

Bullous mastocytosis in child: case report*

*Mastocitose bolhosa na criança: relato de caso**

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Abstract: Mastocytosis is a rare disease, defined as a disorderly infiltration with mast cells in several tissues. It comprises many different clinical situations varying from indolent cutaneous forms to malignant and systemic conditions. The term bullous mastocytosis describes all the variety in which the cutaneous bullae represent the predominant feature and generally indicates cases of diffuse cutaneous mastocytosis. Its presence is more common during the childhood and has a more reserved prognosis. This case report emphasizes the extreme diversity of its clinical manifestations and complications.

Keywords: Child; Mastocytosis; Mastocytosis, cutaneous

Resumo: A mastocitose é doença rara, definida como a infiltração desordenada de mastócitos em vários tecidos. Compreende diferentes quadros clínicos, variando de formas cutâneas indolentes a condições sistêmicas e malignas. O termo mastocitose bolhosa descreve a variedade na qual a lesão cutânea bolhosa é o aspecto predominante e geralmente indica casos de mastocitose cutânea. É mais comum na criança e possui prognóstico mais reservado. Este relato de caso enfatiza a diversidade de suas manifestações clínicas e as complicações decorrentes.

Palavras-chave: Criança; Mastocitose; Mastocitose cutânea

INTRODUCTION

Mastocytosis is a rare disease characterized by a disorderly mast cell accumulation in various organs, such as skin, bone marrow, liver, spleen, lymph nodes and gastrointestinal tract, manifesting through a wide range of clinical alterations.^{1,2} Prevalence in general population is hard to determine, because many cases are self-limited and/or not diagnosed,^{3,4} but it is estimated that each 1.000-8.000 patients is affected,^{1,3,5} a proportion that, in childhood, is close to 5.4 cases out of 1000 children seen in dermatological pediatrics clinics.⁶ The onset of manifestations of mastocytosis in over half of the patients is seen between birth and the second year of life,^{4,8} displaying a certain preference for males.⁷

The most common presentation is cutaneous, considered to be benign during childhood, with spontaneous involution in puberty.⁹ Among the cutaneous forms, the subtype characterized by the predominance of bullous eruptions is called Bullous Mastocytosis (BM), with a more reserved progno-

sis.^{10,11} In this report, a case of an infant bearing BM with unfavorable evolution is described and discussed, depicting the complexity of manifestations and the prognosis of the disease.

CASE REPORT

Four-month old infant, male, brown skin, natural from and living in José de Freitas, PI. Born through transpelvic route, with good vitality, with an uneventful birth and neonatal period. Under exclusive breast-feeding and updated vaccination. He was referred for investigation of bullous skin lesions with an onset three days before, associated to vomiting. At two months of age, pruritic purple maculae appeared evenly distributed throughout the body surface, evolving with skin dryness and spontaneous resolution with no use of topic or systemic medication. He had a good general state, no fever, weighing 7,400kg. There were confluent bullous eruptions, either tense or ruptured, with serous content, on a

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FIGURE 1: Tense, confluent bullous eruption on the cervical region



FIGURE 2: Vesicles and bullous eruptions distributed through trunk and cervical region

non-urticated base, located mainly on the cervical region (Figure 1) and trunk (Figure 2), with some lesions present on the right upper limb and scalp. Mucosae were whole. On the abdomen, there were discretely elevated rough-surfaced hypochromic maculae, as well as grouped vesicular-bullous lesions. Physiologic pulmonary auscultation, absence of lymphadenomegalies or abdominal visceromegalies. Normal hematological and renal laboratorial evaluation; negative secretion bacterioscopy. Thoracic skin biopsy revealed, by hematoxylin-eosin staining (HE) and by toluidin blue, supraepidermal blister with great edema in superficial dris (Figure 3) and a dense inflammatory infiltrate, with predominance of mast cells (Figure 4), thus confirming diagnosis of bullous mastocytosis. The child received local care and antimicrobial medication, with good evolution, rupture of the blisters and formation of crusts on the surface. He was then dismissed from the hospital and his parents were oriented on the importance of dermatological follow-up. Fourteen days later, the child presented an episode of diarrhea, having been seen at the medical service of his town, where, according to the father, he received a non-specified intravenous medication. About an hour later, the child rapidly developed bullous eruptions with hemorrhagic content in the entire body surface, being referred to the Emergency Room Service in Teresina. However, by the time he was seen by a physician, he had already died, with no need for any reanimation maneuvers.

DISCUSSION

Mast cells originate from bone marrow pluripotent primordial cells, becoming completely granulous cells, capable of generating a great amount

of mediators that are responsible for effects in target organs.³ The term mastocytosis refers two a spectrum of rare affections with an increased number of mast cells in the skin and, in some cases, in other organs. It is more often reported in Caucasians and in males.¹² Around 65% of the cases occur up to the 15th. year of age, having 30% of those an onset within the first six months of life,¹ as in the case described here. Even though this disease has a favorable course during childhood, generally the bullous mastocytosis subtype holds a more reserved prognosis,^{5,14} as observed in the present case.

