

## **Systemic Mastocytosis in Children: About a Case**

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### **Abstract**

Mastocytosis is a group of rare pathologies linked to the clonal accumulation of abnormal mast cell infiltrates in one or more organs. Their pathophysiology is dominated by activating mutations affecting C-Kit (Stem Cell Factor receptor).

There are many clinical forms, ranging from isolated cutaneous mastocytosis mainly affecting children, to aggressive systemic mastocytosis described mainly in adults with predilective bone marrow involvement.

According to the 2016 WHO classification of hematologic malignancies, systemic mastocytosis is considered a new entity of "myeloid neoplasias and acute leukemias" which combines cytology (abnormal mast cells) with other genetic and molecular criteria.

**Keywords:** mastocytosis, child, diagnosis, myelogram

### **INTRODUCTION:**

Mastocytosis is a group of rare pathologies linked to the clonal accumulation of abnormal mast cell infiltrates in one or more organs. Their pathophysiology is dominated by activating mutations affecting C-Kit (Stem Cell Factor receptor). [1]

Clinically, systemic mastocytosis is revealed by allergic skin manifestations (pruritus, urticaria, angioedema), cardiovascular (vascular collapse, anaphylactic shock, etc.) mainly due to pro-inflammatory mediators released by mast cells, gastrointestinal disorders (abdominal pain, diarrhea, nausea, etc.), haematological (Hepatosplenomegaly, lymph node and medullary damage) and more rarely bone and neurological damage. [2,3]

The laboratory tests necessary for the diagnosis of mastocytosis derive from the diagnostic criteria for the pathology described by the WHO in 2016 [4].

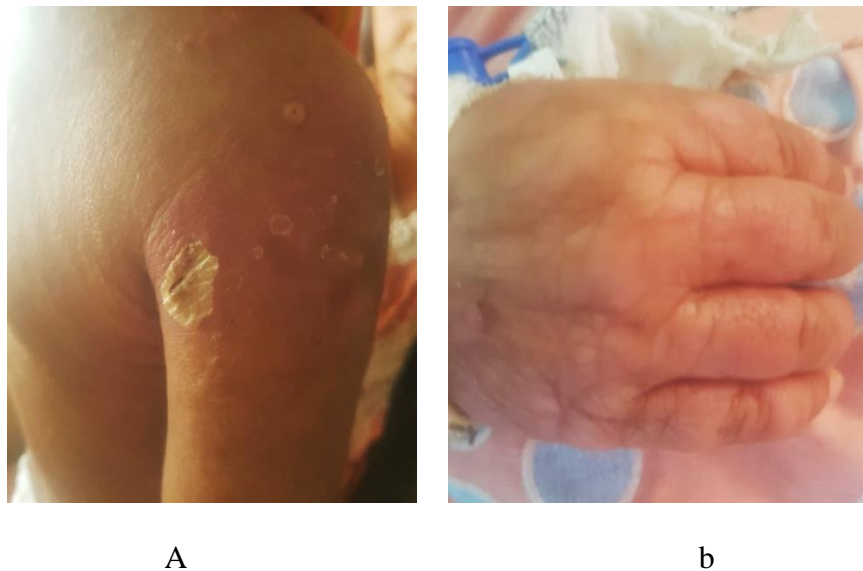
### **OBJECTIVE:**

The objective of the work is to report an exceptional case of systemic mastocytosis in a 2-year-old child

**METHOD:**

This is the 2-year-old child who presents 15 days ago for skin lesions (whitish papules) all over the body itchy then appearance of bubbles (figure 1.a) with clear or haematic content. which spontaneously regresses, forming either crusts or achromic spots (figure 1.b) in places without other associated signs, the whole evolving in a context of conservation of the general condition.

An abdominal ultrasound was performed and which objectified a discrete hepato-splenomegaly, the chest X-ray was normal.



