Hyponatremia as a Presenting Sign of a Pituitary Intrasellar Cyst

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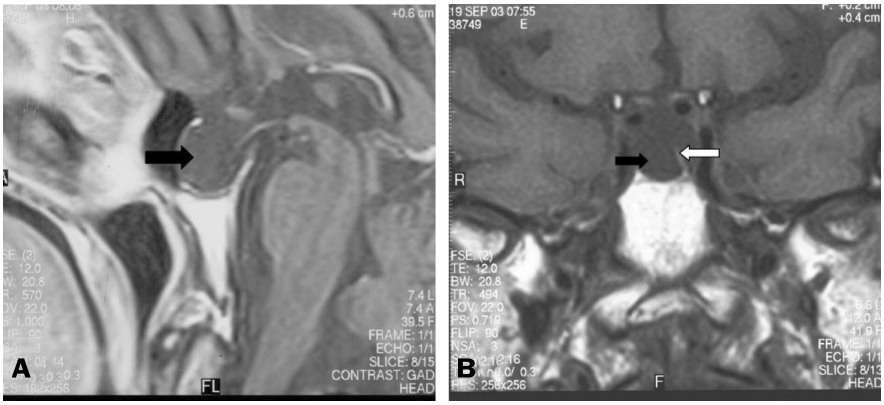
Hyponatremia is one of the most frequently occurring electrolyte disturbances in hospitalized patients. The syndrome of inappropriate antiduretic hormone secretion and SIADH-like conditions are the most common cause of hyponatremic euvolemic hypo-osmolality states. Although pituitary failure should always be considered as a cause of hyponatremia, it is frequently overlooked especially in elderly patients. We report an uncommon case where hyponatremia was the presenting sign of hypopituitarism due to a pituitary intrasellar cyst.

Patient Description

A 66 year old woman was hospitalized because of generalized weakness accompanied by lethargy, occasional vomiting and anorexia that had begun several weeks previously. Her only prior hospitalization had been 10 months earlier in another hospital, because of hyponatremia of 125 mmol/L. SIADH and hypothyroidism were diagnosed, and levothyroxine, 50 μg daily, was started and was her only medication.

Upon admission the patient appeared lethargic. Blood pressure was 135/70 mmHg with no orthostatic decrease. Heart rate was 80 beats per minute and regular, temperature was 36.2°C. The neurologic examination and the rest of the physical examination were non-contributory. Laboratory tests showed a normal complete blood count; hyponatremia was 115 mmol/L, potassium level 3.6 mmol/L, urea 38 mg/dl, creatinine 1.0 mg/dl and glucose 75 mg/dl. Creatine kinase level was markedly elevated (2,794 U/L, mostly of muscular origin) and aspartate amino-transferase (57 U/L) and lactate dehydrogenase (660 U/L) were mildly elevated. Serum levels of albumin, globulins, lipids and other routine blood and urine tests were normal, as was chest radiography. Urine osmolality was 413 mOsmol/kg, urine sodium excretion 133 mmol/L, and serum osmolality 236 mOsmol/kg. Free thyroxine was 0.31 ng/dl (normal 0.9–9.1), total triiodothyronine 46 μg/dl (normal 80–200) and thyrotropin was normal. The normal thyroid-stimulating hormone in the presence of decreased thyroxine and triiodothyronine raised the suspicion of secondary hypothyroidism and possible hypopituitarism. A morning cortisol level was 3.5 μg/dl (normal 5–25). One hour after an intravenous injection of 250 μg cosyntropin, the blood cortisol level increased from 3.1 to 10.7 μg/dl (normal response >18). Serum levels of lueteinizing hormone (<0.1 U/L), follicle-stimulating hormone (<0.2 U/L), and ACTH (<10 pg/ml) were reduced, confirming anterior pituitary failure. Prolactin level was normal. Prednisone, 30 mg daily, was co-administered with levothyroxine leading to a marked clinical improvement and resolution of the hyponatremia.



[A] Gadolinium-enhanced T1-weighted MRI sagital view, showing enlarged sella with hypodense cystic-like structure with flattened pituitary tissue (black arrow). **[B]** Coronal view, showing right cystic structure (black arrow) with stalk deviation to the left (white arrow).

Visual fields examination showed left optic neuropathy. Contrast-enhanced computed tomography and gadolinium-enhanced magnetic resonance imaging [Figure] showed an enlarged sella with a hypodense cystic-like structure of 1.4 cm that was causing flattening of the pituitary tissue, deviation of the pituitary stalk and an upward deviation of the optic chiasm, but with no pressure on it. Based on the benign nature of the lesion and the clinical improvement, the neurosurgeon recommended continuation of corticosteroid and levothyroxine, with regular follow-up and no surgical intervention. One month after discharge the patient was feeling well, and her serum sodium, creatine kinase, free thyroxine and triiodothyronine levels were normal whereas TSH remained unchanged.

