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【 CASE REPORT 】

Ketoacidosis due to a Low-carbohydrate Diet in an Elderly Woman with Dementia and Abnormal Eating Behavior

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Abstract:
Strict restriction of carbohydrates can induce symptomatic ketoacidosis. We herein report a 76-year-old demented woman who developed ketoacidosis after 1 month of abnormal eating behavior involving selectively eating hamburger steak (estimated carbohydrate =12.7 g/day). Laboratory tests showed high-anion-gap metabolic acidosis with elevated blood ketone levels. She was successfully treated with intravenous fluids followed by oral intake of a regular diet. She remained relapse-free after correcting her eating habits. Healthcare providers should know that abnormal eating behavior in demented people can lead to an extremely-low-carbohydrate diet and cause atypical ketoacidosis unexplained by diabetes, heavy alcohol intake, or starvation conditions.

Key words: abnormal eating behavior, dementia, ketoacidosis, low carbohydrate diet

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Introduction

A low-carbohydrate diet (LCHD) is a component of dietary programs that restrict carbohydrate content while maintaining higher amount of proteins and various levels of fats (1). Evidence suggests that, despite the superior short-term effectiveness of LCHD in glycemic control and body-weight loss compared with dietary programs that contain higher carbohydrates, the long-term superiority of these effects and safety remains uncertain in patients with type 2 diabetes (2). Recently, several case reports have described potentially life-threatening ketoacidosis in people on LCHDs (3-7). We herein reported a demented elderly woman who developed ketoacidosis because of an LCHD, which most likely resulted from dementia-related abnormal eating behavior.

Case Report

This case report followed the CARE guidelines (8), and informed consent was obtained from the patient for publication of this report. Under our institutional policy, approval of the institutional review board is not required for case reports.

A 76-year-old retired Japanese woman was brought to our emergency department (ED) because of loss of consciousness for five minutes during an exercise activity in a sitting posture at a day-care center. The bystanders did not notice the typical manifestations of vasovagal syncope, such as urination or defecation before loss of consciousness, or an epileptic attack. Furthermore, the patient denied having nausea or vomiting. She had a history of hypertension and diabetes induced by corticosteroids, which she used to take for controlling idiopathic thrombocytopenia. She had maintained stable glycated hemoglobin levels (range, 6.0-6.8%) by following a dietary program as instructed by her dietitians (data not available due to insufficient information) for over 15 years after discontinuing corticosteroids; however, she had been consistently taking antihypertensive medications. In the two months before her presentation, she stopped taking any medications, including antihypertensive agents. No new oral antidiabetic agents, insulin, or antipsychotics were prescribed. She also denied tobacco and alcohol intake.

Over the two years before her presentation, the patient had gradually become withdrawn, avoided social situations, and was unable to keep her bedroom tidy. Her primary care physician referred her to a psychiatrist, who diagnosed her

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Table 1. Laboratory Findings in an Elderly Demented Woman with Ketoacidosis Induced by a Low-carbohydrate Diet.

Complete blood count		Hemoglobin A1c	5.9 (3.1–6.0) %
White blood cells	12,500 (3,200–8,500) /μL	Glucose	93 (70–109) mg/dL
Red blood cells	533 (380–500) 10^4/μL	L-lactate	27.2 (4–16) mg/dL
Hemoglobin	15.7 (11.5–15.0) g/dL	Insulin	20.5 (5.0–10.0) μU/mL
Platelet	23.4 (13.0–34.9) 10^4/μL	C-peptide	2.99 (0.67–2.48) ng/mL
		Glutamic acid decarboxylase autoantibodies	<0.3 (<1.5) U/mL
Blood chemistry		Total ketones	8,509 (≤130) μmol/L
Total protein	7.1 (6.7–8.3) g/dL	Acetoacetate	1,846 (≤55) μmol/L
Albumin	4.3 (4.0–5.0) g/dL	β-hydroxybutyrate	6,663 (≤85) μmol/L
Aspartate aminotransferase	18 (0–35) U/L		
Alanine aminotransferase	9 (0–35) U/L	***Urinalysis***	
Creatine phosphokinase	31 (62–287) U/L	Ketones	3+ (Negative)
Blood urea nitrogen	26.3 (8.0–22.0) mg/dL		
Creatinine	0.83 (0.6–1.1) mg/dL	***Arterial blood gas analysis***	
Sodium	132 (138–146) mEq/L	pH	7.29 (7.35–7.45)
Potassium	4.8 (3.6–4.9) mEq/L	Partial pressure of carbon dioxide	24.9 (37.0–44.0) mmHg
Chloride	93 (99–109) mEq/L	Partial pressure of oxygen	107.9 (74.0–104.0) mmHg
Phosphorus	4.7 (2.5–4.7) mg/dL	Bicarbonate	11.7 (37.0–44.0) mmol/L
Vitamin B_1	40 (24–66) ng/mL		

