Thyroid storm in a postpartum and uncontrolled graves’ disease patient: the challenges of accurate and multidisciplinary disease management

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ABSTRACT

Background: Graves’ disease is an immune system disorder that results in the overproduction of thyroid hormones (hyperthyroidism). Although pregnancy hyperthyroidism is a relatively uncommon, thyroid crisis is a medical emergency caused by hyperthyroidism exacerbation with symptoms of organ decompensation in one or more organs. Therefore, managing this disease in pregnant women is critical as well as the safety of using antithyroid drugs for pregnant women and the foetus.

Case presentation: A 26-year-old woman presented to the Dr Soetomo General Academic Hospital Surabaya, Indonesia with complaints of shortness of breath that had worsened one hour before the admission as well as sudden fever, diarrheal, anxiety, and decreased consciousness. The patient had hyperthyroidism for three years, and the controls were inconsistent. The patient was diagnosed with P1101 postpartum day 1, thyrotoxicosis due to Graves’ disease, thyroid crisis, hypertension, microcystic hypochromic anemia, hypoglycemia, hypoalbuminemia, keratitis, and lagophthalmos. The patient was treated with supportive therapy with an oxygen mask 8 liters per minute (lpm), intravenous fluids, and antipyretic acetaminophen 500 mg every 8 hours. Propylthiouracil 400 mg loading dose followed by maintenance 6x100 mg, 8 drops of Lugol’s solution after propylthiouracil administration, intravenous (IV) dexamethasone 2 mg every 6 hours, and oral propranolol 20 mg every 6 hours. The patient was discharged from the hospital after presented favorable improvement.

Conclusion: This case demonstrates that the stage of the disease determines the management of Grave’s disease during pregnancy, and that multidisciplinary involvement could improve the success and reduce the patient mortality.

Keywords: thyroid crisis, hyperthyroidism, grave’s disease, immune system disorder.


INTRODUCTION

Pregnancy hyperthyroidism is a relatively uncommon condition with a prevalence in the United States is 0.1-0.4%, with Graves’ disease being the most common etiology.1 Hyperthyroidism affects 0.05-3% of all pregnancies worldwide.1 Graves’ disease is one of several autoimmune diseases with incidence rates ranging from 1-2 per 1000 pregnancies.1 Poor hyperthyroidism control during pregnancy is linked to a variety of complications, including intrauterine foetal death, hypertension in pregnancy, preterm labor, low birth weight, intrauterine growth restriction, and maternal congestive heart failure.2-3 Thyroid crisis is one of the most feared complications of hyperthyroidism, with a mortality rate of 10-30%.2,3 A thyroid crisis is a sudden medical emergency caused by hyperthyroidism exacerbation with symptoms of organ decompensation in one or more organs. Surgery, trauma, infection, drugs, noncompliance with antithyroid medication, pregnancy, and childbirth have all been identified as precipitating factors for thyroid crisis.4 There is no specific amount of thyroid hormone in the blood that can cause a thyroid crisis. Clinical challenges in reducing thyroid crisis mortality and morbidity include hemodynamic instability and therapeutic management.4

In this case report, we discuss the management challenges of a pregnant woman with Graves’ disease who has a thyroid crisis, as well as the safety of antithyroid drugs for pregnant women and their fetuses.

CASE PRESENTATION

A woman, 26 years old, Madurese, Muslim, a farmer, married, domiciled in Bangkalan, Surabaya, Indonesia complained that her stomach ached, and a little bloody mucus came out of the patient, then she went to the midwife. The midwife referred the patient to the Bangkalan Hospital due to a lack of equipment, on the way the patient gave birth. The patient complained that her chest was often pounding, the complaints of shortness of breath accompanied by fever and diarrhea 2-3 times a day, dregs (+), no mucus and blood. The patient also complained of shortness of breath accompanied by cough without phlegm since one week before...
hospital admission, intermittent shortness of breath, not affected by activity, and slept daily using one pillow.

Palpitations had been reported for the past three years. In addition, the patient also complained that her body sweated easily, often felt restless, anxious, lost weight, increased appetite, increased frequency of bowel movements, diarrhoea, and denial of menstrual disorders. The appearance of a lump in the neck was denied. Previously, the patient then went to the Bangkalan Hospital’s Internal Medicine Polyclinic. The patient was diagnosed with hyperthyroidism and received 2x10 mg of thyrozol and 1x10 mg of propranolol, but she did not have routine control because she had no complaints. The patient has not taken the medication for a year. Because of frequent nausea and vomiting, the patient’s appetite has decreased since pregnancy. Since then, the patient’s weight has decreased and reports that her body feels weak. Fever complaints were denied. Normal defecation, yellowish in colour, normal urination painful and clear colour. The patient’s first pregnancy occurred at the age of 18, and the child was delivered safely and healthily by the midwife. Previously denied history of diabetes, hypertension, asthma, and allergies. The patient was not controlled by performing laboratory tests or taking antithyroid medication at the start of her second pregnancy.

