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CASE REPORT

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Severe hyponatremia as the presenting manifestation of primary empty sella syndrome

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Abstract

Severe hyponatremia is associated with neurological impairment and mortality. Furthermore, severe hyponatremia can be the first presentation of several diseases. Therefore, an appropriate investigation for the underlying causes of hyponatremia apart from the proper correction of sodium levels, might lead to a diagnosis of occult diseases.

KEYWORDS

empty sella, hyponatremia, hypopituitarism, syndrome of inappropriate antidiuretic hormone secretion

1 | INTRODUCTION

Hyponatremia, which is defined as lowering serum sodium concentration values below 135 mmol/l, is the most common electrolyte disorder in clinical practice.[1] Patients with hyponatremia are associated with neurological symptoms caused by cerebral edema, including headaches, confusion, seizure, and coma. In addition, hyponatremia can be the first presentation of several occult diseases such as lung cancer, cryptococcal, and tuberculosis meningitis.[2–4] The main pathogenesis of hyponatremia is excess water intake or inability of the kidney to excrete water, usually because of elevated serum antidiuretic hormone (ADH) levels.[5] Normally, ADH secretion is stimulated by high plasma osmolality and low effective circulating volume. Persistent ADH release in the presence of low plasma osmolality and normal blood volume is known as the syndrome of inappropriate antidiuretic hormone secretion (SIADH), which can result from various medication conditions. One of the important causes of inappropriate increased ADH secretion is adrenal insufficiency, which frequently presents as SIADH.[6] This report describes a case of a male patient with recurrent symptomatic hyponatremia. Management of serum sodium level together with the comprehensive workup for causes of hyponatremia results in the accurate diagnosis of the occult disease and proper therapy to the patient.

2 | CASE REPORT

A 47-year-old Thai man with no significant past medical history was presented with nausea, lethargy, generalized muscle weakness, and intermittent cramps for 1 month.

He visited the emergency department and had been admitted several times in 3 weeks. The laboratory evaluations on every visit showed severe hyponatremia (ranging from 107 to 112 mmol/L). After hypertonic saline infusion, his symptoms were improved and the laboratory was partially corrected. He was discharged from the hospital and advised to restrict fluid intake. After discharge, he drank water less than 800 ml per day. Five days after the latest admission, he developed nausea, vomiting, and progressive somnolence.

On physical examination, his blood pressure was 108/65 mmHg without orthostatic hypotension. His pulse rate was 70 beats per minute. He had a normal skin appearance and no dry skin or mucous membrane. The neurological examination was normal. He had no edema. The rest of the physical examinations were normal.

His blood chemistry showed serum sodium 111 mmol/L, potassium 3.8 mmol/L, chloride 81 mmol/L, bicarbonate 19 mmol/L, blood urea nitrogen 6 mg/dl, creatinine 0.53 mg/d, plasma glucose 90 mg/dl, and uric acid 1.3 mg/dl. Plasma and urinary osmolalities were 247 mOsm/Kg and 537 mOsm/Kg, respectively. His urinary sodium was 105 mmol/L.

A timeline of events pertaining to this case is shown in Table 1. He was initially treated with intravenous 3%NaCl during an acute phase. Serum sodium had risen to 118 mmol/L in the first 24 h. His clinical of euvolemic hyponatremia was compatible with SIADH. Fluid restriction (less than 600 ml/day) and oral sodium chloride tablets were prescribed. His serum sodium levels were stable at around 118–121 mmol/L. For other investigations, his chest radiograph was normal. Serum morning cortisol (8.00 A.M.) was 6.1 μg/dl. An adrenocorticotrophic hormone (ACTH) stimulation test was performed and revealed inadequate response to low-dose ACTH (serum cortisol levels were 10.11 μg/dl at 30 min and 8.4 μg/dl at 60 min, respectively; normal ≥18 μg/dl). ACTH levels were 18.8 pg/ml (normal 0–46 pg/ml). Serum hormone assays were requested and revealed thyroid-stimulating hormone (TSH) 1.498 mIU/L (normal 0.3–4.1 mIU/L), free thyroid hormone (FT4) 0.61 ng/dl (normal 0.8–1.8 ng/dl), prolactin 4.4 ng/ml (normal 2–25 ng/ml), and testosterone 0.262 nmol/L (normal 5.9 to 25.7 ng/dl). He was diagnosed with hypopituitarism (secondary adrenal insufficiency, central hypothyroidism, and hypogonadism).

