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Molar pregnancy and thyroid storm - literature review

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ABSTRACT
Molar pregnancies results from a tainted fertilization process. Trophoblastic thyroidian hyper function is an unusual complication of a molar pregnancy. The degree of thyroid stimulation and the severity of clinical hyperthyroidism is directly proportional to HCG concentration. Human chorionic gonadotrophin is almost identical with TSH, luteinizing hormone (LH) and follicle-stimulating hormone, this analogy in the structure will cause cross-reactivity with their receptors. Hyperthyroid status can vary from asymptomatic hyper function to thyroid storm. Dilation and curettage represents the treatment for hyperthyroidism in molar pregnancy. Awareness of this condition is important for diagnosis and treatment.

Keywords: hCG, TSH, mimicry, thyroid storm

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Introduction

Gestational trophoblastic disease is a condition that includes a group of tumors defined by abnormal trophoblastic proliferation. Gestational trophoblastic disease can be histological divided depending on the presence or absence of villas into hydatiform moles– or molar pregnancies and non-molar trophoblastic tumors. Hydatiform mole is the most frequent form of gestational trophoblastic tumors and occurs in 1:1000 pregnancies [1,2]. Molar pregnancies results from a tainted fertilization process.

Epidemiology

Among the risk factors for molar pregnancy are included maternal age, history of hydatidiform mole, viral infections, maternal immune mechanisms, cytogenetic abnormality, nutritional status,

multiparity and oral contraception. Also the extreme age - teenagers, respectively premenopausal

women have an increased risk for developing molar pregnancies.

Clinical patterns in molar pregnancy

Vaginal bleeding is the most frequently clinical sign. Gross uterine growth, vomiting, and induced hypertension, pelvic pain due to tecaluteinic cysts represents also traditional presenting features (Figure 1).

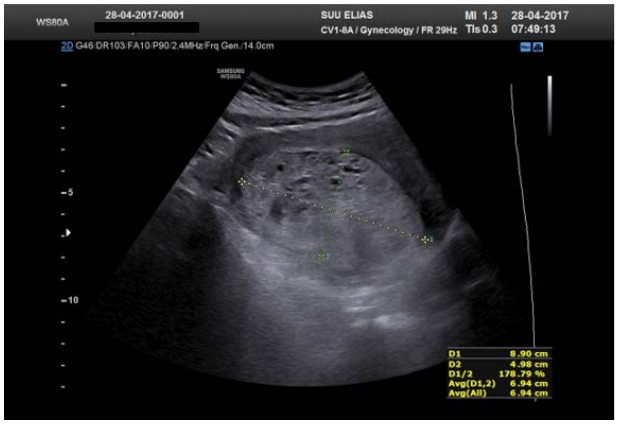

Figure 1. Ultrasonographic aspect of a molar pregnancy . Gross non homogeneous intrauterine mass

Etiology

Trophoblastic thyroidian hyper function is an unusual complication of a molar GTD [3]. The excess of human gonadotropin hormone which characterize the molar pregnancy and which has a intrinsic thyroid stimulating activity induces a thyroid hyper function [4]. Human chorionic gonadotrophin is a glycoprotein consisting of an "a" and a "b" subunit. The "a" subunit is similar to TSH and the gonadotropins (LH and FSH) [5]. The analogy in the structure between hCG and TSH can cause cross-reactivity with their receptors [6]. The degree of thyroid stimulation and the severity of clinical hyperthyroidism is directly proportional to HCG concentration.[7] The LH/HCG receptors share 45% homology with the TSH receptor.[8]TSH and hCG due to a molecular mimicry and have similar effects on the thyroid .[9] High HCG levels stimulate the thyroid gland to produce thyroidal hormones with suppression of pituitary TSH release. It is estimated that HCG serum concentrations above 200,000 mIU/ml suppress TSH in 67% of cases,and levels above 400,000 mIU/ml induces suppression in 100% of cases .[10] [11]

Several studies showed that there is an indirect proportional relationship between TSH and hCG with a hCG peak level at about 10-12 weeks of gestation – in normal pregnancy , and this peak level is associated with an increased level of thyroidian hormones (free T3 and free T4).(Figure 2)[12] [13] Concomitent with the hCG peak the serum levels of TSH are suppressed "in mirror image".[14] As a consequence in the first trimester the normal TSH limits are approximately 0.03-0.08 mIUL-1 secondary to the mimicry and thyrotropic activity of hCG.[14][15]

