

[CASE REPORT]

The Delayed Diagnosis of Thyroid Storm in Patients with Psychosis

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Abstract:

We herein report two cases of patients with thyroid storm with a delayed diagnosis due to psychosis. The patients were a 63-year-old woman with bipolar II disorder and a 37-year-old man with major depressive disorder. The psychoses in both patients were well controlled with medication. Although they both showed symptoms of thyrotoxicosis, the symptoms were ignored, presumably because the psychological manifestations of worsening of psychosis and thyroid storm are similar. When the mental or physical state of patients with psychosis changes, thyroid hormone levels should be measured for early treatment.

Key words: thyroid storm, Graves' disease, central nervous system, psychosis

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Introduction

Thyroid storm is a medical emergency that is associated with multiple-organ dysfunction due to a failure of normal homeostatic mechanisms to cope with excessive thyroid hormone levels. It may develop in patients with thyrotoxicosis who are under severe stress (1). In Japan, thyroid storm has been reported in approximately 0.2 per 100,000 persons per year with a mortality rate that exceeds 10% (2). Central nervous system (CNS) manifestations, including the presence or absence of consciousness disorder, are important for the clinical diagnosis and outcomes of thyroid storm in Japan (1, 3, 4). However, such manifestations can be diverse and easily misinterpreted as psychosis (2, 5), which is confounded in cases where patients with psychosis.

In this study, we report two cases of patients with thyroid storm that were diagnosed late.

Case Reports

Case 1

A 63-year-old Japanese woman with bipolar II disorder had been treated with medication at a psychiatric hospital. Her mental state had been stable for over three years. However, in the past two months, the deterioration of her depression had been noted, accompanied by a decreased food intake and extensive fatigue. She was admitted to a psychiatric hospital with a two-day history of emaciation and difficulty with dietary intake, at which point she experienced disorientation and developed incomprehensible speech and somnolence. Therefore, she was transferred to our hospital.

Her medical history was significant only for sciatica, and her family history was unremarkable. She was treated with mirtazapine, flunitrazepam, lorazepam, haloperidol, biperiden, famotidine, rivaroxaban, and verapamil. On an examination, she had a height of 156 cm, a weight of 40.8 kg, a body temperature of 38.9°C, tachycardia with 177 beats per

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Table 1. Laboratory Findings at Admission in Case 1.

Hematology		Serum chemistry/immunology			
WBC	10,700 / μ L	TP	5 g/dL	TG	64 mg/dL
RBC	4.04 \times 10 ⁶ / μ L	ALB	2.9 g/dL	T-chol	30 mg/dL
Hb	11.5 g/dL	T-Bil	1 mg/dL	HDL-chol	33 mg/dL
Hct	35.8 %	AST	13 IU/L	TnI	10 pg/dL
Plt	0.93 \times 10 ⁵ / μ L	ALT	15 IU/L	CRP	0.23 mg/dL
PT	23.6 Sec	γ -GTP	52 IU/L	PCT	0.031 ng/mL
APTT	27.2 Sec	ALP	287 IU/L	HbA1c (NGSP)	5.9 %
Fib	258 mg/dL	LDH	203 IU/L	Glu	101 mg/dL
		CK	27 IU/L	FT3	16.39 pg/mL
Arterial blood gas		BUN	17 mg/dL	FT4	3.74 ng/dL
pH	7.448	Cr	0.38 mg/dL	TSH	<0.003 μ U/mL
pCO ₂	47.4 mmHg	Na	141 mEq/L	TRAb	21.6 IU/L
pO ₂	42.8 mmHg	K	5 mEq/L	Tg	233.3 ng/mL
HCO ₃ ⁻	32 mmol/L	Cl	106 mEq/L	Tg-Ab	11.66 IU/mL
BE	6.9 mmol/L	Ca	9 mg/dL	TPO-Ab	6.27 IU/mL
		P	3.6 mg/dL	NT-proBNP	3,810 pg/mL

