

CASE REPORT



A rare presentation of angioedema with isolated retropharyngeal and supraglottic involvement

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ABSTRACT

Angiotensin converting-enzyme (ACE) inhibitors are commonly prescribed drugs with multiple indications including congestive heart failure, hypertension, and diabetic nephropathy. ACE inhibitor induced angioedema is commonly seen across emergency departments and clinics, with transient swelling of lips, tongue, and other facial structures being the common presentation. Isolated airway obstruction as a result of pharyngeal and laryngeal swelling without facial swelling is a rare presentation. We present a case of a patient on lisinopril therapy for one year who experienced severe airway compromise without the classic symptoms of ACE inhibitor induced angioedema. He required emergent cricothyroidotomy to secure his airway, as fiberoptic laryngoscopy showed 90% obstruction and inability to visualize true vocal cords. His ACE inhibitor therapy was discontinued, and he was discharged home within a few days with no residual symptoms.

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1. Introduction

Angiotensin converting-enzyme (ACE) inhibitors are widely prescribed across the world, with multiple indications for usage including congestive heart failure, hypertension, and diabetic nephropathy [1,2]. The incidence of ACE inhibitor induced angioedema is estimated to be in the range of 0.1–0.7% [3–5]. ACE inhibitor related angioedema accounts for 30–68% of all angioedema associated visits to the emergency department [6,7]. In terms of demographics, African-American patients are at a 3 times higher risk compared to other races, and women have also been noted to have a 1.5 times increased risk of ACE inhibitor induced angioedema [5,8]. Typically, ACE inhibitor related angioedema is more common within the first four weeks of starting therapy, but a lower but consistent risk remains, even after multiple incidence-free years of ACE inhibitor treatment [5,9].

Patients typically present with swelling of lips, tongue, cheeks, oropharynx, and larynx, and with less common complaints of dysphagia and dyspnea [5,10]. Isolated retropharyngeal involvement devoid of these symptoms is a rare phenomenon [5,6,9,10]. Here we present a unique case of ACE inhibitor induced angioedema with isolated retropharyngeal and supraglottic edema that required cricothyroidotomy due to severe airway compromise.

2. Case presentation

A 52-year-old male presented to the emergency department with chief complaint of feeling like his throat was closing up and difficulty breathing. He noticed the onset of symptoms after eating dinner, which did not consist of any new foods or allergens. Symptoms initially started with globus sensation and difficulty swallowing, later progressing to increasing shortness of breath. Within two hours of onset, he noted drooling and hoarseness of voice, which prompted him to visit the emergency department (ED). After further questioning, he recalled a brief episode of lip swelling three weeks prior to this presentation, which resolved spontaneously on the same day. Of note, patient had been taking lisinopril daily for treatment of hypertension for the past year, the last dose taken on the morning of presentation. Otherwise, patient denied any new exposures, recent nonsteroidal anti-inflammatory drug use, changes in medications, sick contacts, insect bites, or trauma. He also denied pruritus, wheezing, skin changes, or lip or tongue swelling. His past medical history included hypertension and depression, for which he was taking lisinopril and aripiprazole respectively. He denied recent travel history but did admit to drinking, on average, up to three to four cans of beer per week. His vital signs on admission were as follows: blood pressure 159/100 mm Hg, pulse 75 bpm, temp 98.9 F, respiratory rate 18/min with dyspnea, O₂ saturation 98%. On physical

examination, the patient appeared in moderate distress with muffled voice. Examination of the oral cavity revealed no edema of lips, tongue, or uvula. Pulmonary exam revealed coarse upper airway sounds over the neck but no stridor or wheezing.

Initial laboratory tests showed a complete blood count of hemoglobin of 12.7 g/dL, hematocrit of 37.5%, with normal WBC at 5.6 K/mcL and platelet count of 78 K/mcL. His thrombocytopenia was chronic in nature with multiple readings of platelet counts in the range of 90–95 K/mcL noted at least two years prior to current presentation. Comprehensive metabolic panel was unremarkable with Na – 138 mmol/L, K – 4.2 mmol/L, CO₂ – 26 mmol/L, BUN – 15mg/dL, and Cr – 1.01 mg/dL. Lactate level was normal at 1.3 mmol/L. Urinalysis was within normal limits.

