

Carbamazepine-induced hyponatremia

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Abstract: Treatment with some drugs may lead to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), the presence of which is more likely in some populations, including people who are elderly or who take diuretics. Resulting drug-induced hyponatremia is often mild and usually resolves following water restriction and withdrawal of the drug. In some patients, however, it may be a potentially fatal condition that is typically asymptomatic until it becomes severe. In this article, we describe the case of a 59-year-old man with arterial hypertension, already treated with hydrochlorothiazide, who presented with hyponatremia after starting administration of carbamazepine. After excluding other common causes of hyponatremia, a diagnosis of SIADH was established, carbamazepine was withdrawn and SIADH treatment introduced. Our study shows that routine assessment of blood electrolytes is reasonable not only in patients receiving diuretics but also in patients treated with other drugs affecting vasopressin secretion.

Key words: carbamazepine, diagnosis, hydrochlorothiazide, syndrome of inappropriate antidiuretic hormone secretion (SIADH), treatment

INTRODUCTION

Hyponatremia, defined as serum sodium <135 mmol per liter, is the most common electrolyte disorder in hospitalized patients [1,2]. Hyponatremia occurs in 1% of hospitalized patients and subjects at a high risk for the disease are especially children and elderly patients [3]. Because of the fact that sodium is the dominant electrolyte of the extracellular fluid and the primary determinant of serum osmolality, the disturbances of sodium homeostasis can lead to pathologic alterations in cell functions [4,5]. Even asymptomatic hyponatremia is associated with the risk of complications and worsening prognoses for accompanying diseases [1,4]. The main causes of hyponatremia are iatrogenic factors. Diuretics are the most common drugs which induce hyponatremia, but there are a few case reports in literature in which hyponatremia is induced by another therapy [1,3].

CASE REPORT

A 59-year-old man was admitted to hospital because of severe hyponatremia. He was transferred to an emergency room with symptoms attributable to cerebral edema: depressed re-

flexes, weakness, Babinski's sign, seizures and extrapyramidal signs. The patient's blood pressure was 150/90 mmHg. The computer tomography scanning of the brain ruled out a stroke and showed cerebral edema.

A diagnosis of hypertension had been made 3 years earlier and he had been treated with a 10 mg daily dose of amlodipine. Because hypertension was uncontrolled, a 25 mg dose of hydrochlorothiazide per day was added to amlodipine therapy, 24 hours before admission. When after 4 days facial neuralgia developed, carbamazepine was administered in the dose of 200 mg per day. The dose was then increased to 600 mg 2 times a day. After 6 days from initiating the carbamazepine therapy, weakness, mild anorexia and vomiting were observed. Laboratory tests were normal except for a mild hyponatremia (126 mmol per liter) which was probably induced by hydrochlorothiazide, which then was discontinued. However, the patient was still symptomatic on hospital admission.

Laboratory tests revealed hyponatremia (112 mmol per liter), decreased effective osmolality (234 mOsm/kg of water) and increased urinary osmolality (371 mOsm/kg of water) in comparison to serum osmolality. The urine sodium concentration was 88 mmol per liter. The urinary output was 920 ml per day. Other laboratory tests revealed a low concentration of plasma uric acid (95 μ mol per liter), blood urea nitrogen (6.8 mmol per liter), creatinine (28 μ mol per liter) and phosphates (0.74 mmol per liter) in the serum. The serum potassium concentration was normal (4.84 mmol per liter) and remained stable during the rest of the patient's hospitalization. On the basis of these findings the patient was diagnosed with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Because of severe hyponatremia, fluid restriction and the infusion of a 3% saline were administered, since, similarly to other pictures of this syndrome, increased sodium concentrations can

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CASE REPORTS

be achieved when the infused saline osmolality is higher than the urinary osmolality [1,5]. The goal was to raise the serum sodium level by 1 mmol per liter per hour by infusing a 3% saline. The infusion of a 3% saline was discontinued when the serum sodium concentration reached 125 mmol per liter and the patient remained stable because of the risk of central pontine myelinosis. On the 5th day of hospitalization the serum sodium concentration was normal. Based on medical history, the physical examination and laboratory tests, other causes of this syndrome were ruled out (neoplasm, pulmonary diseases, diseases of the central nervous system, acute intermittent porphyria and other causes of iatrogenic hyponatremia, hypovolemic hyponatremia, glucocorticoid deficiency, hypothyroidism, hyponatremia due to fluid abuse, congestive heart failure, cirrhosis and renal failure in the course of nephritic syndrome, pseudohyponatremia and reset osmostat syndrome). Carbamazepine was discontinued on admission because the patient was asymptomatic and there was a relationship between the occurrence of hyponatremia and the use of carbamazepine.

Twelve months later the patient remained stable and hyponatremia was not observed during the repeated measurements. Amlodipine and bisoprolol were continued; the patient's blood pressure was controlled.

DISCUSSION

Iatrogenic hyponatremia is an important clinical problem [4]. In the discussed case hyponatremia developed rapidly and led to the life-threatening condition. At the beginning we supposed that the patient's symptoms were associated with the thiazide therapy and caused by the increasing loss of sodium and water, because the use of this medication can result in the decrease of extracellular fluid, the increased secretion of vasopressin, and the disturbance of free water excretion [6]. Hyponatremia induced by thiazides is not only one of the common causes of iatrogenic hyponatremia, but occurs usually (like in this case) in the first 2–3 weeks of pharmacotherapy [1]. Although the thiazide therapy was discontinued, the sodium level was not normalized, in contrast, the disturbances of electrolytes became severe, thus, we considered that hyponatremia was not due to this drug in the discussed case.

It seems that in our case hyponatremia is due to the use of carbamazepine, one of the three anticonvulsants (besides oxcarbamazepine and lamotrigine) that can lead to iatrogenic hyponatremia [3,6]. Hyponatremia induced by these medications is associated with the modification of vasopressin on renal tubules [3,6].

In the majority of described cases, like in the discussed case, carbamazepine-induced hyponatremia developed shortly after initiating therapy [7,8]. However, contrary to the data from literature, in our case hyponatremia was more severe. Interestingly, the clinical symptoms over the first days of hospitalization were mild and then, over the next few hours the patient's clinical condition deteriorated. A similar clinical course

was observed by other authors in patients with hyponatremia of other etiology [4]. The case report described here concerns nephrogenic diabetes insipidus induced by colchicine. As similar symptoms were observed a few years earlier after treatment with gentamicin, we suggest that some patients may exhibit a genetic predisposition to the development of a drug-induced diabetes insipidus [9]. In the discussed case report despite the withdrawal of thiazide hyponatremia persisted, and even became more severe. It is well known that thiazide can induce hyponatremia, but in our case this tendency was not noticed. It seems that in iatrogenic diabetes insipidus genetic predisposition to develop electrolyte disturbances induced by different medications does not play any role in iatrogenic hyponatremia.

In most cases iatrogenic hyponatremia usually affects certain populations (the elderly and children) and people in the life-threatening condition [6,8]. Moreover, symptomatic hyponatremia occurs more often in females [1,3]. In the discussed case hyponatremia occurred in a man, who did not suffer from other severe concomitant diseases, and hence we think that the risk of an incidental hyponatremia should be taken into consideration in all patients, even those whose initial clinical condition is good and who have no history of hyponatremia. The present study shows that the routine assessment of blood electrolytes is reasonable not only in the case of patients receiving diuretics but also the patients treated with other drugs affecting vasopressin secretion.

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