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Case Report
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Diffuse Cutaneous Mastocytosis

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Abstract

Mastocytosis is a group of disorders characterized by abnormal accumulation of mast cells in the skin and other organs. Diffuse cutaneuos mastocytosis is a rare and most severe variant of cutaneous mastocytosis. In this article, we present you a girl with urtical elements on her skin folds, abdomen and axillae since she was 4 month old that progressed into generalized vesiculobullos rash with positive Darrier's sign. Based on clinical, histological and laboratorial findings the diagnosis of diffuse cutaneous mastocytosis was made at the age of 6 months. Treatment was started at age of 4 months with cetirizine, after the diagnosis was made we increased dose four times, later desloratadine, topical zinc preparations, topical pimecrolimus, montelukast was added but there was no therapeutical effect so at age of 7 months she started therapy with oral glucocorticosteroids. At age of 17 months she started oral cromolyn sodium. This is the first case of DCM in Children's Clinical University hospital Riga as far as we know.

Introduction

Mastocytosis refers to a heterogeneous group of disorders characterized by the pathologic accumulation of mast cells in different tissues or organs, predominantly skin, bone marrow, and visceral organs [1]. Mastocytosis is divided in two main subgroups, Systemic Mastocytosis (SM) and Cutaneous Mastocytosis (CM) [2]. CM is classified into mastocytoma, maculopapular cutaneous mastocytosis or urticaria pigmentosa, telangiectatic cutaneous mastocytosis and diffuse mastocytosis [2-4]. Diffuse Cutaneous Mastocytosis (DCM) is a rare, severe variant of CM, it accounts about 1% to 3% of the cases of CM [2,4]. DCM appears in neonates or in the first month of life and is characterized by intense symptoms due to increased cutaneous infiltration by mast cells [5]. The first sign may be blistering and extensive bullae, which may rupture, leaving erosions and crusts. The blisters can be hemorrhagic. The skin may be leathery and thickened, hyperpigmented. Systemic symptoms, such as body flushing, pruritus, diarrhea, intestinal bleeding, hypotension, anemia, hypovolemic shock, can be present due to the large amount of mast cell mediators released locally and absorbed locally and systemically. Visceral involvement with lymphadenopathy and hepatomegaly may be present. Rarely, all cutaneous forms of mastocytosis in children can present with acute mast cell activation events, including anaphylaxis. [4,6]. Mechanical irritation of skin lesions leads to a release of mast cell mediators (histamine, leukotrienes and prostaglandins) and thus to reddening and urticarial swelling. This reaction is known as Darier's sign and is pathognomonic for all forms of CM [4,7]. Pruritus and flushing can be triggered by many factors, for example, temperature changes, hot showers, emotional stress, spicy food, fever, exercise, friction, and certain drugs [4]. Mastocytosis is also associated with a number of comorbidities such as osteoporosis, gastric and duodenal ulcers, recurrent anaphylaxis and hematologic disorders such as myeloproliferative or myelodysplastic disorders and rarely lymphoproliferative disorders [8].

Unfortunately, there is no standardized treatment for mastocytosis and treatment consists primarily of symptomatic drugs and other treatments that deal with the symptoms experienced by individual patients [2].

Case Presentation

A 4 month old girl developed urticarial elements on her skin folds, abdomen and axillae. She was treated by a local dermatologist with cetirizine, nevertheless after a month she developed generalized vesiculobullous rash. The bullae where flaccid, ruptured easily leaving crusts. When she was 5 month old, she was admitted to a hospital where she was seen for the first time by the authors of this article. During physical examination urticarial elements on her back and skin folds were noted. Yellowish crusts covering erosions secondary to ruptured bullae were observed (Figure 1 and 2). Darrier's sign was positive: upon stroking the back, the patient developed an urticarial reaction.

