CASE REPORT

Alcohol-induced Fasting Hypoglycemia

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Hypoglycemia is an uncommon presentation of alcoholism. As alcoholic patients typically exhibit few of the characteristics of hypoglycemia, they may be treated by the first aid physician as if they were drunk. Furthemore, it is believed that some of the deaths among drunken people that have occurred in police cells are due to alcohol-induced hypoglycemia. Here, we present a case of alcohol-induced fasting hypoglycemia to remind readers of this potentially grave complication of alcohol intoxication. A previously healthy 46-year-old man was sent to the emergency room in a comatose state after drinking 700 cc of 58% alcohol without any food intake for the preceding 24 hours. He regained consciousness after administration of thiamine and 50% dextrose. Laboratory data revealed an extremely low plasma glucose level (0.278 mmol/L (5 mg/dL)) and marked metabolic acidosis. Ethanol level was 6.78 mmol/L (31.21 mg/dL), 24 hours post alcohol consumption. He was discharged in good health after five days of observation. The prognosis for hypoglycemia is excellent if recognition and treatment are prompt. As there are few characteristic hypoglycemic features, awareness of the conditions, a careful history taking, and alertness are important for diagnosis and management of such a patient. **(Mid Taiwan J Med 2003;8:174-8)**

Key words

alcohol, ethanol, hypoglycemia, alcoholic ketoacidosis

INTRODUCTION

Alcoholism is a very common condition; however, hypoglycemia is a rare complication of alcohol abuse. Alcohol-induced hypoglycemia has attracted comparatively little attention, although individual cases [1,2] and small series [3-8] have been reported in many countries. As only a few of the features of typical hypoglycemia are exhibited other than coma [9], and because many symptoms are identical to those of alcohol intoxication, hypoglycemia in such patients may go unrecognized by their families or even the first aid physician [10]. Hypoglycemia often develops slowly and insidiously in the comatose drunk and probably accounts for at least some of the deaths among drunken vagrants and drunks who are confined in police cells and left unsupervised to sober up overnight [11]. Sucov et al found that alcohol associated hypoglycemia at an emergency department constituted only 0.9% of ethanol detectable cases over a three-month period, concluding that initial glucose screening did not appear to be necessary for all of these patients [8]. Measurement of plasma glucose is cheap, quick and not laboratory intensive; however, delaying restoration of blood sugar may lead to permanent brain damage or even death. We present a case of alcohol-induced fasting hypoglycemia to remind readers of the potential for, and consequences of, hypoglycemia in alcoholic patients.

