

Angioedema Associated with Angiotensin-Converting-Enzyme Inhibitor Usage: A Case Report

Anjiyotensin Dönüştürücü Enzim İnhibitörü Kullanımıyla İlişkili Anjiyoödem: Olgu Sunumu

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Summary

Angiotensin-converting-enzyme inhibitors are used for hypertension treatment. One of the adverse drug reaction is angioedema with an incidence of 0.2%–0.7%. This angioedema most commonly affects the oral and perioral regions, and any laryngeal involvement can lead to death. Thus, oral and perioral angioedema must be immediately and adequately treated. If ACE inhibitor-associated angioedema resolves when the drug is stopped, then no further investigations are needed. Angiotensin-receptor blockers can not be considered as a safe alternative. Effective alternatives to control hypertension in such circumstances include calcium channel blockers and beta-blockers.

Key words: Angioedema, drug hypersensitivity, hypertension

Özet

Anjiyotensin dönüştürücü enzim inhibitörleri, hipertansiyon tedavisi için kullanılır. Advers ilaç reaksiyonlarından biri %0,2-%0,7 insidansla anjiyoödemdir. Bu anjiyoödem en çok oral ve perioral bölgeleri etkiler ve herhangi bir laringeal tutulum ölüme neden olabilir. Bu nedenle, oral ve perioral anjiyoödem derhal ve yeterli şekilde tedavi edilmelidir. İlaç kesildiğinde ACE inhibitörü ile ilişkili anjiyoödem düzelse, daha fazla araştırmaya gerek yoktur. Anjiyotensin reseptör blokerleri güvenli bir alternatif olarak düşünülemez. Bu tür durumlarda hipertansiyonu kontrol etmenin etkili alternatifleri arasında kalsiyum kanal blokerleri ve beta blokerleri bulunur.

Anahtar kelimeler: Anjiyoödem, ilaç aşırı duyarlılığı, hipertansiyon

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Introduction

Angioedema is defined as a local, non-inflammatory, and self-limiting edema that occurs due to increased leakage of plasma from capillaries located in the deep layers of the skin and mucosa (1). Many studies have focused on its mechanisms and causative factors, including trauma, stress, infection, and medications, such as non-steroidal anti-inflammatory drugs, antibiotics and angiotensin-converting enzyme (ACE) inhibitors. ACE inhibitors are commonly used for treating hypertension and heart failure (2). Angioedema is a relatively rare adverse drug reaction to ACE inhibitors, with an incidence of

0.2%–0.7% (3). In this case report; it was aimed to discuss ACE inhibitor-associated angioedema.

Case

A 39-year-old female presented at the polyclinic with edema on the face and lips that could be clearly identified as angioedema. It had initiated 2 days ago but she considered it unimportant and temporary sought medical help only when symptoms persisted. She had hypertension since 2 years, which was controlled using lercanidipine (20 mg). She had visited an internal medicine polyclinic 15 days ago, where her medication regimen was changed to perindopril arginine (5 mg) and amlodipine (5 mg), a combination of an

ACE inhibitor and a calcium channel blocker, due to insufficient control of hypertension.

Her clinical examination was normal except the presence of facial angioedema. As an emergency intervention, we treated her with pheniramine (50 mg) and dexamethasone (8 mg, intramuscular). The edema responded well to these medications. As the occurrence of angioedema was attributed to the recent prescription of an ACE inhibitor, ACE inhibitors were stopped and revert to lercanidipine (20 mg). A checklist for blood pressure measurement and a follow-up appointment after 5 days was also provided. At follow-up, her blood pressure (mean pressure systolic 126 diastolic 82) was under control angioedema had subsided.

Discussion

ACE inhibitor-associated angioedema typically involves the lips, tongue, or face and mostly presents with swelling of the tongue (4). Histamines are central to the pathophysiology of allergic urticaria, whereas bradykinins are the main mediators of non-allergic angioedema. The pathogenesis of ACE inhibitor-associated cough and angioedema may involve the vasoactive kinins, bradykinins, substance P and other pro-inflammatory mediators (5). Icatibant, a bradykinin B2 receptor antagonist, is effective in treating ACE inhibitor-induced angioedema (6).

The prevalence of cardiovascular conditions increases with age, ACE inhibitor-associated angioedema presents more frequently in patients aged >40 years (7), and the risk factors include female gender and African-American ethnicity (8) as well as a history of seasonal allergies and antihistamine or corticosteroid usage (9). Smoking and past smoking (9), rheumatoid arthritis, and past transplantation (10) are also associated with an increased risk of ACE inhibitor-associated angioedema.

