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CASE REPORT

# Anesthetic management of a pregnant woman undergoing thyroidectomy following propylthiouracil-induced hepatotoxicity: a case report

Bruna Carvalho Oliveira[1]*, Camila Borges Ferreira[1], Katharina Lanza Japolini[1], Marina Ayres Delgado[1]

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## ABSTRACT

This case report describes the anesthetic management of a pregnant woman with severe hyperthyroidism treated with propylthiouracil, who developed hepatotoxicity, leading to the suspension of the medication and the need for thyroidectomy as the only therapeutic option. The patient, at 24 weeks of gestation, presented with jaundice and drug-induced hepatitis, associated with uncontrolled hyperthyroidism. The surgery was performed under balanced anesthesia, with strict hemodynamic monitoring and precautions to diagnose complications such as thyroid storm. This case highlights the complexity of managing hyperthyroidism during pregnancy and the importance of careful anesthetic planning in high-risk situations.

## KEYWORDS

Hyperthyroidism; Pregnancy; Propylthiouracil; Liver failure; Acute; Thyroidectomy; Thyroid crisis

## INTRODUCTION

Hyperthyroidism is characterized by an abnormal increase in serum concentrations of unbound thyroid hormones. Uncontrolled hyperthyroidism can lead to serious maternal and fetal complications, including pre-eclampsia, pregnancy loss, heart failure, thyroid storm, preterm labor, intrauterine growth restriction, low birth weight, and fetal hyperthyroidism[1].

Current therapies for pregnant patients include antithyroid medications (ATDs) and thyroidectomy. The first-line treatment is propylthiouracil (PTU), which is recommended during the first trimester due to its lower risk of congenital malformations. However, PTU is associated with rare but potentially fatal fulminant hepatic failure[2]. A meta-analysis of 15 studies involving both non-pregnant adults and pregnant women showed increased odds of elevated liver enzyme levels associated with PTU compared to methimazole (OR 2.4, 95% CI 1.16-4.96)[3]. It is estimated that 1 in 10,000 adult patients prescribed PTU will develop hepatotoxicity[4].

Other ATD options, like methimazole or carbimazole, are preferred in non-pregnant women as their use during pregnancy has been associated with severe congenital malformations[1,2]. These medications can also elevate liver enzyme levels, which generally normalize after stopping the drug or improving thyrotoxicosis. Severe adverse reactions like agranulocytosis and hepatitis can occur, albeit rarely[5].

[1] Universidade Federal de Minas Gerais, Hospital das Clínicas, Departamento de Cirurgia, Divisão de Anestesiologia, Belo Horizonte, MG, Brasil

If ATDs cannot be used, thyroidectomy becomes the treatment of choice. This case highlights the anesthetic management of a pregnant woman undergoing thyroidectomy which represents the only feasible yet uncommon therapeutic option in this scenario. The patient provided written informed consent for the publication of this case report.

## CASE REPORT

A 27-year-old woman, 24 weeks pregnant, was admitted with jaundice, choluria, and fecal acholia developing over the past 10 days. She denied fever or prior episodes of jaundice. The patient was treated and followed for hyperthyroidism in high-risk prenatal care. She was taking PTU, methyldopa, acetylsalicylic acid, and calcium supplements. The patient had a poor obstetric background, including preeclampsia and a stillbirth.

Due to suspected drug-induced hepatitis from PTU, her medications were discontinued, and she was admitted to a liver transplantation referral center. Serial exams were conducted to monitor her condition (Table 1), including tests to rule out viral hepatitis. Abdominal ultrasound excluded structural liver abnormalities.

Propranolol was initiated for thyrotoxic symptoms, and two days before surgery, treatment with Lugol's iodine began. The patient underwent total thyroidectomy at 26 weeks and 5 days of gestation. Monitoring included oximetry, continuous electrocardiography, non invasive blood pressure, and bispectral index. Parameters prior to induction were stable, with a heart rate of 88 bpm, blood pressure of 123/77 mmHg, oxygen saturation of 96%, and a temperature of 36.1°C.

