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Hyponatremia in Pulmonary TB

Evidence of Ectopic Antidiuretic Hormone Production

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Hyponatremia is among the most common biochemical abnormalities in hospital inpatients. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is one of several causes of hyponatremia, particularly in patients with pulmonary diseases. The mechanism of SIADH associated with pulmonary infection is, however, poorly understood. We report an unusual case of hyponatremia in a man with pulmonary TB and central diabetes insipidus with biochemical evidence of ectopic antidiuretic hormone production as a possible mechanism causing hyponatremia. ***CHEST 2010; 137(1):207–208***

Abbreviations: ADH = antidiuretic hormone; DI = diabetes insipidus; SIADH = syndrome of inappropriate antidiuretic hormone secretion

The mechanism of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) associated with pulmonary infection is poorly understood.[1] We report a case of hyponatremia in a man with pulmonary TB and diabetes insipidus (DI) with biochemical evidence of ectopic antidiuretic hormone (ADH) production as a possible mechanism causing hyponatremia.

Case Report

A 47-year-old man presented with a 1-month history of hemoptysis. DI was diagnosed 30 years ago. No structural causes were found on CT scanning and pituitary MRI. A water-deprivation test 5 years ago following desmopressin withdrawal confirmed isolated ADH deficiency (clinical dehydration, polyuria, and urine osmolality < 100 mOsm/kg). Past history included renal TB and HIV infection diagnosed 31 and 24 years ago, respectively. He received a full course of anti-TB therapy and had been stable (undetectable viral load, CD4 count 700-800 cells/mL last 3 years) on antiretroviral therapy (tenofovir disoproxil fumarate 300 mg, emtricitabine 200 mg, one tablet/d; lopinavir 200 mg, ritonavir 50 mg, two tablets/d; and lamivudine, 300 mg/d). Eunatremia was maintained by desmopressin therapy (10 μg intranasally twice daily), initiated at diagnosis 30 years ago.

He was clinically euvolemic and euthyroid. Biochemistry revealed hyponatremia with low serum osmolality, inappropriately high urinary osmolality (470 mM/kg), and normal urinary sodium concentration (57 mmol/L), consistent with excessive desmopressin therapy (Fig 1). Morning serum cortisol was sufficient at 581 nmol/L.

Chest radiography demonstrated a 3-cm cavitating lesion in the right upper lobe. Sputum culture was positive for *Mycobacterium* TB, consistent with reactivation of TB. Hyponatremia was initially attributed to desmopressin overtreatment. However, the hyponatremia persisted despite dose reduction, and only improved after stopping desmopressin (Fig 1). When measured 48 h after stopping desmopressin, plasma ADH was 1.2 pmol/L, a level well above the assay detection limit of 0.35 pmol/L (intraassay precision: 4.6%; interassay precision: 10%). The corresponding sodium concentration was 117 mmol/L.

Serum sodium increased to 127 mmol/L after stopping desmopressin for 4 days (see Fig 1). However, the patient became anxious about not receiving his regular therapy and administered 10 μg desmopressin intranasally against medical advice on day 5, resulting in a decrease in serum sodium and osmolality, and an increase in urinary osmolality (540 mM/kg), consistent with ADH action. Stopping desmopressin again improved hyponatremia.

Five days into anti-TB therapy (isoniazid 300 mg daily, ethambutol 1,200 mg daily, and rifampicin 600 mg daily), polyuria recurred. The patient agreed to a reduced dosage (10 μg every other day) of desmopressin, which resolved the polyuria and maintained serum sodium at 125 to 130 mmol/L. The dose of desmopressin was titrated to serum sodium and urine output and was returned to the usual regimen at 3 months follow-up. Serum sodium remained normal, and ADH was undetectable on three occasions (see Fig 1) while taking desmopressin.

