

Crash Call for Tongue Swelling: Is it Anaphylaxis?

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Received: June 20, 2018; Published: July 14, 2018

Abstract

It is important to differentiate between ACEi induced angioedema and anaphylaxis as the pathogenesis and treatment are different. We report a case where a patient was reinstated on Lisinopril on hospital admission who then developed angioedema on day 3 that subsequently resolved spontaneously on withdrawal of the medication with no cardiorespiratory sequelae. We briefly discuss the prevalence and treatment options for ACEi induced angioedema in this article.

Keywords: Angiotensin Converting Enzyme; Angioedema; Anaphylaxis; Tongue Swelling; Bradykinin

Abbreviations

ACEi: Angiotensin Converting Enzyme Inhibitor; C1 INH: C1 Inhibitor; ARB: Angiotensin Receptor Blocker; ITU: Intensive Care Unit; ARB: Angiotensin Receptor Blocker

Introduction

ACEi or ARB is the recommended first line medications for hypertensive patients below the age of 55 years and in those with co-existing diabetes mellitus [1]. Bronchospasm, dyspnea, nephritic syndrome, rash are among the many side effects reported with ACEi. Acquired angioedema is one of the serious side effects involving swelling of the lip, eye, face, throat or mouth [2]. It typically does not respond to adrenaline, antihistamines and steroids due to the condition being related to accumulation of bradykinin and not histamine [3]. Being a potentially lethal condition, it is not often recognised accurately on initial presentation. It is important to establish as early diagnosis with appropriate history and risk assessment to initiate appropriate management plan.

Case Report

90 year old male with history of hypertension being treated conservatively for a humerus fracture 3 days ago, developed progressive tongue swelling that had come on 2-hours ago. The night medical on-call team was asked to review him urgently. His swollen tongue was protruding out of his mouth causing difficulty talking. He denied any food or medication allergy and had not had anything to eat in last 1 - 2 hours or any recent medication started on this admission. He denied having similar episode in the past. He did not have any family history of anaphylaxis or angioedema. On reviewing his drug chart, he was on Lisinopril and had three doses since admission. Looking back at his electronic medication records to confirm his allergy status we noted that Lisinopril was last issued in September, 2016 by his pharmacy. On further enquiry patient acknowledged that his General Practitioner had stopped Lisinopril in 2016 due to cough. He was not started on any other antihypertensive medication, though. On bedside assessment his National Early Warning Score was zero and there were no other features to suggest anaphylaxis or airway compromise. The absence of family history made hereditary angioedema extremely unlikely as it would be extremely late first presentation. Also, based on the absence of haematological risk factor to suggest the possibility of acquired C1 INH deficiency, an even rarer entity, and normal coagulation profile, a diagnosis of ACEi-induced angioedema was made by the on-call team. He was kept under observation overnight. Haematology and ITU on-call registrars were informed of this case due to

potential need for fresh frozen plasma in case of worsening swelling or airway compromise. Further on, the night was uneventful, and the angioedema gradually reduced in size from the next morning completely resolving the following day without any sequelae. He was switched on to calcium channel blocker.

Discussion

ACE inhibitor-induced angioedema has long been a known adverse drug reaction occurring with the whole group of ACE inhibitors. The overall incidence of angioedema is 0.1%-0.42%, mostly occurring within the first year of treatment (0.23%), but can occur up to 12-33 months after being given ACE-i [3-5,11]. A history of ACEi-induced cough can increase the risk of angioedema by 9-fold [6]. Female gender and age of more than 65 year are associated with increased risk of ACEi-induced angioedema, however it has been seen in middle age patients as well [7]. Interestingly, dark-skinned persons have three times higher risk for developing ACEi-induced angioedema compared to Caucasians [8]. Some drugs such as Dipeptidyl peptidase-4 (DPP) inhibitors (for example, gliptins) increase the risk of ACEi-induced angioedema 4 - 5 times higher than ACEi alone [9]. As ACEi is usually seen as first-line therapy for hypertension in patients with type-2 diabetes, the incidence of angioedema, a potentially lethal condition, may become more common now that DPP4 inhibitors are regularly being used. In such cases, adding a DPP4 inhibitor can potentially become the destabilising trigger for an episode of angioedema in patients developing angioedema after many years of stable ACEi use.

The mean duration of resolution of angioedema is thought to be 29-hours [10]. It is important to differentiate between mast-cell mediated angioedema and bradykinin associated angioedema as management for both pathways is different. The offending drug should be stopped immediately. Mast cell mediated angioedema is treated with steroids and anti-histamines whereas C1-INH mediated are acutely treated with plasma derived C1 esterase inhibitor concentrates or Icatibant (bradykinin B2 receptor antagonist) [12,13]. There are case reports of ACE inhibitor angioedema being successfully treated with fresh frozen plasma. Thus, in patients with severe ACE inhibitor angioedema, a trial of a couple of units of fresh frozen plasma can be considered in an attempt to reduce the duration of the attack or to the need for what could be a very difficult intubation [13]. Anti-fibrinolytic agents such as tranexamic acid and rituximab can be prophylactically used for recurrent angioedema from ACEi [14].

Conclusion

One should consider this irregular pattern of ACEi-induced angioedema and regularly monitor patients for this adverse effect. It can take a few presentations for ACEi induced angioedema to be diagnosed specially with milder presentations. The likelihood of underestimation of ACEi angioedema can be potentially fatal.

Conflict of Interest

No Financial or any conflict of interest exists.

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Volume 5 Issue 8 August 2018

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