

No obvious sympathetic excitation after massive levothyroxine overdose

A case report

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Abstract

Rationale: Thyrotoxicosis from an overdose of medicinal thyroid hormone is a condition that may be associated with a significant delay in onset of toxicity. However, limited literature is available regarding thyrotoxicosis attributed to excessive ingestion of exogenous thyroid hormone and most cases described were pediatric clinical researches. Herein, we presented the course of a patient who ingested a massive amount of levothyroxine with no obvious sympathetic excited symptoms exhibited and reviewed feasible treatment options for such overdoses.

Patient concerns: A 41-year-old woman patient with ureteral calculus ingested a massive amount of levothyroxine (120 tablets, equal to 6 mg in total) during her hospitalization. Her transient vital signs were unremarkable after ingestion except for significantly accelerated breathing rate of 45 times per minute. Initial laboratory findings revealed evidently elevated serum levels of thyroxine (T4) >320 nmol/L, free triiodothyronine (fT3) 10.44 pmol/L, and free thyroxine (fT4) >100 pmol/L. The patient had a history of hypothyroidism, which was managed with thyroid hormone replacement (levothyroxine 100 µg per day). Besides, she also suffered from systemic lupus erythematosus and chronic pancreatitis.

Diagnoses: This is a case of excessive ingestion of exogenous thyroid hormone in an adult.

Interventions: The interventions included use propranolol to prevent heart failure; utilize hemodialysis to remove redundant thyroid hormone from blood; closely monitor the vital signs, basal metabolic rate, blood biochemical indicators, and serum levels of thyroid hormone.

Outcomes: The woman had no obvious symptoms of thyrotoxicosis. After 4 weeks, the results of thyroid function indicated that serum thyroid hormone levels were completely recovered to pre-ingestion levels. Accordingly, the levothyroxine was used again as before.

Lessons: Adults often exhibit more severe symptoms after intaking overdose levothyroxine due to their complex medical history and comorbidities than children. As for them, hemodialysis should be considered as soon as possible. Besides, diverse treatments according to specific symptoms and continuously monitoring were indispensable.

Abbreviations: fT3 = free triiodothyronine, fT4 = free thyroxine, ICU = intensive care unit, SLE = systemic lupus erythematosus, T3 = triiodothyronine, T4 = thyroxine, TSH = thyroid-stimulating hormone.

Keywords: levothyroxine, overdose, sympathetic excitation, thyrotoxicosis, treatment

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LZ, ZQ, and RL contributed equally to this work.

The study was conducted in our hospital after approving by the institutional ethical committee of the first affiliated hospital of Nanjing Medical University. All patients included in the study signed an informed consent.

We declare that we have no conflict of interest.

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Table 1**Laboratory results postingestion of levothyroxine.**

Items	Day 1		Day 2	Day 3	Day 4	Day 6	Day 12	Day 28	Reference range
	Pre-hemodialysis	Post-hemodialysis	Post-hemodialysis	Post-hemodialysis					
FT ₃ , pmol/L	10.44	11.37	15.04	14.03	15.47	16.14	6.54	0.98	3.10–6.80
FT ₄ , pmol/L	>100	>100	>100	>100	>100	>100	66.64	6.95	12.00–22.00
T ₃ , nmol/L	2.62	2.86	3.38	3.45	3.77	3.97	2.04	0.65	1.30–3.10
T ₄ , nmol/L	>320	>320	>320	>320	>320	306.3	209.4	47.2	66.0–181.0
TSH, mIU/L	6.43	3.78	0.342	0.123	0.076	0.042	0.038	6.12	0.270–4.200

FT₃=free triiodothyronine; FT₄=free thyroxine; T₃=triiodothyronine; T₄=thyroxine; TSH=thyroid-stimulating hormone.

