

# Pediatric Cutaneous Mastocytosis: A Review of 180 Patients

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## Abstract

**Background:** Mastocytosis is a heterogeneous group of diseases characterized by the abnormal infiltration of mast cells in the skin and, sometimes, other organs. Some patients may experience symptoms related to mast cell mediator release.

**Objective:** To analyze the clinical features of cutaneous mastocytosis in a large series of children.

**Methods:** We conducted a file review of all children clinically diagnosed with cutaneous mastocytosis in our department over the last 20 years. We evaluated gender, age at onset, character and distribution of the lesions, associated symptoms, and course of the disease.

**Results:** Altogether, 180 patients with cutaneous mastocytosis were identified. The male to female ratio was 1.5:1. About one-third of patients had a mastocytoma, which was present at birth in over 40% and appeared during the first year of life in most of the remainder. Urticaria pigmentosa was noted in 65% of the patients, presenting at birth in 20% and during the first year in most of the remainder. The majority of lesions was distributed over the trunk and limbs. Different kinds of associated symptoms were noted. Prognosis in general was good. Only 11% of the cases, all urticaria pigmentosa, were familial.

**Conclusions:** Most cases of pediatric mastocytosis are sporadic and appear during the first 2 years of life, especially on the trunk. Urticaria pigmentosa is the most frequent variant. The prognosis of pediatric mastocytosis, in general, is good.

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The typical lesions of mastocytosis were first described by Nettleship in 1889 as an unusual form of urticaria [1]. Mastocytosis is a heterogeneous group of clinical syndromes characterized by the abnormal infiltration of mast cells into various tissues and the concomitant release of chemical mediators by these cells [2]. The typical presentation of pediatric-onset mastocytosis consists of cutaneous manifestations – namely, mastocytoma, urticaria pigmentosa and, less commonly, diffuse cutaneous mastocytosis. Rubbing a cutaneous mastocytosis lesion results in the formation of a wheal or even a vesicle. This response is known as Darier's sign and is considered clinically diagnostic [3].

We studied 180 pediatric patients with mastocytosis who presented at Beilinson Medical Center and Schneider Children's Medical Center of Israel over a 20 year period, and analyzed the clinical features, associated symptoms and course of the disease. To the best of our knowledge, this report constitutes the largest series of pediatric mastocytosis to date.

## Patients and Methods

We conducted a file review of all cases of mastocytosis seen in our ambulatory Pediatric Dermatology Unit over the last 20

years. The clinical diagnostic criteria for cutaneous mastocytosis were:

- Mastocytoma: one or two lesions, presenting as a slightly elevated red to light-brown plaque or nodule
- Urticaria pigmentosa: multiple reddish-brown hyperpigmented macules, papules or nodules at random distribution
- Diffuse cutaneous mastocytosis: diffuse erythema-increased skin markings and skin infiltration with frequent vesicles.

For all cases, either positive Darier's sign or a compatible histology was required to confirm the diagnosis. Patients' gender, personal and family history, age at onset and diagnosis, type of mastocytosis, and distribution of involvement were recorded. No hematologic or serum chemistry profiles were performed routinely; skeletal surveys or bone marrow aspirations were not conducted during the initial evaluation. Parents were questioned regarding extracutaneous involvement, course of disease and associated symptoms. Follow-up evaluation was based on the physical reexamination of 89 patients (49.4%).

## Results

We identified 180 patients with cutaneous mastocytosis: 117 with urticaria pigmentosa (65%), 62 (34.4%) with mastocytoma, and 1 (0.6%) with diffuse cutaneous mastocytosis. A complete physical examination was undertaken in all patients.

The male to female ratio for the whole sample was 1.5:1. The mastocytoma appeared at birth in 42.5% of patients and during the first year of life in most of the remainder; all the mastocytomas in our series were identified by 2 years of age. By contrast, urticaria pigmentosa presented at birth in only 18.8% of patients, during the first 3 months of life in 32.5%, and after age 2 years in 11.1%. Overall, 92.7% of all cases of pediatric mastocytosis presented during the first 2 years of life.

