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An adult patient with hypernatremia: a case of water balance equipoise

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CASE PRESENTATION

A 67-year-old black man from Cape Verde was admitted to our emergency department with a two-day history of altered mental status and fever. Past medical history included hypertension and a well-controlled HIV infection, previously treated but with treatment abandonment for the past two years. On admission the patient presented with a Glasgow Coma Score of 9, hypotension (97/78 mmHg) and sinusal tachycardia. He had *de novo* impaired renal function (serum creatinine 5.93 mg/dL; previous creatinine was 0.53 mg/dL two years prior), hyperchloremic metabolic acidosis, elevated C-reactive protein, with unremarkable renal ultrasound. Findings on thorax x-ray, electrocardiogram, abdominal and renal ultrasound, serum electrolytes, urine dipstick (specific gravity 1.020) and head computer tomography (CT) scan were unremarkable. Cerebrospinal fluid study was unaltered except for increased proteins (103.2 mg/dl).

The patient was admitted to the intensive care unit (ICU) for septic shock of unknown origin with multiorgan dysfunction (central nervous system, kidney and liver), for which he started IV antibiotics and required vasopressors and mechanical ventilation. On the following days there was steady improvement of renal function and slight improvement of his mental status (to Glasgow Coma Scale 13). CT/MRI angiography revealed a solid hyperdense expansive lesion of the suprasellar cistern of unknown etiology.

After 11 days in the ICU, the patient was transferred to a ward, remaining hypotensive despite normovolemia (BP 80/50 mmHg). For this reason, laboratory assessment of pituitary gland function was requested (Table 1), which was suggestive of anterior hypopituitarism.

Table 1

Pituitary gland function tests

Test	Results	Reference range
tSH	1.42	0.35 –4.94 uUI/mL
fT4	< 0.4	0.70 – 1.48 ng/dL
ACTH	8.68	ND – 46 pg/mL
Plasma cortisol	0.9	Morning: 3.70 – 19.40 ug/dL Afternoon: 2.90 – 17.30 ug/dL
LH	0.13	0.57 – 12.07 mUI/mL
FSH	0.46	0.95 – 11.95 mUI/mL
Total testosterone	0.06	1.424 – 9.231 ng/mL
Free testosterone	< 0.15	5.0 – 28.8 pg/mL
Prolactin	66.81	3.46 – 19.40 ng/mL
GH	0.284	0.003 – 0.971 ng/mL

TSH = thyroid-stimulating hormone, fT4 = free thyroxine, ACTH = adrenocorticotropic hormone, LH = luteinizing hormone, FSH = Follicle-stimulating hormone, GH = Growth hormone.

What is the water disorder most commonly seen in patients with anterior hypopituitarism?

Hyponatremia.

Hormones secreted by the anterior pituitary include thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), growth hormone (GH), prolactin and adrenocorticotropic hormone (ACTH). Reduced production of ACTH in anterior hypopituitarism leads to secondary adrenal insufficiency with reduced levels of glucocorticoids. Glucocorticoid

deficiency can lead to hyponatremia through three distinct mechanisms:

i) Direct water permeability increase in the collecting tubules through an antidiuretic hormone-independent effect, leading to water reabsorption and hyponatremia.[1]

ii) Altered systemic and renal hemodynamics. Glucocorticoids maintain peripheral vascular tonus and have a positive inotropic effect on the heart. Thus, glucocorticoid deficiency results in hypotension and decreased glomerular filtration rate. This prompts an increase of volume absorption at the proximal tubular, limiting delivery of filtrate to the tubules' diluting segment and ultimately impairing the formation of free water.[2]

iii) Antidiuretic hormone (ADH) synthesis by the hypothalamus and its secretion by posterior pituitary lobe is inhibited by glucocorticoids. In the setting of anterior hypopituitarism, an inappropriate increase in ADH secretion additionally impairs the ability to dilute urine.[3]

At this point the patient's serum creatinine had improved to 1.60 mg/dL and he was normonatremic (143 mEq/L). The patient was started on replacement treatment for anterior hypopituitarism with hydrocortisone (50mg q8h iv) and levothyroxine (0.1mg qd po). In the subsequent days the patient developed hypernatremia followed by polyuria (serum sodium reached 173 mEq/L and urinary output reached 5L/day), despite voluminous administration of intravenous normal saline. The calculated serum osmolality was 332 mOsmol/Kg (reference range 275-295), urine dipstick specific gravity 1.005, urinary osmolality 213 mOsmol/Kg and urinary sodium 21 mEq/L.

