International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Review Article

MISDIAGNOSIS OF CHILDHOOD THYROID CRISIS: A CASE AND LITERATURE REVIEW, *A CASE OF CHILDHOOD THYROID CRISIS*

Yifei Zhang[1], Ruobing Chen[2], Shuang Zheng[3] and Dan Liu[4*]

[1,2,3]Department of Pediatrics, Jingzhou No 1 People's Hospital and First Affiliated Hospital of Yangtze University, No. 8 Hangkong Road, Shashi District, Jingzhou City, Hubei Province, China, 434000.

[4]Associate professor, The first clinical medical collage of Yangtze University, No. 8 Hangkong Road, Shashi District, Jingzhou City, Hubei Province, China, 434000.

ABSTRACT

Thyroid crisis is a rare childhood endocrine emergency. It occurs in children with thyrotoxicosis. It is manifested as decompensation of multiple organs caused by infection, fatigue, and severe stress. Its etiology and pathophysiology are not yet clear. Diagnosis and treatment are mainly based on the Burch-Wartofsky point scale (BWPS) and the Japanese Thyroid Association criteria (JTA). We reported a case of hyperthyroidism in a child with fever, vomiting, restlessness, rapid heart rate and increased infection index. After received anti-infection, stomach protection treatment, the symptoms were not relieved and the infection index continued to increase. Later diagnosed as thyroid storm and was treated with hydrocortisone, propylthiouracil, high-dose propranolol, and meropenem combined linezolid anti-infective therapy, the child's condition gradually improved. Hope the case was provided clinical reference.

Keywords: Children, Hyperthyroidism, Thyroid storm, Treatment.

CASE REPORT

A 5-year-old child, without any significant past history, was hospitalized with thin, sweaty and thick neck. Half a year before admission, there was no obvious inducement to lose weight, sweating, restlessness and skin itching. One week ago, her family found that his neck was thick. At presentation her temperature-36.0 ℃, pulse rate-140 beats/per min, respiratory rate-19 breaths/min, blood pressure-82/62 mmHg, weight-17.5kg. The eyes were slightly protruding, the stellwag sign, Graefe sign, Mobius sign and joffroy sign were negative, and the eyelids were slightly swollen. The thyroid is II ° diffusely swelling, soft in quality, without tremor, no obvious vascular murmur, no tenderness, and no palpable nodules. The pharynx was slightly red, bilateral tonsils were swollen at I° without exudation. The apical pulsation was enhanced without tremor, the heart sound was powerful but no pathological murmur was heard.

Her investigation profile showed that the thyroid function test: free triiodothyronine (FT3) > 20.00 pg/mL↑, free thyroxine (FT4) 59.49 ng/dL↑, thyroid stimulating hormone (TSH) <0.0038 μIU /mL↓, thyroglobulin antibody (TG) 10.80 IU/mL↑, anti-thyroid peroxidase antibody (TPO) 278.98 IU/mL↑; thyroid-stimulating hormone receptor antibody (TSHR) 32.02IU/L↑; full type parathyroid hormone determination 69.1pg/mL↑; blood routine: total white blood cells count 6.72*109/L, red blood cell count 4.94*1012/L↑, platelet count 163*109/L, hemoglobin 108.00g/L↓, neutrophil count 2.57*109/L; biochemical indicator: alanine aminotransferase (ALT) 61U/L↑; thyroid color Doppler ultrasound showed diffuse thyroid parenchymal lesions; chest CT showed spneumonia, increased volume and decreased density of thyroid, which was considered as diffuse thyroid disease; Cardiac ultrasound, bilateral orbital CT scans, growth hormone, cortisol, insulin, sex hormones, renal function, electrolytes, myocardial enzymes and C-reactive protein (CRP) were normal.

