Mastocytosis

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KEYWORDS

• Masocytosis • Update • Review • Pathophysiology • Diagnosis • Treatment
• Cutaneous mastocytosis • Systemic mastocytosis

KEY POINTS

- Mastocytosis is a rare disease, characterized by excessive production of mast cells that accumulate in the skin, bone marrow, and other visceral organs.
- The prevalence of mastocytosis is estimated to be 1 in 60,000 in the United States; children tend to have benign forms of mastocytosis, whereas adults may develop aggressive disease.
- The most common mutation is in the C-kit gene, which causes increased proliferation of mast cells; other causes exist but are less frequent.
- Clinical presentation of mastocytosis is variable, often based on the type of mastocytosis, but in all types of mastocytosis there seems to be an increase in the risk of anaphylaxis; patients may present with skin lesions, flushing, diarrhea, lymphadenopathy, hepatosplenomegaly, osteoporosis, and recurrent anaphylaxis.
- For systemic mastocytosis (SM), the preferred method of diagnosing is via bone marrow biopsy.

INTRODUCTION

Mastocytosis is a rare disease, characterized by excessive production of mast cells that accumulate in the skin, bone marrow, and other visceral organs.[1] In a majority of cases, the disorder is due to a nonhereditary somatic mutation in the KIT gene, which leads to heightened proliferation and activation of morphologically and clinically abnormal mast cells.[2] Mast cell activation results in release of mediators by degranulation, and synthesis of lipids and proteins.[3] These mediators are responsible for the clinical manifestations, which include pruritus, flushing, diarrhea, headaches, and life-threatening anaphylaxis.[3] The World Health Organization (WHO) has classified mastocytosis into 7 categories. Broadly, it can be divided into cutaneous mastocytosis (CM) and SM. CM is relatively benign and affects the skin whereas SM involves an extracutaneous organ and has aggressive potential.[4] The most common form of CM is urticarial pigmentosa.[5] SM is subclassified into indolent SM (ISM), associated

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clonal hematologic non–mast cell lineage disease (AHNMD), aggressive SM (ASM), and mast cell leukemia (MCL) (Table 1).

EPIDEMIOLOGY

The prevalence of mastocytosis is estimated to be 1 in 60,000 in the United States. The disease occurs in both children and adults. Children tend to have benign forms of mastocytosis, whereas adults may develop aggressive disease. The true number of cases of mastocytosis is unknown.[1] Its prevalence is estimated to be 1 in 60,000 and incidence 0.5 to 1 per 100,000 per year in the United States.[6] Mastocytosis is a disease of both children and adults, with equal male and female prevalence.[7] A majority of patients are children and are typically affected by CM forms, which carry an excellent prognosis.[8] In many children, symptoms regress spontaneously by puberty.[8] Adults are much more likely to have urticarial pigmentosa and ISM. In adults, the onset of mastocytosis is generally at age 20 to 50 and is diagnosed between 40 and 60 years of age.[3,7] The disease is congenital in approximately 15% to 25% of cases and, in these patients, usually occurs before the age of 2.[3,7,9] In a majority of cases, the disease is spontaneous.[3]

MAST CELL BIOLOGY

Mast cells act as effector cells in allergic and hypersensitivity disorders and are activated through IgE and non-IgE mechanisms. Once activated, they release proinflammatory and vasoactive mediators. Mast cells arise from pluripotent cells in the bone marrow, acquire cytoplasmic granules, and mature in specialized tissues.[1,4,7] They act as sentinels of the innate and adaptive immune system and are abundant in endothelial and mucosal surfaces.[2,6,10,11] Mast cells have a central role in immunomodulation and act as effector cells in allergic and hypersensitivity disorders.[12] Activation and degranulation of mast cells occur through IgE and non-IgE receptor cross-linking.[7,10]

Table 1
World health organization classification of mastocytosis

CM	• Urticaria pigmentosa or maculopapular CM • DCM • Mastocytoma of skin

SM	• ISM
	  ○ Isolated bone marrow mastocytosis
	  ○ Smoldering SM
	• SM-AHNMD
	  ○ SM with acute myeloid leukemia
	  ○ SM with myelodysplastic syndrome
	  ○ SM with myeloproliferative disorder
	  ○ SM with chronic myelomonocytic leukemia
	  ○ SM with hypereosinophilic syndrome
	• ASM
	  ○ Lymphopathic SM with eosinophilia
	• MCL
	  ○ Classic
	  ○ Aleukemic MCL

MCS	
Extracutaneous mastocytoma	

Data from Valent P, Akin C, Wolfgang S, et al. Mastocytosis: pathology, genetics and current options for therapy. Leuk Lymphoma 2005;46:35–48.