

# Impending thyroid storm in a pregnant woman with undiagnosed hyperthyroidism

## A case report and literature review

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### Abstract

**Rationale:** Thyroid storm is a rare complication during caesarean section of patients with hyperthyroidism. It occurs abruptly, with a high mortality rate if not recognized immediately and aggressively treated. Herein, we reported a case of impending thyroid storm during a caesarean section.

**Patient concerns:** A healthy 23-year-old woman with undiagnosed hyperthyroidism underwent an emergency caesarean section under general anesthesia. After tracheal extubation, the patient exhibited abnormal tachycardia, agitation, sweating, and hyperpyrexia.

**Diagnoses:** The clinical manifestation and the following thyroid function test indicate a high index of suspicion for impending thyroid storm.

**Interventions:** Hydrocortisone and esmolol were intravenously administered immediately. Propylthiouracil and propranolol were orally administered after the patient regained complete consciousness.

**Outcomes:** Due to our immediate recognition and aggressive treatment, more serious manifestations of thyroid storm were avoided.

**Lessons:** Good antenatal care is very important for pregnant women, and they should be generally screened for thyroid disorders, especially if the resting heart rate is >100 beats/min and weight increases are inconsistent with gestational age. When hyperthyroidism is suspected, drugs that excite the sympathetic nerves or promote the release of histamine should not be used during caesarean section.

**Abbreviations:** BP = blood pressure, FT3 = free triiodothyronine, FT4 = free thyroxine, HR = heart rate, ICU = intensive care unit, MH = malignant hyperthermia, NA = neuronal noradrenaline, T3 = triiodothyronine, T4 = thyroxine, TGAb = thyroid globulin antibody, TRAb = thyrotrophin receptor antibody, TSH = thyroid-stimulating hormone.

**Keywords:** emergency caesarean section, hyperthyroidism, pregnancy, thyroid storm

## 1. Introduction

Thyroid storm is a rare complication of hyperthyroidism, which can be life threatening, with a high mortality rate of 10% to 30% if not recognized immediately and aggressively treated.<sup>[1]</sup> According to the degree of systemic decompensation, it can be

divided into 2 stages: the early stage (impending storm) and the actual crisis (thyroid storm).<sup>[2]</sup> Currently, there are no uniform diagnostic criteria for impending storm. In most cases, Burch and Wartofsky's<sup>[2]</sup> Point Scale is used. It is generally believed that the impending storm is the intermediate stage of hyperthyroidism that finally develops into thyroid storm. Caution is advised if the original symptoms of hyperthyroidism suddenly aggravate, such as temperature 38°C to 39°C, pulse 120 to 159 beats/min, accompanied by sweating, nausea, irritability, etc. The impending storm is reversible, if it can be diagnosed early and actively treated. If the situation continues to deteriorate, with temperature >39°C, pulse >160 times/min, accompanied by consciousness disorders (delirium, lethargy, coma, etc), it is diagnosed as thyroid storm. The occurrence of thyroid storm is associated with numerous precipitants, including surgery, trauma, delivery, and infection, especially those accompanied by undiagnosed and untreated hyperthyroidism.<sup>[2,3]</sup> Pregnant women with hyperthyroidism are more likely to develop thyroid storm.<sup>[4,5]</sup> Herein, we reported a case of impending thyroid storm during an emergency caesarean section. We also performed a literature review on the management of thyroid storm or impending thyroid storm.

## 2. Case report

This study was approved by the Ethics Committee of West China Second University Hospital of Sichuan University. Written

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informed consent was obtained from the patient for publication of this report.

A 23-year-old, gravida 1, para 0 woman was admitted to the antenatal ward of our hospital, due to tachycardia of the fetus and premature rupture of membranes. She was at 36 weeks and 4 days of gestation and had no unusual medical or family history. She had a regular prenatal examination during pregnancy at another medical institution, and no obvious abnormality was detected. But there was no report of thyroid function test in her record. Physical examination revealed her weight as 57.5 kg, height as 158 cm, temperature of 36.8°C, blood pressure (BP) of 132/88 mm Hg, and heart rate (HR) of 118 beats/min. The fetal position was left sacrum anterior, and the fetal HR was 150 to 200 beats/min. Regular uterine contraction was present. Vaginal examination showed meconium-stained amniotic fluid, and ultrasound revealed a fetus younger than the gestational age. The obstetrician diagnosed fetal distress in utero, which required immediate termination of pregnancy. Thus, an emergency caesarean section was performed under general anesthesia to expedite delivery.

