorphic	MP	28	+	35
P8	DCM	-	Bullous	286	+	49
P9	MPCM	Polymorphic	MP, Plaque	16	+	18
P10	MPCM	Polymorphic	MP, Bullous	15	-	8.6
P11	MPCM	Polymorphic	MP	5	+	14
P12	MPCM	Polymorphic	MP, Plaque	25	+	11
P13	DCM	-	MP, Bullous	25	+	12
P14	MPCM	Monomorphic	Nodular	1	+	13
P15	MPCM	Polymorphic	MP	8	+	19
P16	SM	-	MP, Plaque	1	+	0
P17	MPCM	Monomorphic	MP, Plaque	35	+	24

Abbreviations: MPCM: Maculopapular Cutaneous Mastocytosis; DCM: Diffuse Cutaneous Mastocytosis; MP: Maculopapular; SCORMA: Scoring Index of Mastocytosis; SM: Solitary mastocytoma; WHO World Health Organization; +: Yes; −: No.

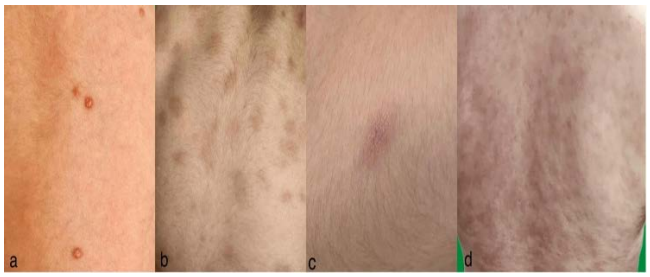

Figure 1: Cutaneous mastocytosis types

a: Maculopapular cutaneous mastocytosis (Monomorphic)

b: Maculopapular cutaneous mastocytosis (Polymorphic)

