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Pediatric Bullous Mastocytosis: Diagnostic Challenges and Therapeutic Strategies

mahmoud ladhar
Hopital Universitaire Hedi Chaker
olfa fendri
Hopital Universitaire Hedi Chaker
manel hsairi
Hopital Universitaire Hedi Chaker
imene moalla
imenemoalla@gmail.com

Hopital Universitaire Hedi Chaker
kmar turki
Hopital Universitaire Hedi Chaker
hamida turki
Hopital Universitaire Hedi Chaker
lamia gargouri
Hopital Universitaire Hedi Chaker
faiza safi
Hopital Universitaire Hedi Chaker

Case Report

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Abstract

Background

Mastocytosis is a rare disorder characterized by abnormal proliferation and accumulation of mast cells. In children, it is most often limited to the skin. Diffuse cutaneous mastocytosis is the rarest form and typically presents during infancy, frequently with extensive bullous lesions. Due to its rarity and clinical resemblance to other bullous dermatoses, early diagnosis remains challenging.

Case presentation

We report the case of a 9-month-old female infant admitted for an extensive pruritic bullous and ecchymotic eruption involving the thorax, limbs, and scalp. Physical examination revealed thickened infiltrated skin and a positive Darier's sign, while mucous membranes were spared. Routine laboratory investigations were normal. Skin biopsy showed a dense subepidermal dermal infiltrate composed predominantly of mast cells arranged in confluent sheets. Immunohistochemical staining demonstrated strong and diffuse CD117 positivity. Serum tryptase levels were elevated, supporting the diagnosis of diffuse cutaneous mastocytosis. The patient was treated with topical corticosteroids, sterile dressings, and oral antihistamines, with complete resolution of skin lesions and no systemic complications.

Conclusion

Diffuse cutaneous mastocytosis should be considered in infants presenting with bullous skin lesions. Histological and immunohistochemical confirmation is essential for diagnosis. Although prognosis is generally favorable, careful follow-up is required due to the risk of severe mediator-related manifestations.

Clinical trial number: not applicable

Introduction

Mastocytosis encompasses a group of rare disorders characterized by abnormal proliferation of mast cells in one or more organs. Clinical expression is highly variable and depends both on mast-cell mediator release and tissue infiltration. Gain-of-function somatic mutations of the KIT gene are identified in more than 80% of pediatric mastocytosis cases (1). In children, cutaneous involvement is the most common manifestation. According to the WHO classification, cutaneous mastocytosis is divided into three clinical forms (2). Urticaria pigmentosa is the most frequent form, accounting for approximately 65% of cases (3), while solitary mastocytoma is observed in 9–35% (3, 4). Diffuse forms, such as bullous mastocytosis, are much rarer but may lead to more severe symptoms. This clinical diversity may complicate diagnosis and highlights the importance of reporting rare or atypical cases. The present case illustrates a particular manifestation of this disease, providing further insight into its clinical variability.

Case Report

We report the case of a 9-month-old female infant from Sfax with no significant past medical history, admitted to the pediatric intensive care unit for management of extensive oozing epidermal detachment. Symptoms began five days prior to admission with a flu-like syndrome, followed by the appearance of an erythematous rash involving the thorax, trunk, and all four limbs, which rapidly progressed to bullous detachment within 24 hours (Fig. 1). A history of symptomatic treatment with paracetamol and homeopathic remedies was reported. Due to the severity and extent of skin lesions associated with respiratory deterioration, the patient was admitted to the intensive care unit. She was febrile, tachypneic with hoarseness, and hemodynamically stable. Dermatological examination revealed areas of epidermal detachment with a 'wet sheet' appearance; Darier's sign was positive in the axillary folds, neck folds, and back. The background skin was ecchymotic with hemorrhagic bullae overlying ecchymotic areas, particularly on the neck (Fig. 2–3). There was no mucosal or diaper area involvement. The scalp was also affected (Fig. 4).

Initial laboratory investigations showed an inflammatory response with CRP of 45 mg/L, leukocyte count of 9,930/mm³, and eosinophils at 20%. Upon admission, the patient was intubated and mechanically ventilated due to respiratory distress. Skin care included sterile wet dressings, paraffin gauze, and petroleum jelly, along with systemic dexamethasone. Toxic epidermal necrolysis and staphylococcal scalded skin syndrome were initially suspected, prompting treatment with intravenous immunoglobulins for two days and antibiotics (teicoplanin combined with amoxicillin–clavulanic acid). Skin swab cultures revealed various staphylococcal species.

