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Thyroid Storm Complicated by Bicytopenia and Disseminated Intravascular Coagulation

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 23
Final Diagnosis: Thyroid storm
Symptoms: Delirium • diarrhea • fever • hypertension • hyperventilation • tachycardia • weight loss
Medication: —
Clinical Procedure: —
Specialty: Endocrinology and Metabolic

Objective: Unusual clinical course

Background: The clinical presentation of thyroid storm includes fever, tachycardia, hypertension, and neurological abnormalities. It is a serious condition with a high mortality rate. Furthermore, some other complications affect the clinical course of thyroid storm. Although it is reported that prognosis is poor when thyroid storm is complicated by disseminated intravascular coagulation syndrome (DIC) and leukopenia, reports of such cases are rare.

Case Report: A 23-year-old man presented with delirium, high pyrexia, diarrhea, and weight loss of 18 kg over 2 months. According to the criteria of Burch and Wartofsky, he was diagnosed with thyroid storm on the basis of his symptom-complex and laboratory data that confirmed the presence of hyperthyroidism. Investigations also found leukopenia, thrombocytopenia, and disseminated intravascular coagulation, all of which are very rare complications of thyroid storm. We successfully treated him with combined therapy including anti-thyroid medication, despite leukopenia.

Conclusions: Early diagnosis and treatment are essential in ensuring a good outcome for patients with this rare combination of medical problems.

MeSH Keywords: Disseminated Intravascular Coagulation – complications • Hyperthyroidism • Thyroid Crisis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/890519

Background

The classic clinical presentation of thyroid storm is a symptom-complex of pyrexia, heart failure, altered mental status, dehydration, vomiting, and diarrhea [1,2]. It is a life-threatening condition that is difficult to treat even when the diagnosis of hyperthyroidism is made promptly [3]. The prognosis is poor when thyroid storm is complicated by disseminated intravascular coagulation syndrome (DIC) and leukopenia; however, reports of such cases are rare.

Graves' disease is an autoimmune disorder characterized by hyperthyroidism, ophthalmopathy, and dermopathy, which can be complicated by various autoimmune blood disorders, including hemolytic anemia [4], idiopathic thrombocytopenic purpura [5], and iron deficiency anemia [6].

Here, we present a case of thyroid storm complicated by bicytopenia and disseminated intravascular coagulation, which was successfully treated as a result of prompt diagnosis and treatment.

Case Report

A 23-year-old man presented with gradual onset consciousness disturbance, high pyrexia, diarrhea, and weight loss of 18 kg over 2months. He was treated with intravenous fluids and oral fosfomycin for 2 days, but was transferred to our hospital after his condition deteriorated. He had developed consciousness disturbance, bicytopenia, and hepatic dysfunction. Abdominal computed tomography showed marked hepatic enlargement and splenomegaly.

On physical examination at admission, his temperature was 40°C, blood pressure 140/97 mm-Hg, pulse rate 97 beats/min with a regular rhythm, respiratory rate 16 breaths/min, and reduced level of consciousness. His pulse rate increased to 110/min later on the same day, and remained thereafter until our treatments showed some effects. An apical systolic murmur (Levine 3/6) was audible. He had a fine tremor in his hands and excessive sweating. The thyroid gland was slightly enlarged.