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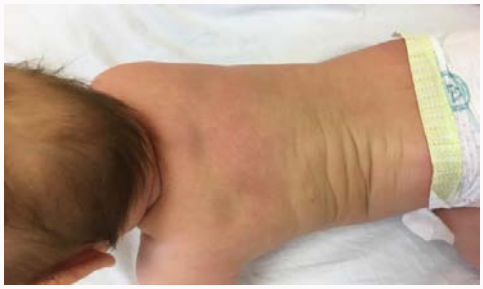


Figure 1:

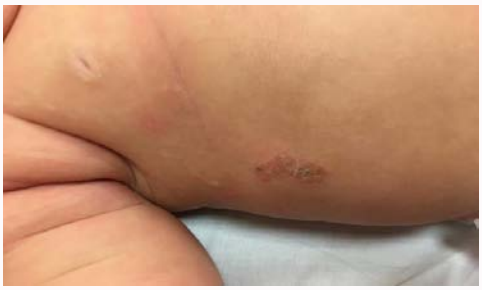


Figure 2:

Palpation and percussion revealed possible hepatomegaly. Her parents admitted that the girl seemed to be anxious for the past few weeks. She woke up several times every night and the skin conditions worsened when she was stressed.

Laboratory examination revealed thrombocytosis and elevated serum tryptase level 129 ng/ml. Further investigations were undertaken to exclude systemic mastocytosis.

Skin biopsy was performed. The histopathological diagnosis fits with bullous mastocytosis (Figure 3a-3c). The day after skin biopsy the patient developed reddish papules, urticarial plaques and new bullous lesions (Figure 4).

Ultrasound examination of the abdominal cavity confirmed hepatosplenomegaly. Computer Tomography (CT) of the thorax demonstrated small, subpleural cysts. Bone marrow biopsy excluded prominent mast cell infiltration. However there was massive lymphocytosis without atypia, hyperplasia of neutrophils. Hematologist recommended periodical observation, no other intervention was needed.

A day after bone marrow biopsy the disease exacerbated. Generalized vesicobullous rash developed (Figure 5 and 6).

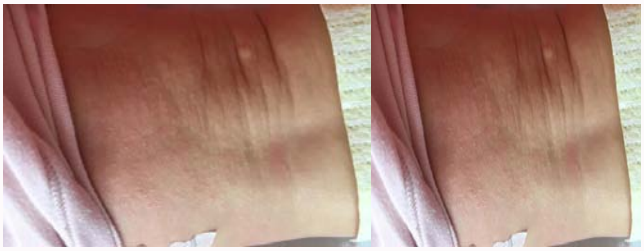


Figure 4:

Figure 5:

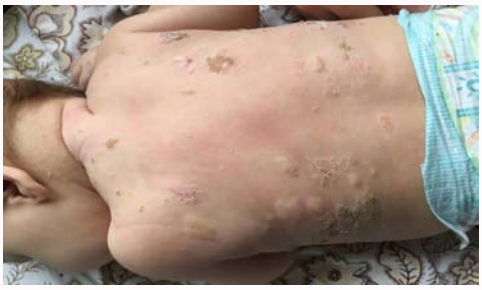
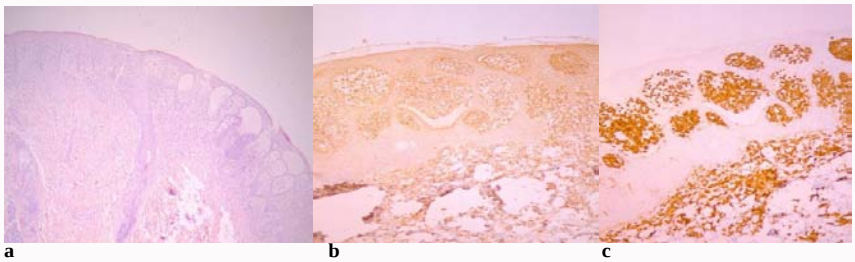


Figure 6:

