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Thyrotoxicosis in pregnancy: A case report

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التسمم الدرقي في الحمل: تقرير حالة

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الملخص: هناك أسباب عديدة لفرط الدرقية أثناء الحمل مثل داء غريفز و التسمم الدرقي بسبب الحمل. ينتج تحفيز الغدة الدرقية من إزدياد مستوى موجهة القند المشيمائية في الدم و الناتج عن أنسجة الأرومة الغاذية في كل من الرحى العدارية والظهاروم المشيمائي. نعرض هنا حالة امرأة حامل مصابة بالرحى العدارية و التي كانت تعاني من أعراض الانسمام الدرقي، و قد زالت تلك الأعراض بعد تفريغ الرحى.

ABSTRACT. There are various causes of hyperthyroidism in pregnancy such as Graves' disease and gestational thyrotoxicosis. The thyroid stimulation results from the excessive levels of circulating human chorionic gonadotropin (hCG) produced by the trophoblastic tissue in both hydatidiform moles and choriocarcinoma. We present a pregnant patient with hydatidiform mole who presented with hyperthyroidism that resolved after evacuation of the mole.

Keywords: thyrotoxicosis, hydatidiform mole, pregnancy, hCG

The prevalence of hyperthyroidism in pregnancy is reported in the range of 0.1–0.2%. The majority of the patients have Graves' disease while other causes of hyperthyroidism occur much less frequently. Data accumulated indicate that human chorionic gonadotropin (hCG) has weak thyroid stimulating activity. Besides its contribution to hyperthyroidism in patients with trophoblastic tumours, the clinical significance of the thyrotrophic action of hCG is now also recognized in normal pregnancy and hyperemesis gravidarum.[1]

THE CASE

A 24-year-old 12-weeks pregnant woman was admitted to the Armed Forces Hospital on June 14, 1999 with history of abdominal pain, vomiting and bleeding per vagina, as well as the history of two previous missed abortions. Clinical examination showed she had tachycardia (150/min). No goitre was seen. Otherwise the vital signs were stable. Pelvic scan was suggestive of molar pregnancy with bilateral ovarian theca lutial cyst. Liver enzymes were raised. Serum BhCG was 370,493 mIU/l. Thyroid function test (TFT) showed FT4 >100 pmol/l and TSH 0.006 uIU/ml.

Table 1. *Patients' serial TFT and BhCG values taken on various dates*

	BhCG *(mIU/l)*	**FT4** *(pmol/l)*	**FT3** *(pmol/l)*	**TSH** *(uIU/l)*
Normal range	*< 5*	*12–22*	*2.8–7.1*	*0.27–4.2*
14 June	>10,000	ND	ND	ND
21 June	>370,493	>100	ND	0.006
24 June	>10,000	ND	ND	ND
28 June	2,806	21.57	ND	0.005
10 July	249.9	7.22	2.94	0.554
13 Sept		11.7	1.25	4.05

BhCG – B human chorionic gonadotropin; FT4 – Free Thyroxine 4; FT3 – Free Thyroxine 3; TSH – Thyroid Stimulating Hormone

ECG showed sinus tachycardia. She was treated with propranolol 40 mg TDS, neomercazole 20 mg TDS, Lugol's Iodine 0.3 ml TDS, and supportive care. Nine days after admission, she had an incomplete abortion after which an evacuation of retained product of conception (ERPC)

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was performed. Histopathology of the endometrium confirmed hydatidiform mole. The anti-thyroid medications were stopped. All the features of hyperthyroidism resolved when the hydatidiform mole was evacuated. A repeat TFT two weeks later showed results within normal limits, and the BhCG level dropped down to 249.9 mIU/l. When the patient was reviewed 2 months later, she remained asymptomatic and a repeat TFT was normal.

DISCUSSION

Graves' disease is the commonest cause of hyperthyroidism in pregnancy while other causes occur much less frequently [Table 2].[11]

In patients with hyperthyroidism caused by trophoblastic tumours, serum hCG levels usually exceed 300 U/ml. However, thyrotrophic potency of hCG varies among its different isoforms, which explains why some patients with trophoblastic tumours and very high serum hCG levels do not manifest hyperthyroidism.[4] Both hCG and thyroid stimulating hormone (TSH) are glycoproteins, which are composed of a common alpha-subunit and a non-covalently linked hormone-specific beta-subunit. This structural homology suggests the basis for cross-reactivity of hCG with the TSH receptor.[3] The diagnosis of hyperthyroidism is established by finding elevated serum free T4 and T3 levels, and suppressed TSH concentration. In most instances, a patient with molar pregnancy has mild hyperthyroidism with a small goitre, and the hyperthyroidism resolves rapidly after surgical removal of the hydatidiform mole. Conversely, patients with choriocarcinoma who manifest hyperthyroidism usually have a large mass, and antithyroid therapy may be required in addition to chemotherapy for the tumour.[5]

The term gestational thyrotoxicosis refers to a subset of hyperemetic patients with clinical and biochemical hyperthyroidism in early pregnancy.[1] It is believed to result from circulating hCG with high biological activity. It usually resolves spontaneously in the latter half of pregnancy. Women with gestational thyrotoxicosis may be differentiated from those with Graves' disease by the absence of goitre and negative antithyroid antibodies whose titre decreases from mid trimester onwards. As gestational thyrotoxicosis is mediated by hCG, no thyroid antibodies should be present. Hyperthyroidism is transient and self-limiting in this condition, and specific antithyroid treatment is not required.