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CASE REPORT

A previously healthy and moderately nourished 46-year-old man was brought to the

emergency room in a comatose state. He was aphasic and pale in appearance after drinking 700 cc of 58% alcohol without any food intake for the preceding 24 hours. The patient was an alcoholic, consuming an estimated daily average of 200 to 300 cc of 58% alcohol for 26 years; however, he denied ever being admitted to hospital in a comatose state before. There was no medication history. Physical examination revealed blood pressure 107/67 mmHg; pulse rate 122/min; respiratory rate 28/min; body temperature 35.1°C; and, Glasgow coma scale 3. The pupils were equal in size (2.5 mm) with prompt light reflex. His skin was cold with no excessive sweating, and the breathing pattern was deep and rapid. Glucometer blood glucose was 0.994 mmol/L (17 mg/dL. Intravenous injection of 100 mg thiamine, three ampoules of 50% dextrose, and intravenous infusion of 10% dextrose were administered after blood was drawn for biochemical, electrolyte and ethanol measurements. The patient regained consciousness about 10 minutes later. Arterial blood gas analysis (breathing room air) revealed marked metabolic acidosis: pH 6.945; $PaCO_2$ 25.9 mmHg; PaO_2 72.8 mmHg; HCO_3^- 9.7 mmol/L; and, increased anion gap 30 mEq/L. Two ampoules of sodium bicarbonate were given by rapid intravenous injection followed by an infusion of another two ampoules. Laboratory data revealed an extremely low plasma glucose level of 0.278 mmol/L (5 mg/dL). Ethanol level was 6.78 mmol/L (31.21 mg/dL), 24 hours after the alcohol consumption. Biochemistry revealed: AST 86 U/L (7-31); ALT 79 U/L (< 29); BUN 7.35 mmol/L (2.1-8) ((21 mg/dL (6-23)); Cr 123.76 μmol/L (4.42-132.6) (1.4 mg/dL (0.5-1.5)); Na 146 mmol/L (135-149); K 3.7 mmol/L (3.7-4.7); and, Cl 109 mmol/L (98-109). Hematology revealed: WBC 31.5×10^3 μL (neutrophils 74.8%, lymphocytes 14.6%, monocytes 8.98%); RBC 5.31×10^6 μL; Hb 18 gm/dL; Hct 53.9%; platelet count 342×10^3 μL; MCV 102 fL; and, MCH 34 pg. The upper BUN and Cr values limits and marked leukocytosis indicated dehydration so the patient was hydrated with 0.9% normal saline 2500 cc plus 5% G/W 500 cc and 10% G/W 500 cc. Coffee-ground vomitus was noted during his stay in the observation room but occult blood was negative. On admission, body height, body weight and body mass index were 158 cm, 53 kg and 21.2 kg/m^2, respectively. Vital signs were: blood pressure 150/90 mmHg, pulse rate 76/min, respiratory rate 22/min and body temperature 36.2°C. A daily infusion of 100 gm of dextrose was administered during hospitalization. Both hepatitis B and C markers were negative. Coarse echogenicity of the liver and an intrahepatic stone in the right lobe were evident from abdominal sonography. Panendoscopy revealed hyperemic esophageal and gastric mucosa, and a healing ulcer over the anterior wall of the duodenal bulb. Pathologic findings included chronic gastritis with mild inflammation. Peripheral blood smear demonstrated reactive leukocytosis. Lactate level was 1.40 mmol/L (0.50-2.18) (12.6 mg/dL (4.5-19.6)) and urine ketone body was negative (nitroprusside reaction) on day two. Cortisol level was 31.45 nmol/dL (11.4 μg/dL) in the morning and 18.48 nmol/dL (6.7 μg/dL) in the evening on day four. Hematological data had returned to normal without antibiotic treatment by day five: WBC 6.25×10^3 μL; RBC 4.25×10^6 μL; Hb 14.8 gm/dL; Hct 41.9%; platelet count 212×10^3 μL; MCV 98.7 fL; and, MCH 34.9 pg. The patient recovered and he was not hypoglycemic during the five days of hospitalization. No recurrence of hypoglycemia was noted during the three months of follow-up at the outpatient clinic.

DISCUSSION

The incidence of alcohol-induced hypoglycemia varies according to the social and ethnic background of the population investigated. Most reports describe individual cases [1,2] or a small series [3-8] only. In adults, the incidence of alcohol-induced hypoglycemia in all hypoglycemic patients is generally less than 1% [9] but can be as high as 4%, according to Sporer et al [3]. In children, it ranges from 3% to 5% [4,9].

Blood glucose homeostasis is based on absorption of dietary carbohydrate, glycogenolysis, and gluconeogenesis. Alcohol-

induced fasting hypoglycemia results from starvation and subsequent depletion of glycogen storage and impairment of gluconeogenesis. In healthy subjects, a minimum of 2 to 3 days of fasting is necessary to deplete hepatic glycogen storage [1]. However, alcohol-induced hypoglycemia could develop in chronically malnourished or acutely food-deprived individuals within 6 to 36 hours of ingestion of a moderate to large amount of alcohol [12]. In ethanol metabolism, excessive amounts of reduced nicotinamide adenine dinucleotide (NADH) is produced during the oxidation of ethanol to acetaldehyde and then to acetate. The increased $NADH/NAD^+$ ratio creates greater conversion of pyruvate to lactate, thus decreasing the conversion of pyruvate to the gluconeogenic precursors for gluconeogenesis. Starvation, depletion of glycogen storage, and impairment of gluconeogenesis cause hypoglycemia. In addition to these well know mechanisms, suppression of counter-regulatory hormone secretion also contributes to alcohol-induced hypoglycemia. In healthy subjects, Flanagan et al found that acute ingestion of alcohol markedly blunts growth-hormone release and impairs epinephrine secretion [13]. Growth hormone is an insulin antagonist. The lack of this antagonism leads to increased insulin sensitivity and a further reduction in blood glucose levels. This effect is more potent after 2 to 3 days of fasting, and is potentially lethal when chronic alcoholics are treated with insulin [14]. Relatively impaired epinephrine secretion may partially explain the atypical presentation of alcohol-induced hypoglycemia. An additional contributor to this type of hypoglycemia is alcohol-induced acute inflammation of the upper gastrointestinal tract which is associated with carbohydrate malabsorption, and which contributes to food deprivation when intake is minimal [15].