Although many organs can be involved, the most common manifestation is the cutaneous, the clinical expressions of which are eruptive teleangiectasia macularis perstans, mastocytoma, diffuse cutaneous mastocytosis and pigmented urticaria (PU).¹⁵ Bullous cutaneous lesions can manifest and be present in all forms of mastocytosis; however, when this is the predominant presentation, it is called bullous mastocytosis (BM), with frequent systemic involvement.^{4,10} Any organ may be affected, but the most commonly affected are bones (osteolytic lesions), spleen, liver (mast cell infiltration an fibrosis) and gastrointestinal tract.¹⁵ Patients suffering from mastocytosis often have cardiovascular manifestations, such as flushing, hypotension, tachycardia, syncope and shock. Such reactions are secondary to the effects of the mediators secreted by mast cells, by agents stimulating their degranulation, such as bacterial toxins, physical stimuli (heat, cold, sun light, friction), poisons (snakes, Hymenoptera), biological peptides (ascaris, jelly fish, lobster, wasp poison and bees), polymers (dextrane), acetylsalicylic acid, codein, morphin, polimixin B, quinine, radiographic contrasts, thiamine,

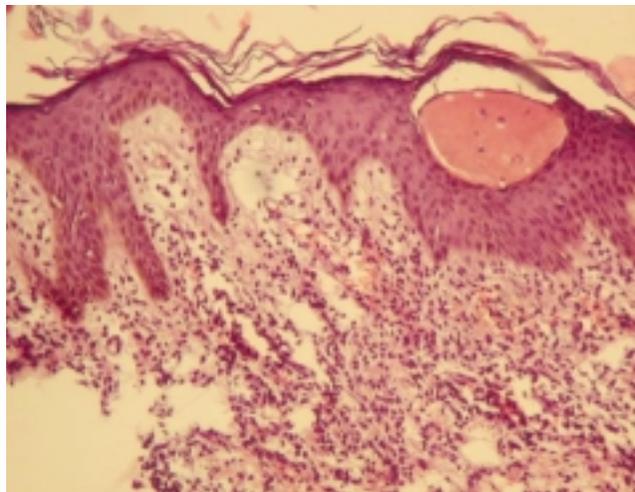


FIGURE 3: Histopathological examination of a skin fragment with supiepidermal blister and great edema in superficial dermis (H&E 40x)

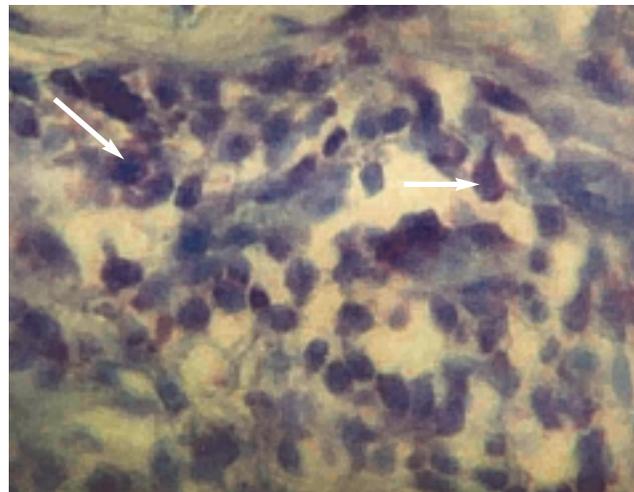


FIGURE 4: Histopathological examination of a skin fragment with dense inflammatory infiltrate and predominance of mast cells (arrows), stained by toluidin blue (400x)

isoproterenol, ephedrine, scopolamine, galamine, decamethonium and reserpine.^{4,5,14}

Patients under high risk of shock or sudden death are those with extensive bullous lesions, symptoms of vasodilation, flushing or hypotension, and those with a very early onset of the disease, i.e., still during the neonatal period.¹¹ Involvement of the gastrointestinal tract by mastocytosis is related in literature as a not-so-common event, but in BM, when there is systemic involvement, that of gastrointestinal tract is more common. Gastric hypersecretion, due to a plasmatic increase in histamine, resulting in peptic ulcer, is the most common problem, as well as diarrhea and abdominal pain, related to malabsorption in up to one third of instances.³ Because it is the most common systemic involvement in this variant,^{6,10} it is interesting to stress the systemic findings of the patient here reported, which could be intestinal compromising as indicated by symptoms (vomiting and diarrhea), even though with no laboratorial proofs, given the quick evolution of the picture.

Bullous mastocytosis is typically characterized by a thickened skin, with an enhancement of cutaneous folds, hyperpigmentation in over half of the cases and present Darier's sign,^{10,13} none of which was observed in the present case. Blisters are tense, with thin walls, initially with clean fluid content, later on becoming pustular or hemorrhagic, varying in size, and linear or grouped, as verified in case description. With extensive compromising of skin complications like secondary cutaneous infections, systemic alterations and shock may occur.¹⁰ The good general state of the child reported here, in spite of the extension of the cutaneous affection, is attention-drawing.