1. Introduction

Thyrotoxicosis is characterized by increased thyroid hormone in the blood circulation, which can lead to excited sympathetic activities and high metabolism syndrome, including diverse symptoms such as fever, irritability, tachycardia, diarrhea, and seizure.^[1–4] Levothyroxine, as an analog of thyroxine, is widely used for hypothyroidism. Although there are large numbers of patients with hypothyroidism using levothyroxine as an alternative treatment, limited cases of levothyroxine overdose were reported worldwide and most of them were pediatric clinical researches.^[5] Despite generally a mild and benign course was followed by levothyroxine intoxication in pediatric cases according to most available literature, some severe manifestations were also shown in several reports such as malignant hyperthermia, cardiac arrhythmias, seizures, coma, and thyroid storm after intaking even low dosages of levothyroxine.^[4,6–8] Herein, we described a case that a 41-year-old woman with ureteral calculus and a history of hypothyroidism and systemic lupus erythematosus (SLE) took in excessive levothyroxine 6 mg in total. However, no obvious sympathetic excited symptoms exhibited after that.

2. Case presentation

A 41-year-old woman was admitted to the hospital for ureter calculus. The second day after ureteroscopy, she was administered with tramadol intramuscular injection due to severe backache. After that, the patient left the ward without permission and was found back to ward by her family members till half a day later. She was extremely mentally unstable and emerged with significant tachypnea and chills at that time. On examination, her vital signs were evidently accelerated respiratory rate 45 breaths per minute, body temperature 36°C, heart rate 85 beats per minute, and blood pressure 130/94 mm Hg. The patient suicidally took in 120 tablets of levothyroxine prescription (50 µg each tablet), equal to 6 mg in total. Initial laboratory findings revealed extremely elevated serum levels of thyroxine (T₄) >320 nmol/L, free triiodothyronine (fT₃) 10.44 pmol/L, and free thyroxine (fT₄) >100 pmol/L. However, serum triiodothyronine (T₃) was 2.26 nmol/L, within the normal range, as well as the thyroid-stimulating hormone (TSH) was 6.430 mIU, above the normal. The patient had a past history of hypothyroidism and managed with long-term thyroid hormone replacement (levothyroxine 100 µg per day). Accordingly, the concentration of TSH suggested that it had not received negative feedback suppression from hypophysis yet. Besides, she also suffered from SLE, which was treated with glucocorticoids and hydroxychloroquine sulfate, and chronic pancreatitis.

We asked department of Endocrinology, department of Nephrology, and intensive care unit (ICU) for a consultation,

and ultimately determined her treatment programs together. First, stop taking the levothyroxine prescription. Then, use propranolol (30 mg per day, 3 times a day) to prevent heart failure. Besides, utilize hemodialysis to remove thyroid hormone from blood. Last but not least, it is essential to closely monitor the vital signs, basal metabolic rate, blood biochemical indicators, and serum degrees of thyroid hormone (Table 1). Although the hemodialysis did not significantly improve the outcomes for this patient, according to the serum thyroid hormone concentrations before and after hemodialysis (Table 1), the patient remained asymptomatic. Three days later, the level of serum T₃ began to escalate (3.77 nmol/L), as well as the degree of serum TSH declined (0.076 mIU/L). Till the sixth day postingestion, an epileptic seizure occurred to her. We administered the patient with phenobarbital intramuscular injection, and then she recovered to normal. In addition, the woman had no more symptoms of thyrotoxicosis since then. After 4 weeks, results of thyroid function revealed the levels of thyroid hormone of this patient were completely recovered to pre-ingestion levels and then levothyroxine was used again as before.

The research protocol was approved by the Institutional Review Board of the Nanjing Medical University, Nanjing, China, and the study was carried out in accordance with the nationally approved guidelines.