Oral prednisolone 15 mg and levothyroxine 50 μg per day were started. Fluid restriction and sodium chloride tablets were discontinued. Serum sodium was normalized in 2 days with complete clinical improvement (Table 1).

The patient denied polyuria or galactorrhea. A pituitary magnetic resonance imaging (MRI) was performed. There was marked thinning of the anterior lobe of the pituitary gland about 1–2 mm in height in shallow sella

TABLE 1 Timeline and laboratory data

	Day −5 (before discharge from the latest admission)	Day 0	Day 1	Day 3	Day 4	Day 5	Day 6	2 weeks after discharge
Serum Na (mmol/L)	123	111	118	121	128	133	137	140
Plasma osmolality (mOsm/Kg)		247						
BUN (mg/dl)	5	6		8		9	10	14
Creatinine (mg/dl)	0.65	0.53		0.70		0.81	0.72	0.75
Urine sp.gr.		1.015		1.009		1.004		1.010
Urine osmolality (mOsm/Kg)	473	537		282				
Urine Na (mmol/L)	132	105		68		24		
Urine K (mmol/L)	12	8		18		19		
Treatment		3%NaCl 200 ml +Restrict fluid <600 ml	Restrict fluid <600 ml/day NaCl (300) 6 tablets per day		Prednisolone 15 mg and levothyroxine 50 μg per day			Prednisolone 7.5 mg and levothyroxine 50 μg per day

turcica without suprasellar or parasellar mass compatible with an empty sella (Figure 1). He was discharged with oral prednisolone 7.5 mg and levothyroxine 50 μg per day. Two weeks after discharge, his serum sodium was 140 mmol/L. Oral prednisolone and levothyroxine were continued, and testosterone replacement therapy was initiated. At a 6-month follow-up, the patient remained stable with a normal serum sodium level.

