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Two Infants Who Have Skin Lesions That React to Minor Trauma

Case 1: Abdulla Gori, MD,* Carlos Tomeria, MD,* Case 2: Victoria M. Kelly, MD,† Barrett J. Zlotoff, MD,† Michael E. Contreras, MD†

Case 1 Presentation
A 2-year-old girl presents to the outpatient clinic for a routine health supervision visit. She was born at term with congenital hydronephrosis requiring antibiotic prophylaxis. Except for one episode of pyelonephritis during infancy, her past medical history has been uneventful. Growth and development are normal for age. Family history is unremarkable.

Routine physical examination reveals a happy, playful, well-developed toddler who has nine skin lesions located on the abdominal wall and back. The lesions range from red to tan to brown and appear as macules, papules, or plaques (Fig. 1). Stroking one of the lesions triggers a wheal and flare reaction at the lesion site (Fig. 2). No respiratory symptoms develop at that time. Findings on the rest of her physical examination are unremarkable.

On additional questioning, her parents recall that the skin lesions developed during infancy, gradually increasing in number. They were not concerned because the lesions did not appear to have any associated signs or symptoms. A clinical diagnosis is made.

Case 2 Presentation
A 5-month-old girl presents to the clinic with a 4-month history of a recurrent “blister” on her left fourth finger. Between episodes of blistering, the finger remains swollen and red. The patient’s mother denies any history of a burn or trauma to the finger. She reports that her daughter often sucks on the finger. Despite bandaging, the blistering continues to occur. The infant is otherwise asymptomatic; she has had no febrile episodes or abdominal or respiratory symptoms. The infant was born at term via vaginal delivery without complications. Past medical history and family history are unremarkable.

Physical examination reveals a well-nourished infant in no acute distress. Skin examination reveals a 1×2 cm reddish-brown papule with an overlying bulla on the dorsal aspect of the left fourth digit (Fig. 3). Rubbing the area produces erythema and enlargement of the bulla. No other lesions are noted elsewhere on the body. A clinical diagnosis is made and confirmed by biopsy.

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Figure 1. Red to tan to brown abdominal macules and papules.

Figure 2. Wheal and flare reaction of skin lesion after stroking.

Figure 3. 1×2 cm reddish-brown plaque that has overlying bulla on dorsum of fourth finger.
Diagnoses: Cutaneous Mastocytosis

Case 1: Urticaria Pigmentosa

The development of a Darier sign (erythema and urticaria on rubbing the pigmented lesion) confirms the clinical diagnosis of urticaria pigmentosa (UP). The Darier sign is a reaction caused by the release of histamine from mast cell degranulation due to mechanical trauma. The wheal and flare response seen in UP can persist 30 minutes to several hours.

Case 2: Solitary Mastocytoma

The findings on clinical presentation and on physical examination are consistent with a solitary mastocytoma that usually presents as a papule, plaque, or nodule and consists of infiltrating mast cells and inflammatory cells in the dermis. With scratching of or minor trauma to the mastocytoma, the mast cells degranulate, releasing histamine, and leading to the development of local erythema, edema, and sometimes blistering.

Discussion

Mastocytosis is a rare disorder in both children and adults caused by an infiltration of excess mast cells within any organ, with the skin being the organ involved most commonly. Following scratching or minor trauma, mast cells degranulate, releasing histamine. Patients who have mastocytosis may have associated systemic signs and symptoms, depending on the concentration of mast cells in other organ systems, such as the gastrointestinal (GI) and respiratory tracts and cardiovascular, hematologic, and lymphoid tissues. Examples of systemic signs and symptoms include flushing, rhinorrhea, wheezing, and diarrhea. The spectrum of mastocytosis ranges from benign cutaneous disease to aggressive mast cell leukemias. Subcategories of cutaneous mastocytosis include solitary mastocytoma, UP, telangiectasia macularis eruptive perstans, and diffuse cutaneous or bullous mastocytosis.