γ -GTP: gamma glutamyl transpeptidase, ALB: albumin, ALT: alanine aminotransferase, APTT: Activated partial thrombin time, AST: aspartate aminotransferase, ALP: alkaline phosphatase, BE: base excess, BUN: blood urea nitrogen, Ca: calcium, CK: creatine kinase, Cl: chloride, Cr: creatinine, CRP: C-reactive protein, Fib: Fibrinogen, FT3: free triiodothyronine, FT4: free thyroxine, Glu: glucose, Hb: hemoglobin, HbA1c (NGSP): hemoglobin A1c (National Glycohemoglobin Standardization Program), HCO₃⁻: bicarbonate, Hct: hematocrit, HDL-chol: high-density lipoprotein cholesterol, K: potassium, LDH: lactate dehydrogenase, LDL-chol: low-density lipoprotein cholesterol, Na: sodium, NT-proBNP: N-terminal proB-type natriuretic peptide, P: phosphorus, pCO₂: partial pressure of carbon dioxide, PCT: procalcitonin, Plt: plate, pO₂: partial pressure of oxygen tension, PT: Prothrombin time, RBC: red blood cells, T-Bil: total bilirubin, T-chol: total cholesterol, Tg: thyroglobulin, Tg-Ab: anti-thyroglobulin antibody, TG: triglyceride, TnI: troponin I, TPO-Ab: thyroid peroxidase antibody, TP: total protein, TRAb: thyroid stimulating hormone receptor antibody, TSH: thyroid stimulating hormone, TSAb: thyroid stimulating antibody, WBC: white blood cells

minute (regular rhythm), and a blood pressure of 122/86 mmHg. Her Glasgow Coma Scale (GCS) score was 13 (eye opening was 3 points, verbal response was 4 points, motor response was 6 points). Although she had a goiter, she had no exophthalmos, cervical lymphadenopathy, foot edema, or any gastrointestinal symptoms. A lung examination revealed clear breath sounds.

The laboratory findings are summarized in Table 1. Electrocardiography revealed tachycardia with 158 beats per minute along with atrial fibrillation. Echocardiography revealed a left ventricular ejection fraction of 40%, a left ventricular diastolic/systolic state diameter of 50/44 mm, and an inferior vena cava measuring 18 mm. Chest X-ray revealed a cardiothoracic ratio of 62% with pleural effusion. Thyroid ultrasonography revealed a clearly enlarged thyroid gland with increased blood flow. Based on the clinical findings of thyrotoxicosis, CNS manifestations, a fever, and tachycardia, she was diagnosed with “definite” thyroid storm according to the diagnostic criteria (1). Subsequently, we treated her with thiamazole, potassium iodide, landiolol, heparin, and bisoprolol fumarate. She did not take her prescription medicine initially and her restlessness worsened. However, she resumed all medications on day 2. Her restlessness subsequently improved, and her GCS normalized by day 7. At this point she was clinically euthyroid, and her general con-

dition had improved, but her activities of daily living had been markedly reduced because she had not walked for a long time. She was therefore transferred to another hospital on day 17 for long-term care (Table 2). Her activities of daily living subsequently improved, and she left the hospital after five months. Her thyroid function stabilized while taking thiamazole and potassium iodide.

Case 2

A 37-year-old Japanese man with major depressive disorder had been treated with medication by his primary care doctor. He had experienced palpitations and chest tightness two years previously but considered it to be due to his major depressive disorder and so took no further action. However, two weeks before presenting to a primary care hospital, he developed a fever, loose bowels, palpitations, dyspnea, and foot edema. At admission, he had clinical thyrotoxicosis and a thyroid stimulating hormone receptor antibody concentration of 32.2 IU/L, so he was diagnosed with Graves' disease and started on oral thiamazole (15 mg/day). However, five days later, his dyspnea and foot edema worsened, and he was transferred to our hospital.

His medical history was significant for tuberculosis at 19 years of age and appendicitis, and his mother had Graves' disease. He was treated with amoxapine, lorazepam, fexofe-

Table 2. Clinical Course in Case 1.

Days	1	2	3	7	9	10	13	14	16	17
GCS	13	14	14	15	15	15	15	15	15	15
BT (°C)	38.3	37.1	36.8	36.5	36.7	36.7	36.8	36.3	36.9	36.7
PR (beats/min)	177	143	143	115	106	99	86	80	70	86
FT3 (pg/mL)	16.39		4.76		3.15		1.95		2.26	
FT4 (ng/dL)	3.74		2.22		1.44		1.00		0.92	
TSH (μU/mL)	<0.003		<0.003				<0.003		<0.003	
TRAb (IU/L)	21.6				18.89					
Thiamazole (mg/day)	15	45	45	45	45	30	30	15	15	15
KI (mg/day)	50	100	200	200	200	200	200	100	100	50
Landiolol (mg/h)	12	19.5	24	19.5	OFF					
Heparin (Unit/h)		400	460	520	520	520	OFF	→ Rivaroxaban 15 mg/day		
Bisoprolol fumarate (mg/day)		0.3125		0.625			1.25		0.625	

GCS: Glasgow coma scale, BT: body temperature, PR: pulse rate, FT3: free triiodothyronine, FT4: free thyroxine, TSH: thyroid stimulating hormone, TRAb: thyroid stimulating hormone receptor antibody, KI: potassium iodide

Table 3. Laboratory Findings at Admission in Case 2.

