

# Diffuse Cutaneous Mastocytosis in a Child - a Case Report

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## Abstract

Mastocytosis refers to a group of diseases characterized by a clonal proliferation and accumulation of mast cells in one or more tissues/organs with different clinical presentations. In children, limited cutaneous forms of mastocytosis are rather frequent, while systemic mastocytosis is rare. The diagnosis of cutaneous mastocytosis is based on clinical findings and histopathology. We present a patient who developed skin lesions at the age of 18 months. Clinical findings, confirmed by histopathology, were consistent with diffuse cutaneous mastocytosis. The follow-up period was 7 years. The treatment included oral antihistamines in combination with mast cell stabilizers, mild topical steroids and avoidance of friction. During the follow-up period, there were no signs of systemic involvement, and the quality of life was preserved, despite the large surface of affected skin. This case report should increase the awareness and knowledge of clinicians about this rare form of cutaneous mastocytosis in the pediatric population.

**Key words:** Mastocytosis, Cutaneous; Child; Diagnosis; Signs and Symptoms; Mast Cells; Dermatologic Agents; Treatment Outcome

## Introduction

Mastocytosis is a rare disease that occurs both in children and in adults. In pediatric patients, mastocytosis is usually cutaneous and transient, while in adults the condition commonly progresses to a systemic form. Mastocytosis is a heterogeneous disorder characterized by clonal proliferation and accumulation of mast cells in one or more organs which may lead to different clinical pictures (1). Pathological accumulation of mast cells may affect the skin, bone marrow, liver, spleen and the lymph nodes.

Cutaneous forms are urticaria pigmentosa (UP), diffuse cutaneous mastocytosis (DCM), and cutaneous mastocytoma. UP and mastocytoma are more frequent forms during childhood and the lesions may be present at birth (1 - 3), while DCM is rare.

The treatment of cutaneous mastocytosis (CM) depends on the severity of lesions. The management is conservative and aimed at counteracting the symptoms due to mast cell mediator release, including avoidance of triggering factors such as cold water, friction, hot or cold air. In case of hypotension, epinephrine may be indicated, and in cases of fre-

quent hospitalizations, imatinib mesylate (a type 2 kinase inhibitor) may be introduced (1).

## Case Report

A 2-year-old boy was admitted to our Department of Pediatric Dermatology with a history of atopic dermatitis since the second month of life. The first cutaneous lesions and blisters on trunk and diaper area appeared at the age of 18 months. On admission, the boy presented with leathery thickened skin on the face, trunk and extremities (Figure 1). Approximately 80% of the body surface area was affected. He also had a marked dermographism and tense blisters in the friction zones (Figure 2). The Darier's sign was positive. Routine laboratory test results (CBC, biochemistry, and urinalysis) were all normal. The levels of serum tryptase were not measured, due to the lack of laboratory tests. Abdominal ultrasonography revealed normal findings of the spleen and liver. He had no lymphadenopathy, gastrointestinal or respiratory symptoms, but had a personal history of perinatal asphyxia with no complications, allergy to peanuts, home dust, orange, nuts and peach.



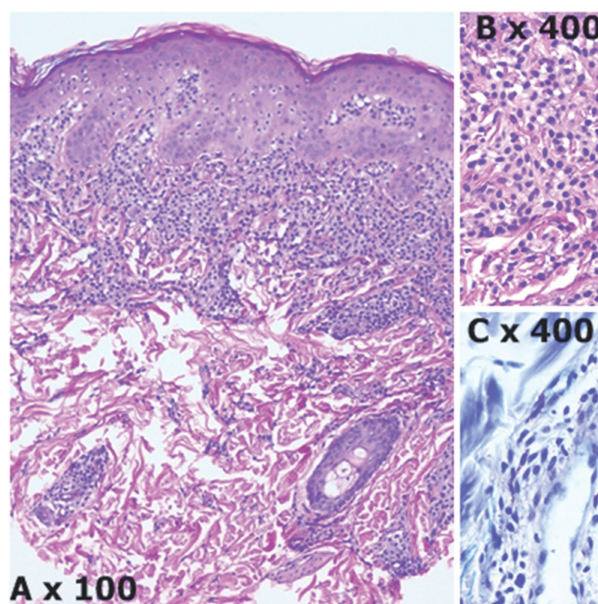
**Figure 1.** Leathery, erythematous thickened skin on the trunk in our patient at the age of 18 months

Histopathology of skin lesions revealed an increased number of mast cells in the papillary dermis, and mast cells aggregates around blood vessels (Figure 3. A; 3. B). Mast cell infiltrations were confirmed by toluidine blue staining (3. C).

