Childhood mastocytosis: results of a single center

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Abstract

Aim: We aimed to retrospectively evaluate histopathological, demographic and clinical findings of children with mastocytosis diagnosed with mastocytosis in our clinic.

Material and Methods: The files of 21 patients diagnosed with mastocytosis between 2000 and 2014 in our clinic were retrospectively analyzed.

Results: All patients had cutaneous mastocytosis, 19 patients had urticaria pigmentosa and 2 patients had mastocytoma. The male-female ratio was: 1/1.6. The median age for onset of disease was 12.1 months and the disease occurred in the newborn period in 3 patients. While all patients had eruption, 10 patients had pruritis, 1 patient had a bullous formation, 1 patient had abdominal pain and 1 patient had attacks of redness throughout the body and a sense of burning in the chest. Two patients had a positive familial history. The diagnosis was confirmed with skin biopsy in all patients. The median follow up time of the patients were 5 years. The patients were treated with H1, H2 antihistaminics, local moisturizing creams and topical corticosteroid drugs. The lesions resolved completely in 4 patients who reached to puberty and 7 patients had marked improvement in a 5.5 year-follow-up period. Ten patients had stabile lesions in a 3.6 year-follow-up period.

Conclusions: Most cases of childhood mastocytosis are observed in the form of cutaneous mastocytosis. The prognosis is good; the disease limits itself and is prone to regress in the adolescent period. (Turk Pediatri Ars 2015; 50: 108-13)

Keywords: Childhood mastocytosis, cutaneous mastocytosis, mastocytoma, urticaria pigmentosa

Introduction

Mastocytosis is a considerably rare disease characterized with episodes of release of mast cell mediators as a result of excessive growth and accumulation of mast cells (1). The disease is mostly observed in infancy; it is examined in two main groups including cutaneous mastocytosis which is characterized only with cutaneous involvement and frequently observed in children and systemic mastocytosis which is observed rarely in the childhood. Childhood cutaneous mastocytosis tends to disappear spontaneously before puberty. Cases which continue in the adulthood may transform into the systemic form. In our study, we aimed to retrospectively evaluate the clinical, demographic, histopathological properties, disease prognosis and treatment results

of the patients who were followed up with a diagnosis of mastocytosis in our clinic in the last 14 years.

Material and Methods

The files of 21 pediatric patients who presented to İstanbul University Cerrahpaşa Medical Faculty, Pediatric Hematology Outpatient Clinic between January 2000 and October 2014 and were diagnosed with mastocytosis were evaluated retrospectively. The diagnosis of mastocytosis was made with histopathological confirmation obtaining cutaneous biopsy samples from patients who were suspected clinically in accordance with the recommendation of World Health Organization (WHO). Histopathological diagnosis was made by observing mast cells showing metachromasia with tol-

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idin blue in full-thickness skin biopsy (2). All patients were evaluated with complete blood count, peripheral blood smear, hepatic and renal function tests and abdominal ultrasonography in terms of systemic mastocytosis involvement and systemic disease was investigated by bone marrow aspiration and bone graphs in the patients who were found to be suspicious.

The age of presentation, age of disease onset, gender, type and localization of the lesions, accompanying complaints, clinical course, familial history, histopathological findings and treatment results were recorded from the files. In our study, classification of cutaneous mastocytosis was made in accordance with the consensus recommended by the WHO and modified by Hartman and Herts (3). In accordance with the classification, cutaneous mastocytosis is examined in five different groups:

1. Maculopapular cutaneous mastocytosis
2. Plaque type cutaneous mastocytosis
3. Nodular cutaneous mastocytosis/mastocytoma
4. Diffuse cutaneous mastocytosis (DCM)
5. Telangiectasic cutaneous mastocytosis

Results

A total of 21 cases of cutaneous mastocytosis were seen between October 2000 and October 2014. Eight of the patients were female and 13 were male. The male/female ratio was found to be: 1:1.6. The median age at presentation was 12.1 months (range: 1-96 months). The mean time of onset of lesions was 11.9 ± 20.8 SD months. 19 of the patients (90%) had urticaria pigmentosa (UP) and the remaining two patients (10%) had nodular mastocytosis (NM). Among the patients who had urticaria pigmentosa, the lesion was in the head-neck, trunk, lower and upper extremities in 8 patients, only in the trunk in 5 patients, in the the trunk and head-neck region in 2 patients, in the trunk and lower extremity in 2 patients and only in the head-neck region in 1 patient (Figure 1). The lesion was in the trunk in one patient who had nodular mastocytosis and in the head-neck region in another patient who had nodular mastocytosis (Figure 2). When the complaints of the patients were evaluated, the main complaint at presentation was eruption. Itching was observed in 10 of the patients (48%), abdominal pain which could be explained by another cause was observed in one patient and burning sensation in the chest and eruption in the whole body following hot bath were observed in one

Figure 1. Urticaria pigmentosa

Figure 2. Nodular mastocytoma

patient. In one patient with nodular mastocytosis, bulla formation occurred following itching. Darier sign was positive in 90% of the patients (n=19). The clinical properties of the patients are summarized in Table 1.

