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**Thyrotoxicosis after a massive levothyroxine ingestion: A case report**

Du F *et al.* Thyrotoxicosis after a massive levothyroxine ingestion

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**Abstract**

**BACKGROUND**

The literature on thyrotoxicosis caused by excessive ingestion of exogenous thyroid hormone is limited, and most cases reported have involved pediatric clinical studies.

**CASE SUMMARY**

A 21-year-old woman initially presented with palpitation and chest tightness after an overdose of levothyroxine (10 mg). The patient transiently lost consciousness and developed atrial fibrillation during hospitalization. We used propylthiouracil to decrease the peripheral conversion of T4 to T3 and inhibit the synthesis of endogenous thyroxine, propranolol to control heart rate, hydrocortisone to correct severe thyrotoxicosis, and hemoperfusion to increase levothyroxine clearance. The patient recovered and was discharged.

**CONCLUSION**

For patients with thyrotoxicosis after taking excess levothyroxine, it is critical to monitor vital signs and initiate effective treatment.

**Key Words:** Levothyroxine; Overdose; Thyrotoxicosis; Thyroid crisis; Treatment; Case report

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**Core Tip:** The literature on thyrotoxicosis caused by excessive ingestion of exogenous thyroid hormone is limited. We report a 21-year-old woman who presented with thyroid crisis after an overdose of levothyroxine. For patients with thyrotoxicosis or even thyroid storm after an overdose of levothyroxine, it is critical to monitor vital signs and symptoms and initiate effective treatment.

## **INTRODUCTION**

Levothyroxine is a commonly used medication for hypothyroidism. Although many patients with hypothyroidism use levothyroxine as an alternative treatment, few cases of acute overdosage have been reported worldwide<sup>[1]</sup>, and a large proportion of them have involved pediatric patients. Most reported levothyroxine intoxication symptoms have been mild<sup>[2,3]</sup>, but severe manifestations including hyperthermia<sup>[3]</sup>, vomiting<sup>[4]</sup>, cardiac arrhythmias<sup>[5]</sup>, seizures<sup>[6]</sup>, coma<sup>[7]</sup>, and thyroid storm<sup>[7,8]</sup> have been reported to occur after massive levothyroxine overdosage.

<sup>1</sup> We report herein a case of a 21-year-old woman with a history of hypothyroidism and depression who took 200 tablets of levothyroxine, more than 10 tablets of clonazepam, and 20 tablets of zolpidem after mental stimulation. She ultimately developed symptoms of thyrotoxicosis, such as arrhythmia, dyspnea, dizziness, and coma.

## <sup>6</sup> **CASE PRESENTATION**

### ***Chief complaints***

A 21-year-old woman was admitted to the emergency department with palpitations and chest tightness.

### *History of present illness*

Fifteen hours earlier, the patient had ingested 200 Levothyroxine tablets (10 mg), more than 10 clonazepam tablets (20 mg), and 20 zolpidem tablets (200 mg), after mental stimulation.

### *History of past illness*

The patient's parents reported that she had been diagnosed with hypothyroidism due to fatigue 3 years ago and was being treated with levothyroxine (12.5-25.0 µg/d) without thyroid function monitoring. In addition, she was diagnosed with depression 2 years previously and was taking clonazepam and zolpidem for intermittent treatment.

### *Personal and family history*

Her family history included maternal hypothyroidism.

### *Physical examination*

On admission, the patient was conscious, presenting with palpitations, dyspnea, dizziness, fatigue, and sweating but with no nausea, vomiting, abdominal pain, nor diarrhea. Her vital signs were a temperature of 37.3 °C, heart rate of 103 beats/min, blood pressure of 100/73 mmHg, respiratory rate of 27 breaths/min, and oxygen saturation of 95% while breathing room air. The thyroid gland was I degree swollen, tough, and without tenderness.

### *Laboratory examinations*

The patient's thyroxine (T4) level was > 320 nmol/L, free thyroxine (FT4) level was > 100 pmol/L, triiodothyronine (T3) level was 6.27 nmol/L, free triiodothyronine (FT3) level was 27.96 pmol/L, thyroid stimulating hormone (TSH) level was < 0.01 mIU/mL,

5 thyroglobulin antibody (TGAb) level was 583.4 IU/mL, thyroid peroxidase antibody (TPOAb) level was 30.8 IU/mL, and thyrotropin receptor antibody (TRAb) level was < 0.3 IU/L (Table 1). Chemistries 4 were within normal limits, except for an alanine aminotransferase level of 74.3 U/L (normal range: 7-40 U/L).