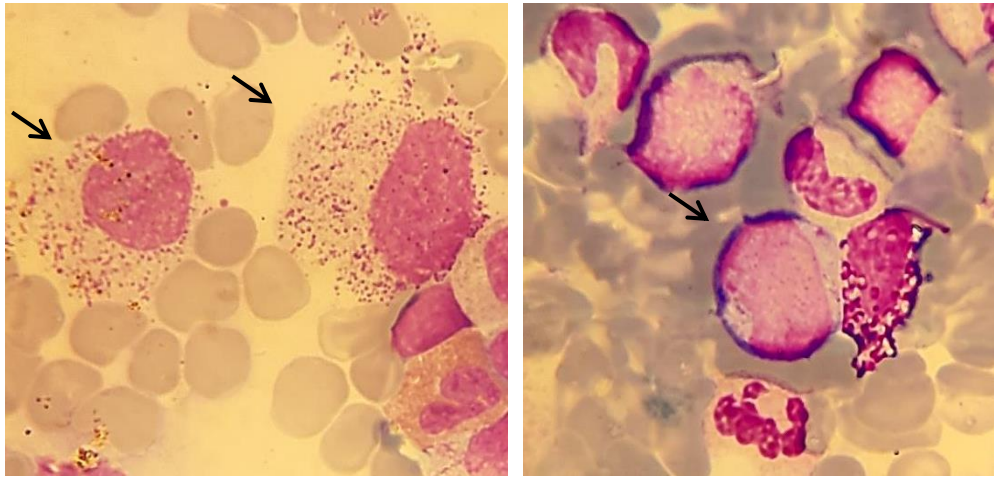
**Figure 1:** aspects of skin lesions bullous lesions (a) and achromic spots after healing (b)

On the complete blood count, hemoglobin was 12.5 G / L, mean blood volume (MCV) at 77.7, Mean corpuscular hemoglobin content (MCHC) at 27.1, white blood cells at 8460 and platelets at 384,000 / L.

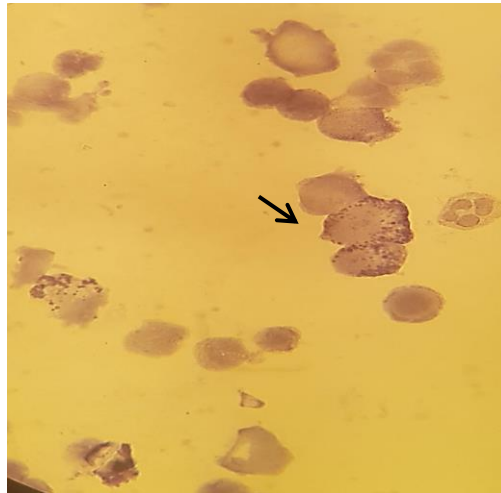
The renal function was normal with a urea level at 0.33 and creatinine at 2. The liver test returned to normal with a normal transaminase level (ALAT at 11, ASAT at 27) and normal cholestasis balance (GGT at 12, PAL to 221). C-reactive protein (CRP) was normal with a level of 6.14., The ionogram was normal and tryptase was elevated with a level of 113 ug / L

A skin biopsy was taken which came back inconclusive.

The myelogram objectified a very rich marrow showing very many megaryocytes with the presence of atypical spindle-shaped cells with a low nucleocytoplasmic ratio with eccentric nucleus and dense chromatin, extended cytoplasm showing basophilic granulations evoking mast cells at 27%, The other lines are well represented and are without notable cytological abnormalities. Toluidine blue staining came back positive (Figure 3).



**Figure 2:** montrant infiltration médullaire par les mastocytes (flèche)



**Figure 3:** mast cells toluidine blue staining (arrow)

A search for the mutation of the gene encoding the c-kit receptor has not been requested, either on blood or skin samples.

The patient was initially put on antiH1, topical corticosteroids and moisturizing gel with good progress.

