Thyroid storm without precipitating factors in a previous healthy child: A case report

Takaaki Mori,[1] Marie Mitani-Konno,[2] Yusuke Hagiwara,[1] Yukihiro Hasegawa[2]

[1]Division of Pediatric Emergency Medicine, Department of Pediatric Emergency and Critical Care Medicine; [2]Division of Endocrinology and Metabolism, Tokyo Metropolitan Children's Medical Center, Fuchu Tokyo, Japan

Abstract

The Thyroid Storm (TS) is the severest form of thyrotoxicosis and is associated with a high mortality rate. TS presents with fever, tachycardia, gastrointestinal symptoms, and central nervous system dysfunction and may be overlooked if patients do not present thyrotoxic symptoms or have precipitating factors. We reported a pediatric case of TS with mild proptosis but no obvious precipitating factors in a previously healthy child. A 9-year-old, female patient with a history of attention-deficit hyperactivity disorder presented with the complaint of frequent vomiting. She was alert but lethargic with fever and tachycardia. Physical examination was unremarkable except for coolness in the extremities and a delayed capillary refill time of two seconds. Fluid resuscitation was ineffective in alleviating the tachycardia. Additional history-taking revealed a one-month history of mild proptosis but no other thyrotoxic findings or precipitating factors were found. Markedly elevated thyroxine and triiodothyronine and suppressed thyroid-stimulating hormone on thyroid function tests led to a diagnosis of TS. Methimazole, potassium iodine, bisoprolol, and hydrocortisone were administered. Her vital signs and thyroid functions gradually improved, and she was discharged 18 days after admission without any serious complications. She is currently euthyroid and clinically stable on 5 mg of methimazole at three months after admission. When tachycardia that is resistant to usual resuscitation is found, careful history-taking and physical examination targeting thyroid disorders should be performed to assess for TS.

Correspondence: Takaaki Mori, Division of Pediatric Emergency Medicine, Department of Pediatric Emergency and Critical Care Medicine, Tokyo Metropolitan Children's Medical Center, 2-8-29 Musashidai, Fuchu, Tokyo 183-8561, Japan.
Tel.: +81.43.300.5111; Fax: +81.43.312.8130.
E-mail: takaakimori001019@gmail.com

Key words: Thyroid storm; healthy child; precipitating factors.

Acknowledgements: We thank Mr. James R. Valera for his assistance with editing this manuscript.

Contributions: TM conceptualized and designed the study, collected data, and drafted the initial manuscript. MMK and YHag coordinated and supervised the data collection and critically reviewed the manuscript for important intellectual content. YHas critically reviewed the manuscript for important intellectual content. All the authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of interests: The Authors declare no conflict of interest.

Availability of data and materials: All data underlying the findings are fully available.

Ethics approval and consent to participate: No ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: The patient's guardian gave her written consent to use the patient's personal data for the publication of this case report and any accompanying images.

Received for publication: 2 October 2021.
Revision received: 10 January 2022.
Accepted for publication: 11 January 2022.

Emergency Care Journal 2022; 18:10165
doi:10.4081/ecj.2022.10165

Introduction

Thyrotoxicosis is rare, having an incidence of only 0.7-6.5/100,000 in children.[1] Its most severe manifestation is the Thyroid Storm (TS), which triggers a variety of complications. The incidence of TS is around 0.2/100,000 per year in hospitalized patients, and the associated mortality rate is □10% although there are no data on pediatric patients with this condition.[2] TS can manifest a wide variety of symptoms, including fever, tachycardia, Gastrointestinal (GI) symptoms, and Central Nervous System (CNS) dysfunctions associated with thyrotoxicosis, such as goiter, proptosis, and palpitation. However, the various combinations of these common symptoms often make diagnosis challenging especially if the patient neither presents thyrotoxic symptoms nor has a history of a thyroid disorder.[2] Furthermore, TS is often triggered by the discontinuation of anti-thyroid medication, surgery or infection, and in the absence of such triggers, diagnosis may be difficult.[2] We herein report a pediatric case of TS without any triggers in a prepubertal child with no previous history of a thyroid disorder.

