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Original Research Paper

Biochemistry

HYPERTHYROIDISM IN GESTATIONAL TROPHOBLASTIC DISEASE

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ABSTRACT

Background: Hyperthyroidism is less common than hypothyroidism in pregnancy. A rare cause of thyrotoxicosis during pregnancy is gestational trophoblastic disease (GTD).

Aims/Objectives : To perform thyroid function testing in two suspected cases of GTD and its follow up.

Material Methods: Two patients of GTD presented for β hCG and TFT measurement, which were estimated by chemiluminescent immunoassay.

Results: First case had β hCG levels 2,34,000 and TFT (TSH = 0.06µIU/ml, FT4 = 1.97 ng/dl, FT3 = 5.16 pg/ml) and second case had β hCG 2,76000 with TFT (TSH – 0.07 µIU/ml; FT4 = 2.14 ng/dl; FT3 = 4.34 pg/ml). TFT and β-hCG was repeated after suction evacuation. They remained elevated and normalised at 5th day in case one while it took 2 weeks to normalise in case two.

Conclusion: The development of hyperthyroidism is largely influenced by hCG level and usually resolves with treatment of GTD. Hyperthyroidism in pregnancy should be diagnosed early and managed efficaciously before suction evacuation of hydatidiform mole.

KEYWORDS : Gestational trophoblastic disease (GTD), Hydatidiform mole (H. mole), Human Chorionic gonadotropin (hCG)

Introduction

Gestational trophoblastic disease (GTD) is a rare complication of pregnancy that may be associated with hyperthyroidism. GTD is a broad term used to define a spectrum comprising of hydatidiform mole (complete or partial), placental site trophoblastic tumor, choriocarcinoma and gestational trophoblastic neoplasia. Out of these most commonly occurring form is the hydatidiform mole (H. mole) which is also known as molar pregnancy [1]. Molar pregnancies result from abnormal genomic duplication associated with monospermic or dispermic fertilization and subsequent loss of the maternal nuclear genome.

The incidence of molar pregnancy in developed countries is about 1 in 1500 pregnancies [2], while in Asia it is almost 3 times higher [3]. In India the incidence of molar pregnancy is 1 in every 400 pregnancies [4].

Complete moles have highest incidence of thyrotoxicosis, mainly affecting younger women with chief complaints of vaginal bleeding. The effect on the thyroid is postulated due to molecular mimicry between HCG subunits and TSH. Hyperthyroidism in hyperemesis graviderum occurs with great frequency than in normal pregnancy. We have described two cases of hyperthyroidism secondary to molar pregnancy emphasizing the rare but important evaluation of Hyperthyroidism in women of child bearing age.

Material and methods:

Two cases of hyperthyroidism secondary to molar pregnancy, one with complete mole (case 1) and other with partial mole (case 2) are reported. Routine and hormonal investigations were done in both the cases. Total β hCG (5th IS) assay and hTSH-sequential two step immunoenzymatic (sandwich) chemiluminiscent immunoassay were done in Access 2 by Beckman. Free T3 (FT3) and free T4 (FT4) were done using competitive binding immunoenzymatic assay in Access 2 by Beckman. Diagnosis of molar pregnancy was confirmed by ultrasonography (USG).

Results:

Case 1was a 22 year old presented at 9th week of gestation with hyperemesis graviderum. She gave history of (h/o) vaginal bleeding with passage of grape like vesicles. On examination she appears dehydrated with tachycardia (110 BPM); there were no h/o tremors, exopthalmous. Case 2 was a 19 year old woman presented for her first ANC visit at 10th weeks of gestation with h/o of tremors and weight loss. She also gave h/o of passage of blood clots with pain in abdomen. On examination she had tachycardia (118 BPM); there was no h/o exopthalmous.

Hormonal profile details of both the cases are given in table 1 & table 2. Diagnosis was confirmed by snowstorm appearance in USG.

Both patient underwent dilatation and curettage for evacuation of the mole. Histopathological examination of the evacuated specimen verified diagnosis of complete H. mole and partial H. mole for case 1 and case 2, respectively.