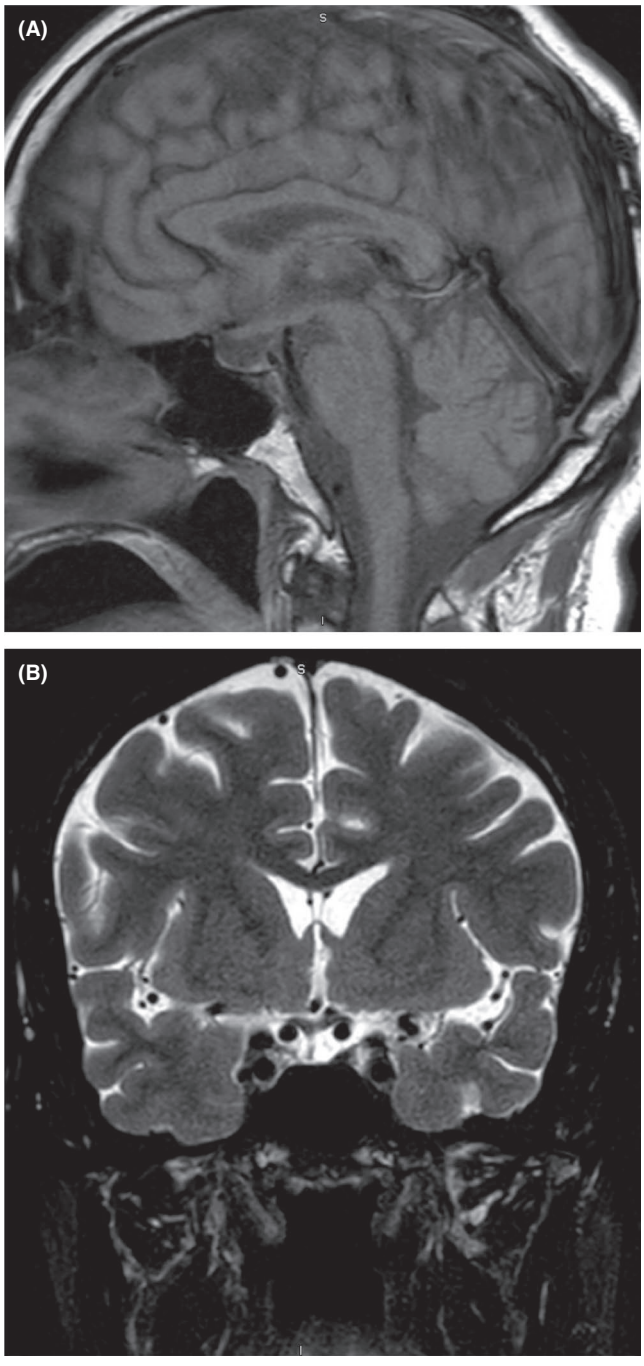

FIGURE 1 Sagittal T1 and coronal T2 sections of magnetic resonance imaging show marked thinning of the anterior lobe of the pituitary gland, about 1–2 mm in height in shallow sella turcica, and no evidence of suprasellar or parasellar mass

3 | FINAL DIAGNOSIS

Severe hyponatremia was due to secondary adrenal insufficiency with primary empty sella syndrome (PES).

4 | DISCUSSION

We report a case of recurrent severe symptomatic hyponatremia, which is defined as serum sodium ≤120 mEq/L.[7] This patient had hypotonic hyponatremia with high urine osmolality and high urine sodium excretion, which represented the effect of ADH and euvolemic status. Very low serum uric acid and blood urea nitrogen in this euvolemic hyponatremia patient suggested SIADH, which is the most common cause of euvolemic hyponatremia.[8] The continuous secretion of ADH despite hypo-osmolality and normal or increased effective circulatory volume results in impaired water excretion and hyponatremia. Numerous common medical conditions can cause SIADH, including malignancy, pulmonary diseases, central nervous system disorders, and various medications. Although most patients who were diagnosed with SIADH had no identifiable etiology, SIADH might be the first presentation of the primary occult disorder.

Our patient did not take any medication and had normal chest radiography. Serum morning cortisol was borderline. Further investigation, including ACTH level and ACTH stimulation test, was compatible with secondary adrenal insufficiency. The pathogenesis of hyponatremia in patients with adrenal insufficiency is mainly attributed to an increase in ADH secretion. ADH is produced together with corticotropin-releasing hormone (CRH) by the paraventricular nuclei of the hypothalamus to activate the synthesis and release of ACTH from the pituitary gland. Thus, as the end-organ hormone, cortisol has negative feedback to inhibit ACTH and CRH production.[9] Also, glucocorticoid appears to directly suppress ADH synthesis in magnocellular cells in the hypothalamus.[10] Therefore, patients with adrenal insufficiency have an inappropriately high ADH level as patients with SIADH can be effectively treated with glucocorticoid supplements. In our patient, severe hyponatremia was dramatically improved after glucocorticoid replacement, which suggested the etiologies of hyponatremia from adrenal insufficiency. Hormonal assays and MRI pituitary gland revealed hypopituitarism due to PES.

Primary empty sella syndrome is characterized by the herniation of the subarachnoid space within the sella, which is often associated with variable degrees of flattening of the pituitary gland in patients without previous pituitary pathologies. The pathogenesis of PES is still not well known but seems to be associated with sellar

diaphragm incompetence and upper sellar factors such as intracranial hypertension and variation of pituitary volume. PES is usually asymptomatic and mostly diagnosed as an incidental radiological finding.[11] Also, patients with PES could be presented with persistent headache or hormonal deficiencies. Severe hyponatremia as the presenting manifestation of empty sella syndrome is rare.

An appropriate investigation for hyponatremia and attentive workup for secondary causes of SIADH led to a diagnosis of hypopituitarism from empty sella syndrome and precise treatment with hormone replacement therapy in this patient. Our report highlights the importance of proper investigation for the underlying causes of hyponatremia apart from the correction of sodium levels.

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None.

CONFLICTS OF INTERESTS

The author(s) declared no potential conflicts of interest.

AUTHOR CONTRIBUTION

KT and AW wrote the initial draft. KT, PK, and SE supervised and revised the manuscript. All authors approved the final manuscript.

CONSENT

The patient provided informed consent for the write-up of this case report.

DATA AVAILABILITY STATEMENT

Data and materials may be made available upon written request to the corresponding author.

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