Endocrine Journal 2009, **56** (6), 747-752

A Case of Atypical Thyroid Storm with Hypoglycemia and Lactic Acidosis

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Abstract. We describe herein a case of thyroid storm with hypoglycemia and lactic acidosis—a rare complication of thyroid storm. The patient was a 50-year-old Japanese woman who suffered cardiopulmonary arrest an hour after hospitalization. Analysis of a blood sample obtained before her cardiopulmonary arrest yielded surprising results: Her plasma glucose level was 14 mg/dL and her lactic acid concentration had increased to 6.238 mM. Thus, if atypical thyroid storm presents with normothermic hypoglycemia, and lactic acidosis, we believe it is necessary to consider a diagnosis of thyroid storm earlier, because this condition requires emergency treatment. Moreover, it is very important to apply standard principles in the treatment of atypical cases of thyroid storm.

Key words: Thyroid storm, Hypoglycemia, Lactic acidosis

(*Endocrine Journal* **56**: 747-752, 2009)

THYROID storm is a rare [1] but severe and dangerous condition; although the symptoms of thyroid storm are similar to those of thyrotoxicosis, they are far more extreme. The formal criterion for thyroid storm has been described by the Japanese Thyroid Association [2].

Thyroid storm is a condition requiring emergent care, and can be deadly if untreated. Although it is the result of uncontrolled thyroid disease, it is usually triggered by the addition of another strong stressor such as surgery, sepsis, or burn injury, among others [1]. Thyroid storm may lead to multiple organ failure as the body attempts to compensate for the condition and is overwhelmed by excess thyroid hormone.

Thyrotoxicosis—in which circulating levels of free T3 and/or free T4 are high—is the underlying condition in thyroid storm cases. Thyroid storm may be diagnosed on the basis of the following five symptoms [2]: (1) Central nervous system irregularities; (2) fever (over 38°C); (3) tachycardia (over 130 beats/min); (4) heart failure; and (5) digestive complaints.

The disease may be confirmed in patients with thyrotoxicosis if the following conditions exist: (1) presentation with symptom number 1 (as listed above) and at least one other symptom or (2) more than three symptoms other than symptom number 1 [2].

The patient may be suspected of having thyroid storm if the following conditions are met: (1) more than two of the symptoms listed above with the exception of symptom number 1 in addition to a diagnosis of thyrotoxicosis; and (2) without a confirmation of thyrotoxicosis, by considering the history of thyroid disease in addition to exophthalmos or goiter, and by considering symptom number 1 with at least one other symptom; or more than three symptoms other than symptom number 1.

Thyroid storm is usually treated with a high dose of methimazole or propylthiouracil, Lugol's iodine or sodium iodide, steroids, or beta blockers. If beta blockers are contraindicated, then calcium channel blockers or digoxin may be substituted [1]. Most cases should be managed in an intensive care unit or a medical high-dependency unit.

Our patient had an atypical presentation of thyroid storm with normotension and normothermia. In addi-

Received Feb. 12, 2009; Accepted May 1, 2009 as K09E-043
Released online in J-STAGE as advance publication Jun. 9, 2009

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Table 1. Laboratory findings on admission

Urinalysis		Serum chemistry/immunology			
pH	5.5	TP	7.4 g/dL	T-chol	77 mg/dL
Prot	3+	Alb	4.1 g/dL	TG	29 mg/dL
Glu	–	T.bil	1.9 mg/dL	HDL	11.0 mg/dL
Ketone	±	D.bil	1.0 mg/dL	LDL	60.2 mg/dL
S.G.	±	AST	44 U/L	FBS	14 mg/dL
O.B.	3+	ALT	22 U/L	HbA_{1C}	4.70%
Bil	–	LDH	204 U/L	CRP	1.14 mg/dL
WBC	±	ALP	592 U/L		
		γGTP	234 U/L	TSH	0.10 μIU/mL
		ChE	103 U/L	fT3	11.72 pg/mL
CBC		CK	57 U/L	fT4	>6.00 ng/dL
WBC	5860 /μL	S-amy	25 U/L	ANA	<20 titer
RBC	474×10^4 /μL	UA	7.1 mg/dL	CH50	63.8 /mL
Hb	9.0 g/dL	BUN	22.3 mg/dL	IgG	1508.0 mg/dL
Hct	30.1 %	Cr	0.55 mg/dL	IgM	617.7 mg/dL
PLT	26.5×10^4 /μL	Na	137 mEq/L	IgA	98.1 mg/dL
		K	4.4 mEq/L	RPR	(–)
		Cl	103 mEq/L	TPHA	(–)
		Ca	9.5 mg/dL	HBs	(–)
		Mg	2.12 mEq/L	HCV	(–)
		P	5.5 mg/dL	BNP	746.6 pg/mL (<18.4)