After simple preoperative visit and airway assessment, anesthesia was induced with ketamine 60 mg, propofol 120 mg, and suxamethonium 100 mg in rapid sequence, followed by tracheal intubation. The fetus was delivered 3 min after incision, with Apgar scores of 10 at both 1 and 5 minutes. The weight of the newborn was 2250 g, and body length was 46 cm. Sufentanil 15 µg along with atracurium 25 mg which was immediately administered. Anesthesia was maintained with sevoflurane 3% and remifentanyl 0.15 µg/kg/min. The patient experienced tachycardia at 110 to 120 beats/min during the surgery, with BP of 115 to 125/75 to 85 mm Hg. The operation was uneventful and lasted 45 minutes. Sufentanil 5 µg was given toward the end of the surgery, while simultaneously terminating the use of sevoflurane and remifentanyl. The patient's HR reached 130 beats/min during tracheal extubation after the patient was able to respond to commands. Another dose of sufentanil 5 µg and additional midazolam 2 mg were intravenously given. Intravenous esmolol was administered intermittently to control the tachycardia. However, the patient's HR continuously increased, and peaked at 160 beats/min. Additionally, the patient exhibited a respiratory rate of 25 breaths/min, BP of 135 to 145/95 to 100 mm Hg, agitation, coupled with profound sweating. However, the patient was able to respond to commands and denied having palpitations, shortness of breath, or postoperative pain. Meanwhile, her temperature reached 38.2°C. Thyroid palpation was performed, which revealed a slightly enlarged thyroid. Notably, when the thyroid was touched, the patient's HR increased. The release of thyroid hormone by touching the thyroid gland may be responsible for this phenomenon. A thyroid function test was immediately conducted to establish a definitive diagnosis. Simultaneously, hydrocortisone 100 mg was administered by intravenous drip, and esmolol 0.15 mg/kg/min was intravenously pumped. The HR was maintained between 130 and 140 beats/min. The patient was then transferred to the intensive care unit (ICU) for further treatment. The thyroid function test revealed triiodothyronine (T<sub>3</sub>) 8.15 nmol/L (normal range: 0.93–3.7), thyroxine (T<sub>4</sub>) >387.0 nmol/L (normal range: 58.1–173), free triiodothyronine (FT<sub>3</sub>) 18.81 pmol/L (normal range: 3.5–6.5), free thyroxine (FT<sub>4</sub>) 70.22 pmol/L (normal range: 11.5–22.7), thyroid-stimulating hormone (TSH) 0.005 mIU/L (normal range: 0.55–4.78), and thyroid globulin antibody (TGAb) 173.8 IU/mL (normal range: <60). Therefore, hyperthy-

roidism was definitively diagnosed. After the patient was completely conscious, propylthiouracil 100 mg and propranolol 10 mg were administered orally 3 times daily, and the patient's HR gradually decreased to <100 beats/min. The patient was transferred out of the ICU after 3 days and discharged from the hospital 3 days later.

The thyroid function test of the newborn at 5 days after birth revealed T<sub>3</sub> 4.84 nmol/L (normal range: 1.4–2.5), T<sub>4</sub> 318.9 nmol/L (normal range: 105–213), TSH 0.007 mIU/L (normal range: 1.7–9.1), and TGAb 113 IU/mL (normal range: <60). Neonatal hyperthyroidism was diagnosed. Propylthiouracil 5 mg was administered orally 3 times daily for 8 weeks. The repeat thyroid function test was normal. The mother continued to take propylthiouracil after discharge. One year later, her thyroid function test showed normal FT<sub>3</sub>, FT<sub>4</sub>, TT<sub>3</sub>, and TT<sub>4</sub> levels, but TSH was reduced to 0.05 mIU/L.

### 3. Discussion

Hyperthyroidism is a rare complication, occurring in 1 to 4/1000 pregnant women,<sup>[6]</sup> with 85% of these cases resulting from Graves' disease.<sup>[7]</sup> Untreated and inadequately controlled thyrotoxicosis is correlated with miscarriage, stillbirth, prematurity, pre-eclampsia, maternal congestive heart failure, low birth weight, and intrauterine growth restriction.<sup>[8–10]</sup> Maternal serum thyrotrophin receptor antibody (TRAb) due to Graves' hyperthyroidism can cross the placenta and stimulate the fetal thyroid, resulting in fetal hyperthyroidism, with signs of intrauterine growth restriction and an increased fetal HR,<sup>[11]</sup> as seen in our patient.

Treatment of hyperthyroidism does not increase the likelihood of an adverse perinatal outcome, but is an independent risk factor for caesarean section.<sup>[12]</sup> However, symptoms of hyperthyroidism, including tachycardia, hyperhidrosis, and anxiety can also occur during a normal pregnancy.<sup>[7]</sup> Moreover, because of the bias towards a Th2 immune state in pregnant women accompanying tolerance of the fetus, symptoms of hyperthyroidism during pregnancy can be alleviated.<sup>[13]</sup> Therefore, there is considerable difficulty in diagnosing hyperthyroidism during pregnancy without thyroid function test. Our patient had no history of hyperthyroidism and was not previously screened for thyroid function during pregnancy. Thus, when she was admitted to the emergency ward of our hospital, the obstetrician focused on the fetal distress and could not differentiate if the tachycardia of the fetus was caused by maternal disease, such as maternal hyperthyroidism.

