The Other Deadly AAA: Allergy, Angioedema, and Anaphylaxis

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A code is called in room 2

- As you run down the hall pulling on your gloves, you see a visitor unravel as she watches a 42 year old woman with two kids become unresponsive while she is talking to her
The patient recently rec’d some IM PCN for her Strep Throat.
She is 240 lbs. Currently has no IV access on she is flushed and warm.
As you push the curtains away and begin to roll her into the code room you begin to ask yourself the following questions...

Objectives

- After this lecture you will:
  - Appreciate the spectrum of Allergic reactions
  - Recognize systemic and non-systemic reactions
  - Formulate your own strategy for dealing with them
  - Become a greater advocate for the distribution of the Epi-Pen

Perspectives

- What to do on a Cruise…
- 1902 Portier and Richet
  - Extract of jellyfish tentacles injected into a dog
    - 1st time tolerated
    - 2nd time death (several weeks later.)
- Anaphylaxis from Greek “against protection”
- (ana, against; phylax, guard or protect)
What does this tell us…

- Early researchers had too much time on their hands
- It takes more than three weeks to cruise the Mediterranean

Spectrum of Allergic reactions

- Non-Systemic
- Systemic

Non-Systemic Allergic Reactions

- Urticaria
- Angioedema
Non-Systemic Allergic Reactions

- Urticaria
- Angioedema

Case: 65 year old man calls 911 for lip and tongue swelling
- He is anxious and meets the ambulance at the curb
- He has a HTN and takes a BP med he can’t remember

Urticaria and Angioedema

- Effects up to 20% of population at some point
- Acute and Self-Limited
  - (some chronic forms exist)
- Similar pathological reaction in different locations
Angioedema
- Reaction deep in dermis and Sub Q tissue.
- Non-Pruritic
- Skin may appear normal
- Face, Eyelids, Tongue
Coexisting??

- Urticaria and Angioedema co-exist in many patients.
- For unknown reasons:
  - Some patients manifest urticaria (40%),
  - Some angioedema (20%),
  - Some both (40%)

Pathogenesis

- Multiple mediators and Pathways
  - Allergen stimulation of IgE -> mast cell
  - Complement Cascade (C3a,4a,5a) -> mast cells directly
  - Hageman factor, via coagulation cascade, induces formation of other mediators bradykinin and kallikrein

Etiology of Angioedema

- Allergic
- Hereditary
- ACE Inhibitor related
- Unknown

Etiology - Hereditary

- Associations with autoimmune disorders
  - SLE (7% of SLE pts. will develop hives/allergic reactions)
  - Rheumatoid Arthritis
- Truly Hereditary
  - HAE - Hereditary Angioedema
  - First described in 1876 (J.L. Milton)

HAE - Hereditary Angioedema

- 1:10000 pts.
- All races
- All sexes
- Recurrent attacks
  - 2-5 days in duration
  - Unresponsive to standard allergic therapy

Angioedema and ACE Inhibitors

- The ACE Inhibitor issue
- Bradykinin response
- ACE (the actual enzyme) works on two substrates
  - Angiotensin I and Bradykinin
- By inhibiting ACE, Bradykinin levels accumulate and cause Angioedema

Angioedema and ACE Inhibitors

- Review of 108 cases of Angioedema
- 69% caused by ACE Inhibitor
- 30 min to 3 days of symptoms
- Single dose to 5 years
- Airway mgmt (intub. or cric) 13%
  - 50% of these were Diabetic
Urticaria and Angioedema - Treatment

First line
- Anti-Histamines (H1 blockers)
  - Diphenhydramine
- H2 blockers
  - Ranitidine, etc.
  - Studies for efficacy are small but do show difference

Steroids??
- Probably…
- 43 pts. acute urticaria.
  - Much improved pruritis and rash at both 2 and 5 days. P<.0001

And gosh darn it…
- Stop the ACE Inhibitor
- Vanderbilt Study with 82 ACE I related cases
  - Recurrence rate 18.7 per 100 person-yrs vs. 1.8 in pts, who didn’t stop taking meds

What if it isn’t allergic????
  - Give C1 esterase inhibitor concentrate
    - 69% resolution in 30 min
    - 95% resolution in 4 hours
  - FFP
Urticaria and Angioedema - Treatment

- Newer Treatments
  - Ecallantide - Blocks the pathway (Kallikrein Inhibitor)
  - Icatibant - Blocks the pathway (Bradykinin B2 receptor antagonist)
    - J Am Acad Derm, Nov 2010
    - Ann Emerg Med, Sep 2010
      - 8 patients. Mean time to sx improvement 51 min. Complete relief 4.4 hrs vs. 47 hx controls relief at 33 hrs

- Obviously advanced airway plans etc. should treatment fail or should the patient decompensate...

- Recent case from last month...

