Case Report

Thyroid storm with encephalopathy and cardiovascular symptoms refractory to medical management in an adolescent

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ABSTRACT

Thyroid storm (TS) is rare in pediatrics, most cases reported in literature responded well to medical therapy. We report the case of an adolescent female presented with TS refractory to anti-thyroid medical management. She had refractory hypertension, tachycardia, and progressive encephalopathy despite aggressive medical management. She underwent subtotal thyroidectomy after 2 weeks of failed medical management with a complete resolution of symptoms within days of surgery. We also learned sodium nitroprusside with its direct vasodilatory effect on conduit vessels, verapamil with its rate control properties, and labetalol with its dual sympathetic blockage property were beneficial in the management of this patient.

Key Words: Encephalopathy, hypertension, pediatric, thyroid storm

INTRODUCTION

Hyperthyroidism is uncommon in pediatrics, with an incidence of 0.1/100,000 in children and 0.3/100,000 in adolescents.[1] Thyroid storm (TS) occurs in <0.3% of all hyperthyroid and 2%–5% of hospitalized hyperthyroid patients of all ages.[2] The main clinical manifestations of TS include fever, tachyarrhythmias, restlessness, delirium, psychosis, convulsion, and coma.[3] The most reported cases of TS in the pediatric age group have shown a significant symptomatic improvement with medical treatment between 5 and 14 days.[4-6]

We present the case of an adolescent female with newly diagnosed thyrotoxicosis and TS with severe hypertension refractory to multiagent anti-hypertensive, an episodic of atrial flutter and progressive encephalopathy despite aggressive medical management. She had a complete resolution of symptoms immediately after total thyroidectomy. Such a complicated course, experience with a large number of cardiac medication and dramatic response to surgical therapy is not described in the pediatric literature.

CASE REPORT

Clinical presentation

A 16-year-old previously healthy female with slurring of speech, diplopia, ataxia, and altered sensorium with vital signs that included temperature of 38.2° C, heart rate of 154/m, and blood pressure of 149/86 mm of Hg on presentation. She was not on any regular medications. There was no personal or family history of autoimmune disorders.

Access this article online
Website: www.ijciis.org
DOI: 10.4103/IJCIIS.IJCIIS_58_19
Quick Response Code:

Cite this article as: Chauhan JC, Frizzola M, McMahon K, Perry S, Hertzog JH. Thyroid storm with encephalopathy and cardiovascular symptoms refractory to medical management in an adolescent. Int J Crit Illn Inj Sci 2020;10:38-41.

Received: 26.08.2019; Revision: 24.10.2019; Accepted: 02.12.2019; Published: 06.03.2020.
Investigations
She had normal electrolytes, cerebrospinal fluid studies, and magnetic resonance imaging (MRI) of the brain and spine. Levels of thyroid-stimulating hormone (TSH) were 0.02 mIU/L (0.5–5.5 mIU/L) with elevated thyroid hormones - total T4 level of >24.9 mcg/dl (5.9–13.2 mcg/dL) and free T4 level of 7 ng/dl (1.0–1.6 ng/dL) [Figure 1]. Her thyroid-stimulating immunoglobulin activity level was 324% (normal <125%) with anti-thyroglobulin antibody levels 2.6 IU/ml (normal <4 IU/ml). Ultrasonography of the thyroid showed an enlarged thyroid with the increased thyroid. Thus, based on the clinical features and laboratory findings, she had grave’s disease. On the application of the Burch and Wartofsky score to our patient, a score >50 was generated consistent with TS.

Interventions and outcomes
Anti-thyroid therapies included propranolol, potassium iodide, methimazole, hydrocortisone, cholestyramine, and dexamethasone. Saturated solution of potassium iodide 5 drops every 6 h, methimazole 20 mg every 6 h, hydrocortisone 100 mg every 6 h, and propranolol 30 mg every 6 h were initial anti-thyroid therapy. Cholestyramine 4 g every 6 h was added to the regimen on day 4 of pediatric intensive care unit (PICU) stay through the nasogastric tube. A small decrease in thyroid hormone levels were noted, as shown in Figure 1. Despite the patient continued to show clinical worsening.

