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“Heterogeneous group of disorders characterized by the presence of abnormal mast cells (MC) in one or multiple organs”. At the early stages of the disease there are:
- No MC proliferation
- No MC accumulation in tissues

As a consequence
- Low MC numbers + Absence of MC aggregates
- An accurate diagnosis cannot be performed on the basis of cytology, histology and immunohistochemistry

Demonstration of the presence of either clonal or phenotypically aberrant MC by highly-sensitive methods becomes essential:
- Advanced flow cytometry = cells present at low frequencies
- Study of KIT mutations in highly purified mast cells

DIAGNOSIS OF MASTOCYTOSIS IN MCAS /ANAPHYLAXIS IS A CHALLENGE!
Diagnostic algorithm in suspected mastocytosis without skin involvement: anaphylaxis/severe symptoms

Complete clinical work-up. Allergic work-up. Abdominal ultrasonography, DEXA scan

Peripherally blood count. Routine biochemistry, serum cholesterol, LDH, B₂-microglobulin, tryptase. Prostaglandins, leukotrienes

Bone marrow aspirate and biopsy. ARE YOU READY?  

STOP HERE

Cytology  
Histology & IHC  
Flow cytometry immunophenotyping  
Cell lineages purification  
Molecular biology in purified cell lineages

Integrated diagnosis & Classification

NO  
STOP HERE

YES
A. Direct criteria. Confirm an “anatomical lesions” or the presence of abnormal mast cells:

1. Anatomical lesion: aggregates of mast cells detected in sections and/or smears in bone marrow or other tissues (Tryptase, c-kit, CD25)

2. Atypical morphology of mast cells

3. Mast cells express CD25 (±CD2)

4. Detection of a $KIT$ mutation (usually in exon 17) in bone marrow, blood or another extracutaneous organ. In women with negative $KIT$ mutation clonality can be demonstrated by the HUMARA test

B. Indirect criteria. Allow to “suspect” a mastocytosis

1. Serum tryptase levels > 11.4 ng/mL

2. Positive REMA score
1. In SM at the early stages of the disease, lacking bone marrow mast cell aggregates, the combined use of cytology, histology and immunohistochemistry is not enough for an accurate diagnosis of SM because the low mast cell numbers

2. Flow cytometry immunophenotyping is the most sensitive and specific method for detecting abnormal (CD25++) mast cells

3. Study of KIT mutations should be performed in “adequate samples” containing enough mast cells. When positive study should be performed in at least one myeloid and if positive in lymphoid lineages = prognosis = risk stratification

4. Reference Centers for mastocytosis should apply the most sensitive and specific method for an accurate diagnosis and classification of the disease

5. Surrogate markers needed for be applied in developing Countries
Suspected mastocytosis in the absence of skin lesions

- Score ≤ 2
  - Anaphylaxis/severe symptoms
    - Non-clonal
      - Adequate treatment
        - NO BM study
        - Follow-up

- Score ≥ 2
  - Probable ISMs
    - Tryptase ≤ 20
      - Adequate treatment
        - DEXA scan
        - Abdominal ultrasonography
        - Follow-up
        - Wait and see
    - Tryptase ≥ 20
      - + Bone marrow study
      - Follow-up
      - Wait and see