Table 2. Estimated Daily Nutrient Intake by the Diet History Questionnaire for Japanese* (9).

Nutrient, unit	Quantity	Dietary reference intake (10)
Protein, g	49.4	50
Fat, g	52.2	33–50
Carbohydrate, g	12.7	188–244

*The estimated daily total energy intake was approximately 750 kcal; however, this estimate may not be accurate because the validity of the questionnaire has been reported to be low (19).

with dementia with moderate cognitive impairment (16 points by the revised Hasegawa dementia scale; no dementia subtype specified) coexisting with depression. Since then, she had become selective with her food and had preferably consumed hamburger steak over regular meals. She had lost 12 kg in the past 9 months. Approximately one month prior to presentation, her selective eating behavior had worsened; at home, she hardly ate any other food except for hamburger steak. According to her daughter, she unwillingly ate the daily lunch that was provided at the day care center only once a week. On the day prior to admission, she was presumed to have eaten only 5 self-prepared, microwaved, frozen hamburger steaks (approximately 500 g, corresponding to approximately 750 kcal), as was her usual habit, according to her daughter's report.

At the ED, the patient was alert and oriented; her vital signs were stable, except for tachycardia, with a body temperature of 36.0℃, pulse rate of 100 beats per minute, respiratory rate of 15 breaths per minute, oxygen saturation of 99% at room air, and blood pressure of 106/94 mmHg. Her body mass index was 22.8 kg/m^2. Other physical examination findings, including those from a neurologic examination, were unremarkable. The bedside Schellong test suggested orthostatic hypotension.

Basic laboratory tests at the ED showed mild polycythemia (hemoglobin 15.6 mg/dL) and elevated blood urea nitrogen (26.3 mg/dL), which suggested dehydration. Other abnormal findings included mild leukocytosis (white blood cell count 12,500/μL), slightly increased blood L-lactate (27.2 mg/dL), 3+ urinary ketones, and mild acidemia (pH 7.28) with high-anion-gap (estimated at 27.3 mEq/L) metabolic acidosis on an arterial blood gas analysis. Her blood glucose level was normal (93 mg/dL). A complete list of the laboratory findings is presented in Table 1. A chest X-ray image was unremarkable, and electrocardiography was not indicative of either arrhythmia or ischemic heart disease. Computed tomography (CT) of the head was unremarkable, except for mild brain atrophy in the frontal and temporal lobes. Chest and abdominal CT without contrast did not reveal any life-threatening cardiovascular lesions or sources of infection that might cause sepsis and subsequent lactic acidosis. A further blood analysis revealed elevated levels of ketones, including acetoacetate and β-hydroxybutyrate (Table 1). Glutamic acid decarboxylase auto-antibodies were absent, and the C-peptide level was slightly elevated (2.99 ng/mL).

Using the Diet History Questionnaire for Japanese (DHQ) (9) and based on her daughter's report, we estimated her dietary intake of carbohydrates to be 12.7 g per day (Table 2), which was below the reference value for elderly Japanese women (188-244 g/day) (10) and thus satisfied the criterion for a very-low-carbohydrate ketogenic diet (20-50 g/day or <10% of the 2,000 kcal/day) (1).