3. Discussion

Massive levothyroxine ingestion can cause excessive thyroid hormone in the blood circulation and then lead to sympathetic excitation. Common symptoms include fever, tachycardia, hypertension, hyperglycemia, irritability, and seizure.^[1–5] Recently, a case of multiorgan failure after high-dose levothyroxine intake was reported.^[9] However, available literature about levothyroxine intoxication is limited and most of the described cases are pediatric clinical researches. Cases of adults ingesting overdose levothyroxine are extremely rare. Most children who ingested overdose levothyroxine always suffer from few or mild clinical complications and no sequela is found.^[3] Contrarily, adults intoxicated with overdose levothyroxine generally have more severe symptoms, including cardiac arrhythmias, coma, malignant hyperthermia, and even renal failure.^[6,8,10] Hartman et al^[11] suggested that children were more tolerant to large overdoses of levothyroxine than adults. Whereas, there are lack of sufficient clinical or physiological evidence to certify this point. Adults who take in massive levothyroxine may always have disorders of mental or spirits and other severe medical histories. Therefore, their conditions could be more serious and complex once they suffer from levothyroxine intoxication.

In our case, the woman acutely took in 6 mg levothyroxine with no obvious sympathetic excited symptoms and a

Table 2**Alternative treatments of thyroxine overdose.**

1.	Decontamination
1.	Gastrointestinal decontamination
	2. Oral activated charcoal
	3. Bile acid sequestrants such as cholestyramine
2. Symptomatic treatment	1. Acetaminophen for fever
	2. Beta-blockade for tachycardia, such as propranolol
	3. Benzodiazepines for agitate and seizure, such as Phenobarbital
3. Decrease conversion of T3 to T4	1. Propylthiouraci
	2. Glucocorticoids
	3. Iopanoic acid and sodium ipodate
4. Reduce serum level of thyroid hormone	Hemodialysis or plasmapheresis
5. Monitor	Prolonged monitoring of vital signs and serum levels of thyroid hormone

T3 = triiodothyronine; T4 = thyroxine.

benign course followed. Given diverse conditions between cases of children and adults, the top choice of management may also have differences. Let us briefly review the management of thyroxine overdose first. Alternative treatments are listed in Table 2. As for children, gastrointestinal decontamination can apparently reduce absorption of levothyroxine within 1 hour after ingestion, particularly the administration of activated charcoal.^[12] In addition, properly symptomatic treatment such as acetaminophen for fever, propranolol for tachycardia, phenobarbital for agitate and seizure, and appropriately monitoring are sufficient to cope with the vast majority of cases. For adults, those with simple condition and mild symptoms can be treated similarly to children. Although for those with complicated conditions and severe symptoms, hemodialysis or plasmapheresis can be considered as soon as possible. They have been reported to be successful in removing part of levothyroxine from the serum and can correct electrolyte disorder.^[13,14] Symptomatic treatment and close monitoring are also indispensable. If necessary, anti-thyroid medication and iopanoic acid and sodium ipodate can also put on use. Furthermore, it is essential to updating treatment at any time according to the progress of illness.

Finally, we explored possible mechanisms why most reported cases show no obvious sympathetic excited symptoms and severe toxicity occurred after investigating excessive levothyroxine by referring to relevant studies. Evidence suggests that the body can respond to large doses of levothyroxine by generating biologically inactive reverse triiodothyronine (rT3) to maintain an euthyroid state.^[10,15] Then, rT3 can inhibit levothyroxine toxicity by competitive binding to receptor.^[16] In addition, levothyroxine can also tightly combine with certain plasma proteins such as thyroid binding globulin (TBG) and this could also prevent its biological activity.^[16] What is more, the liver plays a significant role by increasing the metabolism of excessive levothyroxine. Hence, on account of the powerful compensatory mechanism versus elevated levothyroxine in blood circulation, most patients show no remarkable symptoms. In this patient, although she had a history of hypothyroidism, her metabolic capability directed at thyroid hormone stayed normal. When overdose levothyroxine entered into her body, above-mentioned

compensatory activities began work to reduce redundant free thyroid hormone in serum. In addition, the proper therapeutic measures also played an essential role.

4. Conclusion

As our case showed, the woman had no obvious symptoms after so much levothyroxine ingestion. In our views, we did not recognize the point that children seem to be more tolerant to large overdoses of levothyroxine when compared with adults. Adults often exhibited more severe symptoms due to their complex history and comorbidities than children. As for them, hemodialysis should be considered as soon as possible. Besides, diverse treatments according to specific symptoms and continuously monitoring were indispensable.

Author contributions

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