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Clinical spectrum of patients diagnosed with childhood mastocytosis: a retrospective single center experience

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IMPACT STATEMENT

Although symptoms are difficult to control in cases of pediatric mastocytosis and are sometimes associated with significant morbidity, in most cases the symptoms are limited to the skin and follow a mostly benign course in children.

Introduction

Mastocytosis refers to a rare group of diseases. It is a disease characterized by an increase in abnormal morphology of mast cells in one or more tissues (1, 2). Mastocytosis usually occurs due to activation mutations that affect the c-Kit tyrosine kinase receptor and give function to this receptor (2). Patients diagnosed

with mastocytosis are classified as cutaneous mastocytosis (CM) and systemic mastocytosis (SM) based on the involvement of the affected organ. There are three main groups of childhood mastocytosis (CHM), which are mostly seen in the childhood age group and progress only with skin involvement: urticaria pigmentosa (UP)/maculopapular cutaneous mastocytosis (MPCM), solitary mastocytoma and diffuse CM (1, 3).

Summary

Background. Pediatric cutaneous mastocytosis patients diagnosed and followed up by our specialist were enrolled in this study, and clinical and laboratory evaluations were retrospectively analyzed from patients' archived files. **Methods.** Patients, who applied to the Division of Pediatric Allergy And Immunology Unit of a University Training and Research Hospital between 01 January, 2010 and April 28, 2021, were enrolled in this study. **Results.** Of the 33 patients included in the study, 11 (33.3%) were female and 22 (67.7%) were male. The median age of onset of the patient's complaints was 7 (0-60) months. The median age at diagnosis was 11 (2-64) months. Their complaints' median regression age was 54 (6-192) months. Resistant clinical findings were followed in 13 (39.4%) patients. Itching, redness, gastrointestinal symptoms, and maculopapular eruption were the most common complaints. The rashes were mostly polymorphic and larger than 1 cm. Heat was the most common trigger. Darier's sign was positive in 97% of the patients. Antihistamines were the most commonly used drug for prophylaxis and treatment. The autoinjector prescription rate was 24.2%. **Conclusions.** Quality of life was mildly affected in 48.5% of the patients based on the CDLQI scores. Thus, patients should be followed up through adolescence for the development of systemic signs and symptoms.

Childhood mastocytosis can be seen both in the pediatric age group and in adults if it does not regress with age. 80% of patients are diagnosed in the first year for the pediatric patient group. Generally, the findings are self-limiting and almost completely recovered in adolescence (4, 5). Mastocytosis in children follows a bimodal distribution. The frequency of disease peaks in the first three years, followed by a decline, and a second much smaller increase in CHM cases is observed after age 15 (2, 6). Although there is a slight predominance of males in pediatric cases, it is more likely to occur in females after puberty. There may be a familial history of mastocytosis, but there is no history in family members in most cases (7, 8).

This study aimed to retrospectively evaluate the demographics, clinical characteristics (type of rash, size, age of onset of the lesion, complaints, *etc.*), laboratory characteristics, and treatment plans of patients diagnosed with CHM.

Materials and methods

Between 01 January, 2010 and April 28, 2021, 33 patients diagnosed with CHM at a University Training and Research Hospital were included. Approval was obtained from the local, non-invasive Clinical Research Ethics Committee (date: October 10, 2021, document no: 74636-469). Again, consent was obtained from the child and/or parent to use the related case pictures here. The study started by distinguishing the patients aged 0-21 years with a diagnosis of mastocytosis (Q82.2 in the ICD10 coding system). Then, the patients who were followed up with the diagnosis of CHM in the Pediatric Immunology and Allergy Division after the physical examination [typical skin involvement with positive Darier sign (major criterion)] and clinical findings and/or biopsy results performed by us with the diagnosis of CHM were included in the study. In this study, the diagnosis was confirmed by skin biopsy in approximately 25% of our patients, and biopsy was performed in suspected cases. *c*-Kit mutation could not be examined in any of our cases.

The criteria for exclusion in the study can be listed as being over 21 years old, having a history of co-morbid disease, conversion to SM, and having a history of regularly used drugs due to SM or chronic disease.

