

Stormy Encounter with Partial Hydatidiform Mole

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Abstract

We report a case of a 40-year-old multiparous woman who underwent total abdominal hysterectomy due to massive vaginal bleeding from partial molar pregnancy. Post-operatively, she developed high-grade fever, profuse sweating and shortness of breath. Examination revealed tachycardia, hypertension, elevated jugular venous pressure, and crackles on both lower lung fields, with no palpable thyroid mass. Free thyroxine (FT4) and human chorionic gonadotropin β -subunit (β -hCG) were markedly elevated, while thyroid stimulating hormone (TSH) was significantly suppressed. With a Burch and Wartofsky score of 55, thyroid storm from the molar pregnancy was considered. She was given propylthiouracil (PTU), propranolol and hydrocortisone. Resolution of her signs and symptoms were noted 2 to 3 days following treatment.

Key words: thyroid storm, pregnancy, partial hydatidiform mole, hyperthyroidism

INTRODUCTION

Hyperthyroidism can occur in 0.1 to 0.2% of pregnant women, with Graves' disease as the most common etiology.¹ Transient gestational hyperthyroidism, molar pregnancy, toxic multinodular goiter and toxic adenoma are the other less common causes of hyperthyroidism in pregnancy.² Hyperthyroidism has been documented in 8% of molar pregnancies, but one report has cited its prevalence to be as high as 25 to 64%.^{3,4} Severe hyperthyroidism resulting in thyroid storm rarely occurs in molar pregnancy. In isolated reports, two cases of thyroid storm have been documented in young women, both with partial molar pregnancy.^{5,6}

CASE

A 40-year-old Filipino female with an obstetric score of G15P9 (9059) was admitted due to vaginal bleeding. She was apparently well, with no complaints other than amenorrhea of two months. About 11 weeks prior to her admission, she experienced nausea and mild hypogastric pain associated with minimal vaginal bleeding. She did not have fever, frequent defecation, tremors or excessive sweating. She did not seek any medical consult and attributed her symptoms to a possible pregnancy. Six weeks later, she started to complain of malaise, easy

fatigability and dyspnea on heavy exertion. Progressive weight loss about 25% was also noted. During the following week, she experienced frequent palpitations and hyperdefecation. These symptoms were not associated with tremors, heat intolerance, fever and vomiting. She was not previously diagnosed with thyroid disease.

Due to the persistence of hypogastric pain and vaginal bleeding, she opted to consult a general physician. Her urine pregnancy test was positive and her vaginal bleeding was considered a probable threatened abortion. Pelvic ultrasonography revealed an enlarged uterus (7.6 cm x 10.0 cm x 11.5 cm) with multiple grape-like masses, with no fetal echo or gestational sac. She was diagnosed with molar pregnancy and was subsequently transferred to our institution.

On examination by an obstetrician-gynecologist, she was found to be afebrile (36.9°C), slightly hypertensive (140/90 mm Hg), tachypneic (23 cycles per minute) and tachycardic (108 beats per minute). Other than a 5-month size uterus and blood per examining finger, there were no other significant findings. She was admitted as a case of hydatidiform mole with a management plan of suction curettage. Six hours after her admission, she suddenly had profuse vaginal bleeding, prompting emergency total abdominal hysterectomy.

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Intraoperatively, the uterus was found to be large and boggy, measuring about 16 cm x 10 cm x 6 cm, and filled with vesicular tissues. The uterus, cervix and recovered tissues were sent for histopathologic examination. The patient tolerated the procedure. Blood transfusion was done to correct her anemia.

A few hours after the surgery, she developed fever, shortness of breath and hypertension. She was referred to the Medicine service for evaluation of possible hyperthyroidism. On evaluation, she was noted to be cachectic, awake, restless and in respiratory distress. She was hypertensive (160/90 mm Hg), tachypneic (42 cycles per minute), tachycardic (136 beats per minute) and already febrile (38.4°C). She had pale palpebral conjunctivae and elevated jugular venous pressure (8 cm from sternal angle). She had no exophthalmos and thyromegaly. Examination of the chest revealed crackles on both lower lung fields, and a loud S1 at the cardiac apex and base. The rest of the physical findings were unremarkable.

