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CASE REPORT

A case of congestive heart failure caused by secondary hypocortisolism

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Key Clinical Message

Congestive heart failure caused by secondary hypocortisolism is rare but clinically significant, because its appropriate treatment is effective. Severe hyponatremia with indefinite complaint resembling depression or persisting fever despite antibiotics may be important for establishing this diagnosis.

Keywords

Congestive heart failure, secondary hypocortisolism, severe hyponatremia.

Introduction

Various diseases can cause congestive heart failure. Common causes of left-sided congestive heart failure in adults are ischemic heart disease, arrhythmia, and vulvlar diseases. In addition to these common causes, there are other rare causes of left-sided congestive heart failure. There are a few reports of left ventricular (LV) dysfunction caused by isolated adrenocorticotrophic hormone (ACTH) deficiency [1]. Isolated adrenocorticotrophic hormone deficiency is a rare cause of secondary adrenocortical insufficiency and is difficult to diagnose [2–4]. We experienced a case of congestive heart failure caused by isolated ACTH deficiency. The finding of hyponatremia led to this diagnosis. Isolated ACTH deficiency should be considered when congestive heart failure of unknown origin is found.

Case

A 77-year-old woman was transferred to our hospital for evaluation and treatment of congestive heart failure. She had been followed up for the possibility of depression without antidepressant during the previous 4 months because she complained of prolonged general malaise, loss of appetite, loss of concentration, and insomnia. Finally, she became unable to walk and was admitted to a psychiatric hospital, from which she was referred to our institution. She was only administered clomipramine for 2 days as a psychotropic agent, but it was ineffective. Doctors in the psychiatric hospital began to suspect that she did not have psychiatric disorders. Her plasma sodium level was 125 mEq/dL, and her brain natriuretic peptide (BNP) level was elevated. She was diagnosed with congestive heart failure in the psychiatric hospital and referred to our hospital. She had no past medical history of traumatic brain injury or cerebrovascular diseases. She had no history of steroid or diuretic use. Her vital signs at admission were as follows: blood pressure, 123/73 mmHg; heart rate, 101 beats/min; body temperature, 36.2°C; respiratory rate, 18 breaths/min; and SpO2, 99% at room air. With regard to her general condition, she was disoriented. Her voice was feeble and barely audible. She was thin, had joint contractures, and was no longer able to ambulate. She had pitting edema in both legs. Peripheral blood tests showed mild to low levels of red blood cells ($480 \times 10^4/\mu L$). Biochemical analysis showed low levels of albumin (2.5 g/dL), sodium (119 mEq/L), and chloride (88 mEq/L), and high levels of C-reactive protein (2.21 mg/dL), and BNP (610 pg/mL).

Hyperkalemia, eosinophilia, and hypoglycemia were not present. The plasma osmolity was 243 mosm/kg. The TSH level was slightly high (5.6 mIU/L), but the F-T4 was normal. Urine tests showed a high osmolity (330 mosm/kg) and sodium level (114 mEq/L). The serum vitamin B1 level was normal. Chest radiograph showed cardiomegaly (cardiothoracic ration of 60%) and pleural effusion. Electrocardiogram showed inverted T waves in leads II, III, aVF, and V4-6.

Echocardiography showed diffuse hypokinesis of the left ventricular wall and slight pericardial effusion. There were no valvular abnormalities. Contrast-enhanced computed tomography (CT) showed bilateral pleural effusion, chronic cholecystitis, and no appreciable findings to explain her condition. Computed tomography of the magnetic resonance imaging brain of the brain especially focused on the pituitary gland showed no abnormal findings.

There seemed to be no obvious diseases to explain the patient's condition. We began to compensate for hyponatremia with 3% saline and provided enteral feeding. Because she had no signs of congestion and did not complain of dyspnea, we did not use diuretics or oxygen for her treatment, while we continued to search for a cause. As differential diagnosis of hyponatremia, we considered adrenal insufficiency or SIADH, in our patient because plasma osmolity was low, urinary osmolity was high, the urinary sodium level was greater than 40 mEq/L, the F-T4 was normal, and she has no apparent hypovolemia.

Three days after the patient's admission, she suddenly developed a fever. We examined her but could not detect the cause of fever. We administered antibiotics (CTRX2 g/day) for 1 week without the known cause of the fever, but they were ineffective.