As the patient continued to have refractory hypertension in form of systolic blood pressures >160 mm of Hg, propranolol was replaced by Labetalol on day 4 of PICU stay to get additional benefit of alpha effects, with maximal dosing by day 8 of 80 mg every 4 h. Nicardipine was the first antihypertensive infusion started day 2 of PICU stay and quickly escalated maximum of 5 mcg/kg/min within 24 h. Due to persistent refractory hypertension, sodium nitroprusside was the second IV infusion added on D4 of PICU stay and escalated to a moderately high dosing of 4 mcg/kg/min that allowed Nicardipine to be weaned to 2 mcg/kg/min [Figure 2]. On day 7 of hospitalization, the patient developed atrial flutter needing synchronized cardioversion. A brief trial of esmolol and amlodipine attempted without any benefit, which was later changed to verapamil to provide to get added benefit of rate control, verapamil doses were 120 mg every 6 h. By day 12 of her hospitalization, despite aggressive medical management, the patient continued to have refractory hypertension [Figure 2].

On admission, the patient was communicative and appropriate, although with episodic delirium. Over the next 2 days, she became progressively encephalopathic. A dexmedetomidine infusion and intermittent haloperidol were provided for symptomatic relief, but by day 4 of hospitalization, the patient became obtunded with the loss of protective airway reflexes, necessitating tracheal intubation and mechanical ventilation [Figure 2]. A second MRI of the brain at the time did not reveal posterior reversible encephalopathy syndrome or other pathologies.

Given the progression of life-threatening hypertension and encephalopathy, medical treatment failure was considered, and the decision was made in favor of total thyroidectomy. While surgical intervention in

![Figure 1: T4 (mcg/dl), Free T4 (ng/dl), T3 (ng/ml), and TSH (mU/L) levels after starting treatment with anti-thyroid medications and after thyroidectomy](image-url)
this situation is associated with a high risk of bleeding, worsening of TS, hypocalcemia, and related cardiac arrhythmias, the benefits of surgery were believed to outweigh these risks.

Postoperatively, the patient had hypocalcemia as expected secondary to iatrogenic transient hypoparathyroidism. On postoperative day 1, the patient became normotensive leading to the discontinuation of anti-hypertensive infusions. Tracheal extubation and discontinuation of mechanical ventilatory support were completed 3 days postoperatively as neurological status normalized. Pathology of the thyroid gland reported Grave’s disease.

**DISCUSSION**

TS is a rare critical event precipitated typically by the infection or stress in a person with thyrotoxicosis. The Burch and Wartofsky score and Akamizu criteria are the two scoring systems widely used to diagnose TS in adults, however no such scoring system has been developed for pediatrics. In our patient, the application of either of the system will lead a diagnosis of TS. [2,3]

Hyperthyroidism leads to a decrease in the steady component of afterload determined by systemic vascular resistance (SVR), but an increase in the pulsatile component of the arterial load determined by aortic input impedance and global arterial compliance. The net result is increase in systolic blood pressure and decrease in diastolic blood pressure. There is activation sympathetic and renin–angiotensin aldosterone system resulting in increased blood volume, venous return, heart rate, and stroke volume, which also increases systolic blood pressure. [7] Thyroid hormones strongly affect cardiac electrophysiology and rhythm through diverse effects on the activity of multiple-ion channel subunits, transporters, and exchangers that ultimately regulate the cellular excitability. Accordingly, increased thyroid hormone levels may alter cardiac excitability and conduction, resulting in automatic, triggered, and reentrant supraventricular and ventricular tachyarrhythmias, most commonly atrial fibrillation. [8] Arrhythmias, congestive cardiac failure, and other cardiac manifestations are not frequently described in pediatrics. [9]

