

Blister, Vaccines, and Mast Cells: A Difficult Case of Diffuse Cutaneous Mastocytosis



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Overall Purpose/Goal: To provide excellent case-based reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

Target Audience: Physicians and researchers within the field of allergic disease.

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Learning objectives:

1. To recognize the symptoms of cutaneous mastocytosis.
2. To formulate a management plan for children with suspected cutaneous mastocytosis.
3. To recognize the key differences in cutaneous lesions between pediatric and adult onset disease.

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The Difficult Cases Feature is based on the *Difficult Cases* Course presented at the AAAAI Annual Meeting and coordinated by the AAAAI New Allergist-Immunologist Assembly (NAIA). View the entire presentation and obtain CME or MOC credit by visiting the *JACI: In Practice* homepage www.jaci-inpractice.org.

Key words: Pediatric mastocytosis; Diffuse cutaneous mastocytosis

CASE

A 7-month-old female infant was seen at the Allergy Clinic for a persistent urticarial rash. The rash first appeared at 3 months of age on the back and scalp, manifested as intermittent blistering

and was associated with scratching according to the mother. On examination, the skin had a peau d'orange texture with non tender urticarial lesions on the abdomen and back. On gentle

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FIGURE 1. Darier's sign* elicited in clinic. *Darier's sign: the development of erythema and urticaria after stroking of the skin.

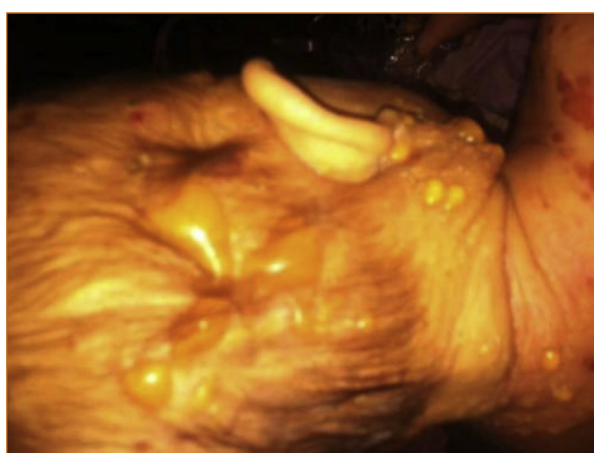


FIGURE 2. Lesions after a viral illness involving vomiting and diarrhea.

stroking of an indurated area, localized erythema and urticaria were induced, indicative of a positive Darier's sign (Figure 1). This led to the suspicion of diffuse cutaneous mastocytosis (DCM), and the serum tryptase level was found to be elevated at 115.0 ng/mL (reference range: <11.4 ng/mL).

A skin biopsy confirmed the diagnosis of cutaneous mastocytosis (CM). Given the highly elevated tryptase level, a bone marrow biopsy was obtained to rule out systemic mastocytosis (SM) and was negative for mast cell aggregates. The skin biopsy, peripheral blood, and bone marrow were all negative for KIT D816V mutation.

The patient was treated with daily H1 and H2 receptor blockers and montelukast. Epinephrine autoinjector was recommended. Intermittent urticaria and blistering occurred with



FIGURE 3. Flare after live viral vaccines.

TABLE I. Tryptase trend (reference range: <11.4 ng/mL)

Level at 7 months of age	Level at 1 year of age	Level after a flare	Level after a flare	Level at 3 years of age	Level at 4 years of age
115.0	93.4	148.0	187.0	61.9	39

TABLE II. Classification of cutaneous mastocytosis^{1,2}

Maculopapular cutaneous mastocytosis (MPCM)*	Most common type; lesions may range from macules to raised papules to plaques and nodules
• Monomorphic	Small lesions—seen usually in adults; occasionally in children
• Polymorphic	Larger asymmetric lesions—seen usually in children
Diffuse cutaneous mastocytosis (DCM)	Rare; involves skin diffusely with thickening; bullous eruptions with hemorrhage may be seen
Mastocytoma of the skin	Solitary to a maximum of 3 lesions; seen typically in infants and young children with spontaneous involution seen most frequently

*MPCM is also known as urticaria pigmentosa.

TABLE III. Triggers of cutaneous mastocytosis*

Physical triggers: Temperature changes, humidity, exercise, stroking of the skin, surgery
Foods: Spicy foods
Medications ³ : Opioids, aspirin, vancomycin, radiocontrast agents, some muscle relaxants
Vaccines, particularly live viral vaccines ⁴ : Most problematic in diffuse cutaneous mastocytosis
Other factors: Infections, emotional stress, teething, fever, alcohol

*This list is not exhaustive.

viral illnesses (Figure 2) and after live viral vaccines (Figure 3). These episodes were treated with topical and oral corticosteroids and topical antibiotics. The tryptase level was followed yearly with the most recent at 4 years of age at 39 ng/mL (Table I).

TABLE IV. Characteristics of cutaneous lesions associated with adulthood-onset and childhood-onset mastocytosis²

Parameter	Adulthood-onset mastocytosis	Childhood-onset mastocytosis
Most common skin lesion	Maculopapular	Maculopapular
Morphology of skin lesion	Monomorphic	Polymorphic
Typical size of lesions	Small	Large
Distribution of lesions	Trunk, thigh	Trunk, head, extremities
Typical course	Chronic	Temporary
Typical tryptase level (µg/L)	>20	<20

DISCUSSION

Mastocytosis is the excessive accumulation of clonal mast cells in tissue(s). Mast cells may be limited to the skin without other organ involvement (CM) or may infiltrate extracutaneous organs (SM). CM can be classified based on the types of lesions (Table II). Symptoms can be elicited by various triggers (Table III) and include pruritus, flushing, urticaria (Darier's sign), and blister formation. Most pediatric patients with CM have a normal serum tryptase. However, in DCM (bullous type), tryptase levels may be elevated with or without systemic involvement. Most lesions, however, resolve by adolescence.

The most common form of mastocytosis in children is CM, with lesions typically being polymorphic. On the other hand, cutaneous lesions of adult-onset mastocytosis are typically monomorphic in nature.⁵ Initial lesions of childhood-onset cutaneous mastocytosis develop within the first year of life (in approximately 80%). Diagnosis is often clinical based on characteristic skin findings, age of onset, and history suggestive of mast cell mediator release. Evaluation involves laboratory tests including serum tryptase, complete blood count with differential, and liver function tests to rule out systemic involvement. Skin biopsy is indicated to confirm the diagnosis. In the absence of systemic symptoms, hepatosplenomegaly, lymphadenopathy, and any laboratory evidence of systemic involvement, the patient can be followed longitudinally. Bone marrow biopsy is not indicated unless tryptase is highly elevated (>20 ng/mL),^{5,6} and/or there is evidence of systemic involvement, including cutaneous

lesions persisting beyond adolescence, or persistently elevated/increasing serum tryptase levels.²

Management of CM involves avoidance of triggers for mast cell activation (Table III), and antihistamines to prevent pruritus, flushing, and blistering. Topical sodium cromolyn (0.21% to 4%) has also been used anecdotally for symptomatic relief.⁷ Epinephrine autoinjector is indicated in patients with elevated tryptase or anaphylactic symptoms. Premedications are recommended before anticipated exposure to triggers, including surgery, vaccinations (specifically before live viral vaccines given in childhood in patients with DCM), and radiological procedures.

Besides CM, skin lesions can also be present in SM. The characteristics of cutaneous lesions associated with adulthood-onset mastocytosis (most commonly SM) and childhood-onset mastocytosis (most commonly CM) are listed in Table IV.

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