EM CASE OF THE WEEK.

BROWARD HEALTH MEDICAL CENTER
DEPARTMENT OF EMERGENCY MEDICINE

BROWARD HEALTH
Care Warriors

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Angioedema

A 55-year-old male with recently diagnosed hypertension presents with 6 hours of increasing angioedema of the face and lips. This is the first time this has happened. The patient denies any allergies or any known allergen exposures. The only medication he takes is lisinopril, which he took this morning. Vital signs are within normal limits. He has no rash, pruritis (itching), or urticaria (hives). He has no edema of the tongue, and is not wheezing or showing any signs of respiratory distress. Which of the following is the best treatment for this patient's condition?

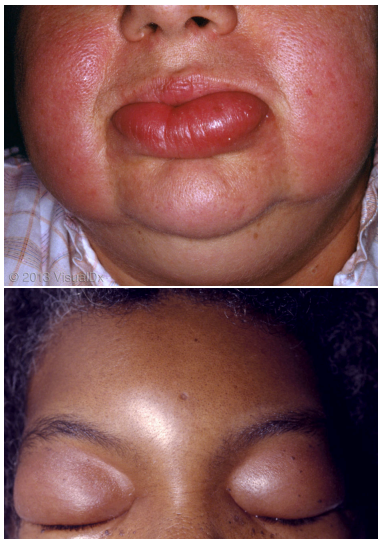
A. 0.5mg epinephrine IM

B. 50mg diphenhydramine IV

C. 10mg loratadine PO

D. 125 mg methylprednisolone IV

E. Discontinue lisinopril & monitor



Via VisualDx.com

Angioedema is a localized swelling of deep dermal, subcutaneous, and/or submucosal tissues due to the extravasation of fluid from the vessels. Inflammatory mediators, histamine, and bradykinin cause the vasodilation and increased vascular permeability. Areas with loose connective tissue are typically affected, such as the face, lips, mouth, throat, larynx, uvula, bowel wall, extremities, and genitalia.

EM Case of the Week is a weekly "pop quiz" for ED staff.

The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

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The correct answer is E. Discontinuation of the ACE inhibitor is the mainstay of therapy. There is no evidence supporting the use of antihistamines and glucocorticoids in these patients. ACE inhibitors are the leading cause of drug-induced angioedema in the United States, occurring in up to 0.7% of recipients. Although the overall risk to individuals is low, ACE inhibitors are commonly prescribed to those with hypertension, diabetes, myocardial infarction, and congestive heart failure so it is still seen often.

Discussion

The etiologies of angioedema can be subcategorized into the following:

(1) Mast cell mediated / Histaminergic

More commonly associated with urticaria, flushing, pruritis, bronchospasm, and hypotension. Mast cells release histamine and other mediators. When mast cells do not degranulate, but there is an excess of histamine, angioedema and urticaria occur without respiratory symptoms or hypotension.

(2) Bradykinin mediated

Urticaria and pruritis are absent. There is an underlying overproduction or underdegradation of bradykinin. ACE inhibitors (i.e. captopril, lisinopril, enalipril) inhibit the breakdown of bradykinin. Thus, there is an increase in bradykinin, which commonly produces a dry cough in patients using this medication and in higher levels, angioedema that develops rapidly and usually self resolves w/in 72 hours.

