İstanbul Med J 2015; 16: 125-6
DOI: 10.5152/imj.2015.58076

Case Report

Diabetic Ketoacidosis associated with Steroid in a Renal Transplant Recipient

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Abstract

Post-transplant diabetes mellitus is a serious complication of organ transplantation. Post-transplant diabetes mellitus is a form of type 2 diabetes mellitus that is thought to develop in response to a relative insulin deficiency resulting from increased insulin resistance or impaired insulin production or a combination of both. The clinical presentation varies from asymptomatic hyperglycemia to hyperosmolar dehydration or diabetic ketoacidosis. The onset of diabetes is associated with reduced graft function and patient survival. Immunosuppressive drugs, such as corticosteroids and calcineurin inhibitors (cyclosporine and tacrolimus), are known to be diabetogenic. However, the association of diabetic ketoacidosis with the use of systemic corticosteroids is infrequently reported. Here, we report a 27-year-old female recipient of a live renal transplant who developed diabetic ketoacidosis associated with short-term corticosteroid treatment.

Keywords: Diabetes mellitus, diyabetik ketoasidoz, kortikosteroid, renal transplantasyon

Introduction

Post-transplant diabetes mellitus (PTDM) is a major metabolic complication developing after renal transplantation (1). It is accepted as a form of type 2 diabetes mellitus (DM), and it is thought that PTDM develops in association with the use of high-dose corticosteroids and calcineurin inhibitors. The diabetogenic effect of steroids has been known for many years. However, diabetic ketoacidosis (DKA) is a rarely seen complication that occurs in association with steroids. In our study, the case of a 27-year-old patient without a history of DM but having DKA that developed with high-dose steroid use in the early post-transplant period is presented.

Case Report

A 27-year-old female patient, who had been diagnosed with chronic kidney disease (CKD), had undergone peritoneal dialysis for 6 years, and received hemodialysis for the last 10 years, was hospitalized for a renal transplant from her mother. She had no history of DM. There was no pathological finding in her physical examination except a blood pressure of 180/100 mmHg. Her height was 148 cm, weight was 32 kg, and body mass index (BMI) was 14.6 kg/m^2. The results of her blood analysis were 81 mg/dL for fasting blood glucose level, 4.5% for HbA1c level, 118 mg/dL for urea level, and 8.5mg/dL for creatinine level. The donor candidate was 51 years old and had no history of a known disease. Her physical examination results were normal. The donor's height was 154 cm, weight was 61 kg, and BMI was 25.7 kg/m^2. The fasting blood glucose and HbA1c levels were 86 mg/dL and 5.4%, respectively. The patient, whose panel reactive antibodies were negative and who had haplotype 3 compliance with the donor candidate, underwent renal transplantation. As an induction agent, 50-mg antithymocyte globulin and 500-mg methylprednisolone were preoperatively used. Methylprednisolone was given at the dose of 250 mg on the 1st postoperative day and 120 mg on the 2nd postoperative day. The patient, who was previously anuric, had a urination volume of approximately 4.000 cc. The creatinine level decreased to 1.4 mg/dL on the 3rd postoperative, and her blood glucose level was 580 mg/dL. She appeared dehydrated, and her blood pressure was 95/50 mmHg, pulse was 105/min, respiratory rate was 16/min, and body temperature was 36.4°C. Other values were as follows: white blood cell count: 10.500/mm^3, serum sodium level: 136 mEq/L, serum chloride level: 111 mEq/L; in complete urinary analysis: ketone 3+, glucose 4+; in arterial gas: pH: 7,30, HCO3: 7 mEq/L, and anion gap: 18 mEq/L (8–16 mEq/L). After the establishment of the DKA diagnosis according to the clinical and laboratory findings, oral intake was stopped. Physiological serum solution and 0.1 U/kg/h intravenous infusion of crystalline insulin were initiated. After her blood pressure was regulated and urinary ketone became negative, she was given 0.5 U/kg/day dose of subcutaneous insulin as maintenance treatment. At the end of the 3rd month of the follow-up period, the dose of methylprednisolone was decreased to 12 mg per day. With decreased steroid dose, the patient did not need insulin. After the 3rd month, the fasting blood glucose levels varied between 85 and 100 mg/dL with the help

This study was presented at the 4th Current Kidney Diseases, Hypertension and Transplantation Congress, 8-12 April 2015, Sakarya, Türkiye

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Received:
28.02.2015

Accepted:
02.06.2015

of a diabetic diet. This study was prepared after receiving written informed consent from the patient.

