Urticaria & Angioedema

Allergy-Immunology Review

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objectives

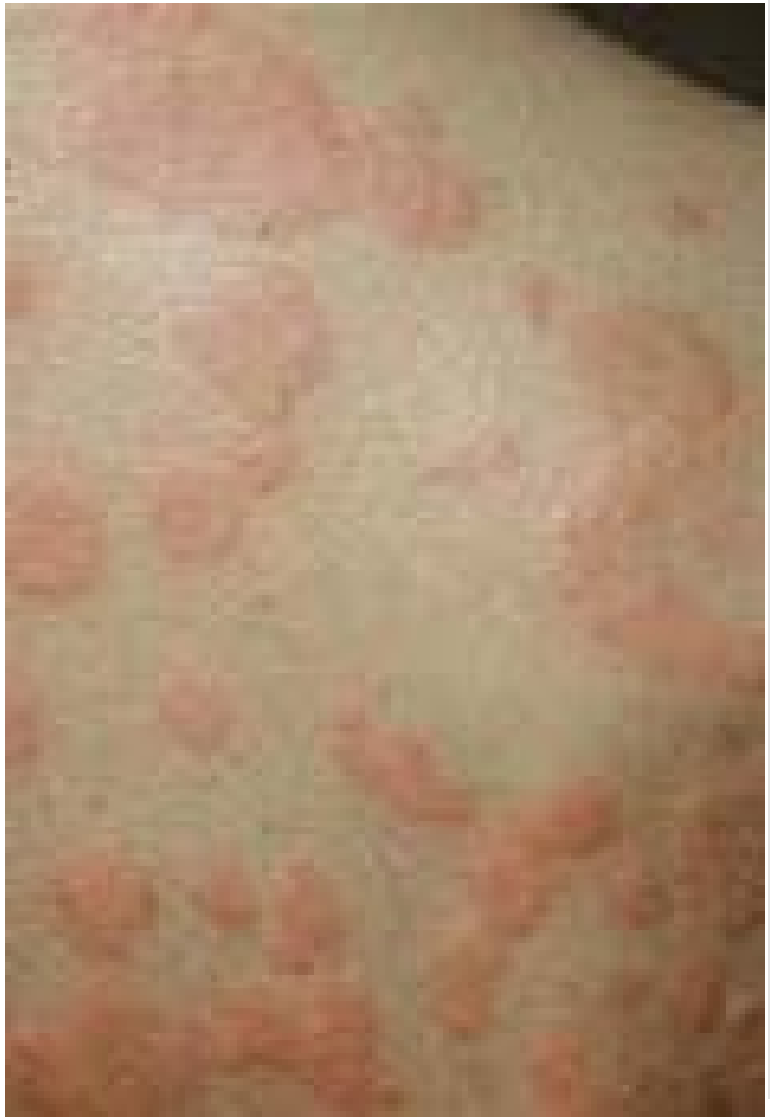
- *Identify the main cell type involved in the inflammatory response that produces both urticaria & angioedema*
- *Be able to distinguish urticaria from other skin lesions*
- *Know what medications are most likely to cause angioedema*
- *Know how to distinguish hereditary angioedema from an allergic reaction*
- *Know how to treat urticaria & angioedema*

urticaria

- *Urticaria (hives) is common, occurring in up to 25% of people at some point in life*
- *Definition:*

  rash that consists of pruritic, erythematous, edematous (swollen), lesions with pale centers (wheals), which are often coalescent

- *Found on the trunk and extremities, but can be found on any part of body*
- *Often transient, lasting <48 hrs*
- *Lesions typically migrate and do not remain in a region for > 24hrs*