In patients who applied to our clinic and were diagnosed with CHM, the age of onset, duration and frequency of complaints, types and distribution of skin lesions (plaque, macule, papule, bullae, *etc.*), accompanying complaints related to other systems, triggering factors, demographic characteristics of patients, chronic medication use, additional allergic disease, other chronic disease states, *etc.*, family history (family history of atopy/allergic disease) were questioned in the anamnesis. Angioedema/anaphylaxis histories and treatment plans of the patients, whether they needed adrenaline autoinjectors or not, were retrospectively scanned from their files. After recording all this history, physical examination

findings, CDLQI (Children's Dermatology Life Quality Index) score, and the results of laboratory tests performed during routine evaluation were evaluated using the 'Statistical Package for Social Science' (IBM SPSS Statistics, Chicago, IL) v21 program.

Statistical analysis

The frequency and percentage ratios of the categorical variables in the study are given together with the tables. Numerical findings are tabulated with mean, standard deviation, and minimum-maximum values. Whether the categorical variables were evenly distributed was evaluated with the chi-square test. Whether the laboratory findings differed according to categorical variables was checked with the Likelihood ratio P-value test, Mann Whitney U, and Kruskal Wallis H tests. Whether there was a relationship between the numerical findings was evaluated with the Spearman correlation test. The study accepted the significance level as ($p < 0.05$).

Results

Of the patients diagnosed with CHM, 11 (33.3%) were girls and 22 (66.7%) were boys. The male/female ratio was found to be 2/1. The median age of onset of complaints in patients with CHM was seven months, and the median age of diagnosis was 11 months. The median age of regression of their complaints was 54 months. Clinical findings continued in 13 (39.4%) patients followed (**table I**).

When the additional allergic diseases of the patients diagnosed with CHM were questioned, sixteen (48.5%) had no concomitant atopic disease, and seventeen (51.5%) had a concomitant allergic disease. Allergic rhinitis in nine (52.9%) patients, allergic asthma in four (23.5%), atopic dermatitis in two (11.8%), food allergy in one (5.9%), food allergy and asthma were found to be together in one case (5.9%) as well.

When the family history of mastocytosis was questioned, it was learned that fourteen (42.4%) had a family history of allergic disease. It was learned that nine (64.3%) of the family mem-

Table I - Demographic and clinical characteristics of the cases.

Variables	
Girl	11 (33.3%)
Boy	22 (66.7%)
Median age of onset (month)	7 (0.00-60.00)
Median age at diagnosis (month)	11 (2.00-64.00)
Age of regression (month)	54 (6.00-192.00)
Tryptase	3.94 (1.00-20.50)
History of allergic disease	17 (51.5%)
Allergic disease in family history	14 (42.4%)

Parenthesis shows minimum-maximum or percentage values.

bers with a history of allergic disease had asthma, two (14.3%) allergic rhinitis, two (14.3%) urticaria/eczema, and one (7.1%) food allergy. Nevertheless, there was no mastocytosis case in the families of the patients. No significant correlation was observed when examining the relationship between additional allergic disease and patient family history ($p > 0.05$).

Figure 1 - Polymorphic maculopapular cutaneous mastocytosis appearance in one of our patients.

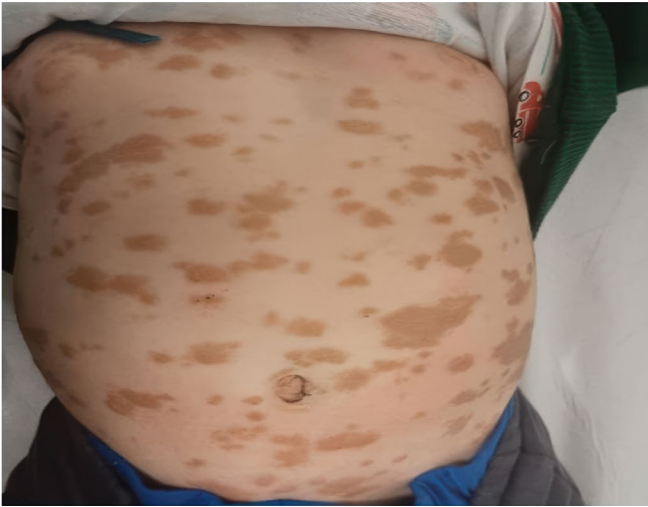


Figure 2 - Diffuse cutaneous mastocytosis appearance in CM patients.



