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## Case Report

# Severe allergic reaction to human insulin in the patient with diabetic ketoacidosis

Nese Colak Oray <sup>a,\*</sup>, Basak Bayram <sup>a</sup>, Emel Altintas <sup>b</sup>, Semra Sivrikaya <sup>c</sup>, Yusuf Savran <sup>d</sup><sup>a</sup> Dokuz Eylul University, Faculty of Medicine, Department of Emergency Medicine, Balçova, 35340, Izmir, Turkey<sup>b</sup> Adiyaman University, Training and Research Hospital, Department of Emergency Medicine, Adiyaman, Turkey<sup>c</sup> Artvin State Hospital, Department of Emergency Medicine, Artvin, Turkey<sup>d</sup> Dokuz Eylul University, Faculty of Medicine, Department of Internal Medicine, Balçova, 35340, Izmir, Turkey

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## ABSTRACT

Diabetic ketoacidosis (DKA) is an acute and major life-threatening complication of diabetes mellitus. Fluid resuscitation, insulin therapy, and electrolyte replacement are essential for DKA treatment. Rarely, life threatening allergic reactions might develop in a patient treated with insulin. If anaphylaxis develops after insulin, the DKA treatment options are restricted. A limited number of case reports have been reported in patients with severe anaphylactic reactions to human insulin who were then treated with synthetic insulin analogues. We present a case of a 45-year-old male patient with allergic reactions to human insulin. The patient was successfully treated with insulin aspart and hemodialysis.

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## 1. Introduction

Diabetic ketoacidosis (DKA) is a potentially fatal crisis of diabetes mellitus (DM). In the treatment of DKA, fluid resuscitation, insulin therapy, and electrolyte replacement are important. Rarely, insulin allergies can be developed in the patient treated with insulin. The most common symptoms of insulin allergies are localized and limited. Life-threatening allergic reactions are rarely reported. Insulin allergies can be managed safely and successfully by desensitization treatment.<sup>1,2</sup> We present treatment of a patient with DKA who developed an insulin allergy. In this case report, we aimed to discuss DKA treatment options in patient with insulin allergies.

## 2. Case report

A 45-year-old male was brought to our emergency department

with chest pain and hyperglycemia. He had a history of type 2 DM and had been using an oral antidiabetic drug for two years, but he had been stopped using for a month. His past medical history did not show any drug allergies. His vitals were measured: 1.) blood pressure of 166/98 mmHg; 2.) pulse 100/min; 3.) respiration number 24/min; 4.) O<sub>2</sub> saturation 98%; and 5.) temperature 36.0 °C. His electrocardiograms (ECG's) were normal. His blood glucose level was 405 mg/dL, urinary ketones 15 mmol/L, pH was 6.8, HCO<sub>3</sub> 4.7 mmol/L, and lactate 3.6 mmol/L. Regular insulin (0.1 unit/kg IV bolus) was initiated in addition to 2000 mL of intravenous saline, and a 0.1 unit/kg/hour infusion was started. He developed a generalized skin rash, hoarseness, and uvular edema at the 30th minute of treatment, which then expanded to the soft palate. The vital findings were normal except for the presence of tachycardia. At that moment his vitals were measured: 1.) blood pressure 126/75 mmHg; 2.) pulse 104/min; 3.) respiration number 24/min; 4.) O<sub>2</sub> saturation 99%; and 5.) temperature 36.0 °C. It was discovered that the patient never had insulin in the past. A human insulin-related allergic reaction was proposed, and insulin treatment was ended. Chlorphenoxamine hydrochloride (10mg), ranitidine (50mg), prednisolone (1mg/kg), and 0.1mg (1/10,000) adrenaline was given intravenously. Uvula edema did not resolve. Emergency hemodialysis was performed due to severe metabolic acidosis refractory to

\* Corresponding author.

