

## Case Report

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# Life Threatening Airway Angioedema Secondary to Captopril

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## INTRODUCTION

Angioedema associated with Angiotensin-Converting Enzyme Inhibitors (ACEI) is an emergency, which can develop in 0.1-1% of the recipients. Severe life-threatening total airway obstruction secondary to angioedema can occur rarely. In this case report, the clinical approach, diagnosis and treatment of ACEI induced angioedema with special focus on the differential diagnosis from hereditary angioedema are discussed.

**KEYWORDS:** Angioedema; Captopril induced angioedema; Hereditary angioedema; Difficult airway.

## CASE DESCRIPTION

A 38 year old female patient was brought to emergency department by the first aid team following an epileptic seizure. She was in a postictal state at arrival. The patient was oriented and cooperative but fell asleep easily. Her Glasgow coma score was 14. Her vital signs were as follows: Blood pressure 190/124 mmHg, pulse 88/min, breathing rate 22/min, temperature 36.5 °C, and oxygen saturation in room air was 99% by pulse oximetry. Her physical impression was normal. She had no active complaints. Her medical history included meningitis in childhood, hypertension, and epilepsy. Her daily medications included sodium valproate 1000 mg/daily and candesartan 8 mg daily. Her elevated blood pressure was treated prehospital with 50 mg of captopril. A finger sticks blood sugar test was 134 mg/dL. Twenty minutes after arrival in the emergency department, tachypnea, perioral oedema, and rhonchi developed. Treatment with methylprednisolone, 100 mg IV, ranitidine, 20 mg IV, and pheniramine, 45.5 mg IV were started immediately. Salbutamol 5 mg was also administered by nebulization. Thirty minutes after arrival rapidly developing bilateral tongue angioedema was observed. Epinephrine 0.3 mg (1:1000) was injected intramuscularly. A room air arterial blood gas measurement demonstrated an oxygen saturation of 58%. When stridor developed, preparation for a cricothyrotomy was done. The patient's clinical status deteriorated rapidly as her oxygen saturation dropped down to 56%, the patient lost consciousness. When a laryngeal mask was inserted, the patient's oxygen saturation was raised to 95%. With these airway interventions cardiac arrest was avoided. Because of severe widespread and indurated submandibular swelling, a tracheostomy was performed instead of oral intubation (Figure 1). Two units of (300 unit/70kg) Fresh Frozen Plasma (FFP) were infused. Within 10 to 15 minutes after administration of the FFP, apparent regression in submandibular hard thickenings was noted (Figure 2). Even so,

the ambulatory support and aspiration, ventilation of the patient could not be restored and the patient had a cardiac arrest, due to an unknown reason after fifteenth minute. Cardiac compressions were immediately initiated. The tracheostomy tube was removed by the emergency physician and a modified endotracheal tube was placed through the tracheostomy site. Ventilation with an ambu bag was successfully accomplished (Figure 2). After 3 minutes of Cardiopulmonary resuscitation (CPR), Return of Spontaneous Circulation (ROSC) was achieved. The patient was further stabilized and admitted to the intensive care unit. In biochemistry, a Na<sup>+</sup> of 103 mmol/L was noted. Renal function tests were normal. Her severe hyponatremia was treated with a hypertonic sodium infusion. Complement testing was achieved by the second day (from blood samples taken during angioedema) and demonstrated a mild decrease in C4 and C1 esterase inhibitor levels, but controls were normal at day 9 and 15 (Table 1). She was discharged neurologically intact on the seventh day and follow up by the allergy clinic was arranged.



Figure 2: Figure shows that, the patient's tongue went back in her mouth and submandibular swelling were regressed after 2 units of FFP.



Figure 1: Tracheostomy was opened using laryngeal mask for the respiration of the patient when tongue went out of her mouth and submandibular wide and hard bulges were developed.

