Letter to Editor
Eurasian Journal of Critical Care

Use of Fresh Frozen Plasma in a Dramatic Case of ACE-Inhibitor Associated Angioedema

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To the Editor,

Angioedema describes a non-dependent, non-pitting and transient edema caused by the accumulation of vasoactive substances in the circulation. These vasoactive substances increase vascular permeability, causing swelling of the deep dermal, submucosal or subcutaneous tissues of the face, lips, neck, extremities or gastrointestinal tract. Urticaria may or may not accompany this condition.1 Angioedema is generally mediated through two pathways: histamine-mediated and bradykinin-mediated. Histamine-mediated angioedema generally responds to standard therapeutic measures (such as antihistamines, steroids and epinephrine), whereas bradykinin-mediated angioedema can be more difficult to manage in emergency departments (ED).2

Angiotensin-converting enzyme inhibitors (ACE-I) are widely prescribed drugs for the treatment of hypertension and heart failure. ACE-I-associated angioedema is one of the well-known side effects of this group of drugs and may sometimes be dramatic and life-threatening. The incidence of angioedema during treatment is 0.1-0.2% and usually occurs in the first week after initiation of the drug.3 Approximately one-third of all cases of angioedema presenting to the ED are ACE-I-related.1,4

Here, we present a patient who presented to our ED with bradykinin-mediated ACE-I-associated dramatic angioedema clinic, did not respond to standard treatments, rapidly improved with fresh frozen plasma (FFP) administration and was discharged after 6 days of follow-up in the emergency critical intensive care unit.

A 65-year-old male patient presented to the ED with swelling of the tongue that developed within hours **(Figure 1a and 1b)**. At presentation, vital signs were stable and consciousness was clear. He had no comorbidities other than hypertension. The patient had no history of any other drug, substance, smoking or alcohol use. The patient was started on a combination of perindopril arginine 10 mg and amlodipine 5 mg for hypertension treatment two weeks ago. The patient had no previous history of angioedema or family history of angioedema. IV fluids, chlorpheniramine and methylprednisolone and intramuscular epinephrine were started in the ED. Despite this treatment, the patient's complaints did not improve and he was hospitalized in the emergency critical intensive care unit. The patient did not respond to additional methylprednisolone and epinephrine treatments was also given IV tranexamic acid and C1-esterase inhibitor treatment. The patient whose complaints did not improve with these treatments for 24 hours was given 3 units of FFP. Then complaints of the patient improved dramatically after treatment was given 2 units of FFP for 2 consecutive days. No intubation or surgical airway procedure was required during hospitalization. The patient was discharged on the 6th day of hospitalization with resolved complaints, good oral intake, normal speech and swallowing, changed antihypertensive medication and recommended dermatology and allergy outpatient follow-up **(Figure 2a and 2b)**.

ACE-I-associated angioedema is more common in blacks, smokers, women, the elderly, patients with

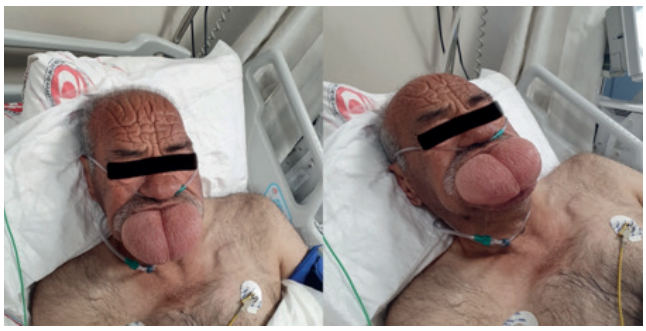

Figure 1a and 1b: Dramatic angioedema of the tongue at the patient's presentation

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Received: 14.04.2023 • **Accepted:** 04.07.2023
DOI: 10.55994/ejcc.1469585

Cite this article as: Güler S, Üçöz Kocaşaban D, Ata MA, Yaş SC, Günaydın YK. Use of Fresh Frozen Plasma in a Dramatic Case of ACE-Inhibitor Associated Angioedema. Eurasian Journal of Critical Care. 2024;6(2): 83-84

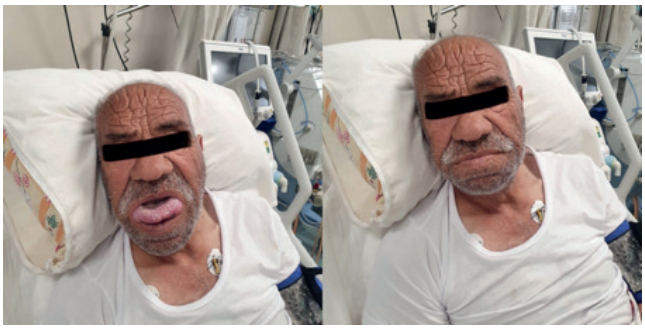

Figure 2a and 2b: Final condition of the patient before discharge after FFP treatment

drug and seasonal allergies, and individuals receiving immunosuppressive therapy.4 Our patient had no history of drug or food allergy and was not receiving any treatment other than antihypertensive therapy. ACE-I therapy may cause an increase in bradykinin and other inflammatory vasoactive peptides, which in turn leads to angioedema due to the development of vasodilation in blood vessels.2 Bradykinin is thought to play a major mediator role in both ACE-I-associated angioedema and hereditary angioedema.3 The ACE enzyme is a primary peptidase that degrades bradykinin under normal conditions, and when the activity of this enzyme is blocked by ACE-I, a very strong vasodilator effect occurs and capillary permeability increases.2 Here, FFP contains Kininase-II, which has similar activity to the ACE enzyme, and this enzyme also degrades bradykinin.2 Because of this feature, it is thought to be effective in cases of refractory angioedema. Although there are studies reporting no statistically significant difference in the duration of hospital or intensive care unit stay and the need for advanced airway interventions in ACE-I-associated angioedema patients with and without FFP therapy5, we believe that FFP therapy may improve patient outcomes in patients with refractory ACE-I-associated angioedema.

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