May 2nd, 12:00 AM

Amlodipine-Induced Angioedema: A Case Report and Literature Review

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Case Presentation: Amlodipine-Induced Angioedema

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Abstract

Angioedema is a medical condition characterized by rapid and localized swelling in the deeper layers of the skin and mucous membranes. Unlike hives (urticaria), which affect the superficial layers of the skin and appear as raised, itchy welts, angioedema involves swelling beneath the skin's surface and commonly affects areas such as the face, lips, tongue, throat, hands, feet, and genitals. This swelling can be dramatic and may cause discomfort, pain, or difficulty with breathing or swallowing, depending on the location and severity of the swelling. Here we present the case of 73 year old patient with amlodipine-induced angioedema. This case highlights the importance of considering dietary factors and potential allergic reactions in patients presenting with acute angioedema. Prompt recognition and appropriate management, including airway protection and supportive care, are essential in preventing complications associated with angioedema. Collaboration between specialties, including allergy and immunology, is crucial for optimizing patient care and preventing future episodes.

Introduction

Angioedema can be classified into two main types based on its underlying causes:

1.Allergic Angioedema: This type of angioedema occurs as a result of an allergic reaction to specific triggers, such as certain foods (e.g., nuts, shellfish, eggs), medications (e.g., antibiotics, nonsteroidal anti-inflammatory drugs [NSAIDs], ACE inhibitors), insect stings, latex, or environmental allergens (e.g., pollen, animal dander). Allergic angioedema typically develops rapidly after exposure to the allergen and may be accompanied by other symptoms of an allergic reaction, such as itching, hives, wheezing, or anaphylaxis.

2.Non-Allergic (Non-Histaminergic) Angioedema: This type of angioedema is not mediated by the immune system and does not involve histamine release. Instead, it may be caused by various factors, including:

1. Medications: Certain drugs, such as angiotensin-converting enzyme (ACE) inhibitors (e.g., lisinopril, enalapril), nonsteroidal anti-inflammatory drugs (NSAIDs), and, less commonly, calcium channel blockers (e.g., amlodipine), can trigger angioedema in susceptible individuals. The mechanism of medication-induced angioedema may involve direct effects on blood vessels or the bradykinin pathway.
2. Genetic Factors: Some individuals may inherit a genetic predisposition to angioedema due to deficiencies or abnormalities in proteins involved in the regulation of blood vessel permeability or inflammation. Hereditary angioedema (HAE) and acquired angioedema (AAE) are two types of angioedema that can be caused by genetic factors.
3. Idiopathic: In some cases, the underlying cause of angioedema remains unknown, leading to a diagnosis of idiopathic angioedema.

Case Report

Patient Information:
Age: 73-year-old female
Past Medical History: Hypertension (HTN), Hyperlipidemia (HLD), Endometrial cancer status post total laparoscopic hysterectomy with right salpingo-oophorectomy and pelvic/para-aortic lymph node dissection, completed adjuvant vaginal brachytherapy, recent cerebrovascular accident (CVA) in June 2023, currently on aspirin 81 mg daily, completed Plavix 75 mg daily for 21 days.
Presenting Complaint: Acute onset left-sided tongue swelling, awakened from sleep due to progressive angioedema. No known environmental or medication allergies reported.
Outpatient Medications: Aspirin 81 mg daily, previously completed Plavix 75 mg daily for 21 days.
Clinical Course:
The patient presented to the Emergency Department (ED) overnight with acute left-sided tongue swelling, which awakened her from sleep. She reported that she recently began a new fasting regimen involving no dietary meats and had consumed new fruits and vegetables for dinner but could not specify which ones. On examination, there was notable angioedema of the tongue, more pronounced on the left side, without periorbital or lip involvement. The oral cavity appeared moist without erythema, and examination was limited due to angioedema.

Management in ED:
Upon presentation, the patient received Decadron, Benadryl, and epinephrine intramuscularly. However, she was unable to tolerate attempted nasopharyngeal airway placement. Despite treatment, the left-sided tongue swelling persisted. Neurological examination revealed intact sensation throughout, with lower extremity and upper extremity strength noted at 3/5, which the patient's husband stated was baseline. The patient reported ambulating at home without the use of a walker or cane.