Laboratory findings on admission are shown in Tables 1 and 2. The patient's complete blood count (CBC) showed bicytopenia, with leukopenia of 1.8×10^3/μL (normal level; $3.9–9.8\times10^3$/μL) and thrombocytopenia of 71×10^3/μL ($13.1–36.2\times10^3$/μL). Serum C-reactive protein (CRP) was 2.88 mg/dL (0.0–0.3 mg/dL). Hepatic dysfunction was evident; aspartate aminotransferase (AST) was 93 IU/L (10–35 IU/L); alanine aminotransferase (ALT) 88 IU/L (5–40 IU/L); lactate dehydrogenase (LDH) 393 IU/L (120–230 IU/L); alkaline phosphatase (ALP) 390 IU/L (110–360 IU/L); and γ-glutamyltranspeptidase (γ-GTP) 91 IU/L (10–50 IU/L). Serum levels of fibrin degradation products and D-dimer were also increased to 82.7 μg/mL (0.0–0.5 μg/mL) and 43.51 μg/mL (0.0–1.0 μg/mL), respectively, diagnostic of DIC (6). Thyroid function test results showed a high free triiodothyronine (FT3) level of 6.5 pg/dL (2.3–4.0 pg/dL), free thyroxine (FT4) level of 4.0 ng/dL (0.9–1.7 ng/dL), and a low thyroid stimulation hormone (TSH) concentration of less than 0.01 μIU/mL (0.5–5.0 μIU/mL). His thyrotoxicosis was diagnosed as a Graves' disease because serum TRAb was detected at a concentration of 3.0 IU/L (under 2.0 IU/L). An electrocardiogram revealed tachycardia and ventricular trigeminy. Ejection fraction was normal on echocardiography. Ultrasound tomogram of the thyroid showed mild enlargement and increased blood flow. His blood culture and fecal culture results were all negative. We diagnosed his condition as a thyroid storm because of the presence of consciousness disturbance, high pyrexia, and diarrhea, with Graves' disease equivalent to Burch-Wartofsky score of 50 out of 140 [8], complicated by bicytopenia and DIC. On the day of admission, we started 20 mg/day of thiamazole for thyroid storm (Figure 1) and continued rehydration, after which his conscious level began to improve. Nevertheless, his fever was unable to be reduced by cooling with ice packs placed on major arteries. Therefore, we added 15 mg/day potassium iodide and 30 mg/day propranolol on the second day. Thereafter, body temperature declined to 37°C, and although his diarrhea persisted for about 4 days, it gradually improved. Blood pressure and pulse rate also normalized. By the sixth day, CBC count showed improvement in the white blood cell counts at 3.6×10^3/μL, and platelet count at 163×10^3/μL. On the thirteenth day of admission, the course of potassium iodide was completed, and on the fifteenth day he was discharged on thiamazole monotherapy.

Discussion

Thyroid storm is a serious condition with a mortality rate in excess of 20%, but it affects less than 10% of patients admitted because of thyrotoxicosis [9]. It is of utmost importance to be aware that the serum-free T3 and T4 concentrations may lie within their respective normal range in thyroid storm, which risks delay in commencing prompt treatment and risking poor outcome [10,11]. Generally, the Thyroid Storm Scoring System proposed by Burch and Wartofsky is used to make the diagnosis [8]. The score of our case was sufficiently high (50 out of 140) to suggest the diagnosis of thyroid storm.

The notable features of this case are the variety and severity of complications. First, the patient had bicytopenia, manifested as leukopenia and thrombocytopenia. Thyroid hormones facilitate the production of blood cells by stimulating hematopoietic stem cells [4]. However, they also reduce the life-span of blood components by a β-adrenergic mechanism [12] or by

Table 1. Laboratory findings on admission.

WBC	1800/μL	TP	7.1 g/dL	Na	132 mEq/L
Neu	73.8%	Alb	3.1 g/dL	K	3.5 mEq/L
Lym	20.8%	BUN	10.9 mg/dL	Cl	99 mEq/L
Mo	4.9%	Cr	0.53 mg/dL	CRP	2.88 mg/dL
Eo	0.0%	T-Bil	0.7 mg/dL	ferritin	954 ng/ml
Baso	0.5%	D-Bil	0.5 mg/dL	IgG	1120 mg/dL
RBC	5.23×10^6/μL	AST	93 IU/L	IgA	105 mg/dL
Hb	15.2 g/dL	ALT	88 IU/L	IgM	89 mg/dL
Ht	42.6%	LDH	393 IU/L	C3	90 mg/dL
Plt	7.1×10^4/μL	ALP	390 IU/L	C4	29 mg/dL
		G-GTP	91 IU/L	CH50	51 mg/dL
		CK	101 IU/L		