#### **DISCUSSION:**

Mastocytosis is a condition characterized by an abnormal tissue accumulation of mast cells, most often in the skin. Cutaneous mastocytosis are benign conditions, usually self-limiting and mainly observed in children [1], as in our case, it is a systemic mastocytosis diagnosed in a 2-year-old child, moreover it can affect children at all ages [5,6,7,8]. The other entity is represented by

systemic mastocytoses (SM) which are rare conditions (10% of all mastocytoses), which are either indolent, be aggressive. [9]

Mastocytosis is considered an autonomous disease and it is no longer part of the classic myeloproliferative neoplasias. A distinction is made between two forms of mastocytosis: on the one hand, the cutaneous form (urticaria pigmentosa), which is limited to the skin and often occurs in children; On the other hand, systemic mastocytosis in which other organs, such as the liver, spleen, gastrointestinal tract or lymph nodes, can be affected from the bone marrow [10].

In the WHO 2016 classification, mastocytosis is one of the entities of the myeloid neoplasia group (Table 1).

<b>WHO CLASSIFICATION:</b> 2008: Myeloproliferative neoplasia 2016: Separate entity in myeloid neoplasias and acute leukaemia
<b>- Cutaneous mastocytosis (CM)</b>
<b>- Systemic mastocytosis (SM)</b>
- Indolent systemic mastocytosis (ISM) *
- Systemic smoldering mastocytosis (SSM) *
- Mastocytosis associated with another hemopathy **
- Aggressive systemic mastocytosis (ASM) *
- Mast cell leukemia (MCL)
<b>- Mast cell sarcoma (MCS)</b>

**Table 1:** 2016 WHO classification of mastocytosis

The diagnosis of mastocytosis is based on a set of clinical, cytological, histological, molecular and phenotypic criteria. According to the WHO 2016 diagnostic criteria for systemic mastocytosis, the diagnosis is confirmed by the association of the major criterion with a minor criterion or the presence of 3 minor criteria.[4](Table 2).

Cytologically, normal mast cells are medium-sized and very chromophilic cells, which allows their microscopic identification on a low-magnification myelogram even if they do not exceed 1% of the bone marrow cells.

With MGG staining, preferably with toluidine blue, the mast cell is a mononuclear cell of 15 to 25 µm, with a round, spherical nucleus, small (nucleocytoplasmic ratio <0.5), central, covered with dense metachromatic granulations of 0.3 at 1.5 µm, stained purple with Giemsa and orange-red with alcian blue at acidic pH. [11.12]

With the use of sensitive analytical methods, it is possible to demonstrate an A2447T somatic mutation in the coding sequence of the KIT gene in 95% of adult cases of SM [13,14]. Less sensitive methods, eg. Sanger sequencing can lead to false negative results in more than 90% of cases [14].

**Major criterion:**

Multifocal dense infiltration of mast cells (> 15 aggregated mast cells) on bone marrow biopsy and/or on sections of other affected organs.

**Minor criteria:**

a. more than 25% spindle cells in sections of marrow or extracutaneous organs affected or more than 25% atypical mast cells of all mast cells observed on a smear of marrow.

b. mutation of codon 816 from c-kit in the marrow or other extra-cutaneous organs analyzed.

vs. detection of Kit + mast cells expressing CD2 and/or CD25

d. controlled serum tryptase > 20 ng / ml apart from another associated blood disease.

**If a major criterion and a minor criterion or three minor criteria are met, the diagnosis of systematic mastocytosis is retained.**

**Table2:** Diagnostic criteria for systemic mastocytosis according to the 2016 WHO classification.

In our study, the atypical mast cell count was 27% of all mast cells observed in the spinal cord smear.

Most pediatric patients with cutaneous mast cell disease do not require treatment. Considering an excellent long-term prognosis, the management is conservative and aims to counter the symptoms due to the release of mast cell mediator. Given the lack of double-blind placebo-controlled studies or therapeutic agents in this area, many of the recommendations below are based on personal experience and/or expert opinion [1].

**CONCLUSION:**

Mastocytosis in children most often presents as isolated skin lesions and is a relatively rare occurrence with an excellent prognosis and spontaneous regression often occurring in adolescence. Systemic mastocytosis with organ system involvement is a more serious condition and may persist into adulthood.

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