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Case Report

Euglycemic Ketoacidosis Induced by Low Carbohydrate Diet in a Non-diabetic Patient: A Case Report

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Abstract

Low-carbohydrate diets are believed to work in reducing body weight. However, prolonged lacking of glucose intake can force body into keto-genesis, causing high anion gap metabolic acidosis. It is a rare condition in non-diabetic patients but we should keep high awareness on high risk populations especially chronic kidney patient since uremic status will complicate the detection of low carbohydrate diet associated ketoacidosis.

Keywords: Euglycemic ketoacidosis; Low carbohydrate diet; Non-diabetic patient; Chronic kidney disease

Abbrevations: ABG- arterial blood gas; AG- Anion gap; CKD- Chronic kidney disease; CVVH- Continuous veno-venous hemofiltration; DM- Diabetes mellitus; euDKA- Euglycemic diabetic ketoacidosis; HCO_3- bicarbonate; HD- Hemodialysis; ICU- Intensive care unit; LCHD- Low carbohydrate diet; PD- peritoneal dialysis; SGLT2i- sodium-glucose cotransporter 2 inhibitor

1. Introduction

ketoacidosis related to prolonged lacking of carbohydrate intake in non-diabetic patients is a rare clinical complication, which may be attributed to lipid metabolism, ketoacidosis or a probably pre-diabetic status. There are emerging evidences in literature reporting cases of low carbohydrate diet (LCHD) related euglycemic ketoacidosis

(euDKA). However, patients from those cases were mainly with diabetes, with increasing risk reported during treatment with sodium-glucose cotransporter 2 inhibitors (SGLT2i) [8, 11, 12]. The incidences of non-diabetic patients were less reported. We reported a 47-year-old male without diabetic history and presented with euDKA after application of strict LCHD.

2. Case Presentation

A 47-year-old man without any medical history was hospitalized due to progressive shortness of breath and generalized edematous change for about 2 months. He complained of poor appetite, nausea sensation and foamy urine for long time. He denied fever episode, upper respiratory tract symptoms, arthralgia or diarrhea. There was no family history of diabetes and he also denied alcohol consumption. According to this patient, he had been practicing strict LCHD for body weight control in recent one month.

He was diagnosed with severe ketoacidosis and was hospitalized in the intensive care unit (ICU) soon after admission. His laboratory test results reveal pH 7.145, bicarbonate (HCO_3^-) 7.3 mmol/L, significant blood ketone bodies, serum sugar 71 mg/dL, (blood urea nitrogen 152.0 mg/dL, creatinine: 16.09 mg/dL, and potassium 7.5 mmol/L. Glycated hemoglobin (HbA1c) was 6.2% and his blood sugar never went above 120 mg/dL during his first three days in ICU admission. Emergent hemodialysis was initiated due to severe azotemia and hyperkalemia, but following up arterial-blood gas (ABG) showed persistent metabolic acidosis (HCO_3^-: from 17.3 to 9.8 mmol/L) even after hemodialysis twice (Table 1).

	Reference Range	Day 1 pre-HD	Day 1 post-HD	Day 2 pre-HD	Day 2 post-HD	Day 3 CVVH
pH	7.35~7.45	7.145	7.282	7.196	7.296	7.357
pCO_2 (mmHg)	35~48	21.6	37.5	26	24.7	33.4
pO_2 (mmHg)	83~108	66.2	50.8	62.2	124.2	98.1
HCO_3^- (mmol/liter)	22~26	7.3	17.3	9.8	11.8	18.3
Base excess (mmol/liter)	-	-19.9	-8.7	-16.7	-13.1	-6.1
Na (mmol/liter)	136~144	134	-	138	139	137
K (mmol/liter)	3.5~5.1	7.5	5.6	6.3	5.8	4.3
Cl (mmol/liter)	99~107	105	-	103	105	107
Anion gap (AG)	-	21.7	-	25.2	22.2	11.7
Glucose (mg/dl)	65~109	71	76	72	86	59
BUN (mg/dl)	8~20	152	124.5	126.6	-	88.9
Creatinine (mg/dl)	0.64~1.27	16.09	-	13.56	-	9.91
Lactate (mmol/liter)	0.5~2.2	-	-	0.5	0.7	-
Ketone (mmol/liter)	< 0.6	-	-	-	5.2	0.5

Abbreviations: HD, hemodialysis; CVVH: Continuous venovenous hemofiltration

Table 1: Laboratory findings following treatment with hemodialysis and continuous veno-venous hemofiltration.