Prot: protein; Glu: glucose; S.G.: specific gravity; O.B.: occult blood; Bil: bilirubin; WBC: white blood cells; RBC: red blood cells; Hb: hemoglobin; Hct: hematocrit; PLT: platelet; TP: total protein; Alb: albumin; T.bil: total bilirubin; D.bil: direct bilirubin; AST: aspartate-aminotransferase; ALT: alanine-aminotransferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; γGTP: γ-glutamyltranspeptidase; ChE: choline esterase; CK: creatine kinase; S-amy: serum amylase; UA: uric acid; BUN: blood urea nitrogen; Cr: creatinine; T-chol: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; FBS: fasting blood sugar; HbA_{1C}: hemoglobin A1C; CRP: C-reactive protein; TSH: thyroid-stimulating hormone; fT3: free triiodothreonine; fT4: free thyroxine; ANA: antinuclear antibody; CH50: 50% hemolytic unit of complement; IgG: immunoglobulin G; IgM: immunoglobulin M; IgA: Immunoglobulin A; RPR: rapid plasma reagin test; TPHA: treponema pallidum hemagglutination; HBs: hepatitis B surface antigen; HCV: hepatitis C virus antibody; BNP: brain natriuretic peptide. Normal values indicated within parentheses.

tion, hypoglycemia and lactic acidosis were also identified. Since this constellation of symptoms is very rare, initial diagnosis was difficult. Thus, because thyroid storm is a condition requiring emergent attention we report this case to encourage swift diagnosis and treatment in cases with atypical presentation.

Case Report

A 50-year-old Japanese woman with foot edema, confusion, and heart failure was referred to our hospital. Initially, she was unable to communicate, which sometimes lasted for several minutes; however, this improved on hospitalization. She had severe foot edema and her heart failure was thought to be worsening. We suspected either brain tumor or cerebral hemorrhage and systemic edema or liver dysfunction with hyperammoniaremia. Hence, we performed computed tomography (CT) of the head and conducted a blood sample analysis. After 1 h of hospitalization, the patient suffered a cardiopulmonary arrest. Thereafter, endotracheal intubation followed by cardiopulmonary resuscitation was performed. She recovered quickly and was transferred to our intensive care unit.

Physical findings at the time of admission were as follows: Consciousness, Japan Coma Scale I–3 (Glasgow Coma Scale, 11/15 [E4V3M4])[3]; height, 150 cm; weight, 35 kg; body mass index, 15.5kg/m^2; heart rate, 182 beats/min; blood pressure, 126/85 mmHg; temperature, 36.8°C; respiratory rate, 20 breaths/min; and SpO_2, 97%. Her cardiac symp-

Table 2. Blood-gas analysis and endocrinological examination on admission

Blood gas (room air)		Pituitary function	
pH	7.324	ACTH	1900.7 pg/mL (7.4–55.7)
pCO_2	29.8 mmHg	IGF-1	<10 ng/mL (121–436)
pO_2	73.1 mmHg	GH	2.12 ng/mL (0.55–3.22)
HCO_3	15.1 mEq/L	ADH	3.6 pg/mL (0.3–4.2)
BE	-9.8 mM/L	prolactin	35.5 ng/mL (6.1–30.5)
O_2sat	94.7%		
Thyroid function and immunology		Adrenal function	
TSH	<0.10 μIU/mL	cortisol	42.1 μg/dL (4.5–21.1)
fT3	11.72 pg/mL		
fT4	>6.00 ng/dL	epinephrin	4356 pg/mL (<100)
TRAb	26.3 IU/L (<1.0)	norepinephrin	6835 pg/mL (100–500)
TSAb	295 % (<180)	dopamin	782 pg/mL (<30)
Thyroglobulin	9.1 ng/mL (<32.7)		
Thyroid test	×1600 (<100)	renin	57.9 ng/mL/h (0.1–2.0)
Microsome test	×6400 (<100)	aldosterone	32.6 ng/dL (3.6–24.0)
Anti-thyroglobulin antibody	78.2 U/mL(<0.3)		
TPO antibody	54.3 U/mL(<0.3)		
GAD antibody and C-peptide		Pyruvic acid and lactic acid	
GAD	<1.3 u/mL	Pyruvic acid	2.2 mg/dL (0.3–0.9)
CPR	0.3 ng/mL (0.8–2.5)	Lactic acid	56.2 mg/dL (4.2–17.0) =6.238 mM

