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OLGU SUNUMU / CASE REPORT

Severe hyponatremia and rhabdomyolysis associated with hypothyroidism

Hipotiroidi ile ilişkili ağır hiponatremi ve rabdomyoliz

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Abstract

Hyponatremia is one of the laboratory feature of hypothyroidism and usually occurs in elderly patients. In this report we presented a young patient with hypothyroidism induced severe hyponatremia and rhabdomyolysis. A nineteen-year-old woman was brought to the hospital with confusion. Because of acute hyponatremia with confusion, she was treated with hypertonic saline. The neurological examination returned to normal after treatment and fluid restriction, then serum sodium level increased to normal. Because of recurrent hyponatremia futher investigations were held. She was diagnosed as Hashimoto's thyroiditis. Hyponatremia improved with levothyroxine therapy and serum sodium level remained normal range. The elevated parameters of rhabdomyolysis decreased with levothyroxine therapy. Hypothyroidism should be considered in patients presenting with hyponatremia and rhabdomyolysis.

Key words: Hypothyroidism, hyponatremia, rhabdomyolysis.

Öz

Hiponatremi hipotiroidinin laboratuvar bulgularından biridir ve daha çok ileri yaştaki hastalarda gelişmektedir. Burada genç bir hastada hipotiroidi zemininde gelişen ciddi bir hiponatremi ve rabdomyoliz olgusu sunulmuştur. Ondokuz yaşında kadın hasta acil servise bilinç kaybı yakınmasıyla başvurdu. Hastada bilinç bulanıklığının da eşlik ettiği akut hiponatremi olması nedeniyle hipertonik salin infüzyonu uygulandı. Tedavi sonrası bilinci düzeldi, serum sodyumu normal değerlere yükseldi. Tekrarlayan hiponatremisi olması nedeniyle ileri tetkikleri yapıldı. Hastaya hashimato tiroiditi tanısı kondu. Hiponatremi levotroksin tedavisiyle geriledi ve serum sodyumu normal aralıkta seyretti. Tiroid hormonu replasman tedavisiyle rabdomyoliz ile uyumlu parametreler de hızlı bir şekilde geriledi. Hiponatremi ve rabdomyolizle gelen hastalarda hipotiroidizm mutlaka akla gelmelidir.

Anahtar kelimeler: Hipotiroidi, hiponatremi, rabdomyoliz.

INTRODUCTION

Hyponatremia, defined as serum sodium concentration below 135mEq/L, is one of the most commonly encountered electrolyte abnormalities in hospitalized patients. It is rarely observed in outpatients and is present in certain chronic diseases. In the absence of pseudohyponatremia or an excess of osmotically active solutes in extracellular fluid, the most important initial step in the diagnosis of hyponatremia is the assessment of the extracellular fluid volume status. Then hyponatremic patients can be grouped into three ategories as hypovolemic, hypervolemic and euvolemic hyponatremia. If there is not a serious renal failure, diminished free water excretion that facilitates euvolemic hyponatremia is almost always the result of a persistent antidiuretic hormone (ADH) secretion. Persistent ADH secretion occurs usually due to one of four conditions; effective circulatory volume depletion, the syndrome of inappropriate antidiuretic hormone secretion, cortisol deficiency or hypothyroidism[1]. Hyponatremia is sometimes associated with moderate to severe hypothyroidism, particularly in patients with primary hypothyroidism and myxedema. Thus, thyroid function should be evaluated in any patient with an otherwise

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unexplained reduction in the plasma sodium concentration. Although the mechanisms influential in the development of hyponatremia have not been fully understood yet, some reports have postulated inappropriate secretion of antidiuretic hormone (SIADH) as being causative while others have implicated a relative deficiency of adrenal cortical hormone or changes in renal function[2]. Here, we present a young patient having severe hyponatremia and rhabdomyolysis induced by hypothyroidism.

CASE

A 19-year-old woman was brought to our hospital due to disturbance of consciousness. Her anamnesis did not reveal any disease or use of any medication while the physical examination showed that she had somnolence, a blood pressure of 100/60 mmHg, temperature of 36.5 °C and pulse rate of 88 beats/min. Systemic examination did not reveal any abnormalities and the electrocardiogram showed a normal sinus rhythm.

The main pathological finding of the tests during admission was low serum sodium concentration (Na: 117 mmol/L). She had mild anaemia. Due to the accompanying elevated liver enzymes (Aspartate aminotransferase (AST), Alanin aminotransferase (ALT)), further tests were performed for liver toxicity. Hepatitis markers were found to be negative and her anamnesis did not reveal any toxic drugs or substances. Parameters (serum bilirubin, alkaline phosphatase. (ALP), gamma glutamyl transferase (GGT), amylase) related with liver and biliary tract were normal. However, consistent with rhabdomyolysis, laboratory findings showed that creatine phosphokinase (CK), myoglobin and lactate dehydrogenase (LDH) were elevated. Spot urine analysis showed that a urine density of 1011, sodium of 79 mEq/l, potassium of 24 mEq/l and osmolality of 486 mOsm/kg. The simultaneous plasma osmolality was 242 mOsm/kg. The patient was considered as having euvolemic hyponatremia. Laboratory tests performed at admission are summarized in Table 1.

