Hymenoptera Envenomation

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…when the bee stings

Case Presentation

- 39 year-old male brought to Emergency Department in respiratory arrest with agonal pulse. He is intubated and cyanotic from the neck up.

Case Presentation

- ALS personnel report that he was helping a friend paint when he was apparently stung by a bee. He walked into the house, saying "I don't feel good," and collapsed.

Case Presentation

- PMH: depression, gastritis, seasonal allergies
- Medications: Ritalin, Zantac, Prozac, Claritin
- No known drug allergies
- No prior reactions to hymenoptera

Case Presentation

- intubated at scene orotracheally
- en route, received endotracheal and intravenous epinephrine, and intravenous Benadryl
- large-bore intravenous of crystalloid wide open

Case Presentation

- on arrival in ED, placed in Trendelenberg position
- PASG with leg compartments inflated
- 2nd IV established, wide-open fluid
- CPR continued

Case Presentation

- dopamine drip
- epinephrine drip
- central line (subclavicular)
- Isuprel drip
- Levophed drip

Case Presentation

- monitor - agonal, wide-complex
- transvenous pacemaker failed to capture
- after 20” prehospital and 30” in hospital resuscitation, no response
- pronounced dead - cause, “Fatal Anaphylactic Reaction”

Case Presentation

- social history gathered in retrospect from wife
- schoolteacher
- 2 daughters, 5 years and 6 months old

What is anaphylaxis?

- systemic reaction of multiple organ systems to an antigen-induced IgE-mediated immunulogic mediator release in a previously sensitized individual

How does it manifest?

- clinical severity varies from mild to fatal
- majority of reactions are respiratory and dermatologic
- innocent early findings may progress to lethal over a short time

What causes the deaths?

- laryngeal edema and acute bronchospasm with respiratory failure account for >70%
- circulatory collapse accounts for 25%
- other <5% - ?brain ?MI

In USA - 400 to 800 deaths/year

- parenterally administered penicillin accounts for 100 to 500 deaths per year
- hymenoptera stings account for 40 to 100 deaths per year
- risk factors: protracted course, beta-blockers, adrenal insufficiency

What does the word mean?

- ‘ana’ means against or backwards
- ‘phylax’ means guard or protect
- anaphylaxis = “without protection”
- prophylaxis = “for protection”

Reactions may be uniphasic, biphasic, or protracted

- glucocorticoids do NOT reproducibly prevent biphasic or protracted anaphylaxis
- laryngeal edema is more common in the protracted (57%) or biphasic (40%) cases

Brief overview of physiology

- mast cells are found in all subcutaneous and submucosal tissues, including conjunctiva, upper and lower respiratory tracts, and the gut
- basophils circulate in the blood

There are four basic mechanisms leading to mast cell degranulation

- IgE-mediated hypersensitivity
- complement activation with synthesis of anaphylatoxins C3a & C5a
- anaphylactoid substances that independently stimulate the mast cell
- inhibition of the arachidonic acid pathway

Major components of a Type I (anaphylactic) reaction are...

- …IgE, a heat-labile glycoprotein
- …mast cells
- …basophils
- …eosinophils
- …histamine releasing factors

IgE...

- …basal level controlled by host factors: age, sex, race, skin and mucosal permeability
- …low IgE level is an autosomal dominant trait
- …95% bound to cells for 3 - 4 weeks

Mast cells...

- …have two distinct populations
  1. connective tissue cells in skin
  2. mucosal mast cells in lung and lamina propria of the gut
- …originate in bone marrow

Basophils...

- …are produced from precursors in the blood and bone marrow
- …are polymorphonuclear leukocytes
- …promote late-phase response

Eosinophils...

- …originate in the bone marrow under the influence of granulocytes
- …are a major component of late-phase response

Histamine releasing factors...

- …are produced by platelets, macrophages, and lymphocytes
- …selectively cause release in atopics
- …may discriminate between “intrinsic” and “extrinsic” asthma and anaphylaxis

Mechanism of "classic" immediate hypersensitivity

- Antigen interacts with antigen-specific cell-surface bound IgE (dimer) on mast cells
- Generates a signal through the cross-linking of Fce IgE receptors
- Initiates membrane lipid and adenine metabolism

Mechanism of "classic" immediate hypersensitivity

- Solubilizes granules to release preformed amines, proteins, peptides, and proteoglycans

Preformed mediators are...

- …histamine
- …ECF-A (from mast cells)
- …HMW-NCF (from mast cells)
- …tryptase (from muscosal mast cells)
- …kallikrein

Newly formed mediators are...

- …PAF (from mast cells, macrophages, neutrophils, and eosinophils)
- …arachidonic acid metabolites (from mast cells and basophils)
- …prostaglandin D2
- …adenosine

Histamine is the...

- …prime mediator of both the local and systemic effects
- …ONLY preformed mediator in humans known to have direct potent vasoactive and smooth muscle spasmogenic effect

There are 3 histamine receptors

- H1
- H2
- H3

(you expected maybe Larry, Moe & Curly?)