DISCUSSION

Angioedema is characterized by sudden development of oedema in the mucosa and submucosa. Angioedema due to ACEI generally develops in face and neck area without urticaria. Sometimes there may be severe abdominal pain due to visceral oedema of the intestines, mimicking symptoms of appendicitis or Familial Mediterranean Fever.<sup>1,2</sup> Accumulation of bradykinin, increased number of mast cells and increasing histamine release play a role in the pathophysiology.<sup>1,2</sup> Female gender, African race, and genetic polymorphism are enhancing risk factors.<sup>3</sup> Major triggers are food, trauma, or an autoimmune event. Angiotensin-Converting-Enzyme Inhibitor (ACEI), such as captopril, lead to bradykinin accumulation because of their kininase-like activity. ACEI's are the cause of 10-25% of all angioedema cases.<sup>4</sup> Defective or reduced substance P and des-Ard9-BK enzymes that metabolize bradykinin, result in an increase of this substance in circulation.<sup>5</sup> Vasodilatation, increased vascular permeability, and oedema develop due to the bradykinin effects. ACEI induced angioedema, causes death by airway obstruction in 10% of cases.<sup>2,6</sup> In 16% of cases angioedema can recur.<sup>6</sup> Captopril induced an-

Complement (Normal range)	C1 INH (15-35 mg/dL)	C4 (16.0-38.0 mg/dL)	C1 esterase inhibitor function (70%-130%)
Durin angioedema	14.1	12.2	
9th day	32.3	26.4	
15th day	19 (N)	37	%90

C1 INH: Complement 1 esterase inhibitor, C4: Complement 4, C1: Complement 1

Table 1: Changes in C1 INH and C4 values by day in angioedema case. Moreover, the C1 esterase inhibitor function was tested.

gioedema is the clinical diagnosis in our case and no family history was reported. Former usage of ACEI was unknown.

There is no concurrence in the treatment of angioedema.<sup>6</sup> Conventional treatment for angioedema due to allergic etiologies includes the administration of antihistamines (H1 and H2), steroids, and epinephrine administration.<sup>4</sup> These treatments, however, are generally not effective against ACEI associated angioedema. Treatment with Complement 1 esterase inhibitors (C1 INH) or with icatibant (Bradykinin B2 receptor antagonist) is successful in Hereditary angioedema (HAE).<sup>7,8</sup> Fresh frozen plasma administration is one of the suggested treatments.<sup>8</sup> FFP prevents bradykinin release by providing kininase II, like Angiotensin-converting enzyme.<sup>9</sup> In our case, conventional treatment was administered, but was not successful. Treatment ultimately succeeded with the infusion of FFP which provided kininase II, like angiotensin-converting enzyme. Afterward, regression in tongue and in submandibular hard swelling occurred (Figures 1 and 2).

Anatomical staging may be used to predict the risk of angioedema-related airway obstruction. Stage I; facial rash, facial and lip oedema. Stage II; soft palate oedema. Stage III; tongue oedema. Stage IV; laryngeal oedema. Admission to intensive care must be done in stages III and IV.<sup>10</sup> Our case did not respond to the initial treatment and, stages III and IV airway obstruction developed rapidly.

In our case, the most important differential diagnosis was HAE. Quantitative (HAE type 1) or functional (HAE type 2) defect occurs in C1 INH by HEA.<sup>11</sup> Low serum C4 levels confirm the diagnosis of HAE type 1. In 15-20% of HAE cases, even when C1 INH level is normal, its function is impaired (HAE type 2). Another possible diagnosis could be acquired C1 INH deficiency that can be seen in autoimmune disease or lymphoma.<sup>12</sup> Normal levels of C1 INH and its function measured in our case led to the diagnosis of ACEI induced angioedema.

## CONCLUSION

This case demonstrates the complications and treatment of severe ACEI induced angioedema. The progressive airway obstruction was treated with a surgical airway and the infusion of Fresh Frozen Plasma (FFP). HAE type 1 and 2 were ruled out from the diagnosis with normal results of C1 INH level and C1 function tests. While other treatment options are currently under study, current options to the emergency physician for the medical management of patients with ACEI associated angioedema and airway obstruction can primarily include the administration of FFP.

## CONFLICTS OF INTEREST

The authors have no commercial associations or sources of support that might pose a conflict of interest.

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