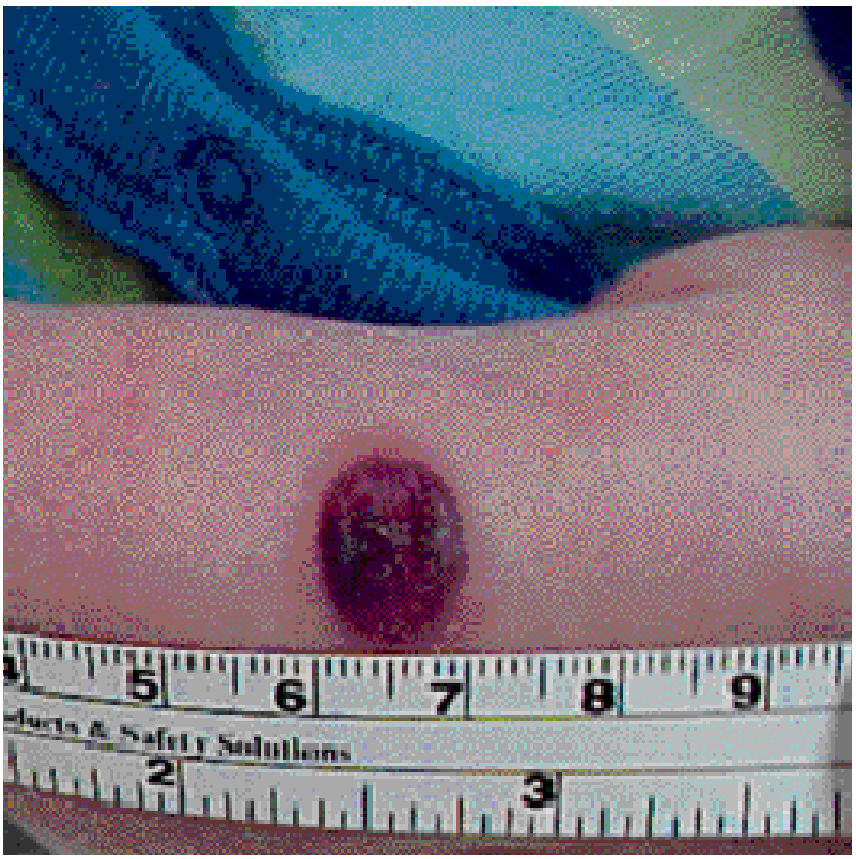
# What Is Your Diagnosis?




A 14-day-old neonate presented with a reddish-brown eroded plaque on his left anterior leg.

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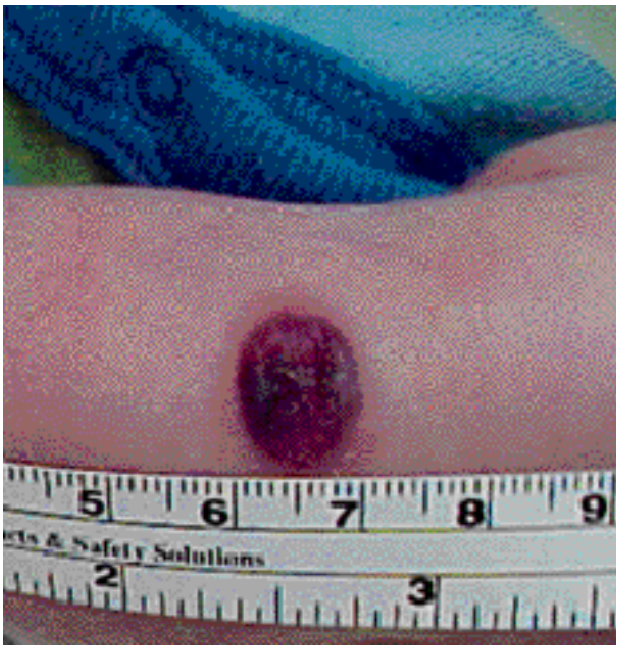
# The Diagnosis: Solitary Mastocytoma

A 14-day-old male neonate presented to the pediatrics clinic with a fever and was admitted for a sepsis workup. The child's parents pointed out a single erythematous blister on his left leg, and the dermatology department was consulted to evaluate the lesion. His mother stated that the lesion was present at birth. From the interview, the dermatologist determined that the lesion initially was a reddish macule, which later evolved into a bulla. The patient's birth was unremarkable, and there was no history of flushing, wheezing, or diarrhea. Results of a 3-mm punch biopsy of the lesion showed a diffuse infiltrate of mast cells in the upper dermis.



The patient presented with the classic history and appearance of a solitary mastocytoma, one of the subtypes of mastocytosis. Mastocytosis, a disorder of mast-cell proliferation, occurs in both cutaneous and systemic forms.

