CASE REPORT

Chronic idiopathic hyponatremia in an elderly patient due to inappropriate antidiuretic hormone secretion (SIADH) syndrome

Kounatidis D, Liakopoulou C, Brozou V, Dimopoulou G, Vallianou N

First Department of Internal Medicine, Evangelismos General Hospital, Athens, Greece

Abstract

Introduction: The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a disorder which is characterized by the inability to suppress the secretion of antidiuretic hormone (ADH), leading to impaired water excretion and hyponatremia. The syndrome should be suspected in any patient with hyponatremia, hypo-osmolality and a urine osmolality >100 mOsm/kg, while urine sodium concentration is above 40 mEq/L.

Case Description: Herein, we present an 84-year-old female patient with chronic idiopathic hyponatremia due to SIADH. Her laboratory tests showed hyponatremia with serum sodium of 120 mEq/L, while urine sodium concentration was 83 mEq/L. Measured serum osmolality was 255 mOsm/kg and urinary osmolality 130 mOsm/kg. In addition to these, her serum glucose, potassium, uric acid, renal, and liver functions were normal, and there were no acid-base disorders. The patient's adrenal function (cortisol, adrenocorticotropic hormone, renin, and aldosterone) showed no abnormalities, as well as her thyroid function.

Discussion: The patient suffered from chronic idiopathic hyponatremia and osteoporosis, which often coexists in patients with chronic idiopathic SIADH and was treated with alendronate/cholecalciferol. The scenario of the presence of SIADH was further strengthened by the fact that hyponatremia did not improve after isotonic normal saline administration, but only with fluid restriction. HIPPOKRATIA 2019, 23(1): 42-44.

Keywords: SIADH, syndrome of inappropriate secretion of antidiuretic hormone, chronic SIADH, elderly, osteoporosis, fluid restriction

Corresponding author: Natalia G. Vallianou, 5 Pyramidon str, 19005, Municipality of Marathonas, Athens, Greece, tel: +302294092359, e-mail: natalia.vallianou@hotmail.com

Introduction

Hyponatremia is a common electrolyte disorder in the elderly population, a phenomenon that can be attributed to drugs (more frequently thiazides and antidepressants) and endocrinopathies, to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and also to other mechanisms, such as the 'tea and toast' syndrome. Age is a strong independent risk factor for hyponatremia[1]. Furthermore, chronic hyponatremia can be associated with osteoporosis through several mechanisms, the most important of which is the activation of osteoclastic resorption[1]. Herein, we describe an 84-year-old female patient with idiopathic chronic hyponatremia due to SIADH.

Case report

An eighty-four years old female patient presented to our hospital due to chest pain, which was typical of musculoskeletal origin. Her past medical history was remarkable for arterial hypertension, for which she was taking manidipine, left nephrectomy due to severe infection and bladder carcinoma, which was successfully treated ten years before her presentation. Apart from manidipine, she did not take any other drugs. Also, she did not complain of diarrhea or vomiting. On initial assessment, she had high blood pressure (160/90 mm Hg), while the clinical examination revealed chest pain worsening with movements. The laboratory tests showed hyponatremia with serum sodium of 120 mEq/L, while urine sodium concentration was 83 mEq/L. Measured serum osmolality was 255 mOsm/kg and urinary osmolality 13 0mOsm/kg. Serum glucose, potassium, uric acid, renal, and liver functions were normal, no hyperproteinemia or hyperlipidemia was present, and HIV test was negative.

Tumor markers and thyroid function [thyroid-stimulating hormone (TSH): 1.02 mcU/ml] were within the normal range. Serologic investigations for autoimmune disorders were performed [antinuclear antibodies (ANA), anti-double stranded DNA (Anti-dsDNA) antibodies, perinuclear and cytoplasmic anti-neutrophil cytoplasmic antibodies (p-ANCA and c-ANCA)] and showed no abnormalities. The chest x-ray and the abdominal ultrasound had no pathological findings. In order to exclude malignancy, given the fact that from the medical history she had a successfully treated bladder carcinoma in the past, we performed computed tomography (CT), which

showed thickening of the right adrenal gland, mild enlargement of the left adrenal gland and findings compatible with osteoporosis, the presence of which was confirmed by the bone scan and the bone density measurement. The value in bone density measurement was 0.499 g/cm^2. Her adrenal function [cortisol, adrenocorticotropic hormone (ACTH), renin, and aldosterone] showed no abnormalities. The main laboratory tests of the patient are depicted in Table 1.

