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A case of overt hyperthyroidism: A forgotten cause of poor maternal-fetal outcome in low-resource settings

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Abstract

Introduction: Overt hyperthyroidism during pregnancy is uncommon, occurring in only 0.7% to 0.9% of pregnancies. The grave disease is the most common cause, accounting for 90–95% of cases. It is characterized by low Thyroid Stimulating Hormone (TSH) and Elevated Levels of Free Thyroxine (T4) and Triiodothyronine (T3). Due to the normal changes in a woman's body during pregnancy and the different levels of thyroid-stimulating hormones in each trimester, overt hyperthyroidism is difficult to diagnose.

Overt hyperthyroidism is associated with adverse maternal-fetal outcomes, including low birth weight, recurrent pregnancy loss, congenital abnormalities, preterm birth, intrauterine growth restriction, preeclampsia, abruptio placenta, and lastly, thyroid storm. Therefore, treatment is required for the management of overt hyperthyroidism during pregnancy, and it is essential to maintain euthyroid status to lessen the severity of the symptoms. Priority should be given to preconception care and achieving euthyroid is recommended prior to conception. Depending on the underlying cause, this can be accomplished through medical management such as antithyroid medication or surgery.

Case presentation: A case of 18-years-old, gravida 2, para 0+1, diagnosed with overt hyperthyroidism with severe preeclampsia and severe Intrauterine Growth Restriction (IUGR), which necessitated preterm delivery at 34 weeks of gestational age. A baby boy weighing 900 g was delivered vaginally and succumbed to early neonatal death on the fourth day of life due to prematurity complications with underlying congenital hypothyroidism.

Conclusion: Health providers must not underestimate the necessity of evaluating thyroid illnesses as a potential cause of miscarriage and poor maternal-fetal outcomes even if thyroid disease is less common. The importance of having euthyroid conditions during pregnancy should be emphasized, as should the requirement for a multidisciplinary approach that prioritizes optimal patient care.

Introduction

Approximately 0.7% to 0.9% of pregnancies are complicated by overt hyperthyroidism. Grave disease is the most prevalent cause, accounting for 90-95% of cases, and is characterized by low TSH and increased free T4 and T3 [1]. Diagnosis of hyperthyroidism is challenging because the level of Thyroid Stimulating Hormones (TSH), Thyroxine (T4), and Triiodothyronine (T3) varies across the trimester, but also impact of Human Chorionic Gonadotrophic Hormone (HCG) on the TSH receptors acting as week agonist, never the fewer symptoms such as tachycardia, tremor, warm and moist skin, and the systolic murmur may be attributed to physiological change on pregnancy [2,3].

Low birth weight, recurrent pregnancy loss, congenital anomalies, preterm delivery, intrauterine growth restriction, preeclampsia, abruption placenta, and last but not least thyroid storm have been connected to hyperthyroidism. Thus, overt hyperthyroidism during pregnancy necessitates treatment, and it is essential to maintain euthyroid in order to lessen the severity of its effects [4,5]. Maternal thyroid illness may have negative effects on the mother, pregnancy, and newborn, necessitating unique treatment considerations for overt hyperthyroidism. Maternal overt hyperthyroidism that is improperly or mistreated may impair pregnancy outcomes. Propylthiouracil (PTU) is indicated as the first-line treatment for hyperthyroidism during the first trimester of pregnancy due to the increased risk of teratogenicity with methimazole derivatives [6]. We present a rare case of overt hyperthyroidism in pregnancy that was diagnosed at our institution and resulted in poor maternal-fetal outcomes due to failure to achieve euthyroid status prior to conception and during pregnancy.

Case presentation

An 18-year-old, gravida 2, para 0+1 patient presented to the Ear, Nose, and Throat (ENT) clinic on March 2021 with a history of cardiac awareness and easy fatigue. She was diagnosed with Hyperthyroidism related to Hashimoto thyroiditis, with a baseline thyroids panel consisting of low Thyroid Stimulating Hormone (TSH) 0.14 U/L (normal range: 0.32-5.2), high free thyroxine (T4) 30.0 ng/dL (normal range: 5-13), and high triiodothyronine (T3) 10 ng/dL (normal range 0.6-2.10). Maternal Thyroid Stimulating Hormone Receptor Antibodies (TRAb) were not performed since they were unavailable in the vicinity. At 6 weeks of gestation, an early obstetric ultrasound revealed a viable Intrauterine Pregnancy (IUP). She was kept on carbimazole 10 mg orally three times per day and propranolol 40 mg once per day. On her next visit to the ENT clinic, she was started on folic acid 5 mg orally daily, switched to Propylthiouracil (PTU) for the next four weeks, and then back to carbimazole. She was also supposed to get antenatal care at an obstetric clinic, but she never showed up. She came in for her first appointment at our Antenatal Care (ANC) when she was 17 weeks pregnant, and she came back for two more appointments after that. She had normal blood pressure readings on both of her first antenatal visits, was blood group O positive, and had normal fasting glucose and hemoglobin levels. However, shehad an abnormal thyroid panel at 22 weeks of pregnancy, with a TSH of 0.05 U/L (normal range, 0.37 mU/L - 3.6 mU/L), T4 of 30.0 ng/dL (normal range, 0.87 pmol/l-1.45 pmol/l), and T3 of 20 ng/d [7]. She was prescribed carbimazole 10 mg be taken orally three times daily, but she stopped taking it in the interim and we lost track of her.