Histamine acts on H1 receptors to cause...

- …smooth muscle contraction
- …increased vascular permeability
- …prostaglandin generation

Histamine acts on H2 receptors to cause...

- …increased vascular permeability
- …gastric acid secretion
- …stimulation of suppressor lymphocytes
- …decreased PMN enzyme release
- …release of more histamine from mast cells and basophils

Histamine acts on H3 receptors to cause...

- …inhibition of central and peripheral nervous system neurotransmitter release
- …inhibition of further histamine formation and release

Insect sting hypersensitivity

- Hymenoptera - yellow jackets, honeybees, hornets, wasps, bumble bees, and imported fire ants
- 90% of reactions are local hives and pruritus
- 10% of reactions show massive local reaction, including swelling beyond two joints of an extremity

Insect sting hypersensitivity

- **1%** will have systemic reaction
- in general, children react less severely than adults
- only 10% will have worse reaction on second sting
- only 28% will have recurrent systemic reaction

Clinical findings...

- …vary in initial signs and symptoms
- …do NOT necessarily correlate with severity, progression, and duration of response

IN GENERAL, the sooner the symptoms start following antigenic exposure, the more severe the reaction will be.

Clinical expression of anaphylaxis depends on...

- …degree of hypersensitivity
- …quantity, route, and rate of antigen exposure
- …pattern of mediator release
- …target organ sensitivity and responsiveness

The first clinical manifestations involve the skin

- warmth and tingling of the face, mouth, upper chest, palms and/or soles, or site of exposure
- pruritus is a universal feature
- may be accompanied by generalized flushing, urticaria, and nonpruritic angioedema

Respiratory symptoms soon follow...

- cough
- chest tightness
- dyspnea
- wheeze
- throat tightness
- odynophagia
- hoarseness

May also complain of...

- …lightheadedness or syncope caused by hypotension or dysrhythmia
- …nasal congestion and sneezing
- …ocular itching and tearing
- …cramping abdominal pain with nausea, vomiting, diarrhea, and tenesmus

May also complain of...

- …bowel or bladder incontinence
- …pelvic pain
- …headache
- …sense of impending doom
- …decreased level of consciousness

Examination may reveal...

- …urticaria, andioedema, rhinitis, conjunctivitis
- …tachypnea, tachycardia, hypotension
- …laryngeal stridor, hypersalivation, hoarseness, angioedema
- ...coughing, wheezing, rhonchi, diminished air flow

Optimal management requires...

- …high index of suspicion
- …early diagnosis
- …pharmaceutical intervention
- …observation
- …disposition

Index of suspicion

- must SUSPECT and TREAT within moments of presentation

The motto of emergency medicine:

TREAT FIRST

ASK QUESTIONS LATER

Differential diagnosis of laryngeal edema includes...

- …epiglottitis and supraglottitis
- …retropharyngeal abscess
- …peritonsilar abscess
- …laryngeal spasm
- …foreign body aspiration
- …tumor
- …factitious anaphylaxis or globus hystericus

ANAPHYLAXIS vs VASOVAGAL

- anaphylaxis
  hypotension
  tachycardia
  diaphoresis
- vasovagal
  hypotension
  bradycardia
  pallor

Other dysrhythmias seen are...

- …premature atrial contractions
- …premature ventricular contractions
- …nodal rhythm
- …atrial fibrillation

Other EKG changes seen are...

- …ischemic ST-T wave changes
- …nonspecific ST-T wave changes
- …right ventricular strain
- …intraventricular conduction delays

Prehospital management for the known allergic patient

- with re-exposure, take Benadryl 50mg p.o.
- at any sign of anaphylaxis, self-administer subcutaneous epinephrine (Epi-Pen, Ana-Kit)
- if short of breath or wheezing, use aerosolized epinephrine (Primatene Mist, Medihaler-Epi)

Does inhaled epinephrine work?

<u>20 "puffs"…</u>

- …is equivalent to 3 mg of epinephrine
- …produces therapeutic plasma levels
- …is easily administerd
- …is rapidly absorbed
- …gives good levels in upper and lower airways

What does all this cost?

diphenhydramine 50mg.....$2.90/100 capsules

Ana-Kit……$23.35/kit

Epi-Pen……$33.49/pen

Primatene Mist……$11.69/inhaler

Medihaler-Epi……$19.29/refill

<u>These costs WHOLESALE to pharmacist</u>

Treating mild anaphylaxis

urticaria, rhinitis, conjunctivitis, mild bronchospasm

- epinephrine 1:1000 0.3cc SQ - may repeat every 5 - 20 minutes prn
- Sus-phrine 0.15cc SQ
- Benadryl 25 - 50mg PO or IM

CONSIDER:

cimetidine or ranitidine, prednisone, inhaled beta-agonists

Treating moderate anaphylaxis...

angioedema or hypotension with BP >80 mm Hg

- epinephrine and Sus-phrine as above, may give SQ or IM
- Benadryl 25 - 50mg IM or IV.....$0.65/dose
- cimetidine 300mg IV.....$1.05/dose
- Solu-Medrol 40 - 125mg IV.....$3.00/dose
- oxygen, IV fluid, cardiac monitor

Local measures include...

