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Case Report

# Diabetic Ketoalkalosis after Steroid Pulse Therapy in a Patient with Pancreas Transplant Rejection

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## Abstract

Diabetic ketoacidosis (DKA) is characterized by excessive production of organic acids leading to a low blood pH. Rarely, because of other complicating factors blood pH may be in the alkalemic range and the term diabetic ketoalkalosis has been coined to describe this condition. So far, less than 30 such cases have been reported in the literature. We report a 34-year-old woman who received methylprednisolone pulse therapy for the treatment of pancreas transplant rejection. Thereafter, she developed vomiting and abdominal pain. Her laboratory data showed high blood sugar, hypokalemia, alkalemic pH, elevated plasma anion gap, and significant ketonemia. She responded well to the treatment of DKA. It was concluded that an alkalemic pH does not rule out the presence of ongoing DKA. In suspected cases, changes in plasma anion gap and bicarbonate and the presence of ketonemia should be noted.

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**Keywords** ● Steroid therapy ● Diabetic ketoacidosis ● Alkalosis

## Introduction

Diabetic ketoacidosis (DKA) is an acute complication of diabetes mellitus and is characterized by excessive production of betahydroxybutyric and acetoacetic acids leading to low blood pH. An arterial pH of less than 7.3 is required in order to diagnose DKA.[1] Rarely, because of other complicating factors, blood pH may be in the alkalemic range and the term diabetic ketoalkalosis has been coined to describe this condition.[2] Currently, less than 30 such cases have been reported in the literature. We report the first case associated with steroid pulse therapy. In this patient an alkalemic blood pH had led to a delay in diagnosis and treatment.

## Case Description

A 34-year-old woman was admitted to the Emergency Department of Nemazee Hospital, Shiraz university of Medical Sciences, because of polyuria and polydipsia. She had been suffering from type 1 diabetes mellitus for 20 years. One year prior to admission she had underwent pancreas transplantation with pancreatoduodenal anastomosis because of repeated episodes of hypoglycemia, diabetic ketoacidosis, and poor diabetic control. After transplantation, she was on immunosuppressant drugs such as mycophenolate mofetil (CellCept) and tacrolimus (Prograf) and had normal blood sugar. She discontinued her immunosuppressant drugs from 2 weeks prior to admission and gradually developed polyuria and polydipsia. At the time

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of admission to the emergency room her laboratory data were as follows: blood sugar: 385 mg/dL, blood pH: 7.41, bicarbonate: 22 meq/L, BUN: 28 mg/dL, creatinine: 1.1 ng/mL, K: 3.9 meq/L, Na: 138 meq/L, negative urine ketone, and 3+ glucosuria.

She was admitted because of acute pancreas transplant rejection. Her immunosuppressant drugs were restarted and she received one pulse of 1000 mg methylprednisolone. During the next 72 hours she received an intravenous infusion of 4 units regular insulin per hour. However, her blood sugar remained high and she had repeated episodes of vomiting and had diffuse abdominal pain and extremity weakness. Because of her deteriorating condition, she was transferred to the intensive care unit (ICU).

At the time of her ICU admission, she was vomiting and complained of abdominal pain. Her vital signs were as follows: temp: 36.5ºC orally, blood pressure: 100/70 mmHg, PR: 110/min, and RR: 34/min. She had dry mucosa and diffused abdominal tenderness. Her initial laboratory data showed: Hb:13.5 g/dL, WBC: 18500/mL, 80% PMN, blood sugar: 385 mg/dL, BUN: 32 mg/dL, creatinine: 1.3 ng/mL, Na: 144 meq/L, K: 2.5 meq/L, blood PH: 7.50, $PaCo_2$: 32 mmHg, bicarbonate: 25 meq/L, chloride: 92 meq/L, serum albumin: 4.2 g/dL, globulin: 2.1 gd/L, calcium: 9.2mg/dL, and magnesium: 1.6mg/dL. Urinalysis showed 3+ glucosuria and 3+ ketonuria. Her serum ketone was positive with nitroprusside test in 1/16 dilution.

The patient was diagnosed as having DKA and mixed metabolic acidosis and metabolic and respiratory alkalosis. Because of her hypokalemia, she received 40 meq potassium chloride and normal saline during the first hour of treatment. The routine treatment of DKA was started with 10 units of regular insulin per hour. During the first 4 hours of treatment, her alkalosis progressed to a pH of 7.64. Face mask was applied to retain $Co_2$ and lower blood pH. Her nausea, vomiting, and abdominal pain subsided after 5 hours of treatment and her serum ketone became negative after 8 hours. She was able to eat after 14 hrs and 2 days later she was discharged on insulin (twice daily). She was in a good general condition at discharge. Because of her undetectable c-peptide level, she was diagnosed as a case of pancreas transplant failure and her immunosuppressant drugs were discontinued.

## Discussion

Our patient had strongly positive serum ketone, but at the same time her blood pH was in the alkalemic range of 7.5. The mean plasma pH in other reported cases has been 7.55.[2] This alkalemic pH in our patient can be explained by the presence of mixed acid-base disturbance. The calculated anion gap was 27 mmol/L which was 11 mmol/L higher than normal. If the patient had pure metabolic acidosis, the serum bicarbonate was expected to drop to 11 meq/L. The serum bicarbonate in our patient had failed to decrease which signifies the presence of concomitant metabolic alkalosis.[3,4] In our patients, repeated vomiting and the effect of a high dose of methylprednisolone were two causes for metabolic alkalosis. Hypokalemia can also maintain alkalosis and contribute to the overall clinical condition. The other acid-base abnormality in our patient was respiratory alkalosis. The patient's serum bicarbonate was 25 meq/L. Moreover, the expected arterial $PaCo_2$ is 40 mmHg, but our patient had an arterial $PaCo_2$ of 32 mmHg, reflecting the presence of respiratory alkalosis. Pain and anxiety can be the causes of respiratory alkalosis in this patient.[5] As expected, treatment of DKA led to the progression of alkalosis, but with therepletion of water and electrolytes, plasma pH gradually returned normal.

In most previously reported cases the main causes of DKA were hypovlemia because of vomiting and use of diuretics,[6] and alcohol ingestion.[7] Gastroparesis is also associated with recurrent ketoalkalosis.[8] Use of diuretics and repeated vomiting result in electrolyte depletion and hypovolemia, leading to bicarbonate reabsorption and alkalosis.[3,6]

Two cases of endogenous Cushing's syndrome because of adrenal adenoma and ectopic adrenocorticotropin (ACTH) production with DKA have also been reported.[2] Our case is the first reported case associated with glucocorticoid pulse therapy. Excess endogenous or exogenous glucocorticoids can promote $H^+$ excretion from the kidneys by their effect on mineralocorticoid receptor and contribute to alkalosis.[9] Respiratory alkalosis, as in our patient, has also been implicated as a contributing factor.[10]

## Conclusion

Vomiting and hypercortisolemia caused by steroid pulse therapy were the causes of DKA in our patient. We conclude that a normal or even alkalemic blood pH does not rule out the presence of DKA. In order to prevent delayed diagnosis and treat this potentially fatal condition, attention should be paid to the changes in plasma anion gap and bicarbonate and the presence of ketonemia.

**Conflict of Interest:** None declared

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