Case Report

A 9-year-old female patient with a history of attention-deficit

hyperactivity disorder presented with frequent non-bilious vomiting of 22 hours' duration. On arrival, she was alert but lethargic with a respiratory rate of 16 breaths/minute, a heart rate of 140 beats/minute, oxygen saturation of 99% on room air, a blood pressure of 141/65 mmHg, and a body temperature of 37.0°C. Her weight was 27.0 kg (-0.8 SD), and her height was 133.5 cm (-0.2 SD). She denied any other symptoms, such as abdominal pain and diarrhea. On physical examination, her lungs were clear. Her heart sounds were normal with no heart murmurs or gallop rhythm. Hepatosplenomegaly was denied. She had coolness in her extremities and a delayed Capillary Refill Time (CRT) of two seconds. Ultrasonography demonstrated adequate left ventricular contraction, and a chest radiography and electrocardiogram revealed no remarkable findings except for sinus tachycardia. Venous blood gas analysis showed metabolic acidosis with hypoglycemia and positive urinary ketone bodies (Table 1). Fluid resuscitation with 20mL/kg of normal saline and 40mL of 20% glucose was initially performed for hypovolemic compensated shock due to frequent vomiting. After fluid resuscitation, her heart rate remained at around 150 beats/minutes despite warmth in the extremities and normal CRT.

Additional history-taking revealed that her mother had noticed a slight protrusion of the patient's eyes one month ago despite the absence of any family history of thyroid disorders. Repeated examinations failed to find a goiter but revealed slight exophthalmos in comparison to a photograph taken two months ago. Her body temperature rose to 38.8°C although the other vital signs and physical examination findings showed no significant change. Laboratory tests (Table 1) found Thyroid-Stimulating Hormone (TSH) suppressed to <0.005µU/mL (normal range: 0.67-4.52µU/mL), Free Thyroxine (FT4) elevated to >7.77ng/dL (normal range: 0.96-1.60ng/dL), and Free Triiodothyronine (FT3) elevated to 22.31pg/mL (normal range: 3.10-4.87pg/mL). Anti-TSH-receptor antibodies and thyroid-stimulating antibody were markedly elevated at 35.2 IU/L, and 2392%, respectively, as seen in Graves' disease. Other laboratory tests demonstrated normal creatinine and elevated urea nitrogen, aspartate aminotransferase, alanine aminotransferase, and total bilirubin. Nasopharyngeal swab, blood, stool, and urine cultures were negative (Table 1).

Graves' disease was diagnosed based on the clinical findings and test findings. TS was confirmed by the Burch-Wartofsky Point Scale and the Japanese Thyroid Association criteria. The patient was admitted to a pediatric intensive care unit for cardiovascular monitoring and anti-thyroid treatment. Methimazole (MMI) 60mg/day, potassium iodide (KI) 150mg/day, bisoprolol 1.4 mg/day, and Hydrocortisone (HDC) 200 mg/day were soon begun in accordance with the guidelines for the treatment of childhood-onset Graves' disease in Japan and the 2016 guidelines for the management of thyroid storm of the Japan Thyroid Association and the Japan Endocrine Society. After treatment, the patient's vital signs and thyroid function tests slowly improved as shown in Figure 1. Thyroid ultrasonography on day 2 showed an enlargement in the right and left lobe to 6.5mL and 5.8mL, respectively, and increased vascularity (upper limit: 4.4mL and 3.6mL) despite the gland being clinically impalpable.

KI and HDC were tapered, then discontinued on hospitalization day 16. MMI was also tapered in accordance with the thyroid function test findings, and the patient was discharged with a prescription for MMI 30 mg and bisoprolol 1.4mg without serious complications, such as severe liver dysfunction or agranulocytosis, 18 days after admission. After discharge, bisoprolol was terminated on day 74. The patient is currently euthyroid and clinically stable with 5 mg of methimazole at three months after admission.

