Case Report

EUGLYCEMIC DIABETIC KETOACIDOSIS WITH ACUTE PANCREATITIS IN A PATIENT NOT KNOWN TO HAVE DIABETES

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ABSTRACT

Objective: Euglycemic diabetic ketoacidosis (DKA) is a less known presentation of DKA. The aim of this case report is to alert physicians to the possibility of euglycemic DKA in a female patient presenting with metabolic ketoacidosis and to highlight the complex physiologic interplay between severe alcohol-related pancreatic injury, ketoacidosis, and starvation.

Methods: We describe a patient with a known history of alcoholism who presented with metabolic acidosis and acute pancreatitis and was not known to have diabetes.

Results: Computed tomography (CT) of the abdomen showed severe pancreatitis. The patient had not eaten for over 1 week. Laboratory work-up showed severe metabolic acidosis and no alcohol. Her acidosis improved only after euglycemic DKA was suspected; intravenous (IV) insulin infusion and dextrose were initiated, and her fluid/electrolyte abnormalities and carbohydrate metabolism were normalized.

Conclusion: Euglycemic DKA occurs in a small subset of patients with DKA and can go undiagnosed at initial presentation. It is thought to be due to starvation and food restriction, which inhibits gluconeogenesis, and is mainly observed in patients with a history of diabetes and insulin deficiency. **(AACE Clinical Case Rep. 2015;2:e88-e91)**

Abbreviations:
AKA = alcoholic ketoacidosis; **DKA** = diabetic ketoacidosis; **HbA1c** = glycated hemoglobin A1c; **IV** = intravenous

INTRODUCTION

Diabetic ketoacidosis (DKA) is usually easily recognized and is characterized by hyperglycemia, metabolic acidosis, and increased ketones (1). Euglycemic DKA, a relatively uncommon presentation, is a less known entity and can go unrecognized at initial presentation. It can be caused by starvation of any cause in conjunction with a current illness (2) and has been described mainly in patients with type 1 diabetes (3,4) but also in subjects with type 2 and gestational diabetes (3,5). We report a case of euglycemic DKA precipitated by starvation and severe pancreatitis in a patient with history of chronic alcoholism and no known underlying diabetes. This case shows the complex interplay among severe alcohol-related pancreatic injury, ketoacidosis, and starvation physiology. It highlights the fact that euglycemic DKA should be considered in the differential diagnosis of an ill patient presenting with metabolic acidosis, even in the absence of hyperglycemia.

CASE REPORT

A 36-year-old female presented to the emergency room with severe epigastric pain with radiation to her back of 3 days duration and a 1-week history of nausea and vomiting. She reported having not eaten for over 1 week and admitted to drinking 1 L of brandy daily for years; her last drink was 3 days prior to admission. She denied taking any medications. Her medical records review revealed a history of hematemesis from a Mallory-Weiss tear and rehabilitation for alcoholism in 2007 and 2008 with subse-

Submitted for publication April 28, 2014
Accepted for publication September 23, 2014
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Published as a Rapid Electronic Article in Press at http://www.journals.aace.com on January 21, 2014.
DOI:10.4158/EP14182.CR

