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Syed Faraz Kazim
Aga Khan University

Muhammad Shahid
Aga Khan University

Case Report

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Syed Faraz Kazim,[1] Muhammad Shahid[2]

Department of Surgery,[1] Department of Emergency Medicine,[2] Aga Khan University Hospital, Karachi, Pakistan.

Abstract

A case of anaphylaxis and angioedema induced by angiotensin II receptor blocker (ARB), losartan is reported. A 37 years old hypertensive female presented to the Emergency Department with swelling over the face especially the lips, urticarial rash all over the body, and dyspnoea within an hour of losartan administration. She did not have any previous history of drug allergies. The patient was managed with epinephrine. Although angioneurotic oedema and anaphylaxis are well documented adverse effects of angiotensin converting enzyme (ACE) inhibitors, very few cases of these adverse reactions with ARBs have been reported in medical literature.

Introduction

Anaphylaxis is an allergic, IgE mediated, hypersensitivity reaction that is rapid in onset and can be life-threatening.[1] Angioedema is an asymmetric, non-pitting swelling of loose tissue, usually skin. Laryngeal swelling from angioedema may lead to severe respiratory distress.[2] The most common etiologic agents of anaphylaxis and angioedema include drugs, insect bites, foods and food additives, transfusion of blood and blood products, radio- contrast media, and latex.[1,2]

In this report, we describe a case of anaphylaxis and angioedema associated with angiotensin II receptor blocker (ARB), losartan.

Case Report

A 37 years old female presented to the Emergency Department (ED) of Aga Khan University Hospital (AKUH), Karachi, with complaints of facial swelling especially over the lips, generalized rash all over the body, and dyspnoea for two hours. The history of presenting complaints revealed that she was started that morning on losartan 50mg by a family physician for the control of hypertension. The patient was previously taking captopril, which incited cough, and was therefore stopped. The patient had no previous history of anaphylaxis or angioedema. Within the first 60 minutes of starting medication, she developed difficulty in breathing along with facial swelling and urticarial rash all over the body. The patient presented to the ED, approximately two and half hours after intake of the medication. On arrival in the ED, her blood pressure was 120/85 mmHg, pulse rate 90 /minute, temperature 37.2°C, respiratory rate 22/minute; and oxygen saturation of 94% at room air. She experienced cold sweats all over the body. Her clinical examination was otherwise within normal limits. Based on her history and physical examination, a diagnosis of anaphylaxis and angioedema was made. Her baseline laboratory investigations including complete blood count (CBC), electrolytes, blood urea nitrogen (BUN) and creatinine, and liver function tests were done and they were within normal limits. Her serum IgE levels, however, were marginally raised. She was managed with epinephrine followed by ranitidine, clemastine, and hydrocortisone. Her symptoms resolved within an hour of treatment. The patient remained in the ED for two more hours and was subsequently transferred to the Internal Medicine Ward. She was discharged

after 24 hours of observation.

Discussion

Losartan is an orally effective ARB, used for the treatment of hypertension, cardiac disease, and renal disease.[3,4] The drug was approved by United States Food and Drug Administration for clinical use in 1995.[3,4] The more widely used angiotensin converting enzyme (ACE) inhibitors, such as captopril, are well known to cause cough (5 to 20% of patients) and angioneurotic oedema (0.1 to 0.2% of patients) because of the accumulation of bradykinin.[3] Initially, it was hypothesized that since losartan does not have ACE activity, it would not block the degradation of bradykinin; and hence there would not be an increase in bradykinin levels.[3-6] The drug was thus publicized to be free of above mentioned adverse effects. Nevertheless, even according to the manufacturers, angioedema occured in 1 out of 4058 initially treated patients.[4] Additionally, few other cases have been reported in medical literature during the past years.[5] Acker and Greenberg in 1995 reported a case of angioedema in a patient induced within 30 minutes of administration of losartan.[6] Their case was a 52 years old male, who had a history of focal segmental glomerulosclerosis and was prescribed losartan for the control of hypertension. Just as the patient being reported here, he too had previously received an ACE inhibitor, captopril, which was discontinued because he was experiencing cough with it. He too did not have any previous history of angioedema. He however, did have a history of allergy to radiographic contrast material. Lately in 2005, Nielson[7] reported a case of hypotensive shock and angioneurotic oedema associated with ARB, irbesartan. According to few authors treatment with losartan may cause anaphylaxis during haemodialysis.[8,9] The better documented anaphylactic reactions associated with ACE inhibitors during dialysis with AN69 membranes have been shown to be due to activation of bradykinin along with bradykinin effects on prostaglandins, leukotrienes, and substance P.[10] However, as mentioned earlier, if ARBs do not have any effect on bradykinin metabolism, they should not cause these adverse reactions.

More recent studies have shown that ARBs may in fact increase the bradykinin levels.[7,11-13] Campbell et al have shown that losartan increases the bradykinin levels by twofold in hypertensive patients.[11] ARBs bind to type 1 angiotensin II receptors (AT1). This binding blocks the cardiovascular effects induced by angiotensin II, e.g. vasoconstriction, water and salt retention, aldosterone synthesis and release. Angiotensin II can still bind to type 2 receptors. This binding may counteract some or all of the above mentioned effects mediated via AT1 receptors, and may do so by increasing bradykinin and nitric oxide.[12] Other mechanisms by which ARB may increase bradykinin is by inhibiting ACE[11] and neutral endopeptidase (NEP).[13] Thus, ARB mediated increase in bradykinin may be responsible for anaphylaxis and angioedema seen with losartan. This may be a class effect, and thus other ARBs should not be prescribed to patients with documented anaphylaxis and/or angioedema secondary to any ARB. Nonetheless, anaphylaxis in the patient under review may be an allergic reaction to antigenic properties of losartan; and thus other ARBs may be well tolerated.

Losartan and other ARBs are widely used in clinical practice in Pakistan. To the best of our knowledge, this is the first case of an ARB associated anaphylaxis and angioedema from Pakistan.

Conclusion

In conjunction with the previously published reports, our case of losartan associated angioedema and anaphylaxis strengthens the evidence that ARBs increase bradykinin levels; and thus may cause allergic reactions in susceptible patients. This may be a class effect; and thus other ARBs should be avoided in such patients. Further research is warranted to explore this side effect of losartan. Meanwhile, the drug should be prescribed with caution.

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