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Angioedema of the airway: an unusual case

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Abstract

We report a case of angioedema caused by angiotensin-converting enzyme inhibitor and topical lignocaine spray, administered during nasendoscopy.

Angioedema induced by angiotensin-converting enzyme inhibitors is a rare but well known entity. Allergy to topical lignocaine has been acknowledged as a rare phenomenon when used for dental surgery and for skin anaesthesia, but it has not previously been reported after topical administration prior to nasendoscopy. In the reported case, our patient was unfortunate enough to be allergic to both lisinopril and lignocaine. The result was life-threatening airway obstruction, and the continued use of lignocaine spray sustained the laryngeal oedema. We advise that patients are asked about any and every allergy – specifically, any previous problems with dental procedures – before administration of local anaesthetic spray to the upper aerodigestive tract.

Key words: Angioedema; Angioneurotic Edema; Angiotensin Converting Enzyme Inhibitor; Local Anesthetic Allergy

Introduction

Angioedema is a non-pitting, symmetrical oedema that occurs in the skin and mucous membranes.[1,2] It can be life-threatening[3] if it causes obstruction to the pharynx or larynx. Angiotensin-converting enzyme (ACE) inhibitors are one of the most common known causes of angioedema of the mouth and upper airway.[1] Angiotensin-converting enzyme inhibitor induced angioedema is an idiosyncratic reaction which occurs because ACE is normally required to metabolise bradykinin, a potent mediator of angioedema. Allergy to topical lignocaine appears to be a much rarer phenomenon. We describe a patient who was unfortunate enough to be exposed to, and to react to, both drugs.

Case report

A 70-year-old man with known type two diabetes mellitus presented to the accident and emergency department with hypoglycaemia. While in this department, his tongue began to swell. He had experienced 10 similar, minor episodes over the previous four months, which had resolved without intervention and for which he had not sought medical help. He had commenced taking lisinopril (25 mg once daily) six months earlier.

The patient was reviewed by the ENT team and flexible nasoendoscopy performed. This showed gross swelling of the tongue and mild oedema of the arytenoid mucosa. The vocal folds were mobile, and, although there was some pooling of saliva, the airway was not compromised. The patient was treated with intravenous steroids, fluids and antihistamines.

Ninety minutes later, the patient suddenly became pale, blue and restless. He had no peripheral or central pulse, had lost his airway and was not spontaneously breathing. The airway compromise prevented ventilation via a nasopharyngeal tube. An emergency tracheostomy was performed and the patient was successfully resuscitated with defibrillation, ventilation and intravenous adrenaline and fluids.

The patient was transferred to the intensive care unit, where he was ventilated. He was apyrexial but had a high white cell count of 18.2×10^9/litre. He was treated empirically with antibiotics. After the arrest in A and E, he had a seizure on the ICU. A computed tomography brain scan showed no evidence of intracranial haemorrhage or infarction. The patient also suffered acute renal failure, which subsequently resolved.

The patient was reviewed by the immunology team and a presumptive diagnosis of ACE inhibitor induced angioedema was made. The immunology team recommended that the lisinopril be stopped permanently and that no further ACE inhibitors be given.

The patient's tongue swelling resolved and his sedation was gradually decreased. Decannulation within the intensive care unit was planned, but a routine, pre-decannulation nasoendoscopy showed some supraglottic oedema. He continued to improve, coping well with downsizing and capping off of his tracheostomy tube. Nasoendoscopy was repeated three times pre-decannulation in order to assess the degree of swelling in the larynx. However, there was no reduction in the supraglottic swelling, so the tracheostomy tube was left in situ.

The patient was reviewed again by the immunology team. Tests for complement (C4) and C1 inhibitor were normal. These tests were performed because angioedema in acquired C1 inhibitor deficiency can sometimes be precipitated by ACE inhibitors. On further questioning by the immunology team, the patient gave a history of mild tongue swelling following a previous dental extraction. This had occurred several years ago, before he had started taking lisinopril. The patient then underwent skin prick testing and then intradermal testing for lignocaine allergy. A 1:10 solution of lignocaine produced a striking wheal and flare reaction. The same solution failed to

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produce a reaction on intradermal injection in a healthy control, suggesting that the patient had an allergy to lignocaine.

Prior to the repeated nasoendoscopies, the patient's nose had been routinely sprayed with a topical solution of lignocaine hydrochloride 5 per cent and phenylephrine hydrochloride 0.5 per cent. This would account for the persistence of the supraglottic oedema.

From then on, the patient underwent nasoendoscopy without the use of the topical solution. The supraglottic swelling decreased, and he was decannulated without difficulty. The tracheostomy tube had been left in situ for nearly a month. The tracheostomy site was sutured without the use of local anaesthetic.

At an out-patient attendance, several weeks after discharge, the patient was re-tested for lignocaine allergy, again with positive results. He was advised to avoid all local anaesthetics, as well as ACE inhibitors.

Discussion

This patient had experienced intermittent, mild tongue swelling as a result of lignocaine injection after a dental procedure several years previously. In the months prior to admission, he had suffered more frequent attacks of tongue swelling as a result of exposure to lisinopril. On admission, he may have been unfortunate enough to be exposed to both drugs simultaneously, resulting in severe laryngeal oedema, hypoxia, and consequent cerebral and renal complications. His subsequent recovery was delayed by repeated re-exposure to lignocaine. The tongue swelling resolved once the lisinopril was stopped, although the laryngeal oedema was maintained due to repeated administration of topical lignocaine. The reactions were not synergistic.

