A Case of Lymphocytic Hypophysitis With Masked Diabetes Insipidus Unveiled by Glucocorticoid Replacement

Chun-Hao Huang, MD, Kang-Ju Chou, MD, Po-Tsang Lee, MD, Chien-Liang Chen, MD, Hsiao-Ming Chung, MD, and Hua-Chang Fang, MD

- Lymphocytic hypophysitis may involve the pituitary gland and various hormonal abnormalities. A 72-year-old man presented with euvoicmic hyponatremia caused by glucocorticoid deficiency. After glucocorticoid replacement, hyponatremia in the presence of dilute urine was found. Central diabetes insipidus (DI) was confirmed later by a significant increase in urine osmolality after vasopressin administration. Brain magnetic resonance imaging showed a pituitary mass and loss of hyperintense signal in the posterior pituitary gland on T1-weighted imaging. The patient underwent a transsphenoidal adenectomy, and pathological examination of dissected tissues showed a typical finding of lymphocytic hypophysitis. Two months after surgery, the patient’s central DI had resolved sufficiently that 1-desamino-8-D-arginine vasopressin therapy was discontinued without polyuria. However, he was kept on glucocorticoid and levothyroxine therapy. In conclusion, lymphocytic hypophysitis may feature a concealed central DI caused by glucocorticoid deficiency–associated hyponatremia. Am J Kidney Dis 45:197–200. © 2004 by the National Kidney Foundation, Inc.

INDEX WORDS: Lymphocytic hypophysitis; hyponatremia; glucocorticoid; central diabetes insipidus (DI).

LYMPHOCYTIC HYPOPHYSITIS was described first in 1962 on an autopsy specimen by Goudie and Pinkerton.1 It can involve the anterior and/or posterior lobe of the pituitary gland and corresponding hormone deficiencies. Thyroid-stimulating hormone and corticotropin (ACTH) are the hormones most commonly affected.2,3 It also may present with isolated antidiuretic hormone (ADH) impairment, previously presumed to be idiopathic central diabetes insipidus (DI).4 Among the pituitary hormone deficiencies, ACTH and ADH impairment may have opposite influences on water balance. The former may cause exaggerated release of ADH and hyponatremia, whereas the latter may result in overt water diuresis and, sometimes, hypernatremia. It therefore is interesting to learn exactly how panhypophysitis will behave in terms of water balance. Investigators of previous relevant reports in which hyponatremia associated with glucocorticoid deficiency or central DI was described did not focus on this issue.2,3

Our patient presented with glucocorticoid deficiency–associated hyponatremia, in which central DI was uncovered by glucocorticoid administration. This rarely has been reported. The pathophysiological process underlying this manifestation is fascinating and noteworthy. In this report, the mechanism of this clinical manifestation is discussed and the relevant literature is reviewed.

CASE REPORT

A 72-year-old man presented with general weakness and diminished appetite that had lasted 1 month. The patient had no history of visual disturbance, headache, polyuria, polydipsia, cold intolerance, or significant body weight change. He denied the use of herbs or diuretics. On physical examination, blood pressure was 120/80 mm Hg, pulse was 51 beats/min, and body temperature was 35.5°C. He had no signs of dehydration or edema. Physical evidence of adrenal insufficiency and hypothyroidism, such as hyperpigmentation of the skin over bony prominences, coarse hair and skin, slow speech and hoarse voice, or dull facial expression, was absent. Neurological examination and other physical findings were unremarkable.

Blood biochemistry tests showed hypo-osmolar hyponatremia, with a sodium level of 124 mmol/L and osmolality of 249 mOsM/kg (mmol/kg). Urine counterparts showed a sodium level of 71 mEq/L (mmol/L) and osmolality of 630 mOsM/kg (mmol/kg). Other blood biochemistry results showed the following values: creatinine, 0.8 mg/dL (70.7 μmol/L); urea nitrogen, 11 mg/dL (3.9 mmol/L); and uric acid, 2.9 mg/dL (172.5 μmol/L). He had a low plasma renin level of 5.7 ng/mL/h (1.58 ng/L/s; standing 1 hour, 3.6 to 63.7 ng/mL/h), indicating a euvolemic state. Euvolemic hyponatremia caused by a syndrome of inappropriate antidiuretic hormone secretion, glucocorticoid deficiency, or hypothyroidism was suggested. We measured the patient’s thy...
roid function and morning cortisol level. Cortisol level was less than 1.0 μg/dL (27.6 nmol/L).