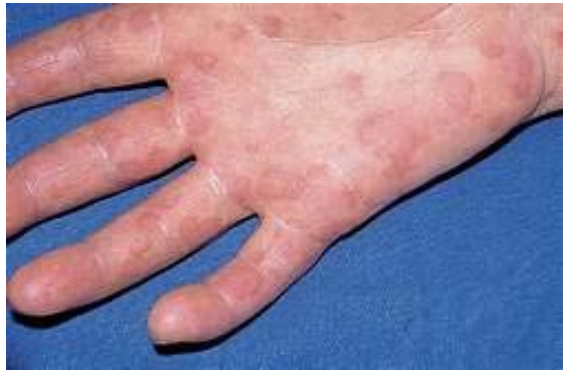
urticaria

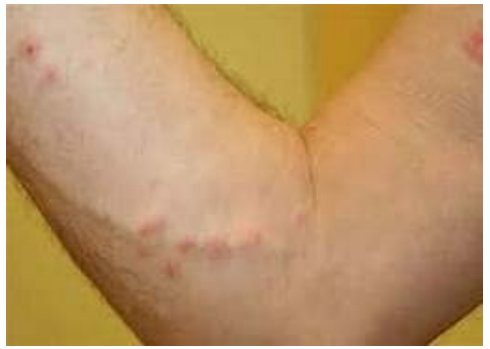
- Classification
  - Acute urticaria: <6 weeks
  - Chronic urticaria: persistent or recurring lesions ≥ 6 weeks
    - Less common in children
- Causes
  - Numerous triggers, which overlap with many of the causes for anaphylaxis
    - Food allergens
    - Medications
    - Insects
    - Pollens, animal dander
    - Cold, pressure, heat, light
    - Viral infections
- Pathophysiology
  - Mast cells are the primary effector cells, degranulation leads to release of leukotrienes, histamine, prostaglandins
  - Leads to vasodilation and leakage of plasma

urticaria

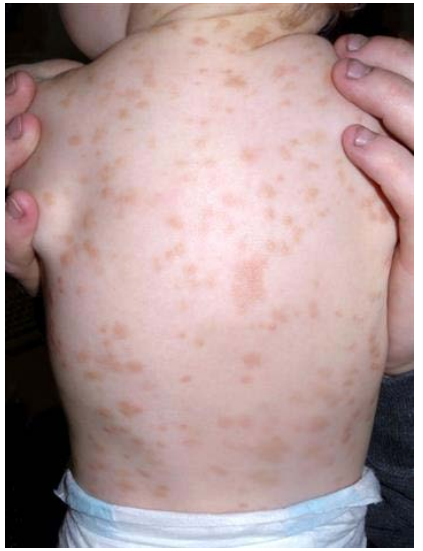
- Differential diagnosis
  - Important to distinguish from other rashes that can mimic urticaria
    - Erythema multiforme
      - Targetoid lesions
    - Papular urticaria: insect bite-induced hypersensitivity
      - Typically clustered or linear
    - Urticaria pigmentosa (mast cell syndrome)

Erythema multiforme





Papular urticaria



Urticaria pigmentosa

urticaria

- Acute urticaria
  - Workup
    - Consider allergy testing to identify causative agent
  - Treatment
    - **Antihistamines**:
      - 1st or 2nd generation antihistamines are both effective
    - Consider adding montelukast (leukotriene inhibitor) if no improvement
    - Reserve corticosteroids for severe cases
    - If signs of anaphylaxis – epinephrine is indicated

urticaria

Chronic Urticaria

- More common in adults
- No exogenous trigger is usually identified
  - Reported triggers: physical factors e.g. cold, pressure, exercise
- Persistent activation of mast cells, unclear mechanism
- Higher morbidity and decreased quality of life
- Labs: chronic urticaria index, measures autoantibodies to IgE receptor
- Treat with antihistamines

angioedema

- Definition: swelling in the deep subcutaneous tissue of the skin or mucous membranes
  - typically in the hands, lips, eyelids
  - in extreme cases affects the tongue or throat
- Angioedema is typically accompanied by urticaria, rarely occurs in the absence of urticaria

angioedema

- Pathophysiology
  - Mast cells are the primary effector cells, as in urticaria
- Causes
  - Foods
  - Medications:
    - NSAIDS and ACE-I most common
  - C1 inhibitor deficiency
    - Hereditary angioedema (HAE)
    - Acquired angioedema (AAE)
- Treatment
  - Antihistamines