Bone marrow aspiration was performed in one patient because of anemia the cause of which could not be found, but mastocytosis involvement was not found. In the remaining patients, bone marrow aspiration was not performed, because physical examination, laboratory values (complete blood count, peripheral blood smear, hepatic and renal function tests) or radiological tests (liver, kidney and spleen ultrasonography) did not suggest systemic mastocytosis. Tissue biopsy was not performed, because organ involvement was not present. Two patients diagnosed with urticaria pigmentosa had a positive familial history (father in one patient and sibling in one patient). Familial history could not be confirmed, since the family members who were reported to have similar lesions did not accept biopsy.

Table 1. Characteristics of the patients

Age of onset of the symptoms	n (%)	
• Birth	3 (14)	
• <6 months	10 (48)	
• 6 months-1 year	3 (14)	
• >1 year	5 (24)	
Localization of the lesion	Urticaria Pigmentosa (n)	Mastocytoma (n)
• Head Neck	2	1
• Trunk	5	1
• Head-Neck+Trunk	2	-
• Trunk+ Extremity	2	-
• Trunk+Head Neck+Extremity	8	-
Symptoms and physical examination findings	Urticaria Pigmentosa (n)	Mastocytoma(n)
• Darier sign(+)	17	2
• Itching	9	1
• Bulla formation	-	1
• Erythema in the whole body and burning in the ches	1	-
• Abdominal pain	1	-

The mean follow-up period of the patients was 5 ± 3.44 years. In the follow-up, the lesions improved spontaneously in four patients who reached puberty. In 6 patients, the eruptions decreased in a 5.5 ± 1.5 year follow-up period. The lesions continued in the same way in 10 patients who were followed up for a mean period of 3.6 ± 1.1 years. In all patients, the complaints of itching and erythema were controlled with antihistaminics and topical steroids used during the complaints. Intermittent abdominal pain observed in one patient and burning sensation observed in another patient regressed with H2 group antihistaminics. No abnormality was found in the laboratory variables in any patient at the time of diagnosis. Anaphylaxis did not occur in any patient.

Discussion

Mastocytosis is a rare clonal disease of hematopoietic stem cells which occurs as a result of accumulation of mast cells in the skin (cutaneous form) alone or in many organs including the bone marrow, liver, spleen and lymph nodes (systemic type) (4). The clinical properties of the disease are shown in Table 2 (5-9). Childhood cutaneous mastocytosis tends to disappear spontaneously in puberty (10). Disease may transform into

the systemic type in 15-30% of the patients symptoms continue in the adulthood (11). Since the disease occurs as a result of spontaneous mutation in the C-kit gene, familial transmission is rare and few familial cases have been reported until the present time (12). In our study, similar eruptions were reported to be present in the family members of two patients. However, familial disease could not be proven because tissue diagnosis was not present.

Although there are no definite data related with the incidence of the disease, the number of new cases has been reported to be 5-10/1 million people (6). The incidence of the disease varies from country to country. While the incidence is 0,54% in Spain, it has been reported to be 0,2% in Mexico (13). In the study of Serarslan et al. (14) reported from Turkey, the rate of childhood cutaneous mastocytosis was found to be 1/234 among the patients who newly presented to the clinic. In our 10-year experience, the rate of cutaneous mastocytosis was found to be 0,8% among all newly diagnosed patients.

Although studies related with childhood cutaneous mastocytosis in the literature have frequently reported that the number of female cases is higher compared to the number of male cases, few publications have reported that male cases constitute the majority as in our

Table 2. Clinical properties of mastocytosis

Age of onset of the disease/frequency	
<1 year	80% (5-8)
>1 year	20% (5-8)
Course of the disease/type of involvement	
Cutaneous mastocytosis	Only skin
Systemic mastocytosis	Skin, bone marrow, liver, lung, spleen, bone
Types/properties of cutaneous mastocytosis observed in the childhood	
Urticaria pigmentosa (UP)	The most common type; diffuse macular or Maculopapular red-brown lesions
Nodular mastocytoma (NM)	The second most common type; single, endurated, in the form of nodule, observed from the neonatal period
Diffuse cutaneous mastocytoma (DCM)	Rare type; diffuse macules or nodular lesions covering the whole body
Symptoms/signs of the patients and frequency	
Darier sign	Development of sudden swelling with mild stimulation of the skin, this sign is positive with a rate of 95% (7).
Itching	The most common finding; emerges following hot Bath and physical irritation.
Bulla formation, erythema in the whole body	This is observed more rarely
Constipation, abdominal pain, diarrhea, Gastrointestinal ulcers, stomach-intestinal Problems, fibromyalgia, osteopenia, Pathological fracture, anxiety, depression	Observed very rarely (9).
Factors triggering symptoms	
Sudden temperature change, massage, narcotic analgesics, non-steroid antiinflammatory drugs, aspirin, snake toxin, insect bite, exercise, infections	

