

Recurrent impending thyroid storm in a girl with Graves' disease: a case report

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Thyroid storm is an acute, life-threatening, hypermetabolic state in children with thyrotoxicosis. Before the thyroid storm occurs, the patient falls into a "warning stage" called impending thyroid storm. Rapid diagnosis and prompt treatment of an impending thyroid storm are crucial to prevent further life-threatening impacts. We describe a pediatric patient who experienced two episodes of impending thyroid storm with negative COVID-19 tests during the COVID-19 pandemic. [Paediatr Indones. 2023;63:517-20; DOI: <https://doi.org/10.14238/pi63.6.2023.517-20>].

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Thyrotoxicosis is a rare disorder in children with an annual incidence of 0.9 per 100,000 children. It is a hypermetabolic state caused by high thyroid hormone levels circulating in the blood. This leads to higher energy demand and higher tissue oxygen consumption, resulting in symptoms such as lethargy, hyperphagia, weight loss and heat intolerance. The metabolic changes lead to increased cardiac output, characterized by tachycardia and hypertension.¹ The most common cause of thyrotoxicosis in children is Graves' disease, which is thought to be six times more common in girls than in boys.² Although Graves' disease is most common in post-pubertal girls, our patient was pre-pubertal.³ Graves' disease is defined as autoimmune hyperthyroidism with a diffuse goiter.² Pediatric patients account for less than 5% of the total number of patients with Graves' disease; the prevalence in children is 0.02%. The remission

rate with antithyroid drugs is lower in children than adults.⁴ Children with thyrotoxicosis show advanced bone age because of higher metabolism.⁵

The case

A 9-year-old girl with Graves' disease had recurrent impending thyroid storm during the COVID-19 pandemic. She came to Dr. Hasan Sadikin General Hospital Pediatric Outpatient Clinic, Bandung, West Java, with chief complaints of palpitation and fatigue since two weeks prior to admission. She also had insomnia, excessive sweating, increased appetite, diarrhea, and weight loss of 2 kg in two months. She had already been diagnosed with Graves' disease two months before admission, with a history of protruding eyes and goiter. On examination, we found thyrotoxicosis signs and symptoms, including resting tremor, tachycardia, hypertension, warm

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periphery, goiter with no nodules and features of bilateral exophthalmos. The patient had short stature concordant with familial short stature with normal bone age. Her thyroid profiles showed elevated T3 (7 ng/mL) and fT4 (>5 ng/dL), and very low TSH (<0.02 μ L/mL). The thyroid scan indicated diffuse toxic goiter. TSH receptor antibody (TRAb) was >40 IU/L.

Cardiologic evaluation showed signs and symptoms consistent with NYHA class I heart failure.⁶ Electrocardiography results showed tachycardia (heart rate 154 times/minute) and enlargement of the left atrium and left ventricle. Chest X-ray showed no intrathoracic struma. There was no abnormal intracardiac finding on echocardiography.

Following a negative COVID-19 antigen swab test, she was admitted to the pediatric emergency room where she was given oral methimazole, propranolol, and hydrocortisone. Her initial Burch-Wartofsky Point Scale score was 40, indicating an impending thyroid storm. After six days of inpatient stabilization, her Burch-Wartofsky Point Scale score had decreased to 5 and she was discharged. She continued to be treated with methimazole and propranolol.

On her follow-up visit to the Pediatric Endocrinology Outpatient Clinic, seven days after discharge, she had shortness of breath since three days after hospital discharge accompanied by fever. Pulse oximetry showed desaturation with good response to oxygen supplementation. Her Burch-Wartofsky Point Scale score was 45. Her chest X-ray showed bilateral pneumonia. Thyroid function evaluation showed a T3 of 3.1 ng/mL, fT4 of 4.8 ng/dL, and TSH of <0.02 μ L/mL. She was again diagnosed as having an impending thyroid storm and hospital-acquired pneumonia (HAP). Her COVID-19 antigen swab was negative.

