

Euglycemic ketoacidosis: Missed complication of Diabetes

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Abstract: Diabetes ketoacidosis is a well known acute complication of Diabetes Mellitus presenting with hyperglycemia, ketoacidosis and electrolyte abnormalities. Similar presentation may be seen with normal blood sugars where the patient presents with nausea, vomiting and abdominal pain, features suggestive of ketoacidosis. This condition is diagnosed by finding metabolic acidosis and ketosis/ ketonuria in presence of normal blood sugars. If hyperglycemia is always considered for diagnosis and further workup, one may miss this condition. We report 2 cases of euglycemic ketoacidosis in Diabetic patients.

Keywords: diabetes mellitus, euglycemic ketoacidosis.

I. Introduction

Diabetic Ketoacidosis (DKA) is a life-threatening condition in which severe insulin deficiency leads to hyperglycaemia, excessive lipolysis, and unrestrained fatty acid oxidation, producing the ketone bodies acetone, β hydroxybutyrate, and acetoacetate. This results in metabolic acidosis, dehydration, and deficits in fluid and electrolytes. DKA is a far more characteristic feature of Type 1 Diabetes Mellitus (T1 DM) than of Type 2 Diabetes Mellitus (T2 DM), but it may be seen in persons with T2DM under conditions of stress such as occur with serious infections, trauma, and cardiovascular or other emergencies^[1].

The serum glucose in DKA is usually in the 500 mg/dL range. However, an entity known as euglycemic DKA has been described, particularly in patients who have decreased oral intake or are pregnant, in which the serum glucose is normal or near normal but the patient requires hydration and insulin therapy for clearance of ketoacidosis¹.

Euglycemic ketoacidosis described first by Munro et al in 1973 and Jenkins et al in 1993 suggested blood glucose level of 200 mg/dl (11.1 mmol/l) or less for defining true euglycemic diabetic ketoacidosis.

Several cases have been reported in literature of true euglycemic ketoacidosis in type 1 diabetes. We report two case of true euglycemic ketoacidosis with almost same presentation in both T 1 and T2 DM, necessitating the assessment of acid/base in patient presenting with nausea and vomiting, even though blood sugars are in normal range.

II .1 Case Report 1:

A 31 year old female known case of T1 DM was admitted with third degree utero-vaginal (UV) prolapse. She was being treated with premixed insulin (30/70 regular/ NPH) of thirty units pre-breakfast and eighteen units pre-dinner and six units of regular insulin pre-lunch. Her haemoglobin A1c (HbA1C) was 6.4%, Fasting blood sugar (FBS) 162 mg/dl, Post-prandial blood sugar (PPBS) 173 mg/dl. Her blood counts, renal and liver functions were normal. Abdominal sling operation was performed with strict sugar control. The patient remained nil per oral for 12 hours post surgery, insulin was given according to requirement with monitoring of sugars by glucometer and the sugars were maintained in the range of 150-200 mg/dl.

On the post-operative day 1, patient developed multiple episodes of vomiting with abdominal pain. On examination patient was tachypneic suggestive of acidotic breathing. Investigations revealed positive for urine ketone bodies (2+), ABG was suggestive of high anion gap metabolic acidosis with compensatory respiratory alkalosis (PH- 7.38, PCo₂ 13.4, HCO₃ 7.8, anion gap 21), hypokalemia (serum potassium 2.2 mEq/L), blood counts were repeated and found to be normal. Patient was started on intravenous saline, regular insulin infusion after potassium supplementation. Patient improved symptomatically and the metabolic parameters including serum electrolytes and urine ketones normalised in 12 hours.

II.2 Case Report 2:

A 38 year old woman with type 2 diabetes on Oral hypoglycaemic agents (Metformin and glibenclamide) for 3 years was admitted second degree UV prolapsed. Blood sugars were well controlled with HbA1C was 6.8%. She underwent hysterectomy with strict preoperative sugar control with regular insulin. Patient was nil per oral for 12 hours post-operatively and her sugars were controlled between 150- 200 mg/dl.

On the second post-operatively day, patient complained of abdominal pain and multiple episodes of vomiting and was tachypneic. Investigations revealed high anion gap metabolic acidosis (pH- 7.39, pCO₂ 11.4, pO₂ 170, HCO₃ 8.5, anion gap 29.5), urine ketone bodies were present (3+), blood counts and renal functions were normal. Patient was treated with intravenous saline and insulin infusion. Patient improved symptomatically and biochemically.

II. Discussion

DKA results from relative or absolute insulin deficiency combined with counter-regulatory hormone excess (glucagon, catecholamine, cortisol, and growth hormone). Both insulin deficiency and glucagon excess, in particular, are necessary for DKA to develop. The decreased ratio of insulin to glucagon promotes gluconeogenesis, glycogenolysis and ketone body formation in the liver, as well as increases the substrate delivery from fat and muscle (free fatty acids, amino acids) to the liver^[2].

Ketosis results from a marked increase in free fatty acid release from adipocytes, with a resultant shift towards ketone body synthesis in the liver. Reduced insulin levels in combination with elevations in catecholamines and growth hormone, increase lipolysis and the release of free fatty acids. Normally, these free fatty acids are converted to triglycerides or very-low-density lipoprotein (VLDL) in the liver².

DKA defined by American Diabetes Association's (ADA) as hyperglycemia ie, bloodglucose >250mg/dl (13.9mmol/l) , acidosis (arterial pH<7.3 and serumbicarbonate <15mEq/l), and ketosis (moderate ketonuria or ketonemia)^{[3],[4]}.

Euglycemic ketoacidosis was described by Munro et al in 1973. They reported a series of 211 episodes of DKA, of which 37 episodes were described as euglycemic ketoacidosis defined as blood glucose less than 300 mg/dl (16.7 mmol/l) and plasma bicarbonate concentration of 10 mEq or less. All were young insulin dependent diabetics, only one being previously undiagnosed. In 1993 Jenkins et al by using above diagnostic criteria reported reported 23 case of euglycemic DKA out of 722 cases. They reported that true euglycemic DKA i.e initial blood glucose 180 mg/dl (10 mmol/l) or less was rare occurring only in 0.8-1.1% of all cases. It was also suggested that glucose readings above 200 mg/dl (11.1 mmol/l) cannot be considered to represent euglycemia, and therefore a blood glucose level of 200 mg/dl (11.1 mmol/l) or less should be used as the cutoff for defining true euglycemic diabetic ketoacidosis^{[5],[6]}.

The suggested etiology for the relative euglycemia is low caloric intake precipitated by starvation and persistent vomiting together with continuation of insulin treatment with excretion of larger amount of glucose in urine or lower rates of hepatic glucose production. Patients with euglycemic ketoacidosis are usually in the fasting state before they become ill. Clinically most patients present with vomiting and some may present with abdominal pain, dysuria, productive cough, thirst and nausea^{[5],[6]}.

In previous reported cases in literature all were insulin dependent/ type 1 diabetes with prolonged starvation. The cases presented include both type 1 and type 2 diabetes patients with similar presentation. The clinical and biochemical picture of both patients represent DKA except for the blood sugar values which were less than 200 mg/dl. Hence the initial blood sugar values may not be a good indicator to predict ketoacidosis. The clinicians need to be watchful for euglycemic ketoacidosis in practice which may be missed if only blood sugars are considered in diagnosis.

III. Conclusion

Euglycemic ketoacidosis is common in clinical practice and may be missed if only blood sugars are considered for diagnosis. Any patient presenting with clinical features of ketoacidosis must be evaluated with blood gas analysis and ketone tests.

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