In the patients' physical examinations, cervical lymphadenopathy (LAP) smaller than 1 cm was reported in 3 patients. Abdominal ultrasonography was performed in 23 of 33 patients; hepato-splenomegaly was not detected, and only one patient had abdominal lymphadenopathy smaller than 1 cm.

In our patients, one (3%) of the rashes was only on the head and neck, three (9.1%) only on the trunk, one (3%) only on the extremities, seven (21.2%) on the head, neck and trunk, nine (27.3%) on trunk and extremities, three (9.1%) on extremities and head-neck, nine (27.3%) on head-neck, trunk and extremities. While rashes were detected in one body area in five (15.2%) patients, they were detected in two or more in thirty (84.8%) patients. As the rash type, macule was seen in nine (27.3%) patients, papule in eight (24.2%) patients, and bullae in two (6.1%) patients (**figures 1 and 2**). There are two cases of diffuse CM in our series. We did not have one patient with only nodules and plaque-type lesions (**figure 3**). In patients with more than one type of rash, the maculopapular rash, the most common type, was seen in fourteen (42.4%) patients. Most of the cases diagnosed with polymorphic MPCM is shown in **figure 1**. When lesion sizes and similarities were compared, the lesions of twenty-six (78.8%) patients were larger than 1 cm, and seven (21.2%) were millimetric. While one (3%) of the patients had monomorphic lesions, thirty (97%) had polymorphic type of MPCM lesions. Darier's sign was positive in 32 of 33 (96.9%) patients diagnosed with CHM.

Considering the itching and redness (rash) rates on the skin from the complaints and findings of the patients, itching was positive in 66.7% and redness in 81.8%. Headache was observed in

Figure 3 - Solitary mastocytoma appearance in CM patients.



only one patient (3%) as a neurological symptom. When gastrointestinal system findings were questioned, they were absent in 29 (88%) patients. One patient (3%) had abdominal pain, one (3%) had nausea and vomiting, one (3%) had reflux, and one (3%) had abdominal pain and nausea. When gastrointestinal complaints were questioned, it was learned that these complaints were of short duration and regressed over time. There were no symptoms or signs of other organs and systems.

Laboratory values were found within the normal range in all routine biochemistry tests (kidney/liver function tests, serum electrolytes, *etc.*). When peripheral smears of patients diagnosed with CHM were examined in terms of systemic involvement, no atypical cells were found in the smear. A hemogram was not obtained from one of the patients. When the hemograms of 32/33 patients diagnosed were examined, 20 (60.6%) were normal. Three (9.4%) patients had anemia, one had neutropenia, six (18.8%) had eosinophilia, and two (6.2%) had thrombocytosis.

Of the 33 patients included in the study, total IgE was measured in 19. 7/17 patients had additional allergic disease and whose total IgE was checked. We had two patients under age 6 with an IgE value of over 100. No statistical significance was found in comparing total IgE values according to additional disease, and there was no correlation between additional allergic disease and total IgE. Sensitization was detected in specific IgE or skin prick tests in six of the patients. Cat sensitivity was detected in one patient, stinging nettle and ash pollens in one patient, grass pollen in one patient, hazelnut in one patient, egg and milk in one patient, and cat with milk sensitivity in one patient.

Vitamin D levels were measured in 15 of the patients with CM. The median vitamin D level of the patients examined was 14.90 ng/ml (7.88-53.0 ng/mL). Vitamin D level is below 12 ng/mL in six patients with vitamin D deficiency; a diagnosis of vitamin D insufficiency was made in 2 patients with a 12-20 ng/ml range. Vitamin D was found in the normal range in 7 (47%) patients, between 20-100 ng/ml. None of the patients had a history of bone-joint pain or spontaneous bone fracture. No clinical findings suggestive of osteoporosis/osteopenia was detected in the patients. There were 16 patients whose tryptase levels were measured in the study. The median tryptase level of the patients whose tryptase levels were measured was 3.88 ng/ml. In one diagnosed patient, the serum tryptase level was above 20. Bone marrow aspiration was performed with the suspicion of SM in the patient, whose serum tryptase level was above 20 ng/mL, and no atypical cells were found in the patient's bone marrow examination, and the patient's annual follow-up was continued. When the patients with tryptase levels were compared according to gender, there was no significant difference between the mean of boys and girls. When the lesion size groups are separated as < 1 cm and \geq 1 cm, there is no significant difference between the patients' mean in comparing the lesion size. When the tryptase value is compared according to the lesion type in the patients, it can be said that

there is no significant difference between the averages of all lesion types. There was no significant difference between the mean of the normal and lymphadenopathy groups in comparing tryptase values in patients.

