

## A case of angioedema involving the tongue and uvula

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A case of late-onset life threatening angioedema because of upper airway obstruction after long term use of angiotensin-converting enzyme inhibitor was reported. The clinical presentation, pitfalls in diagnosis, incidence, current practice in airway management and prognosis were reviewed.

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### Introduction

Angiotensin-converting enzyme inhibitor (ACEi) is a commonly used drug and is gaining popularity for its promising effectiveness in treatment of congestive heart failure, hypertension and proteinuria. Angioedema, as a rare but well known complication of ACEi, contributes to a more sizable presentation to the emergency departments than ever before with the more extensive use of ACEi. With a particular predilection for the head and neck areas, angioedema can be rapidly fatal by causing acute upper airway obstruction. However, late-onset angioedema is frequently overlooked and delayed diagnosis may lead to serious consequences. The importance of early recognition, careful airway evaluation and anticipated difficult intubation in the emergency department is emphasized.

### The Case

A 77-year-old man walked in our Accident and Emergency Department complaining of throat discomfort. At the triage station, his blood pressure was 136/60 mmHg, pulse 73 beats/min,

temperature 36.6°C, respiratory rate 22/min. He was triaged as a 'Semi-Urgent' case. He revealed a history of throat discomfort since early morning associated with lips and jaw swelling. There was no pain over the neck area. Initial examination revealed a conscious and alert man with minimal swelling over the periorbital area, and the lips and jaw were swollen. His voice was not muffled nor hoarse. In view of the possible upper airway compromise, he was subsequently transferred to the resuscitation room for further management.

He revealed a history of hypertension and ischaemic heart disease and had been put on aspirin, captopril, Elantan<sup>®</sup> (isosorbide mononitrate) and Mevacora (lovastatin) for four years without any problems. He also had prostate disease and just finished a course of Tarivid<sup>®</sup> (ofloxacin), Honvan<sup>®</sup> (fosfestrol tetrasodium) and Pyridium<sup>®</sup> (phenazopyridine HCl). On further enquiry, there was a history of having eaten stonefish the day before the swelling occurred.

Physical examination showed that his lips and tongue were swollen and the uvula was grossly oedematous. There was no stridor, nor drooling of saliva and no rash nor itchiness on general examination. The nasal examination was normal, the neck was not swollen, the jugular venous pressure was not elevated. The chest was clear with good air entry. Other physical examination including the abdominal and neurological examination were unremarkable.

The patient was given 100% oxygen via face mask,

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intravenous line was secured and 10 mg of chlorpheniramine and 100 mg hydrocortisone was given.

Lateral neck X ray performed showed markedly swollen tongue base close to the posterior pharyngeal wall. (Figure 1)

At this juncture, the differential diagnosis were: angioedema, food or drug allergy, epiglottitis and others including: peritonsillar abscess, retropharyngeal abscess and Ludwig's angina. Diagnosis apart from angioedema and food allergy are unlikely in view of the nontoxic clinical condition without any pain in the oral or neck area.

The patient was diagnosed to have angioedema with potential airway compromised and was transferred to the intensive care unit (ICU) for close monitoring. He remained in ICU for 24 hours with supportive care and steroid and chlorpheniramine. The uvula swelling subsided after 4 days and intubation was not required.

## Discussion

Angioedema is nonpitting oedema of vascular origin with a predilection for the head and neck area. Acquired and hereditary forms are distinctive.

The causes are often known in the acquired type. Both can cause extensive oral and facial swelling and in particular, the floor of mouth, tongue, larynx and lips. It is a medical emergency in view of the potential rapid progression of gross swelling of oral structure causing acute upper airway obstruction.

