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Case report

Angiotensin-converting enzyme inhibitor- induced unilateral angioedema: A case report and literature review

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Abstract

Background: Angiotensin-converting enzyme inhibitor (ACEI) - induced angioedema is a potentially life-threatening adverse effect that most commonly involves the lips and tongue. Unilateral tongue involvement is rare and may complicate diagnosis.
Case Report: We describe a 63-year-old man with long-standing hypertension treated with enalapril who presented with sudden-onset unilateral left-sided tongue angioedema during sleep. The episode was not associated with pruritus, urticaria, or respiratory distress and resolved spontaneously within several hours under close observation.
Conclusion: This case illustrates the unpredictable presentation of ACEI-induced angioedema, even after prolonged and previously well-tolerated therapy. Early recognition, airway monitoring, and prompt discontinuation of the offending drug are essential to prevent potentially severe complications.

Keywords: Angioedema; Angiotensin-Converting Enzyme Inhibitor; ACEI; Unilateral; Tongue; Bradykinin; Drug-induced angioedema

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Introduction

Angioedema is a localized, non-pitting edema involving subcutaneous or submucosal tissues, most frequently affecting the lips, tongue, face, pharynx, or gastrointestinal tract [1]. Angiotensin-converting enzyme inhibitors (ACEIs) are widely prescribed as first-line therapy for hypertension and other cardiovascular conditions [2]. Despite their overall safety, ACEIs represent the most common cause of drug-induced angioedema, with an estimated incidence of up to 1% [3,4]. ACEI-induced angioedema may occur shortly after treatment initiation or after many years of continuous use, complicating clinical recognition [3-5]. Unlike histaminergic angioedema, it is typically non-pruritic, progresses gradually, and shows limited response to antihistamines, corticosteroids, or epinephrine [1-6].

This reaction is mediated by the accumulation of bradykinin, as ACE plays a key role in its degradation. Increased bradykinin levels enhance vascular permeability, particularly in the tongue and upper airway, posing a risk of airway compromise [1,5,7]. The aim of this report is to describe a rare case of unilateral lingual angioedema induced by enalapril and to review the relevant literature.

Case Report

A 63-year-old male presented to the Department of Stomatology and Dentistry with sudden swelling of the left side of his tongue. He reported awakening at approximately 6:00 a.m. with abrupt tongue enlargement and mild dysarthria. He denied dyspnea, stridor, chest pain, or dysphagia. His medical history was significant for long-standing hypertension treated for several years with enalapril, without recent dose adjustments. He denied recent infections, trauma, allergen exposure, or ingestion of new foods.

On examination, the patient was hemodynamically stable with normal oxygen saturation. Intraoral inspection revealed unilateral left-sided lingual angioedema without involvement of the lips, soft palate, or posterior pharynx (*Figure 1*). No cutaneous manifestations or signs of anaphylaxis were present.

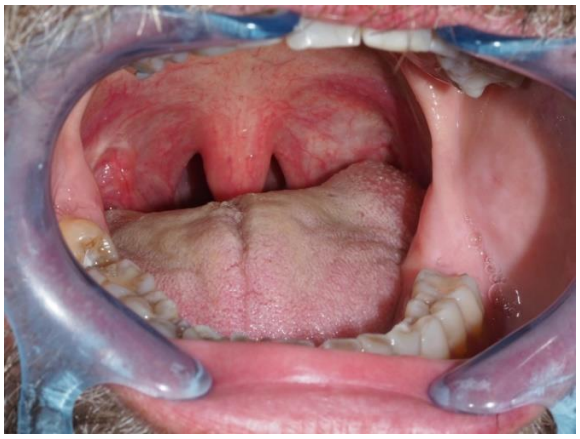

Figure 1: Left- unilateral tongue angioedema.

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Given the clinical presentation and medication history, ACEI-induced angioedema was considered the most likely diagnosis. The patient was admitted for close airway observation. No airway compromise occurred, and no pharmacologic interventions were required. The swelling resolved spontaneously within several hours (*Figure 2*). The ACE inhibitor was permanently discontinued, and alternative antihypertensive therapy was recommended.

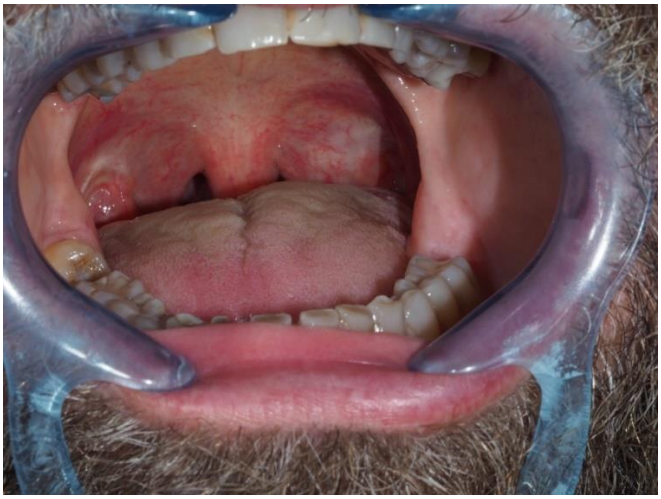

Figure 2: Spontaneous recovery from lingual angioedema.