c: Solitary Mastocytoma

d: Diffuse cutaneous mastocytosis

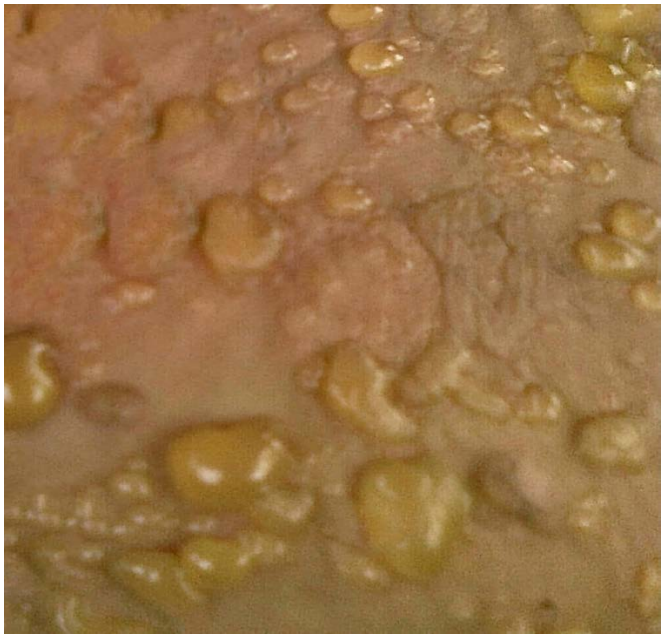

Figure 2: Diffuse cutaneous mastocytosis with bullous lesions

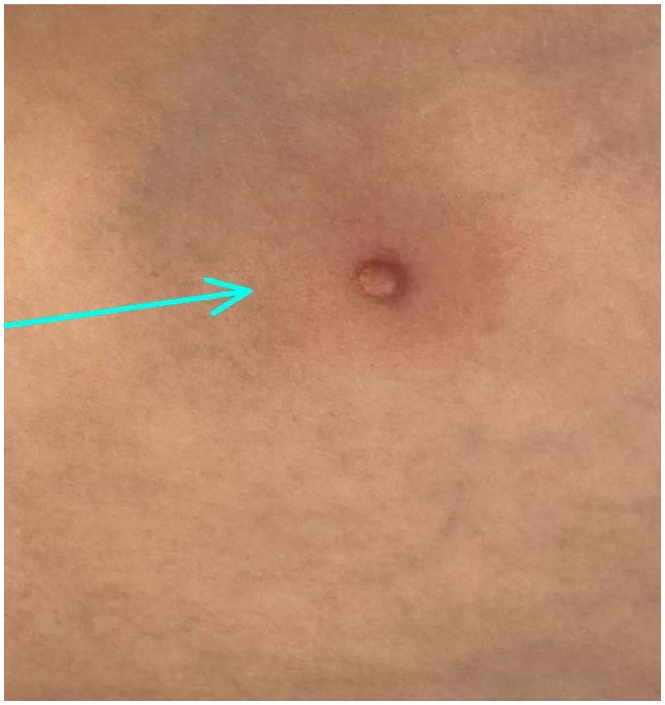

Figure 3: Darier's sign (turquoise arrow)

During this period, the disease progression was primarily stable or regressive: 11.7% (n=2)

achieved complete regression, 47.0% (n=8) showed incomplete regression, and 35.2% (n=6) maintained a stable course. Only one patient (5.8%) experienced an increase in lesion count. Abdominal ultrasonography demonstrated hepatosplenomegaly in 11.7% (n=2) of patients, without any associated organ dysfunction or severe symptoms. No lymphadenopathy was observed. The median serum tryptase level was 5.90 (range: 2.39–16.9) µg/L. An elevated tryptase level (>8 µg/L) was detected in 17.6% (n=3) of patients. Importantly, no systemic mastocytosis transformation or anaphylaxis was observed. Of the patients with elevated tryptase, 66.6% (n=2) had monomorphic lesions. The overall prognosis was benign, and no fatal outcomes were recorded. The most common treatment employed was antihistamines, supplemented by montelukast, topical emollients, and topical corticosteroids, which provided adequate symptom control (Table I).

Allergic and Immunological Characteristics

CBC revealed no abnormalities except for eosinophilia, which was detected in 23.5% (n=4) of the cases. Regarding immune status, all immunoglobulin G, A, and M levels were within age-appropriate reference ranges. Anti-HBs vaccine titers were positive (>10 mIU/mL) in all 12 patients assessed. Elevated IgE levels were found in 17.6% (n=3) of the patients. No clinical evidence suggestive of IEI was detected. Concomitant allergic comorbidities were identified in 41.1% (n=7) of the patients. Allergic rhinitis was the most prevalent (23%, n=4), followed by atopic dermatitis, food allergy, drug allergy, and infantile asthma. Allergic sensitization, confirmed by skin prick test and/or serum-specific IgE, was observed in 29.4% (n=5) of the patients (Table III).

Table III: Allergic and Immunological Characteristics

Patient ID	Allergic Disease	SPT (*)	sIgE (*)	#EOS (×10⁹/L)	IgG (g/L)	IgA (g/L)	IgM (g/L)	IgE (IU/mL)	Anti-HBs (mIU/mL)
P1	-	-	-	0.35	4.63	0.29	0.5	32.2	54.5
P2	-	-	-	1.08	3.62	0.3	0.24	2.33	16.8
P3	Allergic rhinitis, Atopic dermatitis, Drug hypersensitivity	-	+	0.68	4.52	0.32	0.61	27.5	28.7
P4	Drug hypersensitivity	-	-	0.21	11.6	0.39	1.37	16.7	944
P5	Allergic rhinitis, Infantile asthma	-	-	0.32	8.97	0.35	0.42	198	NA
P6	-	-	-	0.17	7.65	0.33	0.58	2.35	NA
P7	-	-	-	0.36	4.93	0.65	0.6	2.16	>1000
P8	Allergic rhinitis, Food allergy	+	-	0.55	6.87	0.36	0.97	24.2	NA
P9	-	-	+	0.14	9.67	1.11	0.73	2.37	28.6
P10	-	-	-	0.31	11.3	1.42	0.72	7.06	14.5
P11	Atopic dermatitis, Food allergy, Drug hypersensitivity	+	-	0.32	10.2	0.45	0.66	92.4	181
P12	-	-	-	0.4	3.25	0.3	0.59	69.6	>1000
P13	Allergic rhinitis	+	-	0.29	10.7	1.23	0.84	369	NA
P14	Atopic dermatitis, Food allergy	-	-	0.02	3.94	0.34	0.3	53.6	1000
P15	-	-	-	0.19	4.5	0.35	0.4	11.7	NA
P16	-	-	-	0.13	9.18	0.95	1.01	2.86	186
P17	-	-	-	0.55	7.77	1.37	0.58	4.48	13.6

Abbreviations: IEI: Inborn Error of Immunity; NA: Not Available; SPT: Skin Prick Test; sIgE: Specific IgE; #EOS: Absolute Eosinophil Count; +: Yes; −: No.