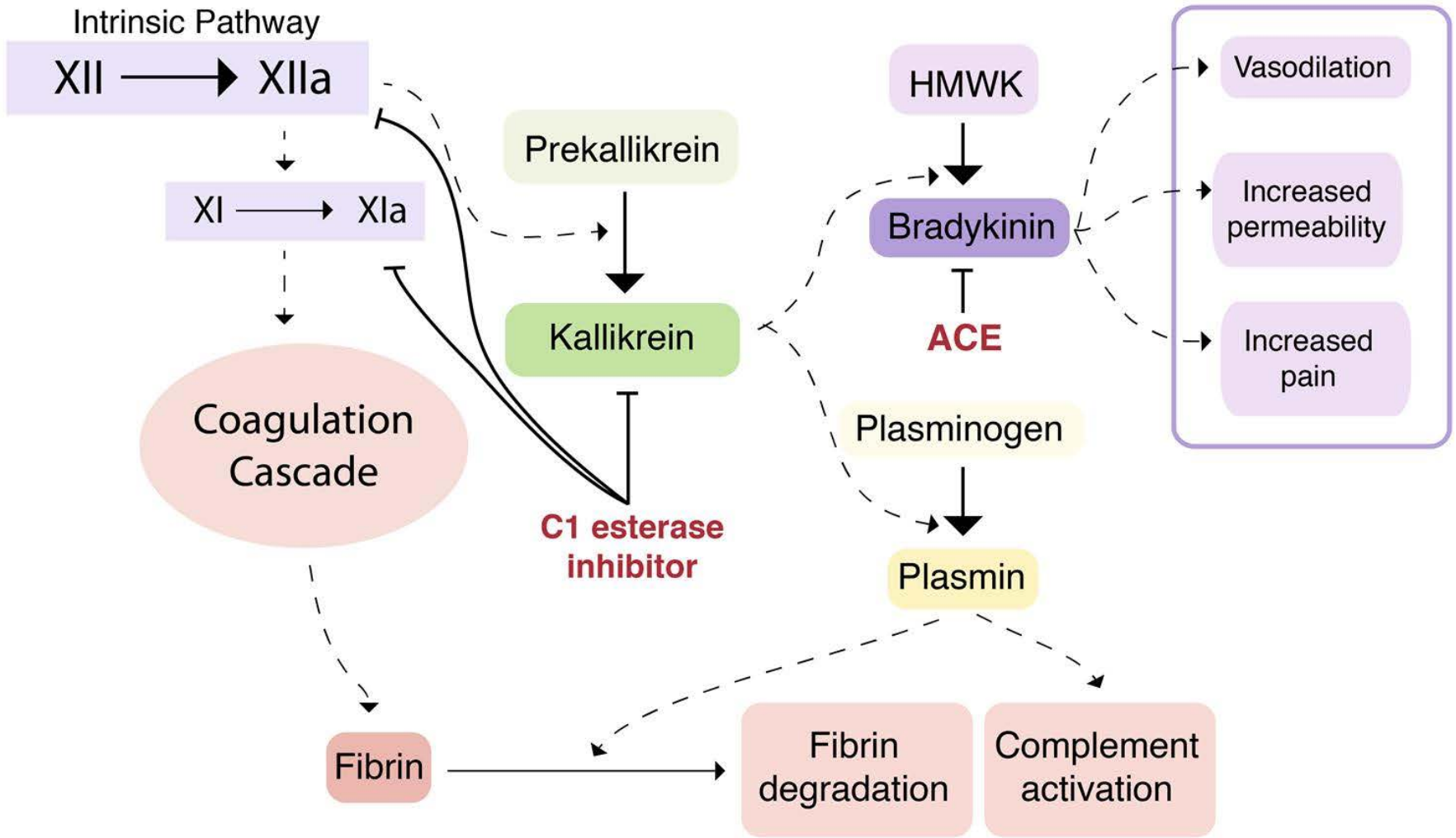
Hereditary angioedema

- Hereditary angioedema
  - Autosomal dominant
  - Onset typically at 8-12 years old
  - Present with recurrent episodic, nonpruritic swelling of skin/mucosal tissues
    - Commonly of face, hands, feet, genitals. May have laryngeal edema, abdominal pain due to intestinal edema in severe cases.
    - Typically develops over 24 hours, and resolves over following 24-36 hours
    - Often no preceding trigger
  - Types of C1 inhibitor deficiency
    - Type 1: insufficient C1 inhibitor levels
    - Type 2: dysfunctional C1 inhibitor

Hereditary angioedema

- Distinguishing HAE from allergic reactions
  - No associated urticaria or pruritis, develops gradually over hours
  - Poor response to antihistamines, corticosteroids, epinephrine
  - Often presents with a prodrome of localized discomfort at site of swelling, or fatigue several hours in advance
- Diagnosis
  - Labs
    - Low C1 inhibitor levels
    - Complement levels – low C4, nml C3 levels
- Treatment
  - Acute attack
    - Stabilization of airway in acute setting
    - C1 inhibitor concentrate
    - Fresh frozen plasma contains C1 inhibitor, 2nd line therapy
  - If history of frequent or severe symptoms, consider prophylactic meds

Kallikrein-Bradykinin Pathway



Lucy Liu

Summary:

- *Angioedema and urticaria are caused by mast cell activation, and often present concurrently*
- *It is important to distinguish urticaria from other similar rashes e.g. erythema multiforme, papular urticaria, urticaria pigmentosa*
- *NSAIDs and ACE-I are common triggers for angioedema*
- *Consider HAE when angioedema presents in the absence of urticaria, and no medication triggers have been identified*
- *Treat both angioedema and urticaria with antihistamines*

Citations:

1. Kanani et al. Allergy, Asthma & Clinical Immunology 2011, 7(Suppl 1):S9
2. Emily W. Langley and Joseph Gigante. Pediatrics in Review June 2013, 34 (6) 247-257; DOI: https://doi.org/10.1542/pir.34-6-247