Diabetes Insipidus and Lymphocytic Hypophysitis

Key words: hyponatremia, SIADH, glucocorticoid deficiency, hypopituitarism

Lymphocytic hypophysitis was first described in an autopsy specimen in 1962 by Goudie and Pinkerton (1). Lymphocytic infiltration of the pituitary gland is associated with complete or partial hypopituitarism and occurs exclusively in women, often during pregnancy or in the postpartum period. Hashimoto et al reviewed 124 cases, including 25 Japanese (2), and Beressi et al also reviewed 145 cases (3). The most common symptoms and signs are headache (60%) and visual field loss (40%) due to a pituitary enlargement occasionally associated with suprasellar extension (2, 3). An inflammatory lesion mainly exists in the anterior pituitary, which is termed "lymphocytic adenohypophysitis", resulting in anterior pituitary hormone deficiency including ACTH, TSH, LH, FSH and GH, either alone or in combination. Interestingly, the prolactin concentration is elevated in 30% of cases. In addition, 16 or 18% of cases of lymphocytic adenohypophysitis have been reported to show diabetes insipidus (DI), resulting from a lymphocytic infiltration to the infundibulum, stalk and posterior lobe of the pituitary gland, i.e. infundibulo-neurohypophysitis, leading to ADH deficiency. Imura et al reported that 9 of 17 patients with idiopathic DI demonstrated thickening of the pituitary stalk, enlargement of the neurohypophysis or both on MRI (4). The etiology of lymphocytic hypophysitis is unknown. However, the coexistence of other autoimmune diseases such as Hashimoto's thyroiditis, Addison's disease and/or type 1 diabetes mellitus strongly suggests autoimmune mechanisms. Therefore, lymphocytic hypophysitis has been considered to be a part of the type I autoimmune polyglandular endocrinopathy.

In this issue of the Journal, Iida et al (5) reported a transient lymphocytic panhypophysitis which demonstrated clinical features of the syndrome of inappropriate secretion of ADH (SIADH) at first followed by DI after glucocorticoid replacement.

See also p 991.

This is a very rare and interesting case when we consider the pathophysiological regulation of ADH secretion and the definition of SIADH. When their patient was admitted, his serum ADH concentration was 1.9 pg/ml, despite hyponatremia (124 mEq/*l*) and hypoosmolality (249 mOsm/*l*) associated with a urinary loss of sodium (157 mEq/*l*) and high urinary osmolality (669 mOsm/*l*). However, after administration of hydrocortisone at 15 mg/day based on the diagnosis of hypopituitarism (plasma ACTH level 7 pg/ml, serum cortisol level 1.4 μg/dl), polyuria amounting to 10 *l*/day appeared. His serum sodium concentration increased to 148 mEq/*l* and plasma osmolality to 307 mOsm/*l* . In response to 5% hypertonic saline infusion, urinary volume was not decreased and urinary osmolality remained low (186 mOsm/*l* at most), confirming the diagnosis of DI, so called "masked DI". It has been well known that glucocorticoid deficiency causes higher plasma ADH levels and impaired water diuresis, resulting in a hyponatremia in some cases (6). Recently, aquaporin 2, vasopressin-dependent water channel has been reported to be enhanced in the absence of glucocorticoid, resulting in an exaggerated action of ADH in the collecting tubules, comprising of the permissive action of glucocorticoid as the attenuator of ADH action (7). In this sense, it seems better for the authors not to use the term "SIADH" in this case with glucocorticoid deficiency. However, as the authors discussed in their article, there are only a few cases of lymphocytic hypophysitis associated with a hyponatremia followed by DI. If so, the marked hyponatremia observed in this case might be attributed to some other concomitant situation such as the leakage of ADH from the posterior pituitary gland during the development of infundibulo-neurohypophysitis. Alternatively, a concomitant hypothyroidism may exaggerate hyponatremia.

Although the majority of such patients have permanent destruction of all or a part of the pituitary gland and require chronic hormone replacement therapy, some patients show a transient course. The case reported in this issue recovered spontaneously five months later, suggesting that total destruction of the whole pituitary gland may not always occur. Thus, these patients should be evaluated at regular intervals to determine the necessity for persistent hormone replacement.

Shigehiro KATAYAMA, MD and Chizuko YOKOTA, MD
Department of Medicine,
Division of Endocrinology and Diabetes,
Saitama Medical School,
38 Morohongo, Moroyama-cho, Iruma-gun,
Saitama 350-0495

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