### *Imaging examinations*

There was no imaging examination.

### **FINAL DIAGNOSIS**

Thyrotoxicosis caused by excessive intake of levothyroxine.

### **TREATMENT**

After fluid rehydration, supplemental oxygen, and emergency hemoperfusion, the patient was transferred to our department. Continuous cardiorespiratory monitoring was begun, propylthiouracil (150 mg 3 times per day) was given to reduce the conversion of T<sub>4</sub> to T<sub>3</sub> and inhibit the synthesis of endogenous thyroxine, propranolol (20 mg every 6 h) to control the heart rate, and intermittent hemoperfusion to increase levothyroxine clearance. Treatment was supplemented with liver protection, adequate energy intake, and other support measures.

On day 3 after admission, the patient lost consciousness without inducement, along with excessive sweating, and without nausea, vomiting, or gatism. Her pupils were sensitive to light, the body temperature was 37.1 °C, the electrocardiogram showed sinus tachycardia, heart rate fluctuations of 120-150 beats/min, blood pressure fluctuations from 90-110/76-94 mmHg, and an oxygen saturation of 94%-96% with a nasal catheter flow of 2 L/min and 40-50 breaths/min. Considering that the patient was in thyroid crisis, intravenous hydrocortisone 100 mg was given and an emergency hemoperfusion was performed. The patient regained consciousness 1 h later.

On day 7 after admission, the patient developed atrial fibrillation, with a heart rate of 100-110 beats/min after emotional agitation; after about 1 h, the patient spontaneously

shifted to sinus rhythm. The patient continued to improve and was discharged on day 15.

### OUTCOME AND FOLLOW-UP

The patient had no discomfort after discharge, and thyroid function gradually returned to normal.

### DISCUSSION

Thyrotoxicosis involves an excess of circulating thyroid hormone that has a number of causes and eventually leads to sympathetic nerve excitation and hypermetabolic syndrome. The symptoms are diverse and include fever, irritability, tachycardia, diarrhea, and seizures.<sup>2</sup> The most common causes of thyrotoxicosis are Graves' disease, toxic multinodular goiter, and thyroiditis. An excess dose of exogenous thyroid hormones can also lead to thyrotoxicosis, but the published literature on levothyroxine intoxication is limited and most of the described cases are pediatric clinical reports.<sup>1</sup> Cases of adults ingesting overdose levothyroxine are extremely rare, and adults who ingest massive doses of levothyroxine nearly always have mental disorders and other relevant medical histories<sup>[2]</sup>. Our case occurred in a woman who presented with severe symptoms of thyrotoxicosis after taking a massive levothyroxine dose. As she took the medication after mental stimulation, it may have been related to her history of depression.

Our patient developed clinical symptoms 15 h after an overdose of levothyroxine, improved with treatment, and was discharged 15 d after admission. Golightly *et al*<sup>[9]</sup> studied levothyroxine ingestion in 41 children who accidentally ingested levothyroxine sodium. The patients were managed by a standard protocol based on the reported amount of ingested levothyroxine, which ranged from 0.05-13 mg.<sup>3</sup> The onset of symptoms ranged from 12 h to 11 d, and all symptoms resolved by 14 d after ingestion.<sup>3</sup> Levothyroxine is a synthetic T4 preparation that needs to be converted to T3 *in vivo* to

exert its effects, and has a long half-life of approximately 7 d. Therefore, the symptoms of levothyroxine overdose may be delayed and may last for several days.

Thyroid storm, also known as thyroid crisis, is a serious clinical manifestation of thyrotoxicosis and is characterized by high fever, sweating, tachycardia, arrhythmia, loss of consciousness, and other symptoms that may be life threatening. Prompt diagnosis and active treatment are essential. The Burch and Wartofsky scoring system<sup>[10]</sup>, based on abnormalities of thermoregulation and the <sup>2</sup>central nervous system, gastrointestinal, and cardiovascular systems can be used to help determine whether a patient is experiencing a thyroid storm. This patient had a total score of 55 points, 30 for disturbance of consciousness and 25 for tachycardia, which met the diagnostic criteria for thyroid storm. Thyroid storm can occur a few days after an overdose of levothyroxine. In the cases reported by Wong *et al*<sup>[7]</sup> and Schottstaedt and Smoller<sup>[11]</sup>, the thyroid storm occurred 3 d after ingestion. The delayed occurrence of the thyroid storm can be attributed to the onset of levothyroxine action, which occurs 3–5 d after oral administration.