The demonstration of mast cell increase in mid and superficial dermis of characteristic cutaneous lesions is the golden standard for the diagnosis of mastocytosis.¹¹ Such diagnostic confirmation is important for an effective therapy or to make projections regarding prognosis, plan life-supporting measures and even genetic counseling. One of the likely death causes in the patient of this report (immediate cause) may have been hypotension secondary to massive mast cell degranulation, triggered by some agent. Among these, can be the use of non-specified intravenous medication, supposedly a trigger for secretion of mediators by mast cells, such as scopolamine or analgesic drugs, according to collected information. Another hypothesis to be considered is the action of bacterial toxins, that could have been present due to gastroenteritis, as mast cells degranulating agents. Unfortunately, because no necropsy was carried out, the question remains open. The main treatment goal of all mastocytosis categories is to control signs and symptoms determined or provoked by releasing of mast cell mediators. Patients should always avoid the use of mast cell degranulating agents. Dissodium cromoglycate inhibits mast cell degranulation and may have some efficacy in the treatment, particularly for the relief of gastrointestinal symptoms, even though it does not decrease seric or urinary levels of histamine.

Among other drugs mentioned in the literature are ketotifen, as a mast cell membrane stabilizer, with anti-histaminic properties; adrenaline, used for vascular collapse episodes. Photochemotherapy with psoralene and ultraviolet A is reported,^{13,15} as is the use of interferon associated or not with systemic steroids, for patients with systemic mastocytosis.^{4,5} Topic glucocorticoids can be used for extensive PU or cutaneous mastocytosis.

Children who present bullous lesions as the first sign of mastocytosis seem to have a worse prognosis when compared to those with diffuse cutaneous mastocytosis, with the later onset of blisters.¹¹ Despite the relative rarity of bullous mastocytosis, its diagnosis is important, both because of the multiplicity of

cutaneous manifestations and of the risk associated with consequent symptoms, illustrating the clinical complexity that may come with the disease, hence the need for knowledge and prevention of agents that trigger release of mast cells mediators and of treatment and orientation of these patients. □

REFERENCES

1. Hartmann K, Henz BM. Mastocytosis: recent advances in defining the disease. *Br J Dermatol.* 2001; 144: 682-95.
2. Mastocytosis Information and Help Site [homepage on the Internet]. Australia: The Mastocytosis Society, Inc.; c1996-2003 [updated 2003 Jan 11; cited Apr 8]. Available from: <http://www.mastocytosis.com/>.
3. Metcalfe DD. Mastocitose. In: Goldman L, Bennett JC. *Tratado de Medicina Interna.* 21a ed. Rio de Janeiro: Guanabara Koogan; 2001. p.1634-6.
4. Fernandes EI, Faria BC de, Cartell A, et al. Mastocitose sistêmica na infância: relato de 3 casos. *J Pediatr.* 2002;78: 176-80.
5. Leblanc L, Monléon JV, Faber V, Beer F, Dalac S, Justrabo E, et al. Mastocytose cutanée bulleuse révélée par un malaise grave secondaire à la prise de morphinique. *Arch Pediatr.* 2001; 8: 512-5.
6. Metcalfe DD. Classification and diagnosis of mastocytosis: current status. *J Invest Dermatol.* 1991; 96:2-4.
7. Kettelhut BV, Metcalfe DD. Pediatric mastocytosis. *J Invest Dermatol.* 1991; 96:15-8.
8. Murphy M, Walsh D, Drumm B, Watson R. Bullous mastocytosis: a fatal outcome. *Pediatr Dermatol.* 1999; 16:452-5.
9. Golkar L, Bernhard JD. Mastocytosis. *Lancet.* 1997; 349: 1379-85.
10. Hartmann K, Metcalfe DD. Pediatrics Mastocytosis. *Hematol Oncol Clin North Am.* 2000;14: 625-40.
11. Sampaio SAP, Rivitti EA. Mastocitoses. In: *Dermatologia.* 2a ed. São Paulo: Artes Médicas; 2001. p. 915-7.
12. Carvalho IM, Friedman H, Medeiros BM. Telangiectasia macularis eruptiva perstans: relato de caso. *An Bras Dermatol.* 2001; 76: 611-4.
13. e.Medicine Instant Access to the Minds of Medicine [homepage on the Internet]. Nebraska: e.Medicine.com, Inc.; c1996-2003 [update 2003 Feb 12; cited 2003 Jul 5]. Available from: <http://www.emedicine.com/derm/index.shtml>.
14. Murphy GF, Mihm EM. A pele. In: Cotran RS, Kumar V, Robbins SL, Schoen FJ. *Patologia estrutural e funcional.* 5a ed. Rio de Janeiro: Guanabara Koogan; 1996. p.1058-93.
15. Kaatz M, Barta U, Wollina U. Mastocitose cutânea difusa na infância: tratamento bem sucedido com PUVA. *An Bras Dermatol.* 2000;75:737-43.

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