Discussion

Post-transplant diabetes mellitus is a well-known complication of organ transplantations, and its frequency rate after transplantation has been revealed to be between 2% and 53% (2). PTDM is believed to be a result of insulin resistance (3). The risk factors for PTDM include cadaveric donors, advanced age (>40 years), African or Hispanic race, familial history of diabetes, obesity, metabolic syndrome, hepatitis C infection, and immunosuppressive treatment (4, 5). In a study, while high BMI was found to be associated with increased risk for type 2 DM, low BMI was found to be related to DKA. Our case was different from cases in literature in that the patient had low BMI (BMI: 14.6 kg/m^2), that transplantation was performed from a living donor, and that she had no familial history.

It is known that corticosteroids and immunosuppressive drugs such as calcineurin inhibitors, which are used in renal transplantation, are diabetogenic. It has been reported that these drugs can cause DKA in renal transplant recipients without a history of DM (4, 6). The clinical presentation of PTDM can vary from asymptomatic hyperglycemia to DKA or hyperglycemic hyperosmolar coma (6). Abbott et al. conducted a retrospective study with 39,628 renal transplant recipients and found that the incidence of DKA was 33.2/1,000 individuals per year among renal transplant recipients with DM and 1.9/1,000 individuals per year among recipients without DM (7).

In the study by Hoitsma et al. (5), it was demonstrated that the risk for the development of PTDM was more apparent in the first 3-month period and that it continued for 12 months. The mechanism of glucocorticoids that lead to the development of diabetes relies on their effects on the metabolism of carbohydrates. It hinders glucose from being taken into the cell in the periphery and from being used. It provides amino acids by increasing protein breakdown and glycerol level by increasing lipolysis. Amino acids and glycerol are also converted into glucose by gluconeogenesis in the liver. This increases the production of glucose and accordingly the blood glucose level (8). This situation can cause the impairment of blood glucose regulation in patients with overt DM and new onset of hyperglycemia in patients predisposed to DM. Glucosuria associated with hyperglycemia and dehydration secondary to it can increase catecholamine synthesis. Increased catecholamine synthesis increases lipolysis and gluconeogenesis, which facilitates the development of ketosis.

Post-transplant diabetes mellitus is important because it is found to be associated with a decrease in graft function in a patient survey (9). It is known that DKA is related to increased mortality in renal transplant recipients.

When the dose of drugs is reduced in hyperglycemia developing in association with steroids, hyperglycemia is generally brought under control (10). However, in the presence of high blood glucose levels, insulin therapy is administered for 2–6 months in addition to diet treatment. The need for insulin disappears in most patients during the follow-up period. In our patient, only a diabetic diet was implemented after giving subcutaneous low-dose insulin for 3 months. At the end of the 3rd month, the blood glucose levels were found to be normal at the follow-up examinations.

Conclusion

It should be kept in mind that DKA, which is an emerging clinical picture, can develop secondary to immunosuppressive agents (especially steroids) in patients undergoing renal transplantation. Therefore, blood glucose levels must be carefully followed, particularly when a high-dose steroid is used in patients.

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ş.K.C., E.Ç.Y.; Design - Ş.K.C., E.Ç.Y.; Supervision - F.D., N.Ö.; Funding - Ş.K.C., N.B.; Materials - Ş.K.C., N.B.; Data Collection and/or Processing -Ş.K.C.; Analysis and/or Interpretation - F.D., N.Ö.; Literature Review - Ş.K.C., E.Ç.Y.; Writer - Ş.K.C.; Critical Review - F.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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