Because diabetic ketoacidosis was considered unlikely and with a primary impression of atypical ketoacidosis with transient loss of consciousness secondary to orthostatic hypotension, we treated the patient with intravenous infusion of 1 L of Ringer-acetate solution with vitamin B at the ED, followed by 500 mL of normal saline at the medical ward. Af-

ter placing her on a normal diet of 1,400 kcal per day for 2 days after admission, her ketoacidosis resolved. Work-up for other causes of syncope, including a 24-hour Holter monitor, transthoracic echocardiography, and electroencephalography, were all negative. She was stabilized and was eventually discharged on day 9. After correcting her eating habits, including the selective intake of hamburger steak, and ensuring she maintained a regular diet for 2 months, she has remained stable and free from relapse of ketoacidosis.

Discussion

We reported the case of an elderly demented woman who developed ketoacidosis due to worsening of abnormal eating behavior involving the select consumption of hamburger steak for a month. Her unbalanced diet contained a moderate amount of protein and high fat content, but extremely low carbohydrate content. She was diagnosed with LCHD-associated ketoacidosis and was successfully treated with intravenous fluids and oral intake of a regular Japanese diet. After discharge, she remained in remission on a regular diet for two months.

In this case, we considered an LCHD as the more likely cause of atypical ketoacidosis than other common causes. Although we did not confirm the absence of an increased osmolality gap, we clinically ruled out alcoholic ketoacidosis because she had not consumed any alcohol. In addition, we excluded the possibility of diabetic ketoacidosis secondary to typical fulminant autoimmune diabetes or atypical latent autoimmune diabetes in adults on the basis of her normal blood glucose level (11, 12), negative glutamic acid decarboxylase auto-antibodies test, and slightly elevated blood level of C-peptide. Atypical causes of ketoacidosis in type 2 diabetes patients, such as the intake of sodium-glucose cotransporter 2 inhibitors (13) and ketosis-prone diabetes (14), were also unlikely based on her clinical history and presentation, although she had a history of steroid-induced diabetes. We did not assess the blood concentrations of formic acid, oxalic acid, hippuric acid, or paraldehyde because organic solvent intoxication was unlikely. Starvation ketoacidosis due to prolonged fasting is a rare but potentially life-threatening complication in the setting of acute starvation in pregnant women (15), perioperative patients (16), or patients with eating disorders (17, 18), among others. Although the limited reliability of the DHQ precluded the accurate evaluation of the total energy intake (19), prolonged abrosia resulting in acute starvation was less likely, regardless of the documented chronic weight loss, because the patient continued to eat food that contained high fat.

As of this writing, at least five cases of LCHD-associated ketoacidosis have been reported (Table 3) (3-7). Similar to the symptoms of diabetic ketoacidosis, nausea and vomiting were reportedly two of the most common symptoms that developed within three days to several months after the initiation of an LCHD. The glucose levels varied, and acidemia was typically only mild to moderate in severity. In cases with hyperglycemia, the diagnostic criteria for diabetic ketoacidosis were also met (11, 12). Insulin therapy was added only when the patients were hyperglycemic. The response to intravenous fluid therapy was generally good, and the symptoms appeared to resolve rapidly. No relapses have been reported after discontinuing the LCHD regimens. However, it is important to note that the follow-up duration in these reports was relatively short. Our case had generally the same findings and clinical course as these previously reported cases, except for the clinical manifestation of syncope and the absence of typical symptoms of nausea and vomiting.

Several limitations associated with the present case report warrant mention. First, we were unable to identify a direct mechanism that accounted for the relationship between the syncopal episode and ketoacidosis. The absence of typical ketoacidosis symptoms led us to speculate that the state of ketoacidosis *per se* may have, at least in part, contributed to the development of the syncope. However, syncope is highly prevalent in people with dementia (20), and orthostatic hypotension due to extracellular volume depletion may also have contributed to her episode of syncope. Therefore, it may be possible that, in this case, the ketoacidosis was completely asymptomatic and was found only by chance. Second, in people with dementia, abnormal eating behavior and dietary changes are common and, theoretically, can result in malnutrition (21). For example, patients with Alzheimer's disease are more likely to merely refuse food, whereas those with frontotemporal dementia, particularly the behavioral variant, frequently experience substantial changes in their diet, which include insisting on favorite foods for every meal as in the present case (21). In our case, the history of abnormal eating behavior together with the morphologic findings on head CT appeared congruent with the characteristics of frontotemporal dementia (22). However, this was only speculative because we did not investigate the cause of her dementia further. Third, the estimated nutrient intake of our patient may be unreliable because she was already moderately demented and we relied exclusively on the daughter's recollection. Lastly, as pointed out previously, the total ketone concentration of 8.5 mmol/L in our case did not reach the estimated anion gap of 27.3 mmol/L, implying that the missing anions may be low-molecular-weight anions, such as citrate, isocitrate, α-ketoglutarate, succinate, malate, and D-lactate (23, 24). However, we lack the necessary data to address this intriguing question because we did not measure the concentrations of these substances.