In children, mastocytoses generally are confined to the skin. Progression to hematologic malignancy with solitary mastocytoma has not been reported; bone marrow involvement in children can occur with the more diffuse cutaneous mastocytoses but is rare and usually transient. Adult-onset disease tends to have a more severe course than childhood-onset and often is associated with a sporadic gene mutation for the c-kit growth factor. Adults also are more likely to manifest bone marrow involvement, including premalignant and malignant hematologic disorders. Myeloid cells can be involved (proliferative and dysplastic disorders), and lymphoproliferative disorder can occur. The Table classifies mastocytoses.

Diagnosing mastocytosis can be difficult in the absence of characteristic skin lesions and the Darier sign. A skin biopsy may demonstrate increased numbers of mast cells identified by toluidine blue, fluorescein isothiocyanate-avidin, or Giemsa stain. Biochemical markers that may indicate increased mast cell degranulation include increased plasma tryptase concentrations, chronically elevated plasma and urinary histamine values (along with high urine concentrations of the histamine metabolite N-methyl-histamine), and increased urine prostaglandin D values.

Urticaria Pigmentosa

UP is the most common form of mastocytosis, occurring in about two thirds of patients who have cutaneous mastocytosis. UP is primarily a disease of children, with the most cases diagnosed between 3 and 9 months of age. The lesions may be present at birth or typically erupt in crops during the first several months to 2 years of age. Cutaneous lesions may be sparse or numerous and usually follow symmetric distribution, most commonly affecting the upper and lower extremities, thorax, and abdomen. The palms, soles, face, and mucous membranes are spared. The skin lesions generally appear as multiple red-yellow brown hyperpigmented macules, papules, or nodular lesions that have ill-defined borders (Fig. 4). Individual lesions usually are round to oval, vary from 1 mm to several centimeters in diameter, and generally are larger in children than in adults. Some lesions may develop as early bullous or urticarial lesions.

### Table. Classification of Mastocytoses

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that fade over time and recur at the same site as fixed, hyperpigmented lesions.

Clinical diagnosis is based on the appearance of erythema and urticaria in response to gentle stroking of the lesion. Ninety percent of patients who have UP and other forms of cutaneous mastocytosis demonstrate this hallmark finding. Other common symptoms of UP include intense pruritus that varies in degree of intensity and chronicity and flushing in association with bathing in hot or cold water, friction of the lesion, and exercise.

Skin lesions tend to resolve by adolescence in about 50% patients; 25% of adults have partial resolution. UP that appears after age 10 years usually persists throughout life and may be associated with systemic disease. Of note, the skin lesions seen in UP also appear in other varieties of mastocytosis.

Solitary Mastocytoma
A solitary mastocytoma is a single, benign skin lesion about 1 to 5 cm in diameter that is created by infiltration of the dermis by mast cells and inflammatory cells. The lesion usually appears at birth or early infancy, increases in size for several months, and eventually regresses within several years. These lesions usually are round to oval and have a thick or rubbery texture, often with a hyperpigmented, “pebbly, orange peel-like” (“peau d’orange”) surface. Solitary mastocytomas may appear at any site, with a predilection for the wrist, neck, and trunk. Stroking of the lesion may result in urticaria at the site. Punch biopsy of a mastocytoma reveals a monomorphic infiltration of mast cells in the dermis, along with mixed inflammatory cells.

Mastocytomas have the most favorable prognosis of all cutaneous forms of mastocytosis, and in children, most solitary mastocytomas spontaneously resolve within 10 years. In most patients, lesions are solitary; occasionally, however, other lesions do appear. Children rarely develop additional mastocytomas more than 2 months after the onset of the initial lesion.

Symptoms usually are local and mild and have no systemic involvement, so no treatment is necessary. However, conservative measures may be employed to ameliorate symptoms. Topical corticosteroids under occlusion or an intralesional corticosteroid injection can reduce irritation.

Diffuse Cutaneous Mastocytosis
Diffuse cutaneous mastocytosis (DCM) is a rare form of cutaneous mastocytosis that occurs primarily in children younger than 3 years of age. Large areas of the dermis are infiltrated with mast cells rather than discrete areas, as seen in UP. The skin surface may appear normal at birth but rapidly evolves into a generalized pink to yellow thickening, orange peel-like appearance. Bullae and blistering are common, and systemic symptoms can be severe.