There is no evidence to support the hypothesis that ACE inhibitors most frequently cause angioedema. However, a study reported lisinopril as the most commonly prescribed ACE inhibitor that caused angioedema (11).

ACE inhibitor-associated angioedema most commonly affects the oral and perioral regions, and any laryngeal involvement can lead to death (12). Thus, oral and perioral angioedema must be

adequately and immediately treated. Antihistamines, corticosteroids, and adrenaline have been traditionally used to treat these patients, although their efficacy remains unproven, and C1-esterase inhibitor concentrate is not beneficial in these patients (13).

ACE inhibitors are contraindicated in patients with a history of angioedema, and alternative antihypertensive drugs should be prescribed. If ACE inhibitor-associated angioedema resolves when the drug is stopped, then no further investigations are needed; however, if symptoms persist several months after stopping the drug, other possible etiologies must be investigated.

Angiotensin-receptor blockers (ARBs) cannot be considered as a safe alternative in patients with a history of ACE inhibitor-associated angioedema because ARB-associated angioedema is known to occur in patients who have previously experienced angioedema while receiving ACE inhibitors (14). Effective alternatives to control hypertension in such circumstances include calcium channel blockers and beta-blockers.

Conclusion

ACE-inhibitor associated angioedema most commonly affects women mainly during the first month of treatment and resolves when the drug is discontinued. Physicians must obtain details regarding seasonal allergies, antihistamine use, corticosteroid use, smoking, rheumatoid arthritis, and transplants, if any, before prescribing ACE inhibitors. Also, when these patients, physicians should be aware of the recurrence of angioedema but not necessarily refrain from prescribing ARB.

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References

1. Cicardi M, Suffritti C, Perego F, Caccia S. Novelty in the diagnosis and treatment of angioedema. *J Investig Allergol Clin Immunol* 2016;26(4):212-21.
2. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC

- Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013;31:1281-357.
3. Toh S, Reichman ME, Houstoun M, Southworth MR, Ding X, Hernandez AF, et al. Comparative risk for angioedema associated with the use of drugs that target the renin-angiotensin-aldosterone system. *Arch Intern Med* 2012;172:1582-9.
 4. Pavletic AJ. Late angio-oedema inpatients taking angiotensin-converting-enzyme inhibitors. *Lancet* 2002;360:493-4.
 5. Maurer M, Bader M, Bas M, Bossi F, Cicardi F, Cugno M. et al. New topics in bradykinin research. *Allergy* 2011;66:1397-406.
 6. Bas M. The angiotensin converting-enzyme-induced angioedema. *Immunol Allergy Clin North Am* 2017;37:183-200.
 7. Bluestein HM, Hoover TA, Banerji AS, Camargo CA, Reshef A, Herscu P. Angiotensin-converting enzyme inhibitor-induced angioedema in a community hospital emergency department. *Ann Allergy Asthma Immunol* 2009;103:502-7.
 8. Miller DR, Oliveria SA, Berlowitz DR, Fincke BG, Stang P, Lillienfeld DE. Angioedema incidence in US veterans initiating angiotensin-converting enzyme inhibitors. *Hypertension* 2008;51:1624-30.
 9. Straka B, Nian H, Sloan C, et al. Pollen count and presentation of angiotensin-converting enzyme inhibitor-associated angioedema. *J Allergy Clin Immunol Pract* 2013;1:468-73.
 10. Kostis JB, Kim HJ, Rusnak J. Incidence and characteristics of angioedema associated with enalapril. *Arch Intern Med* 2005;165:1637-42.
 11. Malde B, Regalado J, Greenberger PA. Investigation of angioedema associated with the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. *Ann Allergy Asthma Immunol* 2007;98:57-63.
 12. Atalay E, Ozdemir MT, Cigsar G, Omurca F, Aslan N, Yildiz M, et al. Angiotensin converting enzyme inhibitor-related angioedema: a case of an unexpected death. *Iran J Allergy Asthma Immunol* 2015;14:642-5.
 13. Powell RJ, Leech SC, Till S, et al. BSACI guideline for the management of chronic urticaria and angioedema. *Clin Exp Allergy* 2015;45:547-65.
 14. Howes LG, Tran D. Can angiotensin receptor antagonists be used safely in patients with previous ACE inhibitor-induced angioedema? *Drug Safety* 2002;25:73-6.

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