Approximately 10 days after the patient's admission, a hormonal assessment was conducted. ACTH and cortisol

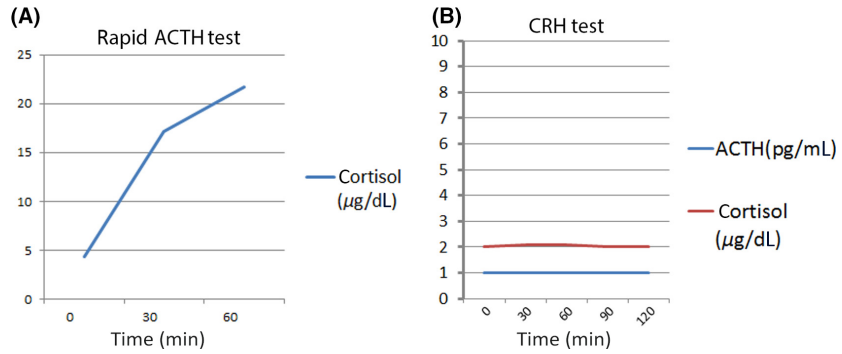

Figure 1. (A) Result of rapid adrenocorticotrophic hormone (ACTH) test. During the test, 250 μg synthetic ACTH was administered as an intravenous bolus for the measurement of serum cortisol after 30 and 60 min. Cortisol response was normal. (B) Result of corticotropin-releasing hormone (CRH) test. During the test, 100 μg human CRH was administered as an intravenous bolus for the measurement of serum adrenocorticotrophic hormone and cortisol during the following 2 h. ACTH and cortisol were unresponsive.

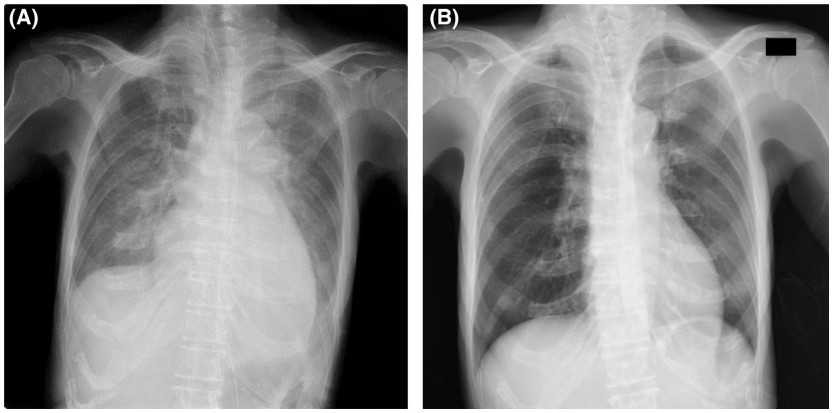

Figure 2. Chest radiograph on admission (A) and on the 47th day of hospitalization (B) at approximately 3 weeks after steroid therapy. Cardiomegaly (CTR; cardiothoracic ration of 60%) and pleural effusion were observed on admission. Effusion disappeared and the CTR had decreased during treatment.

