Angiotensin-Converting Enzyme Inhibitor-Induced Angioedema: A Case Report With a Review of Management Options

Muhammad Atif Ameer 1, Jawaria Mushtaq 2, Haroon Chaudhry 3, Nimi Patel 3, Sonia Ilyas Khan 4

Abstract
Angiotensin-converting enzyme inhibitors (ACEIs) are widely used for heart failure, renal failure, diabetic nephropathy, stroke, arterial hypertension, and a number of other cardiovascular or related conditions. ACEI-induced angioedema is a rare entity but can result in life-threatening emergencies. It mainly occurs in patients starting on ACEI as an antihypertensive. We present a case of lisinopril-induced angioedema in an African American patient managed in the emergency department. After appropriate evaluation, the patient was declared safe to be observed in the emergency department. Intubation was not performed. Early identification of angioedema is paramount, and emergency physicians should maintain airways or intubate such patients if indicated. There should be a high level of suspicion of angioedema in patients taking ACEIs if they present with symptoms of respiratory compromise.

Introduction
Angiotensin-converting enzyme inhibitors (ACEI) are commonly used antihypertensive medications estimated to be used by millions of hypertensive patients globally [1]. The three main indications for ACEI are coronary artery disease, renal disease, and heart failure. ACEI-induced angioedema incidence ranges from 0.1% to 0.7%. It has predilections in elderly individuals, females, and the African American population with a prior history of cutaneous drug eruptions, allergy reactions, and patients on immunomodulatory agents [2]. ACEI-induced angioedema in genetically predisposed individuals is caused by kallikrein activation leading to elevated levels of bradykinin, substance P, and other inflammatory mediators. These inflammatory markers are responsible for causing significant vasodilatation leading to hypotension. Clinical features range from angioedema of the face, lips, and oral mucosa to laryngeal and sub-glottic edema, hoarseness of voice, inspiratory stridor, acute tongue edema leading to pharyngeal tonsils, and uvula leading to airway compromise and asphyxiation [3]. Treatment includes removing offending agent exposure, immediate preservation of the airway, intravenous steroids, histamine receptor antagonists, and IV epinephrine once the patient is stable. Newer and improved treatments include bradykinin receptor antagonists, kallikrein production inhibitors, fresh frozen plasma, and C1 inhibitor concentrate [4]. We present a case of a middle-aged African American male with a history of ACEI-induced angioedema, who presented again with similar features after accidental re-exposure.

Case Presentation
A 48-year-old African American male presented to the emergency department with complaints of difficulty and painful swallowing along with lip swelling for the past six hours. He had a medical history of diverticulitis, gastrointestinal bleeding associated with acute gastritis, hyperlipidemia, hypertension, and spinal stenosis with sciatic pain. The patient takes atorvastatin, bupropion, metformin, cyclobenzaprine, lisinopril, and meloxicam.

On presentation, his blood pressure was 126/84 mmHg, heart rate was 103 bpm, temperature was 97.3°F, and respiratory rate was 15/minute with oxygen saturation of 95% on room air. The patient was visibly anxious with mild distress. The head was normocephalic and atraumatic on physical examination, with no apparent deformities of both ears, rhinorrhea, or nasal swelling. The patient had labial, sublabial mucosal (Figure 1), and gingival edema (white arrows), edematous glossopharyngeal arch, and hyperemic edema palatine tonsils (black arrows), injected and displaced edematous uvula (yellow arrow), and lingual edema (blue arrow). He had moderate cervical lymphadenopathy and swelling of the posterior pharynx and tonsils (Figure 2). Cardiovascular, pulmonary, gastrointestinal, and neurological exam was unremarkable.
FIGURE 1: Asymmetric labial angioedema (white arrows)
The initial symptoms were significant for dysphagia, odynophagia, and palatal angioedema that started approximately 48 hours prior to the presentation. Additionally, the patient reported a feeling of burning sensation, predominantly in the throat and palate, exacerbated by eating or drinking. The patient denied drooling, shortness of breath, facial hyperthermia, or hyperemia. The patient reported allergies to iodine and certain medications but could not recall the specific names.

The patient was started on lisinopril five days ago for his uncontrolled hypertension. He had a similar episode a year ago when he began lisinopril. He did not seek any medical attention for it but discontinued
lisinopril. He did not take this medication until recently when he was found to have uncontrolled hypertension and restarted on lisinopril.