In the ED, patient was given 0.5 mg of 1:1000 Epinephrine IM, 120 mg Methylprednisolone IV, 25 mg Diphenhydramine IV, and 20 mg Famotidine IV. CT scan of the neck with contrast was obtained, which demonstrated marked supraglottic and retropharyngeal edema with severe compromise of the supraglottic airway (Figures 1 and 2). As the patient remained stable, otolaryngology consultation was requested for direct visualization and controlled fiberoptic-guided intubation. Fiberoptic laryngoscopy showed severe edema of the supraglottic and glottic larynx with 90% obstruction of airway along with no visualization of true vocal cords due to severe edema. Due to these findings, along with the possibility of worsening of airway compromise leading to complete obstruction, emergency cricothyrotomy was performed to secure the patient's airway. The ACE inhibitor was stopped, and the blood pressure managed with hydralazine IV as needed.

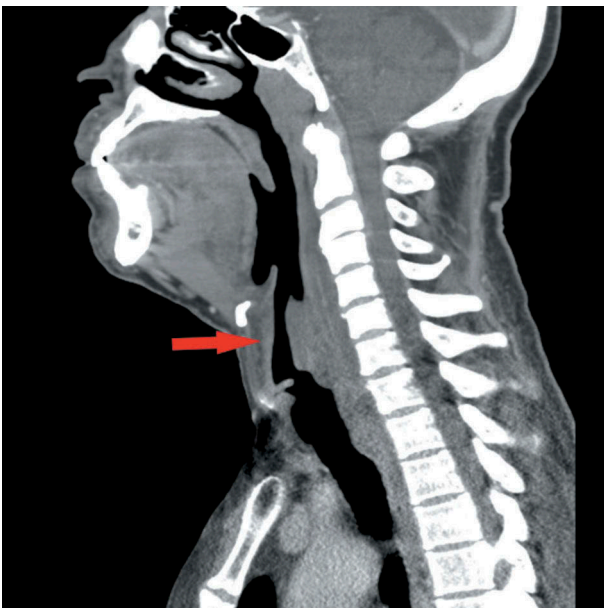


Figure 1. Sagittal view contrast enhanced CT scan of the neck with retropharyngeal, epiglottic, and vocal cord edema.

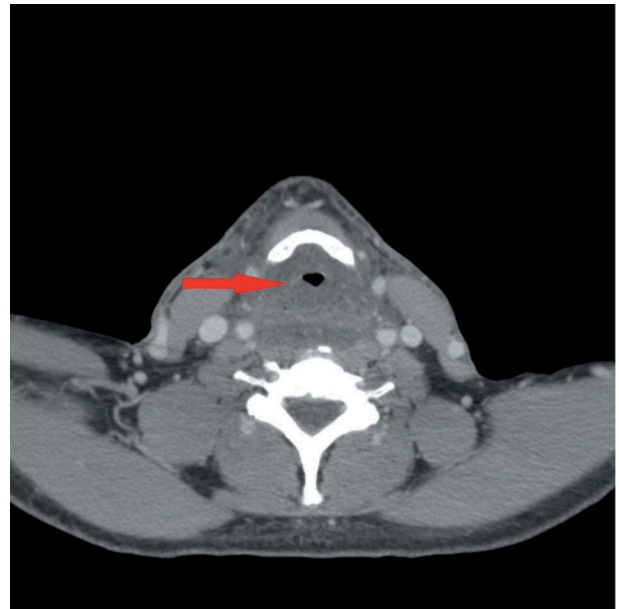


Figure 2. Axial contrast enhanced CT scan of neck soft tissue at the level of hyoid body shows edema of the pharyngeal mucosa and retropharyngeal space with airway narrowing.

On day 2 of admission, repeat fiberoptic laryngoscopy showed persistent but moderate amount of laryngeal edema, but with 40% improvement compared to the previous day. Patient was continued on IV methylprednisolone through day 2 and 3 of admission. On day 4 of admission, repeat fiberoptic laryngoscopy demonstrated near complete resolution of the supraglottic edema. However, vocal cord edema due to submucosal hemorrhage was present, which was in part attributed to the thrombocytopenia. This delayed plans for decannulation, and patient remained on same steroid regimen. On day 5 of admission, patient was decannulated after a final laryngoscopy demonstrated complete resolution of supraglottic and retropharyngeal edema, with a widely patent airway. After observation for another day without complications, patient was discharged home on day 6 without residual symptoms. Long term follow up demonstrated no similar episodes of recurrence or classic facial or oral cavity edema.