Both β hCG and TFT repeated after suction evacuation on the same day. In case 1, both β HCG and TFT remained elevated and normalized to reference range at day 5. while both β HCG and TFT took 2 weeks to normalize in case 2. Thereafter both the patients were advised to come weekly for β hCG levels, which showed progressive decline . (Table 1 & Table 2)

Table 1: Hormonal profiles of case 1

Follow up	β HCG (mIU/mL)	TSH (µIU/mL) (0.1 – 2.5 µIU/mL)	FT4 (ng/dL) (0.70 – 2 ng/dL)	FT3 (pg/mL) (2.11 – 3.83 pg/mL)
Baseline (At presentation)	2,34,000	0.06	2.96	5.16
Day 1 (after evacuation)	1,64,000	0.13	2.54	4.99
Day 5	<5	1.76	1.99	3.76
2 weeks	<5	-	-	-
3 weeks	<5	-	-	-

Table 2: Hormonal profiles of case 2

Follow up	β HCG (mIU/mL)	TSH (µIU/mL) (0.1 – 2.5 µIU/mL)	Ft4 (ng/dL) (0.70 – 2 ng/dL)	FT3 (pg/mL) (2.11 – 3.83 pg/mL)
Baseline (At presentation)	2,76,000	0.07	2.14	4.34
Day 1 (after evacuation)	96,000	0.08	2.04	4.30
Day 5	4300	0.22	2.01	4.00
2 weeks	<5	0.98	1.66	2.64
3 weeks	<5	-	-	-

Discussion

Hyperthyroidism is a rare complication of GTD attributed to the increaesed levels of β hCG released by the tumor [5]. Hormone β hCG act as a specific tumor marker for trophoblastic disease. The homology in hCG and TSH molecule as well as their receptor is responsible for cross reactivity of hCG with the TSH receptors [6]. HCG is a glycoprotein composed of α and β subunits. The α subunit is almost identical to that found in TSH, luteinising hormone (LH) and follicle-stimulating hormone [7]. The subunit consists of a 92-amino-acid chain containing two nitrogen-linked oligosaccharide side chains. In vitro testing has shown low-affinity cross-reactivity between these hormones [7,8].

The HCG subunits all target one or more of the G-protein-coupled seven transmembrane receptors, and have a high degree of homology in their transmembrane domains [9]. The LH/HCG receptors share 45% homology with the TSH receptor [10, 11]. Hyperthyroidism is more common in trophoblastic disease than normal pregnancy. The potency of HCG for TSH receptors is some 4000 times less than TSH and hence, extremely high levels of HCG are usually required for an effect on thyroid function to be seen [12].

Aim of our study was to establish the relationship between β hCG and TFT in both the cases of molar pregnancy. In present study we found overt hyperthyroidism associated with molar pregnancy (β hCG > 200000 mIU/mL) in both cases. Our results were in concordance to result of Bhat S[13], who reported a case of hyperthyroidism secondary to molar pregnancy (β hCG level >1978770 mIU/mL with TSH <0.07 mIU/mL, FT4 5.59 ng/dL & FT3 465 ng/dL). After suction evacuation the hCG & TFT values decrease to within normal limits after 12 weeks. A study done by Anisodowleh et al[14] included 146 cases of molar pregnancies and showed significant inverse corelation between β hCG and TSH (p=0.05) and significant direct corelation between β hCG and FT3 (p=0.01) and FT4 (p=0.01). Therfore establishing raised levels β hCG in molar pregnacies are associated with hyperthyroidism.

The first reported case of hyperthyroidism as a complication of H. mole was reported in 1955 [15]. Glinoer D has estimated that for every 10,000 mU/mL increase in serum hCG, FT4 increases by 0.1 ng/dL and TSH decresase by 0.1 mIU/mL [16]. In approximately 67% cases of H. mole, β hCG level >2,00,000 mIU/mL have been found to suppress TSH ≤ 0.2 µIU/mL while level >4,00,000 mIU/mL can lead to suppression in up to 100% of cases [17].

Molecular variants of hCG found in molar pregnancy have increased thyrotropic potency [18]. Depending on severity of trophoblastic disease, the patient may have clinically asymptomatic elevation of TFT or can present with severe entity like thyrotoxicosis. In patients with uncontrolled hyperthyroidism, surgical interventions like suction evacuation and anesthesia are associated with significant perioperative mortality [19]. Patient can progress to life threatening thyroid storm during surgery for evacuation[20]. Hence it is important to evaluate TFT in every patient of GTD to avoid severe complication during surgical procedure for GTD.

Conclusion

The development of hyperthyroidism is largely influenced by the level of hCG and usually resolves with treatment of GTD. The consideration of this cause of hyperthyroidism in pregnancy should be diagnosed early by perioperative laboratory workup and managed efficaciously before suction evacuation for definitive management of the H.mole to prevent life thretening complication like thyroid storm.

Conflict of interest: NIL

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