AN AUTOPSY CASE OF OVERWHELMING SEPSIS WITH HYPOGLYCEMIA IN A PATIENT WITH ALCOHOLIC LIVER CIRRHOSIS

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Abstract : A 46-year-old man, unconscious, was admitted to our hospital as an emergency case. He was known to have liver disease due to excessive alcohol intake. He had fallen while riding a motorcycle one week before admission. On arrival, he was comatose and in a state of shock. Petechiae and subcutaneous bleeding were observed on his trunk and extremities. His left upper and lower extremities were remarkably swollen, and a discolored, elevated, hard mass was found on the outer side of the left ankle joint. He was diagnosed as having disseminated intravascular coagulation complicated by renal and liver failure. Hypoglycemia (plasma glucose level 29 mg/dl), hyperammonemia and severe metabolic acidosis were found. He was treated with controlled ventilation, plasma expanders, blood transfusion, antibiotics, dopamine, noradrenaline, nafamostate gabexate and hypertonic glucose. Despite this intensive treatment, he died of irreversible shock 20 hours after admission. Postmortem examination revealed small vegetation in the aortic valve and microabscesses in the kidney, heart, thyroid gland, and retroperitoneal adipose tissues. These findings suggest that he had developed sepsis stemming from cellulitis further to alcoholic liver cirrhosis. It is considered imperative that physicians consider the possibility of hypoglycemia in all patients with multiorgan failure.

Key words : hypoglycemia, sepsis, alcoholic liver cirrhosis, disseminated intravascular coagulation, microabscess

INTRODUCTION

Hypoglycemia is a clinical syndrome with diverse causes, in which low levels of plasma glucose eventually lead to neuroglycopenia[1, 2]. If not recognized and treated promptly, hypoglycemia may cause irreversible central nervous system injury or expose the patient to unnecessary procedures; it rarely results in death. We encountered a patient with sepsis and alcoholic liver cirrhosis accompanied by hypoglycemia. The mechanisms responsible for the occurrence of hypoglycemia in this patient are discussed.

CASE REPORT

A 46-year-old comatose man was admitted to Nara Prefectural Mimuro Hospital as an emergency case. He was known to have liver disease due to excessive alcohol intake. He had fallen while riding a motorcycle one week before admission. Subsequently his left extremities gradually became swollen. He was found, having fallen, by his family, early in the morning on July 2, 1998, and was transferred by ambulance to our hospital. On arrival, he was gasping for breath and in shock. Initial vital signs were: blood pressure 80 mmHg systolic;

pulse 120/min; respiration 36 breaths/min (shallow); and temperature 36.0℃. His skin was wet, pale, cyanotic, and mottled over his flanks. Petechiae were found on the anterior neck, and subcutaneous bleeding was observed on the posterior aspect of the left upper extremity. Left-sided upper and lower extremities were remarkably swollen, and a discolored, elevated, hard mass was found on the outer aspect of the left ankle joint. His pupils were dilated to 4 mm, but were responsive to light. Coarse crackles were slightly audible in the bilateral lung fields. The liver was palpated a 3-finger width below the xiphoid process, but the spleen was not palpable. Laboratory findings included a blood hemoglobin concentration of 7.5 g/dl, no red blood cell fragmentation, a white blood cell count of 30,800/mm^3 with a shift to the left, and thrombocytes of 37,000/mm^3. Serum creatinine was 4.4 mg/dl, blood urea nitrogen 54.6 mg/dl, sodium 133 mEq/L, potassium 5.9 mEq/L, and chloride 103 mEq/L. Serum GOT was 229 IU/l, serum GPT 50 IU/l, γ-glutamyl transpeptidase 72 IU/l, albumin 2.04 g/dl, γ-globulin 2.86 g/dl, total bilirubin 13.0 mg/dl, PT 28.6 sec (17 % of control), and FDP 20.0 μg/ml. Viral antibodies to hepatitis B and C were negative. C-reactive protein was 11.3 mg/dl. Serum ammonia was 328 μg/dl. Blood glucose on admission was 29 mg/dl. Blood gas analysis revealed severe metabolic acidosis (pH 7.221, pCO_2 15.7 torr, pO_2 88.7 torr, standard bicarbonate 6.2 mmol/L, base excess −20.3 mmol/L). Endotoxin was elevated to 29.9 pg/ml in stored serum. No culture of blood and urine was performed.