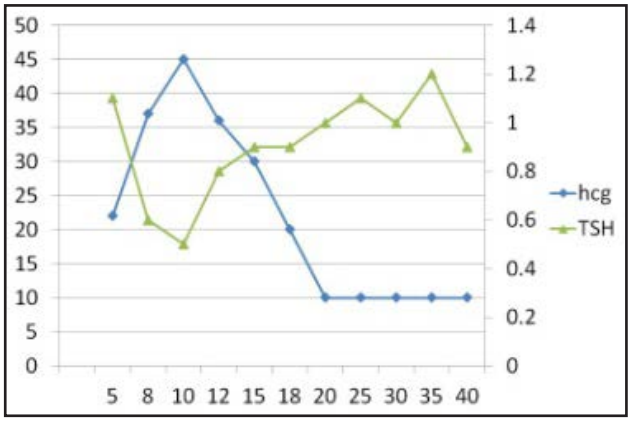

Figure 2. The pattern of serum TSH and HCG changes are shown as a function of time

Complications

Hyperthyroid status can vary from asymptomatic hyper function to thyroid storm. The molar induced thyroidian hyper function clinical features consists of fatigue, weight loss, muscle weakness, excessive sweating, nervousness, increased metabolic rate, heat intolerance, hyperactivity, tremor, accelerated intestinal transit, increased appetite, incapacitation, muscle weakness,tachycardia and minimal enlargement of the thyroid gland. Ophthalmopathy has not been noted. Cardiomyopathy can be manifest and the reflexes become hyper-reactive.

The most severe maternal complications due to hyperthyroid state are cardiac failure and thyroid storm. Thyroid storm is characterized by hyperthermia, hyperpyrexia, severe dehydration, tachycardia,tachypnoea, diaphoresis, diarrhoea, atrial fibrillation, extreme anxiety, delirium, coma, and haemodynamic instability leading to acute pulmonary edema associated with cardiac failure. [16,17]

Clinical manifests of thyroidian hyper function are found in approximately 5% of molar pregnancies cases.[16] Thyrotoxicosis is uncomon in molar pregnancy [19].Chiniwala and co. were the first to describe a thyroid storm caused by a partial hydatiform mole and published their work in 2008. [20]

The first to describe severe hyperthyroidism associated with hydatiform mole and the thyrotropic activity in molar tissue were Hirshman and Higgins in 1971. [21]

Thyroid storm is a rare entity but has a high mortality rate up to 15%. [22] The hyperthyroidism prevalence can reach up to 7% in the cases of hidatiform mole.[23] The pathophysiological

mechanism of induction of hyperthyroidism in molar pregnancy is multifactorial. The most important aspect discussed is molecular mimicries with TSH and the elevated hCG values. [4]

Management

Hyperthyroidism induced by a molar pregnancy is treated by dilation and curettage, with rapidly regression after evacuation. Sometimes, depending on the hyperthyroid state anti-thyroid drugs and β-adrenergic blocking agents can be administered to reverse the cardiovascular and metabolic features. Thyroid storm can be treated using cooling blankets, rapidly hydration with glucose and electrolyte replacement, oxygen, glucocorticoids, anti-thyroid drugs iodine compunds, β, plasma exchange, dantrolene and B-complex multivitamins. [6] The anti-thyroid drugs (methimazole or propylthiouracil) are thyroid hormone synthesis inhibitors and they are used to control the overt of thyroid hormone production. Steroids can inhibit peripheral conversion of T4 to T3, a more potent hormone.[24] Chemotherapy with methotrexat and leucovorine – can also reduce the thyrotoxic complications, but is not a first line treatment. Surgical evacuation of molar tissue represents the cure of thyrotoxic trophoblastic disease.

Conclusions

Biochemical thyroid changes in patients with molar pregnacies are relatively common. Molar hyperthyroidism depends on the level of HCG. High levels of HCG are directly proportional with the clinical manifests of hyperthyroidism. Rarely the thyroid hyper function can be potentially life threatening and requires treatment with anti thiroidians drugs and symptomatic drugs such as b-blockers. Thyroid function is expected to return to normal rapidly after the treatment of the underlying molar pregnancy and the collapse in HCG levels. Awareness of this condition is important for diagnosis and treatment.

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