The patient is the second child of two siblings, no one in the patient’s family suffers from complaints like the patient. The patient works as a farmer, drinks herbal medicine, and denies pain medication. Has been married for 8 years. History of birth control was denied. First child: 9 months, male, AS 9/ 3200 g/7 years. Second child: 7 months, AS 2/1450 g/ died.

A physical examination revealed a general state of weakness and awareness of composition on the Glasgow Coma Scale (GCS 15) (Figure 1). Body weight: 55 kg; height: 155 cm; blood pressure: 147/100 mmHg; pulse: 130 beats per minute; respiration: 28 beats per minute; axillary temperature: 38.5°C; and body mass index: 22.8 kg/m². The score for Burch-Wartofsky was 65.

The conjunctiva contained anaemia, dyspnoea, the sclera was not icterus, the pupil reflex was normal, the eye was staring, the exophthalmos was present, and the stellwag test was positive (Figure 1). The throat, nose, and ears are all within normal ranges. There were no visible enlarged lymph nodes. On thoracic examination, there was wheezing, vesicular breath sounds, symmetrical chest breathing, and no crackles. Cardiac apex beat on intercostal space (ICS) V linea anterior left axilla, single S1 and S2, and no murmurs or gallops were discovered during a cardiac examination. When the abdomen was examined, the stomach did not appear enlarged, there were no ascites, and neither the liver nor the spleen could be felt. Uterine contractions (+) were strong and the uterine fundus was two fingers below the center. There was no edema and the extremities were warm, dry, and red.

Laboratory tests showed Hb 7.7 gr/dL, leukocytes 14,400/mm3, platelets 71,000/mm3, haematocrit 23.5%, granulocytes 58.4%, MCV 77.7 fL, MCHC 32.6 g/dL, SI 29 ug/dL, TIBC 380 ug/dL, LED 2 mm/h, random blood sugar 63 gr/dL, SGOT 42 U/L, SGPT 19 U/L, albumin 2.0 g/dL, BUN 7.0 mg/dL, creatinine 0.44 mg/dL, potassium 2.9 mmol/L, sodium 136 mmol/L, chloride 98 mmol/L, FT4 7.78 ng/dL, T3 4.42 ng/ml, PT 14.4 seconds, APTT 42.7 seconds, TSH <0.05 uIU/ml, HbsAg negative, blood gas analysis pH 7.47, PCO₂ 20 mmHg, PO₂ 174 mmHg, HCO₃⁻ 14.6 mmol/L, BE -8.3 mmol/L, SaO₂ 100 %. Urinalysis: orange colour, pH 5.5, nitrites (-), protein (-), glucose (-), ketones (-), blood 1+, epithelium 3-6, erythrocytes 1-3, leukocytes (-), and no bacteria.

The chest X-ray revealed cardiomegaly with a CTR of 65% (Figure 1). The patient was diagnosed with pro-evaluated cardiomegaly, hypertension stage 1 JNC VII, no signs of acute heart failure, and
there were no signs of acute or chronic respiration in the patient after an evaluation at the department of cardiology and pulmonology. Following consultation with the Department of Ophthalmology, the patient was diagnosed with ophthalmic left and right (ODS) keratitis exposure + ODS lagophthalmos. Based on the initial assessment, the patient was diagnosed with P1101 postpartum day 1, thyrotoxicosis due to Graves’ disease, thyroid crisis, hypertension stage 1 JNC VII, microcytic hypochromic anaemia, hypoglycemia, hypoalbuminemia, ODS keratitis, and lagophthalmos.

The patient was treated with O3 nasal 3 lpm, IV NaCl 0.9% 1500 cc/24 hour, IV dexamethasone 2 mg every 6 hours, drip Dextrose 40% 50 ml, IV albumin 20% 100 ml in 4 hours, and packed red cell (PRC) transfusion 500ml. The patient has also given propylthiouracil (PTU) 300 mg every 6 hours, Lugol 8 drops every 6 hours, propranolol 20 mg every 6 hours, and amiodipine 10 mg every 24 hours orally.

