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Case Report

The hyperthyroidism in gestational trophoblastic disease: a case report

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ABSTRACT

Gestational trophoblastic disease, also referred to as GTD, is an extremely rare form of pregnancy-related complication that can arise. It covers a wide range of conditions, from choriocarcinoma to molar pregnancy. Patients who are diagnosed with gestational trophoblastic disease have an increased likelihood of developing hyperthyroidism. It is speculated that this occurs as a result of molecular mimicry that exists between human chorionic gonadotrophin (hCG) and thyroid-stimulating hormone (TSH), which results in cross-reactivity with the TSH receptor. This would explain why the two molecules would react similarly to each other. The gestational trophoblastic disease-induced thyroid storm is an extremely rare but potentially fatal complication that can arise during pregnancy. It is necessary to detect and treat this complication as soon as possible in order to prevent additional complications from occurring. Once the patient's hemodynamic status has been stabilized, the removal of the mole is the primary component of the definitive treatment that will be administered. In most cases, hyperthyroidism usually resolves once the gestational trophoblastic disease has been successfully treated and the hCG levels have been brought back to normal.

Keywords: Hyperthyroidism, Gestational trophoblastic disease, Thyroid

INTRODUCTION

Gestational trophoblastic disease (GTD) is a comprehensive classification including a range of illnesses linked to pregnancy, characterized by atypical growth of placental trophoblast cells. Both complete and partial hydatidiform moles, as well as gestational trophoblastic neoplasia (GTN), are encompassed within the diagnosis of GTD. GTN encompasses a group of trophoblastic tumors, including invasive moles, choriocarcinomas, placental site trophoblastic tumors (PSTT), and epithelioid trophoblastic tumors (ETT). These subtypes are together classified as trophoblastic tumors.[1] It is estimated that benign GTD occurs in approximately one in one thousand pregnancies, whereas choriocarcinoma occurs in approximately one in forty thousand pregnancies.[2] In the past, GTD has been connected to a significant amount of morbidity and mortality. Before the development of methods for early detection and efficient uterine evacuation, hydatidiform mole was frequently complicated by severe bleeding.[3] A gestational trophoblastic disease (GTD) pregnancy may potentially give rise to several problems, including pre-eclampsia, hyperthyroidism, hyperemesis, and respiratory distress.[4]

Although hyperthyroidism is an uncommon complication of GTD, its presence can result in severe clinical outcomes that are potentially fatal. As a result, it is imperative that hyperthyroidism be detected and treated as soon as possible. However, due to the rarity of the condition, making an accurate diagnosis of hyperthyroidism at an early stage can be difficult.[2]

In addition, since uterine evacuation is the primary treatment for hydatidiform mole and GTN, hyperthyroidism is an important perioperative consideration to keep in mind. Thyrotoxicosis is a potentially lethal condition.[3]

In the following, we report a case of hyperthyroidism in gestational trophoblastic disease that occurred in a 43-year-old woman with no previous history of thyroid disease.

CASE REPORT

A 43-year-old female come to hospital, was consulted by an obstetrics and gynecology specialist with suspicion of hyperthyroidism.

The patient had previously been hospitalized on April 2022 and performed a suction curretage procedure due to abortus incomplete versus mola pregnancy with history of irregular vaginal bleeding. The patient reported her last menstrual period was eight weeks prior to presentation. She complained of nausea and sweating, however no tachycardia, no arrhythmia, no palpitations, no tremor, no increased sensitivity to heat and no unintentional weight loss. Her blood pressure was 120/80 mmHg, heart rate 86 beats per minute, temperature 36 degrees Celsius. At that time, the patient had moderate anemia (Hb was 7,8) and transfusted with 3 bags of PRC (Hb becomes 8,7), β-hCG level 137,398.5 mIU/ml, PP test was positive, TSHs level 0,12 mIU/l, FT4 1,5 ng/dl, and anatomical pathology results: support the clinical diagnosis of incomplete abortus with morphology features suitable for the remainder pregnancy. Patient was then discharged after hospitalized for a total of 5 days.