Skin biopsy was taken in ten (30.3%) of 33 patients with a diagnosis of CM, and the diagnosis was shown to be CM. In the report of the patients whose skin biopsy was taken, an increase in the number of mast cells was found at a rate that met the diagnostic criteria. Immunohistochemical staining was positive in the patients. When the patients' rashes were questioned regarding the triggering factor/agent, it was understood that 19 (57.6%) patients had a trigger factor. When the factors triggering the complaints of the patients were questioned, it was heat increase (fever) in 6 (18.2%) of them, heat increase (fever) and infection in 5 (15.2%), heat increase (fever) and stress were seen as triggering factors in 3 (9.1%) and only one patient, along with heat increase (fever) and food (chocolate). Sun exposure in one of the remaining four patients, heat increase (fever) and sun exposure in one, stress in one, and infection and stress in one were found to be triggering factors.

The patients who were followed up with the diagnosis of CHM and those who needed autoinjector prescription and treatment were examined. There were 8 (24.2%) patients who had an autoinjector report. There were four patients with prophylactic drug use; 2 of them were prescribed antihistamines, and 2 of them were prescribed montelukast. No medication was ever prescribed for 7 (21.2%) patients. Antihistamine was prescribed for 12 (36.4%) patients, local steroids were prescribed for 5 (15.2%), and antihistamine and local steroids were prescribed for 8 (24.2%) patients in whom treatment was initiated in case of active disease. Systemic steroids, cromolyn sodium, omalizumab, and PUVA were not used in any of our patients, and the symptoms regressed with the treatments given.

Discussion and conclusions

Although males are slightly predominately in CHM, females are more affected after puberty (7, 8). In some studies, the incidence rate in boys was 1.4 times higher than in girls (2, 6). In the study of Ben-Amitai *et al.* (7), the male-female ratio was 1,8/1 in patients diagnosed with CHM. In the study of Kiszewski *et al.* (9), the male-female ratio was 1,8/1; Akoğlu *et al.* (10) reported the male-female ratio as 1,5/1. Some sources argue that CM is seen at an equal rate of male-female in children (11, 12). In the study conducted by Wiechers *et al.*, with 144 patients, 73 (50.7%) of the patients were female and 71 (49.3%) were male (11). The patients diagnosed in our study were under 15, and the disease was more common in males. Of the patients diagnosed with CM, 11 (33.3%) were female and 22 (66.7%) were male. The male-female ratio in our study was 2/1, consistent with the literature. The incidence of CM in the pediatric age group increases in the first two years of life and after the age of fifteen; therefore, a bimodal

distribution is observed (12). The age of onset of CM in children is between birth and two years of age in 55% of patients, typically in the first six months of life. 35% of the patients are diagnosed over the age of 15, and the remaining 10% are diagnosed under the age of 15 (2). Hannaford *et al.* detected skin findings at birth in 39 patients, before the 6th month in 102 patients, at 6-12 months in 8 patients, and after the 12th month in 12 patients (13). Kiszewski *et al.* found that the lesions started in 92% of the patients in the first 12 months, and there was no difference in age of onset between the types (9). In their study, Akoğlu *et al.* found that the lesions appeared in the first six months in 41.8% of the patients and by the age of 13 months in 78.2% of the patients; however, they reported that they did not find a congenital form in any of the patients (10). In the study of Heinze *et al.*, the age of onset of complaints was 2.8 (0-42) months, and the age of disappearance of complaints was 10 (3-19) years (14). In our study, there was no patient whose rash started at birth. The age of onset of complaints in all of the patients in our study was under 15. The earliest rash in our patients appeared in the first month. The median age of onset of the complaints of our patients with MPCM was 7 (0.0-60.0) months. The median age at diagnosis of the patients was 11 (2-64) months. Consistent with the literature, 27 (81.8%) of 33 patients were younger than two years of age. Their complaints' median age of regression was 54 (6-192) months. In 13 (39.4%) patients followed up, rashes continued. Mastocytosis is a rare disease, and there is usually no familial transmission. However, rarely familial cases have been described (12). In the study conducted by Hannaford *et al.*, 3/173 patients had a family history of mastocytosis (13). Being twins was found in 1.8% of these patients (6). In the study of Ben-Amir *et al.*, 117 patients were examined, and a family history was found in 13 (11%). In other studies, CM was not found in family members (14, 15). There was no history of mastocytosis in other family members of the patients examined in our study. When the studies were examined, there was no data on allergic diseases in the patients' families. A family history of allergic disease was observed in 14 (42.4%) patients with CM in our study.