On the second treatment day, the patient was agitated, had palpitations, had shortness of breath worsened and began to lose consciousness, had diarrhoea twice daily, and had a fever. The patient’s condition was poor, with GCS 11, blood pressure 104/68 mmHg, pulse 131 beats per minute, respiratory rate (RR) 32 beats per minute, and an axillary temperature of 39.1°C. Burch-Wartofsky rating: 80 (temp 20, agitation 10, tachycardia 20, diarrhea 10, cardiomegaly 10, risk factors for delivery 10). The patient appeared anaemic and short of breath. No murmurs/gallop, vesicular lung sounds, fine moist rales at the bases of both lung fields, and no wheezing. Warm, dry, and red acral covers at the bases of both lung fields, and no short of breath. The patient's condition was poor, with GCS 3X5, blood pressure 132/77 mmHg, pulse 88 beats per minute, RR 20 on ventilator, and a temperature of 37.0°C. The heart was examined and found to be normal, with only minor crackles at the base of the lungs and no wheezing. The echocardiography examination revealed normal heart valves and chamber dimensions, an left ventricle ejection fraction (LVEF) of 72%, and no left ventricular hypertrophy (LVH). Lab results: Hb 7.6 g/dL, leukocytes 21,210/mm³, platelets 171,000/mm³, blood glucose 296 mg/dL, albumin 2.4 g/dL, sodium 138 mmol/l, potassium 2.7 mmol/l, chloride 115 mEq/L, PT 21.6 seconds, APTT 41.8 seconds, procalcitonin 0.63 ng/ml. Electrocardiography revealed heart rate (HR) 125 beats per minute tachycardic sinus rhythm, axis normal.

The patient was intubated on the fourth day of treatment. The patient’s condition was poor, with GCS3X3, blood pressure 149/80 mmHg, pulse 96 beats per minute, RR 20 on ventilator, and a temperature of 37.8°C. The heart was examined and found to be normal, with only minor crackles at the base of the lungs and no wheezing. The echocardiography examination revealed normal heart valves and chamber dimensions, an left ventricle ejection fraction (LVEF) of 72%, and no left ventricular hypertrophy (LVH). Lab results: Hb 7.6 g/dL, leukocytes 21,210/mm³, platelets 171,000/mm³, blood glucose 296 mg/dL, albumin 2.4 g/dL, sodium 138 mmol/l, potassium 2.7 mmol/l, chloride 115 mEq/L, PT 21.6 seconds, APTT 41.8 seconds, procalcitonin 0.63 ng/ml. Electrocardiography revealed heart rate (HR) 125 beats per minute tachycardic sinus rhythm, axis normal.

The sixth day of treatment, the patient was still intubated. The patient’s condition was weak, GCS 3X5, blood pressure 132/77 mmHg, pulse 88 beats per minute, RR 20 on ventilator, temperature 37.0°C. Examination of the thorax and abdomen was within normal limits. Laboratory results Hb 8.1 g/dL, leukocytes 16,010/mm³, platelets 185,000/mm³, haematocrit 26.4%, granulocytes 82.7%.

On the 8th day of treatment, the patient was taken off the ventilator, conscious and had no short of breath. The patient’s condition was weak, GCS 3X5, blood pressure 132/77 mmHg, pulse 88 beats per minute, RR 20 on ventilator, temperature 37.0°C. Examination of the thorax and abdomen was within normal limits. Laboratory results Hb 8.1 g/dL, leukocytes 16,010/mm³, platelets 185,000/mm³, haematocrit 26.4%, granulocytes 82.7%.

The presence of an increase in free thyroxine (FT4) levels accompanied by a decrease in thyrotropin (TSH) levels confirms the diagnosis of Graves’ disease. Although elevated of this hormone can be found in other diseases. The presence of this hormone can be found in other diseases. The presence of this hormone can be found in other diseases. The presence of this hormone can be found in other diseases.

The patient’s condition was mmHg adequate: GCS 456, blood pressure 120/78, pulse 78 beats per minute, RR 19 beats per minute, and temperature 36.6°C. The thorax and abdomen were examined and found to be normal. Hb 10.6 g/dL, leukocytes 10,790/mm³, platelets 34,200/mm³, granulocytes 54.8%, SGOT 26 U/L, SGPT 20 U/L, BUN 11 mg/dL, creatine 0.36 mg/dL, sodium 138 mmol/l, potassium 3.4 mmol/l, chloride 103 mmol/l, direct bilirubin 0.14 mg/dL and total bilirubin 0.37 mg/dL. A soft diet of 2100 kcal/24 hours, oral PTU 200 mg/8 hours, oral propranolol 10 mg/8 hours, and oral amiodipine 10 mg/24 hours were given to the patients. The patient was discharged from the hospital on the 11th day of treatment.

