Case Report

Severe Hyponatremia: A Comorbidity with I-131 Therapy in a Patient with Papillary Thyroid Cancer

Chalermrat Kaewput MD*,
Pawana Pusuwan MD*

** Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Hyponatremia is the most common electrolyte disorder in hospitalized patients, especially in elderly patients, in which morbidity varies widely in severity. A 64-year-old Thai woman with papillary thyroid cancer, who developed hypothyroid state after thyroid hormone withdrawal for preparation of I-131 treatment, had severe hyponatremia within the day of I-131 administration. It is possible that the combination of old age, hypothyroidism, severe nausea and vomiting, and inappropriate secretion of antidiuretic hormone (SIADH) may all have precipitated the severe hyponatremia in the presented case.

Keyword: *Hyponatremia, Hypothyroidism, Thyroid carcinoma*

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According to the revised American Thyroid Association (ATA) guideline, high-risk patients with differentiated thyroid cancer are recommended to be treated with radioactive iodine (I-131) after total thyroidectomy[1]. The efficacy of radioactive iodine depends on the radiation dose delivered to the thyroid tissue. The preparation of patients for I-131 treatment was done by thyroid hormone withdrawal or injecting recombinant human TSH (rhTSH) to produce high serum thyroid-stimulating hormone (TSH). TSH stimulates follicular cells to trap iodine[2,3].

Hyponatremia is a common electrolyte imbalance and hypothyroidism is one of the causes. Although hypothyroidism induced hyponatremia is rare, there are serious and fatal complications if there is no emergency treatment. Therefore, physicians should recognize it well, and adequately manage their patients[4].

The authors described a patient with papillary thyroid cancer who developed severe hyponatremia within the day of I-131 ablation. The mechanisms of this electrolyte imbalance are also discussed.

Case Report

A 64-year-old Thai woman with a history of papillary thyroid carcinoma underwent complete thyroidectomy in December 2010. Three months after complete thyroidectomy, the patient was admitted for ablation therapy with 100 mCi of I-131 after thyroid hormone withdrawal and low iodine diet. She was treated with I-131 without any complications.

In early June 2012, because of residual thyroid remnant seen on the follow-up diagnostic total body scan, the second I-131 therapy was performed with 150 mCi of I-131 after four weeks discontinuation of thyroid hormone replacement and two weeks of low iodine diet, which was not different from the first therapy. She had normal blood pressure and was not taking any medication other than thyroxine. All laboratory results including renal function and electrolytes were normal, except marked low serum T4 level (T4 = 1.7 ug/dl) as well as elevated serum TSH level (TSH >100 mIU/L) due to thyroxine withdrawal. She was advised to maintain good fluid intake to enhance elimination of I-131.

On the first day of admission, about six hours after the ingestion of I-131, she had nausea and vomited more than 10 times. Upon examination, she was fully conscious and oriented. She had euvolemic status and had stable vital signs. A high potency of anti-emetic drug was started every six hours.

In the morning of the second day of admission, she developed dizziness, abdominal discomfort, poor appetite, and vomited several times. She was marked fatigue and had difficulty in walking. At that time, her physical examinations showed drowsiness, lethargy, together with sunken eyeballs, dry lips, and poor skin turgor from hypovolemic dehydration. She still had

Correspondence to:
Kaewput C, Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine Siriraj Hospital, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: 0-2419-6220-1, Fax: 0-2412-7165
E-mail: aung_med@hotmail.com

stable vital signs except only tachycardia with a heart rate of 108/minutes. Laboratory values were summarized in Table 1. Initial blood tests revealed a critical serum sodium concentration of 117 mEq/L (reference range 135-145 mEq/L), which was thought to be the cause of impaired consciousness, together with other electrolytes abnormalities such as hypokalemia, hypocalcemia, and hypomagnesemia. She was treated with intravenous infusion of normal saline with potassium and calcium replacement. Correction was done by administration of 0.9% NaCl with rate of 150 ml/hour, her serum sodium level slightly increased from 117 mmol/L to 119 mmol/L in two hours. Then, 0.9% NaCl was reduced to 100 ml/hour (approximately 2 L over 24 hours); serum sodium was stable at the level of 120 mmol/L. At this time, no clinical evidence of volume depletion was detected. Urine specific gravity was low with the level of 1.005. By restriction of fluid intake below 800 ml/day, her serum sodium slightly increased and returned to normal level within two days. She had sequential laboratory investigation throughout her clinical course. Initial electrolytes were checked every six hours. Her mental status was normal during 48 hours after I-131 treatment.

On the third day of admission, all of her symptoms improved as well as her food intake. All electrolytes imbalance were gradually become normal until discharge in mid-June 2012 with full recovery.