Overwhelming sepsis, stemming from the phlegmone on the left leg, complicated by renal and liver failure, and disseminated intravascular coagulation (DIC) were suspected. The patient was treated with controlled ventilation, plasma expanders, blood transfusion, antibiotics, dopamine, noradrenaline, nafamostate gabexate and hypertonic glucose. Despite this intensive treatment, his blood pressure remained low and he died of irreversible shock 20 hours after admission. Postmortem examination revealed a phlegmone in the left leg (Fig. 1), small vegetation (3×5 mm in size) on the cuspid of the aortic valve (Fig. 2), and microabscess formations in renal glomeruli (Fig. 3), the thyroid gland, myocardium, and retroperitoneal adipose tissues, which were compatible with sepsis. The liver was swollen (2,350 g in weight), and exhibited findings consistent with alcoholic liver cirrhosis, with lipid vacuoles and Mallory bodies in the hepatocytes (Fig. 4).

DISCUSSION

The patient ultimately died of septic shock. He was in a state of multiple organ failure and hypoglycemia was evident. In this case, there was no personal or family history of diabetes mellitus or hypoglycemic episodes, and he had not been taking any drugs associated with hypoglycemia. He developed sepsis from cellulitis further to alcoholic liver cirrhosis. Many factors may cause hypoglycemia. In this case, sepsis may have been one main factor. Postmortem examination revealed a clustering of bacilli and microabscesses in various organs, and a high level of serum endotoxin was detected. Coagulation abnormalities such as DIC were also observed in the patient. DIC *per se* is common in patients with hypotensive septicemia[3]. This means our patient had a severe infection. In infants who have severe infection or sepsis, there is evidence that glucose requirement is increased possibly as a result of an increase in glucose utilization[4]. Lang et al.[5-7] demonstrated that endotoxin in gram-negative infection was able to increase whole-body glucose utilization without

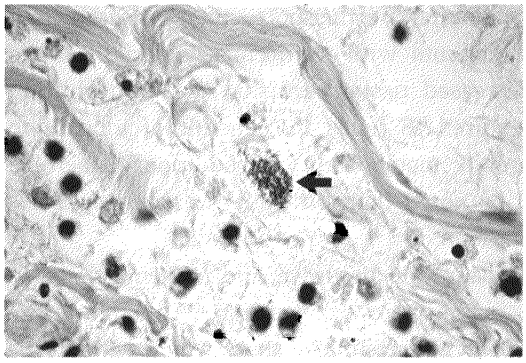

Fig. 1. Bacterial cluster (arrow) with edema and cellular infiltrate in the subcutaneous tissue of the left foot (HE stain, original magnification ×100).

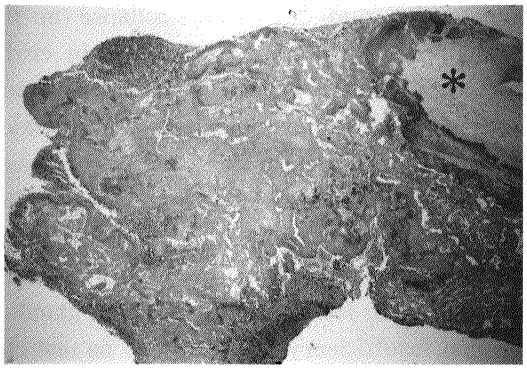

Fig. 2. Vegetation on the aortic valve (asterisk), consisting of fibrin, inflammatory cells, and bacterial organisms (HE stain, original magnification ×4).

