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Prompt Reversal of Airway Obstruction Secondary to Angiotensin Converting Enzyme Inhibitor (ACEI) Induced Angioedema by Ecallantide: A Case Report

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Prompt Reversal of Airway Obstruction Secondary to Angiotensin Converting Enzyme Inhibitor (ACEI) Induced Angioedema by Ecallantide: A Case Report

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INTRODUCTION

- Fatal airway obstruction from ACEI angioedema has been described but effective therapy has not been established. Intubation is sometimes required for progressive airway compromise. Ecallantide is a kallikrein pathway blocker and may offer benefit in reversing ACEI induced angioedema.

Case

- A 54 year old African-American male with a history of hypertension treated with lisinopril daily, remote cocaine abuse associated myocardial infarction, seizures and prostate cancer, presented with a 2 day history of facial and throat swelling along with dysphagia. He was treated in the emergency department with intravenous methylprednisolone, epinephrine and diphenhydramine. He was admitted, but angioedema progressed overnight, confirmed by laryngoscopy. ICU transfer and intubation was undertaken the next morning for airway protection. Tryptase level was 2 ng/ml. C3 and C4 and routine chemistries were normal. Ecallantide 30mg was administered subcutaneously at 1014 hours.
- Medications: Lisinopril 10mg daily, tamsulosin.
- Family History: No history of angioedema. Parents deceased.
- Social history. Denies current alcohol or recreational drug use.
- Review of Systems: Remarkable for hypertension. On disability for back and knee problems.
- Physical Exam: Temp 98.8, Respiratory Rate 15, Heart Rate 61, Blood Pressure 130/80, and Oxygen Saturation 99% on ventilator.
  - HEENT- Oral endotracheal tube, limited exam after intubation by Otolaryngology for airway obstruction and desaturation while sleeping.
  - Respiratory- Lungs were clear and with good air entry on ventilator.
  - Cardiac- Regular heart rate and regular rhythm with no appreciable gallops, murmurs, or rubs.
  - Skin- There was no urticaria, other angioedema or rash.

RESULTS

Tryptase	2ng/ml	Hgb	10.9	pH	7.41	Sodium	145 meq/L	WBC	5.0 K/mm3
C3	134 mg/dL	PTT	33	PaCO2	33 mmHg	Potassium	3.1 meq/L	Hgb	11.8 gm/dL
C4	19 mg/dL	PT	14.1	PaO2	110 mmHg	Chloride	105 meq/L	Hct	35.70%
C2	2.2 mg/dL	INR	1.11	HCO3	21 meq/L	Bicarbonate	30 meq/L	Plt	159 k/mm3
				Base Excess	0.8 meq	BUN	10 mg/dL	Neutrophils	72.80%
						Creatinine	1.1 mg/dL	Lymphocytes	16.10%
						Glucose	104 mg/dL	Monocytes	8.70%
								Eosinophils	2.20%

CLINICAL COURSE AND OUTCOME

- Patient improved over the day and self-extubated prior to 1800 hours. He had no dysphagia or difficulty with respiration and was discharged the next morning.

•ACEI angioedema is a recognized complication of ACEI treatment that can occur months to years after starting therapy. The incidence is thought to be 0.1-0.5% (Warner. Ann Pharmacother 2000; 34: 526). Fatalities from airway obstruction are described (Dean. J Forensic Sci 2001; 46: 1239). Angiotensin converting enzyme is an important enzyme for degradation of bradykinin. Ecallantide selectively and reversibly inhibits plasma kallikrein, preventing bradykinin generation. This case suggests that ecallantide may indeed be effective in reversing ACEI induced angioedema, even in patients requiring intubation for airway protection.

