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Severe Laryngeal Edema after Extubation with Prior Use of ACEi Medications

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INTRODUCTION

Angioedema (AE) is a known adverse effect of angiotensin-converting enzyme inhibitor (ACEi) therapy, usually seen in the outpatient setting shortly after initiating treatment, but also can occur after months or years.[1] The prevalence of ACEi-induced AE has been reported as 28% to 30%.[2] AE is believed to be caused by plasma extravasation secondary to increased vascular permeability within the dermis, subcutaneous, or submucosal tissue.[3] Activation of the kallikrein-kinin system and the classic complement pathway results in the release of inflammatory mediators that lead to vasodilation.

Among patients presenting with AE, facial edema was seen in 85%, followed by lingual swelling in 40% and laryngeal edema in 10%; the condition is self-limiting, with spontaneous resolution of swelling often within two to three days.[4-6] Immediate management of AE focuses on airway protection, as respiratory failure may ensue secondary to airway edema and complete obstruction. In patients with hoarseness, odynophagia, or dyspnea, fiberoptic nasopharyngolaryngoscopy can be a useful technique to evaluate for laryngeal edema.[5,7]

This case reports a patient with a previous history of ACEi use who presented with severe laryngeal edema 20 minutes following extubation. Multiple attempts at reintubation were made utilizing an awake Glidescope™ technique, fiber optic, and blind nasal tube placement.

CASE REPORT

Written, informed consent was obtained from the patient for publication of this case report.

A 67-year-old, 105 kg Caucasian male with atrial fibrillation, insulin-dependent diabetes mellitus, obstructive sleep apnea, and hypertension presented to the operating room for incision and drainage of a left foot wound infection. Notably, the patient reported two previous instances of throat swelling while taking ACEi medications, one of which required intubation. Therefore, he had listed allergies to this class of medication and had discontinued them for two years prior to this incident. On inspection of the oral cavity, the patient had a Mallampati III opening, adequate thyromental distance, and normal dentition. Other than the left foot infection, his vital signs and physical examination were unremarkable.

After the application of routine monitoring devices and premedication with midazolam 1 mg IV, anesthesia was induced with 150 mcg of fentanyl, 100 mg succinylcholine, 200 mg propofol, and 50 mg ketamine IV. Direct laryngoscopy with a Miller 2 blade revealed a Cormack-Lehanegrade-one view, and the patient was intubated without difficulty. Anesthesia was maintained with sevoflurane and the operation was uneventful. Following this case, the patient was extubated without incident, and he was transferred to the post-anesthesia care unit (PACU) with supplemental oxygen for monitoring. The patient's intraoperative course lasted 30 minutes with 20 minutes of tourniquet time.

Hemodynamics were stable upon arrival to PACU. Approximately 20 minutes later, the nurse noted the patient's oxygen saturation had dropped to the mid-90s with swelling at the base of his tongue and no systemic signs of anaphylaxis or subcutaneous emphysema. The patient received 8 mg dexamethasone, 50 mg diphenhydramine, and 20 mg famotidine. Respiratory therapy was called for inhaled racemic epinephrine and a nasopharyngeal airway was inserted.

Despite these efforts, the patient's tongue continued to swell, and intubation was deemed necessary, so the surgery team was notified of possible surgical airway intervention. Initially, an awake Glidescope™ was attempted but was unsuccessful secondary to severe supraglottic and glottic swelling with copious secretions. A fiberoptic scope was introduced for a nasal approach. This was complicated by desaturations to the mid-forties, so bag-mask ventilation was performed while continuing the intubation attempt. Saturations improved to within normal range, but ultimately the tube could not advance through the vocal cords.

A smaller diameter tube was introduced blindly through the nasal passage. Color change capnometry was negative for end-tidal CO_2 and no breath sounds were noted. Bag ventilation was performed through this tube while a Glidescope™ was introduced to visualize the tube's position. Visualization of laryngeal structures was achieved, and the nasal tube was advanced successfully through the cords. Afterward, the patient was transferred to the intensive care unit where he remained intubated for the next two days, during which time he received systemic steroids. He was extubated without incident and discharged home on post-operative day three.

DISCUSSION

The differential diagnosis of post-operative laryngeal swelling includes AE, allergic reaction, anaphylaxis, peritonsillar abscess, hematoma, and superior vena cava syndrome.[8] The patient lacked systemic symptoms, hypotension, and anaphylactic or allergic manifestations, and the physical exam did not indicate hematoma formation. However, he expressed bilateral, soft, non-pitting edema evident of AE. Moreover, he had multiple predisposing conditions that can lead to the diagnosis of AE, including prior use of ACEi medications and a previous episode of AE that required intubation. The patient's symptoms presented in the immediate post-operative period, and recent airway manipulation has been reported to precipitate AE.[5,9]

Inciting factors often are idiopathic, yet 38%-68% of acquired forms arise following the use of ACEis, which interfere with the conversion of angiotensin I to angiotensin II and cause a reduction in the degradation of bradykinin.[3,6,8] Other medications include certain antibiotics, opioids,[7] NSAIDs,[10, 11] and angiotensin II receptor antagonists.[12] The latter is a unique association in that antagonizing the angiotensin II receptor does not increase kinin levels, suggesting a different mechanism may be involved. Additional forms of AE follow a hereditary

pattern and involve deficiencies in the C1 esterase inhibitor protein.[13] These patients are susceptible to acute swelling after physical, dental, or surgical manipulation of the upper airway.[14] Our patient did not have any measurements of C4, C1q, or any functional assays of the complement cascade available for reference.

Varying degrees of laryngeal edema are seen in patients post-extubation. Among patients requiring reintubation, 15% are due to post-extubation laryngeal edema.[9] Other than extubation predisposing to laryngeal edema-indicated reintubation, pre-hospital use of ACEi was found to be an independent risk factor for failed extubation due to unexpected upper airway edema.[15] These two different etiologies often overlap in hospital settings, making it difficult to identify the precise cause of an individual case, though management was often the same.

When AE is suspected, primary management requires discontinuation of the offending agents and evaluation of the airway. Though AE is self-limiting, it is crucial to identify the natural regression of AE to prevent unnecessary surgical intervention. Chiu et al.[16] produced an algorithm for airway management in the AE setting. They categorized AE into three types based on the extent of swelling: Type 1 involves swelling of the face and oral cavity only, Type 2 extends to the floor of the mouth or tongue, and Type 3 extends to the supraglottic structures. In the study, 21% of Type 2, and 33% of Type 3 AE patients required intubation.[16]

Treatment of AE involves steroids, antihistamines, epinephrine, and humidified oxygen. Danazol and stanazol are androgens that increase serum concentrations of C1 esterase inhibitors and can be useful in prophylactic treatment when AE episodes are possible, such as in patients with a hereditary deficiency of C1 esterase.[17] Androgenic steroids typically are used as an illicit drug and not in medical settings, but they can be effective in addressing angioedema, as seen in our patient. Fresh frozen plasma also has been utilized in treatment, but its inclusion of C4 may lead to propagation of the complement system and a worsening of AE and is reserved for prophylaxis and not acute episodes.[18]

CONCLUSIONS

Healthcare providers must be aware of AE presenting in the immediate post-operative environment. Recognition of early signs, including tongue swelling, respiratory decompensation, and difficulty speaking, may be lifesaving. Assessment of the airway and immediate intervention can prevent the mortality and morbidity associated with airway compromise.

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