DISCUSSION

Graves’ disease is an autoimmune disorder characterized by the presence of autoantibodies against the TSH, also known as thyrotropin receptor antibody (TRAb). It is distinguished by hyperthyroidism, orbitopathy, and pretibial myxedema, with symptoms including thyroid gland swelling, exophthalmos, weight loss, palpitations, heat intolerance, and excessive sweating. The presence of an increase in free thyroxine (FT4) levels accompanied by a decrease in thyrotropin (TSH) levels confirms the diagnosis of Graves’ disease. Although elevated of this hormone can be found in other diseases. T3 toxicosis affects about 2% of Graves’ disease patients who have normal FT4 levels but high levels of free triiodothyronine (FT3). The Wayne index uses a scoring system to evaluate existing clinical signs and symptoms; a score of 20 or higher indicates hyperthyroidism.
toxic adenoma.10

In our case, the patient had diffusely enlarged thyroid glands, frequent palpitations, excessive sweating, weight loss, hyper defecation, increased FT4 levels, and decreased TSH, leading to the diagnosis of Thyrotoxicosis caused by Graves’ disease. Graves’ disease is the most common cause of hyperthyroidism in pregnancy. Other diseases that cause hyperthyroidism in pregnancy besides Graves’ disease are gestational transient hyperthyroidism, trophoblastic hyperthyroidism, toxic solitary adenoma, toxic multinodular goiter, and subacute thyroiditis. Graves’ disease can worsen during pregnancy and after delivery.11

The physiological effects of HCG causing a decrease in TSH levels and an increase in TBG levels must be taken into account. Beta HCG shares structural similarities with TSH and has thyroid-stimulating activity. TSH concentrations can reach 0.03 at the end of the first trimester of pregnancy. The TRAB level examination is used to determine whether hyperthyroidism is caused by Graves’ disease or not, and it is also used to evaluate the effectiveness of antithyroid drugs. Thyroid-stimulating immunoglobulin (TSI) and thyroid-binding inhibitory immunoglobulin (TBI) are two TRAbs that can be tested. These autoimmune tests are all elevated in Graves’ disease but not in gestational thyrotoxicosis.12,13
In our case, the patient had typical clinical manifestations, such as diffuse goiter and exophthalmos, and the TRAB examination yielded 28.62, allowing the diagnosis of Graves’ disease to be established.

Since thyrotoxicosis poses a risk to both the mother and the foetus, antithyroid drugs should be started in pregnant women as soon as the diagnosis is made. PTU is preferred over methimazole because it crosses the placental barrier more slowly. In North America, PTU is still the drug of choice during pregnancy because methimazole use is linked to an increased risk of congenital anomalies, particularly cutis aplasia, a very rare event known as methimazole embryopathy syndrome.11,14

The American Food Drug Administration classifies either PTU or methimazole as a category D drug, because of the potential to cause foetal hypothyroidism, so the dose of antithyroid drugs must be minimized to avoid foetal hypothyroidism. However, if pregnant women’s FT4 levels remain above the upper limit of normal, the risk of foetal hypothyroidism is low. In the third trimester of pregnancy, approximately 30% of pregnant women can discontinue antithyroid medications and are still found to be euthyroid. Both PTU and methimazole are safe for nursing mothers to use because they are found in very small amounts in breast milk secretions. Clinical studies show that breastfeeding babies have normal thyroid function and intellectual development.4,11,15

Thyrotoxicosis is a syndrome caused by an increase in thyroid hormone in the blood, with an increase in FT4, FT3, or both, which can be caused by an increase in thyroid hormone biosynthesis and continuous secretion by the thyroid gland. A thyroid crisis is one of the most serious complications of hyperthyroidism; if not treated properly, it can lead to death. Clinical symptoms caused by the effect of increasing thyroid hormone which causes dysfunction of the body’s systems can be grouped into 4 main signs, namely: 1). temperature regulator system (body temperature 38.5–40°C); 2). central nervous system (anxiety, disturbance of consciousness, seizures, coma); 3). hepatic gastrointestinal system (diarrhea, vomiting, jaundice); and 4). cardiovascular system (tachycardia, heart failure, arrhythmia, pounding, atrial fibrillation, and cardiac arrest).