Discussion

The management of high-risk patients with differentiated thyroid carcinoma includes total thyroidectomy and followed by radioactive iodine treatment. Thyroid tissue is able to concentrate iodine under the influence of thyrotropin, which is achieved by withdrawal of thyroid hormone before I-131 therapy, directly resulting in hypothyroidism[1-3].

Hypothyroidism is widely accepted as one of the causes of hyponatremia[4,5]. There were few reported cases of hyponatremia in association with hypothyroidism induced by patient preparation for I-131 therapy in thyroid cancer patients[6-8]. The present case with papillary thyroid cancer had hypothyroidism (TSH level of >100 mIU/L) due to preparation for I-131 therapy, developed severe symptomatic hyponatremia within the day of I-131administration. Baajafer et al demonstrated short-term hypothyroidism induced by pretreatment of I-131therapy in patients with thyroid cancer was rarely complicated by severe hyponatremia[9]. However, the review article by Al Nozha OM et al showed several common characteristic of patients with severe hyponatremia as a consequence of the preparation for radioiodine therapy in thyroid cancer, such as old age (>65 years), use of thiazide diuretics, prolonged low-sodium diet, prolonged hypothyroid state and multiple metastases (lung or brain)[10]. There was no history of diuretics administration or sodium

Table 1. Results of laboratory testing of the patient during hospital admission

Test	Baseline (preadmission)	Day 1 of hospitalization	Day 2 of hospitalization	Day 3 of hospitalization
Na^+ (135-145 mmol/L)	142	117	128	136
K^+ (3.5-5.0 mmol/L)	3.9	3.4	3.8	3.5
Cl^- (98-107 mmol/L)	102	81	94	103
HCO_3^- (98-107 mmol/L)	31	22	22	24
Anion gap (8.1-10.4 mg/dl)	9.0	14.0	12.0	9.0
Total calcium (8.1-10.4 mg/dl)	9.0	7.6		
Albumin (3.5-5.5 g/dl)	4.6	4.5		
Phosphorus (2.2-5.0 mg/dl)	3.4	2.8		
Magnesium (1.9-2.6 mg/dl)		1.7		
BUN (7-20 mg/dl)	11.6	8.9		
Cr (0.5-1.5 mg/dl)	0.9	0.9		
Serum osmolarity (275-295 mOsm/kg)		244		
Urine osmolarity (50-1400 mOsm/kg)		418		
Urine sodium (40-220 mOsm/kg)		134		

BUN = blood urea nitrogen

restriction in the presented case. She had no evidence of pulmonary or brain metastases. In this context, old age and hypothyroidism were thought to be the main risk of hyponatremia in the presented case. There was a report that an important factor in the expression of hypothyroidism-associated hyponatremia may be from the severity of hypothyroidism (TSH ranged from 30-180 mIU/L)[9], which was similar to the presented case.

Hypothyroidism has been associated with several reversible changes in renal function including decreased renal blood flow, decreased glomerular filtration rate, and hyponatremia. The mechanisms involved in hypothyroidism-associated kidney derangements are direct effect of thyroid hormone on the cardiovascular system, such as increased peripheral resistance and reduction of myocardial contraction and stroke volume[11-15].

The present case showed severe hyponatremia together with other electrolytes imbalance such as hypokalemia, hypomagnesemia, hypochloremia, and hypocalcemia. These additional electrolyte disturbances are frequently observed in patients with hyponatremia of any origin[16]. Since she developed poor appetite, nausea, and severe vomiting approximately 6 hours after I-131 administration. She had clinical evidence of plasma volume contraction with low level of serum sodium at the same time. After intravenous infusion of normal saline, serum sodium level slightly increased. Thus, severe vomiting caused hypovolemia may be responsible for hyponatremia in the early period of admission as well as hypokalemia. Both reduced intake of potassium and extrarenal potassium loss were thought to be the cause. Hypomagnesemia was a result of hypokalemia. It was reported that hypophosphatemia was the most frequent electrolyte disorder especially in the patient with hyponatremia due to SIADH[16]. Hypocalcemia may be from transient hypoparathyroidism after I-131 treatment[17].

Nausea is one of the side effect of I-131 therapy but it is extremely rare (seen less than 1%). At least 50% of patients experience nausea to some degree, which usually begin a few hours after taking I-131 and resolve within 24 to 36 hours. The mechanism of nausea from I-131 therapy is not known. It may be due to radiation-induced gastritis from the high accumulation of radioiodine in the parietal cells of the stomach or related anxiety. Nausea is more likely and more severe with increasing I-131 dose. Nausea to the point of vomiting occurs in about 10% of patients who receive 150 mCi of I-131 treatment[18]. Therefore, the higher dose of I-131 administered in the second session as compared to the first admission was a possible reason for severe nausea and vomiting in the presented case.