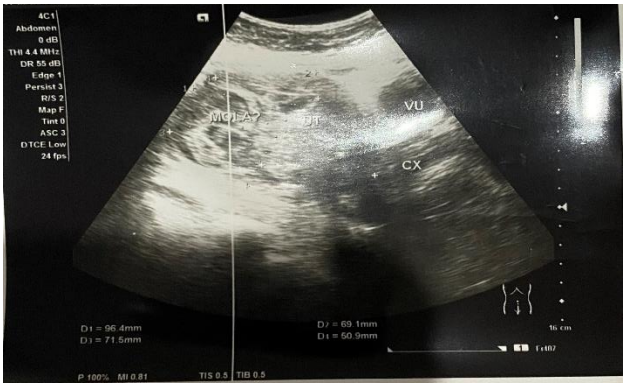

Figure 1: Pelvic ultrasound showed an empty uterus and a mass arising in the right side of the pelvis.

The patient was rehospitalized on May 2022 because of irregular vaginal bleeding for two weeks prior to hospitalization and reported changing around four to five pads per day. She was planned to do dilatation and curettage (DnC) PA. The patient still didn't have any complain of tachycardia, arrhythmia, palpitations, tremor, increased sensitivity to heat nor weight loss. On physical examination, fundus was palpable halfway between the umbilicus and symphysis, other within normal limit. Her blood pressure was 110/70 mmHg, heart rate 99 beats per minute, and temperature 36 degrees Celsius. From the laboratory test, hB 11,1 g/dl, WBC 7,27×10^3/ul, FT4 1,8 ng/dl, TSHs level 0,01 mIU/l. Thorax photo showed within normal limit. The patient was given PTU 200 mg every 12 hours, propranolol 10 mg once daily and intravenous injection of 100 mg hydrocortisone every 12 hours. USG thyroid showed there was no abnormalities in right and left thyroid and isthmus and no specific lymphadenopathy on the right neck. However, on the 4th day of treatment, the β-hCG level results was 540,916.6 mIU/ml, the patient then was recommended to underwent total abdominal hysterectomy bilateral salpingo oophorectomy (TAH-BSO).

Ideally the procedure in hyperthyroid patients was be done if the clinical hyperthyroidism improved, patient was euthyroid, or FT4 within normal limit, however consider that the procedure to evacuate the mola must be done immediately to exterminated the cause of hyperthyroid, the patient were prepared to underwent the procedure, so the risk of thyroid crisis or even worse like thyroid storm can be avoided.

The patient second FT4 test was 1,7 ng/dl. PTU 200mg four times a day, propanolol 10 mg once daily, and intravenous injection of 100 mg hydrocortisone was given to the patient, however because the hydrocortisone was out of stock at the pharmacy, the patient then given intravenous injection of dexamethasone 2,5 mg three times a day. The patient was treated with 2 gr of ceftriaxone as prophylaxis. After the procedure, patient was then started 1 gram of ceftriaxone every 12 hours intravenously. Dexamethasone and propranolol was stopped and PTU was tapering down to 100 mg twice a day in the next day. Lab results after the procedure was her hemoglobin dropped to 8,5 g/dl, WBC was 16.39×10^3/ul, β-hCG level was 95,188.1 mIU/ml. The anatomic pathology result shows invasive hydatidiform of mole (myometrial, vascular, and endocervical invasion), leiomyoma uteri subserosa, follicle cyst on left ovarium, and non-specific chronic cervicitis. After being 10 days hospitalized the patient was discharged.

