Macroglossia secondary to lisinopril-induced acute angioedema

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ABSTRACT

Presented here are two cases of acute acquired macroglossia in adults caused by angioedema resulting from a reaction to angiotensin-converting enzyme inhibitors (ACEIs). Angioedema can be caused by a variety of factors, but ACEIs are the most common precipitating factor. Symptoms such as swelling of the lips, face, tongue, and throat can lead to life-threatening airway compromise. Early management of acute angioedema and macroglossia includes antihistamines, steroids, and occasionally epinephrine, yet a small percentage of patients progress toward airway obstruction and will require intubation. Edema within the lips, face, and throat usually subsides within a week, but the tongue can remain edematous for prolonged periods if biting trauma occurs. If the patient's macroglossia does not resolve in a reasonable amount of time, a partial glossectomy may be indicated.

KEYWORDS ACE inhibitor; angioedema; glossectomy; lisinopril; macroglossia

Macroglossia is a clinical condition resulting in enlargement of the tongue beyond the anterior teeth.¹ The condition is caused by vascular anomalies, allergic reactions,^{2,3} or congenital conditions.^{4–8} Angiotensin-converting enzyme inhibitors (ACEIs) are the most common medication causing angioedema.^{9,10} Studies found that the incidence of ACEI angioedema is higher in older adults, patients with chronic heart failure, and African American women.¹¹ ACEIs also inhibit the kallikrein-kinin system from degrading bradykinin, leading to increased vasodilation.^{12,13} Angioedema can cause significant swelling, resulting in acute airway obstruction and eventual death.^{5,12,14} Partial glossectomy is a valid treatment option for macroglossia that does not resolve with medication.^{5,7} This case report documents the diagnoses and surgical treatment of two cases of ACEI-induced angioedema and macroglossia treated at Baylor University Medical Center (BUMC) at Dallas.

CASE PRESENTATIONS

Patient 1

A 50-year-old black woman presented to an outside hospital emergency room with complaints of progressively worsening swelling of her tongue and shortness of breath (*Figure 1a*). The patient's medical history included a recent diagnosis of hypertension, for which she was started on lisinopril and hydrochlorothiazide. Her onset of symptoms occurred within 48 hours of taking the new medications. The decision to intubate her was made in the emergency room. Attempts at intubation were unsuccessful, and a complicated emergent tracheostomy resulted in an anoxic brain injury. She was subsequently transferred to BUMC. Encephalopathy resulted in the patient persistently biting her tongue, resulting in near transection in certain areas (*Figure 1b*). Oral and maxillofacial surgeons at BUMC performed a partial glossectomy using a U-shaped incision through the existing bite marks (*Figures 1c, 1d*).

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Figure 1. (a) Patient 1 preoperatively with a (b) near tongue transection. (c) Partial glossectomy incision through existing bite marks. (d) Postoperative sutures of partial glossectomy.

Postoperatively, the patient had no complications and the edema subsided over the course of 10 to 14 days. She was seen 1 month after surgery and had no tongue edema. She had significant neurologic deficits from her anoxic brain injury that had not resolved.

Patient 2

A 49-year-old black woman presented to the BUMC emergency department with complaints of shortness of breath and generalized edema. Workup revealed significant congestive heart failure. Aspirin, carvedilol, lisinopril, and supplemental oxygen were initiated. During hospital day 1, she went into cardiac arrest secondary to acute respiratory failure. Return of spontaneous circulation occurred after 18 minutes of cardiopulmonary resuscitation; however, she was neurologically devastated, with magnetic resonance imaging findings of anoxic brain injury. On hospital day 2, her tongue had enlarged beyond the confines of her teeth. Lisinopril was stopped on hospital day 2 secondary to acute kidney injury, and she remained intubated until hospital day 10, when she received a tracheostomy. Her neurologic status did not improve over the next 2 weeks, and she was transferred to a long-term acute care facility, with no improvement in her macroglossia and marked biting on her tongue noted. Her tracheostomy became dislodged after 2 weeks at the long-term acute care facility, and she was transferred urgently to BUMC for evaluation. She was intubated in the emergency department via a fiberoptic nasotracheal approach due to extensive tongue edema. On evaluation from oral and maxillofacial surgery, she had significant tongue edema, and portions of her tongue had been nearly avulsed due to bite trauma. She was taken to the operating room where a partial glossectomy using a keyhole incision was conducted, retaining mucosal flaps for reconstruction

after tongue reduction. Postoperatively she was no longer able to bite on her tongue, and the swelling subsequently subsided over 1 week.

DISCUSSION

The incidence of ACEI angioedema is relatively small compared to the large number of patients treated with these medications, with a reported incidence of 0.3% in a meta-analysis of 26 randomized trials that included 74,875 patients.¹⁵ Though the incidence is low, ACEI angioedema accounts for approximately one-third of all cases of angioedema. The interval between initiation of ACEI therapy and onset of angioedema is widely variable. The Omapatrilat Cardiovascular Treatment vs Enalapril (OCTAVE) trial looked at 12,634 patients taking enalapril and found that most patients developing angioedema had an onset of symptoms within the first month.¹⁶ Both of the patients presented in this report developed angioedema within 48 hours of administration of lisinopril.

Angioedema usually resolves within several days of onset with medical therapy; however, some patients experience persistent macroglossia that can last weeks to months. In the encephalopathic patient, the cause of prolonged tongue edema is usually related to bite trauma. Biting trauma results in venous congestion and impaired lymphatic drainage, which can cause edema for prolonged periods. Bite blocks placed between the teeth can stop patients from biting but are rarely effective long term. Unless the patient's mental status improves, the only effective long-term option is partial glossectomy. Multiple techniques are described in the literature for partial glossectomy. Postoperatively, patients should have regular follow up with a speech therapist, because issues with glosal function, speech deficiency, and deglutition are common.

The first patient in this report undoubtedly sustained an anoxic brain injury secondary to airway compromise from angioedema. The second patient had several confounding factors that led to her cardiac arrest and subsequent anoxic brain injury, but her macroglossia was likely related to lisinopril administered on hospital day 1. In both of these patients, encephalopathy resulted in persistent bite trauma, causing prolonged edema of the tongue. Partial glossectomy was demonstrated to be an effective treatment option for both cases.

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