The patient’s comprehensive metabolic panel and complete blood count are given in Table 1 and Table 2, respectively. Urine drug screen and urinalysis were negative for any significant findings.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Patient value</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na)</td>
<td>138 mEq/L</td>
<td>135-145 mEq/L</td>
</tr>
<tr>
<td>Potassium (K)</td>
<td>4 mEq/L</td>
<td>3.5-5.0 mEq/L</td>
</tr>
<tr>
<td>Chloride (CL)</td>
<td>101 mEq/L</td>
<td>96-106 mEq/L</td>
</tr>
<tr>
<td>Bicarbonate (HCO3)</td>
<td>28.4 mEq/L</td>
<td>23-29 mEq/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>141 mg/dL</td>
<td>70-100 mg/dL</td>
</tr>
<tr>
<td>Bilirubin (total)</td>
<td>0.3 mg/dL</td>
<td>0.1-1.2 mg/dL</td>
</tr>
<tr>
<td>Blood urea nitrogen (BUN)</td>
<td>14 mg/dL</td>
<td>6-24 mg/dL</td>
</tr>
<tr>
<td>Creatinine (Cr)</td>
<td>0.9 mg/dL</td>
<td>0.5-1.0 mg/dL</td>
</tr>
<tr>
<td>Aspartate aminotransferase (AST)</td>
<td>21 U/L</td>
<td>8-33 U/L</td>
</tr>
<tr>
<td>Alanine aminotransferase (ALT)</td>
<td>38 U/L</td>
<td>7-56 U/L</td>
</tr>
<tr>
<td>Alkaline phosphatase (Alk Phos)</td>
<td>119 U/L</td>
<td>30-120 U/L</td>
</tr>
<tr>
<td>Magnesium (Mg)</td>
<td>2 mEq/L</td>
<td>1.3-2.1 mEq/L</td>
</tr>
<tr>
<td>Calcium (Ca)</td>
<td>8.9 mEq/L</td>
<td>8.5-10.2 mEq/L</td>
</tr>
</tbody>
</table>

### TABLE 1: Comprehensive metabolic panel

<table>
<thead>
<tr>
<th>Lab</th>
<th>Patient value</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell (WBC)</td>
<td>7.6 x 10⁹/L</td>
<td>4.5-11.0 x 10⁹/L</td>
</tr>
<tr>
<td>Red blood cells (RBC)</td>
<td>5.7 cells per mcL</td>
<td>4.7-6.1 cells per mcL</td>
</tr>
<tr>
<td>Hemoglobin (Hgb)</td>
<td>14.2 g/dL</td>
<td>13.8-17.2 g/dL</td>
</tr>
<tr>
<td>Hematocrit (Hct)</td>
<td>44.60%</td>
<td>41%-50%</td>
</tr>
<tr>
<td>Platelets</td>
<td>350 x 10⁹/L</td>
<td>150-400 x 10⁹/L</td>
</tr>
<tr>
<td>Mean corpuscular volume (MCV)</td>
<td>77.2 fl</td>
<td>80-100 fl</td>
</tr>
<tr>
<td>Mean corpuscular hemoglobin (MCH)</td>
<td>24.6 pg</td>
<td>27.5-33.2 pg</td>
</tr>
<tr>
<td>Mean corpuscular hemoglobin concentration (MCHC)</td>
<td>31.9 g /dL</td>
<td>32-36 g /dL</td>
</tr>
<tr>
<td>Red blood cell distribution with (RDW)</td>
<td>15.80%</td>
<td>11.8-14.5%</td>
</tr>
<tr>
<td>Mean platelets volume (MPV)</td>
<td>7.9 fl</td>
<td>7.2-11.7 fl</td>
</tr>
</tbody>
</table>

### TABLE 2: Complete blood count

The patient was managed with dexamethasone 10 mg IV, diphenhydramine 50 mg IV, and famotidine 20 mg IV. Lisinopril was discontinued from the patient’s regimen, and the patient was initiated on hydrochlorothiazide for his hypertension management.

**Discussion**

Angioedema is a medical condition characterized by non-dependent, non-pitting swelling of deep dermal
ACEI-induced angioedema is a rare adverse effect of one of the most commonly used antihypertensive therapies, it shows comparable relief after a single dose [12]. In rare instances, ACEI-induced angioedema can also improve from purified C1 concentrate. Ecallantide has not always been effective in treating ACEI-induced angioedema, even though it has been used to treat genetic angioedema [12]. Antihistamines, epinephrine, and steroids are the standard treatments for angioedema. However, despite their use, there is limited proof of their effectiveness, specifically in ACEI-induced angioedema. It can be challenging to diagnose the pathology correctly, but it may be essential to starting the right treatment [13].

Conclusions

ACEI-induced angioedema is a rare adverse effect of one of the most commonly used antihypertensive

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medications. It can result in life-threatening complications and/or airway obstruction. Whenever such patients are encountered, this differential should be kept in mind. In addition to protecting the airway, the inciting agent should be promptly discontinued. Sometimes, these patients may not initially respond to steroids, epinephrine, or antihistamines, so the airway should be secured via endotracheal intubation or surgically if a respiratory compromise is suspected. Purified C1, icatibant, and sometimes fresh frozen plasma can also be used if the condition is unresponsive to the initial treatment.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References