pCO_2: partial pressure of carbon dioxide; pO_2: partial pressure of oxygen tension; HCO_3: bicarbonate; BE: base excess; O_2sat: oxygen saturation; TSH: thyroid-stimulating hormone; fT3: free triiodothreonine; fT4: free thyroxine; TRAb: TSH receptor antibody; TSAb: thyroid stimulating antibody; TPO: thyroid peroxidase; GAD: glutamic acid decarboxylase; CPR: C-peptide immunoreactivity; ACTH: adrenocorticotropic hormone; IGF-1: insulin-like growth factor-1; GH: growth hormone; ADH: antidiuretic hormone, vasopressin. Normal values indicated within parentheses.

toms corresponded to the NYHA (New York Heart Association) class IV and Killip IV degrees [4]. Her heart sounds were weak and rapid because of atrial fibrillation, and hence, not studied in detail. Respiratory sounds were weak and not audible in the lower right lung. A goiter was palpated in her neck. Her abdomen was distended and fluctuation was found. Her extremities were so edematous that her reflexes could not be studied reliably. Our patient had been diagnosed with Graves' disease at the age of 20 but did not visit the hospital regularly and had discontinued medication after 2 years.

Details of the laboratory data collected on admission are shown in Table 1. Her thyroid hormone levels were markedly increased and her antithyroid receptor antibody test was positive. Based on these findings, she was again diagnosed with Graves' disease. In addition to physical findings, atrial fibrillation, shock, and psychological impairment were also observed. Furthermore, family history revealed that her cousin had been diagnosed with Hashimoto's disease.

A subsequent cardiac echographic study revealed her LVEF (left ventricular ejection fraction) as 55%, her LVDd/s (left ventricular diameter diastolic/systolic state) as 46/33 mm, and her IVC (inferior vena cava) measurement as 18 mm. Her condition met the criteria for thyroid crisis as described by the Japanese Thyroid Association [2] and Burch and Wartofsky (score, 90/140) [5]. Hence, we concluded that she was experiencing a thyroid storm. The level of plasma glucose, pH value, and lactic acid concentration were 14 mg/dL, 7.324, and 6.238 mM (Table 2), respective-

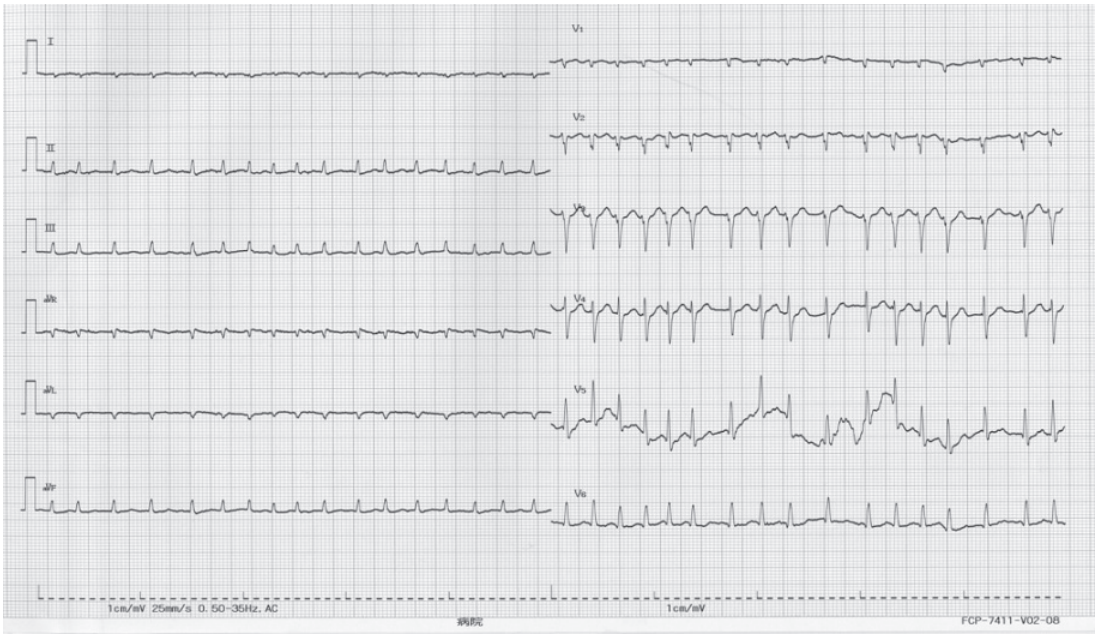

Fig 1. Electrocardiogram obtained at the time of admission.