Nicardipine and Esmolol exert their effect primarily on SVR which is already lowered in hyperthyroidism,
where as Nitroprusside exerts direct vasodilator effect on muscular conduit vessels in addition to lowering SVR as shown in human studies.[10] Verapamil with its rate control property without adversely affecting systolic function was a very useful agent in addition to beta blockade with propranolol/labetalol.[11] Thus, the combination of sodium nitroprusside, labetalol, and verapamil was most effective to manage cardiovascular instability in our case. Ultimately, the most beneficial effect resulted from total thyroidectomy with rapid improvement in all cardiovascular manifestations. Surgical management has been reported in pediatric populations, mostly in cases where the symptoms of long-term hyperthyroidism have an adverse effect on patient’s overall outlook, not in the case of TS as reported by us.[12]

Neurological symptoms such as encephalopathy and seizure are also not common in children.[4] In our case, encephalopathy progressively worsened and responded only to subtotal thyroidectomy, which to our knowledge has not been previously reported.

CONCLUSION

We described a case of refractory TS in an adolescent female despite aggressive medical management. Our experience also suggests that sodium nitroprusside, verapamil, and labetalol were the most beneficial of all the antihypertensive administered. In such cases, emergent surgical removal of the thyroid gland may be life-saving.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) or legally authorized representative(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patient(s) / representative(s) understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed. The authors followed applicable EQUATOR Network (http://www.equator-network.org/) guidelines during the preparation of this report.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Lavard L, Ranlev I, Perrild H, Andersen O, Jacobsen BB. Incidence of juvenile thyrotoxicosis in Denmark, 1982-1988. A nationwide study. Eur J Endocrinol 1994;130:565-8.
2. Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, Tsuboi K, et al. 2016 Guidelines for the management of thyroid storm from the Japan Thyroid Association and Japan Endocrine Society (First edition). Endocr J 2016;63:1025-64.
3. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. Endocrinol Metab Clin North Am 1993;22:263-77.
4. Lee HS, Hwang JS. Seizure and encephalopathy associated with thyroid storm in children. J Child Neurol 2011;26:526-8.
5. Aslan IR, Baca EA, Charlton RW, Rosenthal SM. Respiratory syncytial virus infection as a precipitant of thyroid storm in a previously undiagnosed case of Graves' disease in a prepubertal girl. Int J Pediatr Endocrinol 2011;2011:138903.
6. Underland LJ, Villeda GA, Pal A, Lam L. A case of thyroid storm associated with cardiomyopathy and poststreptococcal glomerulonephritis. Case Rep Pediatr 2016;2016:7192359.
7. Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of thyroid hormone on cardiac function: The relative importance of heart rate, loading conditions, and myocardial contractility in the regulation of cardiac performance in human hyperthyroidism. J Clin Endocrinol Metab 2002;87:968-74.
8. Cappola AR, Desai AS, Medici M, Cooper LS, Egan D, Sopko G, et al. Thyroid and Cardiovascular Disease: Research Agenda for Enhancing Knowledge, Prevention, and Treatment. Thyroid 2019;29:760-77.
9. Razvi S, Jabbar A, Pingitore A, Danzi S, Biondi B, Klein L, et al. Thyroid hormones and cardiovascular function and diseases. J Am Coll Cardiol 2018;71:1781-96.
10. Fok H, Jiang B, Clapp B, Chowienczyk P. Regulation of vascular tone and pulse wave velocity in human muscular conduit arteries: Selective effects of nitric oxide donors to dilate muscular arteries relative to resistance vessels. Hypertension 2012;60:1220-5.
11. Dahlstrøm CG, Ladeoged SD. Verapamil in atrial fibrillation in hyperthyroidism. Br Med J (Clin Res Ed) 1987;294:1384.
12. Bauer AJ. Approach to the pediatric patient with Graves’ disease: When is definitive therapy warranted? J Clin Endocrinol Metab 2011;96:580-8.