Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow

**World Health Organization Criteria for Systemic Mastocytosis (SM)**

Diagnosis of SM can be established if at least 1 major AND 1 minor OR 3 minor criteria are met

- **Major criteria**
  - Multifocal dense infiltrates of mast cells (MC) in bone marrow (BM) biopsies or in section of other extracutaneous organs

- **Minor criteria**
  1. More than 25% of all MCs are atypical (type I or II) or spindle-shaped
  2. *KIT* Asp816Val point mutation present
  3. MCs exhibit CD2 or CD25
  4. Baseline serum tryptase is >20 ng/mL, unless there is an associated myeloid neoplasm, in which case this parameter is not valid.

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**Perform initial testing:**

- TRYPT / Tryptase, Serum
- KITVS / KIT Asp816Val Mutation Analysis, Varies
- PATHC / Pathology Consultation for immunohistochemical (IHC) stains: tryptase or CD117, and CD25

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**Mast cells observed**

1. World Health Organization systemic mastocytosis (SM) diagnostic criteria met
   - If BM aspirate and biopsy also display features of a hematologic neoplasm
     - Diagnostic for systemic mastocytosis with an associated hematological neoplasm
     - Perform disease specific workup of the associated hematologic malignancy

2. If KIT Asp816Val is negative
   - Consider monoclonal mast cell activation syndrome (MMAS) if CD25 or *KIT* Asp816 Val positive

3. Consider possible sampling issue.
   - Resample and retest if clinically appropriate

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**<2 minor SM diagnostic criteria met**

**Normal BM morphology and tryptase Negative KIT mutation**

**Evaluate BM aspirate smear and biopsy for possible non-mast cell hematologic neoplasms**

**STOP**

**No additional testing required**

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**Normal BM morphology and tryptase Negative KIT mutation**

**Perform:**

- CHRBM / Chromosome Analysis, Hematologic Disorder, Bone Marrow
- EXHR / Chromosome Analysis, DNA and RNA Extract and Hold, Varies

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**Other hematologic cells observed**

1. Perform:
   - CHRBM / Chromosome Analysis, Hematologic Disorder, Bone Marrow
   - EXHR / Chromosome Analysis, DNA and RNA Extract and Hold, Varies

2. On a case by case basis; if the bone marrow aspirate shows:
   - Mast cell burden is >15%
   - Mast cell burden is >5%

   **Normal BM morphology**

**Perform:**

- KITE / KIT Mutation Exons 8-11 and 17, Hematologic Neoplasms, Sequencing, Varies
- NGSHM / MayoComplete Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing, Varies

**ABNORMAL**

**Disease-specific workup**

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**If bone marrow (BM) biopsy and IHC stains are inadequate, order:**

- LCMS / Leukemia/Lymphoma Immunophenotyping, Flow Cytometry, Varies

Note reason for referral as Mast cells