quent relapses. Her family history was significant for coronary artery disease, diabetes, and hypertension, and her mother also struggled with alcoholism. Physical examination revealed a temperature of 36.6°C, blood pressure 123/71 mm Hg, respiratory rate 24 per minute, heart rate 80 per minute, oxygen saturation 100% on room air, height 60 inches, weight 50 kg, and body mass index 20 kg/m^2. She was in mild distress due to abdominal pain, lethargic, easily arousable, and followed commands. She had hypoactive bowel sounds and epigastric tenderness. Laboratory investigation showed the following: anemia (hemoglobin: 10.2 g/dL, hematocrit: 32.8%, mean corpuscular volume at 90.9 fL), sodium 134 mmol/L, potassium 4.4 mmol/L, chloride 97 mmol/L, bicarbonate 10 mmol/L, blood urea nitrogen 7 mg/dL, creatinine 0.7 mg/dL, glucose 86 mg/dL, total bilirubin 2.0 mg/dL, aspartate transaminase 320 U/L, alanine transaminase 88 U/L, elevated amylase at 208 U/L, and initial lipase at 3,378 U/L with >10,000 U/L the next day. Her anion gap was 27 mmol/L. Arterial blood gases revealed metabolic acidosis (pH 7.21, pCO_2 19 mm Hg). Further work-up revealed ketonuria (80 mg/dL), ketonemia (acetone qualitative reported as large), negative lactic acid, negative alcohol level, and positive urine toxicology for opioids. Computed tomography (CT) of the abdomen showed severe pancreatitis with peripancreatic phlegmon, edema, and severe infiltration of regional fat. She was admitted to the intensive care unit. Increased anion gap metabolic acidosis was thought to be secondary to ketoacidosis from alcoholism. Methanol and ethylene glycol ingestion was not confirmed by history or clinical presentation, and there was an absence of calcium oxalate crystals in the urine. Patient was kept nil per os, intravenous (IV) fluid resuscitation was initiated (Fig. 1), and abdominal pain was managed with morphine. Piperacillin/tazobactam was started for possible pancreatic necrosis. Elevated liver function tests were attributed to the history of alcoholism. Eighteen hours after intensive fluid resuscitation bicarbonate level remained low at 9 mmol/L, anion gap was still elevated at 22 mmol/L however glucose increased to 315 mg/dL. Urinalysis showed severe glucosuria and ketonuria. Euglycemic DKA was suspected, and IV infusion of regular insulin was initiated (Fig. 1). Seven hours later bicarbonate level increased to 16 mmol/L, anion gap normalized at 11 mmol/L, ketonuria and ketoacidosis resolved and the patient was still glucosuric. Her glycated hemoglobin A1C (HbA1C) was 4%. Unfortunately, insulin, C-peptide, and glutamic acid decarboxylase and anti-islet cells antibody levels were not tested. She was switched to subcutaneous lispro insulin and was requiring almost a total of 6 to 9 U/day. Her hyperglycemia resolved after 1 week of hospitalization, and she did not require further insulin therapy. It should be noted that the patient's hospi-

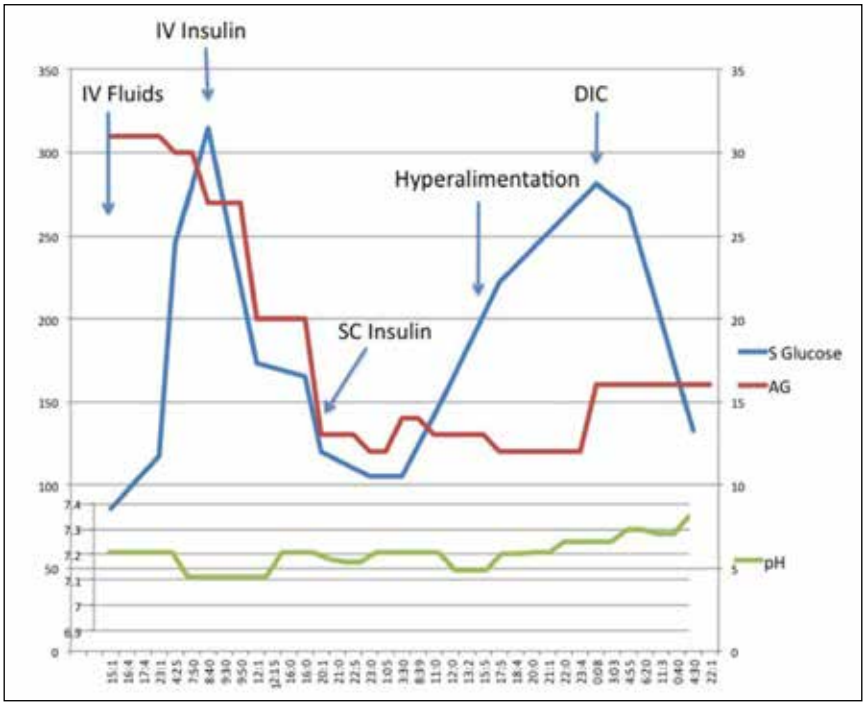

Fig. 1. The time course of events. The horizontal axis lists the exact times, with the first time at admission. The left vertical axis corresponds to serum glucose levels in mg/dL, and the right vertical axis shows the anion gap in mmol/L. The pH levels are shown in the smaller scale. IV fluids initially consisted of 5% dextrose and normal saline and were switched to 5% dextrose and half normal saline on day 2. The patient initially received IV regular insulin and was switched to SC lispro insulin thereafter. *AG* = anion gap; *DIC* = disseminated intravascular coagulation; *IV* = intravenous; *SC* = subcutaneous; *S Glucose* = serum glucose.

tal stay was prolonged due to disseminated intravascular coagulation observed on day 4, abdominal compartment syndrome, and acute respiratory distress syndrome. She was discharged home after 19 days of hospitalization with a recommendation to follow-up on an outpatient basis, which she ignored.