She was treated with ceftriaxone and cloxacillin for HAP, 100 mg propylthiouracil (PTU) three times a day followed by a taper, and propranolol. After two weeks of hospitalization, she had improved clinically and was discharged with 50 mg PTU and 20 mg propranolol three times a day. In addition, she had resumed taking methimazole at the appropriate dose as before. She remains under regular outpatient follow-up at the Pediatric Endocrinology Outpatient Clinic.

Discussion

One of the most severe complications of hyperthyroidism is thyroid crisis, also known as thyroid storm.² Thyroid storm is life-threatening, can include end-organ damage, seizure, hyperthermia, agitation, severe tachycardia, and raised blood pressure, leading to cardiac failure. The estimated mortality rate of this rare but potentially fatal complication ranges from 10% to 30%. There is usually a thyroid storm precipitator, such as infection, surgery, trauma, non-compliance to antithyroid medication, abrupt cessation of antithyroid medication, or radioactive iodine ablation.^{3,7,8} In this case, there was no known precipitating event in the first thyroid storm episode, but the second episode was precipitated by HAP.

While there are no specific diagnostic criteria for children with impending thyroid storm or thyroid storm, the diagnostic criteria derived from adult thyroid guidelines. The most commonly used is the Burch-Wartofsky Point Scale.⁹ The scale includes central nervous system effects, gastrointestinal-hepatic dysfunction, cardiovascular dysfunction/heart failure, and the presence of a precipitating event. A total score of <25 indicates that a thyroid storm is unlikely, a score of 25 to 45 suggests an impending thyroid storm, and a score of >45 indicates a thyroid storm.⁹ Our patient had a score of 40 in the first episode and 45 in the second episode of thyroid storm.

The first-choice antithyroid drug for children is methimazole. The *American Thyroid Association*, *American Association of Clinical Endocrinologists*, and the *2011 Guidelines for the Treatment of Graves Diseases in Japan* discourage the use of PTU in children.^{2,4} Some cases of Graves' disease in children require more definitive treatment such as surgery or radioactive iodine.⁷

An impending thyroid storm is reversible if it is diagnosed early and actively treated. Some case reports in children differed in their Burch-Wartofsky Point Scale score classifications. A study further classified children with a score of ≥ 45 as thyroid storm 1 (TS1) or thyroid storm 2 (TS2) based on the presence of evidence of systemic decompensation requiring aggressive therapy. Children with scores between 25 and 44 are classified into impending thyroid storm, and should be treated as thyroid storm.⁸ Meanwhile, treatment with antithyroid drugs, such as PTU or

methimazole, need concomitant administration of a saturated potassium iodide solution or a beta blocker to aggressively reverse thyrotoxicosis. In addition, other supportive treatments, such as corticosteroids, abundant oxygen therapy, volume resuscitation, effective temperature control with antipyretics or a cooling blanket, and correction of electrolyte imbalance are needed.^{7,10}

A previous report described an impending thyroid storm in a 16-year-old child with a severe electrical burn injury. The patient was treated with propranolol, methimazole, and hydrocortisone. Following treatment, his tachycardia gradually resolved in the span of a few hours.¹¹ Some beta-blockers, such as atenolol and metoprolol, are selective beta-1 blockers that are well-tolerated in reactive respiratory tract disease and have longer half-lives. Propranolol is a non-selective beta-blocker with a shorter half-life that requires the patient to take more than one dose daily. Propranolol inhibits the activity of type-1 monodeiodinase that converts T4 to the biologically more active T3. PTU has 3 to 4 times the effect of blocking conversion compared to methimazole.¹¹⁻¹³ For this reason, we treated our patient with PTU on her second admission.

Another report described an impending thyroid storm in a patient with subacute thyroiditis following influenza vaccination. Hydrocortisone, methimazole, and a beta-blocker effectively stopped disease progression into thyroid storm. The patient responded dramatically to treatment and was discharged within 24 hours on an eight-week prednisone and metoprolol taper. The patient's thyroid function test normalized within three months.¹⁴

We report a case of recurrent impending thyroid storm in a 9-year-old Indonesian girl with Graves' disease occurring during the COVID-19 pandemic. This case is unique because of the low incidence of thyroid storm in pediatric population and highlights the importance of preventing recurrence of impending thyroid storms in a child. In this case, due to immediate recognition and aggressive treatment, the patient's symptoms were effectively controlled and a thyroid storm could be prevented.