(*)Food sensitivity was examined in children under 2 years of age, and aeroallergen sensitivity in children over 2 years of age.

DISCUSSION

Pediatric CM is a rare, typically benign, and self-limiting condition characterized by skin lesions and a positive Darier's sign[3]. Although allergic comorbidities may occur, our findings demonstrate that humoral immune function is generally preserved. These results suggest that routine, extensive immunologic screening may not be necessary in all patients and should instead be guided by clinical indication, thereby reducing unnecessary healthcare burden. To our knowledge, this is one of the few studies evaluating both allergic and immunologic profiles in pediatric CM.

In line with previous reports, MPCM was the predominant subtype in our cohort, followed by DCM and SM[3]. This distribution is consistent with established pediatric series. Characteristic lesions in DCM may present as maculopapular, nodular, bullous, or generalized erythrodermic forms, typically with a yellow–orange appearance, and bullous lesions were observed in 17.6% of our patients[9].

Our cohort demonstrated a clear male predominance and early disease onset, with most patients presenting before two years of age. These findings are consistent with prior studies indicating that pediatric CM is typically an early-onset condition with a slight male predominance[10]. Although familial clustering is uncommon, the presence of parental consanguinity and a positive family history in a subset of patients is in line with previous reports suggesting a potential genetic contribution in selected cases[11].

Disease severity was generally mild, as reflected by low SCORMA scores. Histopathological evaluation confirmed increased dermal mast cell density, demonstrated by CD117 positivity, fulfilling established diagnostic criteria[12]. Darier's sign was present in most patients, supporting its continued value as a clinical hallmark of CM[13].

Serum tryptase levels exceeded 8 μg/L in 17.6% of cases; however, no patient progressed to systemic mastocytosis during follow-up. Notably, most patients with elevated tryptase levels exhibited monomorphic MPCM lesions, supporting previous observations linking monomorphic morphology with increased mast cell burden[14]. In contrast, patients with earlier disease onset tended to have normal tryptase levels, consistent with prior reports[15]. These findings further support the role of serum tryptase as a useful, albeit non-specific, marker for disease burden and follow-up rather than a reliable predictor of systemic involvement[16].

Clinical features remain central to risk stratification in pediatric CM. Extensive skin involvement, persistently elevated tryptase levels, and organomegaly have been associated with an increased risk of mediator-related symptoms and potential systemic disease[4]. In our study, hepatosplenomegaly was observed in a small number of patients without associated clinical deterioration, and invasive procedures such as bone marrow examination were not indicated, in accordance with current recommendations reserving such investigations for selected high-risk patients[17].

Treatment was primarily symptomatic and achieved adequate disease control with antihistamines, topical therapies, and leukotriene receptor antagonists, consistent with current management strategies[18]. Spontaneous improvement is a well-recognized feature of pediatric CM4, and in our cohort, most patients demonstrated either regression or disease stability over time.

Mast cells are central effectors in allergic inflammation and Th2 polarization, contributing to chronic conditions such as asthma and atopy, as well as life-threatening anaphylaxis[19,20]. While MCs are also implicated in immune homeostasis and the pathogenesis of certain IEIs[21,22], their specific role in the clinical interplay between CM and allergic diathesis

remains complex. Interestingly, our findings suggest that the prevalence of allergic comorbidities in pediatric CM does not exceed that of the general population. Although the present study is limited by the absence of a prospective healthy control group, the observed prevalence of allergic comorbidities (41.1%) and allergic sensitization (29.4%) aligns with established epidemiological data for the general pediatric population[5,6]. These findings support the hypothesis that mastocytosis does not inherently predispose patients to de novo IgE-mediated sensitization. Instead, the clinical interplay likely involves an amplification of mediator-related symptoms when independent allergic triggers and mast cell expansion coexist, rather than a direct causal link between mastocytosis and the development of atopy.