On day two of hospitalization, bullous mastocytosis was suspected based on the infiltrated yellowish plaques on the flank, glottic edema, and respiratory distress. Serum tryptase level was markedly elevated at 73.7 µg/L (normal < 8.4 µg/L). The diagnosis of diffuse cutaneous mastocytosis was confirmed by skin biopsy showing a thin epidermis with parakeratotic scales and intra- and subepidermal micro-abscesses. The underlying dermis contained a dense band-like inflammatory infiltrate composed predominantly of confluent sheets of mast cells, with scattered eosinophils and neutrophils. Immunohistochemistry demonstrated intense and diffuse CD117 staining. The patient was treated with topical hydrocortisone, antiseptic cream, and oral antihistamines.

The hospital course was complicated by suspected care-related infection requiring clindamycin, and by right internal jugular vein thrombosis. Skin condition improved within days of treatment, with re-epithelialization, reduced erythema, and absence of new bullae (Fig. 5). The patient was discharged home after 20 days of hospitalization, including 11 days in intensive care and 7 days of mechanical ventilation. Parents received education on trigger avoidance and follow-up care. At 7-month follow-up, complete resolution of lesions was observed (Fig. 6).

Discussion

The prevalence of pediatric mastocytosis is estimated at 1 to 10 cases per 100,000 individuals (5, 6). Between 60% and 80% of patients develop skin lesions during the first year of life (7). In children, most cases are benign, and the cutaneous form is the most frequent. Based on the clinical appearance of skin involvement, cutaneous mastocytosis (CM) is divided into three main forms: maculopapular cutaneous mastocytosis (MPCM), also known as urticaria pigmentosa; diffuse cutaneous mastocytosis (DCM); and cutaneous mastocytoma (8).

MPCM is the most common form and presents as red-brown macules or slightly elevated papules measuring 0.5 to 1 cm, predominantly involving the trunk and extremities, while the face, scalp, palms, and soles are generally spared (9). Mastocytoma is characterized by a nodular or plaque-like lesion, solitary or up to a maximum of three lesions. DCM is a rare and severe form, and its bullous variant is an extremely rare entity, with an estimated occurrence of 1 per 1,000,000 individuals (10). It usually presents at birth (congenital or infantile form) or during early childhood (5). Clinically, it manifests as erythroderma and pachydermia, with thickened, leathery skin showing an “orange peel” appearance due to mast cell infiltration, associated with bullae and blisters (11). A positive Darier’s sign is pathognomonic for all forms of CM (7, 11). Pruritus is frequently present (12), and hyperpigmentation may persist into adulthood. Other systemic symptoms, such as flushing and gastrointestinal disturbances, may occur as a result of histamine and other mast cell mediator release into the bloodstream (6, 13).

In our case, toxic epidermal necrolysis (Lyell syndrome) or a staphylococcal skin infection was initially suspected before the diagnosis of bullous mastocytosis was established. Indeed, the clinical presentation may resemble Stevens–Johnson syndrome/toxic epidermal necrolysis or other pediatric bullous disorders, including staphylococcal scalded skin syndrome, linear IgA bullous dermatosis, epidermolysis bullosa, bullous impetigo, and bullous erythema multiforme (5, 6). The clinical manifestations of bullous diseases in children are often very similar, making clinical diagnosis challenging. Roux et al. (6) reported a similar case that was initially diagnosed and treated as Stevens–Johnson syndrome, with the diagnosis of bullous mastocytosis subsequently confirmed by skin biopsy.

The vast majority of mastocytosis cases result from a somatic mutation of the proto-oncogene c-KIT (7), which encodes the KIT receptor, also known as CD117, a tyrosine kinase receptor responsible for mast cell differentiation, maturation, and proliferation (5, 7). Mutations in c-KIT lead to constitutive activation of the KIT receptor, resulting in mast cell proliferation within tissues (5, 7, 13). Sotlar et al. reported c-KIT gene mutations in skin biopsies from 16 of 37 pediatric patients (43%) with cutaneous involvement (14).

The diagnosis of cutaneous mastocytosis is often challenging and relies on a combination of clinical and biochemical findings (5, 7). Initial evaluation includes a complete clinical and dermatological examination, complete blood count, blood biochemical tests, and serum tryptase measurement, as well as skin biopsy with histological examination. Tryptase is a serine protease primarily synthesized and stored in mast cells (15). Baseline serum tryptase levels reflect the total mast cell burden of the body, making it useful for the diagnostic workup and follow-up of systemic mastocytosis. A baseline serum

tryptase level greater than 20 ng/mL is defined by the WHO as a minor diagnostic criterion for systemic mastocytosis (11), particularly when associated with cytopenias and organomegaly (6, 16). However, elevated tryptase levels may strongly suggest the diagnosis without definitively confirming it. Several other conditions are associated with elevated baseline serum tryptase levels, including hereditary alpha-tryptasemia, allergic diseases, chronic eosinophilic leukemia, and certain nephropathies (17).