A thorough airway assessment was performed, and no predictors of a difficult airway were identified, aside from the physiological changes associated with pregnancy. Therefore, we proceeded with adequate preoxygenation using a face mask with 100% oxygen for 3 minutes, followed by rapid sequence induction. Anesthetic induction included propofol, lidocaine, remifentanil and rocuronium. The procedure was carried out without complications. The patient was positioned with a left lateral tilt to minimize aortocaval compression during surgery. An invasive arterial line was placed to monitor perfusion, and the target mean arterial pressure (MAP) was > 65 mmHg. She was maintained under balanced general anesthesia with remifentanil and sevoflurane with minimal fluctuations in heart rate and blood pressure. She was successfully extubated at the end of the procedure, with stable hemodynamics, and transferred to the ward. The obstetric team confirmed a final fetal heart rate of 128 bpm. Postoperative analgesia was provided with dipyrone and morphine.

Regarding the postoperative period, the hyperthyroid state remained well controlled, despite a transient episode of hypocalcemia, which was promptly corrected. The pregnancy progressed uneventfully, with no maternal or fetal complications observed.

## DISCUSSION

Drug-induced liver injury (DILI) is a condition that encompasses various forms of hepatotoxicity caused by medications, including PTU. PTU is associated with an idiosyncratic DILI, and though potentially fatal, is still extremely rare even in populations with high prevalence of thyroid disorders. The diagnosis is made by exclusion of others causes of hepatitis, through various special tests, and the stages include latency, dechallenge, rechallenge, likelihood, and phenotype, as there are generally no specific markers (Table 2)[6].

However, PTU is the third commonest cause of DILI requiring liver transplantation in the United States, after paracetamol and isoniazid. It is interesting to note that based on "Hy's Law" which describes risk of mortality in DILI, our patient was a match for all the criteria: 1) Serum ALT or AST > 3xULN; 2) Serum total bilirubin elevated to > 2xULN, with no alternative explanation for the combined elevation of ALT and bilirubin[6]. This analysis placed this patient in great risk for acute liver failure (ALF) and for that reason she was transferred to a specialized hospital and follow-up by an expert team.

Fortunately, the patient did not progress to ALF as the medication was discontinued at the onset of clinical presentation and both laboratory tests and clinical condition improved (Table 1). Besides the clinical improvement from the liver injury, her hyperthyroidism condition posed an additional challenge. ADTs are the central hyperthyroidism treatment in pregnancy. However, this patient developed with a serious adverse effect that contraindicates the use of these medications. The Brazilian Federation of Gynecology and Obstetrics Association (FEBRASGO) recommends that ATDs should not be used in cases of agranulocytosis or liver injury, and not to change the medications if one of those triggered the adverse effect[7].

Considering this recommendation, the only option of treatment is thyroidectomy to manage the patient's Grave's disease. This is a common treatment in cases of thyroid cancer but is not usual for hyperthyroidism in pregnancy. It is necessary to consider all the risks from a non-obstetric surgery in a pregnant woman in a context of uncontrolled hyperthyroidism which we believe poses an additional risk to the surgery.

**Table 1.** Evolution of exams during inpatient stay

| Date/Exams | 08/jun (Suspended medication) | 10/jun | 11/jun | 12/jun | 16/jun | 17/jun (Hospitalized at HC-UFMG) | 18/jun | 21/jun | 24/jun | 01/jul | 02/jul (Day before surgery) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Hb / Platelets** | *10.2 (VR 11.0)* | - | *11.3 / 290.000* | *10.5 / 301.000* | *9.8 / 333.000* | *9.8 / 296.000* | *8.5 / 289.000* | *8.4 / 243.000* | *8.7 / 190.000* | - | *9.1 / 182.000* |
| **Cr** | *0.49 (VR < 1.04)* | - | *0.51* | - | *0.22* | *0.3* | *0.31* | *0.3* | *0.35* | - | - |
| **AST** | *1684 (VR 15 -46)* | *1465* | *1521* | *1270* | *458* | *338* | *183* | *64* | *53* | *50* | - |
| **ALT** | *1422 (VR <35)* | *1224* | *1260* | *1120* | *511* | *342* | *220* | *108* | *52* | *32* | - |
| **FA** | *93 (VR 38-126)* | *200* | *208* | *181* | *224* | *164* | *140* | *139* | *122* | *130* | - |
| **GGT** | *122 (VR 12 – 43)* | *122* | *134* | *134* | *105* | *105* | *119* | *172* | - | *79* | - |
| **BT (BD/BI)** | *10.7 (6.7 / 3.9) (VR 0.2 (<0.3 / < 1.1))* | *13.6 (8.09 / 5.51)* | *17.9 (10.2 / 7.6)* | *20.4 (14.6 / 5.8)* | *24.6 (15.5 / 9.1)* | *20.3 (17.7/ 2.6)* | *18.73 (16.26 / 2.47)* | *12.5 (10.7 / 1.8)* | *7.72 (6.15 / 1.57)* | *3.94* | - |
| **INR** | - | *1.41* | - | - | *1.76* | *1.37 (VR <1.25)* | *1.38* | - | *1.07* | *0.98* | - |
| **TSH** | - | - | *< 0.01* | - | - | - | - | *< 0.01* | *< 0.01* | - | *0.0208* |
| **T4** | - | - | *1.96 (VR <1.2)* | - | - | - | - | *6.98* | *6.2* | - | *4.13* |
| **Anti-thyroglobulin** | - | - | - | - | - | - | - | *753.11* | *611.75* | - | - |
| **Anti-TPO** | - | - | - | - | - | - | - | - | *4202.16* | - | - |

