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

<table>
<thead>
<tr>
<th>Mastocytosis Type</th>
<th>Clinical Features</th>
</tr>
</thead>
</table>
| **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 |
# Mastocytosis review

By Mohammed Shanshal, MD

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

| Bone             | o Skull, spine, and pelvis are most commonly involved.  
|                  | o May appear as radio-opacities, radio-lucencies, or mixture of the two  
|                  | o Demineralization → the most common change, followed by osteosclerosis and mixed lesions of osteosclerosis and osteoporosis  
|                  | o Patients may have skeletal pain  
| Gastrointestinal | o Abdominal pain, diarrhea, nausea, and vomiting  
|                  | o Precipitated by alcohol, NSAIDs, aspirin  
|                  | o Malabsorption and peptic ulcer disease with hemorrhage or perforation  
| Spleen and lymph nodes | o Splenomegaly is variable in adults with systemic disease  
|                  | o Lymph node enlargement is uncommon, except in advanced systemic disease  
| Bone marrow (BM) | o BM is involved in nearly all adult patients, but hematologic sequelae are uncommon  
|                  | o 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 | o Pulmonary, genitourinary, and endocrine  

| Management |  
| Histopathology | o Mast cells infiltrate in the dermis of lesional skin, eosinophils, and hyperpigmentation of the basal layer may be present  
|              | o Mast cells special stains → Giemsa, Leder, Toluidine blue or monoclonal antibodies that recognize mast cell tryptase or CD117 (KIT)  
|              | o Leder stain and c-KIT are reliable even in degranulated cells as they stain the cytoplasm in addition to granules  
| Laboratory tests | o 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  
|                | o Urinary histamine metabolites may be detectable but have low sensitivity and specificity, not currently used  
|                | o Plasma levels of IL-6 → correlate with severity of bone marrow pathology and organomegaly  

### Mastocytosis review

**By Mohammed Shanshal, MD**

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
</table>
| o Avoid mast cell degranulating agents and environmental triggers like spicy foods, exercise and friction, medications: aspirin, NSAIDs, narcotics, anticholinergics (e.g. scopolamine), dextromethorphan, polymyxin B sulfate, and some systemic anesthetics **(local injection of lidocaine is safe!)**  
| o After general anesthesia, SM patients **should be monitored for 24 hours as delayed anaphylaxis may occur**  
| o Local therapy for symptom control → topical C/S + TCI  
| o Systemic therapy for symptom control → **antihistamines, oral cromolyn sodium (especially for diarrhea), C/S, omalizumab, epinephrine (for anaphylaxis), and PUVA/UVA1**  
| o 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**