

Teaching Point
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Masked hyperthyroidism in a haemodialysis patient successfully treated by potassium iodide

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Introduction

Hyperthyroidism should be suspected in end-stage renal disease (ESRD) patients who exhibit signs and symptoms including weight loss, tremor, palpitation or atrial fibrillation (Af) [1–5].

This report presents the case of an 82-year-old Japanese female on maintenance haemodialysis (HD) and paroxysmal Af (pAf). Although the serum thyroid hormone levels were within normal reference values for a young healthy control, she was found to have masked hyperthyroidism.

Case report

An 82-year-old female presented with no history of symptoms and signs of hyperthyroidism. She had pregnancy-induced hypertension which had been controlled by medication since 1982, but her blood pressure had not been controlled from 1960 through 1981. She started maintenance HD for ESRD due to pregnancy-induced hypertension since 23 April 2004. She had pAf and cardiomegaly on 12 May 2004, but her thyroid function had not been evaluated.

Her height was 145 cm and body weight before HD was 36.8 kg and 34.9 kg after HD without weight loss. Her blood pressure before HD was 135/61 mmHg and heart rate 72 b.p.m. She had no goiter. The findings of her eyes, chest and abdominal examinations were not remarkable. There was no oedema. The laboratory data before HD in the morning were haemoglobin 103 g/L (10.3 g/dL), white blood cell count $5.0 \times 10^9/L$ (5000/ μ L), platelet count $223 \times 10^9/L$ ($22.3 \times 10^4/\mu$ L), total protein level 60 g/L (6.0 g/dL), albumin 37 g/L (3.7 g/dL), serum creatinine (Cr) 503.9 μ mol/L (5.7 mg/dL), blood urea nitrogen 25.7 mmol/L (72 mg/dL), glutamic oxaloacetic transaminase 12 IU/L, glutamic pyruvic transaminase 9 IU/L, lactic acid dehydrogenase 177 IU/L, alkaline phosphatase (ALP) 738 IU/L, creatine phosphokinase 75 IU/L, uric acid 422.5 μ mol/L (7.1 mg/dL), total cho-

lesterol (TC) 4.09 mmol/L (158 mg/dL), sodium 139 mEq/L, potassium 5.2 mEq/L, calcium 2.18 mmol/L (8.7 mg/dL), phosphorus 1.65 mmol/L (5.1 mg/dL) and C-reactive protein (–). The cardiothoracic ratio (CTR) was 59.4% in a chest X-ray (Table 1). There was pAf in her electrocardiogram (ECG), and mild aortic regurgitation observed in an ultrasonic cardiogram. Thyroid function tests showed that her serum-free thyroxine (fT₄) level was 1.54 (1.01–1.79) ng/dL, free triiodothyronine (fT₃) 2.19 (2.00–4.40) pg/mL, thyroid-stimulating hormone (TSH) <0.01 (0.27–4.20) mU/L and TSH receptor antibody (human) 2.2 (<1.0) IU/L (Table 1), anti-thyroglobulin antibody >100 (<0.3) U/mL and anti-thyroid peroxidase antibody >50 (<0.3) U/mL, on 6 February 2006.

She took 15 mg of methimazole (Mercazole[®]) on 5 April 2006 and 15 mg of propylthiouracil (Thiuragyl[®]) on 17 May 2006, but both of the drugs were immediately withdrawn because of an adverse side effect (skin eruption). She started 50 mg potassium iodide (KI) and the pAf in the ECG disappeared on 14 June 2006. The serum fT₄ level was then 0.92 ng/dL and TSH level became detectable (1.05 mU/L) on July 2007. Although the dosage of KI was gradually reduced to 50 mg 3 days per week, the escape phenomenon from the effect of excess iodide was not observed and serum TSH level remained detectable (3.62 mU/L) until April 2008. The serum fT₄ level (0.97 ng/dL) and fT₃ level (1.66 pg/L) remained constant. As to the blood chemistry, improvement of serum ALP (from 738 to 371 IU/L) and TC (from 4.09 to 5.05 mmol/L) was observed and CTR was also improved from 59.4 to 55.6%. The patient felt much better than before the KI treatment. Gradual decrease in TSH receptor antibody titer was observed from 2.2 to 1.8 IU/L and then to 1.3 IU/L in April 2008, and she displayed ordinary sinus rhythm in the ECG.

