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Transient Hyperthyroidism in Molar Pregnancy

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Abstract :

Gestational trophoblastic disease (GTD) is a rare complication of pregnancy that may be associated with thyrotoxicosis. The incidence of hydatidiform mole in the United States and other developed countries is about 1 in 1500 live births .Complete moles have the highest incidence of thyrotoxicosis, predominantly affect younger women, and present with vaginal bleeding most of the time. Hyperthyroidism in hyperemesis gravidarum occurs with greater frequency than in normal pregnancy.in my report we will discuss four study support the possibility of hyperthyroidism in molar pregnancy⁽¹⁾

Introduction :

Gestational Trophoblastic Diseases is a broad term used to define a spectrum, comprising of hydatidiform mole (complete or partial), placental site trophoblastic tumour, choriocarcinoma and gestational trophoblastic neoplasia. The most commonly occurring form is the hydatidiform mole, which is also known as molar pregnancy. Classification of molar pregnancies can be complete or partial on the basis of gross morphology of the specimen, histopathologic features and karyotype .

Molar pregnancy presents with period of amenorrhea lasting a few weeks to months, followed by vaginal bleeding, abdominal mass, hyperemesis and rarely passage of vesicles per vagina, etc. Bleeding per vagina is the usual complaint (84%), which may or may not be associated with menstrual delay, whereas vomiting is present in 28% of cases that can be refractory to treatment. Hyper-emesis gravidarum is usually seen in cases of hydatidiform mole that have high hCG levels . Additionally, it is also common for such patients to have theca lutein cysts due to ovarian hyperstimulation as a result of high hCG levels. Early diagnosis of molar pregnancy can be made by early prenatal care and timely use of ultrasound. This prevents clinical presentations such as huge hydatidiform moles, passage of vesicles per vagina, severe anemia and emergency situations.⁽²⁾

Hyperthyroidism (overactive thyroid) is a condition in which your thyroid gland produces too much of the hormone thyroxine. Hyperthyroidism can accelerate your body's metabolism significantly, causing sudden Rapid heartbeat (tachycardia) irregular heartbeat (arrhythmia).Tremor usually a fine trembling in your hands and fingers Sweating Changes in menstrual patterns An enlarged thyroid gland (goiter), Fatigue, muscle weakness Difficulty sleeping. Hyperthyroidism is a complication of GTD, attributed to the increased levels of β -hCG released by the tumour.

Studies :

1- A 22-year-old Libyan woman married for 6 years, had delivered a child normally 1 year ago came to the **ALAML out-patient Fertility clinic** with irregular menstrual cycle . She had her menstrual period around 2 months ago for the first time after the delivery and then spotting for 1 day, 20 days ago.

Her gynecological examination revealed an anteverted, 26 weeks size uterus with slight blood staining on the gloved finger during per vaginum examination. Her UPT was negative . Ultrasonography revealed an intrauterine heterogeneous mass with numerous anechoic spaces showing snow storm appearance with absence of fetus in the uterine cavity. Bilateral ovaries were bulky. Repeat UPT was also clearly negative.

On examination she had pallor, mild pedal edema and exophthalmos. She was a febrile but had tachycardia with a heart rate of 110/ m and her BP was 120/80 mm Hg.

On investigation she was found to be having a thyroid-stimulating hormone (TSH) of less than 0.1 mIU/mL with T3 and T4 near upper limit of normal.

Her β HCG level was only 450 mIU/mL to add to the dilemma, as β HCG levels are expected to be very high in a molar pregnancy. However, since her diagnosis was certain because of the ultrasonographic findings, the laboratory reports were considered erroneous. Suction and evacuation of the molar pregnancy was performed and the evacuated grape-like vesicles were sent for histopathologic examination .

2- A 20-year-old nulliparous woman, married since one year, presented to the outpatient department with complaints of three months of amenorrhea followed by increased bleeding per vagina, hyperemesis and abdominal pain of one week duration. She also complained of tremors and palpitation. There was no history of abdominal distension or diarrhea. There was no history of menstrual irregularity prior to the current episode .On examination, her pulse rate was 110 beats per minute and regular in rhythm, blood pressure was 120/78 mmHg, respiratory rate was 16 breaths per minute and oxygen saturation was 99% at room air. She was found to have conjunctival pallor and diffuse non tender enlargement of the thyroid gland.

