ANGIOEDEMA SECONDARY TO ANGIOTENSIN CONVERTING ENZYME INHIBITORS

T. Thiruventhiran[1] and Ho Bee Kiau[2]
[1]Department of Medicine, [2]Department of Primary Care Medicine, Faculty of Medicine, 50603 Kuala Lumpur, Malaysia

ABSTRACT: **Angioedema due to whatever cause is potentially life threatening, especially if it involves the head and neck region. Patients at risk need to be identified and precautionary measures are necessary. The use of Angiotensin Converting Enzyme Inhibitors (ACEIs) has been associated with angioedema of the face and tongue. Its widespread use has resulted in an increased awareness of this rare but important complication. We report here a case of angioedema secondary to ACEIs developing a few months after initiation of therapy and discuss its clinical importance.** *(JUMMEC 1999; 2: 113-114)*

KEYWORDS: Angioedema, Angiotensin Converting Enzyme Inhibitor.

Introduction

Angioedema is a nonpitting oedema of vascular origin, which can involve the floor of the mouth, tongue, larynx, lips and face. There are numerous causes of angioedema including idiopathic causes, C1 esterase deficiency, drugs, sunlight, cold, heat and allergic disorders. Angiotensin Converting Enzyme Inhibitors (ACEIs) was first reported to cause angioedema in 1984, subsequently a retrospective study in a tertiary referral center in United States showed it to be the number one cause of acute angioedema (1).

The use of ACEIs is now established in the treatment of patients with congestive cardiac failure, post myocardial infarction, diabetic microalbuminuria, hypertensive diabetic and non-diabetic chronic renal impairment, resulting in its widespread use in clinical medicine. It has become among the most frequently prescribed drugs in the past several years (1). Though it has a favorable side-effect profile, ACEIs induced angioedema is now more increasingly recognized (1,2,3). Angioedema occurs in 0.1-0.7% of patients on ACEIs and nearly always occurs in the head and neck region, frequently involving the mouth, tongue, pharynx and larynx (2). The onset can be early, however it may be considerably delayed in a significant number of cases.

Case report

A 71 year. old man, a known hypertensive was started on Enalapril after coronary by pass surgery in 1996. Prior to this he had been on Aspirin, Atenolol and Isosorbite dinitrate for 3 years with no adverse-effects. About a month after starting Enalapril, he developed facial swelling affecting his cheeks, lips and tongue. It lasted for 24-48 hours before the swelling resolved spontaneously. Due to its mild nature he didn't think much of it and continued his medication. He developed a second episode 3 months later and subsequently an episode every 2-3 months. He didn't complain about it during his medical follow-up until recently when the swelling got worse. When he was seen at the clinic, there was swelling of the cheeks, lips and tongue resulting in dysarthria. However the was no signs of airway obstruction nor did he have any other cutaneous manifestations. A diagnosis of angioedema was made and Enalapril was replaced with Atenolol and the patient advised to come to clinic daily over the next few days. The angioedema resolved completely by the third day. He denied having a history of angioedema prior to starting Enalapril and there was also no family history of angioedema.

Discussion

Cases of ACEIs induced angioedema are likely to increase in the future, as treatment with this category of drugs becomes widespread. The mechanism of ACEIs induced angioedema is not fully understood. However, it is thought to be a biochemical rather than an immunological reaction for a number of reasons. Firstly, angioedema can occur within hours of the first dose, leaving insufficient time for an immunological response to occur; secondly, the effect can occur with any ACEIs, regardless of its structure (2). ACEIs influences a num-

Corresponding address:
Dr. T Thiruventhiran,
Department of Medicine, University of Malaya
50603 Kuala Lumpur, Malaysia

ber of biochemical pathways including bradykinin, substance P degradation and the renin angiotensin pathway. ACEIs induced angioedema is most likely to involve increased local levels of bradykinin, possibly with the additive effect of reduced angiotensin II (2,3).

Clinical features of ACEIs induced angioedema, include a predilection for the tongue and lips although oedema of the palms, soles, genitalia and visceral oedema have been rarely reported. Urticaria is seen only rarely with ACEIs induced angioedema (2). Captopril was associated with a significantly lower incidence of angioedema compared to long acting agents (1,3).

Episodes of angioedema due to ACEIs are known to resolve spontaneously, even though treatment is continued as seen in the above case. This phenomenon can be confusing to the physician who may attribute it to some other cause and persist in prescribing the drug. It is important to recognize this adverse-effect, as subsequent episodes may be more severe resulting in life threatening upper airway obstruction if treatment is continued (3). In the United States, a study conducted over a period from 1986 to 1992, revealed that physicians often failed to recognize the association between ACEIs and angioedema, despite the fact that angioedema has been included in the United States Food and Drug Administration-approved package inserts since the mid 1980s (2).

Treatment of ACEIs induced angioedema requires stopping the agent and replacing it with another suitable antihypertensive drug. Specific treatment of the angioedema would include antihistamines, steroids, adrenaline and in severe cases airway protection with tracheal intubation or emergency tracheostomy.

In summary, a high index of suspicion is necessary to diagnose ACEIs induced angioedema and necessary measures taken to prevent putting the patient at an increased risk of a life-threatening event.

Reference:

1. Agah R, Bandi V, Guntupalli KK. Angioedema: the role of ACE inhibitors and factors associated with poor clinical outcome. Intensive Care Med 1997; 23: 793-6.
2. Sabroe RA, Black AK. Angiotensin Converting enzyme (ACE) inhibitors and angio-oedema. British Journal of Dermatology 1997; 136: 153-8.
3. Brown NJ, Snowden M, Griffin MR. Recurrent Angiotensin Converting Enzyme Inhibitor-Associated Angioedema. JAMA 1997; 278(3): 232-3.