ACEi is not the only group of drug that causes acquired angioedema, other less commonly known culprits are aspirin, opiates and radiocontrast agents. ACEi as a cause was first reported by Jett GK in 1984.<sup>1</sup> The incidence ranges from 1 in 1000 in the first week of use to 1 in 42000 subsequently.<sup>2</sup> All ACEi have been associated and none of them is spared though the incidence would differ from 0.1% in Captopril to 0.5% in Benazepril.<sup>3</sup>

### ***The Hereditary Angioedema (HAE)***

This disorder is inherited as autosomal dominant and there is an abnormally low levels of plasma inhibitor for the activated first component of complement (C1-inhibitor). It was first reported by Quincke in 1882 and described by Osler in 1888.<sup>4</sup> Unlike other forms of angioedema, there is no known allergic basis to HAE, antihistamines, adrenaline and steroids are ineffective in treating the disorder. However, fresh frozen plasma (FFP)<sup>5,6</sup> and tranexamic acid<sup>7</sup> have been reported to be effective in prophylaxis and therapy.

The pitfall in diagnosis is failure to recognise the



**Figure 1.** Lateral neck X ray performed shown markedly swollen tongue base close to the posterior pharyngeal wall.

late onset cases due to lack of familiarity and inadequate drug history enquiry. Litman et al. in 1992 reported two cases of life-threatening angioedema associated with ACEi that required tracheostomy and one of them experienced four episodes of tongue swelling before ACEi was stopped.<sup>8</sup> Three years later, Weiner JM et al. reported only one out of nine cases of angioedema with ACEi treated at public hospitals in New Zealand had the ACEi stopped.<sup>9</sup> Frontera Y et al. in the same year reported a case with 18 episodes of recurrent left side facial swelling in 3 years before the correct diagnosis was made.<sup>10</sup>

ACEi was the most common known cause of angioedema. The prevalence was estimated to be 0.14%.<sup>11</sup> The association between the clinical findings at the time of presentation and clinical outcome were studied by R. Agah in 1997. It was a retrospective review of 40 patients with angioedema over a period of four years. They concluded that odynophagia and oedema of the tongue were significant predictors for undergoing laryngoscopy ( $p < 0.001$  and  $p < 0.02$ , respectively) and admission to the hospital ( $p < 0.05$ ).

ACE inhibitor associated angioedema is not an allergic reaction. The side-effect can be induced by structurally unrelated ACEi.<sup>12</sup> In most patients, the disorder recur too quickly after restarting or changing the ACEi for specific antibodies to develop.<sup>13</sup> The mechanism is still unknown. Postulated pathophysiology include antibody-antigen interaction, complement system and bradykinin pathway. Bradykinin in angioedema was studied recently by Juerg et al. A plasma bradykinin level of 2 to 12 times the upper limit of normal was observed during acute attack of both acquired and hereditary angioedema, and infusion of C1-esterase inhibitor immediately lowered bradykinin concentrations.<sup>14</sup> This explained why epinephrine, steroids and antihistamine have not been proven to be efficacious.<sup>15</sup> The mainstay of treatment is supportive, directed towards airway protection. Conventional treatment of antihistamine and steroid is justified in cases where anaphylactic shock, rather than angioedema, is the likely cause of the patient's symptoms.<sup>16</sup>

Airway patency should be maintained before patient

arrival at the hospital by paramedics. The main role of an emergency physician is to recognise the need for intubation. Life threatening airway obstruction requiring intubation has been reported in up to 20% of ACEi induced angioedema with an overall mortality of 11%.<sup>11,13</sup> When anticipating difficult airway control, one must be prompt to summon help from experienced personnel and equipment to perform cricothyrotomy should always be available. Oral endotracheal intubation by rapid sequence induction is not recommended as potential complete airway obstruction after muscle relaxation may occur. Nasotracheal intubation is the preferred technique for patient with oral oedema, preferably with fiberoptic bronchoscopic guidance. Surgical airway is restricted to cricothyrotomy for patient older than 12 years old, otherwise, needle cricothyrotomy is the method of choice.

In a retrospective cohort study from 1986 to 1992 by Brown NJ et al,<sup>17</sup> the overall recurrence rate caused by continual exposure was 18.7 per 100 patient-year compared with the rate of 1.6 per 1000 person-year for the first attack of angioedema. The continuing use of ACEi in spite of angioedema results in a markedly increased rate of angioedema recurrence with serious morbidity.

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