Case Report

Recurrent Gestational Transient Thyrotoxicosis Presenting as Hyperemesis

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A 28-year-old G_2P_1 Thai woman presented with severe nausea and vomiting at 12 weeks' gestation. The initial diagnosis was hyperemesis gravidarum. She was clinically euthyroid. Physical examination revealed no thyroid gland enlargement. The serum thyroid stimulating hormone was suppressed while the free thyroxine level was elevated. This patient had a history of hyperthyroidism during her first pregnancy. An anti-thyroid drug was initiated at 16 weeks' gestation and continued throughout her pregnancy. Follow-up thyroid function tests and thyroid antibodies after her first and second gestation were normal. The diagnosis of recurrent gestational thyrotoxicosis was established. There was no need of anti-thyroid drug treatment in this case. No adverse pregnancy outcomes were reported.

Keywords: *Thyrotoxicosis, Recurrent, Pregnancy*

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Thyroid disease is a common endocrine problem in women of reproductive age. Hyperthyroidism occurs in 0.2% of all pregnancies[1]. The incidence of this disease has been increasing. The most frequent type of hyperthyroidism in pregnant women is Graves' disease, which accounts for 85% of all cases[2]. Other causes include gestational trophoblastic disease, solitary toxic adenoma, struma ovarii and TSH producing pituitary tumor[1,3].

Gestational transient thyrotoxicosis (GTT) is a form of non-autoimmune hyperthyroidism with a reported prevalence of 2-11% of pregnancies[4]. It is more prevalent in Asian women, commonly presenting with elevated free thyroxine (FT_4) and suppressed thyroid stimulating hormone (TSH) levels[5]. The prevalence depends on the ethnicity[2], gestational age[6], isoform of human chorionic gonadotropins (hCG)[7] and sensitivity of the testing method. There are few reports of recurrent GTT in the literature[8,9].

This report describes a case of recurrent GTT that initially presented with hyperemesis gravidarum in the subsequent pregnancy. Also, favorable maternal and neonatal outcomes are presented.

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Case Report

A 28-year-old Thai woman, gravida 2, parity 1, came to the out-patient clinic with a 2-day history of severe nausea and vomiting. Her pregnancy was 12 weeks of gestation. She did not have fever, headache, abdominal pain, or vaginal bleeding. She had no palpitations, heat intolerance, tremors, or nervousness, but had lost 4 kg of weight in the past month. She was prescribed antiemetic drugs and vitamin B_6 to relieve her symptoms, but there was no improvement. The symptoms deteriorated and she could not ingest anything. As a result, she came to the hospital.

Her past medical history was significant for a diagnosis of hyperthyroidism during her first gestation (heat intolerance, palpitation and tachycardia), during which proplythiouracil (PTU) 100 mg orally per day was started at mid-trimester then the dosage decreased to 50 mg per day later and continued until delivery. Spontaneous recovery to a normal thyroid state was achieved within 6 weeks postpartum. Consecutive annual check-ups of her thyroid function were also normal, reflecting no evidence of recurrent hyperthyroid disease. She had no family history of thyroid diseases and GTT.

Physical examination revealed a blood pressure of 118/80 mmHg and a pulse rate of 104 beats per minute. She was lethargic and had poor skin turgor and sunken eyeballs. Her conjunctivae were mildly pale. Eyelid retraction, lid lag, chemosis and exophthalmos were not observed. Her thyroid gland was not enlarged.

The fundal height of her uterus was 1/3 higher than the pubic symphysis. Pelvic examination was not performed. The initial diagnosis was hyperemesis gravidarum with a moderate degree of dehydration.

Initially, she had marked ketonuria (4+) and hyponatremia. Intravenous fluid hydration and electrolytes were replaced. The following serum tests were obtained: TSH of 0.008 (normal, 0.27-4.20 uIU/mL), FT_4 of 1.86 (normal, 0.9-1.7 ng/dL) and negative anti-microsomal and thyroglobulin antibodies. An internist was consulted and after comprehensive evaluation, the diagnosis of gestational thyrotoxicosis was suggested. PTU 50 mg orally per day was initiated at 16 weeks' gestation and increased to 100 mg per day at 6 weeks later. After laboratory euthyroid status was achieved, PTU 50 mg per day was continued throughout her pregnancy. Follow-up thyroid function tests are presented in Table 1.

Her antenatal care was uneventful. Screening ultrasonography at mid-gestation showed a single fetus without any abnormality. At 37 weeks' gestation, she had delivered a 2,900 grams healthy female baby. There was no exacerbation of the disease during labor or postpartum period. The patient was discharged three days after delivery. Thyroid function tests were obtained 2 weeks later and confirmed the euthyroid state of the patient without any evidence of thyroid auto-antibodies. PTU was stopped at this time. The follow-up study of thyroid function tests in the next 6 months postpartum remained normal. Thereafter, she was scheduled for the thyroid function testing annually.

Discussion

Pregnancy is associated with significant changes in maternal thyroid functions, including an increase in thyroxine binding globulin, a decline in the availability of iodine due to increased renal clearance, and thyroid stimulation by hCG especially in first trimester[10]. These changes can lead to confusion in the diagnosis of thyroid diseases during normal pregnancy and several abnormal conditions such as gestational trophoblastic disease and hyperemesis gravidarum. The impact of gestational age on the measurement of TSH level must be considered, while the use of non-pregnant FT4 thresholds is recommended[11]. In the first trimester, serum TSH may be transiently suppressed in 10-20% of euthyroid women (< 2.0 uIU/mL) at the time of peak hCG levels. Clinical features of hyperthyroidism can also be confused with those typical of pregnancy.