The symptoms of hyperthyroidism are often worsened by the precipitating events, ultimately leading to thyroid storm.<sup>[3,4]</sup> Patients with hyperthyroidism during pregnancy are 10 times more likely to develop a thyroid storm than in the nongestation period.<sup>[5]</sup> Various stress conditions, such as surgery, childbirth, infection, pre-eclampsia, induced labor, diabetic ketoacidosis, etc, can induce maternal thyroid storm. Therefore, the choice of anesthetic technique and drugs for caesarean section are particularly important in pregnant women with hyperthyroidism. As compared to neuraxial anesthesia, general anesthesia can avoid the stimulation of patients via invasive preoperative manipulation. However, narcotic drugs should be carefully chosen, and the use of anesthetics that could excite the sympathetic nerves and release histamine should be avoided. Ketamine is a potent analgesic with lighter respiratory depression. In spite of ketamine's avid transfer from the placenta, it does

not lead to reduced Apgar scores in the neonate, making it a part of the small group of drugs that are approved for the induction of caesarean section.<sup>[14]</sup> However, ketamine obviously activates sympathetic function via inhibiting neuronal noradrenaline (NA) uptake at the sympathetic nerve endings,<sup>[15]</sup> and spontaneously evokes NA release, which is exocytosis-independent and insensitive to NA transport.<sup>[16]</sup> In addition, histamine concentrations increase dramatically when atracurium is administered at  $\geq 0.5$  mg/kg, which exerts positive inotropic and chronotropic effects on the H<sub>2</sub> receptors of the myocardia and increases the HR.<sup>[17,18]</sup> We speculate that the use of atracurium and ketamine in our patient may have been a key factor for inducing the impending thyroid storm.

For surgery patients, the symptoms of thyroid storm may be atypical due to the effects of narcotic drugs. If a patient's hemodynamics drastically change and the increase of arterial pressure or HR is inconsistent with the depth of anesthesia, thyroid storm should be considered. However, other hypermetabolic conditions should be differentiated from thyroid storm, such as malignant hyperthermia (MH) and inadequate analgesia. In our case, sufentanil was intravenously given twice at the end of the operation and the patient denied any postoperative pain. Most MH patients developed signs of muscle rigidity and higher carbon dioxide,<sup>[19]</sup> which did not occur in our patient. Therefore, thyroid storm was highly suspected. Thyroid storm can be divided into 2 stages: the early stage (impending storm) and the actual crisis (thyroid storm).<sup>[20]</sup> In 1993, precise criteria for thyroid storm were defined by Burch and Wartofsky<sup>[2]</sup> based on the patient's clinical symptoms, including thermoregulatory and cardiovascular dysfunction, gastrointestinal–hepatic dysfunction, and central nervous system disturbance. Our patient exhibited abnormal tachycardia, agitation, sweating, and hyperpyrexia after extubation, with a high index of suspicion for thyroid storm. However, the patient's temperature did not exceed 39°C, and there was no vomiting, diarrhea, psychosis, stupor, or coma. The Burch and Wartofsky score of the patient was 45 implying that she was still in the stage of impending thyroid storm. But if not recognized in time and treated properly, it might have developed into a thyroid storm. As thyroid storm occurs abruptly and with a high mortality rate, people who are highly suspected of impending storm should be treated as thyroid storm. Thyroid function should be examined to establish a definite diagnosis. Meanwhile, antithyroid drugs, such as propylthiouracil, a saturated solution of potassium iodide or  $\beta$ -blockers, should be aggressively used to reverse the thyrotoxicosis. In addition, other multimodality treatment should be provided, including corticosteroid therapy, abundant oxygen, volume resuscitation, effective temperature control with antipyretics or cooling blankets, and correction of electrolyte imbalance.<sup>[7,20]</sup> In the present case, due to immediate recognition and aggressive treatment, we effectively controlled the condition and avoided more serious symptoms of thyroid storm.

Notably, our patient exhibited some unusual phenomena during the third trimester of pregnancy, despite the absence of thyroid function test results. According to the prenatal examination records, the patient's weight only increased by about 1500 g in the last 7 weeks. Her HR maintained at 100 to 120 beats/min in the past 2 months. Bulimia, hyperhidrosis and anxiety were also considered to be normal by the patient and her previous obstetrician. The neglect of these symptoms led to the missed diagnosis of hyperthyroidism. Inadequate preoperative

preparation resulted in the occurrence of impending thyroid storm during the operation.

#### 4. Conclusions

Herein, a pregnant woman with undiagnosed hyperthyroidism who developed impending thyroid storm was reported. Good antenatal care is very important for pregnant women, and they should be generally screened for thyroid disorders, especially if the resting HR is  $>100$  beats/min and weight increases are inconsistent with gestational age. When hyperthyroidism is suspected, drugs that excite the sympathetic nerves or promote the release of histamine should not be used during caesarean section. Once symptoms similar to thyroid storm occur, aggressive treatment should be administered without hesitation to prevent worsening of the condition.

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