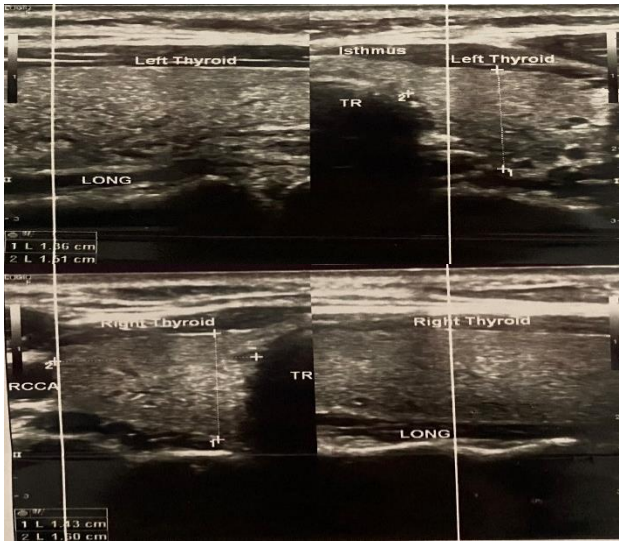

Figure 2: USG thyroid showed there was no abnormalities in right and left thyroid, isthmus and no specific lymphadenopathy on the right neck.

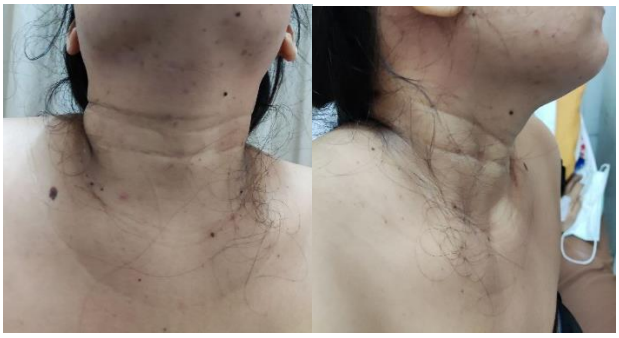

Figure 3: Clinical feature of the neck area.

DISCUSSION

Out of every 100,000 pregnancies in the US, 121 pregnancies result in gestational trophoblastic disorders (GTD), which can include molar pregnancies. Hydatidiform moles arise as a result of aberrant fertilization, giving rise to the excessive growth of trophoblastic tissues and the subsequent vesicular enlargement of placental villi. These modifications confer upon the mole its characteristic "grapelike" morphology. The predominant occurrence in complete moles is the presence of a haploid number of 46, XX. This is attributed to the fertilization of an empty ovum by either a duplicated haploid sperm or the fusion of two sperm. Partial moles predominantly arise from the fertilization of a typical ovum by two sperm, leading to the formation of a triploid (69, XXY) karyotype instead of the usual diploid (23, XY) configuration.[3]

Vaginal bleeding between 6 and 16-week gestation is the prevailing manifestation observed in the majority of complete hydatidiform mole cases, accounting for roughly 80-90% of occurrences.[2] Other common symptoms include an enlarged uterus that is not consistent with the gestational age as well as extreme nausea and vomiting. Patients have elevated levels of beta-hCG, above those observed in normal pregnancies, typically exceeding 100,000 mIU/ml. Also, the absence of fetal heart tones is reported. A considerable proportion of cases initially show signs that indicate a potential occurrence of an abortion that was either missed or incomplete. Despite the fact that ultrasound can only detect 30-50% of hydatidiform moles, a complete mole would have a visual pattern resembling a "snowstorm" of granules during the ultrasound examination.[5,6]

It has been shown that a significant proportion of patients diagnosed with gestational trophoblastic disease (GTD) also have associated hyperthyroidism. Due to the structural resemblance between the beta subunit of human chorionic gonadotropin (hCG) and thyroid-stimulating hormone (TSH), hCG has the capability to interact with the TSH receptor located on thyroid follicular cells.[5] According to available reports, a variable range of 25% to 64% of individuals diagnosed with hydatidiform mole exhibit elevated thyroid function. However, only a small proportion, approximately 5%, of these patients manifest observable symptoms of hyperthyroidism. According to reports, the maintenance of -hCG levels at or above 200,000 m[IU]/ml for a prolonged period is necessary to produce clinical hyperthyroidism.[4] For every 10,000 mlU/ml increase in blood hCG levels, itis estimated that TSH levels will fall by 0.1 mlU/ml and free T4 levels will incr ease by 0.1 ng/dl.[5]