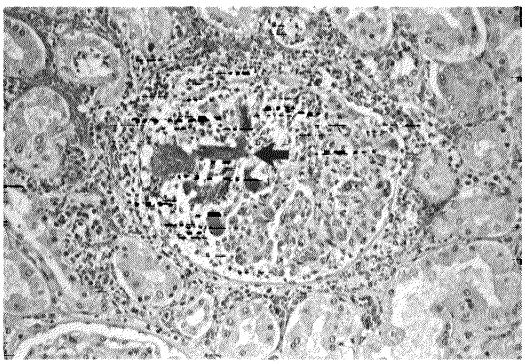

Fig. 3. Neutrophilic infiltration in and around the glomerulus, associated with clustering of bacilli (arrow) in the glomerular tuft (HE stain, original magnification ×20).

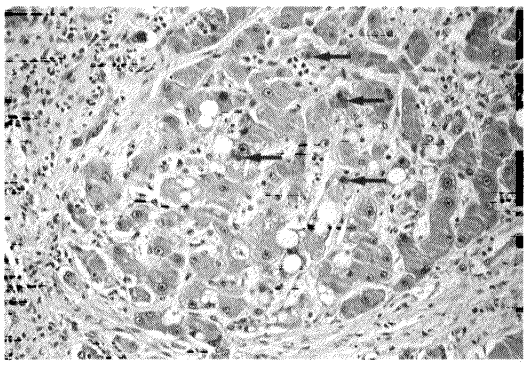

Fig. 4. Alcoholic liver cirrhosis showing lipid vacuoles and Mallory bodies (arrow) in the hepatocytes (HE stain, original magnification ×20).

hyperinsulinemia, and that it also inhibited hepatic gluconeogenesis in rats with experimentally-induced sepsis. What causes the increase in glucose utilization during sepsis remains to be determined, but cytokines, particularly interleukin-1, which is produced mainly by monocytes-macrophages in the inflammatory process, may play a crucial role in the alteration of glucose homeostasis in sepsis[8-10].

Some factors other than sepsis have been suggested to aggravate hypoglycemia. Ethanol abuse has been shown to predispose to hypoglycemia by reducing stores of hepatic glycogen and inhibiting of gluconeogenesis[11]. Glycogen depletion occurs as a result of a diet limited in nutritional intake and comprised primarily of alcohol[11]. In this case, alcoholic liver cirrhosis was confirmed on postmortem examination. Nouel et al.[12] observed a high prevalence (50 %) of low glucose level in cirrhotic patients with septicemia and emphasized the presence of

hypotension and circulatory collapse in their patients. Furthermore, they stressed that hypoglycemia should be considered in cirrhotic patients with septicemia, especially when circulatory failure develops. Hypotension and decreased tissue perfusion result in shifting from aerobic to anaerobic metabolism, which requires 18 times the amount of glucose to produce the same amount of energy as aerobic metabolism. In addition, anaerobic metabolism results in lactic acidosis[13]. It should be noted that our patient exhibited severe metabolic acidosis, although lactic acid was not measured.

Plasma levels of cortisol and ACTH were not measured in this case, and no hemorrhage or necrosis was found in the adrenal glands on postmortem examination. Although acute adrenal insufficiency is thought to be one cause of hypoglycemia[1,2], there would seem to be little likelihood of acute adrenal insufficiency in this case.

In conclusion, we encountered a patient with overwhelming sepsis and alcoholic liver cirrhosis, accompanied by hypoglycemia. The combination of hypoglycemia and septic shock has a poor prognosis[14]. Although the detection and treatment of hypoglycemia in critically-ill patients may not always decrease the mortality rate, it may help to decrease the burden of multiple metabolic disturbances. Blood glucose should be checked at regular intervals while the patient's condition is critical.

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