

Three interesting cases of syndrome of inappropriate antidiuretic hormone secretion

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Abstract

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is an etiologically-diverse pathological condition resulting from the elevation in both ectopic and autonomic secretion of the antidiuretic hormone (ADH) by neoplastic tissue; excessive stimulation of the hypothalamic-pituitary axis, e.g. in pulmonary diseases, central nervous system (CNS) abnormalities, endocrine glands dysfunction or due to the use of some medications; intensification of renal ADH action by certain medications and action of substances chemically-related to vasopressin. The clinical characteristics of the syndrome are comprised of the presence of inadequately concentrated urine, hyponatremia, and hypo-osmolal blood serum, as well as weight gain. To show the variety of its causes and courses the article presents three cases of patients diagnosed with SIADH in the Department of Internal Medicine. In each of them the syndrome of inappropriate antidiuretic hormone secretion manifested in clinical laboratory tests in the form of hyponatremia.

Key words

syndrome of inappropriate antidiuretic hormone secretion, hyponatremia, diagnostics

INTRODUCTION

The name 'syndrome of inappropriate antidiuretic hormone secretion' (SIADH) is reserved for etiologically-diverse pathological conditions resulting from the elevation in both ectopic and autonomic secretion of the antidiuretic hormone (ADH) by neoplastic tissue [1, 2, 3]; excessive stimulation of the hypothalamic-pituitary axis or due to use of some medications [4, 5, 6]; intensification of renal ADH action by certain medications and action of the substances chemically-related to vasopressin. The clinical characteristics of the syndrome are comprised of the presence of inadequately concentrated urine, hyponatremia, and hypo-osmolal blood serum, as well as weight gain. Yet, surprisingly, in this syndrome neither peripheral edema nor ascites are present [7]. To show the variety of its causes and courses three interesting cases of SIADH are presented

CASE 1

SIADH as a result of central nervous system ischemia. A 54-year-old female patient with no history of chronic diseases was admitted to the Department of Internal Medicine due to hyponatremia stated in the ambulatory test. The patient had been undergoing complex neurological diagnostics for the previous month in order to determine the underlying cause of her collapse; which was further accompanied by the occipital headaches as well as balance disorders. A head CT scan was performed during the patient's stay at the Department of

Neurology and revealed two hypodense lesions, indicating ischemic damage of the brain. The patient did not report any symptoms at the time of admission to the Department of Internal Medicine. The physical examination was unremarkable. Further laboratory data indicated an advanced hyponatremia with sodium levels of 121–122 mmol/l. The blood morphology results, urinalysis, as well as potassium, creatinine, glucose, transaminases, TSH, adrenocorticotrophic hormone and fasting cortisol concentrations were within normal ranges. Arterial blood analysis indicated low serum osmolality measured as 249 mOsm/kg H₂O (norm: 270–300 mOsm/kg H₂O), whereas the urinary sodium excretion was unaltered, at the level of 122 mmol/24h (norm: 40–220 mmol/24h – this is a standard specified by the central laboratory where the sample was analyzed).

Ultrasound examination of the abdominal cavity and chest X-ray revealed no significant anomalies. In addition to the proper kidney, thyroid and adrenal gland function, along with low plasma osmolality, the diagnosis of the SIADH was made. An abdominal CT was performed as a part of diagnostic measures taken to discover the underlying cause of the SIADH syndrome, and was found to be unremarkable. The treatment regimen included restriction in daily fluid supply to 1.5 l, as well as additional sodium chloride supplementation. This allowed for an increase in the plasma sodium concentration (137 mmol/l), together with normalization of the serum osmolality.

CASE 2

SIADH syndrome associated with neoplastic process. A 73-year-old male patient presented to the Psychiatry Clinic with complaints of progressive deterioration of his psychological condition, loss of appetite, sleep disturbances,

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anhedonia, and suicidal thoughts for the past three months. His past medical history included controlled chronic hypertension, hyperthyroidism, paroxysmal atrial fibrillation and transurethral prostatic resection due to prostatic hyperplasia. As the patient was under observation in the clinic, his mental condition improved systematically, with the suicidal thoughts subsiding and a significant improvement in mood. Routine laboratory tests demonstrated an advanced hyponatremia, sodium concentrations measured from two samples amounted to 118 and 120 mmol/l, respectively. The patient was transferred to the Internal Medicine Department in order to conduct further diagnostics. After admission, the patient exhibited recurrent episodes of vomiting, general malaise, loss of appetite and considerable weight loss (approximately 10 kg within 2 months). The physical examination was unremarkable, except for the patient being cachectic (BMI 18.4 kg/m²). Further laboratory testing showed remaining hyponatremia with sodium level of 128 mmol/l. No significant pathologies were observed with reference to both blood morphology, as well as remaining electrolyte, urea, creatinine, glucose, TSH and cortisol concentrations. A plasma hypo-osmolality (250 mOsm/kg H₂O) was revealed through blood gasometry testing; nonetheless, the sodium excretion measured in routine 24-hour urine collection remained normal – 153 mmol/24h. In order to determine the underlying cause of the SIADH and because of patient's weight loss along with nausea and vomiting, a chest X-ray was performed in which radiolucent, emphysematous spaces were depicted over the lung fields. The abdominal ultrasound examination demonstrated an image suggesting multiple metastatic lesions throughout the liver. The neoplastic characteristics of the lesions was confirmed with MRI of the abdomen. Furthermore, the MRI revealed extra neoplastic foci located in lumbar spine vertebrae, the sacrum, pelvis and ribs. Considering the patient's mental disturbances and nausea, as well as recurring emetic episodes, a head CT scan was performed, revealing several hypodense areas located in the cerebral hemispheres, most probably of metastatic characteristics. In order to localize the primary neoplastic focus, a chest CT was performed and the patient scheduled for both gastro- and colonoscopy.