The patient started her therapy with cetirizine at the age of 4 months. After a month the dosage increased four times. Afterwards desloratadine, montelukast, topical zinc preparations and pimecrolimus cream were added. The parents were consulted about the necessity to avoid disease triggers and given instructions on the use of the Epinephrin injector. The girl was refractory to the prescribed therapy. The disease progressed. New bullae developed almost every day. Therefore, it was decided to initiate systemic methylprednisolone 1 mg/kg (12 mg) therapy at age of 7 months. There was good therapeutic response. Bullae formation ceased, even though the Darrier's sign remained positive. Abdominal ultrasound



a b c

Figure 3 (a;b;c): Histopathology shows minimal orthokeratosis in epidermis and acanthosis. Monomorphic mast cells with round and oval, hyperchromatic nuclei and eosinophilic cytoplasm are located in the dermis. Giemsa staining demonstrates multiple small metachromatic granules in the cytoplasm – characteristic for mast cells. There is also positive antibody staining to CD117 and Mast cell tryptase antigen. Intraepidermal bullae and vesicles filled with fluid containing eosinophils and mast cells can be seen.

Table 1: Who Classification of Mastocytosis.

Variants	Subvariants
Cutaneous mastocytosis	Mastocytoma, Urticaria pigmentosa (maculopapular), diffuse
Indolent systemic mastocytosis	Smoldering systemic mastocytosis, isolated bone marrow mastocytosis
Systemic mastocytosis with associated clonal hematological non-mast-cell-lineage disease	Associated with myeloproliferative disorder, CMML, myelodisplastic disorder, AML, non-Hodgkin lymphoma, HES
Aggressive systemic mastocytosis	Lymphadenopathic with eosinophilia
Mast cell leukemia	Aleukemic
Mast cell sarcoma	
Extracutaneous mastocytoma	

Table 2: Who Criteria for the Diagnosis of Systemic Mastocytosis.

Major Criterion
Multifocal, dense infiltrates of mast cells (aggregates of ≥15 mast cells) in bone marrow or extracutaneous tissues
Minor Criterion
1. >25% of mast cells in bone marrow samples or extracutaneous tissues are spindle-shaped or otherwise atypical
2. Expression of CD25 and/or CD2 by extracutaneous mast cells (often determined by bone marrow flow cytometry)
3. Presence of activating KIT codon 816 mutation in blood, bone marrow, or extracutaneous tissues
4. Serum total tryptase level persistently >20 ng/ml (unless there is an associated clonal myeloid disorder, in which case this parameter is not valid)

Requires either the major criterion plus one minor criterion or three minor criteria.

monitoring was repeated in a month and no hepatosplenomegaly was seen. The methylprednisolone was tapered to the minimal effective dose of 4 mg of methylprednisolone once in three days. Each time it was tried to tapper or cancel the therapy bullae broke out. At the age of 17 months oral cromolyn sodium 20 mg/kg was added and methylprednisolone was canceled. Comely sodium is not widely available in Latvia, so it was ordered from United Kingdom. At the moment the patient has been receiving oral therapy with cromolyn sodium for 3 months. During this period the Darrier's sign is still positive and her mother observed development of cutaneous bullae for 3 times.

Discussion

Mastocytosis is diagnosed on the basis of clinical history, presenting sign and symptoms, histopathology and laboratory examinations [9]. The World Health Organization (WHO) classifies mastocytosis into 7 categories (Table 1). WHO has also developed criteria for systemic mastocytosis (Table 2) [8].

A physical examination with a positive Darier's sign, serum tryptase level, blood count and a skin biopsy should be evaluated initially. In addition to the skin biopsy, bone marrow studies are recommended if the tryptase is significantly elevated. Severe systemic symptoms are present, if there is associated organomegaly or if there is no significant response to initial symptomatic therapy [4]. In children with tryptase <100 ng/ml the diagnosis of CM may be decided upon without bone marrow biopsy, unless other signs of SM are present. Rising tryptase levels or those that exceed 100 ng/ml are an indication for bone marrow biopsy regardless of age [7]. Tryptase levels correlate with mast cells numbers in the skin. Elevations of tryptase is seen in patients with a more severe disease [4].