Alcoholic ketoacidosis is another complication of ethanol-associated metabolic disorders. During the fasting state, it begins to deplete hepatic glycogen storage. Fat is subsequently mobilized from adipose tissue to the liver as an alternative energy source [16]. Hepatic free fatty acid oxidation produces acetyl CoA. In an excess-energy state, acetyl CoA is either synthesized to fatty acid for energy storage or enters the Krebs cycle to generate ATP [16]. When alcohol is the only available source of energy, however, fatty acid synthesis is not favored. Also, the introduction of acetyl CoA into the Krebs cycle is significantly suppressed because of the alcohol-associated thiamine deficiency. Thus, most of the acetyl CoA is shunted into ketogenesis to form acetoacetate [16]. Furthermore, acetate, which is the final product of ethanol metabolism, is also available to react with the acetyl CoA to form more acetoacetate [16]. Eventually, ketoacidosis occurs. In fact, ethanol partially inhibits ketogenesis by interfering with fatty acid oxidation. Therefore, ketoacidosis during alcohol withdrawal is not usually observed until the ethanol level falls [17,18]. On physical examination, the fruity odor of the ketone body may be detected on the patient's breath; Kussmaul respiration with central nervous system dysfunction is another common presentation. Laboratory analysis usually reveals a high anion gap, with metabolic acidosis and minimal to mild elevation of ketone body levels in the blood and urine, although total ketone body production increases. This is due to the elevated $NADH/NAD^+$ ratio which causes the conversion of acetoacetate to beta-hydroxybutyrate [16]. Therefore, the routine laboratory test for ketone body (nitroprusside reaction) measures only acetoacetate and acetone and not beta-hydroxybutyrate. Thus, the detectable fraction of total ketone body remains low [16]. The negative urine ketone body determined in our patient may have been due to the measurement method (nitroprusside reaction) and/or delay (day 2). Although lactic acid may contribute to the acidosis and anion gap, these two conditions usually result from hypoperfusion associated with volume depletion rather than from the conversion of pyruvate to lactate [16]. Lactate levels increase in only a minority of patients with this syndrome [17]. Ishii et al reported two cases of hypoglycemia associated with severe alcohol-related lactic acidosis [5], and Lien et al reported

one case [2]. These three patients suffered from hypotension and profound dehydration. Our patient also suffered from dehydration but his lactate level was normal. This discrepancy was due to the fact that the blood sample in our case was collected after restoration of blood volume on day 2.

Hypothermia frequently accompanies alcohol-induced hypoglycemia; however, the adrenergic symptoms of typical hypoglycemia are often absent which makes diagnosis difficult if immediate blood glucose measurements are not available [18]. This is of particular concern given the high mortality rates in adults (10%) and in infants (25%) [9]. Patients presenting in a comatose state due to alcohol-induced hypoglycemia usually recover immediately following the restoration of blood sugar by intravenous glucose administration. Recovery is permanent and relapse does not occur if there is no further abuse [9]. Prolonged coma may respond to intensive treatment with dexamethasone and intravenous mannitol which should always be instituted if the patient does not completely recover within 15 minutes of intravenous glucose supplementation [9]. Glucagon is ineffective because of glycogen depletion and should never be given [9].

In conclusion, the management of alcoholic hypoglycemia is straightforward and, with early treatment, the prognosis is excellent. However, delaying restoration of plasma glucose may lead to permanent brain damage or even death. As there are relatively few typical hypoglycemic presentations, a careful history taking, knowledge of a moderate to large amount of alcohol consumption (50 to 300 g) without any nourishment during the preceding 6 to 36 h [9], and alertness are particularly important for the diagnosis and management of alcohol-induced fasting hypoglycemia.

