

Severe Gestational Transient Thyrotoxicosis: A Case Report

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Abstract

We present a case of gestational transient thyrotoxicosis (GTT) associated with hyperemesis gravidarum (HG) highlighting the abnormally elevated free T4 (FT4) found in this instance. This case also highlights that GTT can present as severe and symptomatic hyperthyroidism contrary to its usual presentation of subclinical or mild overt hyperthyroidism.

Learning Points

1. Gestational thyrotoxicosis associated with HG can present with severe toxicosis.
2. Symptomatic treatment may be sufficient for the management of this condition.

Background

One of the etiologies of hyperthyroidism in pregnancy is GTT. Typically, GTT is a mild, self-limiting condition caused by stimulation of the TSH receptor by human chorionic gonadotropin (hCG).

Introduction

The two most common causes of thyrotoxicosis in pregnancy are Graves' disease and gestational transient thyrotoxicosis (GTT) [1].

In the first trimester of pregnancy, human chorionic gonadotropin (hCG) levels rise and peak at around weeks 8-11 [1]. Having an alpha subunit in common with thyroid stimulating hormone (TSH), hCG can activate the TSH receptor, although to a much lesser degree when compared to TSH2. Extremely high concentrations of hCG, usually associated with hyperemesis gravidarum (HG), multiple gestation, or molar pregnancy, can lead to activation of the TSH receptor, and in turn may result in mild suppression of TSH and elevation of FT4 [2]. The level of TSH suppression is correlated to serum hCG concentrations; i.e. serum hCG levels of 100,000 IU/L – 200,000 IU/L are considered to cause TSH suppression, serum hCG levels greater than 200,000 IU/L are more likely to cause suppression of TSH, and serum hCG greater than 400,000 IU/L most consistently cause suppression of TSH [3].

Case presentation

We present a case of a 20-year-old female G2P1001 at 10w1d gestation admitted for palpitations, dizziness, dyspnea on exertion, vision disturbances, progressively worsening nausea and vomiting. Her symptoms had been ongoing for five weeks and had led to poor oral intake and inability to gain weight. On

initial presentation she was diagnosed with supraventricular tachycardia treated in the Emergency Department with IV adenosine, with return to sinus rhythm. Subsequently on physical exam her blood pressure was 107/59 mmHg, heart rate 140 beats per minute and regular rhythm. Other pertinent findings included no goiter appreciated, no orbitopathy, mild restlessness, slightly warm moist skin, and mild hand tremor.

She had no significant past medical history, and she was not taking chronic medications except for prenatal vitamins.

Initial lab findings included serum sodium 129 mmol/L (reference range 136-145 mmol/L), serum potassium 2.3 mmol/L (reference range 3.5-5.1 mmol/L), serum chloride 82 mmol/L (reference range 98-107 mmol/L), aspartate aminotransferase (AST) 160 IU/L (reference range 13-39 IU/L), alanine transaminase (ALT) 369 IU/L (reference range 7-52 IU/L).

TSH < 0.020 uIU/L (reference 0.4-4.5 uIU/L), FT4 4.22 ng/dL (reference range 0.58-1.64 ng/dL), FT3 5.28 pg/mL (reference range 2.20-4.10 pg/mL) hCG 212,563.8 mIU/L.

Thyroid stimulating immunoglobulin (TSI) < 0.10 IU/L (0.54 or less IU/L consistent with healthy thyroid function). Thyroid peroxidase antibody (anti-TPO) < 0.3 IU/mL (0.0-9.0 IU/mL is the reference range). Anti-thyroglobulin antibody < 0.9 IU/mL (less than 4.0 IU/mL indicates a negative result).

For her sinus tachycardia, she was started on metoprolol succinate 25 mg once daily. She was diagnosed with hyperemesis

gravidarum and started on IV fluids and ondansetron 4 mg every 8 hours as needed with improvement in nausea and vomiting.

Two days later, repeat TSH 0.006 uIU/L, FT4 3.48 ng/dL. Serum sodium increased to 134 mmol/L, serum potassium to 3.9 mmol/L, and serum chloride 104 mmol/L. Meanwhile, AST decreased to 26 IU/L and ALT to 111 IU/L. Over the next several days, the TSH remained the same, however, FT4 continued to improve to 2.37 ng/dL and subsequently, 1.80 ng/dL. With improving thyroid function tests and with clinical improvement, anti-thyroid medications were not started. Instead, the patient was discharged with recommendations to closely monitor her thyroid function tests.

Eight days after her initial presentation, repeat TSH 0.005 uIU/L, FT4 0.84 ng/dL. Furthermore, serum sodium 137 mmol/L, serum potassium 3.8 mmol/L, serum chloride 103, AST 12 IU/L, and ALT 26 IU/L. With improvement in nausea, patient was able to gain weight. She denied any tremors, excess sweating, or diarrhea. She continued to take metoprolol succinate 25 mg daily and denied any palpitations. Twenty-six days after initial presentation, at 13w d6, TSH 0.535 uIU/L, FT4 0.69 ng/dL. At this point she no longer had any symptoms of nausea or vomiting. Her weight continued to increase. She again denied any tremors, excess sweating, or palpitations. She had stopped metoprolol succinate 25 mg daily.