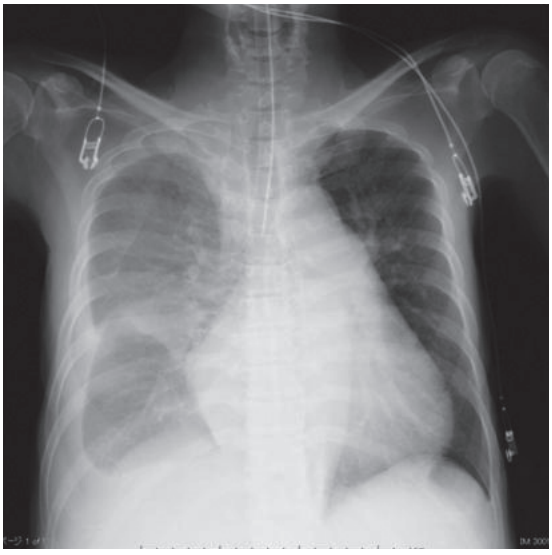

Fig. 2A. X-ray of the chest on admission.

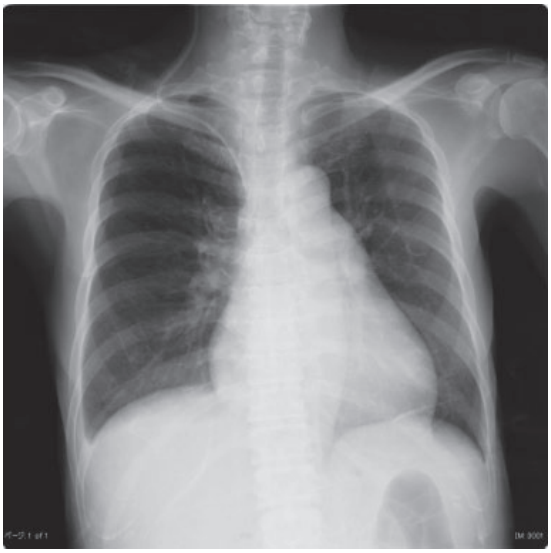

Fig 2B. X-ray of the chest 12th day after admission.

ly. Therefore, we also diagnosed hypoglycemia and lactic acidosis.

The CT of the patient's head performed on admission revealed normal findings. An electrocardiogram disclosed atrial fibrillation, as shown in Fig.1. The chest X-ray film (Fig. 2A) and elevated brain natriuretic peptide levels suggested severe heart failure. On comparing the X-ray film of the chest on admission with that obtained on the 12th day after admission (Fig. 2B), we noted that the patient's cardiothoracic ratio had changed from 69.2% to 57.4%; thus, we thought her heart failure had been ameliorated.

We treated the patient with methimazole, catecholamine, and a beta blocker. For hypoglycemia, 20 ml of 50% dextrose was intravenously injected twice, followed by total parenteral nutrition. Lactic acidosis was treated by maintaining circulating blood volume; iodine was not used since her family reported a past

history of allergic reaction. However, it was confirmed later that the patient did not have an iodine allergy.

The patient recovered in 6 weeks and was discharged from the hospital. After treatment with iodine radiation, her thyrotoxicosis gradually ameliorated.

Discussion

The findings in this case were consistent with the new criteria for thyroid storm as defined by the Japanese Thyroid Association [2] and criteria put forth by Burch and Wartofsky [5]. The patient presented with confusion as a central nerve system disorder, tachycardia with atrial fibrillation, and heart failure. Hyperthermia and digestive symptoms were not observed.

The occurrence of thyroid storm in conjunction with hypoglycemia and lactic acidosis is rare. Jiang *et al.* described a very similar case [6] of thyroid storm with normothermic and normotensive findings in a 44-year-old African–American female. The case described by Jiang *et al.* presented with several difficult diagnostic features, including increased potassium and bilirubin concentrations at the time of admission and the possible effects of race. There were little difference between this case and ours. We tried to identify the condition that occurred due to lactic acidosis and hypoglycemia, but the data available was insufficient.