Discussion

Our case illustrates a diagnostic dilemma of hyponatremia in a man with DI with biochemistry suggestive of an ectopic ADH source causing SIADH. While SIADH is a well-known complication of pulmonary inflammatory and infective diseases, the mechanism is poorly understood and has been attributed to hypoxia and decreased vascular volume.[2,3] Hyponatremia is attributed to the inappropriate production of ADH from the posterior pituitary, which is therefore eutopic. SIADH secondary to ectopic ADH production is only a recognized phenomenon of a paraneoplastic syndrome, most commonly associated with small-cell lung carcinoma, as confirmed by *in vitro* demonstration of ectopic hormone secretion in tumor cells.[4] Ectopic ADH production has not been demonstrated in infectious conditions such as TB. An elevated ADH level in the presence of hyponatremia in our patient with long-standing proven DI who was taken off desmopressin (see Fig 1), is suggestive of ectopic ADH production. Although non-osmoregulated ADH production stimulated by pulmonary disease has been described,[5,6] a water-deprivation test resulted in urine

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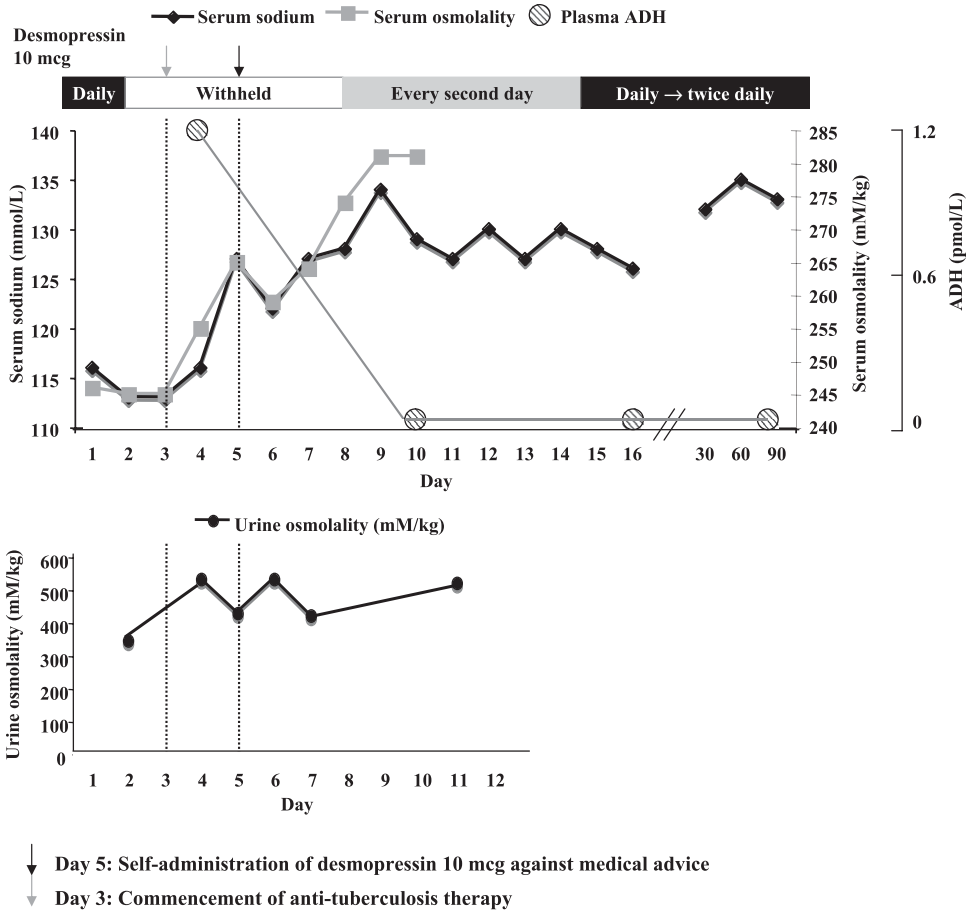

FIGURE 1. Biochemical changes in relation to desmopressin therapy. Patient self-administered a dose of desmopressin on day 5 (black arrow) against medical advice. Anti-TB therapy was commenced on day 3 (gray arrow). ADH = antidiuretic hormone.

osmolality < 100 mOsm/kg in our case, thus arguing against a diagnosis of partial DI with residual central arginine vasopressin production.

The measured ADH is unlikely to represent cross-reactivity to covert desmopressin use, as the radioimmunoassay used (Bühlmann Laboratories; Basel, Switzerland) does not recognize desmopressin. All subsequent measurements following anti-TB therapy revealed undetectable ADH levels, further supporting the validity of the result.

In conclusion, our case provides evidence of ectopic ADH production triggered by a nonneoplastic infective/inflammatory condition, which resolves when this is controlled. Patients with DI on desmopressin who develop pulmonary conditions should be closely monitored for hyponatremia, and the dose of replacement therapy may require reduction or temporary cessation as the result of the possible ectopic ADH production causing SIADH.

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