In our case, serum tryptase levels were elevated in the absence of other signs of systemic involvement. Elevated serum tryptase levels are commonly observed in patients with extensive skin involvement, particularly those with diffuse cutaneous mastocytosis (11). The diagnostic gold standard relies on formalin-fixed skin biopsy with CD117 immunostaining, demonstrating significant dermal infiltration by mast cells (5, 7, 13). The major histological criterion for diagnosis, with a specificity ≥ 95%, is a mast cell density greater than 139 mast cells/mm² in the superficial dermis (18). However, skin biopsy is not systematically required and is mainly indicated in doubtful cases, when Darier's sign is not evident or when skin lesions are atypical (18, 19). Genetic analysis for activating KIT mutations in skin and peripheral blood is particularly important in uncertain cases, as it represents the most specific criterion for cutaneous mastocytosis lesions. Determination of KIT D816V mutational status using highly sensitive quantitative real-time PCR is recommended (18).

To date, no curative pharmacological treatment exists for mastocytosis (5). The main goal of cutaneous mastocytosis management is to reduce and control mast cell mediator release (5, 7, 10, 13). The first and most important preventive measure is avoidance of triggering factors. Numerous environmental and pharmacological factors may induce mediator release, including extreme temperatures (heat and cold), fever, infections, stress, physical exercise, skin friction, nonsteroidal anti-inflammatory drugs, opioids, contrast agents, dextromethorphan, and certain antibiotics such as quinolones (7, 13). This highlights the importance of parental education prior to discharge and during follow-up visits. In our case, paracetamol was not considered a risk medication, but a preceding infection may have acted as the triggering factor. The use of an epinephrine auto-injector in cases of severe hypotension or shock is recommended, particularly in children with extensive skin involvement, a history of severe systemic symptoms or anaphylaxis, and markedly elevated serum tryptase levels.

Symptomatic treatment of diffuse cutaneous mastocytosis can be achieved under sterile conditions through the application of topical therapies and oral medications, such as topical corticosteroids or topical sodium cromoglycate, and oral antihistamines (7, 13). The use of systemic corticosteroids is limited by their numerous side effects but may be indicated for short durations in cases of extensive lesions and recurrent bullae (6, 8). Refractory cases may be treated with omalizumab (an anti-IgE monoclonal antibody) or psoralen plus ultraviolet A photochemotherapy (7, 8). Follow-up is recommended every 6 to 12 months. Parents should be informed of the rare possibility of progression to systemic disease (7). A recent literature review showed that approximately 1 in 100 children with cutaneous mastocytosis may develop a systemic form (20).

During follow-up, our patient experienced an episode of wheezing dyspnea. Disease evolution may be characterized by complete absence of symptoms or, conversely, by the occurrence of mediator-related symptoms such as pruritus, flushing, bullae, wheezing, abdominal pain, diarrhea, hypotension, headaches, and depression (8). In general, most pediatric patients with cutaneous mastocytosis experience spontaneous regression around puberty and have a favorable prognosis (5, 18, 21), despite a reported mortality rate of up to 24%, mainly due to anaphylactic shock and gastrointestinal hemorrhage (8). A recent prospective study evaluating the long-term outcome of pediatric mastocytosis in 28 children reported diffuse bullous involvement in 6% of cases, with a favorable outcome observed in 25% of those patients (22).

Conclusion

Pediatric bullous mastocytosis is a rare and underdiagnosed condition. Early recognition relies on careful correlation of clinical, histopathological, and biological findings. Identification of Darier's sign, CD117-positive mast-cell infiltration, and elevated serum tryptase are essential for diagnosis. Symptomatic management is usually effective, but vigilant monitoring remains necessary given the potential for severe systemic manifestations.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with ethical standards, and ethical principles were fully respected.

Consent for publication

Informed written consent was obtained from the parents of the patients for publication of the paper and all informations within it. The proof of consent can be requested at any time

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the study conception, data collection, analysis, and manuscript preparation. All authors read and approved the final manuscript.

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Figures



Figure 1

Initial papules slightly raised, 0.5 to 1 cm in diameter, located on the trunk, yellowish-brown in color



Figure 2

Appearance upon admission to intensive care showing areas of epidermal detachment overlying an ecchymotic areas



Figure 3

Wet line appearance resting on a bruised base



Figure 4

Erythematous-necrotic appearance with blisters on the scalp



Figure 5

Absence of new blisters or vesicles with hyperemic scars



Figure 6

The erosions are healing and the post-inflammatory hypopigmentation is minimal.