- …loose tourniquet proximal to antigenic site - remove 1 minute every 10 minutes
- …dependent position for extremity
- …ice to site - 15 minutes every 30 minutes
- …local infiltration of epinephrine
- …if stinger present, flick it away with credit card or fingernail

Treating severe anaphylaxis

laryngeal edema, respiratory failure, shock

- Epinephrine 1cc of 1:10,000 IV over 5 minutes, repeat every 3 - 5 minutes prn, maximum 5cc every 15 - 30 minutes
- Benadryl 50 - 100mg IV over 3 minutes
- Oxygen
- Crystalloid wide open intravenously

Treating severe anaphylaxis

laryngeal edema, respiratory failure, shock

- cimetidine or ranitidine
- Solu-Medrol or hydrocortisone
- If upper airway signs: racemic epinephrine 2.25% by nebulization
- If brochospasm: albuterol 5mg/cc by nebulization

CONSIDER: aminophylline

Laryngeal edema

- hyperextend neck, chin lift, jaw thrust
- naso- or oropharyngeal airway
- 80% helium / 20% oxygen gas mixture
- racemic epinephrine 0.5cc by nebulization
- tracheal intubation PRN
- surgical airway PRN

Persistent brochospasm

- albuterol by continuous nebulization
- aminophylline 5.6 mg/kg IV over 20 - 30 minutes
- Atrovent 0.5 mg in 2.5cc NS by nebulization
- steroids
- intubate and ventilate PRN

Persistent hypotension

- Trendelenberg position
- volume repletion with minimum 2 large-bore IVs infusing crystalloid
- monitor urine output and CVP
- PASG

Consider:

naloxone 0.4 - 0.8mg IV; if responsive

IV drip infusion

Persistent hypotension

VASOPRESSORS

- dopamine 5 - 20 mcg/kg/min
- isoproterenol 2 - 20 mg/min
- levarterenol 8 - 32 mg/min

What about glucagon?

- when epinephrine contraindicated, glucagon may be an option
- positive inotropic and chronotropic cardiac effects mediated independently of alpha- and beta-receptors
- thought to enhance cAMP synthesis in myocardium, GI and GU tracts

Consider glucagon in...

- …patients on beta-blockers
- …patients with known CAD
- …pregnant women (category B drug)
- …patients not responding to other drugs

Usefulness is anecdotal only -
no controlled trials

Disposition

- Regardless of response to therapy, all patients with systemic features must be observed for 6 to 8 hours
- There is no accurate way to predict which patients will experience a biphasic reaction

Admission is mandatory…

- …for any patient with moderate to severe reaction, even if they respond rapidly to emergency intervention

This includes anyone who showed signs of upper airway obstruction or hypotension.

Consider admission for...

- …the elderly patient
- …the patient with cardiovascular disease
- …the patient with asthma
- …the patient taking a beta-blocker

May be discharged home if...

- …mild anaphylaxis
- …no hypotension
- …no signs of upper airway obstruction
- …rapid response to ED therapy
- …observed for 6 hours without recurrence
- …safe discharge to care of responsible adult

Outpatient management includes...

- …two-day course of H1 antihistamine

diphenhydramine Q6H x 48hrs……..$0.24

- …two-day course of H2 antihistamine

cimetidine BID x 48hrs……..$2.20

- …two-day course of steroid

prednisone 50mg/day x 2 days……$0.30

AND REFERRAL TO AN ALLERGIST

How to avoid future stings

1. Don't "smell like a rose" - avoid scented soaps and fragrances
2. Wear garments that fit close to the body. Insects can become trapped in loose-fitting clothing and will sting defensively.
3. Wear shoes outdoors at all times, in addition to long pants and long-sleeved shirts.

How to avoid future stings

4. Wear clothing in colors not attractive to bees: **white, red, grey**. Avoid floral designs and **brown** clothing, which may mimic the color of the bee's natural predator, the brown bear.
5. Wasp or hornet nests or beehives near the home should be destroyed by a professional exterminator.

How to avoid future stings

6. Stay away from insect feeding grounds: flower beds, fields of clover, garbage, orchards with ripe fruit.
7. Avoid outdoor picnics.
8. If it is necessary to dispose of garbage, the area should be sprayed first with an effective, rapid-acting insecticide.

How to avoid future stings

9. Keep automobile windows closed. Aside from the sting from a trapped insect, its very presence can arouse such terror in a sting-sensitive individual as to cause an accident.

AND…

Don’t forget to carry a Medic Alert bracelet or necklace

Medic Alert Foundation

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