She was treated with 50 mg KI everyday, -August 2006; 50 mg KI 3 days per week, -June 2008; KI 50 mg 2 days per week, -February 2010 and KI 50 mg 1 day per week. She was scheduled to receive KI 50 mg 1 day per week for the next 2 years.

Discussion

An 82-year-old female with ESRD on maintenance HD presented hyperthyroidism. Her pAf seemed to be the only sign suggesting thyrotoxicosis. Since she was allergic to thionamide anti-thyroid drug, she was treated with 50 mg KI. The improvement of the laboratory values after successful KI treatment, including serum thyroid hormone levels, ALP and cholesterol level, suggested that these abnormalities were induced by long-standing hyperthyroidism since 2004. Although she was almost asymptomatic before the treatment, she felt much better following KI treatment.

The most characteristic finding in this patient was that the serum-free thyroid hormone levels were within the normal reference values for a young healthy control. Although no thyroidal radioactive iodine uptake test was performed, the suppressed serum TSH level and positive TSH receptor antibody suggested that the patient had Graves' hyperthyroidism. The serum thyroid hormone levels were lower than those in healthy controls in patients with non-thyroidal illness including ESRD. Moreover, the thyroid hormone levels may be lower and signs and symptoms of thyrotoxicosis may be masked in elderly individuals [6]. This indicates that the thyroid function must be carefully evaluated in elderly patients with non-thyroidal illness.

The prevalence of heat intolerance, irritability, increased perspiration or excessive appetite is lower among Graves' hyperthyroidism patients aged ≥ 50 years of age than among younger patients [7]. pAf was the only sign suggesting the presence of hyperthyroidism in this patient.

Primary hyperthyroidism is extremely rare in patients with chronic renal failure. However, the frequency of hyperthyroidism is not significantly different, at 1.0% in patients with

ESRD in comparison to 0.3–0.5% in the general population [1]. A previous study showed hyperthyroidism in 2/1252 cases (0.9%), with 3 definite (0.2%) and 9 borderline cases (0.7%) among the Hisayama residents in general [8]. Previous studies show that the prevalence of Af at the time diagnosis of overt hyperthyroidism ranges from 2 to 30% [6, 7, 9] and the prevalence is higher among patients aged ≥ 60 years of age [6]. A low serum TSH concentration among those ≥ 60 years of age is associated with a 3-fold higher possibility that Af will develop in the subsequent decade [9].

A literature search revealed 10 other cases (Table 2). In Japan, hyperthyroidism is commonly treated with anti-thyroid agents, methimazole (Mercazole[®]) or propylthiouracil (Thiuragyl[®]). Methimazole (Mercazole[®]) or propylthiouracil (Thiuragyl[®]) was administered for the treatment of hyperthyroidism, but both the drugs were withdrawn because of skin eruptions (this patient). She was successfully treated with 50 mg KI (Table 2) [1–5, 10–14].

In Japan, hyperthyroidism is commonly treated with thionamide anti-thyroid drugs, such as methimazole or propylthiouracil. Since she was allergic to these drugs, she was then treated with 50 mg KI. KI therapy had been popular before thionamide anti-thyroid drugs became available. KI therapy is now not popular because it is believed that escape from the KI effect is observed. However, escape was not observed in our case and the patient remained well with a small dosage of KI for about 4 years.

Iodide is mainly excreted through the kidneys, and the serum inorganic iodide level has been found to be increased several fold in patients with renal failure, in comparison to normal controls [15]. In our study, a high prevalence of iodide-induced reversible hypothyroidism was found due to retention of excess iodide in ESRD on HD.

