DERMATOLOGY WORLD
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Mastocytosis review

By Mohammed Shanshal, MD

- ❖ Mastocytosis is a **pathologic accumulation of mast cells in tissues**
- ❖ Somatic activating mutations of ***c-kit*** **tyrosine kinase receptor** (frequently involving codon 816) expressed on mast cells.
- ❖ Mutation of ***c-kit*** protooncogene receptor also occurs in→ **piebaldism, in addition to acral and mucosal melanomas as well as melanomas on CSD sites**

• Cutaneous manifestations→

- ○ The most frequently involved organ in mast cell disease is the skin
- ○ Childhood-onset mastocytosis generally has a benign course with spontaneous remission prior to puberty, whereas adult-onset mastocytosis typically persists and may be associated with systemic involvement

Urticaria pigmentosa (UP, maculopapular or plaque mastocytosis)	○ **The most common** clinical variant of mastocytosis ○ Multiple pink-tan to red-brown macules and papules mainly on the **trunk** and usually sparing palms, soles, and face ○ **Darier's sign**→ local erythema or urticarial wheal after friction or rubbing (vs. **Pseudo Darier Sign**: a distinctive finding for congenital smooth muscle hamartoma, in which stroking of the lesion induces transient induration with piloerection) ○ **Pruritus and flushing** may be seen ○ **Bullous mastocytosis** may occur due to mast cell release of **serine proteases**, more common before age 5 ○ Patients with more lesions are more likely to have systemic symptoms (flushing, diarrhea, abdominal pain, dyspnea)
Solitary mastocytoma	○ Single tan/yellow-tan plaque/ nodule with **leathery, peau d'orange texture** ○ Most commonly seen on **distal extremities** ○ **More likely to develop Darier's sign than UP due to higher mast cell density**
Diffuse cutaneous mastocytosis	○ Rare variant, seen almost exclusively in infants ○ Infiltrated, red-brown, leathery plaques, which can coalesce leading to doughy thickening of skin ○ Associated with↑incidence of **systemic mastocytosis**
Telangiectasia macularis eruptive perstans (TMEP)	○ Rare, and is seen almost exclusively in adults ○ Telangiectatic macules and patches **without significant hyperpigmentation and rare or absent Darier's sign**
Nodular mastocytosis	○ Red–purple nodules on the **axillae and inguinal** region, occurs mainly in adults

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• **Systemic manifestations** → rare in childhood mastocytosis, commonly occur in systemic mastocytosis (indolent systemic mastocytosis, mast cell leukemia, and aggressive systemic mastocytosis)

Bone	○ **Skull, spine, and pelvis** are most commonly involved. ○ May appear as **radio-opacities, radio-lucencies, or mixture of the two** ○ **Demineralization**→ the **most common change**, followed by **osteosclerosis and mixed lesions of osteosclerosis and osteoporosis** ○ Patients may have skeletal pain
Gastrointestinal	○ **Abdominal pain, diarrhea**, nausea, and vomiting ○ Precipitated by **alcohol, NSAIDs, aspirin** ○ Malabsorption and peptic ulcer disease with hemorrhage or perforation
Spleen and lymph nodes	○ Splenomegaly is variable in adults with systemic disease ○ Lymph node enlargement is uncommon, except in advanced systemic disease
Bone marrow (BM)	○ BM is involved in nearly all adult patients, but hematologic sequelae are uncommon ○ BM biopsy is not required in children or adults with indolent mastocytosis and normal hematologic parameters, **especially if there is limited cutaneous disease and serum tryptase is normal**
Organs relatively spared	○ Pulmonary, genitourinary, and endocrine
Management	
Histopathology	○ Mast cells infiltrate in the dermis of lesional skin, eosinophils, and hyperpigmentation of the basal layer may be present ○ Mast cells special stains→ **Giemsa, Leder, Toluidine blue** or monoclonal antibodies that recognize mast cell **tryptase or CD117 (KIT)** ○ **Leder stain and c-KIT are reliable even in degranulated cells** as they stain the cytoplasm in addition to granules
Laboratory tests	○ **Serum tryptase may be elevated but is often normal.** Two forms are identified → **α-tryptase** that is elevated in SM whether or not they are experiencing acute symptoms and useful in assessing the total body mast cell burden → **β-tryptase** usually detected in patients who are experiencing anaphylactic symptoms in both patients with and without mastocytosis ○ **Urinary histamine metabolites** may be detectable but have low sensitivity and specificity, not currently used ○ **Plasma levels of IL-6** → correlate with severity of bone marrow pathology and organomegaly

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Treatment	○ Avoid mast cell degranulating agents and environmental triggers like spicy foods, exercise and friction, mediations: aspirin, NSAIDs, narcotics, anticholinergics (e.g. scopolamine), dextromethorphan, polymyxin B sulfate, and some systemic anesthetics **(local injection of lidocaine is safe!)** ○ After general anesthesia, SM patients **should be monitored for 24 hours as delayed anaphylaxis may occur** ○ Local therapy for symptom control→ topical C/S + TCI ○ Systemic therapy for symptom control→ **antihistamines, oral cromolyn sodium (especially for diarrhea)**, C/S, omalizumab, epinephrine (for anaphylaxis), and PUVA/UVA1 ○ Systemic therapy for aggressive/severe mastocytosis→ ❖ **Intravenous cladribine** (shown to be **effective** in advanced SM including patients with D816 c-KIT mutation) ❖ **Imatinib** for patients with FIP1L1-PDGFRA fusion gene who are D816-negative

List of abbreviations:
BM= bone marrow
CSD= chronically sun damaged
CSF= colony-stimulating factor
PGD2= prostaglandin D2
C/S=corticosteroid
TCI= topical calcineurin inhibitors
SM= systemic mastocytosis

References

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