Table 1. Laboratory data on admission

Variable	Value
White blood eell (lmm3)	9070 (3600- 9400)
Hemoglobin (grldL)	11.8 (12-16)
Hemotocrit (%)	% 34.3 (36-46)
Platelets (lmm3)	399000 (142- 424)
Mean eorpuscular volume (MCV)	88(80-100)
Glueose (mg/dL)	106 (80-105)
Blood urea nitrogene (mg/dL)	4.6 (6-20)
Creatinine (mg/dL)	0.5 (0.6-1.1)
Urie asid (mg/dL)	2.5 (2.6-6)
Sodium (mmol/L)	117 (136-145)
Potassium (mmol/L)	4.9 (3.5-5.1)
Calcium (rnq/dl.)	9.1 (8.4-10.2)
Cloride (mrnol/l.)	86 (98-107)
Phosphorus (mg/dL)	3.4 (2.3 - 4.7)
Albumine (g/dL)	4.2 (3.5-5)
Total protein (g/dL)	7.0 (6-8)
Creatine phosphokinaze (CK)(IU/L)	44469 (29-168)
Lactate dehydrogenase (lU/Ll	1869 (125-243)
Aspartate aminotransferase (IU/L)	201 (5-35)
Alanin aminotransferase (IU/L)	108 (10-36)
Alkaline phosphatase (IU/L)	53 (25-100)
Total bilirubin(mg/dL)	0.35 (0.2-1.2)
CK-MB (ng/ml)	5.1 (0-5)
Myoglobin (ng/ml)	31 (0-106)
Direct bilirubin (mgldL)	0.19 (0-0.5)
Plasma osmolality (mOsm/kg)	242 (280-290)

Due to acute hyponatremia with disturbance of consciousness, the patient was first treated by hypertonic saline. After hypertonic saline treatment, her disturbance of consciousness was ameliorated and the concurrent fluid restriction caused serum sodium concentration to rise to 142 mmol/L. However, serum sodium concentration decreased progressively and hyponatremia developed once again (Na: 121 mmol/L).

Further tests were performed to detect the underlying cause of euvolemic hyponatremia. Plasma adrenocorticotropin and cortisol levels were found to be within the normal range. Abdominal ultrasonography showed normal adrenal glands and thus Addison disease was excluded. Neither the medical history nor any of the diagnostic procedures revealed any underlying pathology explaining the SIADH.

The chest X-ray was normal. On cranial magnetic resonance imaging, the sella turcica was normal in shape and size. Endocrinological tests revealed a low level of free triiodothyronine (FT3) and free thyroxine (FT4) and a high level of thyroid stimulating hormone (TSH) and both anti-thyroglobulin (Anti-TG Ab) and anti-thyroperoxidase (Anti- TPO Ab) antibodies were positive. The hormone profile of the patient is shown in Table 2.

Table 2. Endocrinological tests

Variable	Value
Adrenocorticotropic hormone (ACTH) (pq/ml.)	43 (0-46)
Cortisol (mg/dL)	10 (2.3-19.4)
Free triiodothyronine (FT3) (pg/mL)	1.58 (1.71-3.71)
Free thyroxine (FT4) (ng/dL)	0.6 (0.7-1.48)
Thyroid stimulating hormone (mIU/mL)	9.56 (0.35-4.95)
Anti thyroglobulin Ab (lU/mi)	86 (0-4.1)
Anti thyroperoxidase Ab (lU/mi)	416.78 (0-5.6)

She was diagnosed as primary hypothyroidism due to Hashimoto's thyroiditis based on the seropositivity of anti-thyroglobulin and anti-thyroperoxidase antibody and thyroid gland heterogeneity in the thyroid ultrasonography. Levothyroxine was initiated at a dose of 25 μg/day and increased every week until reaching to 100 μg/day. The patient recovered dramatically and her serum sodium level remained between 135-140 mmol/L on a maintenance dose of levothyroxine (100 mg/day). The baseline laboratory parameters consistent with rhabdomyolysis went back to normal ranges (CK:150 IU/L , LDH:194 IU/L , AST:21 IU/L , ALT:23 IU/L) with thyroid hormone replacement treatment. Tests performed one month after discharging from the hospital revealed that the thyroid hormone, serum sodium and CK levels (FT3: 1.83 pg/mL, FT4: 1.01 ng/dL , TSH:3.14 mIU/mL, Na: 139 mmol/L and CK:102 IU/L, respectively) were normal.