Table 1. Changes in the laboratory findings^a

	6 February 2006	5 April 2006	17 May 2006	14 June 2006	2 July 2007	7 April 2008
fT ₄ (ng/dL)	1.54	1.83	1.12	0.67	0.92	0.97
fT ₃ (pg/mL)	2.19	n.d.	n.d.	1.15	n.d.	1.66
TSH (mIU/L)	<0.01	<0.01	0.01	0.39	1.05	3.62
TRAb (IU/L)	2.2	n.d.	n.d.	1.8	n.d.	1.3
ALP (IU/L)	738	639	669	474	491	371
BUN (mmol/L)	25.7	30.4	29.3	25.7	27.9	24.3
Cr (μ mol/L)	503.9	539.2	627.6	565.8	698.4	795.6
TC (mmol/L)	4.09	4.01	3.94	5.28	5.13	5.05
CPK (U/L)	75	76	49	46	107	76
CTR (%)	59.4	58.9	59.4	57.9	56.5	55.6

^afT₄, free thyroxine; fT₃, free triiodothyronine; TRAb, TSH receptor antibody (human); BUN, blood urea nitrogen; Cr, creatinine; CPK, creatine phosphokinase; n.d., not done.

Table 2. Hyperthyroidism in a patient on HD; reported cases^a

Case	Age/sex	Cause of CKD	Onset of hyperthyroidism	Treatment	Ref.
1	83/F	Urinary tract infection	Before HD	ND	[10]
2	32/F	ND	ND	Methimazole	[1]
3	38/F	Diabetic nephropathy	4 Years after HD	¹³¹ I	[11]
4	64/F	Diabetic nephropathy	7 Months after HD	Propylthiouracil	[2]
5	25/F	Chronic pyelonephritis	5 Months after HD	¹³¹ I	[3]
6	64/F	Obstructive uropathy	1 Year after HD	¹³¹ I	[5]
7	38/F	ND	3 Years after HD	¹³¹ I	[12]
8	37/F	ND	At the same time as HD	Propylthiouracil	[4]
9	62/F	Chronic glomerulonephritis	10 Months after HD	¹³¹ I	[13]
10	63/M	Chronic glomerulonephritis	28 Years after HD	Propylthiouracil	[14]
11	82/F	Pregnancy induced hypertension	1 Month after HD	Potassium iodide	This case

^aCKD, chronic kidney disease; ref., reference; ND, not described.

One study [15] suggests that impaired urinary excretion of iodide is also responsible for elevation of serum iodide levels and that urinary iodine excretion might play an important role in the escape phenomenon from the effect of excess iodide.

The thyroid function should be checked in patients, even if only a few signs of thyrotoxicosis are observed, such as weight loss, tachycardia or Af, since the signs and symptoms of thyrotoxicosis may be masked in elderly people. The suppressed serum TSH level is the most sensitive test for masked thyrotoxicosis since the reference values for serum-free thyroid hormones may be lower in those patients, and positive TSH receptor antibody is useful for the diagnosis of mild Graves' hyperthyroidism, together with anti-thyroglobulin or anti-thyroid peroxidase antibodies as markers for the presence of autoimmune thyroid disease. KI may be one of the drugs of choice in these patients with masked and mild-type Graves' hyperthyroidism, without serious side effects.

In conclusion, this clinical course suggested that the normal reference values for a young healthy control may be higher for the older patients undergoing maintenance HD and that KI therapy would be effective in those with mild hyperthyroidism suffering from renal dysfunction without causing the escape phenomenon.

Teaching points

- (1) Hyperthyroidism is exceedingly rare in patients treated by maintenance HD.
- (2) PAF can be the only revealing symptom of this endocrine disorder.
- (3) The normal reference values for serum-free thyroid hormones can be low in these patients and positive anti-TSH receptor antibodies, anti-thyroglobulin and anti-thyroid peroxidase antibody assays are required to lead to the diagnosis.
- (4) Treatment with potassium iodide is efficient in such patients and devoid of the escape phenomenon.

Conflict of interest statement. None declared.

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