Discussion

In the present case, the presence of tachycardia resistant to the initial treatment raised suspicion of a thyroid disorder. Tachycardia in children can be caused by any one of a variety of conditions, including sympathetic hyperactivity triggered by fever, anxiety or exercise; life-threatening conditions, such as sepsis, hypovolemic shock or intoxication; and thyrotoxicosis.[3] The combination of fever, frequent vomiting and tachycardia initially pointed to hypo-

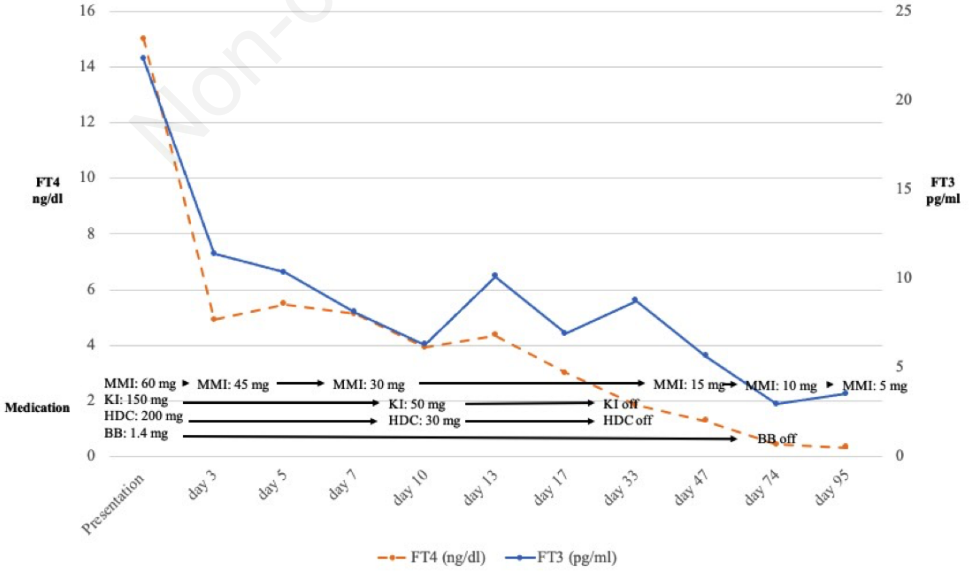

Figure 1. Time course of patient's thyroid hormone levels (FT4 indicated by dashed line and FT3 indicated by solid line). MMI: methimazole; KI: potassium iodine; HDC: hydrocortisone; BB: beta-blocker (bisoprolol).

Table 1. Laboratory test results on admission.

Complete blood count		Endocrinological analysis	(Normal range)
White blood cell	8970 /μL	Free thyroxine (FT4)	>7.77 ng/dL (0.96-1.60)
Hemoglobin	10.4 g/dL	Free triiodothyronine (FT3)	22.31 pg/mL (3.10-4.87)
Platelet	297,000 /μL	Thyroid stimulating hormone (TSH) Cortisol	<0.005 μU/mL (0.67-4.52) 11.5 μg/dL (3-12)
Biochemistry test		Adrenocorticotropic hormone (ACTH)	53.6 μg/dL (7.2-63.3)
Aspartate aminotransferase	61 U/l	Anti-thyroid peroxidase antibody	<9 IU/mL (<16)
Alanine aminotransferase	80 U/l	Anti-thyroglobulin antibody	10 IU/mL (<28)
Total bilirubin	1.0 mg/dL	Anti-TSH stimulating antibody	2392 % (<120)
Direct bilirubin	0.1 mg/dL		
Urea nitrogen	22.6 mg/dL	Blood culture	Negative
Creatinine	0.4 mg/dL		
Na	142 mEq/L	Urine culture	Negative
K	5.5 mEq/mL		
Cl	104 mEq/mL	Stool Culture	Negative
Ca	10.4 mg/dL		
P	7 mg/dL	Nasopharyngeal swab	Negative
C-reactive protein	0.03 mg/dL	SARS-CoV-2 Adenovirus	Negative Negative
Blood gas analysis (venous)		Coronavirus 229E/HKU1/NL63/OC43	Negative
pH	7.23	Human-metapneumovirus	Negative
pCO_2	40.9 mmHg	Rhino/Enterovirus	Negative
HCO_3	16.5 mmol/L	Influenza virus A/B	Negative
Base excess	-10.3 mmol/L	Para-influenza virus 1/2/3/4	Negative
Lactate	1.9 mg/dL	Respiratory syncytial virus Bordetella pertussis	Negative Negative
Urinalysis		Chlamydia pneumoniae	Negative
Nitrate	Negative	Mycoplasma pneumoniae	Negative
Ketone	3+		
White blood cell	Negative		

Table 2. Pediatric cases of thyroid storm with no past history of thyroid diseases or precipitating factors.