#### *Alternative treatments of levothyroxine overdose*

**Conservative monitoring:** This is recommended if the patient is asymptomatic or only mildly symptomatic.

**Gastrointestinal decontamination:** There are no standard criteria for when to perform gastrointestinal decontamination. Ritowitz and White<sup>[12]</sup> studied 78 children who were all about 12 years of age and had accidentally ingested levothyroxine. They recommended that children with ingestion of  $\leq 0.5$  mg should not be treated by gastrointestinal purification, those ingesting 0.5–3.0 mg can be treated by ipecac-induced emesis at home, and those ingesting  $> 3.0$  mg should be treated by ipecac-induced emesis followed by activated charcoal. Tunget *et al*<sup>[13]</sup> recommend that children who ingest  $> 5.0$  mg of levothyroxine be given activated charcoal, as it can reduce systemic absorption if given within 1 h of the levothyroxine. Bouchard<sup>[14]</sup> recommended



that adults with a levothyroxine intake of > 5.0 mg be given activated charcoal.<sup>2</sup> There is a limited role for gastric lavage in this setting, except very soon after a massive overdose (e.g., > 10 mg).

**Symptomatic treatment:** Pay close attention to the patient's vital signs and symptoms, and deal with them promptly. Beta-blockers are recommended for symptomatic treatment of patients with sympathetic overexcitation, such as tachycardia, and propranolol is the first choice. In addition to cardiac benefits, propranolol also reduces the conversion of FT4 to FT3 in peripheral blood. Our patient had palpitations and a heart rate of more than 100 beats/min, so propranolol was given to control the heart rate. Physical cooling and acetaminophen are recommended for patients with fever. Benzodiazepines can be considered if the patient is severely agitated and irritable<sup>[14]</sup>, and antiepileptic drugs, such as phenobarbital, may be considered for patients with seizures<sup>[2]</sup>.

**Decrease peripheral conversion of T4 to T3:** Propylthiouracil can reduce the peripheral conversion of T4 to T3 and inhibit the synthesis of endogenous thyroxine. Dexamethasone<sup>[15]</sup>, prednisone<sup>[16]</sup>, and hydrocortisone<sup>[17]</sup> can be useful in severe thyrotoxicosis because they also reduce T4 to T3 conversion. Kirstie *et al*<sup>[1]</sup> recommend the use of corticosteroids in patients with an overdose of levothyroxine (> 10.0 mg), especially when the initial FT4 Level is above the upper limit, or in any patient with associated adrenal insufficiency. In our case, we used propylthiouracil upon admission and we also used hydrocortisone when the patient developed a coma. If necessary, sodium ipodate can also be used because it inhibits type I iodothyronine 5'-monodeiodinase, which catalyzes the T4 to T3 conversion<sup>[3]</sup>.

**Increase thyroid hormone clearance:** It has been reported that hemoperfusion<sup>[17,18]</sup> and plasmapheresis<sup>[17]</sup> remove levothyroxine from serum and can be used to treat acute and severe thyrotoxicosis. Our patient had taken a high dose of thyroxine and thyroid storm



was considered, so hemoperfusion was used. Levothyroxine has a high rate of binding to specific transporters of about 99.97%, and plasmapheresis seems to be more effective than hemoperfusion for the clearance of T4. In addition, patients can be given cholestyramine, which reduces thyroid hormone levels by decreasing levothyroxine enterohepatic recycling and enhancing elimination<sup>[19]</sup>.

## **CONCLUSION**

Although most patients with levothyroxine overdose are asymptomatic or have only mild symptoms, severe cases and delayed symptoms have also been reported. Levothyroxine overdose can usually be diagnosed by the patient's history and examination results. Treatment of a thyroxine overdose should be based on the levothyroxine dose and the patient's clinical symptoms and signs.

## **ACKNOWLEDGEMENTS**

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