Three years before presentation, her serum sodium levels were compatible with mild hyponatremia, i.e. 135 mEq/L. Regarding the existence of symptoms and signs of chronic hyponatremia, the patient complained of fatigue and had cognitive impairment, but we cannot overlook the fact that this cognitive impairment could merely be the result of the aging process, as she was eighty-four years old. However, due to the reasons mentioned above and mainly to the exclusion of other causes of hyponatremia, we concluded that the patient suffered from chronic idiopathic hyponatremia and osteoporosis, which often coexists in patients with chronic idiopathic SIADH and was treated with alendronate/cholecalciferol. The scenario of the presence of SIADH was further strengthened by the fact that hyponatremia did not improve after isotonic normal saline administration, but only with fluid restriction. Unfortunately, we do not have any follow-up of the patient; thus, we do not know her last serum sodium levels.

Discussion

SIADH is best defined by the presence of the Schwartz and Bartter criteria, as follows: serum sodium less than 135 mEq/L, serum osmolality less than 275 mOsm/kg, urine sodium greater than 40 mEq/L, and urine osmolality greater than 100 mOsm/kg in the absence of clinical evidence of volume depletion and other causes of hyponatremia, such as adrenal insufficiency, hypothyroidism, cardiac failure, pituitary insufficiency, renal disease with salt wastage, hepatic disease, and drugs that impair renal water excretion[2]. There are many causes of SIADH, such as central nervous system (CNS) disturbances, malignancies, surgery, pulmonary diseases, hormone deficiency and administration, HIV infection, hereditary SIADH, and drugs. In some cases, there is a chronic idiopathic SIADH, which is usually described in elderly patients[3]. The elderly are at high risk of developing hyponatremia due to the aging-related impaired water excretory capacity and due to the frequent exposure to drugs and diseases associated with hyponatremia. Furthermore, a higher sensitivity to osmotic stimuli can be present in these patients. The main factors that can decrease the water excretion capacity are the reduction of glomerular filtration rate (GFR) and the reduced intrarenal generation of prostaglandins. Although these mechanisms are very important, the clinical practice shows that eventually, hyponatremia develops only in the presence of increased water intake and other leading factors, the most important of which are the exposure to medications and diseases that can cause SIADH[3]. Miller et al demonstrated that aging is a risk factor for the development of SIADH-like hyponatremia. This syndrome, which was latterly called chronic idiopathic SIADH, usually develops in a subset of older patients, who do not have an apparent underlying etiology. Thus, aging *per se* seems to be an independent etiologic factor for the development of chronic idiopathic SIADH[4].

A number of drugs are related to hyponatremia, with diuretics, antidepressants [selective serotonin reuptake inhibitors (SSRIs) and tricyclic], and anticonvulsants (carbamazepine) being the most common causes. Thiazides are usually associated with hyponatremia, while loop diuretics only occasionally induce hyponatremia[5]. Furthermore, angiotensin-converting-enzyme inhibitors (ACEIs) are associated with hyponatremia through a mechanism that is not clear, although some theories suggest that ACEIs may cause polydipsia as a result of its inhibition of angiotensin-converting enzyme in the peripheral renin-angiotensin system. Other medications that can cause hyponatremia are antipsychotics, anticancer drugs (especially cyclophosphamide), antidiabetics, vasopressin analogs, amiodarone, proton pump inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs)[6]. Our patient was treated for arterial hypertension with manidipine, which is not described to be among the causes of hyponatremia. From her past medical history, she had not undergone any recent surgery and, in addition to this, her CT of the brain and chest did not show any findings that could be associated with SIADH. Surgical procedures often cause hypersecretion of antidiuretic hormone (ADH), a response that is probably mediated by pain. Furthermore, CNS disorders (stroke, infection, hemorrhage, trauma, psychosis) can enhance ADH release, through water retention and urinary sodium losses, while pulmonary diseases (especially pneumonia) can lead to the SIADH, through a mechanism which is not clear yet. Given the fact that the patient had undergone surgery for bladder carcinoma in the past, we aimed to exclude the possibility of tumor recurrence by measuring tumor markers and performing CT of the brain, chest, and abdomen, which showed no pathological findings. Ectopic production of ADH by a tumor is most often due to

Table 1: The main laboratory tests of the 84-year-old female patient with chronic idiopathic hyponatremia due to syndrome of inappropriate secretion of antidiuretic hormone, at the time of her admission at and discharge from the hospital.

	Na	K	Urea	Creat	ALT	AST	TSH	ALDO
Admission	120	3.8	29	0.8	12	22	1.02	
Discharge	128	4.2	35	1.0	18	21		84.4

Na: serum sodium, K: serum potassium, Creat: creatinine, ALT: alanine aminotransferase, AST: aspartate aminotransferase, TSH: thyroid-stimulating hormone, ALDO: aldosterone (normal range: 10-300 pg/mL).

a small-cell carcinoma of the lung, although rarely can be caused from head and neck tumors, extrapulmonary small cell carcinomas, and neuroblastoma[6,7].

