Hyponatremia and pituitary adenoma: Think twice about the etiopathogenesis

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ABSTRACT. Pituitary adenomas may be the cause of the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), although few cases have so far been reported. We described a case of hypotonic hyponatremia in a 76-yr-old man with a pituitary macroadenoma. He had a recent history of two syncopal attacks which had occurred in the last two months. Baseline assessment demonstrated a sodium serum level of 114 mEq/l. Clinically, the patient appeared euvoletic. Thyroid and adrenal function testing did not show any abnormality. Plasma and urinary osmolalities (238 and 186 mOsm/kg, respectively) were in agreement with the diagnosis of SIADH. Accordingly, 3% hypertonic saline solution was started, followed by water intake restriction when natremia reached 126 mEq/l. A computed tomography (CT) scan of the chest revealed the presence of a 2-cm lesion in the azygos-esophageal recess. Because the nature of the lesion appeared uncertain, antibiotic therapy was initiated. After one month, a new CT scan did not show any evidence of the mediastinic mass. Sodium serum level was within the normal range (141 mEq/l) and remained stable thereafter, without fluid restriction. This case very well demonstrates that, in the presence of hyponatremia due to SIADH, more frequently associated co-morbidities (ie mediastinic diseases) have to be searched, even in the presence of a possible, yet rare, cause of this syndrome (ie pituitary adenoma).


INTRODUCTION

Hypotonic hyponatremia in the presence of a normal volume of extracellular fluid is the hallmark of the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) (1, 2). SIADH may be due to tumoral ectopic ADH production (ie lung, kidney, bladder, pancreas, prostate cancer, thymoma, mesothelioma, hematological malignancies) or to release from the posterior pituitary gland. The latter may be associated with diseases of the central nervous system, with pulmonary disorders, with drugs or stressful situations such as those following surgery (3). Hyponatremia may be present in patients affected by pituitary tumors. In these cases, reduced sodium levels are usually due to the presence of secondary hypothyroidism and/or hypocortisolism (4). However, a few reports described SIADH as the cause of hyponatremia in the presence of pituitary tumors, without any evidence of pituitary dysfunction (5-7). In these cases transsphenoidal surgery for the removal of the adenoma may cure SIADH. Admittedly, the pathogenesis of SIADH associated to pituitary tumors remains elusive; however, both mechanical and chemical stimuli have been hypothesized to affect the hypothalamus-neurohypophyseal system (5). Here we describe the case of a 76-yr-old man with a pituitary adenoma, admitted to our University Hospital for the presence of a symptomatic hyponatremia (114 mEq/l).

CASE REPORT

A 76-yr-old man was admitted to the Endocrine Unit ward at the University Hospital in Florence. He had a recent history of two syncopal attacks occurring in the last two months, not associated to seizures or urinary loss. He also reported poor appetite and asthenia in the same period of time. Following a third episode, he was brought to the Emergency Department...
of the University Hospital. He was taking transdermal nitrates for ischemic cardiomyopathy. No other major illness or surgical intervention resulted from his clinical history. Physical findings were: height 170 cm, weight 57 kg, blood pressure 110/80 mmHg, pulse rate 66 beats/min with regular rhythm. He was not thirsty, and neither dry skin or tongue, nor peripheral edema was present. No abnormality was found at neurological examination. Laboratory findings showed severe hyponatremia (114 mEq/l). Red blood cells were 4.08 x 10^{12}/l, white blood cells 4.65 x 10^{9}/l, hemoglobin 11.1 g/dl, hematocrit 32.1%, blood urea nitrogen 0.17 g/l, serum creatinine 0.9 mg/dl, serum uric acid 1.7 mg/dl, potassium 3.5 mEq/l, erythrocyte sedimentation rate (ESR) 56 mm/h (2-25), fibrinogen 512 mg/dl (200-450). A computed tomography (CT) scan of the brain revealed the presence of a pituitary mass (2x2x1.8 cm). A chest X-ray film did not show any pathological finding. The patient was hospitalized and assigned to our Unit. Baseline assessment revealed a plasma osmolality of 238 mOsm/kg, whereas urinary osmolality was 186 mOsm/kg and urinary sodium excretion was 45 mEq/die (urinary volume 1200 ml). Pituitary function was assessed, which revealed partial anterior hypopituitarism. In fact, GH was 0.22 ng/ml, IGF-I 15 ng/ml (80-197), FSH 1.66 U/l (1.7-11), LH 0.7 U/l (0.6-7), testosterone <0.5 nmol/l (10.4-34.6), whereas no abnormality was observed in the level of TSH (0.87 mU/l, normal values 0.25-3.5), free T_{4} (fT_{4}) (12.29 pmol/l, nv 10.3-19.4), free T_{3} (fT_{3}) (3.68 pmol/l, nv 3.5-6.4), ACTH (22.3 ng/l, nv 9-52) and cortisol (431 nmol/l at 08:00 h, nv 160-690). PRL was slightly elevated (332 mU/l, nv 72-288). ADH concentration was 6 pg/ml (<8). Altogether, these findings strongly suggested a condition of SIADH (1). Infusion with hypertonic saline solution (3%) was started in order to correct hyponatremia (3). After 24 h serum sodium was 126 mEq/l. Saline infusion was then stopped and followed by water intake restriction and furosemide 25 mg/die orally. Sodium level further increased up to 134 mEq/l and was maintained in the low range of normality afterwards. A nuclear magnetic resonance (NMR) of the pituitary gland confirmed the presence of a macroadenoma (maximum diameter 2 cm), with sovrasellar extension and pituitary stalk deviation (Fig. 1, A and B). However, the lesion did not reach the optic chiasm. Accordingly, visual field assessment showed no abnormality. A CT scan of the chest and abdomen was also performed and revealed the presence of a slightly hyperdense lesion (maximum diameter 2 cm) in the azygos-esophageal recess (Fig. 2, A and B). The nature of the lesion (ie neoplastic, inflammatory) appeared uncertain, and it was decided to re-evaluate the patient after a short period of time, following treatment with a broad spectrum antibiotic. Thus, amoxicillin plus clavulanic acid (1 g, twice a day orally) was given for 10 days and the patient was discharged with the following additional therapeutic prescriptions: testosterone gel 50 mg/die and moderate fluid intake restriction. Serum sodium level was assessed weekly and the values were between 135 and 139 mEq/l. After a month, CT scan of the chest was repeated and showed no evidence of the previously described lesion (Fig. 3). At that time natremia was 141 mEq/l. Fluid restriction was