Laboratory and Imaging Findings:
Initial laboratory workup revealed a white blood cell count (WBC) of 11.2, hemoglobin (Hb) 12.3 g/dL, hematocrit (Hct) 37%, serum creatinine (Cr) 1.08 mg/dL, sodium (Na) 140 mmol/L, potassium (K) 4.2 mmol/L, prothrombin time (PT) 11.7 seconds, international normalized ratio (INR) 1.04, and partial thromboplastin time (PTT) 40 seconds. An electrocardiogram (EKG) demonstrated normal sinus rhythm, and a chest x-ray was pending at the time of this report.

Further Management:
Despite administration of steroids and Benadryl, the left-sided tongue swelling persisted. The patient was administered 2 units of fresh frozen plasma (FFP), resulting in complete resolution of the angioedema. She was able to tolerate a diet without difficulty and remained hemodynamically stable, prompting her downgrade from ICU.

Discharge and Follow-up:
Amlodipine was discontinued, and it was added to the list of allergies. The patient was instructed to follow up outpatient with her Primary Care Physician (PCP) and Cardiology for further management of her hypertension. Additionally, follow-up with an allergist was recommended for further evaluation of the cause of angioedema. She was discharged home with a 3-day course of oral prednisone and an EpiPen, with instructions to return to the Emergency Room if her symptoms recurred.

Discussion: mechanism of action/Treatment

Calcium channel blockers have been associated with causing angioedema, but the mechanism is not well understood. It is thought that bradykinin and vascular nitrous oxide production play a role in calcium channel blocker angioedema by causing vasodilation and vascular permeability.**1**

Treatment may depend on the classification of angioedema. Histamine-induced angioedema presents as anaphylaxis with symptoms of bronchospasm, wheezing, hypotension and urticaria. These symptoms generally have a rapid onset and a brief time of attack. Bradykinin-induced angioedema presents with abdominal symptoms and has a slower onset with a longer duration. The standard of treatment for a patient presenting with angioedema is epinephrine, antihistamines and/or corticosteroids since histamine-induced angioedema is most common. However, concern for bradykinin-mediated angioedema rises if the patient is resistant to these agents and symptoms do not subside after treatment. There is some evidence to suggest fresh frozen plasma (FFP), ACE (Kininanse II), and other enzymes block bradykinin degradation which may help ACE-I induced angioedema caused by excessive bradykinin accumulation.**4**

The treatment options for CCB induced angioedema are similar to those for ACE-I angioedema. Our patient received epinephrine, steroids, diphenhydramine, famotidine, and tranexamic acid.

Tranexamic acid is a lysine receptor inhibitor that stops the conversion of plasminogen to plasmin resulting in inhibition of bradykinin formation. The inhibition of plasmin activity causes haults activation of C1 esterase inhibitor (C1-INH) which decreases the inflammation with hereditary angioedema.**5**

H1 antihistamines, such as diphenhydramine, work as antagonists at the H-1 receptors and reduce allergy symptoms by decreasing histamine levels.**7**

Famotidine which is a competitive histamine H-receptor antagonist (H2RA) which binds to H-receptors mainly in stomach and can be used off-label for chronic spontaneous urticaria in combination with an H1 antihistamine.

Corticosteroids can be used in patients with new onset urticaria with significant angioedema or if patients are unresponsive to antihistamines.**6** They decrease inflammation by reducing proinflammatory cytokines and enzymes that proliferate the inflammatory process.**8**

Discussion continued

It's worth noting that angioedema induced by CCBs is relatively rare compared to other adverse effects associated with these medications. The incidence of angioedema with CCBs varies depending on the specific drug within this class, patient factors, and other medications being taken concurrently.

Research and clinical reports have documented cases of angioedema associated with CCB use, but the exact frequency may not be well-documented in the literature. Angioedema caused by CCBs typically occurs as a non-allergic reaction and is thought to be related to the direct effects of these drugs on blood vessels rather than an immune-mediated response.

Patients who experience angioedema while taking CCBs may need to discontinue the medication and explore alternative treatment options under the guidance of a healthcare provider. It's essential for healthcare professionals to remain vigilant for signs of angioedema in patients taking CCBs and to educate patients about the symptoms of this condition so that it can be promptly recognized and managed.

Conclusion

Conclusion: This case highlights the importance of considering dietary factors and potential allergic reactions in patients presenting with acute angioedema. Prompt recognition and appropriate management, including airway protection and supportive care, are essential in preventing complications associated with angioedema. Collaboration between specialties, including allergy and immunology, is crucial for optimizing patient care and preventing future episodes.

References

References available upon request