Case Report

A Case of Postpartum Hypopituitarism (Sheehan's syndrome) Associated with Severe Hyponatremia and Congestive Heart Failure.

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A case of a 69-year-old woman with postpartum hypopituitarism (Sheehan's syndrome) associated with congestive heart failure and severe hyponatremia is reported. She developed congestive heart failure after cholecystectomy, and marked improvement was noted by treatment with oxygen, digoxin, furosemide, and dopamine. Two weeks after surgery, she became confused, and hyponatremia, 106 mEq/l, was detected. She was referred to us. Past history revealed postpartum hemorrhage at the age of 34, followed by a failure to lactate, amenorrhea, and loss of pubic hair and axillary hair. Hypertonic saline (1.5%) infusion and water restriction increased her serum sodium concentration into the low normal range. Despite hyponatremia, serum vasopressin was not suppressed. Basal levels of pituitary hormones were low, and they did not respond to provocation tests. Marked impairment of water excretion was noted, and plasma vasopressin was not suppressed during a water-loading test. These results suggest that inappropriately increased vasopressin played an important role in impaired water excretion, and this defect could have been responsible for the development of hyponatremia and congestive heart failure in this patient.

Key Words: Vasopressin, Hyponatremia, Water loading test, Impaired water excretion

Postpartum pituitary insufficiency (Sheehan's syndrome) is a rare disorder typically presenting several signs and symptoms. Hyponatremia may be an accompanying abnormality of this syndrome and is believed to be a result of impaired water excretion by the kidney.1,2 However, the mechanisms responsible for the development of hyponatremia are still controversial, and cortisol deficiency3,4, abnormal vasopressin release5-8, decreased aldosterone production9,10, and thyroid hormone deficiency11 have been proposed. We described a patient with hypopituitarism with severe hyponatremia and congestive heart failure.

CASE REPORT

A 69-year-old woman was referred to our department from the department of surgery for evaluation and treatment of severe hyponatremia. Right hypochondralgia had developed five weeks previously, cholelithiasis was diagnosed and cholecystectomy was performed. Mild cardiomegaly (cardio-thoracic ratio, 60%) was present before the operation, and the signs and symptoms of congestive heart failure developed on the second day after surgery (Fig. 1). Oxygen, digoxin, furosemide, and dopamine were given, and marked improvement was noted in one week. Serum sodium concentrations were 133-136 mEq/l during this period. Two weeks after surgery, while 500 ml of 5% dextrose in water was being administered...
daily, the patient became confused and dis-orientated. Hyponatremia, 106 mEq/l, was diagnosed, and the patient was referred to our department.

This woman had been followed by our department for treatment of rheumatoid arthritis and congestive heart failure for 10 years, and her serum sodium concentrations were within normal limits during that period. Her previous pregnancies in which lactation did occur were unremarkable. However, the third pregnancy at age 34 had been followed by massive postpartum hemorrhage, and several hundred milliliters of blood were transfused. She did not lactate after delivery; furthermore, she did not menstruate afterward and progressive loss of axillary hair and pubic hair was noted.

Physical examination revealed hypothermia (34.6°C), blood pressure was 120/80 mmHg without orthostatic change, and heart rate was 72 beats/min. Heart sounds were normal, and no rale was audible. There was no axillary hair or pubic hair, and the skin was dry without any hyperpigmentation. The thyroid was normal. No pitting edema was present in her legs. Neurologically, she was confused and disorientated, but no focal sign was found.

Laboratory data disclosed marked hyponatremia and hypochloremia with normal serum potassium. Despite low serum osmolality (235 mOsm/kg), urine osmolality was higher than that of the serum (460 mOsm/kg), and urinary sodium concentration was high (70 mEq/l, Table 1). Furthermore, plasma vasopressin was not suppressed (Table 2). Mild elevations of transaminases and moderate elevations of creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) were noted.

External warming with blankets was started to treat the hypothermia, and hypertonic saline (1.5%) was given intravenously. Serum sodium concentrations increased to 114, 119, and 127 mEq/l on the second, third, and fourth days after starting the infusion of hypertonic saline. Hypertonic saline was discontinued on the sixth day. Her sensorium gradually cleared in parallel with the increase in serum sodium concentrations, and her temperature became normal on the third day. Thereafter, her serum sodium concentration remained stable, around 130 mEq/l, with a water restriction of 700 ml/day and a dietary sodium chloride intake of 10 g/day. Electrocardiogram was normal. Echocardiogram revealed no ab-
normalities except mild left ventricular hypertrophy.