Discussion

Normal pregnancy is associated with significant thyroid physiological changes. Since hCG shares the same alpha subunit with TSH, and its beta subunit is homologous with the beta subunit of TSH, hCG can function as a weak thyroid stimulating hormone, causing both slight suppression in TSH and a slight increase in the levels of FT4 and FT3[1, 2]. These effects are most evident at the end of the first trimester (week 12) in parallel with the hCG peak[2]. In most normal pregnancies at this timepoint, the TSH is slightly suppressed or at the lower limit of the normal pregnancy specific reference range, and the FT4 increases slightly, however, still at the upper limit of the normal pregnancy specific reference range. In about 15% of healthy pregnant women, the TSH is suppressed below the normal pregnancy specific reference range by the end of the first trimester [2]. This condition is transient and physiological, with complete recovery once the hCG levels decline.

Various studies have demonstrated a correlation between the levels of serum hCG and the suppressive effect on TSH; levels of hCG > 400,000 IU/L were always associated with suppressed TSH [3]. Such elevated serum hCG levels are seen in multiple gestations, hyperemesis gravidarum, and gestational trophoblastic disease. Furthermore, certain hCG isoforms were identified with longer half-life, and higher thyroid stimulation potency which result in a more significant suppressive effect on TSH at lower hCG levels [4].

Gestational transient thyrotoxicosis (GTT) denotes hyperthyroidism that occurs at the end of the first trimester

(week 10-12) induced by elevated hCG. Women may be slightly symptomatic, the TSH may be suppressed, and the FT4 may be mildly elevated; however, characteristically, this condition will resolve spontaneously during the beginning of the second trimester, when serum hCG level decline[2, 3].

Although GTT may be the most plausible etiology of hyperthyroidism in a pregnant woman during the end of her first trimester, other causes of hyperthyroidism should be excluded, especially Graves' disease which represents the second most common etiology of hyperthyroidism in pregnancy.

In Graves' disease the patient may present with hyperthyroidism, however, the physical exam will characteristically demonstrate a goiter, orbitopathy, occasionally dermopathy, and the serology will be positive for thyroid receptor stimulating autoantibodies.

GTT may be associated with hyperemesis gravidarum (HG). Both occur in the presence of abnormally high levels of hCG. HG can lead to significant nausea and vomiting. It is diagnosed by 5 % weight loss, dehydration, and ketonuria. HG usually leads to hyponatremia, hypokalemia, hypochloremia, alkalosis, and abnormal liver function tests as well. Therefore, symptoms of HG can overlap with symptoms of thyrotoxicosis. Symptoms of thyrotoxicosis, however, also include sweating or heat intolerance, tachycardia, and tremor[2, 7].

GTT is uncommon, only affecting approximately 1-5% of pregnancies and HG is also uncommon, occurring in about 0.3-1.0% of pregnancies[1]. Lockwood et al demonstrated that out of 15,597 pregnant women tested, only 63 women had serum hCG concentration greater than 200,000 IU/L. 67% of those had suppressed TSH less than 0.2 uIU/mL while 37% also had HG. Women that had a serum hCG of 200,000 – 400,000 IU/L had a median FT4 level was 1.14 ng/dL. Eighty percent of women with serum hCG greater than 400,000 IU/L had a FT4 greater than 1.8 ng/dL[3]. Sun et al has shown that FT4 was not higher than 3.61 ng/dL looking at 65 cases of HG with GTT[8].

Our patient presented with HG and significant thyrotoxicosis (TSH was suppressed and her FT4 was elevated at 4.2 ng/dL). She had no stigmata of Graves' disease and her thyroid stimulating antibodies were negative. Although she was 10 weeks pregnant and suffering from HG, she presented with significant thyrotoxicosis that was uncharacteristic of GTT. In most reports GTT is associated with less thyrotoxicosis and with lower FT4 levels. Furthermore, the serum hCG level our patient had was 212,563.8 mIU/L which was relatively lower than the values reported by others to be associated with such a significant thyrotoxicosis. One explanation could be that our patient's hCG had a longer half-life, or higher thyroid stimulation potency which resulted in a more potent thyroid stimulation.

Most women with GTT do not require antithyroid treatment[1, 5]. Thyroid function tests should be followed for the duration of the pregnancy. Symptomatic management with beta-blockers for tachycardia may be appropriate[7]. Furthermore, symptomatic management of HG with intravenous fluids, antiemetic

medications, and correction of electrolyte abnormalities is appropriate[7].

Conclusion

We highlight a case of gestational transient thyrotoxicosis with exceptionally elevated FT4 associated with hyperemesis gravidarum. It is important to realize the potential for and transient nature of GTT. Without anti-thyroid medication, the thyroid function progressively normalized with complete resolution. In this instance, less is more. Symptom management was enough.

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