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Cases of Childhood Mastocytosis: A Single Center Experience

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Abstract: Cutaneous mastocytosis, primarily affecting children, is confined to the skin and generally carries a good prognosis. In our study, we aimed to evaluate the clinical findings, laboratory values and treatment-related data of 10 patients who were followed up with a diagnosis of mastocytosis in our clinic between 2014 and 2022. Age, gender, family history, clinical findings, type of lesions, laboratory values and treatment-related data of the patients were analyzed within the scope of the study. Skin biopsy was taken from clinically suspected patients and the diagnosis was made with histopathologic confirmation. Histopathologic diagnosis was made by demonstration of mast cells showing metachromasia with toluidine blue in full-thickness skin biopsy. The median age at presentation was 10.0 months (min-max: 1.0-117.0). While rash and pruritus were the most common complaints seen in all patients; erythema was seen in 9 (90%) patients. The most common rash type was maculopapular. One (10.0%) patient had nodules and mastocytoma. When the laboratory findings of the patients were evaluated, no patient had thrombocytopenia or leukopenia. One patient had anemia. The median value of total IgE values was 65.0 IU/ml (8.0-1719.0). In our study, all patients had symptoms of rash and pruritus. The most common lesion type in our study was maculopapular rash (UP type) seen in 4 patients (40%). Nodules and mastocytoma (NM type) were seen in 1 patient (10%). In our study covering an eight-year period, all of our patients had cutaneous mastocytosis and none of them had systemic involvement. ©2024 NTMS.

Keywords: Mastocytosis; Rash; Urticaria Pigmentosa.

1. Introduction

Mastocytosis is an uncommon and diverse disorder marked by the abnormal proliferation and activation of morphologically and immunophenotypically atypical mast cells (MCs) in different tissues, such as bone marrow, lymph nodes, liver and spleen. This condition is notably observed in the skin (cutaneous mastocytosis-CM) and internal organs (systemic mastocytosis-SM) [1-3]. The classification by WHO categorizes cutaneous mastocytosis (CM) into three primary groups: maculopapular cutaneous

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mastocytosis (MPCM), diffuse cutaneous mastocytosis (DCM), and cutaneous mastocytoma only. Cutaneous mastocytosis, primarily affecting children, is confined to the skin and generally carries a good prognosis. If cutaneous mastocytosis (CM) comprises three or fewer lesions, they are identified as mastocytomas, whereas maculopapular cutaneous mastocytosis (MPCM) is defined by the presence of 4 to 100 lesions. The diffuse cutaneous mastocytosis (DCM) classification encompasses widespread skin involvement [4-6].

Mast cells arise from the bone marrow and travel in a precursor state to connective tissue, where they fulfill diverse functions. Although pediatric mastocytosis is typically viewed as a sporadic condition, a few uncommon familial cases have been documented [7-9]. Despite some progress, the precise pathogenesis remains inadequately comprehended. Clinical manifestations and course of mastocytosis are examined under two main categories as 'childhood (pediatric)' and 'adult-onset' depending on the age of onset. Generally, childhood mastocytosis is diagnosed before the age of two years and the most common type of childhood mastocytosis is characterized by a skin disease called urticaria pigmentosa (UP) [10]. Lesions develop in the first year of life in 60-80% of patients. Mastocytoma and UP lesions can be seen even at birth [11-12].

Cases of cutaneous mastocytosis (CM) can lead to symptoms related to mast cell (MC) mediators, either locally and/or systemically. Flushing is a commonly observed symptom, while cyanosis, respiratory arrest, arterial hypotension and anaphylactic reactions are less frequent in maculopapular cutaneous mastocytosis (MPCM). Additionally, CM cases may manifest with gastrointestinal symptoms, such as abdominal pain, diarrhea, hyperacidity or peptic ulcers [4]. In instances of (solitary) mastocytomas or polymorphic MPCM with nodular dermal lesions or plaque, blistering may seldom develop in early childhood period, especially in response to mechanical irritation, but typically recovers without leaving a scar [6].

In cases of mastocytosis in adults, the causes of anaphylaxis vary compared to pediatric cutaneous mastocytosis (CM). In two-thirds of pediatric cases, a specific trigger cannot be identified, leading to idiopathic anaphylaxis. Food allergies have been reported in 10-20% of cases, drugs in less than 10% and toxic animals do not seem to be the primary triggers of anaphylactic reactions in children as much as in adults [6].

In our study, we aimed to evaluate the clinical findings, laboratory values and treatment-related data of 10 patients who were followed up with a diagnosis of mastocytosis in our clinic between 2014 and 2022.