Last Week
An add’l tip for oxygenation

- Can Achieve
  - 20-30 LPM
- Temporizing
Spectrum of Allergic reactions

- Non-Systemic
- Systemic

Systemic Allergic reactions - Anaphylaxis

- First fatal anaphylaxis 4000 years ago - Hymenoptera sting
  - Currently, iatros more common than Hymenoptera
- Hymenoptera venom (yellow jackets, hornets, honeybees, bumblebees, wasps)
  - 50 deaths per year in the United States
  - Far outnumbering deaths from snake bites
  - Only 9-25% of fatal stings report previous hymenoptera allergy

- Anaphylactic reactions to foods
  - Shellfish, nuts (esp. peanuts), and eggs
Anaphylaxis - Pathophysiology

- IgE mediated hypersensitivity reaction
- Similar to allergic rhinitis but more profound
  - Histamine and other pre-formed mediators
  - Overwhelming vascular permeability
- Anaphylactoid reactions (non IgE-mediated)
  - Clinically indistinguishable from true anaphylaxis

Anaphylaxis - Onset of Symptoms

- Most occur within seconds to minutes
- Few are asymptomatic for an hour and THEN develop symptoms

Anaphylaxis - Duration of Symptoms

- Most patients
  - Predictable - **uniphasic** course which resolves with treatment
- 20% of patients - have **biphasic** reactions
  - A second episode up to eight hours following apparent recovery from the initial event
- Rarely, symptoms may persist >1 day

Anaphylaxis - Duration of Symptoms

- NO particular test or spectrum of clinical symptoms predicts who will have biphasic or protracted responses
Anaphylaxis - Symptoms

- Multi-System Spectrum
  - CV - HypoTN, Shock, CP, MI, Arrhythmias
  - RESP - Wheezing, Bronchospasm
  - Neuro - Anxiety, Confusion, Dizziness, SZ
  - Derm - Pruritis, Angioedema, Urticaria
  - GI - N/V, Diarrhea

Anaphylaxis – “New” definitions

1 – Acute onset of skin, mucosal tissue and either
  - Respiratory Compromise
  - Or
  - Reduced BP with end organ evidence

2nd Criteria

- Two or more of the following after exposure to likely allergen
  - Skin/mucosal inflammation
  - Resp. compromise
  - Reduced BP
  - Persistent GI symptoms (Vomiting, pain)

3rd Criteria

- Reduced BP after exposure to a KNOWN allergen for that patient
  - <90 mm HG or a drop of 30% from baseline
    - To detect reaction in patients with only 1 organ system affected but clearly known to be allergic (peanuts, bee stings)
Anaphylaxis - Causes of Death
- Airway Obstruction
- Cardiovascular Collapse
- Target Therapies Accordingly

Anaphylaxis - Treatment
- Consider Anaphylaxis as one end of an Allergic spectrum
- While it may share characteristics with Angioedema, it is wise to think of them as the same identity (at least initially)
- The initial treatment is the same

Anaphylaxis - Treatment
- Preparation
- Make sure you know where your difficult airway tools are
  - Nasal vasoconstrictors
  - Cricothyrotomy kit
  - Fiberoptic Intubating Bronchoscope

Anaphylaxis - Treatment
- Universal Initial Therapy
- Critical Care Room
- Get ALL the relevant Data
- ABC’s
- Vital Signs
Anaphylaxis - Treatment

First Line
- Epinephrine (If IV, NEVER undiluted)
- Fluids
- Antihistamines (prob H1 and H2)

Second Line
- Steroids (may help with rebound anaphylaxis)
- Glucagon? (theoretical benefit)

Anaphylaxis - Treatment - Side Effects

Epinephrine - associated with DISASTROUS side-effects – esp if fast IV infusion
- Hypertensive crisis
  - causing cerebral hemorrhage, pulmonary edema
- Arrhythmias or myocardial infarction

Epinephrine is the drug of choice for treatment of systemic anaphylaxis
- Alpha - reverses peripheral vasodilation
  - Systolic and diastolic blood pressure
  - Angioedema and urticaria
- Beta - bronchodilation, cardiac inotropy and chronotropy

Epinephrine - IM/SQ epinephrine is recommended, even with mild presentations, if truly anaphylactic
- 0.3 mg to IM/SQ q 15-20 minutes until symptoms abate
- A systolic blood pressure of 60 mmHg is sufficient to absorb IM or SQ epinephrine
- IM actually works better - J All Clin Imm 2001
Anaphylaxis - Treatment

- Airway obstruction
- Severe bronchospasm
- Hypotension
- ALL Require IV epinephrine !!!

The dose of IV epinephrine is controversial
- No studies have established a definitive dose
  - safe
  - therapeutic

Anaphylaxis - Treatment

- Slow, low-dose infusion rates stimulate beta-receptors more than alpha-receptors
  - Bronchodilation and modest increase in systolic blood pressure

- Fast, high-dose infusions appear to preferentially stimulate alpha-receptors
  - causing severe hypertension, arrhythmias, and myocardial ischemia

Anaphylaxis - Treatment

- Epinephrine Drip
- Or
- How to give IV EPI and not kill my patient!!!
Anaphylaxis - Treatment

- Epinephrine Drip
- Best Method.
  - 1 mg of epinephrine (code cart) in 1000 cc NS
  - to give a concentration of 1 mcg/cc

- 2-10 ml per minute IV

- PEDS patients, the infusion rate begins at 0.1 mcg/kg/min

DISPOSITION

- Mild Anaphylaxis
  - OBSERVE 6-8 hours

- Anything but Mild
  - Admit for 24 hour monitoring for Biphasic reaction

AND FINALLY....

- ALL patients should receive a self-injectable kit
  - Epi-pen (0.3mg SQ)
  - Epi-pen, Jr. (0.15mg SQ)
- Instructed in its use

- 40% of children with hymenoptera allergy did not receive an epinephrine prescription

FINAL Take Home Points

- Use Both H1 and H2 blockers (though may not help in HAE or ACE AE)
- Use Steroids (though may not help)
- Be PREPARED to get Surgical Airway
- Don’t EVER push undiluted EPI IV
A Return to our objectives…

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Thanks!!