Angiotensin Converting Enzyme Inhibitors Induce Unilateral Tongue Edema

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CLINICAL IMAGE

While angioedema is a well-recognized adverse event of angiotensin enzyme (ACE) inhibitors regardless of duration of use and related to the effect of ACE-inhibitors on the renin angiotensin aldosterone system increasing levels of angiotensin I and Bradykinin. The culprit here is the production of Bradykinin which induces vasodilation and swelling that occurs slowly distinguishing it from the histamine mediated angioedema. It is imperative that internists and hospitalists recognize the rare occurrence of unilateral tongue involvement as a side effect of ACE inhibitors.[1]

The patient was informed that data concerning the case would be submitted for publication, and he provided an informed consent. We report a case of 69-year-old Caucasian male with a sedentary lifestyle, smoker 87pack/yr., and significant past medical history of essential hypertension, hyperlipidemia, coronary artery disease, type 2 diabetes mellitus and significant psychiatric history. The patient denied any history of allergy to medications or food or any history of asthma. The patient presented with an episode of tongue swelling primarily on the right side that he discovered on waking up. It was associated with difficulty in speaking. He denied any hives, lip swellings, flushing, facial swelling, increasing shortness of breath or stridor. The patient denied chest pain, palpitation, fever, night sweats, shortness of breath, orthopnea, paroxysmal nocturnal, dyspnea or any gastroenterology or urinary symptoms. His family history was unremarkable, and no history of hereditary angioedema reported. Pertinent to the case he was notably taking Lisinopril 20 mg once daily for past 10 years. In the emergency room patient was noted for primarily right tongue swelling consistent with angioedema. He denied any prior history of angioedema or similar presentation. On a physical exam, the patient had a BM of 32.1 Kg/m², alert and oriented to time, person and place, vital signs were unremarkable (blood pressure 118/79 mmHg, heart rate 99 beats per minute, 98.1 F temperature, respiratory rate 15/min and the patient was saturating 99% on room air). Head and Neck exams
showing a supple, good range of motion without pain, no masses, or palpable lymphadenopathies. Oropharyngeal exam showed pink throat without exudates or lesions, and moist mucus membranes. The tongue was swollen more on the right side than the left (Figure 1 and 2), with normal visible uvula and normal lips without swelling. Chest and Heart examinations showed equal breathing sounds bilateral, without any wheezes or rhonchi. Distant heart sounds (due to body habitus) but regular S1 and S2, right sided S3, no murmurs, rubs, or gallops or jugular venous distention. Abdominal examination was unremarkable with no evidence of organomegaly. Extremities examination showed no clubbing, cyanosis, or edema. Skin examination showed no rashes or lesions. Chest X-ray showed a normal cardiac silhouette with no focal pulmonary consolidation or pleural effusion. Electrocardiogram (EKG) demonstrated normal sinus rhythm. Labs included: Serum creatinine of 0.69 mg/dl (reference range 0.6-1.25 mg/dL), BUN 12 (reference range 9-20 mg/dL) and eGFR of 100 ml/min/1.73. Serum potassium, sodium, calcium, magnesium and phosphorus and complete blood picture were all within normal limit. COVID 19 test was negative.

Patient was admitted to the ICU for observation due to his angioedema. Benadryl, Intravenous Solu-Medrol and one dose of Tranexamic acid were given. The patient’s symptoms and his tongue swelling improved within 12 hours. The patient was offered educational and counseling about the appropriateness of discontinuing Lisinopril and clinical follow-up in the outpatient setting.

Diagnosing of ACE-inhibitor angioedema is usually made based on the clinical presentation with typical symptoms localized to swelling of the face, with flushing but no pruritus and is followed by spontaneous remission in 72 hours. [1] ACE-Inhibitors induced unilateral tongue involvement is rare and may be the initial presentation before progressing to bilateral tongue edema. There is only a handful of cases have been reported (in age ranges 62 - 74 years old, ACE-inhibitors included perindopril, and lisinopril, with duration of use ranging from 2 days to 10 years, and resolution of angioedema from hours to 48 hours). [2-7] Prompt recognition and diagnosis of unilateral tongue edema secondary to ACE inhibitors use is crucial to initiate management. Hospitalization time varies depending on the severity and the mainstay of management is securing airway and mechanical ventilation if warranted. [1] Corticosteroid and antihistamines are usually given as part of the management. Additionally, in life-threatening resistant angioedema, successful reversal with fresh-frozen plasma has been reported. [1] While the bradykinin receptor antagonist Icatibant have been approved by the FDA for management of hereditary angioedema, there is not enough data to support their use in ACEI-induced angioedema. [8] Similarly, there is not enough supporting data to use Complement C1 inhibitor concentrates as a treatment for ACE-inhibitors induced angioedema.

Patient education and counselling about the recurrence of angioedema within weeks of ACE-inhibitors cessation. Hence, outpatient follow-up of these patients is important to ensure the absence of recurrence of angioedema and to adjust to a different class of antihypertensive medications. Weighing the risk and benefits, angiotensin receptor blocker (ARB) can be used, however there is Cross-reactivity occurring in 10% of cases. Hence patient counseling and education should be emphasized.

**Keywords:** Unilateral tongue angioedema; ACE inhibitors
**Figure 1:** On Admission Day 1, the patient’s tongue showed unilateral (right side) tongue swelling.

**Figure 2:** Focused View of the Unilateral Tongue edema (on the right side).

**REFERENCES**

