Mastocytosis Mimics: Cutting through the Clutter

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Joseph Butterfield, MD Mayo Clinic
Melody Carter, MD National Institutes of Health
Symptoms: Pediatrics

- Pruritus: 90%
- Flushing: 60%
- Bullae: 50%
- Abd pain: 40%
- Mus/skel: 25%
- Headache: 15%
Clinical
- Historical
  - Mast cell-mediator symptoms
  - Less atopic disease than general population
- Cutaneous
  - Permanent pigmented lesions with a general distribution or diffuse thickening “peau d’ orange” appearance
- Other organ systems-mainly systemic disease

Laboratory
- Tryptase-reflects overall mast cell burden
  - May trend down over time and elevates with mast cell activation
- Urinary metabolites-correlates with serum tryptase
- Hematologic-Usually WNL; may see ↑ lymphs, ↑ PT/PTT, ↑Plts

Sonographic-Hepatosplenomegaly with systemic disease, rare lymphadenopathy
Most Likely

- Diffuse or localized hyper-pigmented macules
  - Café au lait spots
  - Neurofibromatosis
  - Albright syndrome

- Bullous Lesions
  - Chronic bullous disease of childhood
  - Linear IgA dermatosis

- Solitary or multiple nodules
  - Congenital nevus
  - Juvenile Xanthogranuloma
Consider

- No lesions
  - Idiopathic flushing

- Diffuse or localized hyper-pigmented macules
  - Post-inflammatory hyperpigmentation
  - Secondary syphilis
  - Chronic urticaria
  - Atopic dermatitis

- Bullous Lesions
  - Staphylococcus infection
  - Drug eruption
  - Incontinentia pigmenti
  - Bullous pemphigoid

- Solitary or multiple nodules
Always Rule Out

- No lesions
  - Identifiable causes of anaphylaxis
  - Idiopathic anaphylaxis
- Diffuse or localized hyper-pigmented macules or papules
  - Secondary Syphilis
  - Addison’s disease
  - Lentigo

- Bullous Lesions
  - Bullous impetigo of infancy
  - Incongenta pigmenta

- Solitary or multiple nodules
  - Leukemia
  - Lymphoma
Clinical symptoms/signs unlikely to be mastocytosis or mast cell activation

- Hypertensive spells
- Symptoms that improve with medications not targeting mast cell mediators or their effects: Ex: medications for anxiety or depression
- Seizure activity; incontinence
- (Delayed) problems with memory
- Dementia
- Arthritic complaints involving small joints or involving muscles.
- Chronic recurrent headaches
- Chronic hives; atopic dermatitis or eczema
- Delayed reactions to medications
- Rhinitis or rhinosinusitis
- Food allergy
- Non-anaphylactic reactions to beestings, fire ants, horseflies
Urticaria pigmentosa; positive Darier’s sign

Mast cell mediator-related symptoms:
  - Flushing/warmth/pruritus/abdominal cramps/diarrhea/bronchospasm/tachycardia/ (pre)syncope
  - The symptoms respond to epinephrine administration & administration of medications targeting mast cell mediators such as antihistamines, sodium cromolyn

Anaphylaxis to bee stings

Recurring episodes of tachycardia not responding to cardiac medications (β-blockers) or a pacemaker

“Idiopathic” anaphylaxis

Males with osteoporosis

Eosinophilia

Anaphylactic response to NSAIDs (90-95% of mastocytosis patients do tolerate them)
What are other common pitfalls when diagnosing mastocytosis?

- Carcinoid: Briefer flush, worsened by epinephrine vs SM
- Common flushing/climacteric flushing
- Disorders of hyper/hypo hidrosis
- Spells- various types
  - 1. Endocrine (ex: pheochromocytoma, thyrotoxicosis, medullary thyroid carcinoma, insulinoma, hypoglycemia)
  - 2. Cardiovascular (labile HTN, deconditioning, pulmonary edema, syncope, orthostatic hypotension, paroxysmal arrhythmias)
  - 3. Psychologic (somatization disorder, hyperventilation)
  - 4. Pharmacologic (withdrawal of adrenergic inhibitor, MAO treatment + tyramine, sympathomimetic ingestion, illegal drug ingestion, chlorpropamide-alcohol flush, vancomycin-red-man syndrome)
  - 5. Neurologic (postural orthostatic tachycardia syndrome, autonomic neuropathy, migraine headache, seizure disorders, stroke, cerebrovascular insufficiency)

- Panic attacks
- Simple faint; vasovagal episodes
A Word about Flushing

- **Neurogenic-“Wet flushing”**-sympathetic cholinergic neurons stimulate sweat glands
  - Example: “Hot Flash”

- **Dry flushing** - direct vasodilation from vasoactive chemicals; no perspiration
  - Example: Histamine, kinins, prostaglandins, nicotinic acid, amyl nitrite
  - Most cases of “idiopathic” flushing
Urinary Histamine Measurements
  - May only reflect commensal bladder bacterial production
  - Better to use Urinary MIAA or n-Methyl Histamine levels

Serum Histamine Measurements: must be processed rapidly
- Urinary 5-HIAA-for diagnosing carcinoid
- Bone Scans-nonspecific
- Intestinal Biopsies-variability in interpretation, sampling and the degree of infiltration required for diagnosing mast cell involvement
What to look for

- Urticaria pigmentosa (UP)-most adults with UP have systemic mastocytosis
- Mediator symptoms, other suggestive clinical features (bee sting anaphylaxis, idiopathic anaphylaxis)
- Good response to MC mediator blockade
- Increased (baseline or symptom-associated) mast cell mediator levels:
  - Tryptase > 20 ng/mL;
  - Elevated 24 hour Urinary N-methyl histamine; 11β-PGF2α; LTE4
- Confirmatory: bone marrow biopsy
  - Tryptase staining
  - Mast cell morphology
  - Mast cell phenotype
  - C-kit Asp816Val mutation