WBC – white blood cells; Neu – neutrophil; Lym – lymphocyte; Mo – monocyte; Eo – eosinophil; Baso – basophil; RBC – red blood cells; Hb – hemoglobin; Ht – hematocrit; Plt – platelets; TP – total protein; Alb – albumin; BUN – blood urea nitrogen; Cr – creatinine; T-Bil – total bilirubin; D-Bil – direct bilirubin; AST – asparate-aminotransferase; ALT – alanine-aminotransferase; LDH – lactate dehydrogenase; ALP – alkaline phosphatase; G-GTP – γ-glutamyltranspeptidase; CK – creatine kinase; CRP – c-reactive protein.

Table 2. Laboratory findings on admission.

TSH	<0.01 μIU/mL	ANA	<40
fT4	4.0 ng/dL	dsDNA-IgG	<10 IU/mL
fT3	6.5 pg/dL	HBs-Ag	0.00 IU/mL
TRAb	3.0 IU/L	HCV-Ab	0.10 S/CO
TSI	110%	HIV-AgAb	0.08 S/CO
Antithyroglobulin antibody	<10 IU/mL	EB-IgG anti-VCM	1.0(+)
PT%	81.7%	EB-IgM anti-VCM	0.0(–)
APTT%	88.6%	EB-EBNA-IgG	3.2(+)
Fib	273 mg/dL	CMV-IgG	2.6(+–)
FDP	82.7 μg/mL	CMV-IgM	0.3(–)
AT3	93.8%		
D-dimer	43.5 μg/mL		

TSH – thyroid stimulating hormone; fT4 – free T4; fT3 – free T3; TRAb – thyroid stimulating hormone receptor antibody; TSI – thyroid stimulating immunoglobulins; PT – prothrombin time; APTT – activated partial thromboplatin time; Fib – fibrinogen; FDP – fibrin degradation product; AT3 – antithrombin III; ANA – antinuclear antibodies; dsDNA-IgG – double-stranded DNA-IgG; HBs-Ag – hepatitis B virus antigen; HCV-Ab – hepatitis C virus antibody; HIV-AgAb – human immunodeficiency virus antigen antibody; EB-IgG anti-VCM – Epstein-Barr virus-IgG anti-VCM; EB-IgM anti-VCM – Epstein-Barr virus-IgM anti-VCM; EB-EBNA-IgG – Epstein-Barr virus nuclear antigen-IgG; CMV-IgG – cytomegalovirus-IgG; CMV-IgM – cytomegalovirus-IgM.

stimulation of the reticulo-endothelial system. Although this suggests that pancytopenia is likely to be a complication of thyrotoxicosis, cases of isolated anemia or thrombocytopenia are more frequently reported [4,5]. Autoimmune mechanisms may also play a role, suggested by the potential complication of idiopathic thrombocytopenic purpura (ITP) and pernicious anemia [4,5], and there have been reports that thyrotoxicosis might directly suppress hematopoiesis in the bone marrow [12]. However, examination of the blood film and bone marrow aspirate excluded these in our case. In this case, bicytopenia