After glucocorticoid replacement, the patient’s symptoms were dramatically reduced. However, 4 days after glucocorticoid replacement, his serum sodium level increased to 154 mEq/L (mmol/L). In the meantime, urine osmolality was 156 mOsm/kg (mmol/kg). The patient experienced polyuria and body weight loss. Although the patient was thirsty, he followed our prescribed restrictions on fluid intake. Next, vasopressin, 10 units, was administered subcutaneously to distinguish central DI from nephrogenic DI. One hour after administration, we observed a significant increase in urine osmolality to 353 mOsm/kg (mmol/kg), indicating central DI. Together, findings strongly suggested a hypothalamic-pituitary lesion (Table 1). These hormone levels were normal, except for a slight decrease in free thyroxine of 0.4 ng/dL (5.1 pmol/L). Although they were within the reference ranges, a serum thyroid-stimulating hormone level of 1.6 mIU/L and ACTH level of 17.2 pg/mL (3.8 pmol/L) were low. In addition to 1-desamino-8-D-arginine vasopressin (Minirin, Ferring, Copenhagen, Denmark) and glucocorticoid, levothyroxine was administered.

Brain magnetic resonance imaging showed a 5 × 6 × 14-mm pituitary mass without compression on surrounding tissues and loss of hyperintense signal in the posterior pituitary on T1-weighted imaging (Fig 1). Because image study results suggested a pituitary adenoma, the patient underwent a transsphenoidal adenectomy. Pathological examination of dissected tissues showed diffuse lymphoplasmacytic infiltrates, a typical finding of lymphocytic hypophysitis (Fig 2). Two months after surgery, the patient’s central DI resolved and vasopressin therapy was discontinued without causing polyuria. However, he continued to take glucocorticoid and levothyroxine.

Table 1. Hormonal Levels at Presentation and After Surgery

<table>
<thead>
<tr>
<th></th>
<th>At Presentation and Before Surgery</th>
<th>6 Days After Surgery</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (μg/dL)</td>
<td>&lt;1.0</td>
<td>10.8</td>
<td>Morning, 9-23</td>
</tr>
<tr>
<td>ACTH (pg/mL)</td>
<td>17.2</td>
<td>6.8</td>
<td>0-46</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (mIU/L)</td>
<td>1.60</td>
<td>1.15</td>
<td>0.49-4.67</td>
</tr>
<tr>
<td>Free thyroxine (μg/dL)</td>
<td>0.4</td>
<td>Not done</td>
<td>0.8-1.9</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>10.7</td>
<td>5.8</td>
<td>Male, 2.8-12.1</td>
</tr>
<tr>
<td>Follicle-stimulating hormone (mIU/mL)</td>
<td>9.82</td>
<td>7.94</td>
<td>Male, 0.85-8.5</td>
</tr>
<tr>
<td>Luteinizing hormone (mIU/mL)</td>
<td>4.09</td>
<td>3.62</td>
<td>Male, 1.15-4.20</td>
</tr>
</tbody>
</table>

NOTE. To convert serum cortisol in μg/dL to nmol/L, multiply by 27.59; ACTH in pg/mL to pmol/L, multiply by 0.22; free thyroxine in ng/dL to pmol/L, multiply by 12.87; prolactin in ng/mL to μg/L, multiply by 1.