2. Material and Methods

2.1. Study Type and Design

Our descriptive study was carried out by retrospective examination of the database of Istanbul Umraniye Training and Research Hospital. The files of 10 patients diagnosed with mastocytosis between 2014 and 2022 were retrospectively evaluated. This study was conducted in accordance with the Declaration of Helsinki and informed consent was obtained from all participants.

2.2. Evaluation

Patients with diagnosis code Q82.2 were identified. Age, gender, family history, clinical findings, type of lesions, laboratory values and treatment-related data were analyzed in the study. Mastocytosis was classified according to WHO. The WHO classification distinguishes three main manifestations: maculopapular cutaneous mastocytosis (MPCM), diffuse cutaneous mastocytosis (DCM) and cutaneous mastocytoma. MPCM is defined as urticaria pigmentosa [13]. Skin biopsy was obtained from clinically suspected patients and the diagnosis was made with histopathologic confirmation. Histopathologic diagnosis was made by observation of mast cells showing metachromasia with toluidine blue on full-thickness skin biopsy [14]. Patients were evaluated with complete blood count, liver and renal function tests and abdominal ultrasonography for systemic mastocytosis involvement and referred to pediatric hematology and oncology.

2.3. Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 25.0 was used for data recording. Normal distrubition was evaluated with *Kolmogorov Smirnov test and* the *Shapiro-Wilk tests.* Descriptive results were presented with median, minimum, maximum values, numbers (n), and percentages (%).

2.4. Ethics

Ethics committee approval was obtained from the Ethics Committee of Umraniye Training and Research Hospital with decision number 26 on February 23, 2023 for the conduct of the study.

3. Results

The data of 10 pediatric cases with mastocytosis were evaluated in the study. All ten patients had cutaneous mastocytosis. None of the patients had systemic findings. Six (60.0%) of the patients were male and 4 (40.0%) were female. Family history was positive in one (10.0%) patient. The median age at presentation was 10.0 months (min-max: 1.0-117.0). While rash and pruritus were the most common complaints in all patients, erythema was observed in 9 (90%) patients. Abdominal pain, reflux, diarrhea, myalgia and bone pain were other symptoms. The most common rash type was maculopapular. One (10.0%) patient had nodules and mastocytoma (Table 1).

Four (40%) patients had additional allergic diseases. The diagnoses of the four patients with comorbidities were allergic rhinitis, allergic rhinitis and atopic dermatitis, asthma and atopic dermatitis, allergic rhinitis and food allergy, respectively.

When the laboratory findings of the patients were evaluated, there were no patients with thrombocytopenia or leukopenia. One patient had anemia. The median value of total IgE values was 65.0 IU/ml (8.0-1719.0). The median AST and ALT values were 27.0 (18.0-52.0) and 19.0 (11.0-50.0), respectively. Immunoglobulin values and other laboratory data are given in Table 2.

Table 1: Clinical characteristics and demographic data of the patients.

		Median (min-max)
Age at onset of symptoms (months)		10.0 (1-117.0)
Age at diagnosis (months)		33.0 (8-120.0)
		N (%)
Positive family history		1 (10.0)
Gender	Male	6 (60.0)
	Female	4 (40.0)
Complaints	Rash	10 (100.0)
	Itching	10 (100.0)
	Redness	9 (90.0)
	Reflux	5 (50.0)
	Diarrhea	1 (10.0)
	Abdominal pain	1 (10.0)
	Vomiting	1 (10.0)
	Muscle pain	1 (10.0)
	Bone pain	1 (10.0)
Lesion size	≤1 cm	7 (70.0)
	>1 cm	3 (30.0)
Lesion type	Maculopapular rash	4 (40.0)
	Macular rash	3 (30.0)
	Nodule and mastocytoma	1 (10.0)
	Papular rash	1 (10.0)
	Macular rash and plaque	1 (10.0)
Treatment	Antihistamines and humidifiers	10 (100)
	Montelukast	1 (10.0)

Antihistamines and humidifiers were used in the treatment of all patients, while montelukast was additionally used in one patient. Prophylactic medication was used in 7 patients (70.0%). Antihistamines and montelukast were used in prophylaxis in one patient.

Table 2: Laboratory values of the patients.