The treatment included oral antihistamines in combination with mast cell stabilizers, mild topical steroids and avoidance of friction. During the following 7 years, the boy was followed up by a pediatrician and a dermatologist. There was no need for hospital treatment. The skin lesions were slowly regressing (Figure 4). The Darier's sign remained positive (Figure 5). He had no blisters since the age of 2 years. Oral and topical treatment was adjusted according to the clin-



**Figure 2.** Erythema, marked dermographism and tense blisters in the diaper area



**Figure 3 A, 3 B.** Increased number of mast cells in the papillary dermis (x 100) and mast cell aggregates around the blood vessels (x 400); 3. C. Mast cells infiltrations confirmed by toluidine blue staining (x 400)

ical flares. During summer months, due to increased friction (sports activities, sweating), antihistamines and/or mast cell stabilizers were increased, while during autumn and winter months he was periodically without treatment. He developed no signs of systemic mastocytosis or growth retardation. However, the parents were advised to carry his medical records, just in case of skin manifestations worsening. The parents were also informed that radio contrast substances containing iodine, as well as drugs such as aspirin, NSAIDs, codeine, morphine, may be associated with exacerbations, and that they have to inform medical workers about DCM.

## Discussion

Based on limited data, it is believed that males and females are equally affected by mastocytosis and that there is no racial predominance. In children, internal organ involvement is not frequent (4).

Our patient developed skin lesion before the age of 2, without systemic involvement. His initial presentations were in line with data published by other authors: pediatric-onset





**Figure 4.** Slightly erythematous leathery skin on the trunk in a nine-year-old boy

of mastocytosis is commonly diagnosed prior to 2 years of age, and it is usually a cutaneous disease (4). Despite its clinical forms, the prognosis of mastocytosis depends on the age of onset. Therefore, the condition may be divided into childhood onset mastocytosis and adult onset mastocytosis (5 - 9). The age of mastocytosis onset is very important because it has prognostic implications (10). The majority of children with CM experience spontaneous resolution of skin lesions by adolescence, whereas adult-onset mastocytosis is chronic and tends to progress to the systemic form (7, 9, 10).

DCM is rare, but can present with more severe symptoms. It accounts for 1 – 3% of cases of CM, and it may involve the whole body, the central region and scalp being most affected. DCM can appear at birth (congenital and neonatal) or in early infancy (4). Blistering and bullae are the most common symptoms, and the blisters may be hemorrhagic. The skin may be leathery and thickened. Hyperpigmentation may persist into adulthood and

with prominent dermographism (4). Due to the extent of the lesions and their severity, systemic symptoms can be present due to the large amount of mast cell mediators released locally and absorbed locally and systemically. Whole body flushing, pruritus, diarrhea, intestinal bleeding, hypotension, anemia, hypovolemic shock and deaths have been reported (11). Visceral involvement with lymphadenopathy and hepatomegaly may be present (12). DCM skin lesions often resolve by adolescence. In contrast, a small minority of patients with DCM and familial mastocytosis exhibit a chronic course with persistently elevated serum tryptase levels and extracutaneous mast cell infiltrates due to germline mutations in c-KIT (3, 14, 15).

During the 10-year period (2006 to 2015), 40 children with mastocytosis were hospitalized at our Department of Pediatric Dermatology. Among them, 30 patients (75%) had urticaria pigmentosa; 7 patients (17.5%) had mastocytoma, and 3 patients (7.5%) had DCM. Our data are in line with a retrospective study from Mexico that reviewed 71 cases of CM in children, of whom 53 had urticaria pigmentosa, 12 had mastocytomas, and 6 had DCM. A positive Darier's sign was found in 94% of patients. In the Mexican study, in 92% of cases the disease onset was recorded in the first year of life. About 80% of patients presented with an improvement or had a spontaneous resolution of the disease (15). Our patient did not have associated symptoms. In the Mexican study, associated symptoms and signs were absent in those with mastocytomas, except for itching.



**Figure 5.** Positive Darier's sign in a nine-year-old boy

Diarrhea was seen in 7/36 cases of urticaria pigmentosa, and 2/5 cases of DCM (15).

In our patient the treatment was symptomatic and included oral antihistamines in combination with mast cell stabilizers, mild topical steroids and avoidance of friction. This approach is in the line with guidelines for diagnosis and treatment of CM in children (4). According to the guidelines, avoidance of triggering factors includes hot temperatures and to a lesser extent, cold temperatures, anxiety and stress. Systemic therapy in pediatric mastocytosis includes H1 antihistamines; combined treatment with H1 and H2 antihistamines; oral cromolyn sodium; oral methoxypsoralen therapy with long-wave psoralen plus ultraviolet A radiation (PUVA). The PUVA is most effective in non-hyperpigmented DCM. Nonetheless, there are some suggestions about peri-operative considerations since patients with mastocytosis have an increased mast cell burden and mast cells are implicated in the pathophysiology of anaphylaxis. Because of understandable concern about adverse reactions which may follow administration of pharmacologic agents in the peri-operative period, various opioids, muscle relaxants, analgesics, and anesthetics should be used with caution. The authors suggest administration of slow intravenous injections, rather than a single bolus of needed drugs (opioids, muscle relaxants) known to activate mast cells. So, the medically indicated drugs (opioids, muscle relaxants) should not be eliminated from therapeutic consideration in the perioperative period, unless there is a clear prior history of sensitivity (4).

