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Chronic ACE-Inhibitor Induced Angioedema Requiring Emergent Nasotracheal Intubation: A Case Report

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Abstract

ACE-inhibitor induced angioedema is a rare, potentially life-threatening phenomenon with unpredictable symptoms. With advanced angioedema, orotracheal intubation may not be possible necessitating nasotracheal intubation or cricothyroidotomy. This case describes a 76-year-old male with a history of hypertension controlled with lisinopril-hydrochlorothiazide who developed sudden-onset angioedema. Additionally, this case was complicated by the patient's anticoagulation after recent abdominal aortic aneurysm repair. The patient's acute respiratory distress was managed with nasotracheal intubation because of severe edema of the oral cavity including at the base of the tongue without improvement with epinephrine, a corticosteroid, or an antihistamine. He was extubated the following day, but mild edema of the oral cavity and left side of face persisted at discharge 4 days after presentation. When presenting to the emergency room with angioedema mediated via ACE-inhibitor use, time is of the essence to avoid cardiopulmonary arrest secondary to hypoxemia. Rapid identification and management of this condition is key to improve outcomes. After acute management, patients should be advised to avoid all ACE-inhibitors in the future.

Keywords

Angiotensin-Converting Enzyme Inhibitors, Lisinopril, Angioedema, Nasotracheal Intubation, Case Report

Abbreviations

ACE: Angiotensin-Converting Enzyme

Introduction

Angiotensin-converting enzyme (ACE) inhibitors are the main cause of drug-induced angioedema in the United States [1]. While they contribute heavily to the development of drug-induced angioedema, ACE-inhibitor induced angioedema is a relatively rare occurrence. Anywhere from 0.1 to 0.7% of recipients are affected [2]. Of these cases, more than one-half of ACE-inhibitor induced angioedema occurs within one week of starting the medication [3]. This case is unique in that the patient had been taking this medication to manage his blood pressure for years prior to developing angioedema. Most cases of angioedema resolve without complications, but some

cases may present with a compromised airway. In these patients, endotracheal intubation may be necessary. In severe cases of angioedema without a patent airway, nasotracheal intubation or emergency tracheostomy is performed. These cases are extremely dangerous, necessitating quick action by the medical team. This case describes a patient presenting to the emergency department with severe angioedema, in the setting of chronic lisinopril use, who required nasotracheal intubation. It is important for physicians to quickly recognize and manage such life-threatening cases.

Case Summary

A 76-year-old male presented to the emergency department by ambulance with significant tongue and left-sided facial swelling. Past medical history was pertinent for being one week status post abdominal aortic aneurysm repair, anticoagulation with Warfarin, hypertension treated with lisinopril-hydrochlorothiazide, diabetes, obstructive sleep apnea, and obesity. He reported the sudden onset of symptoms after dinner about 2 hours prior to presentation. The patient denied food allergies or history of anaphylaxis, but did report allergies to clopidogrel, fenofibrate, and pregabalin.

On arrival, his respiratory rate was elevated at 21 breaths/minute. Other vitals were stable with heart rate of 85 bpm, blood pressure of 123/66 mmHg, and pulse oximetry reading of 98% on room air. Physical exam revealed significant edema to the left side of the face, floor of mouth, tongue, left upper and lower lip, soft palate, and uvula. Additionally, the physical exam was significant for rhonchi and rare patches of mild urticaria. The patient was maintaining his airway and conversing with rhonchorous speech.

En route to the hospital, the patient was given intramuscular diphenhydramine. In the emergency department, the patient was treated with 0.3 mg intramuscular epinephrine, 0.5 mL nebulized racemic epinephrine, 125 mg IV solumedrol, and 20 mg IV famotidine. He received 10 mg IV vitamin K to reverse his anticoagulation in case of surgical management. The use of epinephrine, a corticosteroid, and an antihistamine resulted in minimally improved swelling, making anaphylaxis a less likely diagnosis.

Chest x-ray done in the emergency department revealed bibasilar infiltrates. Initial labs were pertinent for high WBC of 18.1 K/uL, glucose of 170 mg/dL, blood urea nitrogen of 29 mg/dl, globulin of 4.1 dm/dL, AST of 65 IntUnit/L, and ALT of 70 IntUnit/L. He was being anticoagulated with Warfarin at presentation, with INR of 1.38 and PT of 15.7. Electrolytes including calcium, magnesium, and especially potassium were low.

ENT was consulted and bedside flexible fiberoptic laryngoscopy was performed. The scope was passed into the right nasal passage to the level of the hypopharynx for visualization of the airway. Findings were significant for severe symmetric edema of the base of tongue with effacement of the vallecula and mild retroflexion of the epiglottis causing remarkable narrowing at this level of the airway. Moreover, he was found to have edema of the pharynx, interarytenoid mucosa, false vocal cords, true vocal cords, and arytenoids.

The decision was made to take the patient to the operating room for elective controlled intubation, with possibility of tracheostomy if necessary, due to the risk of complete airway obstruction. The anesthesiologist performed fiberoptic nasotracheal intubation through the right nasal passage without complications. The placement was verified by visualization of tracheal rings and carina below the end of the tube. Subsequently, the patient was transferred to the ICU in stable condition.