Postpartum hypopituitarism was suspected from her history, and endocrine examinations were performed. Plasma levels of thyroid hormones were low, and thyroid-stimulating hormone (TSH) in plasma did not increase in response to thyrotropin-releasing hormone (TRH). Responses of prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and growth hormone (GH) to their stimulation tests were all blunted (Table 3). Basal levels of adrenocorticotropic hormone (ACTH) and cortisol were lower than normal. Finally, a water-loading test (20 ml/kg) revealed markedly impaired urinary excretion of water (only 20.5% of loaded volume in four hours), despite decreases in serum sodium and osmolality during water loading. Urinary sodium concentration and osmolality remained high. Plasma vasopressin were not suppressed (Fig. 2).
DISCUSSION

The present patient had a history of postpartum hemorrhage, followed by a failure to lactate, menorrhagia, and loss of pubic hair and axillary hair. Endocrine examination revealed panhypopituitarism, as evidenced by low basal levels of pituitary hormones and failure to respond to provocation tests. Therefore, the patient was diagnosed as having postpartum pituitary insufficiency (Sheehan’s syndrome).

Hyponatremia in hypopituitarism occurs more frequently than is generally recognized\(^2\). Purnell et al.\(^12\) reported 9 of 13 patients with Sheehan’s syndrome had low serum sodium, less than 133 mEq/l. Bethure and Nelson\(^13\) have emphasized this feature of decreased pituitary function and suggested that the diagnosis of pituitary insufficiency should be considered in all patients with unexplained hyponatremia. The mechanisms responsible for the development of hyponatremia in patients with hypopituitarism have been shown to be multifactorial. These factors are 1) increased secretion of vasopressin because of glucocorticoid deficiency or other factors, such as decreased volume or cardiac output; 2) urinary loss of sodium caused by aldosterone deficiency; 3) impaired water excretion because of thyroid hormone deficiency; and 4) impaired water excretion caused by vasopressin independent factors, such as decreased tubular fluid delivery to the diluting site\(^4\). Hyponatremia in hypopituitarism may in part be a result of impaired water excretion, i.e., a defect in renal diluting capacity\(^1,2,14\). Vasopressin-independent mechanisms, such as decreased tubular fluid delivery to the diluting site because of a decrease in cardiac output\(^9\), impairment of the function of the ascending limb\(^15\), and a change in the permeability of the distal nephron caused by factors other than vasopressin, such as glucocorticoid or mineralocorticoid, have been proposed\(^3,15\). However, it has been shown that inappropriately elevated levels of vasopressin play an important role in the pathogenesis of the development of hyponatremia\(^5,8\). An effective or absolute decrease in circulating blood volume because of glucocorticoid or mineralocorticoid deficiency have been shown to stimulate vasopressin release nonosmotically\(^4,7\), and cortisol has an important role in the maintenance of the normal inhibition of vasopressin in response to hypotonicity\(^6,16\). The present case demonstrated high urine osmolality and assayable plasma vasopressin level in the face of marked hypotonicity and low serum osmolality. Moreover, water excretion was impaired, and plasma vasopressin remained unchanged despite a decrease in serum sodium and osmolality during the water-loading test. These results suggest that hyponatremia in this case was at least in part a result of inappropriately increased vasopressin. On the other hand, the role of aldosterone deficiency for the development of hyponatremia in this patient seems less probable, because plasma aldosterone level was normal and signs of volume depletion, hyperkalemia and prerenal azotemia were not found, which are usually seen in patients with aldosterone deficiency\(^14\). Also, we could not rule out the possibility of the role of thyroid hormone deficiency for the development of hyponatremia. However, it has been shown that in patients with myxedema, plasma vasopressin was elevated and could not be suppressed during water loading\(^11\). Therefore, it is possible that vasopressin might have some role in the patient’s inability to excrete water not only in glucocorticoid deficiency, but also in thyroid hormone deficiency.

The other interesting point in this case is the development of congestive heart failure immediately after operation. Although the patient had been followed for congestive heart failure, she had no signs or symptoms of failure before surgery. However, congestive heart failure developed while she was given the usual amount of intravenous fluid after operation. Because she did not develop hypovolemic shock, which is a characteristic sign during adrenal crisis, and because her congestive heart failure improved without glucocorticoid replacement\(^17\), it therefore seems unlikely that this episode was due to acute adrenal insufficiency. Also, hypothyroidism did not seem to play an important role in the genesis of congestive heart failure because pericardial effusion was not present and her congestive heart failure improved without replacement by thyroid hormone. It is well known that plasma vasopressin levels increase...
markedly immediately after an operation and gradually fall to preoperative levels after three or four days, and these increased levels of vasopressin can be associated with excess water retention¹⁸,¹⁹. In the present case, besides severely impaired water excretion, evidenced during water loading, plasma vasopressin levels might have increased after the operation. Therefore, it seems possible that in the present case congestive heart failure was caused not only by impaired water excretion because of pituitary hormone deficiency, but also by a possible increase in vasopressin after the operation that might have been an aggravating factor in the pathogenesis of the development of congestive heart failure.

REFERENCES