Thyroid storm, thyrotoxicosis, and subclinical hyperthyroidism are all possible manifestations of an overactive thyroid.[7] The thyroid storm is a potentially life-threatening illness that manifests with symptoms such as rapid heart rate, elevated body temperature, restlessness, and changes in cognitive function. The mortality rate has a range of 10 to 30 percent.[8,9] Prompt diagnosis and a high degree of suspicion are imperative to prevent the severe complications associated with thyroid storm, which may include stroke, death, arrhythmia, myocardial infarction, liver dysfunction and rhabdomyolysis.[10] Individuals diagnosed with hyperthyroidism caused by gestational trophoblastic disease (GTD) generally do not manifest the typical clinical manifestations commonly associated with Grave's disease, such as ophthalmoplegia and pretibial myxedema. This is a fact that is extremely helpful in making a diagnostic determination. This is probably due to the fact that trophoblast-induced hyperthyroidism only persists for a short amount of time.[6]

After the molar pregnancy has been surgically removed, there are some situations in which the patient has a thyroid storm. This is probably because of a combination of elevated hCG levels and stress brought on by the loss of blood. Although there are people who develop or present with clinical signs of thyroid storm while they are still in the hospital, there are also instances in which thyroid storm develops after the molar pregnancy has been surgically removed. As a result of this, it is of the utmost need to do a pre-operative examination for hyperthyroidism.[11]

The management of hyperthyroidism in GTD shares similarities with the treatment strategies used for hyperthyroidism caused by primary thyroid disorders. The majority of those who are diagnosed with clinical hyperthyroidism generally demonstrate beneficial responses to anti-thyroid drugs and get supportive care, which may include the injection of beta blockers.[12-14]

The administration of steroids has been demonstrated to be efficacious in the management of hyperthyroidism. Steroids function in the management of hyperthyroidism by impeding the peripheral conversion of thyroxine to triiodothyronine and by inhibiting the release of thyroxine from the thyroid gland.[15] After patient’s hemodynamics have been brought under control, the removal of the mole is the primary component of definitive treatment.[6] In most cases, the most effective method of evacuation is suction combined with curettage. In certain cases, a hysterectomy may be conducted on patients who do not wish to conceive in the future. Conducting post-evacuation follow-up with

serial quantitative -hCG assessments is crucial to assess the potential existence of persistent molar tissue or the appearance of choriocarcinoma. The incidence of these problems is estimated to be around 15-20% in individuals with a complete mole and approximately 1-5% in people with a partial mole.[2] After undergoing the surgical procedure, almost all of the patients achieved euthyroid status, ceased exhibiting clinical indications of hyperthyroidism, and did not need any additional medication in the weeks after they were discharged from the hospital. There have been a few cases documented of severe hyperthyroidism in GTD that was unresponsive to medical treatment approaches.

As a result, the patients needed to go through therapeutic plasmaphoresis in order to get ready for surgery as quickly as it could be scheduled. Patients who do not react to more conventional methods of medical treatment or who experience undesirable side effects as a result of the medications they are administered, may be candidates for therapeutic plasmaphoresis.[12-14]

In this report patient showed no sign of thyrotoxicosis, however FT4 was found elevated (FT4 1,8 ng/dl, normal 0,5- 1,4 ng/dl) with low TSHs level 0,01 mIU/l (normal 0,35-5,10 mIU/l). The second test of the FT4 still found elevated (FT4 1,7 ng/dl) and β-hCG level results was 540,916.6 mIU/ml. The patient underwent total abdominal hysterectomy bilateral salpingo oophorectomy with well preparation before the procedure. After the procedure patients are hemodynamically stable, and the β-hCG level lower to 95,188.1 mIU/ml. The patient was then planned for periodic thyroid evaluation at the outpatient care.