Hyperemesis gravidarum occurs in about 1–3% of pregnancies and most investigators believe in the putative role of hCG in cases of hyperemesis and hyperthyroidism. Circulating free T4 and free T3 levels were frequently elevated in hyperemetic patients suggesting a relationship between the severity of the hyperemesis and the biochemical evidence of hyperthyroidism. However, the hCG levels in women with hyperemesis compared to those without emesis are similar, but the former have increased serum thyroid stimulating activity. Kimura *et al* hypothesized that the hyperemetic patients produce molecular variants of hCG with increased thyroid stimulating activity.[1]

Table 2. *Causes of hyperthyroidism in pregnancy*

Primary thyroid disease	**Destructive thyroiditis**
Graves' disease *	Subacute thyroiditis
Multinodular goitre	Exogeneous
Toxic adenoma	Treatment with excessive thyroid hormones*
Pregnancy-related	Thyrotoxicosis factitia
Gestational thyrotoxicosis*	**Others**
Trophoblastic tumours:	TSH-secreting pituitary tumour
Hydatidiform mole	Struma ovarii
Choriocarcinoma	

**Commoner causes*

Graves' disease often remits in mid-trimester and recurs after delivery. If untreated, this condition can lead to significant morbidity and mortality in both mother and fetus.

Beta blockers are effective in controlling hypermetabolic symptoms and may be used in combination with thionamides until the symptoms abate. Propylthiouracil and carbimazole are similarly effective in (blocking thyroid hormone synthesis.[7] Propylthiouracil appears to have some advantage over carbimazole as it inhibits the peripheral conversion of T4 to T3, crosses the placenta less than methimazole does and is less readily secreted in breast milk. They should be administered in the lowest possible dose to target maternal serum free T4 concentration in the upper limits of normal as both the drugs can cross the placenta and can cause fetal goitre and hypothyroidism. Block-replacement regimen is contraindicated in pregnancy because thyroxine crosses the placenta less well than carbimazole and foetal goitre and hypothyroidism may result and the mother must also be given more methimazole if maternal hyperthyroidism is to be prevented. Further, the rare congenital abnormality of congenital aplasia cutis congenita may be associated with the use of methimazole in pregnancy. Dosage of thionamides should be reduced progressively in anticipation of the usual steady amelioration in the disease as pregnancy advances and treatment can eventually be discontinued in approximately 30% of patients.[6] Surgery is reserved for patients who are

not responding to antithyroid drugs because of non-compliance or allergy to both the drugs. Thyroidectomy can be safely performed in the second trimester. Radioactive iodine therapy is contraindicated in pregnancy because of potential congenital malformations or congenital hypothyroidism.[8] Hyperthyroid pregnant patients should be seen at 4–6weeks intervals, with a collaborative effort between the treating physician and obstetrician. Thyroid-stimulating immunoglobulin (TSI) titres obtained in the last trimester may predict the likelihood of neonatal hyperthyroidism. Any newborn from a mother who has a history of hyperthyroidism should be observed for this possibility, due to the transplacental transfer of TSI. The earliest clinical sign of fetal thyrotoxicosis is fetal tachycardia [>160/min]. Serum thyroid stimulating hormone and Thyroxine concentration should be measured in neonates whose mothers have or have ever had Grave's disease.

Postpartum thyroiditis (PPT) is an autoimmune condition that occurs in approximately 5% of women during the first year of postpartum. The well-recognized improvement in clinically overt and biochemically proven autoimmune thyroid disease in pregnancy is due to the state of relative immune suppression in the mother. This is characterized by a rebound in antibody activity in the postpartum period. This is frequently associated with hyperthyroid phase occurring in the first 3 months of postpartum, followed by hypothyroid phase between 3 to 6 months after delivery with spontaneous recovery in the majority of patients.[9] Thyrotoxocosis in postpartum thyroiditis (PPT) is usually mild and self-limiting (2–8weeks duration) and is distinguished from Grave's disease by a low Radio Active Iodine Uptake[RAIU] (study contraindicated if the mother is breast-feeding). Beta-blockers can be administered if symptoms are severe. Antithyroid drugs are not useful in PPT because thyrotoxicosis is secondary to hormone release from the damaged gland[9]. The importance of recognition of this syndrome is two fold: (i) a clear association has been established between the development of this syndrome and alteration in the mood and behaviour that occurs during postpartum period. (ii) There is clear evidence that in a significant number of women the transient syndrome may go onto permanent hypothyroidism.[10]

CONCLUSION

Thyroid problem is the most common pre-existing endocrine disorder during pregnancy reflecting in part a predilection for thyroid problems in women of childbearing age. Maternal thyrotoxicosis occurs about once in every 500 pregnancies, and the diagnosis may be difficult because the increase in cardiac output, tachycardia, skin warmth and heat intolerance typical of pregnancy can mimic hyperthyroidism. The diagnosis of thyroid disease is complicated by many important physiological changes in thyroid metabolism and laboratory values observed in pregnancy. Measurement of TSAb concentration in women with active Grave's disease in late pregnancy or with previous ablative therapy for Graves' disease is useful to predict neonatal Graves' disease. Also, systemic thyroid autoantibody screening in the early stages of gestation may improve obstetric outcome and identify women at risk of PPT. Proper understanding of all this is essential for the effective management of thyroid disease in pregnancy.

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