In the study of Gonzalez *et al.*, additional allergic diseases were found in 21 (44.7%) of 45 pediatric patients diagnosed with mastocytosis. It was reported that 9 (19.1%) of these patients had allergic conjunctivitis, 7 (14.9%) allergic rhinitis, 5 (10.6%) asthma, and 3 (6.4%) atopic dermatitis (16). In a study by Brockow *et al.* in which pediatric and adult patients were included, the frequency of allergic disease was similar to the population, and concomitant allergic disease was found in 31% of the patients (17). In the study of Azaña *et al.*, the history of concomitant allergic disease in patients diagnosed with mastocytosis and their families was 6% (4). In the study of Caplan *et al.*, it was found to be 47% (18). In our research, concomitant allergic disease was found in 17 (51.5%) of our patients, which is compatible with the literature but at a higher rate. Of those with a history of additional

allergic disease, 9 (52.9%) had allergic rhinitis, four (23.5%) had allergic asthma, two (11.8%) had atopic dermatitis, one (5.9%) had a food allergy, one (5%), were found to have a food allergy and allergic asthma.

Itching is among the most common complaints and symptoms in patients with mastocytosis due to excessive secretion of mast cell mediators. Blistering and sudden redness of the rash are other common complaints (6, 14, 15). Although it is said that itching is a common symptom, Hannaford *et al.* included 173 patients in their study. Sudden redness and blistering complaints were common in these patients, and itching was found in only five patients (13). Kiszewski *et al.* reported that 61% of their patients had itching in their study (9). Similar to other studies, in the study of Lange *et al.*, itching was observed in 68% of the patients, sudden rash in 29%, diarrhea in 22%, headache in 18%, hypotension in 16%, and anaphylaxis in 6% (15). In the review of Meni *et al.*, itching was 4% in patients; blistering in skin lesions was 34.5%; sudden redness was 24.5%; findings related to the gastrointestinal tract were found in 19.5% and bone pain in 13.7% (6). In our study, when the itching and rash rates of the patients were analyzed, itching was positive in 63.2% of patients and rash in 81.6% of patients. Symptoms suggestive of respiratory, cardiovascular system, and oncological disorders were absent in patients. Headache was detected in only one patient (3%) as a neurological symptom. When the gastrointestinal system findings were questioned, symptoms were detected in 4 patients (12%). It was found that one of the patients (3%) had abdominal pain, one (3%) had nausea, one (3%) had reflux, and one (3%) had abdominal pain and nausea.

Skin manifestations consist mainly of maculopapular lesions; lesions are brownish or reddish. Among the findings, plaques and nodules may coexist. MPCM lesions can be monomorphic or, more often, polymorphic. Polymorphic lesions are more common and have a better prognosis. In MPCM, large lesions are usually seen at less than seven months, and small lesions are seen in patients over two years of age. Small-sized skin rashes take longer to disappear (\geq eight years) than large-sized skin rashes in children with MPCM (11). In a study by Lange *et al.* in which 101 patients were included, it was reported that 45% of the lesions were plaque, 37% were maculopapular, 25% were bullae, 2% were nodules, and in 6% of the patients, the lesions completely infiltrated the skin (diffuse) (15). In their study with 71 patients, Kiszewski *et al.* examined the rash type of CM patients and found that the most common was macular rash in their patients. Macules in 46 patients, 30 plaques, 27 papules, 16 bullae, and 5 nodules were detected (9). In our study, it was observed that there were patients with one type of rash and patients with multiple types of rashes at the same time. The most common maculopapular rash was detected in the patients. In patients with a uniform rash, macules were 9 (27.3%), papules were 8 (24.2%), and bullae were 2 (6.1%). We did not have any patients with only nod-