The urine anion gap was positive (urine sodium 49 mmol/L, urine potassium 35.8 mmol/L, urine chloride 49 mmol/L, and urine osmolality 349 mOsm/kg). This patient received continuous veno-venous hemofiltration (CVVH) with glucose water supplement. The metabolic ketoacidosis regressed within 3 days after CVVH (Table 2), therefore the dialysis treatment was shifted to intermittent hemodialysis due to persisted oliguria and severe azotemia. This patient received vascular access creation and long term hemodialysis treatment due to no recovery in kidney function after treatment for one months.

	Reference Range	**Day 0 post-HD**	**Day 1 CVVH**	**Day 2 CVVH**	**Day 3 CVVH**
pH	7.35~7.45	7.296	7.34	7.357	7.381
$pCO_{2\ (mmHg)}$	35~48	24.7	20.9	33.4	38.6
$pO_{2\ (mmHg)}$	83~108	124.2	140.3	98.1	83.9
$HCO_3^{-\ (mmol/liter)}$	22~26	11.8	11	18.3	22.4
Base excess (mmol/liter)	-13.1		-13.1	-6.1	-2.3
Na (mmol/liter)	136~144	139	139	137	134
K (mmol/liter)	3.5~5.1	5.8	5.8	4.3	4.1
Cl (mmol/liter)	99~107	105	102	107	100
Anion gap (AG)		22.2	26	11.7	11.6
Glucose (mg/dl)	65~109	86	113	59	92
BUN (mg/dl)	8~20	124.5	126.6	88.9	47.9
Creatinine(mg/dl)	0.64~1.27		13.56	9.91	5.74
Lactate (mmol/liter)	0.5~2.2	0.7	0.7		
Ketone (mmol/liter)	< 0.6	5.2	5.6	0.5	

Abbreviations: HD, hemodialysis; CVVH: Continuous veno-venous hemofiltration

Table 2: Laboratory findings following treatment with continuous veno-venous hemofiltration for 3 days.

3. Discussion

euDKA is a rare complication in non-diabetic patients. In previously published literatures, only few cases regarding the same situation were mentioned, including non-diabetic patients combined with dementia [11, 12], patients with abnormal eating behavior [11, 12, 15], or in lactating women [13]. In aerobic status, energy is produced through the oxidation of acetyl-coenzyme A derived from carbohydrates, fats and proteins into adenosine triphosphate. The glucose is the main substrate of Kreb cycle [14]; in the absence of tissue glucose intake, the organism would shift its energy production to lipid oxidation, which increases free fatty acids production and leads to keto-genesis [14].

The American Diabetes Association defines diabetic ketoacidosis (DKA) as having a combination of hyperglycemia (serum glucose >250 mg/ dL), acidosis (arterial pH <7.3 and bicarbonate <15 mEq/L) and ketosis (moderate ketonuria or ketonemia) [9]. The glycemic control in human body is believed to be organized by the balance

between the levels of insulin and counter-regulatory of hormones such as glucagon, growth hormones, glucocorticoid, and epinephrine. Therefore, DKA occurs when the above balance collapsed, causing hyperglycemia. Due to comparative lack of insulin, the end organs are unable to uptake the available glucose and lead to lipolysis resulting excessive keto-genesis. The most common cause of ketoacidosis is diabetic ketoacidosis or acute infection related uncontrolled hyperglycemic status; others are fasting and alcoholic ketoacidosis, which might occur in abnormal intake behavior or malnutrition.

The possible mechanism of euDKA may be either decreased hepato-gluconeogenesis during fasting status or increased urinary excretion of glucose induced by the counter-regulatory hormones. The possible conditions of keto-genesis and euDKA development include current illness such as infection, physiological stressors, prolonged starvation, LCHD, malnutrition with extremely poor intake, heavy alcohol consumption, chronic substance abuse, diabetic treatment with sodium-glucose cotransporter 2 inhibitors (SGLT2i) [15], and pregnant or lactating women in relatively insulin insufficiency status [13]. Besides, the clinical symptoms of LCHD-associated ketoacidosis are similar to DKA [12, 13], including malaise, dyspnea, abdominal pain, nausea and vomiting. The laboratory data of LCHD-associated ketoacidosis were described as high anion-gap (AG) metabolic acidosis with elevated blood ketone level, varied in glucose level and acidemia.