DCM may present with symptoms of intense generalized pruritus as well as systemic signs and symptoms such as emesis, diarrhea, abdominal pain, GI ulceration, and acute respiratory distress. Spontaneous resolution is the rule, although persistence and systemic involvement extending into adulthood are risks.

Systemic Mastocytosis
Systemic mastocytosis refers to mast cell infiltration of extracutaneous organs, including the bone marrow, liver, spleen, lymph nodes, and GI tract. The cause and prevalence of cutaneous and systemic mastocytosis are unknown. The prevalence of systemic mastocytosis may be higher than what is reported due to misdiagnosis of UP, solitary mastocytomas, and systemic disease without the cutaneous manifestations. However, systemic mastocytosis becomes more prevalent with age, with symptoms seen more commonly in adults than in children. Signs and symptoms include pruritus, flushing, urticaria, rhinorrhea, wheezing, abdominal pain, nausea, vomiting, diarrhea, bone pain and fractures, hypotension, and headaches. A distinction is made between cases of systemic mastocytosis that have an associated hematologic nonmast cell disorder and those that do not.
Differential Diagnosis
The differential diagnoses for cutaneous mastocytoses include acute urticaria and angioedema (caused by an allergic immunoglobulin E-mediated reaction), bullous impetigo, juvenile xanthogranuloma (nonpruritic, firm, dome-shaped, yellow-to-orange papules or nodules located in the skin and other organs), and allergic contact dermatitis (T-cell-mediated hypersensitivity reaction to a specific antigen applied to the skin surface).

Treatment
Cutaneous mastocytosis has no curative treatment. Treatment is directed toward providing symptomatic relief. Patients and parents should be counseled to avoid key triggers for mast cell degranulation, such as being exposed to extreme temperatures, ingesting spicy foods, and receiving certain medications. Drugs that can cause mast cell degranulation include opiates, polymyxin B, vancomycin, succinylcholine, procaine, aspirin, and iodinated radiocontrast media. Over-the-counter cough preparations that contain dextromethorphan or codeine may induce significant histamine release and blistering. Fortunately, the symptoms of pediatric-onset cutaneous disease usually are less severe than those observed in patients who have adult-onset mastocytosis. Pruritus is the most common symptom.

The treatment of choice for controlling pruritus, flushing, and urticaria is administration of an antihistamine to block the H1 effects of histamine. Hydroxyzine and, more recently, cetirizine and loratadine, both of which have less sedating properties, can be administered. The addition of an H2 antagonist may be useful to alleviate the symptoms associated with hypersecretion of gastric acid. Doxepin, which affects both H1 and H2, can be administered to children older than 12 years of age. Cyproheptadine, which has the advantage of both antihistamine and antiserotonin activity, has been effective for treating cutaneous mastocytosis. Oral cromolyn sodium has been helpful in managing disease that has GI involvement, urticaria, and blistering associated with bullous and diffuse cutaneous forms. Although potent topical and intralesional corticosteroids have been used to clear cosmetically significant or symptomatic lesions, such treatments usually are not recommended for general use. Alfa 2-b interferon and long-wave ultraviolet light (PUVA) also have been used, although relapses may occur after PUVA therapy, and severe anaphylactic reactions have occurred with the use of interferon.

Conclusion
Case 1
The parents were counseled about the patient’s general prognosis as well as the possible need for administering an antihistamine. The patient has remained asymptomatic.

Case 2
One week after the biopsy, the blister was unchanged, with the biopsy site healing well. The patient’s mother was counseled regarding the benignity and natural regression of a solitary mastocytoma. The lesion was treated with topical triamcinolone ointment under occlusion at bedtime for 6 weeks. At the 6-month follow-up visit, the blistering was completely resolved.

Summary
Cutaneous mastocytosis should be considered a possible diagnosis for the infant or child who seeks medical attention for a pruritic skin lesion that usually becomes urticarial after being rubbed or exposed to a hot bath. In the pediatric population, cutaneous mastocytosis generally presents as either UP or solitary mastocytoma, and the diagnosis is based solely on clinical presentation and the presence of the Darier sign. Additional evaluation is not necessary because UP and solitary mastocytoma have favorable prognoses, with lesions typically regressing by puberty. Treatment is directed toward providing symptomatic relief, most commonly with H1 and H2 blockers.

Suggested Reading
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