After volume contraction occurs, the renin-angiotensin-aldosterone system is stimulated, directly resulting in decreased urine sodium level. However, SIADH should be suspected in any patient with hyponatremia, hypoosmolality with urine osmolality above 100 mOsmol/kg, and urine sodium concentration above 40 mEq/L[19], as seen in the presented case. It was suspected to be one of the causes of hyponatremia. It is possible that the combination of primary hypothyroidism and SIADH will overcome the renal conservation of sodium, resulting in inappropriate sodium excretion. After fluid restriction, hyponatremia gradually resolved and finally returned to normal, although, serum ADH level was not determined in this patient. It was reported that the occurrence of hyponatremia in patients with hypothyroidism might be caused by both ADH dependent and ADH independent mechanism, especially in myxedema patients who had low effective circulartory volume due to bradycardia and low cardiac output[20]. However, SIADH commonly develops in clinical disorders such as pulmonary tumors or central nervous disorders. Both conditions were not found in the presented case, and one criteria required to make a diagnosis of SIADH include exclusion of hypothyroidism.

The presented case underwent I-131 therapy one time before this admission. The pretreatment preparation was the same in both treatments, but severe hyponatremia only occurred in the second session. It was possible that severe nausea and vomiting during admission was a specific trigger of severe hyponatremia precipitated by prolonged hypothyroidism and SIADH. It is realized that symptomatic hyponatremia may occur in patients with severe vomiting who had normal serum electrolyte on the baseline study before admission.

Conclusion

An elderly papillary thyroid cancer patient without evidence of metastasis developed severe hyponatremia during admission possible from multifactorial causes such as prolonged hypothyroidism after thyroxine withdrawal, severe nausea, and vomiting, and possible SIADH. Thus, screening of risk factor, careful monitoring of symptoms after I-131 treatment, and urgent appropriate treatment may prevent severe hyponatremia in hypothyroidism patients whose baseline serum electrolyte levels before admission were normal.

What is already known on this topic?

Hypothyroidism is known to be one of the causes of hyponatremia[4,5]. The data from a retrospective study of 128 patients with thyroid cancer by Baajafer et al demonstrated that hypothyroidism induced by pretreatment of I-131 therapy were rarely complicated by severe hyponatremia[9]. However, there were several common characteristics of thyroid cancer patients with severe hyponatremia as a consequence of the preparation for radioiodine therapy, such as old age (>65 years), use of thiazide diuretics, prolonged low-sodium diet, prolonged hypothyroid state, and multiple metastases (lung and brain) in the review article by Al Nozha OM et al[10].

What this study adds?

Symptomatic hyponatremia may occur in an elderly papillary thyroid cancer patient who had severe nausea and vomiting as a specific trigger during admission for I-131 treatment, precipitated by prolonged hypothyroidism and SIADH, although, baseline serum electrolyte levels before admission were normal.

The authors hope that the presented case will be recognized by the physician to screen for risk factor, careful monitor symptoms after I-131 treatment, and urgently appropriate treat their patients, which may prevent severe hyponatremia in hypothyroidism patients.

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Potential conflicts of interest

None.

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ภาวะโซเดียมในซีรัมต่ำอย่างรุนแรง: ความผิดปกติที่เกิดร่วมกับการรักษาด้วยไอโอดีน 131 ในผู้ป่วยมะเร็งไทรอยด์ชนิด papillary

เฉลิมรัตน์ แก้วพุด, ภาวนา ภูสุวรรณ

ภาวะโซเดียมในซีรัมต่ำเป็นความผิดปกติของเกลือแร่ในร่างกายที่พบได้บ่อยที่สุดในผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาล โดยเฉพาะในผู้ป่วยสูงอายุซึ่งจะมีระดับความรุนแรงที่แตกต่างกันไป กรณีผู้ป่วยหญิงไทยอายุ 64 ปี มีประวัติมะเร็งไทรอยด์ชนิด papillary ซึ่งมีภาวะขาดฮอร์โมนไทรอยด์จากการหยุดยาฮอร์โมนไทรอยด์เพื่อเตรียมตัวสำหรับการรักษาด้วยไอโอดีน 131 ได้เกิดภาวะโซเดียมในซีรัมต่ำอย่างรุนแรงภายใน 1 วัน นับจากได้รับไอโอดีน 131 โดยอาจเป็นไปได้ว่าภาวะโซเดียมในซีรัมต่ำที่เกิดขึ้นในผู้ป่วยรายนี้อาจมีสาเหตุร่วมกันระหว่างสูงอายุ ภาวะขาดไทรอยด์ฮอร์โมน ภาวะคลื่นไส้อาเจียนอย่างรุนแรง และภาวะ inappropriate secretion of ADH