Allergy/Immunology Update
Brad Mcclimon, PharmD, MD
October 29, 2016
Angioedema

- Self-limited, localized subcutaneous (or submucosal) swelling, which results from extravasation of fluid into interstitial tissues
- Face, lips, mouth, larynx, uvula, extremities, bowel wall and genitalia.

Three Types

- Mast Cell (histamine) Mediated
- Bradykinin Mediated
- Idiopathic
Mast Cell Mediated

- May be allergen related (foods, meds, bee stings, latex, contrast)
- Typically has other systemic symptoms—urticaria, bronchospasm, flushing, pruritis, hypotension
- Typically responds well to epinephrine and antihistamines
- Comes and goes fast
- Tryptase may be elevated

Bradykinin Induced

- Complement abnormalities, ACEI
- not associated with urticaria, bronchospasm, or other symptoms of allergic reactions
- More prolonged course
- Not as responsive to antihistamine, epinephrine or steroids
- Complement 4
An Allergist Plea

- Draw Complement 4 and Tryptase at time of the event

Mast Cell or Bradykinnin Mediated?
Mast Cell or Bradykinnin Mediated?

Treatment

- Airway Protection
- Hemodynamics
Treatment–Mast Cell Mediated

- Fluids
- Anti-histamines
- Steroids
- Epinephrine

Treatment–Bradykinnin Mediated

- C1 inhibitor concentrate (Cinryze, Berinert, or Ruconest)–IV.
- Ecallantide (Kalbitor)–kallikrein inhibitor–SQ
- Icatibant (Firazyr)–bradykinin–B₂–receptor antagonist–SQ
- FFP–likely contains ACE and C1 inhibitor
Drug therapy for angioedema: Mechanisms of action

The renin-angiotensin (AT)-bradykinin (BK) system and sites of drug action.

**Bold** text: drugs.
**Italicized** text: enzymes.

ACE: angiotensin-converting enzyme; BK: bradykinin; ARB: angiotensin II receptor blocker.


Pathways involved in kinin-mediated angioedema and actions of drugs

<table>
<thead>
<tr>
<th>A: Complement cascade</th>
<th>B: Contact - kinin system</th>
<th>C: Coagulation/Fibrinolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clr, Cls, MASPL2</td>
<td>Prekallikrein</td>
<td>Tissue-type plasminogen activator (tPA)</td>
</tr>
<tr>
<td></td>
<td>Prokallikrein</td>
<td>Activated Factor XII (F13a)</td>
</tr>
<tr>
<td></td>
<td>Kallikrein</td>
<td>Activated Factor XI (F11a)</td>
</tr>
<tr>
<td></td>
<td>High molecular weight kininogen</td>
<td>Factor Xa</td>
</tr>
<tr>
<td></td>
<td>Bradykinin type 2 receptor on endothelial cells</td>
<td>Factor Xa</td>
</tr>
<tr>
<td></td>
<td>Endothelial cell activation and capillary plasma leakage</td>
<td>Fibrin split products (FDP)</td>
</tr>
<tr>
<td></td>
<td>INFLAMMATION</td>
<td>ANGIOEDEMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>INCREASED CLOTTING</td>
</tr>
</tbody>
</table>

**X**: Steps normally inhibited by C1 inhibitor
**E**: Site of action of ecallantide
**I**: Site of action of icatibant

The figure illustrates the different functions of C1 esterase inhibitor (also known as C1 inhibitor). The functions in the middle panel are directly relevant to angioedema.

C1r: r subunit of complement component 1; C1s: s subunit of complement component 1; MASPL2: mannose-binding lectin-associated serine protease 2; C4: complement component 4; C2: complement component 2; FDP: fibrin degradation products.

Data from: