Hypoglycemic Coma Masquerading Thyrotoxic Storm

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A 59-year-old woman was hospitalized in hypoglycemic coma. Although hypoglycemia was promptly reversed, she was in a somnolent, restless state with tachycardia, tremor, profuse sweating, and high body temperature. Thyrotoxic storm was highly suspected and vigorous antithyroid regimens gradually brought her up to normal mental and cardiovascular states in several days. However, profound generalized myopathy necessitated the maintenance with a respirator. One month later, an episode of angina pectoris was followed by generalized convulsion, coma, and death in a few days. Neuroimaging study disclosed posterior leukoencephalopathy syndrome. This case is instructive in that hypoglycemic coma may masquerade the major symptomatology of thyrotoxic storm, and that profound myopathy and angiopathic or angiospastic processes of the brain and the heart may interfere with the outcome.

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Introduction

Although thyrotoxic crisis is often accompanied by hyperglycemic state, profound hypoglycemia has been seldom encountered. In fact, the hypoglycemic coma may masquerade the underlying life-threatening process of thyrotoxicity. Here, we describe a case of thyrotoxic storm in whom hypoglycemic coma was the presenting symptom; the clinical importance of this association is discussed.

Case Report

A 59-year-old woman had been easily fatigued, distracted and nervous for several weeks prior to hospitalization. On November 13, 1996 she was slightly febrile, lost her appetite and was brought to a hospital the following morning because she was behaving abnormally. In the emergency room she was drowsy, hypoglycemic (blood glucose 38 mg/dl) and found to have marked leucocytosis (WBC 79,300/mm³). Intravenous glucose and methylprednisolone sodium succinate 500 mg was given, followed by imipenem/cilastatin sodium 500 mg. Her consciousness was slightly improved for a short period of time, but soon she lapsed into lethargy. When transferred to our hospital, the woman was emaciated and in a comatose state. Her blood pressure was 105/68 mmHg, heart rate 123/min, regular, and respiratory rate 36/min. Her surface body temperature was 38.0°C. The lungs were clear to auscultation and systolic heart murmur was audible over the apex. The abdomen was soft, without organomegaly or mass. The thyroid gland was moderately and diffusely enlarged, but soft and smooth. Bruit was audible over the thyroid gland. When pain stimuli were given she responded by moving her extremities. Her pupils were round and reactive to light sluggishly. Oculocephalic reflex was full to all directions. She was immediately given 100 ml of 50% glucose and fursultiamine hydrochloride 100 mg intravenously as her blood glucose was 12 mg/dl. Her consciousness level improved up to lethargy with motor restlessness and profuse sweating. Her head CT study and chest roentgenograms revealed no abnormality, and electrocardiograms showed sinus tachycardia.

The CBC and blood chemistry indicated marked leukocytosis (white blood cell count 30,790/mm³, neutrophil 94%), mild normocytic anemia (red blood cell count 339×10⁴/mm³, hemoglobin 9.4 g/dl, hematocrit 27.2%, mean cell volume 80 fl, mean cell hemoglobin 27.7 pg and mean cell hemoglobin concentration 34.6%), and platelets 12.5×10⁴/mm³. C-reactive protein was 12.6 mg/dl, prothrombin time 15.1 seconds (10-13.5 sec), activated partial thromboplastin time 44.2 seconds, and fibrinogen 434 mg/dl (200-400 mg/dl). Serum electrolytes revealed hyponatremia of 124 mEq/l, potassium 4.0 mEq/dl, and chloride 92 mEq/dl. Hypoproteinemia was present; total protein was 5.6 g/dl. (albumin 2.7 g/dl) and uric acid was high 9.4 mg/dl. Blood urea nitrogen was 23 mg/dl and creatinine 1.0 mg/dl. Arterial blood gas showed pH 7.38, PCO₂ 28.6 mmHg, PO₂ 60.2 mmHg, HCO₃ 17.2 mmol/l and BE -6.1. Serum lipids were decreased; triglyceride 76 mg/dl, total cho-
lesterol 66 mg/dl, and high density lipoprotein 34 mg/dl. Total bilirubin was high (4.53 mg/dl) and, liver and muscle enzymes were moderately increased: aspartate aminotransferase (AST) 200 IU/l, alanine aminotransferase (ALT) 91 IU/l, LDH 775 IU/l, and CPK 399 IU/l (normal 24–195 IU/l). Plasma ketone bodies were; total ketone 93 mol/ml (26–122 mol/mg), acetoacetetic acid 39 μmol/l (13–69 μmol/l), and 3-hydroxybutyric acid 54 μmol/ml (0–76 μmol/l). CSF (cerebrospinal fluid) examination on November 14, 1996 revealed normal opening pressure (170 mmH2O); it was watery clear, cell counts 7/mm3, sugar 18 mg/dl, and protein 32 mg/dl.