The earliest case of cutaneous mastocytosis was described by Nettleship[1] in 1889. The incidence of mastocytosis is unknown, with 55% of patients presenting between birth and 2 years of age and another 10% developing the disease, either cutaneous or systemic, by 15 years of age.[2]

The skin is the most frequent site of involvement in patients with any form of mastocytosis.[3] The types of cutaneous mastocytosis include mastocytoma, urticaria pigmentosa, diffuse erythrodermic cutaneous mastocytosis, and telangiectasia macularis eruptiva perstans.[4] Urticaria pigmentosa presents as tan to reddish-brown macules, usually on the trunk, that spread symmetrically and may evolve into papules, nodules, or plaques. Some authors state that urticaria pigmentosa occurs more frequently than solitary mastocytoma,[4,5] and others report solitary mastocytoma as the most common type of skin lesion manifested in mast-cell disorders.[1,6]

Table 1.

**Mast Cell Mediators and Their Effects***

| Mast Cell Mediators | Clinical Manifestations |
|---|---|
| Histamine | Increased vasopermeability, systemic hypotension, urticaria, pruritus, bronchoconstriction, gastric hypersecretion |
| Heparin | Local anticoagulation, osteoporosis |
| Tryptases/chymase | Fibrinogen degradation, activation of procollagenase and tissue remodeling, stimulation of fibroblast proliferation |
| Leukotrienes: $LTD_4$, $LTC_4$, $LTE_4$ | Vasopermeability, vasodilatation, bronchoconstriction |
| Prostaglandins: $PGD_2$ | Bronchoconstriction, vasodilatation |
| Platelet-activating factor | Vasopermeability, vasodilatation |
| Cytokines: TNF-α, TGF-β, NGF | Activation of vascular endothelial cells, cachexia |
| Growth factors: IL-3, IL-5 | Mast-cell growth, eosinophilia |

*LT indicates leukotriene; $PGD_2$, prostaglandin $D_2$; TNF, tumor necrosis factor; TGF, transforming growth factor; NGF, nerve growth factor; IL, interleukin.

Table 2.

**Systemic Mastocytosis**

| System | Symptoms | Diagnostic Workup |
|---|---|---|
| Hematologic | Anemia, bruising | Complete blood count; consider bone marrow biopsy |
| Gastrointestinal | Abdominal pain, diarrhea | Abdominal ultrasound, endoscopy |
| Reticuloendothelial | Hepatosplenomegaly | Liver/spleen scan |
| Skeletal system | Bone pain, fractures | Skeletal survey and bone scan |

Telangiectasia macularis eruptive perstans, an extremely rare form of mastocytosis, occurs almost exclusively in adults.[2]

Solitary mastocytomas may be present at birth, and most appear by 3 months of age. Mastocytomas occur with equal frequency in both sexes and seem to affect mostly Caucasians.[7] These lesions usually occur on the extremities or trunk but occasionally appear on the palms or soles, as noted by Lee et al[8] who reported a case of solitary mastocytoma on the left thenar eminence of a Korean infant. Scalp lesions also have been reported.[5] Dissemination may occur from a solitary lesion, but this usually occurs within 2 to 3 months of appearance of the initial lesion.[6] Patients typically present with a reddish-brown nodule, plaque, or macule with an associated bulla. The blistering is caused by mast-cell degranulation at the dermal-epidermal junction, with accumulation of edema. Darier sign, or a wheal-and-erythema reaction, may occur from stroking or rubbing the lesion. Clinically, mastocytomas may resemble pigmented nevi or xanthomas.[5] The lesions usually regress spontaneously during childhood without scarring. To our knowledge, there have been no reports in the literature of progression from solitary mastocytoma to systemic involvement.[9]

Systemic mastocytosis occurs in less than 10% of all patients with pediatric mastocytosis.[7] The gastrointestinal tract, lymphoid tissue and spleen, bone marrow, and musculoskeletal system frequently are involved in systemic mastocytosis.[1] Pediatric patients with cutaneous lesions that persist into adulthood are more likely to develop systemic mastocytosis.[6]

Both systemic and cutaneous mastocytosis may cause symptoms related to local and systemic release of mast-cell mediators, such as leukotrienes, prostaglandins, and platelet-activating factor.[10] The release of histamine from the mast cells causes urticaria and pruritus. Mast-cell mediators and their effects are listed in Table 1. Histologically, a diffuse infiltration of mast cells in the dermis is characteristic. Toluidine blue or Giemsa stains highlight the mast-cell granules.

Immunohistochemical studies may demonstrate the c-kit proto-oncogene.[1] C-kit receptor is a growth factor receptor normally expressed on mast cells, hematopoietic stem cells, and melanocytes. It has been proposed that c-kit mutations cause proliferation and accumulation of mast cells.[11,12] Whether the accumulation of mast cells is caused by increased proliferation or decreased apoptosis has not been determined.[9] Adults with mast-cell disease often express activating mutations in the c-kit proto-oncogene. Most pediatric patients with mastocytosis lack mutations in c-kit, though some activating mutations of c-kit have been reported and may be associated with progressive disease.[9]

Laboratory evaluation for systemic mastocytosis may be limited to patients presenting with specific symptoms (Table 2). Measurement of histamine in a 24-hour urine collection and serum levels of beta and total tryptases can aid in the diagnosis.[13]