A pathological infiltration of not only the right lung hilum, but also the right main bronchus and superior vena cava, along with numerous enlarged mediastinal lymph nodes were depicted. The diagnostic material for histopathological examination was obtained from the mediastinal lymph node during endobronchial ultrasound procedure. The results of the histopathological investigation confirmed the diagnosis of a small cell carcinoma of the lung.

CASE 3

SIADH – cause unknown. A 79-year-old female patient treated for chronic hypertension was admitted to the Department of Internal Medicine due to consecutive episode of bilious vomiting and hyponatremia of 111 mmol/l. During past 2 years, the patient was hospitalized in the Internal Medicine Ward for three times. Each hospitalization carried the same complaints of persistent vomiting accompanied by severe electrolyte disturbances in form of hyponatremia (laboratory data of plasma sodium content on admission were 114, 114 and 117 mmol/l, respectively). All the diagnostic

imaging procedures (chest X-ray, abdominal ultrasound examination), as well as basic laboratory testing (blood morphology, serum K⁺ concentration, transaminases, fasting glucose, TSH, fasting cortisol concentrations, double designation circadian rhythm of cortisol secretion) performed during consecutive hospitalizations did not exhibit any considerable deviations from the normal ranges. A head CT scan performed due to the patient's serious condition and alteration in consciousness during one of the admissions, excluded the existence of any notable pathologies. The arterial blood acid alkaline balance revealed low osmolality of the blood plasma – 250 mOsm/kg H₂O; however, the urinary sodium excretion level was indicated as 69 mmol/24h. On the basis of the above-mentioned, exclusion of kidney failure, as well as both adrenal and thyroid insufficiency (for which the patient was examined during previous hospitalizations), the SIADH was diagnosed. Unfortunately, the patient refused further diagnostic procedures concerning investigation of the possible cause of her ailment. The treatment regimen consisted of fluid supply restriction to a maximum of 1l/day, with additional sodium chloride compensation. These proceedings led to stabilization of the plasma sodium concentrations within normal limits.

In each of the three presented cases of patients diagnosed of SIADH in the Department of Internal Medicine, the syndrome of inappropriate antidiuretic hormone secretion manifested in clinical laboratory tests in the form of hyponatremia – one of the most common abnormalities of electrolyte balance [1, 4, 8]. The frequency of its occurrence was calculated as 1% in the total population and over 15% of in-patients [9]. Low serum level of sodium can be a sign of numerous medical conditions including SIADH. Pahdi et al. [6] conducted a big (n=730), prospective study to assess the frequency, risk factors, and outcome in Intensive Care Unit patients with critical conditions and hyponatraemia. On admission, hyponatraemia was diagnosed in 34.3% patients, the main cause of which was SIADH as a consequence of pneumonia. Other predisposing factors included: severe sepsis, trauma, surgery, drugs, renal failure, heart failure, liver cirrhosis, subarachnoid haemorrhage, hypothyroidism and hypocortisolism.

However, hyponatremia accompanied by normovolemia tends to form a typical constellation, most often indicating the SIADH syndrome. Except for these two abnormalities, SIADH is always associated with: extracellular fluid hypo-osmolality at levels below 275 mOsm/kg H₂O, inadequate urine concentration, commonly exceeding the osmolality level of 100 mOsm/kg H₂O, lack of edema or dehydration signs (isovolemia), urinary sodium excretion >40 mmol/24h (despite regular sodium and water supply). The latter parameter stayed within recommended normal values, in spite of serum hyponatraemia, although the drop in urine sodium excretion would be expected in this clinical situation. In every single case, the exclusion of other conditions leading to normovolemic hypo-osmolality is mandatory.

The mechanism of these disorders is complex and depends on the triggering cause of the SIADH syndrome. The common element is abnormally high secretion of vasopressin, despite the absence of states stimulating the secretion such as increase of plasma osmolality or decrease in effective intravascular fluid volume. The high concentration of anti-diuretic hormone by stimulating receptors V₂ in the kidney leads to the water retention, increase in urinary sodium excretion and



hyponatraemia. In 14% of SIADH there occurs very low concentrations of vasopressin. This phenomenon may be caused by mutations in the genes for receptor proteins in the kidney that causes tubular hypersensitivity of antidiuretic hormone secretion or vasopressin acting like oxytocin e.g. [9].

The professional literature includes numerous descriptions of lung cancer-related SIADH syndrome in which the syndrome's metabolic, endocrine or mental disorders symptoms, as in presented Case 2, camouflaged or even delayed the diagnosis and proper treatment of the underlying lung carcinoma.

In spite of all the SIADH causes mentioned throughout the presented case studies, the conditions such as neoplasms located in systems other than respiratory – for instance, digestive tract tumours (pancreas, stomach, duodenum), nasopharyngeal tumours or lymphomas – can also be listed as possible initiators of inadequate vasopressin secretion. Furthermore, the CNS pathologies such as: stroke, meningitis, brain tumours, trauma, haemorrhage, Guillain-Barre syndrome or neurosurgical interventions, may also be responsible for the appearance of the Schwartz-Bartter syndrome, as observed in Case 1 [10, 11, 12, 13, 14].

For numerous reasons the underlying condition of SIADH often remains unknown. In the presented Case 3, the definite cause was the lack of patient's consent for the proposed diagnostic procedures. It has been proved that hyponatraemia is the independent risk factor for increased mortality [6, 15, 16]; therefore, no significant observation may be drawn also from the author's clinical experiences – every case of hyponatremia manifested in random laboratory tests should be given an in-depth clinical differentiation including the SIADH, as it may advance revealing the proper underlying disease and making a life-saving diagnosis.

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