Endocrinopathies are one of the most common causes of hyponatremia in the elderly. Some studies suggest that hypopituitarism is present in 40 % of patients aged 65 years or older since these patients have pituitary/adrenal dysfunction[6]. The recognition of hypopituitarism is often overlooked since symptoms, such as weakness is often attributed to aging or other comorbidities. Furthermore, hyponatremia can be present in patients with hypothyroidism, especially to those with myxedema. In these cases, the main responsible mechanism is the secretion of ADH via the carotid sinus receptor, with the reduction of the cardiac output being the major stimulus[8]. In our case, TSH, cortisol, ACTH, renin, and aldosterone were all within the normal range, while CT of the brain showed no abnormalities. As we have already mentioned, our patient suffered from osteoporosis. We already know that a large percentage of body sodium is stored in bones, suggesting that bone may act as a potential sodium reservoir during periods of homeostatic stress. Chronic hyponatremia is a significant risk factor for osteoporosis and fracture. Several factors have been implicated, the most important being the activation of osteoclastic bone resorption, while at the same time, hypogonadism may play an essential role in its pathogenesis[9].

While symptomatic hyponatremia is easily detected and treated, prognosis and therapeutic challenges in mild chronic hyponatremia have only recently been pointed out. It is noteworthy that the poor outcomes related to this condition are mainly due to the tendency to falls[10]. Amongst the elderly, falls are a common medical problem, with an annual incidence of 30 to 60 % in the community[10]. Falls in the elderly may result in hip fractures, hospitalizations, severe head injuries, and consequent admission to long term care facilities. Moreover, data from the Rotterdam study showed a significant association between chronic mild hyponatremia and falls, as well as vertebral and non-vertebral fractures[9,10].

Excluding all the possible causes of hyponatremia, we concluded that our patient suffered from chronic idiopathic hyponatremia due to SIADH, which was treated successfully with a combination of fluid restriction and diet rich in salt and proteins, while the concurrent osteoporosis was treated with alendronate/cholecalciferol. If water restriction and a diet rich in salt is not adequate, researchers suggest the addition of urea at an initial dose of 30 g daily[11]. Hyponatremia is usually modest in these patients, and although it has little clinical significance, these patients may be at risk of developing severe symptomatic hyponatremia with seizures, especially in the presence of infections[12].

Conflict of interest

Authors declare no conflict of interest regarding this manuscript.

References

1. Filippatos TD, Makri A, Elisaf MS, Liamis G. Hyponatremia in the elderly: challenges and solutions. Clin Interv Aging. 2017; 12: 1957-1965.
2. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. Am J Med. 1967; 42: 790-806.
3. Anpalahan M. Chronic idiopathic hyponatremia in older people due to syndrome of inappropriate antidiuretic hormone secretion (SIADH) possibly related to aging. J Am Geriatr Soc. 2001; 49: 788-792.
4. Miller M, Hecker MS, Friedlander DA, Carter JM. Apparent idiopathic hyponatremia in an ambulatory geriatric population. J Am Geriatr Soc. 1996; 44: 404-408.
5. Moritz ML. Syndrome of Inappropriate Antidiuresis. Pediatr Clin North Am. 2019; 66: 209-226.
6. Wang D, Lai J, Lu S, Huang M, Hu S, Xu Y. Rapid-onset hyponatremia and delirium following duloxetine treatment for postherpetic neuralgia: Case report and literature review. Medicine (Baltimore). 2018; 97: e13178.
7. Sejling AS, Thorsteinsson AL, Pedersen-Bjergaard U, Eiken P. Recovery from SIADH-associated osteoporosis: a case report. J Clin Endocrinol Metab. 2014; 99: 3527-3530.
8. Hoorn EJ, Rivadeneira F, van Meurs JB, Ziere G, Stricker BH, Hofman A, et al. Mild hyponatremia as a risk factor for fractures: the Rotterdam Study. J Bone Miner Res. 2011; 26: 1822-1828.
9. Renneboog B, Musch W, Vandemergel X, Manto MU, Decaux G. Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. Am J Med. 2006; 119: 71.e1-71.e8.
10. Rubenstein LZ, Josephson KR. Falls and their prevention in elderly people: what does the evidence show? Med Clin North Am. 2006; 90: 807-824.
11. Lockett J, Berkman KE, Dimeski G, Russell AW, Inder WJ. Urea treatment in fluid restriction-refractory hyponatremia. Clin Endocrinol (Oxf). 2019; 90: 630-636.
12. Ganguli A, Mascarenhas RC, Jamshed N, Tefera E, Veis JH. Hyponatremia: incidence, risk factors, and consequences in the elderly in a home-based primary care program. Clin Nephrol. 2015; 84: 75-85.