The patient was extubated the following day and transferred out of the ICU to a patient floor. He continued his home medication of 5 mg oral amlodipine daily and was started on 25 mg oral hydralazine every 6 hours for blood pressure control. During his hospital stay he received 50 mg/mL IV diphenhydramine twice daily, 10 mg/mL famotidine every 10 hours, 40 mg/mL methylprednisolone sodium succinate injection every 12 hours, and 2 mg oral warfarin daily. Mild left sided facial swelling persisted at discharge. The patient was discharged from the hospital 4 days after presenting. His airway edema had

significantly improved. He was instructed to discontinue use of any ACE inhibitors. He was discharged with new prescriptions for 10 mg prednisone, 10 mg loratadine, and 25 mg hydralazine (**Table-1**).

Discussion

Fluid extravasation into interstitial tissue leads to the swelling characteristic of angioedema. This swelling commonly involves structures of the airway, oral cavity, face, genitalia, and extremities. The intestines may also be involved, leading to abdominal pain with symptoms such as diarrhea. Angioedema may be deadly in cases of airway obstruction secondary to airway, laryngeal, or tongue swelling [4].

The discussed patient developed angioedema and resulting airway compromise in the setting of ACE-inhibitor use. This reaction may be due to the inhibition of metabolism of molecules such as bradykinin, as a result of ACE-inhibitor implementation [5]. Other etiologies of bradykinin-mediated angioedema include hereditary and acquired C1 inhibitor deficiency. This is in contrast to allergic etiologies of angioedema, which are mediated via histamine and may be a part of anaphylaxis. Angioedema occurring as a consequence of bradykinin typically lacks the findings commonly associated with allergic etiologies such as urticaria, pruritus, bronchospasm, and hemodynamic instability [4]. Minor urticaria, such as in our patient, may be present in ACE-inhibitor angioedema, but this process is largely mediated by histamine rather than bradykinin [6].

Table-1: Significant lab results at presentation to the emergency department

GFR - Non African American	55 mL/min/1.72^2 (low)
White Blood Cell Count	18.1 K/uL (high)
Absolute Neutrophil Count	12.0 K/uL (high)
Absolute Lymphocyte Count	4.2 K/uL (high)
Absolute Monocyte Count	1.4 K/uL (high)
Red Blood Cell Count	3.27 M/uL (low)
Hemoglobin	10.3 gm/dL (low)
Hematocrit	31.3% (low)
Prothrombin Time	15.7 sec (high)
International Normalized Ratio	1.38 (high)
Potassium	2.9 mmol/L (low)
Calcium	8.1 mg/dL (low)
Magnesium	1.3 mg/dL (low)
Glucose	170 mg/dL (high)
Blood Urea Nitrogen	29 mg/dL (high)
Albumin	2.9 gm/dL (low)
Globulin	4.1 gm/dL (high)
AST	65 IntUnit/L (high)
ALT	70 IntUnit/L (high)
Lipase	20 units/L (low)

In cases of suspected angioedema secondary to ACE-inhibitor use, the diagnosis is established clinically, as was done for the discussed patient. Acute management of airway compromise necessitates that the airway be secured in order to prevent asphyxiation. There have been rare cases of fatal asphyxiation reported [7]. Similar to our patient, there have been a few cases of others requiring intubation [8, 9]. There is a case of a patient developing angioedema in the setting of ACE-inhibitor use, who was initially given antihistamines and steroids, but similar to our patient these medications did not lead to resolution of symptoms;

endotracheal intubation was performed on this patient, rather than nasotracheal intubation [9]. Medications such as antihistamines, steroids, and epinephrine are successful in management of histamine-mediated rather than bradykinin-mediated angioedema. In regards to long-term management, cessation of ACE-inhibitor is vital in preventing future recurrences [4]. This patient was appropriately managed in that his airway was secured promptly, avoiding asphyxiation. His long term recommendation of ACE-inhibitor use cessation was appropriate as well.

There is limited evidence that some medical therapies may be helpful in the management of ACE-inhibitor angioedema. There are multiple case reports of patients presenting with angioedema secondary to ACE-inhibitor use being successfully managed with purified C1 inhibitor concentrate [10, 11, 12, 13]. Additionally, there are case reports discussing effective treatment with fresh frozen plasma [14, 15]. Literature reporting success with Tranexamic acid has also been reported [16, 17]. Icatibant was initially demonstrated to be a useful treatment, but when considering later studies the implementation of this drug is not supported [18].

Conclusion

ACE-inhibitors are a common cause of drug induced angioedema. Although it is rare for patients using ACE-inhibitors to develop this reaction, angioedema may be life-threatening in cases of airway compromise. Such cases necessitate quick treatment via procedures such as intubation or possible surgical airway management. Moreover, it is important for patients to avoid ACE-inhibitors in the future to prevent recurrence of symptoms. It is important for physicians, especially emergency physicians, to be cognizant of the fact that ACE-inhibitors are a potential cause of angioedema requiring prompt management.

Conflicts of Interest

The authors have all read and approved the final version of the manuscript. The authors have no conflicts of interest to disclose.

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