In our case, we reported a 47-year-old male who received strict LCHD to control his body weight and developed euglycemic ketoacidosis without diabetes status. We had excluded the possibility of substance ingestion since his delta anion gap/ delta bicarbonate is 1.27 with osmolal gap of 6.04, which is not favored of substance ingestion. The possible etiologies of euDKA in our case were attributed to low carbohydrate, fat-rich meals which can enhance alpha cell secretion of glucagon and lower insulin concentrations, and the unawareness clinical symptoms in pre-existing risk populations such as chronic kidney disease (CKD), and would have adverse metabolic sequelae if not treated promptly.

4. Conclusion

Ketogenic diet such as low carbohydrate diet may induced ketoacidosis in persons with a pre-existing risk factor such as chronic kidney disease, and contributed to adverse metabolic sequelae. Physicians should keep high awareness on high risk populations especially chronic kidney patient since uremic status will complicate the detection of low carbohydrate diet associated ketoacidosis.

Competing Interests

The authors declare that they have no competing interests

Ethical Consideration

Not applicable

Acknowledgements

Not applicable

References

1. Exton JH, Corbin JG, Harper SC. Control of gluconeogenesis in liver. V. Effects of fasting, diabetes, and glucagon on lactate and endogenous metabolism in the perfused rat liver. J Biol Chem 247 (1972): 4996-5003.
2. Fukita Y, Gotto AM, Unger RH. Basal and postprotein insulin and glucagon levels during a high and low carbohydrate intake and their relationships to plasma triglycerides. Diabetes 24 (1975): 552-528.
3. Owen OE, Caprio S, Reichard GA, et al. Ketosis of starvation: A revisit and new perspectives. Clin Endocrinol Metab 12 (1983): 359-379.
4. Gutniak M, Grill V, Efendic S. Effect of composition of mixed meals - low- versus high-carbohydrate content - on insulin, glucagon, and somatostatin release in healthy humans and in patients with NIDDM. Diabetes Care 9 (1986): 244-249.
5. Bisschop PH, De Sain-Van Der Velden MG, Stellaard F, et al. Dietary carbohydrate deprivation increases 24-hour nitrogen excretion without affecting postabsorptive hepatic or whole body protein metabolism in healthy men. J Clin Endocrinol Metab 88 (2003): 3801-3805.
6. Bravata DM, Sanders L, Huang J, et al. Efficacy and safety of low-carbohydrate diets: a systematic review. JAMA 289 (2003): 1837-1850.
7. Hilton PJ, McKinnon W. Life-threatening complications of the Atkins diet? Lancet 368 (2006): 23-24.
8. Louise von Geijer, Magnus Ekelund. Ketoacidosis associated with low-carbohydrate diet in a non-diabetic lactating woman: a case report. von Geijer and Ekelund Journal of Medical Case Reports 9 (2015): 224.
9. Nyenwe EA, Kitabchi AE. The evolution of diabetic ketoacidosis: an update of its etiology, pathogenesis and management. Metabolism 65 (2015): 507-521.
10. Mostert M, Bonavia A. Starvation ketoacidosis as a cause of unexplained metabolic acidosis in the perioperative period. Am J Case Rep 17 (2016): 755-758.
11. Bae EH, Lho H. Severe ketoacidosis in a patient with an eating disorder. Chonnam Med J 52 (2016): 141-142.
12. Hitoshi Iwata, Seiichiro Tsuzuki, Mitsunaga Iwata, Teruhiko Terasawa. Ketoacidosis due to a Low-carbohydrate Diet in an Elderly Woman with Dementia and Abnormal Eating Behavior; Intern Med 56 (2017): 2671-2675.
13. Gordon Sloan, Amjad Ali, Jonathan Webster. A rare cause of metabolic acidosis: ketoacidosis in a non-diabetic lactating woman (2017): 17-73.
14. Alice Larroumet, Marion Camoin, Ninon Foussard, Laure Alexandre, et al. Euglycemic ketoacidosis induced by therapeutic fasting in a non-diabetic patient; Nutrition 72 (2020): 110668.

15. Yuita Fukuyama, Kenji Numata, Kaede Yoshino, et al. Euglycemic diabetic ketoaxcidosis due to a strict low carbohydrate diet during treatment with sodium-glucose cotransporter 2 inhibitors. Acute Medicine and Surgery 7 (2020): e480.

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