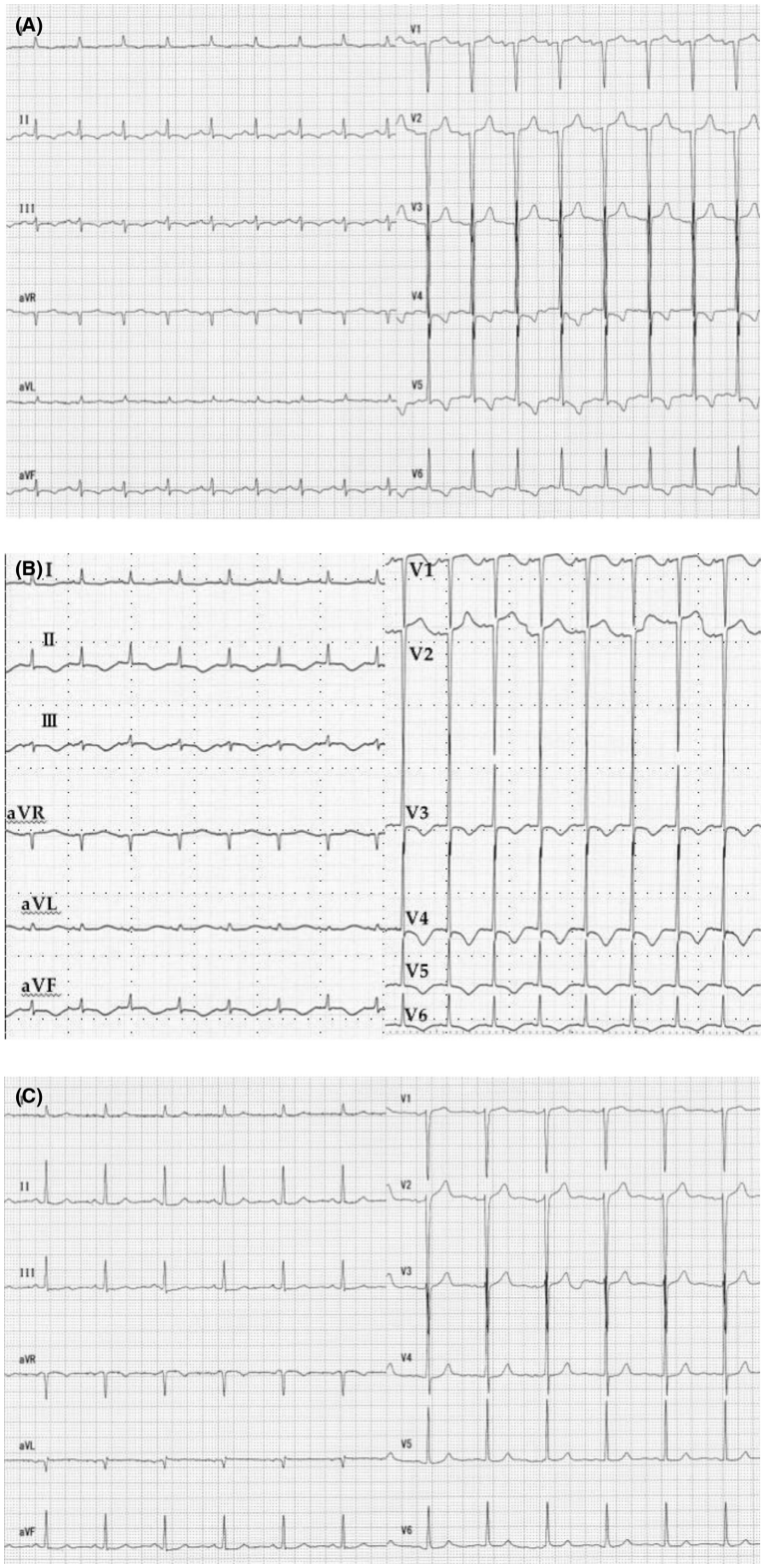

Figure 3. (A) ECG on admission: Inverted T waves were observed in the II, III, aVF, and V4–6 leads. (B) ECG on the 51st day of hospitalization just before discharge: Inverted T waves were normalized at about 4 weeks after steroid therapy. (C) ECG on the 3rd day of hospitalization when takotsubo cardiomyopathy was suspected: Inverted T waves with QT prolongation can be observed in the II, III, aVF, and V3–6 leads.

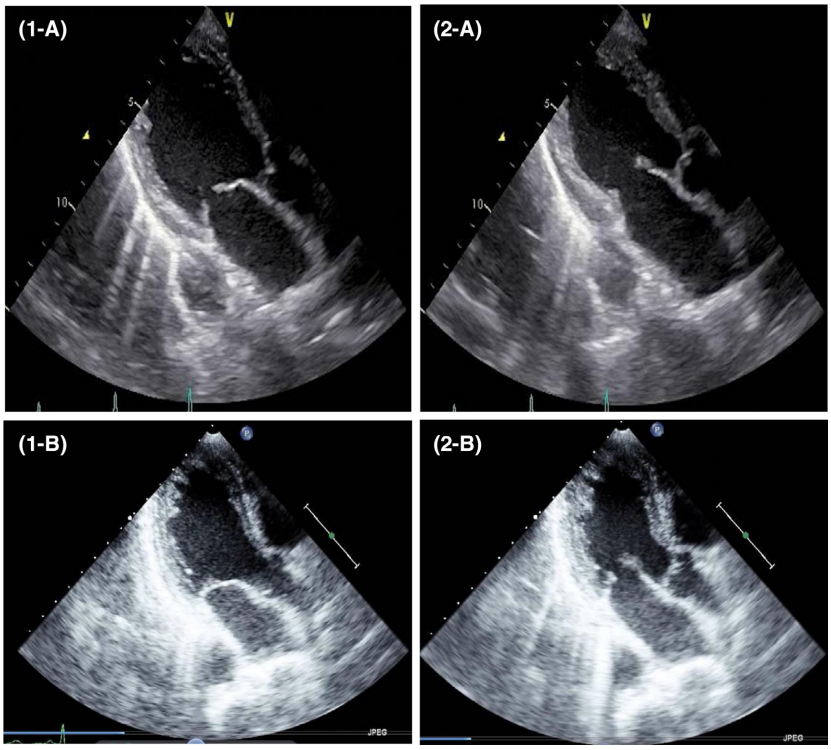

Figure 4. (1) Echocardiography performed on the 9th day of hospitalization just before starting steroid therapy. Diffuse hypokinetic and slight LV dilation can be seen. (1-A) Systolic phase and (1-B) diastolic phase. (2) Repeated echocardiography performed on the 51st day of hospitalization at approximately 4 weeks after steroid therapy. LV wall motion was normalized. (2-A) Systolic phase and (2-B) diastolic phase.