References

1. Pandya M, Garcia A, Awori J. Thyrotoxicosis in a pediatric patient with supraventricular tachycardia and borderline features of thyroid storm. *AACE Clin Case Rep.* 2019;5:393-5. DOI: <https://doi.org/10.4158/ACCR-2019-0261>.
2. Huang SA, LaFranchi SH. Hyperthyroidism. In: Kliegman R, Stanton B, St Geme JW, Schor NF, Behrman RE, Nelson WE (eds). *Nelson Textbook of Pediatrics.* 21st ed. Philadelphia: Elsevier; 2016. p2680.
3. Underland LJ, Villeda GAV, Pal A, Lam L. A case of thyroid storm associated with cardiomyopathy and poststreptococcal glomerulonephritis. *Case Rep Pediatr.* 2016;7:192359. DOI: <https://doi.org/10.1155/2016/7192359>.
4. Committee on Pharmaceutical Affairs, Japanese Society for Pediatric Endocrinology, and the Pediatric Thyroid Disease Committee, Japan Thyroid Association (Taskforce for the Revision of the Guidelines for the Treatment of Childhood-Onset Graves' Disease); Minamitani K, Sato H, Ohye H, Harada S, Arisaka O. Guidelines for the treatment of childhood-onset Graves' disease in Japan. *Clin Pediatr Endocrinol.* 2017;26:29-62. DOI: <https://doi.org/10.1297/cpe.26.29>.
5. Williams GR, Bassett JHD. Thyroid diseases and bone health. *J Endocrinol Invest.* 2018;41:99-109. DOI: <https://doi.org/10.1007/s40618-017-0753-4>.
6. Zhang R, Ma S, Shanahan L, Munroe J, Horn S, Speedie S. Discovering and identifying New York Heart Association Classification from Electronic Health Records. *BMC.* 2018;2:1-13. DOI: <https://doi.org/10.1186/s1291-018-0625-7>.
7. Bonfield A, Shenoy S. Thyrotoxic crisis as an acute clinical presentation in children. *BMJ Case Rep.* 2018 Mar 23:bcr2017222850. DOI: <https://doi.org/10.1136/bcr-2017-222850>.
8. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid.* 2016;26:1343-421. DOI: <https://doi.org/10.1089/thy.2016.0229>.
9. The American Thyroid Association and American Association of Clinical Endocrinologists Taskforce on Hyperthyroidism and Other Causes of Thyrotoxicosis; Bahn RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid.* 2011;21:593-646. DOI: <https://doi.org/10.1089/>

- thy.2010.0417.
10. Carroll R, Matfin G. Endocrine and metabolic emergencies: thyroid storm. *Ther Adv Endocrinol Metab.* 2010;1:139-45. DOI: <https://doi.org/10.1177/2042018810382481>.
 11. Sen S, Palmieri T, Greenhalgh D. Thyroid storm in a pediatric high voltage electrical burn injury. *Burns Open.* 2018;2:76-8. DOI: <https://doi.org/10.1016/j.burnso.2017.09.003>.
 12. Creo AL, Cannon BC, Pittock ST. Thyroid storm after choking. *J Pediatr Endocrinol Metab.* 2018;31:933-6. DOI: <https://doi.org/10.1515/jpem-2018-0072>.
 13. Srinivasan S, Misra M. Hyperthyroidism in children. *Pediatr Rev.* 2015;36:239-48. DOI: <https://doi.org/10.1542/pir.36-6-239>.
 14. Stefan S, Hillary WB. A case of impending thyroid storm in a patient with subacute thyroiditis following an influenza vaccine. *J Endocr Soc.* 2020;4:1. DOI: <https://doi.org/10.1210%2Fjendo%2Fbvaa046.1814>.