The majority of urticaria pigmentosa lesions (88%) was distributed over the trunk, compared to only 48% of the mastocytomas. Transient vesicular formation was frequent in both subgroups (24% and 33%, respectively).

Associated symptoms and signs were noted in 8% of the patients with mastocytoma and in 26.5% with urticaria pigmentosa [Table 1]. The most frequent symptom was flushing, characterized by an erythematous hue or a feeling of warmth, which was present in 6.5% and 12.8% of the subgroups, respectively. No triggers of flushing were identified. Bronchospasms and asthma attacks were noted in 10% of the patients with urticaria pigmentosa but in none of those

**Table 1.** Associated symptoms

	<b>Mastocytoma (%) (n=62)</b>	<b>Urticaria pigmentosa (%) (n=117)</b>
Bronchial asthma		12 (10.3%)
Flushing	4 (6.5%)	15 (12.8%)
Fever		2 (1.7%)
Abdominal pain		1 (0.85%)
Duodenal pain		1 (0.85%)
Melena	1 (1.6%)	
<b>Total</b>	<b>8.1%</b>	<b>26.5%</b>

**Table 2.** Follow-up of pediatric mastocytosis

	<b>Complete resolution</b>	<b>Partial resolution</b>	<b>No change</b>
Mastocytoma (n=27)	74% (n=20)	18.5% (n=5)	7.5% (n=2)
Average duration	7.4 yrs	5.6 yrs	2.4 yrs
Urticaria pigmentosa (n=62)	56.4% (n=35)	24.2% (n=15)	19.4% (n=12)
Average duration	10.2 yrs	7.1 yrs	2.8 yrs

with mastocytoma. Gastrointestinal symptoms were noted in three patients and included an episode of melena in a patient with mastocytoma, and recurrent abdominal pain and peptic disease in two patients with urticaria pigmentosa. No other associated gastrointestinal symptoms, such as nausea, vomiting and diarrhea, were noted. No associated malignancies were diagnosed in our series.

Of the 117 cases of urticaria pigmentosa, 13 (11%) were familial. In all five families involved, only one generation (namely, siblings) was affected. No history of familial disease was noted among the patients with mastocytoma.

Eighty-nine patients (49%) were followed for 1–15 years: 27 with mastocytoma and 62 with urticaria pigmentosa. Twenty of the 27 patients with mastocytoma (75%) showed complete resolution during the follow-up period as compared to 35 of the 62 patients with urticaria pigmentosa (56%) [Table 2].

## Discussion

The term mastocytosis refers to a group of disorders characterized by the accumulation of mast cells, most commonly in the skin, with or without other organ system involvement [1]. The cause is still unknown [4]. Mastocytosis limited to the skin is primarily a disease of children and can be accompanied by systemic symptoms without systemic infiltration. The typical cutaneous manifestation consists of mastocytoma, urticaria pigmentosa or, less commonly, diffuse cutaneous mastocytosis [5]. Typically, the diagnosis of pediatric-onset mastocytosis is based on the clinical appearance of the cutaneous lesions and positive Darier sign [6,7]. Confirmation is provided by the presence of significant mast cell hyperplasia on histologic study. Skin biopsies must be taken carefully to avoid degranulation of the mast cells, which makes their identification impossible [4,7].

In our series of mastocytosis, about two-thirds of the patients had urticaria pigmentosa, similar to the prevalence in the literature [5]. However, the rate of urticaria pigmentosa may be biased upward because of the referral of patients with multiple lesions.

Though males and females are reported to be affected equally [2,5], we found a male to female ratio of 1.5:1. The male predominance was more pronounced in the urticaria pigmentosa subgroup (1.77:1) than in the mastocytoma subgroup (1.44:1). Our male to female ratio for the urticaria pigmentosa subgroup is similar to that reported by Caplan [8] in a retrospective study of 112 patients. In another retrospective study with 71 patients, Kiszewski et al. [9] reported a male predominance of 1.8:1.

