CASE REPORT

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Late-Onset Anaphylaxis due to Irbesartan

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ABSTRACT In the current study, a case of anaphylaxis induced by irbesartan is reported. A 67-year-old female patient presented to our clinic with the complaint of itching after irbesartan use. Oral provocation test was planned with irbesartan. At the end of the third hour, anaphylaxis developed when the test was about to end. The patient was managed with epinephrine. Six weeks later, the patient underwent a prick test with irbesartan. The test was positive. To the best of our knowledge, a case of late-onset anaphylaxis with irbesartan is presented for the first time.

Keywords: Angiotensin II receptor blocker; irbesartan; late onset anaphylaxis

Anaphylaxis is an allergic, IgE mediated, hypersensitivity reaction that is rapid in onset and can be life threatening.[1] 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] Irbesartan is an orally effective angiotensin II receptor blocker (ARB), used for the treatment of hypertension, cardiac disease, and renal disease.[3] In the current study, a case of anaphylaxis induced by irbesartan is reported.

CASE REPORT

A 67-year-old female patient presented to our outpatient clinic with the complaint of itching after ARB use. In the patient's history, ARB group anti-hypertensive drug was started instead of angiotensin-converting enzyme (ACE) inhibitor due to cough 2 weeks ago. She said that a few hours after the last use of ARB, itching on the her hands began, and then itching spread throughout her body, but there were no skin symptoms and systemic complaints. Oral provocation test was planned with irbesartan. At the end of the third hour, when the test was about to be terminated, itching started on the palms of the patient. Next, urticaria developed on the trunk, arms and legs, her voice became muffled, swelling in her hands and redness in the eyes were observed (Figure 1). On examination, uvula was edematous and respiratory sounds were coarse.At the beginning of the test, the patient's blood pressure was 160/100 mmHg, the pulse rate was 86/minute, and oxygen saturation in the room air was 93%, after the reaction occurred, the blood pressure was 120/80 mmHg, the pulse rate was 110/minute and oxygen saturation was 95%. There was also a noticable increase in the number of breaths per minute. Even if the drop in blood pressure was considered to be the class effect of the drug, respiratory symptoms and skin findings were sufficient to diagnose the patient as an anaphylaxis. Adrenaline was administered intramuscularly at a dose of 0.5 mg. Next, 45.5 mg of phenyramine, 40 mg of methylprednisolone, 50 mg of ranitidine were administered intravenously. The patient's clinical condition improved within one hour.

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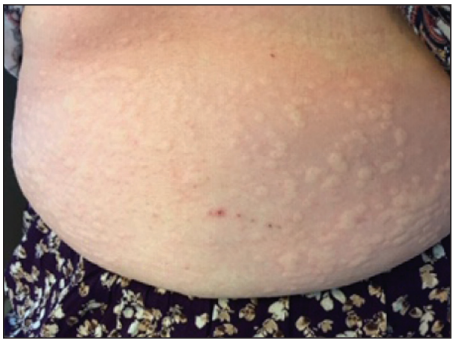

FIGURE 1: Urticaria.

DISCUSSION

Drugs are the second most common cause of anaphylaxis; it is the first among adults.They are also the most common cause of fatal anaphylaxis.[4] Beta-lactam antibiotics and neuromuscular blocking drugs are the most common drug groups leading to anaphylaxis by IgE-mediated mechanisms.[4,5] Irbesartan class C ARB is an antihypertensive drug. ARBs lack side effects, such as cough and angioedema associated with ACE inhibitors. Although angioneurotic edema and anaphylaxis are well documented adverse effects of ACE inhibitors, very few cases of these adverse reactions with ARBs have been reported in medical literature. Anaphylaxis with ARBs has been reported very rarely.

Anaphylaxis is diagnosed with history and physical examination using widely accepted clinical criteria.[6] Even if the drop in blood pressure resulted from the class effect of the drug, our patient was diagnosed as anaphylaxis considering the respiratory symptoms and skin findings.

Laboratory tests are of limited importance in the diagnosis of anaphylaxis. Measurement of tryptase level is the most important sign. It is recommended the serum/plasma tryptase levels to be measured within 3 hours after the appearance of anaphylaxis symptoms. We took blood from the patient for tryptase 1 hour after the development of anaphylaxis. There was no significant difference between the level of triptase assessed during anaphylaxis and basal triptase level (respectively 5.1 ug/L, 5 ug/L). The diagnosis of drug hypersensitivity is usually based on the patient's history. One reason for this is the lack of appropriate skin test extract to show IgE-mediated sensitivity for many drugs. Six weeks later than the reaction, the patient underwent a prick test with irbesartan. Since the drug had no other form than the tablet form, it was diluted with physiological saline after crushing and dripped onto the forearm and tested (KARVEA® 75 mg irbesartan ATC code: C09CA04 Sanofi-Synthélabo). Irbesartan prick test was positive (Figure 2). To demonstrate that the test positivity was not caused by the irritant effect of the drug, 10 volunteer hypertensive patients were tested with irbesartan and none were positive.

Drug provocation test in patients with anaphylaxis can be performed by evaluating the profit-loss ratio of patients with other diagnostic methods.[7] We performed a drug provocation test with irbesartan because there was no other diagnostic method and the previous reaction was only pruritus. Nielson reported a case of irbesartan-related hypotensive shock and angioneurotic edema in 2005.[8] He emphasized that despite the tryptase elevation, the reaction may have been due to the class effect of the drug. Anaphylaxis with another ARB losartan has been reported in hemodialysis patients.[9,10] There are studies showing that ARBs can increase bradykinin levels.[8] ARB-mediated increase in bradykinin may be responsible for anaphylaxis and angioedema. In such cases, it should be identified whether it is dependent on the class effect or the antigenic property of the molecule. In our case, urticaria was more prominent than angioedema therefore, it should be considered as IgE-mediated anaphylaxis rather than bradykinin-mediated reaction. This situation is supported by the fact that irbesartan is positive in the skin prick test.

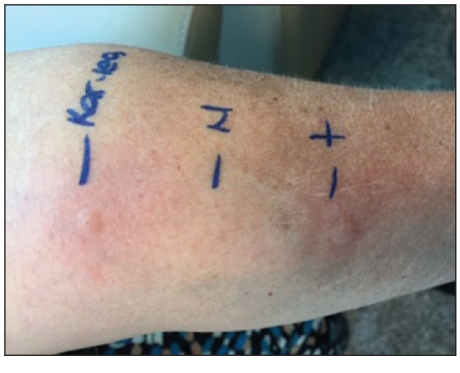

FIGURE 2: Irbesartan prick test.

Symptoms and signs of anaphylaxis usually occur within 2 hours after exposure to allergen.[11] Rare cases of late-onset anaphylaxis for B-lactams and intramuscular L-asparaginase have been reported.[12,13] In addition, cases of delayed anaphylaxis with mAb treatments have been reported.[14] The pathophysiology of late-onset anaphylaxis is unclear and multiple mechanisms may be responsible. To the best of our knowledge, a case of late-onset anaphylaxis with irbesartan is presented for the first time.

Informed Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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