On November 15, 1996 we examined the following endocrine studies. Thyroid stimulating hormone (TSH) was less than 0.08 μU/ml (normal range 0.52–3.79 μU/ml), free T4 4.7 ng/dl (normal range 1.0–1.9 ng/dl) and T3 156 ng/dl (normal range 80–180 ng/dl). Anti-TSH receptor antibody was 41.7% (normal range ±15%), thyroxine-binding globulin 11.9 μg/ml (normal range 14–28 μg/ml), and thyroglobulin 79 ng/ml (normal range below 30 ng/ml). Anti-microsomal and anti-thyroglobulin antibodies were negative. Glucose regulatory hormones, measured after intravenous administration of methylprednisolone sodium succinate 500 mg, revealed GH 2.4 ng/ml (normal range 0.28–8.70 ng/ml), glucagon 81 pg/ml (normal range 23–197 pg/ml), and ACTH 11.9 pg/ml (normal range 7.1–53.8 pg/ml). Serum immunoreactive insulin (IRI) ranged from 11.8 to 21.2 μU/ml and urine C-peptide immunoreactivity was 268 μg/day (41–145 μg/day). Anti-insulin (4%), anti-glutamate aspartate 1-decarboxylase (GAD) and anti-pancreas cell antibodies were all negative. Urine 17-OHCS after steroid administration (November 15, 1996) was 20.6 mg/day (1.6–8.8 mg/day).

**Clinical Course**

After correction of hypoglycemia, intravenous high-caloric fluid therapy was started and in 24 hours she became hypoglycemic requiring intravenous continuous insulin infusion. Despite her being maintained in a normoglycemic state, she remained lethargic and restless together with persistent tachycardia, profuse sweating, fever and limb tremor. Since thyro-

![Figure 1. Clinical course of the patient. JCS: Japan coma scale, BT: body temperature, RR: respiratory rate, HR: heart rate, BP: blood pressure, WBC: white blood cell, CPK: creatine phosphokinase, CRP: c-reactive protein, BS: blood sugar, iv: intravenous injection.]
Hypoglycemic Coma with Thyrotoxic Storm

Toxic storm was most likely complicating the clinical picture, we initiated anti-thyroid therapies from November 18, without awaiting the results of thyroid function studies (Fig. 1). Propranolol 2 mg was intravenously given slowly under cardiac monitoring, immediately followed by oral thiamazole (20 mg) and, after one hour, iodide (40 mg) via the nasogastric tube. Totally, thiamazole 120 mg and iodides 166 mg were given that day and thereafter. Methylprednisolone (200 mg) was also infused intravenously for the first 3 days and then 6 mg of dexamethasone for the following 4 days. Respiratory failure became apparent, however, due to respiratory muscle weakness (pH 7.104, PaO₂ 66.1 mmHg, PaCO₂ 100.8 mmHg, HCO₃⁻ 31.5 mmHg, O₂SAT 83.6%), necessitating the respirator assist. It was also apparent that she had already developed profound thyrotoxic myopathy, characterized by marked weakness and severe wasting of the muscles involving the four extremities and trunk. Her consciousness improved and became almost alert in a few days, and WBC and CRP were gradually normalized. Thiamazole was then reduced to 60 mg/day and dexamethasone to 2 mg/day. However, ten days after initiation of antithyroid treatment (November 26, 1996), she became somnolent again. She was slightly febrile (37.1°C), heart rate up to 160/min and CRP 6.3 mg/dl. Chest roentgenograms revealed infiltrating shadows in the right inferior lung field with pleural effusion, and pseudomonas maltophilia was found by sputum culture. She became mentally clear again, as the pneumonia was under control. However, on December 9, she complained of chest pain, and was tachycardic (150/min) with blood pressure of 150/90 mmHg. She was given a sublingual nitroglycerin (Nitropen 0.3 mg), as ECG showed a slight elevation of ST in precordial recordings, and soon it became normal. Because of persistent tachycardia, she was given propranolol hydrochloride 2 mg intravenously on December 10 and from December 11, 30 mg via the nasogastric tube. However, on December 12, she suddenly developed generalized convulsions and remained comatose. Despite resuscitative efforts, she developed cardiopulmonary arrest and died two days later. CT immediately after seizures disclosed bilateral low density area of the posterior hemispheric white matter, indicating the presence of posterior leukoencephalopathy syndrome (PLES) (Fig. 2).