DISCUSSION

DKA is defined by the American Diabetes Association's diagnostic criteria for hyperglycemia (glucose >250 mg/dL, acidosis [arterial pH <7.3 and bicarbonate <15 mEq/L], and ketosis [moderate ketonuria or ketonemia]) (1). In 1973, Munro et al.(3) reported 37 (17.5%) euglycemic DKA cases out of 211 DKA episodes, and in 1993 Jenkins et al (6) reported 23 (3%) euglycemic DKA cases out of 722 DKA episodes. They defined euglycemia as glucose level ≤300 mg/dL and acidosis as a bicarbonate level ≤10 mEq/L (3). Currently it is advocated that a glucose level ≤200 mg/dL (11.1 mmol/L) should be used to define true euglycemic DKA (2,7). Based on this, only 16 of the 37 episodes in the study by Munro et al (3) and 6 of the 23 episodes in the study by Jenkins et al (6) would be considered as euglycemic DKA, representing 7.6% and 0.8% of DKA patients, respectively. Starvation ketosis and alcoholic ketoacidosis (AKA) are included in the differential. Ketoacidosis without hyperglycemia in an alcoholic patient may be diagnostic of AKA where acidosis usually occurs following heavy alcohol consumption with abrupt cessation in chronically malnourished alcoholics (8). The undetectable alcohol level in our patient argues against AKA. Moreover, if the sole underlying reason was AKA, one would expect improvement with dextrose/normal saline infusion without a need for insulin infusion. In comparison, ketoacid levels usually do not exceed 10 mEq/L with prolonged fasting alone, and the bicarbonate concentration is typically above 14 mEq/L (9). The initial low bicarbonate level of 10 mEq/L in this patient suggests another additional mechanism for her ketoacidosis. The low HbA1c level may reflect acute onset diabetes, probably secondary to severe pancreatitis as evidenced by the marked pancreatic changes seen on CT. Of course this low HbA1c is not evidence that she was not diabetic. Falsely low readings in the presence of diabetes can be seen with any condition that shortens erythrocyte survival (hemolytic anemia, acute blood loss) with secondary increased erythropoesis, after a recent transfusion, with some hemoglobin variants like sickle cell anemia, vitamin A or C supplementation, and in the setting of recurrent hypoglycemic episodes. The fact that ketoacidosis in this patient did not resolve until IV insulin was initiated supports the hypothesis of pancreatic beta cell reserve depletion. On one hand, severe acute destruction of beta cells due to severe pancreatitis on top of chronic alcohol-induced destruction of those cells would lead to acute decompensation and resultant insulin deficiency (10). On the other hand, a decreased glycogen reserve secondary to chronic alcoholism and prolonged fasting would have lead to the euglycemic state. In practice, there might be an overlap between starvation ketoacidosis and euglycemic DKA as the relative normoglycemia in subjects with euglycemic DKA is the result of prolonged fasting (3,6,7). In the latter context, near total glycogen depletion contributes to normoglycemia as metabolic acidosis continues to develop (11,12). Hyperglycemia develops once dextrose infusion is initiated, as in the present case. Severe infection along with increases in inflammatory markers and counterregulatory hormones (mainly catecholamines, cortisol, and glucagon) are also major contributors to hyperglycemia in this setting of acute complicated pancreatitis.

The major limitations of this case report are the lack of antibody and C-peptide measurements and our inability to follow-up after discharge. This would have been particularly important because we could have confirmed the presence and type (type 1 or 2, ketosis prone, or diabetes secondary to islet cell damage from pancreatitis) of diabetes in the ambulatory setting.

CONCLUSION

Although euglycemic DKA is a rare entity, it must be correctly diagnosed to tailor an appropriate therapy. It should be considered in the differential diagnosis of ketoacidosis since IV insulin infusion and dextrose, correction of fluid/electrolyte abnormalities, and restoration of carbohydrate metabolism (1,2,3,13) are the mainstays of therapy. The present case is additional evidence that DKA can occur in the setting of normal glucose concentration.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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