According to the literature, 65% of all cases of mastocytosis begin in childhood, with approximately 85% occurring between birth and 2 years of age, and the remaining 15% between the ages of 2 and 15 years [10]. In our center, more than 40% of the mastocytomas were present at birth and most of the others appeared during the first year of life. By contrast, only 20% of the patients with urticaria pigmentosa presented at birth, but almost 80% did so by age 9 months, similar to the findings of a retrospective study of 112 patients [8] and a prospective study of 67 patients [11].

The majority of urticaria pigmentosa lesions was distributed over the trunk and limbs, similar to published rates [5,8]. The rate of trunk involvement for mastocytoma was lower than that for urticaria pigmentosa but higher than the rate predicted by random distribution according to surface area.

Vesicles and bullae were noted in 33% of our patients with mastocytoma, whereas Caplan [8] reported an incidence of 91.6%. Our rate of 24% for the urticaria pigmentosa subgroup was closer to the range of published studies: 25.3–53% [8,11,12]. In all our patients who had vesicle and bullae formation, the onset of disease was in the first 6 months of life, as noted by others [8,11].

The variation of associated symptoms in our patients was similar to that reported in the literature [2,4,11,13]. Flushing was the most frequent symptom in both the urticaria pigmentosa and mastocytoma subgroups. Bronchial asthma was noted only in patients with urticaria pigmentosa, but not more frequently than in the normal pediatric population.

Two of our patients with urticaria pigmentosa had recurrent episodes of fever of undetermined origin. Fever as a symptom of cutaneous mastocytosis has rarely been reported [4,14]. Hematologic abnormalities have been described in adults with systemic mastocytosis [15] but are quite rare in pediatric mastocytosis [16]. None of our patients had any hematologic abnormality. In the absence of hematologic abnormalities or bone pain, no bone marrow aspirations were performed.

The association of urticaria pigmentosa with malignancy has been reported, but it appears to be less frequent in children [1,2]. Of our 117 patients with urticaria pigmentosa, no case of associated malignancy was diagnosed.

Only about 50 familial cases of urticaria pigmentosa have been described in the literature [17], and they were attributed to autosomal recessive [17], autosomal dominant [18], or multifactorial mode of inheritance [19]. All our patients with familial urticaria pigmentosa were siblings, with no history of affected family members from other generations, suggesting an autosomal recessive mode of inheritance. Clinicians should be aware that a child with a lesion in an area where urticaria is unlikely or hard to

see (scalp, gluteal cleft) may go undiagnosed and, as an adult, would give a negative history for mastocytosis. Inheritance for this condition should be studied in a prospective fashion in order to be substantiated.

The treatment for most forms of pediatric mastocytosis is conservative and symptomatic. Patients are instructed to avoid precipitating causes of immunologic and non-immunologic mast cell degranulation, including certain foods (crawfish, lobster, alcohol, spicy foods, cheese, hot beverages) and medications (aspirin, non-steroidal anti-inflammatory drugs, codeine, morphine, alcohol, thiamine, quinine, opiates, gallamine, decamethonium, procaine, radiographic dyes, dextran, polymyxin B, scopolamine, D-tubocurarine) [20].

The prognosis in children with mastocytoma is good. In the present study we observed either a total disappearance of the lesions or marked improvement in 92.5% of the patients, similar to published rates [8,21]. In the urticaria pigmentosa subgroup, improvement was noted in 80.6%, with complete resolution in only 56.4%, similar to reported rates [8]. Complete resolution occurred after an average of 10.2 years and partial resolution after 7.1 years. In 19.4% of our patients, no change was noted, but their follow-up period was shorter (2.8 years). Although constitutional symptoms as well as several laboratory findings have been reported to be associated with poor prognosis [22], we were unable to identify any such indicators.

In conclusion, most cases of pediatric mastocytosis appear during the first 2 years of life, especially on the trunk. Urticaria pigmentosa is the most frequent variant, and about one-tenth of cases are familial. The prognosis of pediatric mastocytosis, in general, is good.

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