Fever began to appear on the third day of admission, the highest body temperature was 39.4℃, accompanied by vomiting, non-jetting, gastric contents, no coffee grounds, noisy and disturbed, at presentation her temperature-39.4 ℃, pulse rate-148 beats/per min, respiratory rate-27 breaths/min, blood pressure-92/63 mmHg. Her investigation profile showed that blood routine: total white blood cells count 27.82*109/L, red blood cell count 4.92*1012/L↑, platelet count 342*109/L, hemoglobin 108.00g/L↓, neutrophil count 25.84*109/L; C-reactive protein (CRP) 27.50mg/L↑, PCT 62.93ng/ml↑; coagulation analysis: prothrombin time (PT) 14.50 second ↑, prothrombin time activity (PT%) 68.50%↓, international normalized ratio (INR) 1.26↑, fibrinogen (FIB) 3.20g/L, activated partial thromboplastin time (APTT) 33.10 seconds, coagulation Enzyme time (TT) 16.30 seconds, D-dimer (DD) 16.07 mg/L↑, fibrin degradation product 57.49μg/mL↑; biochemical indicators were normal. Burch-Wartofsky point scale(BWPS) was 55, Japanese Thyroid Association criteria (JTA) was TS1, combined application of BWPS and JTA standards [1-3], the children diagnosed thyroid storm. Immediately gave hydrocortisone, propylthiouracil, and high-dose propranolol to inhibit the transition from peripheral T4 to T3, combined the meropenem and linezolid to anti-infection treatment. Then re-check blood routine, biochemical indicators, electrolytes, myocardial enzyme spectrum, coagulation function, CRP, PCT are normal; the thyroid function test: free triiodothyronine (FT3) 4.47pg/mL↑, free thyroxine (FT4) 19.38ng/dL↑,

thyroid stimulating hormone (TSH) <0.0038 μIU /mL↓. Then she was discharged from the hospital for improvement. The case report was approved by the patient.

DISCUSSION

Hyperthyroidism is caused by increased thyroid hormone secretion due to overactive thyroid or passive release of stored hormones, and can also be caused by overtreatment of thyroid hormones [4]. The prevalence of hyperthyroidism is 0.8% in Europe[5] and 1.3% in the United States [6]. Hyperthyroidism increases with age and is more common in women, which is 5-10 times higher than men [7]. Hyperthyroidism in children accounts for about 5% of the total cases. There are many causes of hyperthyroidism. In patients with adequate iodine intake (150μg/d), the incidence of diffuse toxic goiter Graves disease, GD) is about 80%. In iodine-deficient people, toxic multinodular goiter (TMNG) is the most common cause, with about 5% of cases caused by toxic thyroid adenomas (TA), also known as Plummer disease. Other causes include TSH hyperthyroidism and thyroiditis. GD and TA peak around 40 years old, while TMNG usually occurs between 30 and 60 years old [8].

The clinical manifestations of hyperthyroidism include increased sympathetic excitability, increased basal metabolic rate, such as palpitations, fatigue, tremor, anxiety, sleep disturbance, weight loss, and heat intolerance. Some patients are accompanied by goitre and Graves' ophthalmopathy. In severe cases, thyroid crisis such as delirium, fever, vomiting, dehydration and even disturbance of consciousness may occur. The degree of thyroid dysfunction is clinically assessed by measuring T4 and TSH levels. TPOAb and TgAb are important thyroid tissue antibodies, which can directly reflect the degree of thyroid function damage [9].

Treatment of hyperthyroidism depends on the etiology and severity of the disease, as well as the patient's age, goiter size, complications, etc. The goal of treatment is to correct hypermetabolism state, reduce side effects and avoid hypothyroidism. Antithyroid drugs (ATDs), radioactive iodine and surgery are the main treatment options for persistent hyperthyroidism, while β blockers and iodides are used as adjuvant therapy. The main action of anti-thyroid drugs is to inhibit the organization and coupling of iodine, thus inhibiting thyroid hormone levels. Radioactive iodine is the preferred treatment for most GD and TMNG patients in the United States. It is still controversial, but increasingly accepted, in the treatment of hyperthyroidism in children. Radioactive iodine is gradually replacing surgery for hyperthyroidism. the most common surgical treatment is subtotal thyroidectomy, which preserves some thyroid tissue and reduces the incidence of hypothyroidism to 25%, but 8% of patients develop persistent or recurrent hyperthyroidism; total thyroidectomy is used only in patients with severe or enlarged goitres, where recurrence is problematic and also increases the risk of hyperparathyroidism and laryngeal nerve damage. Beta blockers such as propranolol provide rapid relief from adrenergic symptoms of hyperthyroidism, such as tremors, palpitations, fear of heat, and nervousness. Iodide blocks peripheral conversion of T4 to T3 and inhibits the release of hormones, which can be used as adjunct therapy before non-emergency thyroid surgery, but not for routine treatment of hyperthyroidism due to hormone release that may occur with long-term use [10].

