DISCLOSURE

Current Relevant Financial Relationship(s)
None
Outline of Talk

• Mast Cells
• Mastocytosis
  – Types
  – Diagnosis
  – Therapy
Mast Cell Normal Function

- Found in normal tissues esp skin, lungs, and GI track
- Normal function to aid in inflammation
- Can selectively release granules or all at once
- Contains and creates chemical mediators (> 200)
- Lead to symptoms: flushing, urticaria, itching, wheezing etc.
Mast Cell Mediators

- Histamine: wheezing, flushing, itching, angioedema
- Prostaglandins: wheezing, diarrhea, cramping, abdomen pain, hypotension
- Serotonin: flushing, diarrhea
Mastocytosis

- Etiology due to overactive or too numerous mast cells
- Incidence ~10/10,000
- Under recognized
Types of Mastocytosis

- “Mast Cell Activation Syndrome”
- Cutaneous Mastocytosis
- Indolent systemic Mastocytosis
- Smoldering Mastocytosis
- Aggressive Mastocytosis
- Mastocytosis with hematological malignancy
- Mast cell leukemia
Mast Cell Activation Syndrome

- Not clonal
- **Strict** Diagnostic criteria
  1. Symptoms in two or more organ systems
  2. Markers of mast cell activation present (high tryptase etc.)
  3. Responds to mast cell therapy
Cutaneous Mastocytosis

- Most often in children and resolves by adulthood
- Systemic issues rare
- Adults can have cutaneous signs as part of more systemic disease
Indolent Systemic Mastocytosis

- Most common
  - ~50% of patients
- Clonal
- Issues revolve around excessive mast cell activation
Indolent Systemic Mastocytosis

- Symptoms
  - Mast cell release symptoms
  - Gastrointestinal especially
- No impact on survival
- Rare conversion to more aggressive mastocytosis (~1%)
- Symptoms control biggest issue
  - 70% functional limitation
Indolent Subtypes

- Bone marrow MC
  - Mast cells only in marrow
  - Can have mast cell release symptoms
  - Sometimes asymptomatic
- Smoldering
Smoldering Mastocytosis

• Diagnosis
  -> 30% marrow involvement
  – Hepatomegaly
• Inferior survival
• Higher rate of progression (18%)
Aggressive Mastocytosis

- End organ damage
- Less mast cell activation symptoms – more “cancer”
- Tryptase > 200 ng/ml
- Poor survival
When Should You Suspect Mastocytosis?

- Anaphylaxis
- Mast cell release symptoms
- Skin disease
- GI symptoms
- Osteoporosis
Anaphylaxis

- Idiopathic
  - Especially recurrent
- Stings (most common)
  - 12% of anaphylaxis due to bee stings have mastocytosis
- Higher tryptase = higher risk
- IgE levels lower
  - Can lead to false negative testing
Skin

- Itching
- Urticaria not predominant
- Dermatographism
- Darier sign
Darier Sign

- Rubbing an area of skin affected by mastocytosis may also activate the mast cells. The rubbed skin becomes reddened, swollen and itchy within a few minutes (Darier sign). In young children, the rubbed area may later blister.
Gastrointestinal

- Very common
- Often major issue
- N/V/D
- Peptic ulcers
- Abdominal pain
Diagnosis

• Major: aggregates of > 15 mast cells in a non-skin biopsy

• Minor:
  – Abnormal mast cell morphology
  – Abnormal proteins on mast cell surface
  – D816V KIT mutations
  – Tryptase > 20ng/ml
Laboratory

- Tryptase most specific
- 24-hour urine for PGD2
- Blood for c-KIT mutation
- Biopsy
  - Consider bone marrow, GI, or skin biopsy
  - May need special stains – alert pathologist to diagnosis
Tryptase

• Can be elevated with acute anaphylaxis
• Opioids can elevate
• > 20 ng/ml criteria
• Persistently high also worrisome
C-KIT Mutation

- Growth factor receptor
- Key mutation in mastocytosis
- > 90% have D816V mutation
  - Rest in other areas of C-KIT
- Key test for mastocytosis
C-KIT

• Marrow testing used to be recommended
• Now can test on peripheral blood
• Low suspicion – negative test rules out
• Positive test – helps diagnosis
Evaluation

- Blood for c-KIT
- Biopsy of suspicious areas
- Serum tryptase
- Bone marrow for staging and equivocal cases
General

- Symptom trigger avoidance
- Therapy of mast cell mediator release
- Treatment of bone disease
- Cytoreduction
Hereditary Alpha Tryptasemia

- Extra tryptase gene leads to higher serum tryptases
- Some patients with increased mast cells and symptoms
- Proprietary genetic test
- DX: high tryptase negative work-up
- RX: like indolent mastocytosis
Epi-Pens

- Anaphylaxis common
- Mastocytosis kits
  - Epi-pens
  - Antihistamines
  - Steroids
Antihistamines

- Antihistamines (sometimes need high dose)
  - Diphenhydramine toxicity can be an issue
- Cyproheptadine
  - Also blocks serotonin
  - Diarrhea, flushing, headaches
- Doxepin
  - Itching
Dosing

• Can dose escalate
  – Cetirizine 10mg qid
  – Fexofenadine 180mg bid
  – Hydroxyzine 25mg qid

• Non sedating during day and sedating at night

• Allergy/Immunology can help!
H2 blockers

• Helps with GI symptoms
  – Cramping, nausea, vomiting
• May help with other symptoms
• Sometimes adding PPI can help
Cromolyn

• Mast cell stabilizer
  – GI, skin, neuropsychiatric
• Dose: 1-200mg qid
• Can see GI symptoms
  – May need to start low and build up
Bisphosphonates

• Bone pain and osteoporosis major issues
• Oral or IV
• Vitamin D should be checked
• All patients need bone densitometry
Steroids

- May help with flares
- Many long term issues