Author, year	Age (years old)	Gender	TS symptoms	Thyrotoxicosis associated symptoms	PE	Past history of TD	Family history of TD	Precipitating factors
Ladd, 2020	2	Female	CNS, fever, tachycardia, GI	Weight loss, excessive sweating	Goiter	None	Present	None
Bonfield, 2018	4	Female	Tachycardia	Weight loss, increased appetite, tiredness, sleep disturbance,	Goiter, exophthalmos, tremor	None	None	None
Hecht, 2012	7	Female	CNS, fever, tachycardia	None	Goiter	None	None	None
Matsubara, 2021	9	Female	CNS, fever, tachycardia, GI	Weight loss	N.A.	None	None	None
Darby, 1962	9	Female	Fever, tachycardia, CHF, GI	Weight loss, heat intolerance	Goiter, exophthalmos, tremor	None	None	None
Grossman, 1961	10	Female	CNS, fever, tachycardia, GI	Weight loss	Goiter	None	None	None
Albeert, 2014	12	Female	CNS, fever, tachycardia, GI	Weight loss, jitteriness, anxiety	Goiter	None	None	None
Present case	9	Female	Fever, tachycardia, GI	None	Mild exophthalmos	None	None	None

GI, gastrointestinal symptoms such as nausea, vomiting, diarrhea, and increased total bilirubin level over 3.0 0mg/dL; CNS, central nervous system dysfunction including decreased consciousness, seizure, somnolence/lethargy, restlessness, delirium, mental abrasion/psychosis; CHF; congestive heart failure including pulmonary edema, moist rale in more than half of the lung field, Class by the New York Heart Association, or Class in Killip classification, or cardiogenic shock; TS, thyroid storm; TD, thyroid disease; PE, physical examination

volemia caused by frequent vomiting, but fluid resuscitation was ineffective in alleviating the symptoms. According to the 2020 Pediatric Advanced Life Support Guidelines, if the initial treatment for tachycardia is unsuccessful, the patient should be re-evaluated and rare causes of tachycardia, such as thyrotoxicosis, should be considered.[4]

The frequent vomiting in the present patient was considered a potential symptom of TS. Hyperthermia, tachycardia, heart failure, and CNS and GI dysfunctions are the chief presenting symptoms of TS.[2] In adults, TS manifests marked tachycardia and CNS impairment rather than fever, GI symptoms or heart failure.[5] Although no epidemiological studies of TS in children have been published, tachycardia, fever, GI dysfunction is common symptoms in pediatric TS cases.[6-18] In the present case, the patient denied abdominal pain and diarrhea, and anti-thyroid therapy quickly alleviated the vomiting, suggesting that the latter was a symptom of TS rather than acute gastroenteritis.

It is often more difficult to diagnose childhood Graves' disease than in adults. Pediatric Graves' disease predominantly occurs in adolescent females and its incidence rate in prepubertal patients is around 0.4/100,000, or less than one-fifth of that in adolescent.[1] The median time to diagnose from the onset of symptoms in the entire pediatric patients is three months (0-36 months).[1]