She returned to our facility at 34 weeks and 1 day gestation complaining of a throbbing headache accompanied by vomiting, lower limb edema, and awareness of her heartbeat. However, the patient had normal vision and there were no reports of difficulty breathing, loss of consciousness, or convulsions. On the same day, she was admitted to the hospital. She was awake, afebrile, not pale, not jaundiced, and had bilateral pitting edema upon examination. No obvious neck mass swelling was seen. Blood pressure was elevated at 173/113 mmHg, and the pulse rate was 118 beats per minute. On abdominal examination, she was found to have a pregnant abdomen, a symphysio-fundal height of 26 cm, a cephalic presentation, and a fetal heart rate of 142 beats per minute. The results of laboratory investigations were as follows: With a platelet count of 287 x 10^9/L and a hemoglobin level of 11.3 g/dl, the complete blood count was essentially normal. This time, her Thyroid panel was T3-6.761 ng/ml (high), T4-17.17 ng/ml (high), and TSH-0.014 U/L (Low). Her serum levels of urea (2.73 mmol/L) and creatinine (50 µmol/L) were normal. Both Alanine Aminotransferase (ALT) and Aspartate Transaminase (AST) were within normal limits at 17.3 U/L and 26.4 U/L, respectively. Uric acid: 382 mol/L (Mild Elevated). Sodium was essentially normal at 135.9 mEq/L, potassium at 4.65 mEq/L, chloride at 110.2 mEq/L, and serum calcium at 2.1 mEq/L. Using biometry (Biparietal Diameter, Head Circumference, Abdominal Circumference, and Femur Length), obstetric ultrasound determined that the gestational age was 28 weeks and 5 days. Estimated fetal weight of 825 grams, adequate volume of amniotic fluid, and posterior fundal placenta. According to the 2017-WHO fetal growth curve, the fetus was below the third percentile, indicating severe IUGR. Umbilical artery Doppler scan revealed reverse end diastolic velocimetry with a resistance index of 0.72 and a pulsatility index of 1.36 (normal). The Middle Cerebral Artery (MCA) doppler scan revealed normal Resistance Index (RI) and Pulsatility Index (PI) values of 0.67 and 1.44, respectively.

She was treated for hyperthyroidism with severe preeclampsia and intrauterine growth restriction. The Pritchard magnesium sulfate regime was initiated, carbimazole 10 mg orally three times daily, propranolol 20 mg orally once daily, methyldopa 500 mg orally three times daily, hydralazine 25 mg orally three times daily, and dexamethasone 6 mg intramuscularly twice daily for two days. On the basis of a panel discussion and an informed discussion with the mother, a decision was made regarding anticipated maternal-fetal complications.

On the fifth day after admission, misoprostol 25 mcg was administered vaginally every six hours to induce labor. She gave birth vaginally to a live male fetus with APGAR scores of 8 and 10 at first and fifth min respectively, and a birth weight of 900 grams. Due to extremely low birth weight, premature birth, and primary hypothyroidism, the infant was admitted to the Neonatal Intensive Care Unit (NICU). The newborn thyroid panel results were T3-0.46 ng/dL (Low), T4-3.6 ng/dL (low) (Normal: greater than 7 mg/dl), and TSH 7.34 U/L (High) (normal 0.32-5.20). The infant died on its fourth day of life. Prematurity complications, severe low birth weight, and congenital hypothyroidism were cited as potential immediate causes of death. The mother was discharged after receiving carbimazole 10 mg orally three times daily and hydralazine 25 mg orally three times

daily for two weeks. A month after giving birth, her thyroid panel (TSH-2.25 U/L, T3-1.98 ng/dl, and T4-6.42 ng/dl), her blood pressure was 125/78 mmHg, and pulse rate was 89 beats/min. Her blood pressure and thyroid were normal. Counseling was provided regarding the necessity and significance of preconception care in subsequent pregnancies, as well as the significance of being in euthyroidstate before and during pregnancy.

Discussion

Overt hyperthyroidism is rare; it accounts for 0.7% to 0.9% of all pregnancies [1]. Normal physiological changes that happen during pregnancy, such as the thyroid gland getting 30–50% bigger, the number of Thyroid Binding Globulins (TBG) going up, and the level of thyroid stimulating hormone changing from trimester to trimester. Still, the effects of hyperthyroidism caused by Human Chorionic Gonadotrophic Hormone (HCG) are similar to the symptoms of hyperthyroidism, which makes it hard to diagnose [8]. Given the association between thyroid disease and unfavorable pregnancy outcomes, the question of whether or not universal thyroid screening during pregnancy should be implemented has sparked debate. The low prevalence of thyroid disorders reported in the literature and the varying levels of thyroid-stimulating hormone across the globe are central to this discussion [9].