Angioedema can occur in the face, lips, tongue, pharynx and larynx.[3] It can be life-threatening by causing airway obstruction and respiratory distress. Reactions to drugs, foods, inhalants and other substances are relatively frequent and are mediated variably by allergic and non-allergic mechanisms. Hereditary angioedema accounts for a small percentage of cases.

Angiotensin-converting enzyme inhibitors are a well known cause of laryngeal angioedema. They decrease systemic vascular resistance, venous pressure and the levels of circulating catecholamines. Angiotensin-converting enzyme normally metabolises bradykinin into inactive peptides. Thus, ACE inhibitors increase levels of bradykinin, which are thought to be responsible for angioedema.[4] The subcutaneous and submucosal swelling is caused by alterations in vascular permeability.[5] Most reactions occur within the first six months of therapy,[2] as was the case with our patient.

Angioedema is reported to occur in 0.1 to 0.2 per cent[1] of patients taking ACE inhibitors. The predisposing factors for angioedema in such patients are not known. Angiotensin-converting enzyme inhibitors are used to treat hypertension and heart failure and to slow diabetic nephropathy.[6] Over recent years, the number of people taking ACE inhibitors has increased (currently over 40 million people are estimated to take these drugs).[1] This could lead to an increasing number of cases of ACE inhibitor associated angioedema. A report by Cohen and Soliman found that as many as 58 per cent of patients presenting with angioedema were taking an ACE inhibitor.[3] Predisposing factors include previous angioedema, African-American race and transplant-related immuncompromise.[2] Angiotensin-converting enzyme inhibitor induced cough is also associated with angioedema.[7] Sondhi *et al.* reported that angioedema does not occur more frequently with any one ACE inhibitor.[1] Angiotensin-converting enzyme inhibitors are known to increase the frequency and severity of angioedema in patients with hereditary angioedema.

Angiotensin-converting enzyme inhibitor induced angioedema is not trivial; 40 per cent of patients attending emergency departments with angioedema may require intensive care unit admission.[1] Patients commencing ACE inhibitors should be advised to report any episodes of tongue swelling or difficult breathing. If they suffer from such episodes, the ACE inhibitor should be discontinued. This information is available for the patient in the manufacturer's information sheet and in the *British National Formulary*.

The primary pharmacological treatment for angioedema is adrenaline, 300 μg intramuscularly. Any airway compromise must be addressed. In our case, this required a tracheostomy. Mortalities from airway obstruction have been reported.[8]

Lignocaine allergy is thought to be much less common than ACE inhibitor induced angioedema, although the true incidence is unknown.[9] Local anaesthetic allergy can only be accurately diagnosed by specific allergy testing, using a combination of skin prick and intradermal challenge.[9–11]

Lignocaine is widely used as a local anaesthetic. It is an amide (as opposed to an ester) type agent. Allergies to lignocaine are rare. Both immediate allergic reaction (i.e. type one) and delayed type sensitivity have been described,[12] with the former being most common. Mackley *et al.* stated that the delayed type is probably more common than previously thought.[13] However, reported reactions to the dental use of lignocaine may be over-reported and may represent hysterical reactions rather than true allergy.[9]

Lignocaine is a common drug used daily in many operative and trauma situations. Not all reactions to lignocaine and related drugs are life-threatening, as they will not all affect the airway. Less severe reactions may not always be recognised and reported. In addition, reactions to local anaesthetics are not enquired about routinely in the same way as, for example, reactions to penicillin.

A patient with a lignocaine allergy could have an allergic reaction after infiltration with local anaesthetic while under general anaesthesia. Local anaesthetics should only be used after the patient has been asked if they have previously had a reaction, particularly during dental procedures. If patients have had such symptoms, local anaesthetics should be avoided, pending referral to the allergy or immunology service. The immunology team can then confirm the presence of lignocaine allergy and seek safe alternatives.

Conclusion

This was an unusual and life-threatening case of airway obstruction in a patient who developed angioedema of the airway induced by ACE inhibitors and maintained by lignocaine. Two independent pathological processes produced similar symptoms; the allergy to topical lignocaine was suspected when the supraglottic oedema failed to resolve. Lignocaine-based topical anaesthetic sprays are commonly used during nasoendoscopy. This case highlights the importance of asking patients if they have any allergies before the use of any pharmacological agent. It also highlights the importance of obtaining a more detailed history when a patient presents acutely, after the initial critical event has passed. When dealing with a patient with a lignocaine allergy, it is important that they be fully informed so that they can advise medical staff involved in any future procedures. This is particularly important when considering the wide usage of lignocaine and related local anaesthetics. Lignocaine allergy should be documented very clearly in the patient's hospital notes.

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There are also implications when such patients undergo dental procedures.

Even though reactions to ACE inhibitors are rare, doctors in all fields should seriously consider any minor reactions reported, as these may progress to life-threatening airway compromise,[14] resulting in prolonged ventilation and significant sequelae such as renal failure and seizures, as in our case.

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