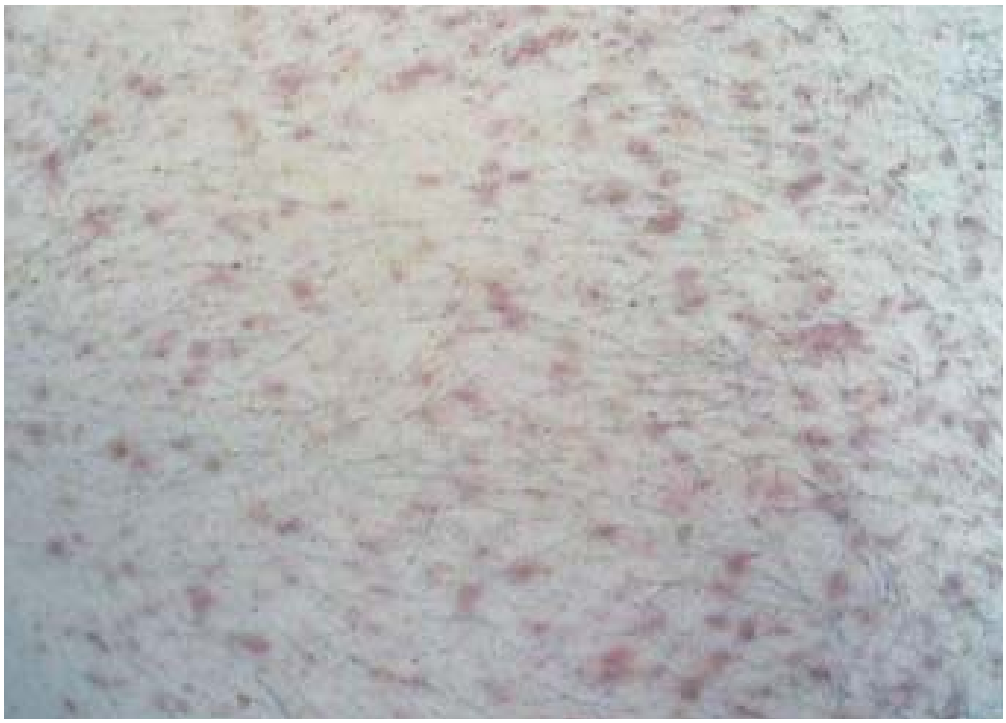
cutis® photo quiz

Thomas N. Helm, MD
Department of Dermatology
Buffalo Medical Group
6255 Sheridan Drive, Suite 208
Williamsville, NY 14221

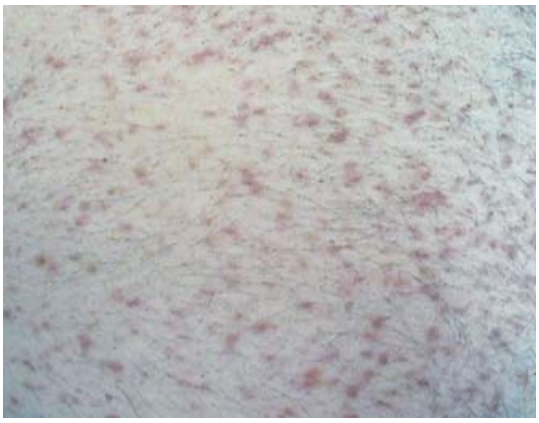


A 45-year-old businessman presents with a widespread pruritic dermatosis. He reports having intermittent trouble with diarrhea and is bothered by the appearance of his skin.

What is your diagnosis?

PLEASE TURN TO PAGE 177 FOR DISCUSSION

The Diagnosis



Discussion

The diagnosis is urticaria pigmentosa, the most common form of mastocytosis. Mastocytosis is a hyperplasia of mast cells that may involve the skin, gastrointestinal (GI) tract, bone marrow, liver, spleen, and lymph nodes.[1] Flushing, pruritus, urticaria, abdominal pain, nausea, headache, and bone pain are associated with extensive mastocytosis, and males are affected slightly more often than females. Mast cell disease is typically classified as being either indolent, associated with hematologic disorders, lymphadenopathic mastocytosis with eosinophilia, or mastocytic leukemia. Individuals with aggressive mast cell disease progress rapidly, and their symptoms are difficult to control with medical therapy. Mast cell leukemia is uncommon and a peripheral blood smear demonstrates immature mast cells.