ule and plaque-type lesions. In patients with more than one rash type, maculopapular rash was detected in 14 (42.4%) patients. Darier's sign is pathognomonic for the diagnosis of CM. In the final classification of mastocytosis in the pediatric age group, it is included among the major criteria for the diagnosis of CM and is positive in almost all patients (19). Darier's sign: in the study (10) conducted by Akoğlu *et al.* in patients with a diagnosis of CM, 89.5%, Darier's sign was found to be positive between 90% and 100% in patients diagnosed with CM in different studies (6,14). In our research, Darier's sign was positive in 32 of 33 patients diagnosed with CM, and Darier's sign was negative in one (3%). In our study, Darier's sign positivity was 97%.

Evaluation of the examinations of patients diagnosed with CHM is necessary to understand whether there is systemic involvement. By evaluating the hemogram and peripheral smears of the patients, it is evaluated whether there is bone marrow infiltration of mast cells. Hemograms, liver function tests, and tryptase levels should be evaluated to exclude SM (20, 21). In their study, Carter *et al.* found anemia due to iron deficiency in 3 patients, lymphocytosis in 22 patients, monocytosis in 3 patients, and thrombocytosis in 12 patients, and evaluated these findings independently of the CM clinic (22). Kiszewski *et al.* evaluated the complete blood count of 28 of 71 patients and reported that six patients had anemia, three had eosinophilia, and one had thrombocytopenia (9). In this study, the examinations of the patients were reviewed retrospectively. Hemograms were obtained from 32 of 33 patients. Anemia in three patients (9.1%), neutropenia in one (3%), eosinophilia in six (18.2%), and thrombocytosis in two (6.1%) patients were detected. Atypia was not observed in the peripheral smears of the patients. Later hemograms taken during follow-up showed that these parameters were within normal limits.

The serum tryptase level indicates the mast cell load in the body, and sudden increases and persistent elevations in the serum tryptase level should be a warning for SM. It should be kept in mind that serum tryptase levels can be found to be high in diffuse CM and monomorphic MPCM in the pediatric age group (2). In children diagnosed with CM, high basal serum tryptase levels and skin findings carry the risk of developing serious symptoms due to mast cell activation (23). There was no effect of having a male or female gender on tryptase level (24). It has been observed that pediatric patients with smaller lesions diagnosed with CM have higher baseline tryptase levels and have a worse clinical picture than those with larger lesions (25). In a retrospective study involving 102 children with CM, high tryptase levels were significant in predicting anaphylaxis in children (26). In the study of Carter *et al.*, it was observed that the serum tryptase level in patients remained stable or decreased over time, and the increase in SM and tryptase levels was found to be related (22). In the study of Şahiner *et al.*, serum tryptase levels decreased with age; it was observed that there was no difference between tryptase levels in healthy boys and girls (26). This study measured serum tryptase

levels in 16 (48.5%) patients. No significant difference was found between the mean of girls and boys in comparing tryptase values to gender in patients whose tryptase levels were checked. Since the patients were not tested for recurrent tryptase, no comment could be made about the decrease with age. Again, tryptase was tested in 17 of the 33 patients included in our study, and no significant correlation was found between the type of rash, age of onset of rash, age of regression, and age of diagnosis.

In addition to various system involvements, bone lesions that can be detected radiologically as osteoporotic or osteosclerotic can be seen in SM. Caksen *et al.* detected rickets in a 12-month-old patient diagnosed with CM. In the patient's examinations, calcium and phosphorus were within normal limits, and alkaline phosphatase was as high as 1401 U/L. The left wrist radiograph showed osteoporosis on the radius and distal end of the ulna. The patient was started on vitamin D therapy. The coexistence of CM and rickets in the patient was evaluated incidentally due to vitamin D deficiency in our country (27). In our study, vitamin D levels were checked in 15 of our patients. The patients' median vitamin D level was 14.9 (7.88-53.0 ng/mL). Vitamin D levels were below 12 ng/mL in 6 patients with vitamin D deficiency; a diagnosis of vitamin D insufficiency was made in 2 patients with a 12-20 ng/ml range. Vitamin D levels were within the normal range (20-100 ng/mL) in 7 patients. None of the patients had a history of bone-joint pain or spontaneous bone fracture. Clinical findings of osteoporosis/osteopenia were not detected in the patients.