Urine pregnancy test was found to be positive. Transvaginal ultrasound of pelvis revealed uterus which measured 10.6x7 cm, with intrauterine gestational sac measuring 4.3 cm and presence of anechoic areas likely to be cystic, suggestive of molar pregnancy. Bilateral ovaries on ultrasound showed theca lutein cysts with the largest measuring 18 mm. Laboratory data showed β -hCG levels of 8,04,578 mIU/ml, hemoglobin of 8.4 g/dl, peripheral smear showed microcytic hypochromic picture, (TSH levels of 0.015 mIU/ml), (T3 of 3.07 ng/ml)and (T4 of 24.86 μ g/dl).

An ultrasound guided suction evacuation of products of conception was done under general anaesthesia three days following admission. Histopathology report of specimen confirmed diagnosis of hydatidiform mole . A repeat ultrasound scan done following evacuation showed retained products of conception and laboratory data showed (β -hCG of 89,677 mIU/ml), (TSH of 0.015 mIU/ml),(T3 of 1.37 ng/ml) and (T4 of 17.47 μ g/dl). She was discharged with the instruction not to conceive for the next six months. The patient was advised to come weekly for β -hCG levels which showed progressive decline. At six weeks following evacuation, her β -hCG was found to be 17.6 mIU/ml and thyroid parameters were normal (TSH of 1.82 mIU/ml, T3 of 1.08 ng/ml and T4 of 7.86 μ g/dl).⁽²⁾

3- A case is reported of a patient admitted after two weeks after ICSI trial for hydatiform mole. The serum human Chorionic Gonadotropin concentration (hCG) was 900,000 iu. The patient was recognized to be clinically hyperthyroid with raised T4 and T3 values, but a very low TSH concentration. After two days of beta adrenergic blocker and carbimazole, a suction curettage was performed under general anaesthesia. Propranolol was again administered 6 hours after the surgery. Thyroid function returned to normal level two weeks after removal of the mole.⁽³⁾

4- Various aspects of thyroid hormone economy were examined in 15 patients with molar pregnancy. None of the patients with molar pregnancy was clinically thyrotoxic , though serum thyroxin (T4) was increased in 13 and free T4 concentrations were above normal in four of ten in whom measurements were made. In 2 patients with elevated serum T4 levels and in one patient with normal serum T4 levels, the daily rate of T4 disposal was increase, and most of 131I derived from 131I-T4 was excreted into urine in two patients in whom estimation of urinary excretion was made. Serum total triiodothyronine (T3) concentrations closely paralleled those of serum T4, but T3/T4 ratios were lower than those previously found in patients with toxic diffuse goiter of Graves' disease . Human chorionic gonadotropin (hCG) concentrations in serum ranged from 0.5 to 2830 IU/ml and were less than 200 IU/ml in 36% of the patients, possibly because molar pregnancy was diagnosed by ultrasonography, rather than high titers of urinary or serum hCG.

Serum thyroid stimulating activity measured by the McKenzie bioassay closely paralleled values for hCG . All thyroid abnormalities disappeared quickly after removal of the mole.⁽⁴⁾

Discussion:

Our patients had features of molar pregnancy at presentation with hyperthyroidism which was controlled with β -blockers. The hCG molecule is made of α and β subunits; which have a similarity in structure to the TSH molecule. Since hCG and TSH receptors are similar, hCG acts directly on the TSH receptors that are present in the thyroid resulting in an increased level of thyroid hormones T3 and T4 and decreased TSH levels . In approximately 67% of the cases, β -hCG levels greater than 2,00,000 mIU/ml have been found to suppress TSH (lower or equal to 0.2 mIU/ml), while levels above 4,00,000 mIU/ml can lead to suppression in upto 100% of cases . Depending on the severity of the trophoblastic disease, the patient may have clinically asymptomatic elevations of thyroid hormones or can have something as severe as thyrotoxicosis. Patients with clinically evident hyperthyroidism can have varying signs and symptoms such as weight loss, easy fatigability, increased sweating, heat intolerance, palpitations, tremors, ophthalmopathy and clinically enlarged thyroid gland. Serum hCG concentrations closely paralleled those of free thyroxin .

Recommendations:

From the previous we can concluded that the association between the molar pregnancy and the transient Hyperthyroidism is very remarkable and almost all cases will be free of the hyperthyroidism signs and symptoms as soon as the molar pregnancy is evacuated and the Beta hCG levels decrease.

Conclusion:

A physician should be aware of the possibility of transient hyperthyroidism with molar pregnancy. The thyroid abnormality usually subsides with evacuation of hydatidiform mole and may rarely require treatment with antithyroid drugs. In our patient, only ultrasound guided suction evacuation of products of conception was done to regain euthyroidism without the need for antithyroid drugs.⁽²⁾

References:

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