A thyroid crisis is diagnosed based on clinical symptoms. No specific symptoms can be used as diagnostic criteria for all patients due to the wide variety of symptoms that arise. There are 2 kinds of criteria in diagnosing thyroid crisis, namely: 1). Goiter-orbital-precipitant (GOP) Score is a classic. If the GOP score is greater than 50, the patient is in a thyroid crisis; and 2). Non-classical: Burch-Wartofsky (BW) score, is a diagnostic scale used to determine thyroid crisis; if a BW score of 45 or higher is obtained, the patient is considered to be suffering from thyroid crisis. Classic thyroid crisis can be diagnosed by the presence of a goiter (G) and/or orbit (O), the presence of precipitants (P), temperature > 39.5°C, and tachycardia 120 beats per minute.5,16,17,18

A thyroid crisis can occur in hyperthyroid patients who have previously been exposed to certain precipitating factors. Sepsis, trauma, discontinuation of antithyroid drugs, and use of sympathomimetic medications can all precipitate a thyroid crisis. After the diagnosis of thyroid crisis is established, medical treatment must be carried out immediately. Therapy for thyroid crisis is divided into 2 parts, supportive therapy, and special therapy.

Supportive therapy includes giving fluids to treat dehydration, administering oxygen, placing a nasogastric tube if needed, cold compresses, and acetaminophen to treat fever. Avoid using aspirin to reduce fever in patients because it prevents a decrease in protein binding, which can cause an increase in FT3 and FT4. Maintain electrolyte balance based on laboratory results, and administer sedatives as necessary. Meanwhile, specialized therapy is developed based on each hospital’s clinical experience. Based on Tjokroprawiro’s clinical experience, special therapy with the formula TS 41668 - 24 - 6 is the formula used in Dr Soetomo General Academic Hospital for the management of thyroid crisis.

In this case, the patient received supportive therapy with an oxygen mask at 8 lpm, intravenous fluids 0.9% NaCl, and antipyretic acetaminophen 500 mg every 8 hours. PTU 400 mg loading dose followed by maintenance 100 mg every 4 hours, 8 drops of Lugol’s solution after PTU administration, IV dexamethasone 2 mg every 6 hours, and oral propranolol 20 mg every 6 hours is the special therapy for thyroid crisis. Propranolol is classified as category C by the FDA, which means that at high doses in animals, it causes embryotoxicity, so it should only be used in pregnant women if the benefits outweigh the risks. Propranolol has foetal side effects, but because a thyroid crisis causes pregnancy termination, propranolol is still given orally at a dose of 40 mg every 8 hours. However, potential propranolol side effects such as hypotension, bradycardia, and hypoglycemia should be monitored.18

Thyroid crisis has a poor prognosis, with a mortality rate of 0-20% if it is not properly
detected or managed, with precipitating factors or underlying disease being the main causes of death.

CONCLUSION
Thyroid crisis is a medical emergency caused by an acute exacerbation of hyperthyroidism characterized by organ decompensation. A 26-year-old woman P1101 postpartum spontaneously had a headache for six hours and presented to the Dr Soetomo General Academic Hospital with complaints of shortness of breath that had gotten worse since one hour before entering the hospital, as well as sudden fever, diarrhoea, anxiety, and decreased consciousness. The patient has a history of hyperthyroidism for three years, and the controls were irregular. On the second day of treatment, there were signs of thyroid crisis with a Burch-Wartofsky score of 80, and therefore the diagnosis was made as a postpartum woman with Graves’ disease who has thyroid crisis with labour triggers and medication irregularity. The patient was then given thyroid crisis therapy according to the formula, with favourable improvement.

PATIENT CONSENT
The patient signed informed consent prior to the study and agreed that the case will be published in an academic journal without revealing the patient’s identity.

DISCLOSURE OF CONFLICTS OF INTEREST
The authors declare no conflict of interest.

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AUTHOR CONTRIBUTION
RRF contributed to the study conceptual, data acquisition, clinical data assessment, follow-up of the patient and during manuscript preparation. HN contributed to the study conceptual, data validation and during manuscript revision.

REFERENCES
9. Mahmud AA, Anu UH, Foyusal KA, Hasan M, Szib SM, Ragib AA, et al. Elevated serum malondialdehyde (MDA), insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and thyroid-stimulating hormone (TSH), and reduced antioxidant vitamins in polycystic ovarian syndrome patients. Narra J. 2022;2(1). Available from: http://dx.doi.org/10.52225/narra.v2i1.56