Hematology		Serum chemistry/immunology			
WBC	4,500 /μL	TP	5.6 g/dL	P	2.8 mg/dL
RBC	4.35×10 ⁶ /μL	ALB	3.4 g/dL	TG	48 mg/dL
Hb	11.6 g/dL	T-Bil	1.5 mg/dL	T-chol	91 mg/dL
Hct	36.1 %	AST	29 IU/L	HDL-chol	43 mg/dL
Plt	1.93×10 ⁵ /μL	ALT	28 IU/L	LDL-chol	40 mg/dL
PT	18.7 Sec	γ-GTP	176 IU/L	CRP	0.65 mg/dL
APTT	28 Sec	ALP	817 IU/L	HbA1c(NGSP)	5.9 %
Fib	307 mg/dL	LDH	223 IU/L	Glu	150 mg/dL
		CK	27 IU/L	FT3	>20.00 pg/mL
		BUN	13 mg/dL	FT4	4.67 ng/dL
		Cr	0.41 mg/dL	TSH	<0.003 μU/mL
		Na	140 mEq/L	TRAb	32.45 IU/L
		K	4.1 mEq/L	TSAb	4,230 %
		Cl	109 mEq/L	Tg	1,230 ng/mL
		Ca	8.8 mg/dL	NT-proBNP	1,974 pg/mL

γ-GTP: gamma glutamyl transpeptidase, ALB: albumin, ALT: alanine aminotransferase, APTT: Activated partial thrombin time, AST: aspartate aminotransferase, ALP: alkaline phosphatase, BUN: blood urea nitrogen, Ca: calcium, CK: creatine kinase, Cl: chloride, Cre: creatinine, CRP: C-reactive protein, Fib: Fibrinogen, FT3: free triiodothyronine, FT4: free thyroxine, Glu: glucose, Hb: hemoglobin, HbA1c (NGSP): hemoglobin A1c (National Glycohemoglobin Standardization Program), Hct: hematocrit, HDL-chol: high-density lipoprotein cholesterol, K: potassium, LDH: lactate dehydrogenase, LDL-chol: low-density lipoprotein cholesterol, Na: sodium, NT-proBNP: N-terminal proB-type natriuretic peptide, P: phosphorus, Plt: plate, PT: Prothrombin time, RBC: red blood cells, T-Bil: total bilirubin, T-chol: total cholesterol, Tg: thyroglobulin, TG: triglyceride, TP: total protein, TRAb: thyroid stimulating hormone receptor antibody, TSH: thyroid stimulating hormone, TSAb: thyroid stimulating antibody, WBC: white blood cells

nadine hydrochloride, brotizolam, thiamazole, ambroxol hydrochloride, L-carbocysteine, tipecidine hybenzate, clarithromycin, and acetaminophen. On examination, he had a height of 165 cm, a weight of 54.4 kg, a body temperature of 37.4°C, a pulse rate of 140 beats per minute (regular), and a blood pressure of 129/75 mmHg. His GCS score was 15. Although he had both goiter and foot edema, he had no exophthalmos, cervical lymphadenopathy, gastrointestinal symptoms, or abnormal breath sounds.

The laboratory findings are summarized in Table 3. Elec-

trocardiography revealed sinus tachycardia at 125 beats per minute. Echocardiography revealed a left ventricular ejection fraction of 40-50%, a left ventricular diastolic/systolic diameter of 46.1/37.5 mm, and an inferior vena cava measuring 19.3 mm. Chest X-ray revealed pleural effusion, a cardiothoracic ratio of 72%, and an infiltrative shadow in the right lower lobe. Thyroid ultrasonography revealed an enlarged thyroid gland with increased blood flow. Based on the clinical findings of thyrotoxicosis, tachycardia, and congestive heart failure, he was diagnosed with “suspected” thy-

Table 4. Clinical Course in Case 2.