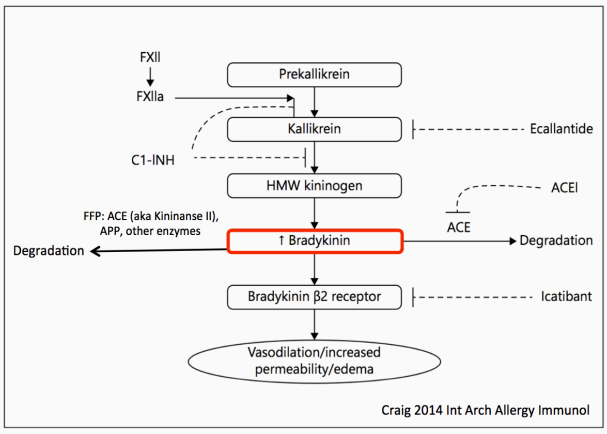
(3) C1 esterase inhibitor deficiency

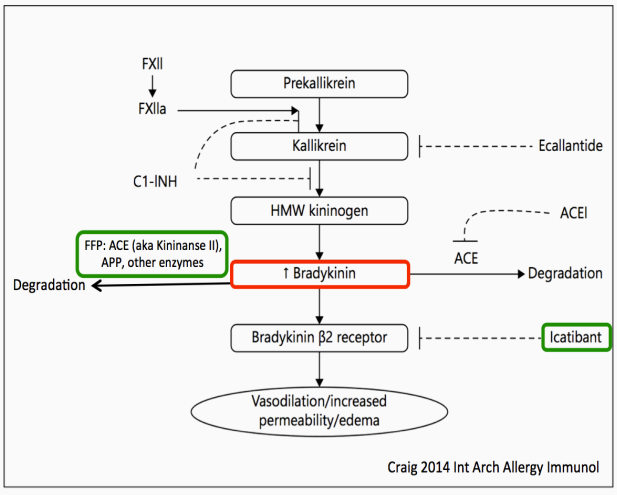
Can be hereditary or acquired. There is a lack of C1 esterase, responsible for breaking down C1 of the complement cascade (part of the innate immune system). Therefore, with the abundance of C1 and complement activation, there is an overproduction of bradykinin. These patients often have recurrent acute attacks of angioedema without any identifiable cause.

(4) Idiopathic Causes

Diagnosis

Angioedema is primarily a clinical diagnosis and it is important that a detailed history is taken including previous episodes, recent exposures/activities, foods last eaten, current medications, and any other ingestions. If suspicious of C1 esterase inhibitor deficiency, obtain C4, C1q, and C1 inhibitor antigenic levels. If all are low, then tests for C1 inhibitor function should be obtained (required for diagosis).





Physiology of ACE-inhibitor induced angioedema and treatment pathways. Illustrations via http://emcrit.org/pulmcrit/treatment-of-acei-induced-angioedema/

For a list of educational lectures, grand rounds, workshops, and didactics please visit ***BrowardER.com*** and **click** on the ***"Conference"*** **link**.

All are welcome to attend!

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Treatment

(1) Mast cell mediated / Histaminergic
Angioedema with anaphylaxis or airway compromise must be treated with IM epinephrine (0.01 mg/kg of a 1:1000 [1 mg/mL] solution, to a maximum of 0.5 mg in adults). Remember, Airway-Breathing-Circulation must be assessed first. Intubate to protect the airway if necessary and bolus fluids in the setting of hypotension. For less severe reactions, antihistamines (i.e. diphenhydramine 50mg IV) and glucocorticoids (methylprednisolone 60-80 mg IV) are first line.

(2) Bradykinin Mediated
If the patient is on an ACE inhibitor, discontinue. The bradykinin antagonist, icatibant 30mg SQ (Grade 1B) is recommended, especially if there is airway involvement. If it is not available, give fresh frozen plasma, C1 inhibitor concentrate, or encallantide (Grade 2C).

(3) C1 esterase inhibitor deficiency
Plasma derived C1 inhibitor concentrate 20units/kg is first line (Grade 2C). Other agents that may be effective are encallantide, icatibant, and FFP.

- Note that icatibant can cost over $10,000. Therefore, it is typically reserved for those with bradykinin-induced angioedema with airway involvement. However, multiple case reports have described rapid improvement of patients following infusion of fresh frozen plasma in bradykinin-induced angioedema. Hence, it may be reasonable to administer this therapy in severe bradykinin mediated angioedema without respiratory symptoms or hypotension.

Take Home Points

- Angioedema can be isolated or as a component of anaphylaxis. The major categories are mast cell mediated/histaminergic, bradykinin mediated, C1 esterase inhibitor deficiency, and idiopathic.
- First assess the ABCs of a patient, intubate if there is significant respiratory distress, and bolus fluids as necessary.
- Get a detailed history including exposures and ingestions. Look and ask for urticaria/pruritis to further differentiate between histaminergic vs. bradykinin-mediated angioedema.
- Treatment is not always necessarily diphenhydramine and steroids (i.e. bradykinin mediated or C1 esterase inhibitor deficiency).

ABOUT THE AUTHOR

This month's case was written by Ravi Patel. Ravi is a 4th year medical student from NSU-COM. He did his emergency medicine rotation at BHMC in November 2016. Ravi plans on pursuing a career in Internal Medicine after graduation.

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