Thyroid storm with hypoglycemia has rarely been reported [7, 8]. Complications such as those seen in our patient are certainly uncommon, but the literature does show that this condition can have a variety of causes. For example, Kobayashi *et al.* [7] described a case of thyroid storm with hypoglycemia due to starvation. Therefore, we considered why hypoglycemia and lactic acidosis happened in our case.

First, we examined why hypoglycemia occurred. The patient's insulin antibody level was within normal limits, a CT scan did not reveal any pancreatic tumor, and the serum C-peptide level at the time of hypoglycemia was 0.3 ng/mL (normal levels, 0.8–2.5). We were able to rule out insulin injection as the cause since the patient had not used it for several years. Further, she did not exercise or consume alcohol during this period. Her adrenal hormone levels were also noted to be high. Thus, we thought that her hypoglycemia could not have been caused by iatrogenic hyperinsulinemia, adrenal dysfunction, alcoholism, or drug abuse.

Next, we examined secondary hypoglycemia. Hormonal hyposecretion, sepsis, renal dysfunction, liver dysfunction, congestive heart failure, lactic acidosis, emaciation, shock, tumor, and postoperative effects of pheochromatosis have all been reported as causes of hypoglycemia [9]. Our case exhibited liver dysfunction, congestive heart failure, lactic acidosis, emaciation over 14 days, and shock. It is possible that each of these factors played a causative role in our patient's hypoglycemia. Unfortunately, we could not indicate which factor actually precipitated the hypoglycemia because we were unable to obtain sufficient evidence to pinpoint the exact cause.

We also examined the possible causes of lactic acidosis, which can be caused by various factors. In our case, hypoglycemia, shock, heart failure, and the lack of thiamine may have been responsible. Since thiamine levels were not investigated due to the lack of serum, it was unclear whether thiamine levels were below normal at the time of admission. After recovery, we examined the patient's adrenal function and found it to be normal. Although sepsis and diabetes were not detected, slight liver dysfunction was noted. No renal failure was observed. There was no malignancy. Hence, we concluded that the causative agents of lactic acidosis were hypoglycemia and shock.

And we considered iodine treatment. Iodine is necessary for treatment of thyroid storm; however, we could not use it due to the possibility of iodine allergy. Although we are pleased that the patient's life was saved even without the use of iodine therapy, we are at a loss to say how this happened. In the case of Kobayashi *et al.* [7], the patient was treated with potassium iodide 4 days after onset of hypoglycemia with a successful outcome. It is therefore evident that a variety of factors are involved in patient survival and recovery, but these factors remain to be explained.

Kearney and Dang [10] reported that iodine could block the conversion of T4 to T3 and that lithium carbonate could be used for this purpose instead. Although we could not measure the conversion rate of T4 to T3 in our case, we believe that if iodine had been used, she would have recovered more quickly, although it is impossible to prove this now. In addition, we did not use lithium because the publication by Kearney and Dang [10] did not appear until after the treatment of our patient concluded.

Independent of the poor prognosis associated with thyroid storm, severe hypoglycemia and lactic aci-

dosis are, by themselves, very serious conditions. Therefore, it may be necessary to monitor blood glucose and lactic acid levels in cases involving complications of thyroid storm such as these. In the future, we hope that the relationship between thyroid storm, hypoglycemia, and lactic acidosis is elucidated.

Finally, in this case, it is evident that the patient's condition was too complex to be recognized immediately and explained precisely. The doctor who referred the patient to our hospital sent detailed documents about her past history, medications, and current status. Although this information was of great help in understanding her status and condition, the symptoms were confusing and our comprehension of the case was poor. The indications of normotension, normothermia, hypoglycemia, and lactic acidosis proved to be too atypical for us to correctly diagnose thyroid storm. We initially believed that these symptoms obscured other diseases such as infection or myocardial infarction; this caused us to hesitate using steroids. However, the clinical course and laboratory data did not indicate these diseases.

Although the chance of a similar case occurring is rare, we believe that it is necessary to consider a diagnosis of thyroid storm earlier, even if the presentation is very atypical, because of the necessity of responding emergently to this condition. Thus, we believe that this report and others will be helpful in understanding similar cases that may occur in the future. In addition, it is very important to realize that treatment of an atypical thyroid storm case, such as the one described here, should be guided by the same principles used in normal thyroid storm.

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