In summary, the strict restriction of carbohydrates, not only as part of diet therapy programs but also as a consequence of abnormal eating behavior, can induce ketoacidosis. Healthcare providers should be aware that abnormal eating behavior in demented people can lead to extreme LCHD, resulting in atypical ketoacidosis unexplained by diabetes, heavy alcohol intake, or typical starvation conditions.

The authors state that they have no Conflict of Interest (COI).

Table 3. Clinical Characteristics of Published Case Reports on Ketoacidosis Associated with a Low-carbohydrate Diet*.

Case (Reference)	(3)†	(4)	(5)	(6)	(7)
Country	United States	United States	United States	United States	Sweden
Age, years	51	40	30	42	32
Sex	Female	Female	Male	Female	Female
Ethnicity	White	White	Caucasian	Iranian	White
Body mass index, kg/m^2 [weight loss, kg (duration, weeks)]	21.7 [13.6 (ND)]	41.6 [9 (4)]	27.1 [7.3 (3)]	25.6 (ND)	ND [4 (1.4)]
Co-morbidities	ND‡	ND	None	None	None
Medications	None	ND	None	None	Occasional acetaminophen
Alcohol intake	None	None	Occasional‖	None	None
Carbohydrate, g/day	<20	Atkins diet§	<20	Dukan diet¶	<20
Onset from start of LCHD	"Several" months	1 month	3 weeks	3 days	10 days
Potential contributors	ND	Dehydration	ND	Ramadan	Breastfeeding for 10 months
Symptoms	Vomiting	N/V, dyspnea	N/V, abdominal pain	N/V, chills	N/V, palpitations, chills, extremity spasm
Partial pressure of carbon dioxide, mmHg	ND	29	23	22	21
Bicarbonate, mEq/L	ND	8	12	8	ND
Anion gap, mEq/L	26–35	26	"High"	26	ND
Lactate, mg/dL	7.2–10.8	ND	ND	ND	9
Ketones	ND	Acetone+; BHB 390 μg/mL (reference range, 0–44)	Positive	ND	7.1 mmol/L (reference range, 0–0.5)
Urinary ketones	"Large"	"Positive"	"Positive"	>150	ND
Acute treatment (short-term outcome)	IV fluids and insulin (remission)	5% dextrose and 150 mmol/L sodium bicarbonate (remission in 4 days)	Isotonic saline and insulin (remission in 1 day)	Normal saline with phosphorus replacement and antiemetics (remission in 2 days)	10% glucose and vitamin B (remission in 3 days)
Long-term outcome	No more episodes after normal carbohydrate intake	ND	No episodes for 2 years after normal carbohydrate intake	ND	Full recovery upon discontinuation of LCHD at 1 month

*We searched PubMed from inception through October 31, 2016, using "low carbohydrate" and "ketoacidosis" as free text search terms. We also searched Ichushi-Web (Japan Medical Abstracts Society database) using the terms "ketoacidosis," "carbohydrate," "carbohydrate restriction," and "low carb" in Japanese. The search was supplemented by an examination of the reference lists of pertinent reports and of the titles and abstracts of all articles that cited at least one of the publications included, using the citation-tracking function of Google Scholar. Only case reports that explicitly described specific diet programs that employed low carbohydrate intake and those with quantitative data on daily carbohydrate intake were eligible.

†Four episodes during the four-year period of low-carbohydrate diet were reported.

‡Hepatic steatosis was revealed by computed tomography on admission.

§Starting at 20–25 g/day of carbohydrates.

‖Approximately 17 g/day of ethanol was consumed the day before the onset of symptoms.

¶No data on daily carbohydrate intake.

BHB: β-hydroxybutyrate, IV: intravenous, LCHD: low carbohydrate diet, ND: no data, NL: normal, N/V: nausea and vomiting

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