Thyroid storm (TS) rarely occurs in children, which can occur when infection, fatigue and inadequate preparation before surgery occur during the disease. It is extremely easy to occur when mental trauma occurs. TS is a life-threatening disease that requires urgent treatment [11]. The pathogenesis of TS is still unclear. Studies have shown that the sharp increase of T4 or T3 release plays a role in the development of TS, and infection and body susceptibility also affect the development of TS [4,11].

The diagnosis of TS is mainly based on clinical manifestations. The Burch-Wartofsky point scale (BWPS) [4] proposed in 1993 is a scoring system based on clinical experience, which considers the severity of multiple organ involvement, including thermoregulatory dysfunction, central nervous system symptoms, tachycardia and atrial fibrillation, congestive heart failure, gastrointestinal/hepatic insufficiency, the central nervous system symptoms and predisposing factors, BWPS score > 45 points indicate TS, BWPS has been widely used in the diagnosis of TS, but the diagnosis standard is too sensitive and the false positive rate is high. In 2012, JIA proposed new diagnostic criteria for TS [4]. The prerequisite for diagnosis is thyrotoxicosis with elevated T3 or T4 levels, combine with central nervous system symptoms and fever, tachycardia, heart failure or gastrointestinal/hepatic insufficiency, which is TS1; combination of at least three of the following symptoms: fever, tachycardia, heart failure or gastrointestinal/hepatic insufficiency is a TS1 replacement combination; combine the following two symptoms: fever, tachycardia, heart failure, or gastrointestinal/hepatic insufficiency, which is TS2; atients meets the diagnostic conditions of TS1, but T3 or T4 was normal as a TS2 replacement combination. TS1 was confirmed TS, and TS2 was suspected TS. Clinically, the BWPS and JIA criteria are combined to diagnose thyroid crisis to improve the clinical diagnostic criteria [11].

The treatment of TS mainly includes ATDs, inorganic iodides, glucocorticoids, β - blockers. Its purpose is to reduce the synthesis and secretion of thyroid hormone, antagonize the peripheral effect of thyroid hormone, and reverse systemic decompensation. The antithyroid drug propylthiouracil can inhibit the activity of type I deiodinase in the thyroid and other peripheral organs, lower the level of T3 faster than methimazole, and can inhibit the conversion of peripheral T4 to T3 [12], as a result, the American Thyroid Association and Clinical Endocrine Physicians jointly issued guidelines recommend thyroid crisis in preferred propylthiouracil [13]. At the same time of ATDs treatment, inorganic iodide can be used in combination, large-dose inorganic iodide can reduce thyroid hormone synthesis by inhibiting the oxidation and organization of iodine and rapidly inhibit the release of thyroid hormone in the thyroid follicular cavity [14]. The hypermetabolic state of thyroid crisis can cause relative adrenal cortical insufficiency, and glucocorticoid supplementation should be given, and glucocorticoids have been shown to inhibit the synthesis of thyroid hormones and the conversion of peripheral T4 to T3 [15]. Propranolol is the most commonly used β -blocker in the treatment of thyroid crisis, it is a non-selective β -adrenergic receptor antagonist and can block the conversion of peripheral T4 to T3 [16], combined with ATDs, the clinical symptoms of thyroid crisis can be controlled quickly. Oxygen inhalation, antipyretic, sedation, infection control and other symptomatic support treatment is also very important.