Discussion

The case presented here was unusual in that profound hypoglycemia was masquerading the underlying thyrotoxic storm. In fact, when transferred to our hospital, she was hypoglycemic, quietly comatose and profoundly hypothermic. In general, a quiescent coma accompanied by cold skin or a lowered body temperature indicates excess ingestion of CNS-depr-
sant drugs, exogenous hypothermia, hypoglycemia, Wernicke's encephalopathy, or hypothryoidism. The fact that prompt correction of hypoglycemia did not improve her consciousness to full wakefulness, was in part explained by the damage to the CNS, as her hypoglycemic state had been prolonged before glucose infusion. However, our initial interpretation was not substantialized. The reversal of hypoglycemia brought about a clinically overt thyrotoxic storm that was characterized by restless-stuporous state associated with hyperthermia, tachypnea, tachycardia, and metabolic acidosis.

Hypoglycemia in the face of thyrotoxic storm is a rare event and it is difficult to explain why this case manifested profound hypoglycemia. The blood glucose level is influenced by multiple hormonal factors, that include thyroid hormones, glucagon, growth hormone, cortisol and catecholamines (1). Hyperthyroidism is a disorder of excess calorie expenditure. The mechanisms of hypoglycemia in this severely thyrotoxic patient might be explained in several ways. First, the facilitated glucose utility in the presence of hyperinsulinemia was not accompanied by the expected drive by glucagon, or other gluconeogenic factors, although the emergency situation did not allow us to measure necessary parameters prior to treatment. Glucagon plays a major role in the counterregulatory response in the hypoglycemic state (2). In the majority of the reported cases of thyrotoxic crisis, insulin resistance was apparently due to recruitment of gluconeogenic hormones and decreased insulin receptor binding (3), and often hyperglycemia is obvious. In hyperthyroid patients plasma glucose recovery from hypoglycemia is known to be faster than in healthy controls (2). However, during the glucagon tolerance test, plasma glucose shows a lower peak than in the normals (4). The glucagon level of the present case was in the normal range unexpectedly, and this might explain in part the hypoglycemic event.

Secondly, she was in a pre-adrenergic failure state. The original hypothesis has been advanced in the literature (5) in that the thyroid crisis occurs on the basis of a relative adrenocortical failure. Adrenal insufficiency occurs with a greater frequency in Graves’ disease on an autoimmune basis. Even in the absence of adrenal insufficiency, adrenal reserve may be deprived in thyrotoxic crisis, because of the inability of the adrenal gland to meet the accelerated turnover and disposal of glucocorticoids (5). The low level of serum sodium might support the presence of adrenocortical failure, although there was no chance to study in depth the adrenocortical function. However, the third and a major additional reason would be that the glycogen necessary for maintaining an adequate blood glucose level had been deprived in this particular patient, since she did not feed herself adequately and vomited frequently prior to hospitalization.

Remarkable in this patient was the appearance of profound generalized myopathy. Respiratory decompensation was apparent despite adequate control of thyroid function, and this indicates the compromised respiratory muscles, as has been reported (6, 7). The major reason why this patient developed a profound myopathy to the degree of respiratory failure, might be due to the delay in initiation of antithyroid therapy, as hypoglycemia did obscure the thyrotoxic state. Angina, a frequent complication in thyrotoxic patients, was explained by coronary artery spasm in the face of increased demand (8). This might be related to the occurrence of a final event; that is, PLES, as the CT demonstrated a characteristic hypodensity area in the posterior lobe bilaterally (9). The syndrome of PLES is characterized by neuroimaging evidence of the posterior hemispheric white matter edema, in the presence of seizure, impaired consciousness and visual phenomena. This syndrome is often associated with diverse systemic disorders; e.g., hypertensive encephalopathy, uremia, eclampsia, and the use of cyclosporine A, tacrolimus, interferon alpha and erythropoietin. Profound vasogenic edema due to angiospasm or angiopathy of the vessels supplying the posterior cerebral hemispheres is thought to be the mechanism (10, 11). To date, no association of PLES is reported with thyrotoxic storm. Although PLES is initially regarded to be reversible, our experience together with others indicates that the outcome may not be favorable (12, 13).

The important lessons in the present case is that hypoglycemia may masquerade the underlying thyrotoxic crisis, and that if recovery from hypoglycemic coma is delayed despite normalization of blood glucose, attention should be focused on the manifestation of thyrotoxic crisis.

References