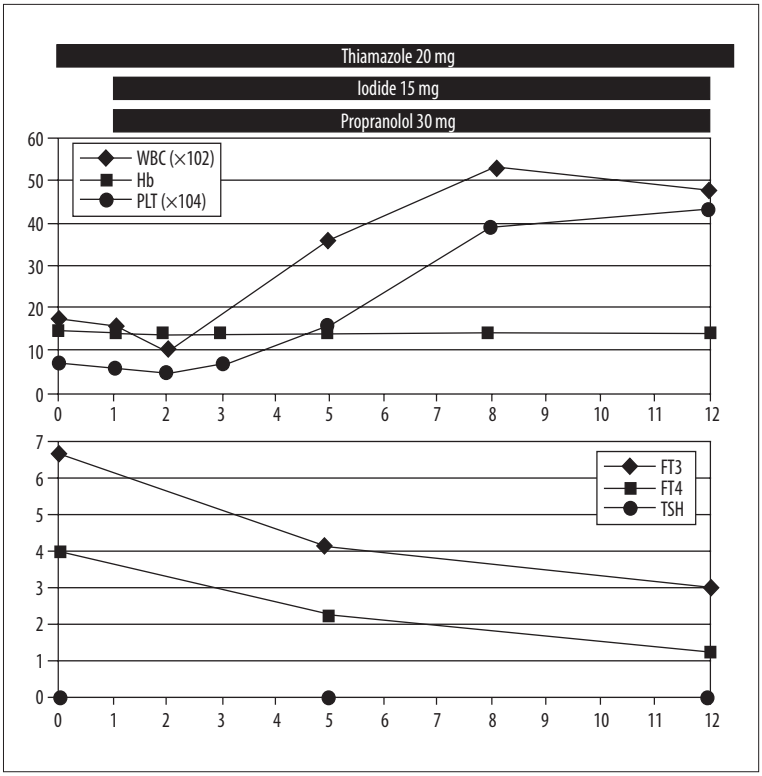

Figure 1. Clinical course of our patient. After admission, thiamazole 20 mg/day was administered. Tachycardia improved gradually after potassium iodide and propranolol were co-administered. There were also steady improvements in complete blood count parameters and serum thyroid concentrations.

resolved rapidly as thyroid function returned to normal, suggesting that a direct effect of thyroid hormones on blood cell lifespan was likely to be the underlying mechanism.

The treatments for thyroid storm consist of: a) suppression of production and excretion of thyroid hormones; b) inhibition of the peripheral effects of circulating thyroid hormones; c) general supportive care; and d) treatment of underlying disorders [13]. Generally, anti-thyroid drugs such as propylthiouracil and methimazole are used to suppress the level of circulating thyroid hormones. Because it can take about 3–4 days for these drugs to act, inorganic iodine and β-adrenoceptor blockers are administered at the same time. One of the serious adverse effects of anti-thyroid drugs is agranulocytosis [14]. We initially considered avoiding an anti-thyroid drug, since our patient had leukopenia on admission. Nevertheless, the leucopenia improved with combined therapy that included thiamazole, suggesting that the leucopenia was a direct consequence of the thyroid storm. In our case, we ruled-out septic state caused by enteric bacteremia, because his blood culture and fecal culture were all negative. Furthermore, this patient's condition improved 3 days after starting inorganic iodine and β-adrenoceptor blockers. A septic state would not have improved so easily and so fast.

The clinical course in this case was also characterized by DIC, which could have been another cause of thrombocytopenia in this case. Although there has been a report of DIC complicating multiple organ failure caused by congestive heart failure in a thyroid storm, this complication is very rare [10]. Infection, surgical intervention, or trauma may cause thyroid storm, which can also induce DIC. However, we could not ascertain the apparent cause in this case. We considered whether it may have been triggered by Epstein-Barr virus or cytomegalovirus infection, hemophagocytic syndrome, or myeloproliferative diseases, but these differential diagnoses were excluded on further investigation. Furthermore, because the DIC also resolved as the thyroid storm was treated, we hypothesize that in this case the thyroid storm directly provoked DIC.

Conclusions

In conclusion, we report a case of thyroid storm complicated by bicytopenia and DIC, an extremely rare combination of pathophysiologic conditions. Rapid diagnosis and prompt treatment, including anti-thyroid drugs, despite the presence of leucopenia, ensure a good outcome for these patients.

Conflict of interest statement

The authors state that they have no conflicts of interest to declare.

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