In our situation, overt hyperthyroidism was diagnosed based on a baseline thyroid panel that revealed a low TSH of 0.14 U/L (normal range: 0.32-5.2), a high free thyroxine (T4) of 30.0 ng/dL (normal range: 5-13), and a high (T3) of 10 ng/dL (normal range 0.6-2.10). However, the patient attended the ENT clinic with nonspecific symptoms and it was unknown that she was pregnant. At 6 weeks, the evaluation indicated an intrauterine pregnancy. The patient was advised to consult with an obstetrician. She did not, however, attend the antenatal clinic at the beginning. She should have been directed straight to the obstetrician or brought up in a multidisciplinary meeting. Sadly, these meetings have never existed in the majority of low-resource environments, including BMC. Due to the unavailability of an endocrinologist at our institution, the case was initially managed by a general ENT surgeon and then by an obstetrician who lacked the experience and expertise to manage such a difficult case

Due to teratogenicity and hepatotoxicity, methimazole derivatives and Propylthiouracil (PTU) cannot be used in the first trimester, making anti-thyroid medication selection difficult. On her second visit to an ENT clinic, our patient was moved from carbimazole to PTU, but she did not take the prescription and was lost to follow-up. She couldn't explain why she didn't take her medications or attend an early antenatal clinic. We believe a number of circumstances led to her lack of adherence to treatment, including the fact that she purchased all of her drugs out of her savings because she lacked medical insurance. She also incurred travel expenses of approximately 160 km from Shinyanga to reach our center, which is the only specialized tertiary facility in the area. All of these factors make it more difficult to manage difficult cases like this in locations with inadequate resources.

Despite the well-documented consequences of hyperthyroidism, routine screening remains controversial. In our case, she had a previous history of miscarriage at 12 weeks, the cause of which was unknown, but we suspect her disease also played a role. However, as has been described in previous research, she did experience a number of pregnancy-related complications, including severe intrauterine growth restriction, hypertension, a low birth weight, and fetal hypothyroidism [10–12]. Unable to establish euthyroid during pregnancy due to poor treatment adherence further complicated our outcome. Reaching and maintaining euthyroid is crucial for both the mother and the baby.

The care of newborns with congenital hypothyroidism is difficult. Thyroid hormonal panel measurements should be made on a regular basis. This is because transient hypothyroidism usually resolves on its own. However, levothyroxine is recommended for persistent cases. Despite the fact that 0.0025% of methimazole derivatives and propylthiouracil are excreted in breast milk, breastfeeding is not prohibited; instead, fetal growth and thyroid function must be evaluated [7]. In our case, the newborn succumbed to early neonatal death as the result of prematurity with probably underlying congenital hypothyroidism.

The timing of delivery in pregnant women with hyperthyroidism is the same as in other normal pregnancies, so the pregnancy can continue to term as long as the euthyroid is preserved [4]. Failure to achieve euthyroid status has a negative maternal-fetal outcome; thus, severe preeclampsia or severe IUGR may warrant early pregnancy termination. In our case, the decision to deliver came at 34 weeks of pregnancy. This was required due to severe preeclampsia and intrauterine growth restriction. This has also been reported in other cases of obvious hyperthyroidism [11,13].

It is critical to provide preconception care to patients who have hyperthyroidism. Pregnancy is generally not advised for those with an uncontrolled thyroid level until the euthyroid is achieved [14]. PTU is strongly advised during the first trimester, after which a switch to methimazole derivatives should be considered [6,14]. In this case, she did not get preconception care because she was diagnosed while she was pregnant. She also did not reach euthyroid. So, she is taking antithyroid drugs and getting counseling, and it has been stressed how important it is for her to be euthyroid before getting pregnant.

Conclusion

Despite the fact that thyroid disease is less common, health providers at various levels of care must consider thyroid diseases as potential causes of miscarriage and poor maternal-fetal outcomes. The importance of euthyroidin pregnancy must be emphasized, as well as the need for a multidisciplinary approach involving (obstetricians, ENT surgeons, endocrinologists, pediatricians, and neonatologists) to maximize patient care.

Declarations

Patient perspective: The care was delivered on time, with a thorough explanation of the diagnosis and treatment plan.

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Author's contributions: OA: participated in the management of the patient and drafted the first manuscript; DM: evaluated the paper; EN: reviewed the manuscript and did major revisions, language proofreading, and publication submission. The rest were involved in patient care and management.

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Consent for publication: Written informed consent was obtained from the patient for the publication of this case. A copy of the written consent is available for review by the editor-in-chief of this journal. Additionally, consent was sought and granted by the Catholic University of Health and Allied Sciences Directorate of Research and Publication to publish this work. The Editor-in-Chief of this journal can also look at a copy of the clearance document.

Competing interest: Author declares that they have no competing interest.

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