VR: reference value; Hb: hemoglobin; Cr: creatinine; AST: aspartate aminotransferase; ALT: alanine aminotransferase; FA: alkaline phosphatase; GGT: gamma-glutamyl transferase; BT: total bilirubin; BD: direct bilirrubin; BI: indirect bilirubin; INR: international normalized ratio; TSH: thyroid stimulating hormone; T4: Thyroxine; Anti-TPO: anti-thyroid peroxidase antibodies; HC-UFMG: Hospital das Clínicas UFMG.

**Table 2.** Differential diagnosis of liver failure in pregnancy

| *Condition* | *Gestational Age* | *Clinical Features* | *Laboratory Findings* |
|---|---|---|---|
| **Acute Fatty Liver of Pregnancy (AFLP)** | Third trimester | Nausea, vomiting, abdominal pain, jaundice, encephalopathy | ↑LFT, hypoglycemia, leukocytosis |
| **HELLP Syndrome** | Third trimester | Hypertension, proteinuria, RUQ pain, hemolysis | Hemolysis, ↑LFT, ↓platelets |
| **Intrahepatic Cholestasis of Pregnancy (ICP)** | Second to third trimester | Pruritus (esp. palms/soles), mild jaundice | ↑Bile acids, mild ↑ LFT |
| **Viral Hepatitis (A, B, C, E)** | Any trimester | Malaise, jaundice, right upper quadrant pain | ↑AST/ALT (often >1000), positive viral serologies |
| **Drug-induced Liver Injury** | Variable | Depend on agent; jaundice, nausea | Variable; ↑LFTs depending on mechanism |
| **Budd-Chiari Syndrome** | Any trimester | Abdominal pain, ascites, hepatomegaly | ↑LFTs; |
| **Sepsis/Ischemic Hepatitis** | Variable | Hypotension, multiorgan failure | Markedly ↑AST/ALT, ↑lactate |

LFT: Liver Function Tests; AST: aspartate aminotransferase; ALT: alanine aminotransferase; FA: alkaline phosphatase; GGT: gamma-glutamyl transferase; BT: total bilirubin INR: international normalized ratio; ↑ increase; ↓ decrease.

One of the main complications of thyroidectomy in a pregnant patient with poorly controlled hyperthyroidism is thyroid storm, which is a rare but potentially fatal endocrine emergency. Studies have reported that 5–16% of all patients admitted with thyrotoxicosis experience thyroid storm. In pregnancy, this incidence is approximately 0.2–0.9%, with a higher rate in the first trimester. The mortality rate can range from 10% to 30% if not recognized and immediately treated[8].

The most common cause of thyroid storm is hyperthyroidism secondary to Graves' disease[1,3]. Untreated and uncontrolled hyperthyroidism is a significant risk factor for the development of thyroid storm during pregnancy. Like the general population, thyroid storm in pregnancy can be precipitated by acute stressors such as infection, surgery, trauma, and drugs/toxins. Additionally, pregnancy-related causes such as anemia, pre-eclampsia, placenta previa, induction of labor/C-section, and chorioamnionitis can contribute[1].