Days	1	2	3	4	5	6	8	9	10	11	12
BT (°C)	37.4	37.3	37.2	37.7	37.6	37.3	36.2	37.0	36.7	36.8	
PR (beats/min)	140	120	111	115	103	95	84	86	95	85	
FT3 (pg/mL)	>20.00		5.09		3.83		2.43			2.17	
FT4 (ng/dL)	4.67		2.94		2.08		1.38			0.91	
TSH (μU/mL)	<0.003		<0.003		<0.003					<0.003	
TRAb (IU/L)	21.6										
Thiamazole (mg/day)	30	30	30	30	20	20	20	20	20	20	20
KI (mg/day)	200	100	200	200	200	200	200	100	100	100	50
Hydrocortisone (mg/day)	100	100	100								
Landiolol (mg/h)	5	5	5	5	5	OFF					
Heparin (Unit/h)		400	400	400	400	OFF	→Rivaroxaban 15 mg/day				
Bisoprolol fumarate (mg/day)			0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625
Furosemide (mg/day)	20	20	20	20	20	20	20	20	20	20	20
Spirolactone (mg/day)				25	25	25	OFF				

BT: body temperature, PR: pulse rate, FT3: free triiodothyronine, FT4: free thyroxine, TSH: thyroid stimulating hormone, TRAb: thyroid stimulating hormone receptor antibody, KI: potassium iodide

roid storm according to the diagnostic criteria (1). Subsequently, we treated him with thiamazole, potassium iodide, hydrocortisone, landiolol, and furosemide. In the hospital, he developed atrial fibrillation and required heparinization. He was euthyroid by day 8 and therefore left our hospital on day 12 (Table 4). He received isotope treatment after four months, and his thyroid function was stable.

Discussion

In the first case, the patient recognized worsening of her depression, a decreased food intake, and extensive fatigue. However, she adopted the “wait and see” approach, presuming her CNS symptoms associated with thyroid storm to be psychiatric in origin. In the second case, the patient had a history of palpitation and chest tightness. However, he initially discounted the symptoms and not informed his doctor. Thyroid storm is a lethal disease that requires early detection and treatment (1). If these patients had undergone thyroid hormone measurements when their mental or physical statuses had changed, we might have been able to detect and treat their thyroid conditions earlier.

CNS manifestations of thyroid storm may include restlessness, delirium, mental aberration, somnolence, convulsions, and coma (2). However, depression, hypomania, and anxiety disorders are the most frequently reported psychiatric findings in patients with hyperthyroidism (6). The mechanisms for underlying these are thought to involve sympathetic nerve activation, increased β -adrenergic activity, and the autoimmune process (6). In addition, thyroid hormones are thought to have a modulating effect on the serotonin system in the brain (7) and induce direct effects on cerebral tissue, which cause electroencephalogram abnormalities (8). However, why CNS manifestations appear during a thyroid storm are unclear.

In Japan, CNS manifestations were been reported in 67.4% of patients with thyroid storm and 84.4% of patients

with a definite diagnosis. More than half of patients with a definite diagnosis had an abnormal GCS (53.5%) and/or Japan Coma Scale score (62.6%) (2). A lower GCS has been significantly associated with the development of irreversible deficits (2), making it essential that we correctly identify CNS manifestations in patients with a thyroid storm.

Bipolar disorder affects more than 1% of the world's population, irrespective of nationality, ethnic origin, or socioeconomic status (9), and patients may present with hypomanic or depressive episodes. By contrast, major depressive disorder is more common, with a worldwide prevalence of 4.4% (10), and patients may present with loss of interest, suppressed thinking, anxiety, fretfulness, sleep disorder, eating disorder, and suicidal ideation. Mental status changes associated with thyroid storm and worsening psychosis can be indistinguishable from these symptoms. Therefore, if the patients have no history of thyroid disease and do not have their thyroid hormone levels measured, their thyroid storm may be overlooked, leading to an unfortunate outcome. However, if we consider the possibility of thyroid storm and measure their thyroid hormone levels, it is not very difficult to distinguish thyroid storm from worsening psychosis.

In conclusion, when the mental or physical state of patients with previously stable psychotic disease changes, we should measure their thyroid hormone levels in order to facilitate early treatment.

The authors state that they have no Conflict of Interest (COI).

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