## Conclusion

Diffuse cutaneous mastocytosis is rare in pediatric patients and it is usually not associated with systemic manifestations. However, regular check-ups, including personal history of gastrointestinal manifestations and lymphadenopathy, should be adopted with caution. The serum tryptase level should be monitored, since it may indicate increased mast cell activation and instability.

## Abbreviations

UP - urticaria pigmentosa

DCM - diffuse cutaneous mastocytosis

CBC - complete blood count

NSAID – non-steroidal anti-inflammatory drug

CM - cutaneous mastocytosis

PUVA - psoralen plus ultraviolet A radiation

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## References

1. Tamay Z, Özçeker D. Current approach to cutaneous mastocytosis in childhood. *Turk Pediatri Ars.* 2016;51(3):123-7.
2. Kettelhut BV, Parker RI, Travis WD, Metcalfe DD. Hematopathology of the bone marrow in pediatric cutaneous mastocytosis. A study of 17 patients. *Am J Clin Pathol.* 1989;91(5):558–62.
3. Kettelhut BV, Metcalfe DD. [Pediatric mastocytosis.](#) *Ann Allergy.* 1994;73(3):197–202.
4. Castells M, Metcalfe DD, Escribano L. [Diagnosis and treatment of cutaneous mastocytosis in children: practical recommendations.](#) *Am J Clin Dermatol.* 2011;12(4):259-70.
5. Escribano L, Akin C, Castells M, Orfao A, Metcalfe DD. [Mastocytosis: current concepts in diagnosis and treatment.](#) *Ann Hematol.* 2002;81(12):677–90.
6. Horny HP, Sotlar K, Valent P, Hartmann K. Mastocytosis a disease of the hematopoietic stem cell. *Dtsch Arztebl Int.* 2008;105(40):686–92.
7. Hartmann K, Henz BM. [Mastocytosis: recent advances in defining the disease.](#) *Br J Dermatol.* 2001;144(4):682–95.
8. Hartmann K, Metcalfe DD. Pediatric mastocytosis. *Hematol Oncol Clin North Am.* 2000;14(3):625–40.
9. Carter MC, Metcalfe DD. [Paediatric mastocytosis.](#) *Arch Dis Child.* 2002;86(5):315–9.
10. Middelkamp Hup MA, Heide R, Tank B, Mulder PG, Oranje AP. Comparison of mastocytosis with onset in children and adults. *J Eur Acad Dermatol Venereol.* 2002;16(2):115–20.
11. Murphy M, Walsh D, Drumm B, Watson R. [Bullous mastocytosis: a fatal outcome.](#) *Pediatr Dermatol.* 1999;16(6):452–5.
12. Walker T, von Komorowski G, Scheurlen W, Dorn-Beineke A, Back W, Bayerl C. Neonatal mastocytosis with pachydermic bullous skin without c-Kit 816 mutation. *Dermatology.* 2006;212(1):70–2.
13. Hannaford R, Rogers M. Presentation of cutaneous mastocytosis in 173 children. *Australas J Dermatol.* 2001;42(1):15–21.

14. Akoglu G, Erkin G, Cakir B, Boztepe G, Sahin S, Kaduman A, et al. Cutaneous mastocytosis: demographic aspects and clinical features of 55 patients. *J Eur Acad Dermatol Venereol.* 2006;20(8):969–73.
15. Kiszewski AE, Duran-Mckinster C, Orozco-Covarrubias L, Gutierrez-Castrellon P, Ruiz-Maldonado R. Cutaneous mastocytosis in children: a clinical analysis of 71 cases. *J Eur Acad Dermatol Venereol.* 2004;18(3):285–90.

## Difuzna kutana mastocitoza u dečjem uzrastu – prikaz slučaja

### Sažetak

Mastocitoze predstavljaju grupu bolesti koje karakterišu klonalna proliferacija i akumulacija mastocita u jednom ili više organa/tkiva, sa različitim kliničkim prezentacijama. Kod dece su najčešće kutane forme mastocitoze, dok je sistemska mastocitoza retka. Dijagnoza kutanih formi mastocitoze postavlja se na osnovu kliničke slike i histopatološkog nalaza. Prikazujemo pacijenta kod koga su se prve promene na koži pojavile u uzrastu od 18 meseci. Klinička slika i histopatološki nalaz bili su karak-

teristični za difuznu kutanu mastocitozu. Period praćenja bio je sedam godina. Terapija je podrazumevala primenu H1 antihistaminika per os, stabilizatore membrane mastocita, blage kortikosteroidne preparate za lokalnu primenu i izbegavanje frikcije. Tokom perioda praćenja, postepeno je dolazilo do delimične regresije kožnih promena i poboljšanja kvaliteta života pacijenta. Ovaj prikaz slučaja treba da poveća svest i znanje kliničara o ovom retkom obliku kutane mastocitoze u dečjem uzrastu.

**Ključne reči:** Kutana mastocitoza; Dete; Dijagnoza; Znaci i simptomi; Mastociti; Dermatološki preparati; Ishod terapije