SIADH = syndrome of inappropriate antiduretic hormone

TSH = thyroid-stimulating hormone

Comment

This patient had hypotonic hyponatremia, representing an excess of water in relation to the body's sodium stores. In the presence of normal kidney function, the retention of water is due to inappropriate antidiuresis caused by a high plasma level of arginine vasopressin despite serum hypotonicity [1]. AVP is the primary hormone implicated in water homeostasis. Increased AVP may be secondary to low effective blood volume either in edematous (type 1, sodium-retaining) conditions such as cirrhosis, nephrosis or heart failure, or in hypovolemic (type 2, sodium-depleted) states such as gastroenteritis. Primary increase in AVP secretion in euvolemic states (type 3) is referred to as SIADH. In this patient, the diagnosis of hyponatremia presenting as an SIADH-like syndrome was based on the accepted criteria of hyponatremia, serum hypo-osmolality natriuresis and inappropriately high urine osmolality in a clinically euvolemic patient [2]. Although elevated serum AVP levels could confirm the diagnosis, this test is not easily performed and is therefore not a required criterion for the diagnosis.

The differential diagnosis of SIADH includes various causes, mainly neoplasms, infections, head trauma, and drugs. However, as demonstrated here, both hypothyroidism and adrenal failure should always be excluded [2], since each one may cause the same laboratory abnormalities as in SIADH. Serum thyrotropin level is the most commonly used test to determine the thyroid gland status. In more than 99% of hypothyroid patients, the cause is primary failure of the thyroid gland and their thyrotropin is expected to be elevated. A normal thyrotropin level excludes primary but not secondary hypothyroidism. A normal thyrotropin level along with low serum thyroid hormones, as in our patient, should always raise suspicion of secondary hypothyroidism. Since isolated thyrotropin failure is very rare, evaluation of other endocrine functions of the anterior hypophysis seemed prudent.

Diagnosing adrenal failure is of utmost importance, because if left unrecognized or untreated it may become life threatening. Secretion of AVP is inhibited by glucocorticoids and their deficiency is a stimulus for AVP secretion. Altered renal sensitivity to AVP due to up-regulation of the aquaporin-2 water channel may also be involved. In primary adrenal failure, the decrease in both glucocorticoids and mineralocorticoids causes dehydration, hyperkalemia and severe depletional hyponatremia, whereas secondary hypoadrenalism – where only ACTH and not aldosterone is deficient – may cause dilutional hyponatremia mimicking SIADH. Determination of adrenal function is recommended in SIADH, yet it is still often overlooked. The ACTH test is convenient, easy and frequently used for evaluating adrenal failure. A subnormal response does not necessarily mean primary adrenal failure because, as in our patient, it may also be due to a prolonged decreased secretion of ACTH causing secondary adrenal suppression [3]. The low serum levels of both ACTH and gonadotropins confirmed hypopituitarism as the plausible unifying diagnosis accounting for the entire clinical presentation of the patient. Tertiary hypoadrenalism as a result of hypothyrodism seems unlikely due to the fact that hypoadrenalism persisted after thyroxine replacement and the imaging finding of an intrasellar cystic mass. As revealed by the MRI, the hypopituitarism was caused by an intrasellar lesion, commonly caused by primary cystic lesions (such as epidermoid and arachnoid cysts) or an empty sella [4]. In our patient, the deviation of the pituitary stalk, the upward deviation of the optic chiasm and the density of the lesion (which was not identical to that seen in the cerebrospinal fluid) support the diagnosis of an intrasellar cyst. Considering the marked clinical and biochemical improvement with levothyroxine and corticosteroids replacement, and the fact that the benign sellar process caused no danger to the optic chiasma, continuing drug therapy with regular follow-up and avoiding surgical intervention seemed to be the appropriate approach.

In this patient hyponatremia was the presenting sign leading to the diagnosis of hypopituitarism. Indeed, severe hyponatremia has been reported to be a frequent informative sign of hypopituitarism in the elderly [5]. In one report, in 43% of elderly patients with recurrent hospitalizations due to hyponatremia, hypopituitarism was finally diagnosed [4]. Both intrasellar cysts and empty sella have been reported as an infrequent cause of hyponatremia mimicking SIADH [4]. The administration of low dose corticosteroids brings recovery within a few days, whereas infusion of hypertonic saline is less effective. Interestingly, the non-suppressible release of AVP and the hyponatremia in secondary adrenal failure are more exaggerated in elderly patients as compared to younger patients. The case described here is a good reminder that hypopituitarism should be ruled out in all patients with an unexplained SIADH-like situation.

AVP = arginine vasopressin

References

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Do not resent growing old. Many are denied the privilege.

Irish proverb