All patients in the present study demonstrated normal age-adjusted immunoglobulin (IgG, IgA, IgM) levels and adequate vaccine responses, as evidenced by positive anti-HBs titers. These findings are consistent with previous reports indicating generally preserved humoral immunity in CM and support the recommendation that routine immunologic evaluation should be reserved for clinically indicated cases[23]. Elevated IgE levels were identified in a subset of patients, all of whom had concomitant allergic comorbidities, in line with previous observations[10]. Although mastocytosis has been associated with hematologic malignancies[24], no such cases were identified in our study. Apart from mild eosinophilia observed in some patients, complete blood counts were otherwise unremarkable.

The prevalence of food allergy and other atopic conditions in pediatric mastocytosis is generally comparable to that of the general population; however, these patients have a significantly increased risk of anaphylaxis[5,6]. High-risk groups include patients with diffuse skin involvement, persistently elevated tryptase levels, or a history of prior anaphylaxis, for whom epinephrine auto-injectors are recommended[5,6]. Although food-related reactions are frequently reported, specific IgE sensitization is confirmed in only a minority of cases[25], and unnecessary dietary restrictions should be avoided unless a true allergy is objectively demonstrated[26]. Importantly, mastocytosis itself does not directly cause food or drug allergy but may increase the severity of reactions due to an increased mast cell burden[27].

Notably, no episodes of anaphylaxis were observed in this current research despite the inclusion of patients with diffuse disease. This may be related to relatively low baseline tryptase levels (median 5.90 μg/L) and the limited sample size. Overall, the predominantly stable or regressive disease course observed in our study is consistent with the known natural history of pediatric CM[4] and supports its generally favorable prognosis.

Our findings demonstrate that although mast cells are central to allergic inflammation, they do not appear to compromise overall immune competence in pediatric CM. The preserved immunoglobulin profiles and adequate vaccine responses further support a clinically guided, rather than routine, approach to immunologic evaluation.

Clinical Implications

The findings of this study have significant implications for the clinical management and economic burden of pediatric cutaneous mastocytosis. Our data demonstrate that humoral immune function is characteristically preserved in these patients, with immunoglobulin levels and vaccine responses remaining within age-appropriate reference ranges. Consequently, we propose that routine, extensive immunological screening in asymptomatic children with CM is not clinically warranted. Shifting from a routine to a

clinically-guided diagnostic approach can prevent unnecessary laboratory investigations, reduce healthcare costs, and alleviate the emotional stress on families associated with invasive testing. These results advocate for a more targeted and cost-effective management strategy, prioritizing advanced investigations only for patients presenting with recurrent infections or clinical red flags for inborn errors of immunity.

CONCLUSION

In conclusion, pediatric cutaneous mastocytosis is predominantly a skin-limited disorder with a favorable clinical course. Although allergic comorbidities may be present, humoral immune function remains intact in most patients. Therefore, immunologic evaluation should be guided by clinical findings rather than performed routinely, allowing for a more targeted and cost-effective approach in clinical practice.

Strengths and Limitations

The strengths of this study include the comprehensive clinical characterization of pediatric CM with histopathologically confirmed diagnoses. The integration of standardized disease severity scoring, detailed allergic evaluation, and a targeted assessment of baseline humoral immunity through immunoglobulin levels and vaccine responses enhances the clinical relevance of our findings. In addition, the longitudinal follow-up enabled the assessment of disease course, progression, and clinical outcomes over time.

However, several limitations should be acknowledged. First, the retrospective design and relatively small sample size—largely attributable to the rarity of pediatric CM—may limit the generalizability of the results. Second, the single-center nature of the study and the absence of a control group may restrict the external validity and comparative interpretation of the findings. Furthermore, molecular analysis of KIT mutations, which constitutes an important component of the diagnostic and prognostic evaluation in mastocytosis, could not be performed in the present study due to technical and financial constraints. The absence of mutational data limits the ability to establish genotype–phenotype correlations and represents an additional constraint of the study.

Ethics Committee Approval: Ethical approval was granted by the Non-Interventional Research Ethics Committee of Fırat University on September 4, 2025 (approval number: 2025/12-10).

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