At least the following three factors hindered the diagnosis of TS in the present case. First, the patient had no history of Grave's disease. Epidemiological studies in Asia have shown that more than 60% of adult TS cases occurred in patients with a history of thyroid disorder.[5] However, only 15% of pediatric patients with TS reportedly have a history of thyroid disorder.[8-10,12,16,17] Second, difficulty in detecting the patient's proptosis at the initial examination delayed the diagnosis of Graves' disease. The triad of Graves' disease is goiter, tachycardia, and proptosis. However, proptosis is uncommon in childhood Grave's disease compared with goiter and tachycardia where its incidence is around 40%,[19] and it is often mild.[20] Lastly, the patient had no precipitating factors of TS. In adult TS, the discontinuation of anti-thyroid medication, surgery, infection, pregnancy, and emotional stress are often recognized as precipitating factors.[2] There are just several cases where pediatric patients had precipitating factors. Table 2 shows previous cases of TS in children without precipitating factors,[6,7,11,13-15,18]

Conclusions

When patients present with marked tachycardia that is resistant to initial resuscitation, TS should be considered even if no typical thyrotoxic findings, a past history of thyroid disorder or precipitating factors are found.

References

1. Williamson S, Greene SA. Incidence of thyrotoxicosis in childhood: a national population based study in the UK and Ireland. Clin Endocrinol (Oxf) 2010;72:358-63.
2. Chiha M, Samarasinghe S, Kabaker AS. Thyroid storm: an updated review. J Intensive Care Med 2015;30:131-40.
3. Fleisher GR, Ludwig S, Bachur RG, et al. Textbook of pediatric emergency medicine. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health 2015.
4. Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2020;142:S469-S523.
5. Kornelius E, Chang KL, Yang YS, et al. Epidemiology and factors associated with mortality of thyroid storm in Taiwan: a nationwide population-based study. Intern Emerg Med 2021;16:601-07.
6. Albert BB, Eckersley LG, Skinner JR, et al. QT prolongation in a child with thyroid storm. BMJ Case Rep 2014;2014:bcr2013202595.
7. Bonfield A, Shenoy S. Thyrotoxic crisis as an acute clinical presentation in a child. BMJ Case Rep 2018;2018:bcr2017222850.
8. Chantra M, Limsuwan A, Mahachoklertwattana P. Low cardiac output thyroid storm in a girl with Graves' disease. Pediatr Int 2016;58:1080-83.
9. Creo AL, Cannon BC, Pittock ST. Thyroid storm after choking. J Pediatr Endocrinol Metab 2018;31:933-36.
10. Dahl IL. Thyroid crisis in a 3-year-old girl. Acta Paediatr Scand 1968;57:55-8.
11. Darby CP. Three episodes of spontaneous thyroid storm occurring in a nine-year-old child. Pediatrics 1962;30:927-31.
12. Galaburda M, Rosman NP, Haddow JE. Thyroid storm in an 11-year-old boy managed by propranolol. Pediatrics 1974;53:920-2.
13. Grossman A, Waldstein SS. Apathetic thyroid storm in a 10-year-old child. Pediatrics 1961;28:447-51.
14. Hecht T, Brand J, Vlaho S. Encephalopathy and sinustachycardia in childhood—a possible differential diagnosis. J Pediatr Endocrinol Metab 2012;25:149-51.
15. Ladd JM, Sabsabi B, von Oettingen JE. Thyroid Storm in a Toddler Presenting as a Febrile Seizure. Pediatrics 2020;145:e20191920.
16. Landgraf L, Grubina R, Chinsky J. Altered mental status in a 16-year-old girl: the calm before the storm. Clinical Pediatrics 2008;47:720-4.
17. Lawless ST, Reeves G, Bowen JR. The development of thyroid storm in a child with McCune-Albright syndrome after orthopedic surgery. Am J Dis Child 1992;146:1099-102.
18. Matsubara K, Kuki I, Yamamoto N, et al. Thyroid crisis mimicking clinically mild encephalitis/encephalopathy with a reversible splenial lesion: A pediatric case report. Brain Dev 2021;43:596-600.
19. Sato H, Minamitani K, Minagawa M, et al. Clinical features at diagnosis and responses to antithyroid drugs in younger children with Graves' disease compared with adolescent patients. J Pediatr Endocrinol Metab 2014;27:677-83.
20. Goldstein SM, Katowitz WR, Moshang T, et al. Pediatric thyroid-associated orbitopathy: the Children's Hospital of Philadelphia experience and literature review. Thyroid 2008;18:997-9.