

EM CASE OF THE WEEK.

BROWARD HEALTH MEDICAL CENTER
DEPARTMENT OF EMERGENCY MEDICINE



Care Warriors

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ACE Inhibitor-Induced Angioedema

63-year-old African American female with a medical history of type 2 diabetes, hypertension, hyperlipidemia presents to the ER with facial, tongue swelling, and shortness of breath that started approximately 7 hours ago. She has difficulty speaking but was able to drive herself to the ER. She denies skin rashes, itching, trauma, recent dental work, fevers, chest pain, and abdominal pain. She is allergic to oxycodone/acetaminophen but denies any recent use. Per chart review, no previous tobacco, alcohol or illicit drug use. Her home medications include amlodipine, lisinopril and metformin. Her temperature is 97.9, pulse is 110, respirations are 32, and blood pressure is 160/90. Examination shows intercostal and subcostal retractions. Lungs are clear to auscultation. Heart and abdominal exams are within normal limit. She has trace edema of the lower extremities. There is no extremity weakness. Head and neck examination reveals findings as shown.

Which of the following is the most appropriate next step in management of this patient?

- A) Epinephrine
- B) Diphenhydramine, famotidine, and methylprednisolone
- C) Albuterol and ipratropium
- D) Purified C1 inhibitor concentrate
- E) Intubation and mechanical ventilation



Google image

Angioedema is the rapid swelling of the skin, mucosa and submucosa tissues. It is a potentially life threatening condition. Most commonly, it occurs on the lips, tongue, face, hands or feet.

ACE-I is the leading cause of drug-induced angioedema. However, angioedema has been reported as a side effect of some other medications including NSAIDs, statins, PPIs, SSRIs, and antidepressants.

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.

The primary treatment of ACE inhibitor-induced angioedema is acute airway management if the mouth or throat is involved. Prompt intubation and mechanical ventilation are required for airway protection.

Discussion

Angioedema is an asymptomatic, non-pitting swelling of the subcutaneous or submucosal tissues. Most commonly reported to affect the lips, tongue, face, and upper airway. There is an absence of itching or urticarial in ACE inhibitor-induced angioedema.

Early signs of laryngeal edema may include hoarseness of the throat and inspiratory stridor, which may progress to airway obstruction. The intestine can also be involved, presenting as acute abdominal pain with diarrhea or other GI symptoms such as vomiting, ascites. This presentation is less well-known and the diagnosis may be delayed by months to years because clinicians are not as aware of this potential presentation of ACE inhibitor-induced angioedema.

ACE inhibitors-induce angioedema occurs in 0.1 to 0.7 percent of recipients. The incidence of ACE inhibitor-induced angioedema is about five times greater in African Americans. In more than half of cases, angioedema occurs during the first week of exposure, although it may occur any time during the course of therapy from hours to even years of uneventful and stable treatment.

The pathophysiology of ACE inhibitor-induced angioedema is related to elevated levels of bradykinin, an inflammatory vasoactive peptide, which leads to vasodilation of blood vessels. High level of bradykinin stimulates vasodilation and increases vascular permeability of the post-capillary venules and allows for plasma leaking into the submucosal tissue, leading to angioedema.

In differential diagnosis, consider rare disorder of bradykinin-mediated angioedema including Hereditary Angioedema (HAE), acquired angioedema with deficiency of C1 inhibitor, which is associated with lymphoproliferative disorders, and mast-cell mediated (histamine) angioedema

Possible risk factors include history of previous episodes of angioedema, female sex, African American, age older than 65, ASA or NSAIDs use, history of angioedema related to NSAIDs use, seasonal allergies.

Diagnosis is made clinically, based upon the characteristic presentation of angioedema, without itching or urticarial, in a patient taking ACE inhibitors.

There is no definite laboratory tests to diagnose. However, a serum level of complement protein 4 (C4) should be obtained if there is clinical suspicion that another cause of bradykinin-mediated angioedema could be present. A low C4 level requires a more complete laboratory evaluation, including C1 inhibitor function and protein levels, C1q levels. C4 level is definitely indicated if the patient has a family history of angioedema or has an underlying lymphoproliferative disorder (such as MGUS) or other malignancy.

Treatment

Acute treatment of ACE inhibitor-induced angioedema includes airway management and discontinuation of the drug. If the mouth or throat is involved, the airway should be immediately evaluated and repeatedly monitored until the swelling is clearly resolving. Prompt intubation and mechanical ventilation may be required for airway protection.

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!

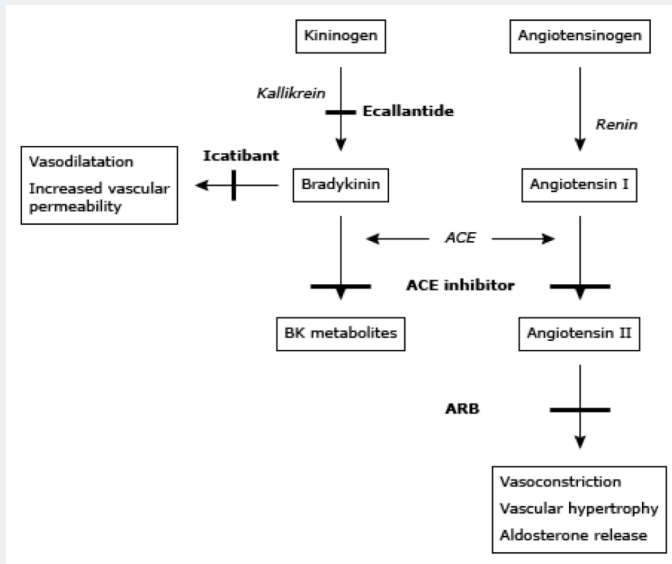


Diagram from UpToDate



ABOUT THE AUTHOR

This month's case was written by John Vu. John is a 4th year medical student from NSU-COM. He did his emergency medicine rotation at BHMC in October 2017. John plans on pursuing a career in Internal Medicine after graduation.

Take Home Points

- ACE inhibitors are the leading cause of drug-induced angioedema
- ACE inhibitor-induced angioedema usually affects the lips, tongue, and face. Urticarial and itching are absent.
- The primary acute treatment of ACE inhibitor-induced angioedema is supportive care until the angioedema resolves. If tongue or laryngeal swelling is present, intubation and mechanical ventilation may be required due to impending airway obstruction.
- Therapies for hereditary angioedema may be beneficial in patients presenting with severe angioedema that began no more than approximately 6 hours earlier.
- Patient should be advised that angioedema can recur in the first few months after stopping an ACE inhibitor and should immediately go the ER if there is swelling of tongue and throat.

REFERENCES

Guyer, A., & Banerji, A. (2017). ACE inhibitor-induced angioedema. *UpToDate*.