■ Why did the patient develop hypernatremia and polyuria?

Hypernatremia is caused by a decrease in total body water relative to electrolyte content. This disturbance is common in patients with altered mental status because they lack independent access to water. However, our patient was normonatremic and normovolemic before hydrocortisone was started. Should hydrocortisone alone be blamed? Hypernatremia could result from hydrocortisone replacement therapy because it improves systemic hemodynamics and quickly suppress ADH secretion. In turn, urine volume increases, whereas sodium reabsorption is still at maximum.[4] While this alone could justify polyuria other causes were investigated.

Polyuria (urine output exceeding 3 L/day) is due to a defect in water balance leading to the excretion of large volumes of dilute urine (urine osmolality usually below 250 mOsmol/kg). It can occur in the setting of osmotic diuresis, primary polydipsia, central or nephrogenic diabetes insipidus (DI). Our patient did not present polydipsia, and low urinary osmolality excluded osmotic diuresis (osmolality typically above 300 mOsmol/kg). Differentiation between central DI (deficient secretion of ADH) and nephrogenic DI (normal ADH secretion with renal resistance to its water-retaining effect) can be established by the administration of exogenous ADH.

For this reason the patient was started on IV desmopressin (2 mcg twice a day) and normal saline was switched to 5% glucose. An expedite correction of hypernatremia was achieved – Table 2. Thus, adequate response to ADH confirmed the diagnosis of central DI, most likely in the context of the newly diagnosed suprasellar cistern mass.

Table 2

Laboratory work after initiation of hydrocortisone replacement therapy

Test	D1	D2	D5	D7	D8	Reference range
Serum sodium	148	153	158	164	173	136 – 145 mEq/L
Serum potassium	4.0	2.8	3.0	3.3	4.3	3.5 – 5.1 mEq/L
Serum chloride	121	124	129	137	142	98 – 107 mEq/L
Serum creatinine	1.61	1.41	1.14	1.17		0.72 – 1.25 mg/dL
Serum urea	43	42	42	39		18 – 55 mg/dL
Calculated serum osmolality				332		275 – 300 mOsmol/Kg
Urinary osmolality				213		50 – 1200 mOsmol/Kg
Urinary sodium				21		mmol/L

Table 3

Laboratory work after initiation of desmopressin

Test	D1	D2	D3	D4	Reference range
Serum sodium	173	158	141	130	136 – 145 mEq/L
Serum potassium	4.2	3.8	4.3	4.5	3.5 – 5.1 mEq/L
Serum chlorine	143	128	112	103	98 – 107 mEq/L
Serum creatinine	1.69	1.48	1.3	1.16	0.72 – 1.25 mg/dL
Serum urea	57	48	40	42	18 – 55 mg/dL
Calculated serum osmolality				263	275 – 300 mOsmol/Kg
Urinary osmolality				439	50 – 1200 mOsmol/Kg
Urinary sodium				160	mmol/L

While still under desmopressin, the patient developed hyponatremia, and after dosage fine-tuning, normal natremia was obtained. The patient subsequently developed infective endocarditis leading to his death. The nature of the cranial mass remained unidentified.

■ Why was the patient's sodium normal before hydrocortisone administration?

Before the correction of his anterior hypopituitarism with hydrocortisone, the patient was normonatremic because he simultaneously presented two antagonic disturbances of water balance, creating a normonatremic equipoise. While the patient presented anterior hypopituitarism (favoring hyponatremia) he also had, unrecognized until that point, posterior hypopituitarism. Posterior hypopituitarism or neurohypophyseal failure, causes central diabetes insipidus (DI) by decreased production of ADH, favoring the development of hypernatremia. Therefore, the administration of hydrocortisone to our patient with anterior pituitary insufficiency unmasked his posterior hypopituitarism, allowing the development of hypernatremia and polyuria driven by the previously present, but silenced, central DI.

The pathophysiology of hypopituitarism is dependent on the underlying cause and coexistence of both anterior and posterior deficits may occur in specific clinical settings, such as traumatic brain injury, pituitary surgery, sarcoidosis or tumors.[5] It is important for physicians to be aware that the correction of one of the disorders may unmask the other.

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