Cutaneous mast cells are thought to arise from bone marrow. Mast cell differentiation involves the C-Kit ligand (stem cell factor).[2] Mutations have been identified in some individuals and are thought to play an etiologic role with mast cell hyperplasia.[3] The increased number of mast cells gives rise to the clinical features, including hyperpigmented macules on the skin. Skin lesions may urticate with rubbing (Darier's sign). Increased flushing and pruritus may be provoked by changes in temperature, rubbing of the skin, or ingestion of alcohol or medications such as morphine and codeine.

GI symptoms are common, and elevated plasma histamine levels may lead to gastritis and peptic ulcer formation. Abdominal pain, cramping, and diarrhea may be noted and can result in malabsorption. Bone marrow involvement consists of aggregates of spindle-shaped mast cells intermixed with eosinophils, lymphocytes, and plasma cells. Although radiographic surveys have been recommended in the past, skeletal bone scans are more accurate at detecting areas of involvement. Pathologic fractures may occur in individuals with advanced mast cell disease. The diagnosis of mastocytosis is usually established by skin examination and biopsy, but bone marrow biopsy and 24-hour urine collection for histamine metabolites may also be helpful. Twenty-four–hour urine histamine often exceeds 50 μg, and 9 alpha-hydroxy-11,15-dioxo-2,3,18,19-tetranorprost-5-ene-1,20-dioic acid is often greater than 350 ng. Bone scans, upper GI series, and electroencephalogram studies may be helpful in diagnosis, but they are obtained only when certain abnormalities warrant a specific diagnostic evaluation.

The diagnosis of mastocytosis is most often made on skin biopsy alone. If clinical information is not provided to the histopathologist, the increased number of mast cells may be overlooked. This is especially true for the telangiectasia macularis eruptiva perstans variety of mastocytosis in which the increase in the number of mast cells may be slight. Special stains such as Giemsa or ASD chloroacetate esterase (Leder stain) help confirm the diagnosis. Twenty-four–hour urine 5-hydroxyindoleacetic acid and urinary metanephrines are helpful to exclude the possibility of a carcinoid tumor or pheochromocytoma, which may be considered in the clinical differential diagnosis when patients present with flushing and diarrhea. Twenty-four–hour urine collection for 1,4-methylimidazole acetic acid may help estimate tumor load in mastocytosis, but it is now considered experimental and is not widely available at most clinical laboratories.

Treatment with H_1 and H_2 receptor antagonists is helpful. Hydroxyzine, loratadine, and doxepin are most commonly used. Disodium cromoglycate slows mast cell degranulation and seems to be particularly effective for individuals with extensive GI involvement.[4] As in other cases of anaphylaxis, epinephrine is necessary in episodes of severe hypotension. Psor-

alen and ultraviolet A therapy has been shown to relieve pruritus and whealing; however, several months of this treatment are required before improvement is noted, and pruritus and cutaneous symptoms recur 3 to 6 months after discontinuing therapy. Topical corticosteroids can be helpful for localized areas of involvement, and interferon-α therapy may be helpful for aggressive forms of mastocytosis.[5] Although chemotherapy is often used as a treatment for mast cell leukemia, no impressive results in terms of prolonged survival have yet been identified.

REFERENCES

1. Travis WD, Li CY, Bergstralh EJ, et al. Systemic mast cell disease: analysis of 58 cases in literature review. *Medicine*. 1988;67:345-368.
2. Longley BJ, Tyrrell L, Lu SZ, et al. Somatic C-Kit activating mutation and urticaria pigmentosa in aggressive mastocytosis: establishment of clonality in a human mast cell neoplasm. *Nat Genet*. 1996;12:312-314.
3. Zsebo KM, Williams DA, Geissler EN, et al. Stem cell factor is encoded at the S1 locus of the mouse and is the ligand for the C-Kit tyrosine kinase receptor. *Cell*. 1990;63:213-224.
4. Horan RF, Sheffer AL, Austen KF. Cromolyn sodium in the management of systemic mastocytosis. *J Allergy Clin Immunol*. 1990;85:852-855.
5. Castells MC, Friend DS, Bunnell CA, et al. The presence of membrane-bound stem cell factor on highly immature nonmetachromatic mast cells in the peripheral blood of a patient with aggressive systemic mastocytosis. *J Allergy Clin Immunol*. 1996;98:831-840.