DISCUSSION

It is well known that hypothyroidism may give rise to hyponatremia. There exist hypothyroid cases applying to hospitals with disturbance of consciousness due to hyponatremia. This usually occurs in older patients, but can be seen in young patients too. Our patient is unusual for two causes. Firstly, she was young and secondly she presented with loss of consciousness but had no complaints related to hypothyroidism. Hyponatremia in hypothyroidism is commonly observed in myxedema coma but mechanism of its development remains to be elucidated. Adreno-corticol dysfunction and inappropriate secretion of ADH are the most elaborate hypotheses. It has been suggested that there is impaired osmoregulation of ADH release and/or a decrease in the metabolic clearance of ADH[3]. ADH has been reported to enhance renal water reabsorption in the collecting duct by ADHV2-receptors. Increase in plasma ADH levels decreases the free water excretion and results in water retention which leads to hyponatremia. Beside this, decreases in the glomerular filtration rate, renal plasma flow and tubular excretory capacity, which are the potential causes of hyponatremia, are also observed in hypothyroidism[4].

Decrease in cardiac output and increase in peripheral resistance have been shown in hypothyroidism too. These give rise to hypovolemia

and increase ADH release. All these hypofunctions diminished water reabsorption in the collecting duct and lead to a reduction in free water excreation by falling urine flow in distal tubule and/or inpairing osmotic gradient in the renal medulla. Moreover, plasma atrial natriuretic peptide (ANP) level decreases due to a reduction in ANP synthesis and its release in hypothyroidism. Decreased plasma ANP value leads to a reduction in renal glomerular filtration rate and renal blood flow[5]. When considered altogether, over secretion of ADH and renal hypofunction in hypothyrodisim cause a decrease in free water clearance, leading to hyponatremia. In our case, hyponatremia improved transiently by fluid restriction and sodium supplementation. However, hyponatremia occured again and improved with thyroid hormon replacement theraphy. In our case, after excluding neurologic, cardiologic or muscle diseases and use of toxic drugs, rhabdomyolysis was associated with hypothyroidism related hyponatremia. Coexistence of hyponatremia and elevated creatine phosphokinase levels has been previously described in case report as psychiatric patients having water intoxication and rhabdomyolysis[6] and hypothyroidism[7]. In hypothyroidism, creatine phosphokinase elevation is thought to be related to mild cardiac or skeletal muscle damage or decreased clearance of normal enzyme concentrations. In hyponatremia associated with hypothyroidism, the mechanism of which serum levels of sodium affect creatine kinase remains to be elucidated. It could be due to subclinical myocyte damage through intracellular movement of water and swelling of cells induced by hyponatremia[8].

In hypothyroidism, CK levels usually remain persistently elevated and are associated with raised levels of other enzymes as AST and LDH[7]. The elevated enzyme levels regress progressively with levothyroxine therapy. Before associating elevated enzyme levels with hypothyroidism, differential diagnoses such as myocardial infarction, muscle disease, skeletal muscle trauma, vigorous exercise, stroke, convulsions and intramuscular injections must be excluded. Having high rhabdomyolysis parameters at the laboratory tests but observing a recovery with levothyroxine therapy in our case supports the notion that hypothyroidism induced hyponatremia has also a facilitating effect on rhabdomyolysis.

As a result hypothyroidism should be considered in patients presenting with hyponatremia and rhabdomyolysis and thyroid hormone replacement treatment should be started as soon as the diagnosis is established.

REFERENCES

1. Rennke HG, Denker BM. Böbrek Fizyopatolojisi Temel Bilgiler. 2. Baskı, İstanbul, İstanbul Medikal Yayıncılık, 2008.
2. Nakano M, Higa M. Hyponatraemia with increased plasma antidiuretic hormone in a case of hypothyroidism. Intern Med. 2000;39:1075-8.
3. Kimura T. Potential mechanisms of hypothyroidism-induced hyponatremia. Intern Med. 2000;39:1002-3.
4. Montenegro J, Gonzales O, Saracho R. Changes in renal function in primary hypothyroidism. Am J Kidney Dis. 1996;27:195-8.
5. Kohno M, Takaori K, Matsuura T, Murakawa K, Kanayama Y, Takada T. Atrial natriuretic polypeptide in atrial and plasma in experimental hyperthyroidism and hypothyroidism. Biochem Biophys Res Commun. 1986;134:178-183.
6. Akasaki Y, Nagatomo L, Nomaguchi M, Matsumoto K. Water intoxication in a schizophrenic patient with rhabdomyolysis. Jpn J Psychiatry Neurol. 1993;47:843-6.
7. Iwasaki Y, Oiso Y, Yamauchi K. Osmoregulation of plasma vasopressin in myxedema. J Clin Endocrinol Metab. 1990;70:534-9.
8. Goldenberg I, Jonas M, Thaler M, Grossman E. Elevated levels of serum creatine kinase induced by hyponatraemia. Postgrad Med J. 1997;73:511-2.