This case demonstrated the rare condition of recurrent GTT that presented with hyperemesis gravidarum in a subsequent pregnancy. The diagnosis of GTT is based on 4 criteria: firstly, abnormal thyroid function tests, confirmed by suppressed TSH and elevation in FT_4 levels; secondly, no evidence of hyperthyroidism before pregnancy; thirdly, the absence of physical findings of Graves' disease and finally, the absence of thyroid autoantibody titers[12]. This case met all of the diagnostic criteria described above and was subsequently treated with an anti-thyroid drug.

Pathogenic mechanisms that contribute to the development of GTT include thyrotropic stimulation of the thyroid gland by circulating hCG, especially the asialo-hCG isoform[13,14], dysregulation of hCG production, hypersensitivity of the thyrotrophin receptor to hCG[15] and increased sensitivity of the thyroid gland to thyroid stimulation[16]. Still, the precise mechanism of GTT is not fully understood. A significantly positive correlation between serum levels of FT_4 and those of the hCG in the first trimester were reported by some researchers[4,5].

GTT is usually of transient nature, characterized by a short duration and spontaneous resolution

Table 1. Thyroid function tests and thyroid antibodies detection in this patient

Gestational age	TSH (uIU/mL)	FT_4(ng/dL)	FT_3(pg/mL)	Thyroid antibodies
12 weeks	0.008	1.86	-	Negative
22 weeks	0.043	1.23	2.69	-
26 weeks	2.860	-	1.91	-
31 weeks	1.860	0.90	2.15	-
2 weeks PP	2.400	1.08	2.56	-
6 weeks PP	1.240	1.36	2.87	Negative

PP = postpartum
Normal reference value: TSH = 0.27-4.20 uIU/mL, FT_4 = 0.9-1.7 ng/dL, FT_3 = 1.8-4.6 pg/mL
Thyroid antibodies = Anti-microsomal and Anti-thyroglobulin antibodies

with the decline hCG[1]. Symptoms and serum FT_4 levels usually normalize in parallel with hCG levels as pregnancy progresses. Notably, TSH levels may remain partially depressed for several weeks. Clinical manifestations of this disorder are not always apparent. Hyperemesis is frequently associated with severe cases[17]. The combination of high hCG and estradiol levels, as well as increased FT_4 concentrations transiently promotes emesis near the period of peak hCG[18,19]. GTT has not been associated with a less favorable pregnancy outcome. It should be distinguished from Graves' disease during pregnancy[15]. Determination of TSH receptor antibody (TRAb) is indicated just in case the clinical diagnosis is in doubt[20].

In most cases of the GTT, no specific treatment is required. In severe clinical features might warrant treatment with anti-thyroid drugs, usually for a few weeks[12]. In the present case, PTU was given from mid-gestation until 2 weeks' postpartum. Importantly, awareness against overtreatment is recommended because it may cause hypothyroidism in both the pregnant woman and her fetus. Serial sonographic measurements of the fetal thyroid were reported to assist in monitoring the maternal anti-thyroid drug dosage[21]. Obstetricians should be aware of GTT because a few of these patients need extensive care. There were a few reports of GTT associated with acute Wernicke's encephalopathy that should be treated with thiamine as soon as possible[22,23].

At present, there is no recommendation for routine screening of thyroid function in early pregnancy[24,25]. Investigations of this test are based on symptoms and signs of the patients, which can mimic normal physiologic changes of pregnancy. There are some adverse outcomes from hyperthyroidism during pregnancy, but the incidence of these conditions is very low[1].

This case is an example of early recognition of recurrent GTT that no clinical signs of thyrotoxicosis in the first trimester. A high index of suspicion and specific thyroid function tests are very helpful in the diagnosis of this condition.

Conclusion

Pregnancy has profound effects on thyroid function that need to be recognized and properly managed. GTT can also present with hyperemesis gravidarum in the first trimester. Early diagnosis makes this disorder amenable to appropriate care; no specific anti-thyroid drug required and prevents further complications.

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Potential conflicts of interest

None.

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การกลับเป็นซ้ำของไทรอยด์เป็นพิษชั่วคราวขณะตั้งครรภ์ที่มาด้วยอาการแพ้ท้องมาก

เมธาพันธ์ กิจพรธีรานันท์

หญิงไทย อายุ 28 ปี ตั้งครรภ์ครั้งที่ 2 เคยคลอดบุตร 1 ครั้ง ที่อายุครรภ์ 12 สัปดาห์ มีอาการคลื่นไส้และอาเจียนมาก วินิจฉัยเบื้องต้นว่าแพ้ท้องชนิดรุนแรง เธอมีอาการทางคลินิกของไทรอยด์ปกติ ตรวจร่างกายไม่พบต่อมไทรอยด์โต ตรวจเลือดพบค่าฮอร์โมนกระตุ้นต่อมไทรอยด์ถูกกดในขณะที่ฮอร์โมนไทรอยด์สูงผิดปกติ ผู้ป่วยเคยมีประวัติไทรอยด์ทำงานมากผิดปกติระหว่างตั้งครรภ์แรก ผู้ป่วยได้รับยาต้านไทรอยด์ตั้งแต่อายุครรภ์ 16 สัปดาห์จนตลอดการตั้งครรภ์ การติดตามการทำงานของต่อมไทรอยด์และภูมิต้านทานต่อไทรอยด์หลังจากตั้งครรภ์ครั้งแรกและครั้งที่ 2 พบว่าปกติ วินิจฉัยว่าการกลับเป็นซ้ำของไทรอยด์เป็นพิษขณะตั้งครรภ์ ในรายนี้ไม่มีความจำเป็นต้องได้รับการรักษาด้วยยาต้านไทรอยด์ ไม่พบผลเสียต่อการตั้งครรภ์