The main challenge is diagnosing thyroid storm in an anesthetized patient, as symptoms may be atypical or masked by the effects of narcotic drugs and general anesthesia. Intraoperative signs such as tachycardia, agitation, and hyperthermia may overlap with normal physiological responses to pregnancy, surgical stress, or medication effects. The absence of specific diagnostic tools, combined with the need for rapid decision-making, further complicates timely recognition. If a patient hemodynamics change drastically with increases in heart rate or blood pressure that are inconsistent with the depth of anesthesia and an abnormal hypermetabolic state with fluctuating temperature is observed, thyroid storm should be strongly suspected[9].

Thyroidectomy is preferable, even with the risk of thyroid storm, rather than continuing clinical treatment that increases the incidence of fulminant hepatitis, preeclampsia, and miscarriage. While thyroid storm is a rare but potentially fatal complication, the alternative—ongoing treatment with antithyroid drugs (ATDs) such as propylthiouracil (PTU)—carries a significant risk of liver failure, which can be fatal and lead to the need for liver transplantation. Given these risks, thyroidectomy becomes a more favorable option, despite the potential for thyroid storm, as it offers a direct solution to uncontrolled hyperthyroidism, thereby preventing the more dangerous systemic complications associated with long-term medical management. Then, anesthesia was carefully designed with the goal to avoid the potential risks for the pregnancy. In this sense, the surgery was programmed to occur in the second trimester because the risk of spontaneous abortion is lower than in the first trimester, and the incidence of preterm labor and delivery is lower than in the third trimester[10].

Thyroidectomy is a surgery performed under general anesthesia. So, after weighing risks and benefits on the both difficult and failed intubation in pregnant women, rapid-sequence induction was planned. Data suggest that the risk of aspiration in non-obese pregnant patients who have adhered to appropriate fasting guidelines is low and likely not significantly different from that of non-pregnant patients. Although the use of rapid sequence induction (RSI) remains subject of debate, many anesthesiologists still choose to perform RSI in women beyond 15 to 18 weeks of gestation, despite evidence indicating that the risk of aspiration in this population is rare[10].

We chose to monitor the pregnant patient with ASA standard for basic monitoring and additionally with an invasive arterial line and bispectral index. The reason for the invasive arterial line was to maintain maternal blood pressure between 80–100% of baseline and, given the risks of performing a surgery in a patient with uncontrolled hyperthyroidism, to note any hemodynamic instability in this patient that we should promptly treat. Moreover, we planned to use phenylephrine to correct blood pressure due to its action as a selective alpha-1 adrenergic receptor agonist without beta-adrenergic effects. This latter effect could lead to a wrong diagnosis of thyroid storm. The bispectral index was used as our parameter of adequate anesthetic depth, though any hemodynamic alteration could also suggest the idea of a symptom of thyroid storm.

The decision to withhold continuous fetal heart rate (FHR) monitoring during non-obstetric surgery in this case was based on the limited evidence supporting its routine use. Given the absence of guidelines and the limited utility of FHR monitoring—particularly when immediate obstetric intervention is not possible—we opted for pre- and postoperative fetal assessments instead. While fetal monitoring may offer indirect insight into maternal stability and could be considered in cases with a higher risk of maternal decompensation, its omission here reflects an individualized, evidence-informed approach consistent with good obstetric practice.

Since effective surgical analgesia plays a crucial role in maintaining maternal hemodynamic stability and reducing the neuroendocrine stress response, the appropriate use of analgesics is essential not only to ensure maternal comfort but also to minimize stress-related physiological responses that could increase the risk of preterm labor.

## CONCLUSION

Managing hyperthyroidism in pregnancy is complex and requires careful consideration for the health of both mother and fetus. In our case, although the patient was treated with ATDs, hepatotoxicity led to medication suspension. This left her with uncontrolled disease, emphasizing the need for careful management during surgery. Thyroid storm is rare but can be devastating, requiring prompt action. This case shows an uncommon treatment for hyperthyroidism in pregnancy. Additionally, it underscores the importance of meticulous anesthetic planning, given the high risk of serious complications in patients with hyperthyroidism undergoing surgery.

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**Correspondence**
Bruna Carvalho Oliveira
Universidade Federal de Minas Gerais, Hospital das Clínicas, Department of Surgery, Division of Anesthesiology
Av. Alfredo Balena, 110, Santa Efigênia, CEP 30130-100, Belo Horizonte, MG, Brasil.
Phone: +55 (031) 99235-2608
brucoliveira23@gmail.com