E-mail addresses: [nese.oray@deu.edu.tr](mailto:nese.oray@deu.edu.tr) (N.C. Oray), [basakdr@yahoo.com](mailto:basakdr@yahoo.com) (B. Bayram), [emel\\_korkmaz@yahoo.com](mailto:emel_korkmaz@yahoo.com) (E. Altintas), [semra.sivrikaya@deu.edu.tr](mailto:semra.sivrikaya@deu.edu.tr) (S. Sivrikaya), [yusufsavran@yahoo.com](mailto:yusufsavran@yahoo.com) (Y. Savran).

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intravenous sodium bicarbonate. After hemodialysis, pH was 7.2 and HCO<sub>3</sub> was 8.9 mmol/L. Also, his symptoms had not regressed. Antihistamines, steroids, and adrenaline were re-administered. He was intubated in order to secure the airway. Because of the lack of response to treatment, hereditary angioedema was considered, and two units of fresh frozen plasma were given. Subcutaneous insulin aspart (15–20 units; NovoRapid, Novo Nordisk Pharmaceuticals Pty Ltd, Australia) was administered due to ongoing complaints and ketoacidosis. Insulin aspart treatment was continued, and hemodialysis was applied intermittently for metabolic acidosis and acute renal failure. On the 3rd day of follow-up, uvula edema, ketonemia, and metabolic acidosis had completely resolved. The patient was extubated on the 5th day and discharged on the 23rd day with basal insulin glargine and nateglinide treatments.

### 3. Discussion

Allergic reaction to the human insulin was rarely (0.1–3%) reported.<sup>1</sup> Most of these cases were simple allergic reactions such as an injection site swelling, erythema, and itching. However life-threatening angioedema and anaphylaxis were also reported.<sup>2,4</sup> The patient's past medical history did not indicate any allergies, and this allergic reaction developed after the first contact with human insulin.

DKA is one of the most common complications of DM. Regular insulin is essential for DKA treatment. Despite its uncommon occurrence, an insulin allergy is an important clinical dilemma, both because of its life-threatening anaphylaxis and the effects on diabetic management. Both clinical conditions are mortal when they are not treated. The treatment options are limited in these situations and should involve correcting symptoms and switching insulin preparations.

Kaya et al. reported a case in which allergic reaction to human insulin develops after the first dose of regular human insulin. In the patient, desensitization treatment was started. At the follow-up DKA developed, and regular human insulin was re-administered. After that, a severe anaphylactic reaction developed, and the patient died despite all medical interventions.<sup>3</sup> We report a case of successful treatment of severe allergic reaction to human insulin in a patient with DKA.

The first step in the treatment of moderate allergic reactions is discontinuation of the suspect agent and antihistamine administration. Severe allergic reactions may be treated with combinations of antihistamines in addition to systemic steroids and adrenaline. Adrenaline should be administered to the patient with angioedema and/or cardiovascular collapse due to anaphylaxis.

If the allergen drug must be used in the treatment, another

equivalent group of drugs can be applied or started desensitization/immunotherapy. Desensitization treatment/immunotherapy is efficient for diabetic patients with allergies to insulin, however, these treatments are not appropriate for DKA patients.<sup>2–6</sup> On the other hand, these treatment options are not useful in emergency situations. Repeated hemodialysis is another treatment choice for correction of resistant metabolic acidosis and removal of ketone bodies, but it is inadequate overall. A limited number of case reports about severe anaphylactic reactions to human insulin in a diabetic patient treatment with synthetic insulin analogues have been reported.<sup>2,7</sup> Insulin glargine, detemir, and aspart are human insulin analogues. Synthetic insulin analogues decrease the risks of insulin allergies due to their differences at the amino acid level.<sup>1,6</sup> In our case, we have successfully managed by switching to a subcutaneous insulin aspart.

In summary, life threatening allergic reactions to regular insulin might develop. Synthetic insulin analogues and hemodialysis can be used in DKA patients with insulin allergies.

### Conflict of interest statement

The authors have no commercial associations or sources of support that might pose a conflict of interest.

### Transparency document

Transparency document related to this article can be found online at <http://dx.doi.org/10.1016/j.tjem.2017.07.004>.

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