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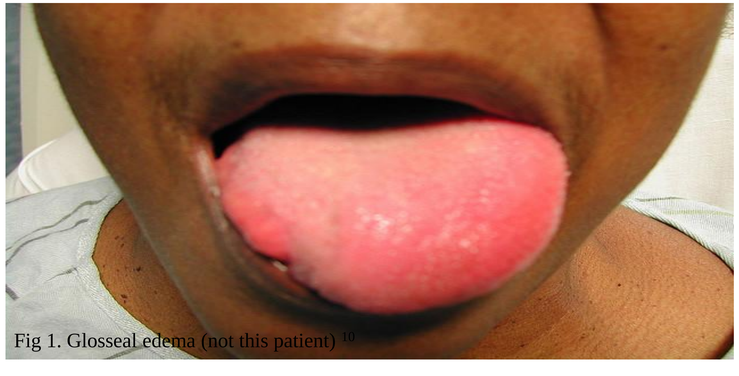

Fig 1. Glosseal edema (not this patient) [10]

CONCLUSION

- The mechanism of ACEI angioedema is thought to be from blockade of angiotensin converting enzyme, the major enzyme for degradation of bradykinin.
- Bradykinin and substance P have been linked to the pathogenesis of ACEI induced angioedema. Angiotensin converting enzyme (ACE) is a kinase that breaks down bradykinin [4]. The inhibition of ACE therefore leads to the inhibition of bradykinin catabolism. Bradykinin formation causes vasodilatation and increased vascular permeability by interaction with B-2 receptors. The inhibition of bradykinin catabolism thus leads to angioedema.
- Antihistamines, corticosteroids and epinephrine are ineffective in acute attacks of non-allergic angioedema. The mainstay of treatment currently is airway protection and supportive care. Theoretically, glucocorticoids could lead to a decrease in mucosal swelling. However, there is no demonstrated beneficial effect in patients with angioedema. Inhaled epinephrine may also be effective in laryngeal angioedema [8].
- Ecallantide is approved treatment of hereditary angioedema. It selectively and reversibly inhibits plasma kallikrein, preventing bradykinin generation. It is theorized that ecallantide can be used to treat other forms of kallikrein dependant angioedema.
- The length of hospitalization for patients with ACEI induced angioedema has ranged from 2 days to 4.8 days [5, 9]. Our patient self-extubated a few hours after emergent intubation and was discharged the next day after he remained stable overnight and without distress.
- This case suggests that ecallantide may indeed be effective in the cessation of ACEI induced angioedema. Additional randomized studies are underway to confirm these findings

REFERENCES

1. Warner KK, et al. Angiotensin II receptor blockers in patients with ACE inhibitor-induced angioedema. Ann Pharmacother 2000;34:526
2. Gibbs CR, et al. Angioedema due to ACE inhibitors: increased risk in patients of African origin.. Br J Clin Pharmacol 1999; 48:861
3. Dean DE, et al. Asphyxia due to angiotensin converting enzyme (ACE) inhibitor mediated angioedema of the tongue during the treatment of hypertensive heart disease. J Forensic Sci 2001;46:1239
4. Witherow FN, et al. Bradykinin contributes to the vasodilator effects of chronic angiotensin-converting enzyme inhibition in patients with heart failure. Circulation. 2001;104(18):2177
5. Bluestein HM. Et al. Angiotensin-converting enzyme inhibitor-induced angioedema in a community hospital emergency department. Ann Allergy Asthma Immunol 2009;103:502-507.
6. Gelee B, et al. Angiotensin-converting enzyme inhibitor-related angioedema: emergency treatment with complement C1 inhibitor concentrate. Rev Med Interne 2008; 29:516)
7. Karim MY, et al. Fresh –frozen plasma as a treatment for life threatening ACE Inhibitor angioedema. J Allergy Clin Immunol 2002; 109: 370)
8. Bas M, et al. Nonallergic angioedema: the role of bradykinin. Allergy. 2007; Aug;62(8):842-56.
9. Lin RY, et al. Pattern of hospitalizations for angioedema in New York between 1990 and 2003. Ann Allergy Asthma Immunol 2005;95:159-166.
10. Image from http://farm4.static.flickr.com/3102/3255202675_c2a61abcf3_z.jpg