3. Discussion

The mechanism causing ACE inhibitor induced angioedema is not clearly understood, but it is thought to be multifactorial. Elevated levels of bradykinin and decreased activity of substance P are postulated to play a major role in patients with ACE inhibitor induced angioedema [11,12]. Angiotensin-converting enzyme is responsible for degradation of bradykinin, an inflammatory mediator that has vasodilatory effects in addition to causing an increase in vascular permeability. Abnormal levels of substance

P have also been noted to be a predisposing factor in patients with ACE inhibitor induced angioedema [12].

Several studies have looked at angioedema incidence, common presenting symptoms, and the location of swelling. Malde et al found that the area above the neck is the most affected among 64 patients with ACE inhibitor induced angioedema, with lips and tongue being the most common locations of swelling [13]. Another retrospective study found similar presentations, with lip and tongue swelling, in all 45 patients with ACE inhibitor induced angioedema in their series [9]. Banerji et al found the presence of lip swelling, tongue swelling, and shortness of breath as the most common initial presenting symptoms among 220 patients who visited ED for ACE inhibitor induced angioedema [6]. Two other studies observed swelling of lips and face as the predominant presentation among patients with ACE inhibitor induced angioedema [5,10]. Other less common swelling sites include eyelids, pharynx, larynx, extremities and visceral organs; common presenting symptoms also include dysphagia, hoarseness, globus sensation, and shortness of breath [5,6,9,10,14].

Airway compromise is not uncommon among patients with ACE inhibitor induced angioedema; however, the majority of those patients presented with concurrent swelling in other locations as well [5,6,9,10,13]. Of patients who experience airway compromise due to ACE inhibitor related angioedema, up to 10% required mechanical ventilation through intubation or tracheostomy [5,6,9,10,13]. Review of the English literature suggests that isolated angioedema without involvement of lips or oral cavity is exceedingly rare. Most of those cases present as isolated visceral angioedema [14–16]; a comprehensive search identified four reports of ACE inhibitor angioedema presenting only with isolated pharyngeal and uvular involvement [14–20].

Case reports of isolated uvular angioedema also exist, albeit such cases are rare and do not mention any obvious airway compromise [17,18]. Isolated retropharyngeal edema precipitated by pharyngitis was reported in a patient with hereditary angioedema [19], and in another case, a patient presented with globus sensation and dysphagia and was discovered to have isolated esophageal angioedema in the setting of recent ACE inhibitor usage [20]. Chiu et al found no cases of isolated supraglottic or laryngeal swelling among 108 angioedema patients studied [7].

The initial differential diagnosis in our patient focused on anaphylactic reaction vs ACE inhibitor induced angioedema. The absence of systemic findings of urticaria, pruritus, hypotension, or tachycardia, along with lack of any obvious inciting allergens, made allergen induced anaphylaxis reaction less likely. Discontinuation of lisinopril and subsequent

resolution of symptoms is consistent with ACE inhibitor induced angioedema. Though ACE inhibitor related angioedema may occur at any point during therapy, it is more common within first month of starting ACE inhibitor therapy [5,9].

As the exact mechanism of ACE inhibitor induced angioedema is not established, management focuses on discontinuation of ACE inhibitor and supportive care rather than treatment with targeted reversal agents. While efficacy of epinephrine and antihistaminergic medication is not established in ACE inhibitor induced angioedema, the consensus is to initiate these therapies in patients with signs of respiratory compromise due to inability to rule out an allergic/anaphylactic reaction [7,9]. Airway assessment with direct fiberoptic visualization is recommended in the setting of oropharyngeal involvement, followed by intubation of cricothyrotomy if airway obstruction is present [7]. Corticosteroids are also used to reduce swelling and inflammation throughout the hospital admission, though there is no consensus for post discharge steroid usage [7,9]. The usage of bradykinin receptor antagonists is indicated in acute attacks of hereditary angioedema and hence these agents have been trialed in ACE inhibitor induced angioedema [21,22]. These studies have shown such agents to be inefficacious and hence their use is controversial among patients with ACE inhibitor induced angioedema [21,22].

4. Conclusion

Angioedema induced by ACE inhibitor is a well-recognized phenomenon, based on the widespread usage and multiple indications of ACE inhibitors. Our case highlights the potential for isolated supraglottic and retropharyngeal involvement without any of the classic symptoms of facial and oral cavity swelling. It demonstrates the importance of quick airway evaluation and imaging in a patient that otherwise appears to show no obvious signs of respiratory distress. Though our patient presented with globus sensation and the feeling of throat closure, the oral cavity examination was normal. Entertaining the possibility of isolated retropharyngeal angioedema in such patients may prevent the life-threatening consequences from impending airway failure.

Disclosure statement

No potential conflict of interest was reported by the authors.

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