CONCLUSION

Hyperthyroidism is a common endocrine disease, but less incidence of children, and there are many causes of hyperthyroidism. In childhood, it is mainly diffuse goiter-type hyperthyroidism, basically the same as the adult treatment, but the preferred drug treatment, the treatment course about 2 to 3 years, although children rarely occur a risk of thyroid storm, but still need to closely observe, avoid infection, fatigue, trauma and other inducements, and master the diagnostic criteria of thyroid storm. If it occurs, timely diagnosis and early intervention are required.

Authors' contributions:

Dan Liu designed the manuscript and give the intellectual input. Yifei Zhang, Ruobing Chen，Shuang Zheng, Dan Liu treated and managed the patient. Yifei Zhang summarized his clinical data, consulted relevant literature, etc. Yifei Zhang contributed to this work and should be considered as first authors. Yifei Zhang and Dan Liu revised the manuscript and edited the final version of the manuscript. All authors have read and approved the final manuscript.

Funding: No.

Declaration of Competing Interest: The authors report no declarations of interest.

Acknowledgements: This study was supported by the Department of Pediatrics and Neonatology, Jingzhou No 1 People's Hospital and First Affiliated Hospital of Yangtze University.

REFERENCES

1. De Leo S, Lee SY, Braverman LE (2016) Hyperthyroidism. *Lancet* 388: 906-918.
2. Burch HB, Wartofsky L (1993) Life-threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am* 22: 263-77.
3. Akamizu T (2018) Thyroid Storm: A Japanese Perspective. *Thyroid* 28: 32-40.
4. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, *et al*. (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 136: 359-86.
5. Reddy V, Taha W, Kundumadam S, Khan M (2017) Atrial fibrillation and hyperthyroidism: A literature review. *Indian Heart J* 69: 545-550.
6. Garmendia Madariaga A, Santos Palacios S, Guillén-Grima F, Galofré JC (2014) The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis. *J Clin Endocrinol Metab* 99: 923-31.
7. Journy NMY, Bernier MO, Doody MM, Alexander BH, Linet MS, *et al*. (2017) Hyperthyroidism, Hypothyroidism, and Cause-Specific Mortality in a Large Cohort of Women. *Thyroid* 27: 1001-1010.
8. Mariani G, Tonacchera M, Grosso M, Orsolini F, Vitti P, *et al*. (2021) The Role of Nuclear Medicine in the Clinical Management of Benign Thyroid Disorders, Part 1: Hyperthyroidism. *J Nucl Med* 62: 304-312.
9. Reid JR, Wheeler SF (2005) Hyperthyroidism: diagnosis and treatment. *Am Fam Physician* 72: 623-30.
10. Keyal NK, Pokharel N, Khanal S (2020) Thyroid storm presenting as septic shock in the intensive care unit: A Case Series. *JNMA J Nepal Med Assoc* 58: 48-51.

11. Akamizu T, Satoh T, Isozaki O, Suzuki A, Wakino S, *et al*. (2012) Diagnostic criteria, clinical features, and incidence of thyroid storm on nationwide surveys. *Thyroid. Jul* 22: 661–79.
12. Maia AL, Kim BW, Huang SA, Harney JW, Larsen PR (2005) Type 2 iodothyronine deiodinase is the major source of plasma T3 in euthyroid humans. *J Clin Invest* 115: 2524-33.
13. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, *et al*. (2011) Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid* 21: 593-646.
14. Okamura K, Sato K, Fujikawa M, Bandai S, Ikenoue H, *et al*. (2014) Remission after potassium iodide therapy in patients with Graves' hyperthyroidism exhibiting thionamide-associated side effects. *J Clin Endocrinol Metab* 99: 3995-4002.
15. Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, *et al*. (2016) Guidelines for the management of thyroid storm from The Japan Thyroid Association and Japan Endocrine Society (First edition). *Endocr J* 63: 1025-1064.
16. Chiha, M., S. Samarasinghe and A.S. Kabaker (2015) Thyroid storm: an updated review. *J Intensive Care Med* 30: 131-40.