Discussion

ACE inhibitor–induced angioedema is a bradykinin-mediated adverse reaction that may present unpredictably, even after years of well-tolerated therapy, as illustrated in this case. Although tongue involvement is a common manifestation, unilateral presentation is distinctly uncommon and may pose diagnostic challenges. Given the potential for rapid progression, early airway evaluation and close clinical monitoring are essential. While many episodes resolve spontaneously, recurrence is possible if the ACE inhibitor is continued; therefore, permanent discontinuation of the offending agent is mandatory. Alternative antihypertensive therapies—such as angiotensin receptor blockers, calcium channel blockers, or thiazide diuretics—should be selected according to the individual patient's cardiovascular profile.

This case highlights the importance of considering ACE inhibitor–induced angioedema in the differential diagnosis of acute tongue swelling, even in patients receiving long-term therapy without prior adverse effects. Prompt airway assessment, observation, and withdrawal of the ACE inhibitor remain the cornerstone of management.

Despite its clinical relevance, ACE inhibitor–induced angioedema remains underrecognized, particularly when presenting atypically. As noted by Papapostolou et al. [1], the condition is frequently underestimated despite the widespread use of ACE inhibitors for hypertension and cardiovascular

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disease, supported by decades of evidence confirming their overall efficacy and safety[2]. This paradox underscores the complexity of the underlying pathophysiology.

The mechanism is fundamentally related to bradykinin accumulation. Inhibition of ACE reduces the degradation of bradykinin and other vasoactive peptides, and compensatory pathways—such as aminopeptidase P, neprilysin, and dipeptidyl peptidase-4—may be insufficient in susceptible individuals [1]. This explains the unpredictable timing of onset and the association with risk factors including advanced age, smoking, allergic predisposition, prior angioedema episodes, and genetic variability in bradykinin metabolism, as demonstrated by Dubrall et al. [7].

Although most cases involve bilateral swelling of the lips, tongue, or face[5], unilateral lingual angioedema is rare and can mimic infectious, traumatic, or neoplastic processes. Multiple reports—including those by Ee et al. [8], Al-Hoqani et al. [9], Eloff and Oosthuizen [10], Imai et al.[11], de Ruiter et al. [12], Mlynarek et al. [13], Gil Braga et al.[14], Kuhlen and Forcucci [15], Chan et al. [16], Leung et al. [17,18], and earlier observations by Lehmke [19]—consistently emphasize the diagnostic difficulty posed by this atypical laterality. In emergency settings, such presentations may initially be misattributed to localized lingual pathology, delaying recognition of the bradykinin-mediated etiology.

Airway compromise remains the principal concern. Mudd et al. [6] reported that a substantial proportion of patients require hospital observation, with up to one-third admitted, particularly in cases involving the tongue. Although most episodes resolve following ACE inhibitor discontinuation and supportive care, a small but clinically significant percentage progress to airway obstruction necessitating intubation [4,5]. Because this reaction is bradykinin-mediated rather than histaminergic, conventional therapies such as antihistamines, corticosteroids, and epinephrine generally have limited efficacy, reinforcing the importance of vigilant airway monitoring [1,3].

Given the shared pathophysiology with hereditary angioedema, targeted therapies such as C1 esterase inhibitor concentrate, icatibant, and ecallantide have been explored. While Perza et al. [4] reported potential benefit in selected cases, broader analyses by Wilkerson and Winters [3] and Papapostolou et al. [1] indicate inconsistent results, with insufficient evidence to support routine use. Consequently, cessation of the ACE inhibitor remains the only universally accepted intervention, with adjunctive treatments considered selectively.

In summary, unilateral lingual angioedema represents a rare but well-documented manifestation of ACE inhibitor toxicity. Its deceptive presentation, variable latency, and poor response to standard allergy-directed therapy underscore the need for heightened clinical awareness. As ACE inhibitors continue to play a central role in cardiovascular management, recognition of this atypical adverse effect is essential to ensure timely diagnosis, airway protection, and appropriate care [2].

This case report has several limitations. As with most reports of ACE inhibitor–induced angioedema, the diagnosis is clinical, and no definitive laboratory marker exists to confirm a bradykinin-mediated mechanism. Although alternative infectious, allergic, and structural causes were considered unlikely based on clinical evolution, imaging or specialist evaluation was not performed at all stages, limiting

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complete exclusion of other etiologies. Furthermore, unilateral lingual angioedema remains rare and poorly understood, restricting the generalizability of conclusions drawn from isolated cases. The unpredictable nature of ACE inhibitor reactions also hampers identification of precipitating factors and individual susceptibility beyond known risk associations. Finally, therapeutic evidence remains limited by the lack of randomized studies, leaving uncertainty regarding optimal pharmacologic management in severe or refractory cases.

Conclusions

ACE inhibitor–induced angioedema is a clinically significant adverse reaction that may present atypically as unilateral tongue swelling, even after years of uneventful therapy. This case highlights the importance of maintaining clinical suspicion in patients presenting with acute lingual edema. Prompt recognition, airway monitoring, and permanent discontinuation of the ACE inhibitor are essential to ensure patient safety. Increased awareness of this rare presentation may help reduce diagnostic delays and prevent serious complications.

Declarations:

Patient Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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