REFERENCES

1. Yang CC, Yang LY, Deng JF. Hypoglycemia following ethanol ingestion in children: repot of a case. [Review] *J Formos Med Assoc* 1995;94:267-70.
2. Lien D, Mader TJ. Survival from profound alcohol-related lactic acidosis. [Review] *J Emerg Med* 1999;17:841-6.
3. Sporer KA, Ernst AA, Conte A, et al. The incidence of ethanol-induced hypoglycemia. *Am J Emerg Med* 1992;10:403-5.
4. Ernst AA, Jones K, Nick TG, et al. Ethanol ingestion and related hypoglycemia in a pediatric and adolescent emergency department population. *Acad Emerg Med* 1996;3:46-9.
5. Ishii K, Kumashiro R, Koga Y, et al. Two survival cases of alcoholic lactic acidosis complicated with diabetes mellitus and alcoholic liver disease. *Alcohol Clin Exp Res* 1996;20(9 Suppl):387-90.
6. Hart SP, Frier BM. Causes, management and morbidity of acute hypoglycemia in adults requiring hospital admission. *QJM* 1998;91:505-10.
7. Feher MD, Grout P, Kennedy A, et al. Hypoglycemia in an inner-city accident and emergency department: a 12-month survey. *Arch Emerg Med* 1989;6:183-8.
8. Sucov A, Woolard RH. Ethanol-associated hypoglycemia is uncommon. *Acad Emerg Med* 1995;2;185-9.
9. Marks V, Teale JD. Drug-induced hypoglycemia. [Review] *Endocrinol Metab Clin North Am* 1999;28: 555-77.
10. Berczeller PH. Alcohol hypoglycemia. *Hosp Pract (Off Ed)* 1993;28:41-2.
11. Scheen AJ, Lefebvre PJ. Hypoglycemia. In: Porte D Jr, Rifkin H, eds. Diabetes Mellitus-Theory and Practice. New York: Elsevier Science, 1991:896-910.
12. Marks V. Alcohol and carbohydrate metabolism. *Clin Endocrinol Metab* 1978;7:333-49.
13. Flanagan D, Wood P, Sherwin R, et al. Gin and tonic and reactive hypoglycemia: what is important-the gin, the tonic, or both? *J Clin Endocrinol Metab* 1998;83: 796-800.
14. Arky RA, Veverbrants E, Abramson EA. Irreversible hypoglycemia. A complication of alcohol and insulin. *JAMA* 1968;206:575-8.
15. Gottfried EB, Korsten MA, Lieber CS, et al. Gastritis and duodenitis induced by alcohol: an endoscopic and histologic assessment. [Abstract] *Gastroenterology* 1976;70:890.
16. Hoffman RS, Goldfrank LR. Ethanol-associated metabolic disorders. [Review] *Emerg Med Clin North Am* 1989;7:943-61.
17. Williams HE. Alcoholic hypoglycemia and ketoacidosis. [Review] *Med Clin North Am* 1984;68: 33-8.
18. Kuiper JJ. Fainting spells. *Hosp Pract (Off Ed)* 1993;28:14.

酒精造成的空腹低血糖

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低血糖是酒精成癮者不常見的表現，因爲酒精造成的低血糖，症狀並不典型，因此這類病人可能被當成酒醉來處理。據信，某些喝醉酒而在警局拘留室死亡的人，有一部分是死於酒精所造成的低血糖。在此，我們報告一例因酒精所產生的空腹低血糖的案例，以提醒讀者酒精中毒，可能產生這種危險的合併症。一位先前健康的46歲男性，在飲酒前24小時內，未進食任何食物，於喝了58%高粱酒700 cc後，因爲意識昏迷而被送到急診室。在給予thiamine及50%的葡萄糖注射液後，他的意識恢復清醒。實驗檢查呈現極度低血糖（血漿血糖濃度0.278 mmol/L (5 mg/dL)），及嚴重代謝性酸血症，乙醇濃度是6.78 mmol/L (31.21 mg/dL)（飲酒後24小時）。在5天的觀察後，他健康的出院了。我們的結論是，如果能及早診斷與治療，低血糖的預後是很好的，因爲這類病人的低血糖表現較不典型，因此詳細的詢問病史以及對酒精造成低血糖的警覺性，對於診斷與治療是很重要的。（中台灣醫誌 **2003;8:174-8**）

關鍵詞

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