levels were low (<2.0 pg/mL and 2.9 μg/dL, respectively). Her urinary free cortisol level was low. These findings were suggestive of isolated ACTH deficiency. Neither ACTH nor cortisol levels adequately increased in response to administration of corticotropin-releasing hormone (Fig. 1). However, the cortisol level increased in response to administration of ACTH. The finding suggested that her adrenal glands remained functional. Based on these laboratory and clinical findings, we established a diagnosis of secondary adrenal insufficiency caused by isolated ACTH deficiency. We could not measure other hormonal data at this point. We measured LH, FSH, PRL, and GH 1 month later, and all values were normal.

Based on this diagnosis, hydrocortisone was started at 20 mg/day. Shortly after this administration, her sodium level normalized, and her fever subsided. After a few days of initiation of steroid replacement therapy, the inverted T waves that were observed in previous electrocardiograms were normalized. The small pericardial effusion disappeared on echocardiography, and there was improvement of the LV ejection fraction. The patient's physical condition gradually improved, and she was finally able to ambulate unassisted. Her cognitive status also improved and her sense of orientation was normalized. A few days before her discharge, she obtained a perfect score in Hasegawa's Dementia Rating Scale (Figs 2–4).

Discussion

We experienced a rare case of congestive heart failure caused by secondary hypocortisolism. There have been a few previous reports of secondary hypocortisolism, in which this condition leads to lethal arrhythmias or takotsubo cardiomyopathy [5–8]. A adrenocortical insufficiency can also cause nonspecific electrocardiographic abnormalities, such as flat or inverted T waves, a prolonged QT interval, low voltage, a prolonged PR or QRS interval, and a depressed ST segment [9]. Additionally, LV dysfunction rarely occurs with adrenocortical insufficiency. Previous reports have indicated that severe myocardial dysfunction is an uncommon but serious complication of adrenal insufficiency [1, 10]. In such cases, electrocardiographic and echocardiographic abnormalities normalized after steroid replacement therapy. As in previous reports, the ST changes and LV dysfunction in this case were reversed shortly after initiating steroid therapy.

Unlike other cases of congestive heart failure, the progression to congestive heart failure was atypical in our case. The patient's condition progressively worsened during the course of 4 months. Therefore, in our case, the disease course evolved too quickly to be a neuromuscular disease and too slowly to be myocarditis. We considered a systemic illness, such as collagen or endocrine disease, as the potential cause. However, LV dysfunction on echocardiography was apparent but unspecific. Typical features of coronary artery disease, such as asynergy of wall motion, septal thinning, and concentric thickening of the myocardium and local aneurysms, were not observed. Finally, CT coronary angiography excluded coronary artery disease.

Some of the laboratory data were helpful for the differential diagnosis of our patient. Her sodium level was low, but the levels of other electrolytes were normal. The level of TSH was slightly high, and free T4 was normal. Finally, the low levels of ACTH and cortisol led to the patient's diagnosis. After steroid replacement therapy, the patient achieved a full recovery. Isolated ACTH deficiency clearly explained her condition and symptoms.

Diagnosing adrenal insufficiency is difficult because hyponatremia and depression are often concomitant with heart failure. Many reports have shown hyponatremia is one of the most common electrolyte abnormalities in patients with heart failure, with a prevalence ranging from 10% to −54%. Additionally, hyponatremia is an independent poor prognostic factor of heart failure [11–16]. However, severe hyponatremia with serum sodium levels below 130 mEq/dL rarely occurs, with a prevalence of 2–5% in patients with acute decompensated heart failure [17, 18]. In our case, the serum sodium level at admission was 119 mEq/L, which is a relatively low value for heart failure. This was an important factor for establishing the diagnosis. When treating a patient with heart failure with severe hyponatremia (serum sodium level <130 mEq/L), another cause for the hyponatremia should be considered. Furthermore, among differential diagnosis of hyponatremia, when the patients have history of indefinite complaint resembling depression and fever with unknown cause, adrenal insufficiency is likely.

Conflict of Interest

None declared.

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