Because most solitary mastocytomas resolve spontaneously in childhood, the only special instruction to parents is to avoid activities that cause friction on the lesion, such as rubbing with a bath towel or wearing tight clothing.[3] Most solitary mastocytomas do not manifest significant symptoms and should simply be observed. Potent topical corticosteroids may be used to control symptomatic or bullous lesions. Two cases of solitary mastocytoma in Japan were treated with the oral mast-cell–stabilizing agent tranilast. The lesions on the 2 neonates described resolved within 2 months of initiating tranilast treatment, though a second biopsy of the lesions was not performed to determine a decrease in the number of mast cells. Tranilast is extracted from the plant *Nandina domestica* and is used in Japan to treat asthma, atopic dermatitis, and allergic rhinitis.[14]

Patients with cutaneous mastocytosis should avoid triggering factors that cause release of mast-cell mediators, such as insect stings, codeine and aspirin use (among other drugs), rapid changes in

Table 3.

**Stimuli for Mast-Cell Mediator Release**

| |
|---|
| **Physical Stimuli** |
| Mechanical irritation |
| Massage |
| Friction |
| Exercise |
| **Infections** |
| Bacterial |
| Viral |
| *Ascaris* |
| **Environmental** |
| Temperature changes |
| Cold |
| Heat |
| Sunlight |
| **Insect Stings/Poisons** |
| Crayfish |
| Hymenoptera |
| Jellyfish |
| Lobster |
| Snakes |
| **Drugs** |
| Amphotericin B |
| Aspirin and nonsteroidal anti-inflammatory agents |
| Dextromethorphan |
| Ethanol |
| Gallium |
| Muscle relaxants |
| Narcotic analgesics |
| Quinine |
| Others |

temperature, alcohol consumption, and mechanical irritation (Table 3).

Clinicians may advise their patients with cutaneous mastocytosis to wear a medical alert bracelet and carry an adrenaline-filled syringe. Shock due to mastocytosis is treated in the same manner as anaphylactic shock, with fluids, antihistamines, adrenaline, and pressor agents, if necessary.[15] Patients with any form of mastocytosis should probably not be given iodinated radiocontrast media. Oral cromolyn sodium may reduce pruritus, flushing, and wheal formation.[6] H1 antihistamines such as hydroxyzine can reduce pruritus and flushing, and H1 and H2 antihistamines may be useful for gastrointestinal symptoms.[2] Surgical excision of a solitary mastocytoma is curative if the lesion does not resolve spontaneously.[6]

## REFERENCES


1. Kacker A, Huo J, Huang R, et al. Solitary mastocytoma in an infant. case report with review of literature. *Int J Pediatr Otorhinolaryngol*. 2000;52:93-95.
2. Kumar S. Mastocytosis. *Pediatr Rev*. 2001;22:33-34.
3. Krowchuk DP, Willford PM, Jorizzo JL, et al. Solitary mastocytoma producing symptoms mimicking those of a seizure disorder. *J Child Neurol*. 1994;9:451-453.
4. Soter NA. Mastocytosis and the skin. *Hematol Oncol Clin North Am*. 2000;14:537-555.
5. Munro CS, Farr PM. Solitary mastocytoma causing recurrent blistering in infancy. *Arch Dis Child*. 1992;67:1038-1039.
6. Metcalfe DD, Kettelhut BV. Pediatric mastocytosis. *Ann Allergy*. 1994;73:197-201.
7. Lewis RA. Mastocytosis. *J Allergy Clin Immunol*. 1984;74:755-765.
8. Lee HP, Yoon DH, Kim CW, et al. Solitary mastocytoma on the palm. *Pediatr Dermatol*. 1998;15:386-387.
9. Hartmann K, Metcalfe DD. Pediatric mastocytosis. *Hematol Oncol Clin North Am*. 2000;14:625-640.
10. Alto WA, Clarco L. Cutaneous and systemic manifestations of mastocytosis. *Am Fam Physician*. 1999;59:3047-3054, 3059-3060.
11. Galli SJ, Tsai M, Wershil BK. The c-kit receptor, stem cell factor, and mast cells. what each is teaching us about the others. *Am J Pathol*. 1993;142:965-974.
12. Furitsu T, Tsujimura T, Tone T, et al. Identification of mutations in the coding sequence of the proto-oncogene c-kit in a human mast cell leukemia cell line causing ligand-independent activation of c-kit product. *J Clin Invest*. 1993;92:1736-1744.
13. Rottem M, Okada T, Goff JP, et al. Mast cells cultured from the peripheral blood of normal donors and patients with mastocytosis originate from a CD34+/Fc epsilon RI-call population. *Blood*. 1994;84:2489-2496.
14. Katoh N, Hirano S, Yasuno H. Solitary mastocytoma treated with tranilast. *J Dermatol*. 1996;23:335-339.
15. Kamajian G, Felix J. Acute mastocytosis: a potential dermatologic emergency. *J Am Osteopath Assoc*. 1993;93:792-796.