Fig 1. Magnetic resonance imaging of the brain and sella on sagittal T1-weighted imaging (A) before and (B) after gadolinium enhancement shows the absence of the hyperintense signal of the posterior pituitary gland (white arrow) and a 5 × 6 × 14-mm mass lesion (white arrow) within the anterior pituitary without compression of surrounding tissues, indicating a pituitary adenoma.
DISCUSSION

Interestingly, our patient’s central DI was masked by the presence of glucocorticoid deficiency–associated hyponatremia. This was uncovered after the patient received glucocorticoid replacement therapy. Among the reported cases of lymphocytic hypophysitis, our patient had a very unique presentation. A similar case was reported, but no definite diagnosis by pathological examination was made.5

ADH is synthesized in both supraoptic and paraventricular nuclei in the hypothalamus and transported within secretory granules through the supraoptic-hypophysial tract to the posterior pituitary, where granules are stored and secreted under osmotic stimulation.6,7 However, ADH produced in the paraventricular nucleus also gains access to the systemic circulation by entering the cerebrospinal fluid and portal system of the median eminence in the hypothalamus.7 Therefore, a lesion below the median eminence or a lesion of the posterior pituitary usually does not cause permanent DI. In addition, the synthesis and secretion of ADH and ACTH-releasing hormone is enhanced in the paraventricular nucleus of the hypothalamus after adrenalectomy, which removes negative feedback from the glucocorticoid.8-10

The brain imaging study of our patient showed a lesion confined to the anterior pituitary and sparing the surrounding tissues. Low serum ACTH and undetectable serum cortisol levels accounted for the initial presentation of hyponatremia that was caused by a lack of negative feedback from glucocorticoids on secretion of ADH and ACTH-releasing hormone from the spared paraventricular nucleus. Glucocorticoid replacement reestablished inhibition of glucocorticoid on ADH secretion from the paraventricular nucleus. This unveiled a masked posterior pituitary involvement and central DI. The pathophysiological process was well shown in our patient, who presented with water diuresis and hypernatremia after glucocorticoid therapy.

Hypothyroidism is a well-established cause of hyponatremia, although the mechanism is not well characterized.11-13 Hyponatremia in this clinical setting frequently is subtle and rarely draws significant attention in clinical practice.14 However, hypothyroidism in combination with secondary adrenal insufficiency may have contributed to our patient’s hyponatremia. In our investigation, glucocorticoid replacement without thyroxine was able to increase the patient’s sodium level, indicating that hypothyroidism did not have an important role in the genesis of his hyponatremia.

Characteristics of lymphocytic hypophysitis seen on brain magnetic resonance imaging have been presented in previous reports and include stalk thickening, diffuse enlargement of the pituitary...
gland, and homogeneous enhancement of gadolinium contrast medium. However, a hypodense lesion on the T1-weighted image after gadolinium enhancement was found in our patient, which is not characteristic of lymphocytic hypophysitis, but indicative of pituitary adenoma. Therefore, a strategy of surgical intervention for both accurate diagnosis and treatment was adopted. Nevertheless, the pituitary lesion in our patient was not big enough to compress the posterior pituitary or other surrounding tissues to compromise ADH secretion. In addition, the absence of a hyperintense signal in the posterior pituitary on T1-weighted imaging noted in our patient was a finding consistent with previously reported cases that presented with central DI. Therefore, even in a patient with an anterior pituitary lesion presenting as an adenoma on an imaging study, simultaneous loss of hyperintense signal in the posterior pituitary suggests an infiltrating disease, such as lymphocytic hypophysitis. Conservative treatment without surgical intervention should be considered in this clinical setting because spontaneous remission may occur.

In conclusion, lymphocytic hypophysitis may feature a concealed central DI caused by glucocorticoid deficiency–associated hyponatremia. Imaging study results for lymphocytic hypophysitis vary, and pathological examination remains the gold standard for accurate diagnosis. However, an anterior pituitary mass lesion free of involvement of the surrounding tissues, but accompanying loss of hyperintense signal in the posterior pituitary, suggests an infiltrating disease, such as lymphocytic hypophysitis.

REFERENCES