study (15). Cutaneous mastocytosis frequently occurs in the early infancy; approximately 15% of the cases are symptomatic from the neonatal period, while the complaints are observed before the age of 2 years in 50% (3.8). The symptoms occurred in the neonatal period in three of our patients (15%) and before the age of two years in 15 patients (90%). Our data were compatible with the literature in terms of time of occurrence of symptoms.

The most commonly reported type of cutaneous mastocytosis is urticaria pigmentosa. In the study of Hanaford et al. (16) in which 173 children were evaluated, NM was reported in 89 of the patients (51%), UP was reported in 81 of the patients (47%) and DCM was reported in 3 of the patients (2%) (systemic involvement was found in two of these three patients). In the study of Alvarez-Twose et al. (17) in which 111 pediatric patients with cutaneous mastocytosis in a 8-year period, UP was reported in 76 of the patients (68%), NM was reported in 22 of the patients (20%), DCM was reported in 9 of the patients (8%) and plaque type cutaneous mastocytosis localized mostly in the trunk and upper extremity

which could not be included in the classical classification was reported in four of the patients. The involvement type (UP in 90% and NM in 20%) and localization (mostly trunk and upper extremity) of the lesions in our patients were compatible with the literature.

In the systemic type of the disease, the bone, liver, spleen, lymph nodes, peripheral blood, gastrointestinal system, skeleton and heart may be involved. It is more common in adults. 10-30% of the patients diagnosed above the age of 10 years and less than 5% of the patients diagnosed below the age of 10 years show systemic involvement (18). In our study which covered a 10-year period, we found no systemic involvement in our patients with mastocytosis. In the literature, systemic involvement was reported in only two of 173 pediatric patients in a study which examined childhood mastocytosis with the highest number of cases (15). Mastocytosis cases with systemic involvement reported are generally single case presentations (19).

In mastocytosis, itching, dermographism, erythema attacks in the whole body, bulla formation, gastrointesti-

Figure 3. A case of acute myeloid leukemia in infancy; nodular lesions in the neck and knee

nal complaints including nausea, abdominal pain, diarrhea and colic and rarely respiratory distress, headache, malaise, lethargy and neuropsychiatric findings may be observed. Anaphylaxis is observed rarely in childhood mastocytosis; it has been reported following bee bite especially in cases of diffuse cutaneous mastocytosis (15). The majority of the cases have no complaints throughout their whole lives or complaints of mild symptoms at times of attacks (8). In recent years, increased serum triptase has been found to be effective on the severity of the complaints (20). In our patients, the second prominent complaint following eruption was itching.

The differential diagnosis of the disease includes milk allergy which frequently occurs with eruption, atopic dermatitis, malign diseases including leukemia of infancy and hemophagocytic lymphohistiocytosis in infancy and chronic urticaria, angioedema, toxic shock syndrome, drug-related eruptions, postinflammatory hyperpigmentation, juvenile xanthogranuloma, pigmented nevus, xanthomas, insect bite and bullous impetigo in adulthood. Before making a diagnosis of mastocytosis, the other diseases in the differential diagnosis should be carefully reviewed. Patients with a prediagnosis of mastocytosis should be carefully investigated in terms of different underlying diseases especially in terms of malignancies. A 6-month old boy presented to our clinic 7 years ago with nodular eruption with macular character at places which occurred at the age of 40 days for the first time (Figure 3). On physical examination, hepatosplenomegaly and lymphadenopathy were not found. The patient was diagnosed with mastocytosis as a result of biopsy performed in another center. Viral serology and abdominal ultrasonography were found to be normal. Neuron specific enolase (NSE) measured in terms

of neuroblastoma was found to be within the normal limits. The biopsy material obtained in another center was requested for further evaluation. 2 weeks later, the patient presented to the emergency department with a complaint of fever. He had bicytopenia and firm mass in the left testicle which emerged in the last one week. Repeated bone marrow aspiration and peripheral smear were found to be normal. The biopsy obtained from the skin lesions before and testicular biopsy were found to be compatible with acute myelocytic leukemia (21). This case is important in terms of reminding that it should be considered in the differential diagnosis.

Conclusively, we can state that childhood mastocytosis cases are mostly cutaneous type mastocytosis based on our long term follow-up periods, though the number of our patients were insufficient, the symptoms can be controlled with symptomatic treatment, the disease limits itself and the children should be carefully evaluated in terms of other diseases before making the diagnosis.

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