CONCLUSION

Hyperthyroidism represents a potentially life-threatening complication that can arise from GTD. Extensive research has been conducted on the underlying mechanisms of trophoblast-induced hyperthyroidism, which can be ascribed to the structural resemblance between hCG and TSH. The present condition is distinguished by increased concentrations of hCG released by trophoblast cells in gestational trophoblastic disease (GTD), resulting in enhanced thyrotropic effects of hCG in GTD.

The majority of hyperthyroidism cases in GTD can be efficiently managed through the use of anti-thyroid medications. However, in instances where patients do not respond to medical treatment or when urgent surgery is necessary, plasmapheresis may serve as a viable alternative therapeutic approach. The sole definitive treatment option for hyperthyroidism in GTD is surgical evacuations of the uterus. The management of hyperthyroidism is a critical aspect to address during the perioperative period for patients with GTD. It is essential to ensure that the patient's hemodynamic condition and thyroid function are adjusted before to surgery to reduce the risk of potential problems.

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REFERENCES

1. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet. 2010;376(9742):717-29.
2. Pereira JV, Lim T. Hyperthyroidism in gestational trophoblastic disease - a literature review. Thyroid Res. 2021;14(1):1.
3. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol. 2010;203(6):531-9.
4. Hershman JM. Physiological and pathological aspects of the effect of human chorionic gonadotropin on the thyroid. Best Pract Res Clin Endocrinol Metab. 2004;18(2):249-65.
5. Kaulfers AM, Bhowmick SK. Molar Pregnancy Causing Thyrotoxicosis in a Teenage Girl With Type 1 Diabetes Mellitus. Glob Pediatr Health. 2015;2:2333794X15574285.
6. Moskovitz JB, Bond MC. Molar pregnancy-induced thyroid storm. J Emerg Med. 2010;38(5):e71-6.
7. Chiniwala NU, Woolf PD, Bruno CP, Kaur S, Spector H, Yacono K. Thyroid storm caused by a partial hydatidiform mole. Thyroid. 2008;18(4):479-81.
8. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011;21(6):593-646.
9. Devereaux D, Tewelde SZ. Hyperthyroidism and thyrotoxicosis. Emerg Med Clin N Am. 2014;32(2):277-92.
10. Kofinas JD, Kruczek A, Sample J, Eglinton GS. Thyroid storm-induced multi-organ failure in the setting of gestational trophoblastic disease. J Emerg Med. 2015;48(1):35-8.
11. Hou JL, Wan XR, Xiang Y, Qi QW, Yang XY. Changes of clinical features in hydatidiform mole: analysis of 113 cases. J Reprod Med. 2008;53(8):629-33.
12. Adali E, Yildizhan R, Kolusari A, Kurdoglu M, Turan N. The use of plasmapheresis for rapid hormonal control in severe hyperthyroidism caused by a partial molar pregnancy. Arch Gynecol Obstet. 2009;279(4):569-71.
13. Azezli A, Bayraktaroglu T, Topuz S, Kalayoglu-Besisik S. Hyperthyroidism in molar pregnancy: rapid preoperative preparation by plasmapheresis and complete improvement after evacuation. Transfus Apheresis Sci. 2007;36(1):87-9.
14. Erbil Y, Tihan D, Azezli A, Salmaslioglu A, Ozluk Y, Buyukoren A, et al. Severe hyperthyroidism

requiring therapeutic plasmapheresis in a patient with hydatidiform mole. Gynecol Endocrinol. 2006;22(7):402-4.
15. Clinical Research Centre. Efficacy and Safety of Cholestyramine and Prednisolone as Adjunctive Therapy in Treatment of Overt Hyperthyroidism. Malaysia. 2017.

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