The approach to treatment of patients with mastocytosis is to stabilize the release of mast cell mediators and to block their effects in order to control the symptoms and signs of the disease such as pruritus, flushing and gastrointestinal cramping [4]. The treatment includes patient counseling, avoidance of trigger factors of mast cell degranulation (environmental stimuli, emotional stress, certain drugs, anesthesia, vaccinations, infections etc), treatment of acute MC mediator-release symptoms (i.e., anaphylaxis), treatment of chronic MC mediator symptoms and treatment of organ infiltration by MC [4,8,9].

The main groups of drugs used in treatment of cutaneuos mastocytosis are antihistamines, leukotriene antagonists, topical and oral cromolyn sodium, local therapy with zinc preparations, steroids, calcineur in inhibitors, NSAID's, phototherapy and PUVA [2,8]. Only few case reports describe the use of oral glucocorticoids in treatment of diffuse cutaneous disease refractory to topical therapy [8].

In our case, the patient did not respond to the common available treatment options, that is why oral corticosteroids were added temporarily. Systemic corticosteroids relieved the symptoms. However, inevitable development of complications prompted search for an alternative treatment. Unfortunately, oral cromolyn sodium is not available in our country, therefore it was ordered from abroad. The treatment proved to be moderately effective with some exacerbations still observed by the child's parents.

Cromolyn sodium is a mast cell stabilizer. Its mechanism of action is unclear. Oral cromolyn sodium has proven to be effective in some children to control diarrhea, abdominal pain, nausea, and vomiting. Despite its low absorption in the intestines, cromolyn sodium is said to be useful in some patients for the treatment of cutaneous symptoms including pruritus [4]. Currently, cromolyn sodium is one of the mainstay treatments of mastocytosis [8]. Mastocytosis treatment can be challenging due to the variability of the cutaneous and systemic disease. Unfortunately, no universal treatment protocol exists [7].

References

1. Vaes M, Benghiat FS, Hermine O. Targeted Treatment Options in Mastocytosis. Front Med (Lausanne). 2017;4:110.
2. Edwards AM, Capkova S. Oral and topical sodium cromoglicate in the treatment of diffuse cutaneous mastocytosis in an infant. BMJ Case Reports. 2011.
3. Rothe M, Grant-Kels JM, Makkar HS. Mast cell disorders: Kids are not just little people. Clinics in Dermatology. 2016;34(6):760-6.

4. Castells M, Metcalfe DD, Escribano L. Guidelines for the Diagnosis and Treatment of Cutaneous Mastocytosis in Children. Am J Clin Dermatol. 2011;12(4):259-70.

5. Azana JM, Torrelo A, Matito A. Update on Mastocytosis (Part 2): Categories, Prognosis, and Treatment. Actas Dermosifiliogr. 2016;107(1):15-22.

6. Bologna JL, Schaffer JV, Cerroni L. Dermatology. Fourth Edition. Section 18. Neoplasms of the Skin: Tharp, Sofen, Mastocytosis. 2102-2112. 2018. Elsevier Limited.

7. Lange M, Nedoszytko B, Gorska A, Anton Żawrocki, Michał Sobjanek, Dariusz Kozlowski. Mastocytosis in children and adults: clinical disease heterogeneity. Arch Med Sci. 2012;8(3):533-41.

8. Cardet JC, Akin C, Lee MJ. Mastocytosis: update on pharmacotherapy and future directions. Expert Opin Pharmacother. 2013;14(15): 2033-45.

9. Carter MC, Metcalde DD, Komarow HD. Mastocytosis. Immunol Allergy Clin North Am. Author; available in PMC 2015 Feb 1.