	Median	**Minimum**	**Maximum**
Total IgE(IU/ml)	65.0	8.0	1719.0
AST (U/L)	27.0	18.0	52.0
ALT (U/L)	19.0	11.0	50.0
IgG (mg/dl)	906.5	391.0	1234.0
IgA (mg/dl)	10.4	1.6	15.0
IgM (mg/dl)	12.1	1.5	15.7

4. Discussion

Mastocytosis is a rare clonal disease of hematopoietic stem cells that develops with the accumulation of mast cells in the skin (cutaneous form) or in multiple organs including bone marrow, spleen, liver and lymph nodes (systemic type) [15]. The identification of hepatosplenomegaly, lymphadenopathy or abnormal blood tests may indicate systemic mastocytosis (SM) and might necessitate additional examinations such as abdominal ultrasound or computed tomography scans and a bone marrow biopsy. In such instances, a thorough set of laboratory tests, including a complete blood count, renal and liver function tests, and serum tryptase levels, should be contemplated [4, 5]. Since our patients did not have systemic involvement, bone marrow biopsy was not performed.

In our study, the male-female ratio of pediatric mastocytosis cases was found to be 1.5. In the literature, the male-female ratio in pediatric mastocytosis is estimated to be 1.4 and this ratio is similar to the results found in our study [16]. Tüysüz et al. also found a male-female ratio of 1.6 in mastocytosis cases in their study [17]. The mean age at the onset of the patients' complaints was 10 months. In the literature, it has been shown that approximately 90% of children develop their first skin lesions in the first two years of their lives [16, 18]. In the study by Tüysüz et al. the median age at presentation in mastocytosis cases was found to be 12.1 months [17].

While the majority of pediatric patients don't exhibit a family history of cutaneous mastocytosis (CM), occasional instances of familial cases have been observed. Reports indicate that familial cases involving a first-degree family member occur in 2% to 4% of cases, and the majority of these cases are linked to c-kit genetic mutations [8]. In our study, family history was found to be positive in 1 (10%) of our patients.

In cases of mastocytosis, inquire about systemic symptoms such as itching, facial flushing, dizziness,

palpitations, fainting, abdominal pain and diarrhea [19]. According to a study conducted by the National Institutes of Health, itching was reported in 83% of patients, rash in 65%, abdominal pain in 41%, vesicles in 53%, bone pain in 18% and headache in 12% [20]. In our study, it was found that all patients had symptoms of rash and pruritus. In the study by Tüysüz et al. Rash was the most common symptom and pruritus was found in the second frequency [17].

In a study of 173 patients investigating childhood mastocytosis in the literature, systemic involvement was reported in only two patients [21]. In our study covering an eight-year period, all of our patients had cutaneous mastocytosis and systemic involvement was not observed in any of them. Our patients are being followed up and no systemic involvement has developed.

In our study, the most common lesion type was maculopapular rash (UP type) seen in 4 patients (40%) and macular rashes were found in 3 patients (30%). Nodules and mastocytoma (NM type) were seen in 1 patient (10%). Hannaford et al. Evaluated 173 patients and reported NM in 51%, UP in 47% and DCM in 2% [21]. Alvarez-Twose et al. Evaluated 111 pediatric patients with cutaneous mastocytosis and reported UP in 68%, NM in 20% and DCM in 8% of the patients [22]. In our study, we found additional allergic diseases in 4 (40%) of the patients. Hannaford et al. Found no increase in asthma, atopic dermatitis and dermographism in their study in patients with mastocytosis [21]. Müller et al. Found no significant difference in the prevalence of atopic disease between urticaria pigmentosa patients and healthy control group in their study. Atopic disease was found in 21% of the patients [23].

5. Conclusion

In conclusion, although the number of cases in our single-center study was small, it can be emphasized that childhood mastocytosis cases are frequently cutaneous type and patients should be evaluated in detail in terms of differential diagnoses before making a diagnosis.

Limitations of the Study

The limitations of the study are small sample size and retrospective design.

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Conflict of Interests

The authors declare that there is no conflict of interest in the preparation and publication of this article.

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Author Contributions

Conceived and designed the experiments; FÇ, AÇ, MYÖ, SÇ. Analyzed and interpreted the data; UA, ZMA, SÇ, MYÖ. Contributed reagents, materials, analysis tools or data; ZMA, SÇ, AÇ, FÇ. Wrote the paper; SÇ, UA. Study of biostatistics; ZMA, UA.

Ethical Approval

Ethics committee approval was obtained from the Ethics Committee of Umraniye Training and Research Hospital with decision number 26 on February 23, 2023 for the conduct of the study.

Data sharing statement

All data relevant to the study are included in the article.

Consent to participate

Consent was obtained from all patients for the use of data under ethical conditions.

Informed Statement

Informed consent forms were obtained from all patients the patient data could be used in the our study.

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