Patients with a diagnosis of mastocytosis should avoid exposures that trigger or exacerbate their symptoms and complaints as much as possible. These exposures include sudden temperature changes (hot/cold), humidity, exercise, dry skin, emotional stress, alcohol, and lack of sleep. In infants and young children, skin rubbing, teething, fever, irritability (anger), and excessive excitement can trigger symptoms (23). Our study determined heat, stress, infection, food, and sun exposure as triggering factors (**table II**).

Table II - Triggering factors in patients with cutaneous mastocytosis.

Triggers	n	%
None	14	42.4
Hot (heat)	6	18.2
Heat and infection	5	13.2
Heat, stress	3	9.1
Stress	1	3
Sun	1	3
Heat, sun	1	3
Infection and stress	1	3
Heat, food	1	3

It has been reported that the risk of anaphylaxis is higher in patients followed up with a diagnosis of mastocytosis (16, 28). The prevalence of anaphylaxis in the community is thought to be 1-3/10,000 patients per year (29). In the study of Gonzalez *et al.*, anaphylaxis was observed in 22% of patients diagnosed with mastocytosis (16). Serum tryptase level was found to be higher in patients who had anaphylaxis (28). Vaccines, food, and sudden contact with cold are the cause of anaphylaxis in CHM patients (28). In the study of Lange *et al.*, ketamine, clindamycin, and radiocontrast material were shown to cause anaphylaxis (15). Anaphylaxis during operation can be the first presenting manifestation of mastocytosis. Cases with mastocytosis using chronic antimediator treatment and/or prophylactic medications before operation had an ordinary surgical progress (30). Since the risk of anaphylaxis increases in patients with mastocytosis with a high serum tryptase level, such as in a large mastocytoma or a diffuse CM, it is recommended that epinephrine autoinjectors be prescribed (15, 31, 32). In our study, 8 (24.2%) patients had an autoinjector prescription. Our patients had no history of anaphylaxis or angioedema. Eight (24.2%) of the patients were prescribed an adrenaline autoinjector to use in case of possible anaphylaxis, similar to other studies (table III). However, it was learned that none of the patients needed an adrenaline autoinjector prescription during their follow-up.

The use of antihistamines is recommended to prevent mediator release in patients with signs of mast cell degranulation (2, 23, 33). In our study, symptomatic medication was not prescribed for 7 (21.2%) patients. In the case of active disease, antihistamine was prescribed to 12 (36.4%) patients, local steroids were prescribed to 5 (15.2%), and antihistamines and local steroids were

prescribed to 8 (24.2%) patients. Again, antihistamine, montelukast, and local steroids were prescribed to 1 patient for therapeutic purposes. Antihistamine was prescribed for 2 (6.1%) patients, and montelukast was prescribed for 2 (6.1%) patients for prophylaxis (table III).

CLDQI is an index that shows the effect of dermatological disease on quality of life in pediatric patients aged 4-16 years. It consists of 10 questions asked to the patients. In our study, this index could only be applied to 18 patients over the age of 4 years. Two (6.1%) patients had no impact on their lives, and sixteen (48.5%) had a slight/mild impact.

Since CHM is a rare disease, the number of cases is limited. Due to the retrospective nature of our study, prospective follow-up of patients with ongoing complaints in terms of SM is required, and our study period is insufficient for this.

In conclusion, childhood mastocytosis is a rare disease that may cause parents concern. Cutaneous mastocytosis has a benign course and is usually limited to the skin in the pediatric age group. However, it should be known that SM may develop years later in very few patients; therefore, there is a possibility of a fatal course (34, 35).

Fundings

None.

Contributions

AMD, ÖÖ: conceptualization, writing - original draft; ÖÖ: writing - review & editing.

Conflict of interests

The authors declare that they have no conflict of interests.

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Table III - Distribution of autoinjectors, prophylactic drugs and treatments in patients.

		n	%
Autoinjector	None	25	75.8
	Yes	8	24.2
Treatment	None	7	21.2
	Used	26	78.8
	Antihistamine	12	36.4
	Local steroid	5	15.2
	Antihistamine, local steroid	8	24.2
	Antihistamine, montelukast, local steroid	1	3
Prophylaxis	None	29	87.8
	Used	4	12.2
	Antihistamine	2	6.1
	Montelukast	2	6.1

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