Laboratory Investigation

Further tests revealed elevated β -hCG titer (>10,000 mIU/mL, reference value 0-1), FT4 (275.20 nmol/L, reference value 66-181) and free triiodothyronine (FT3) (6.69 nmol/L, reference value 1.3-3.1); and suppressed TSH (0.01 μ IU/mL, reference value 0.27-4.2). Histopathologic examination of the vesicular tissues revealed invasive partial hydatidiform mole, with involvement of less than 50% of the myometrial wall and extent of invasion limited to the uterus. Thus, thyroid storm from partial molar pregnancy was considered, with a Burch and Wartofsky score of 55 and probable thyroid storm.⁷

Ultrasonography of the neck to investigate other possible causes of hyperthyroidism revealed a sub-centimeter nodule in the left thyroid lobe with benign features. Thyroid scintigraphy to assess function of the nodule was not done. However, the authors determined that the severe hyperthyroidism resulted from the partial hydatidiform mole, based on the absence of hyperthyroid symptoms prior to pregnancy, the development of hyperthyroidism only during the recent pregnancy, and subsequent resolution of symptoms after removal of the hydatidiform mole.

Differential Diagnosis

One of the probable causes of thyroid storm was a functioning toxic nodule. Thyroid scintigraphy was not available in our setting. We opted to observe the clinical course of the patient after surgery and upon discontinuation of anti-thyroid medications. With the patient remaining euthyroid on follow-up, we considered the molar pregnancy as the sole source of hyperthyroidism resulting to thyroid storm.

Management

The patient was given oral PTU 600 mg as loading dose, followed by 200 mg every 8 hours to rapidly decrease thyroid hormone synthesis. She was also given intravenous hydrocortisone, 50 mg every 8 hours to decrease conversion of FT4 to FT3. Intravenous furosemide 40 mg was administered to address acute pulmonary congestion and intravenous digoxin 0.5 mg to control the heart rate. Digoxin was later shifted to oral propranolol at 160 mg/day after resolution of acute pulmonary congestion. Supersaturated solution of potassium iodide was not available in our setting. Additional anti-hypertensive medication was given to control blood pressure.

With marked improvement of hyperthyroidism noted after 2 to 3 days, PTU was shifted to oral methimazole at 20 mg once daily. Hydrocortisone and propranolol were subsequently discontinued. She underwent chemotherapy with intramuscular methotrexate 0.6 mL for five days and was subsequently discharged.

Follow-up Examination

Two weeks after hospital discharge, the patient was free of clinical manifestations of hyperthyroidism. Repeat FT4 was within normal limits (12.14 pmol/L, reference value 12-22), while β -hCG titer decreased further (85.01 mIU/mL, from 1102 mIU/mL; reference value 0-1). Methimazole was discontinued and the patient remained euthyroid.

DISCUSSION

The incidence of hydatidiform mole in Asia is higher (1 in 125 live births in Taiwan and 2 in 1000 pregnancies in Southeast Asia and Japan) compared to other regions of the world (1 in 1000 in Europe and 1 in 1500 in the USA).^{3,8} In the Philippines, the national prevalence rate is 2.4 in 1000 pregnancies; at the Philippine General Hospital, a national referral center, it is as high as 14 in 1000 pregnancies.⁹ Several risk factors for molar pregnancy were present in our patient, including advanced maternal age, previous miscarriage and smoking.^{4,10}

Human chorionic gonadotropin is secreted in high levels in molar pregnancies, and is associated with hyperthyroidism.¹¹ The thyrotropic activity of hCG is due to the structural homology between the molecules and receptors of hCG and TSH.¹² Both hCG and TSH belong to a family of glycoprotein hormones with a common alpha-subunit and unique beta-subunit. The homology between the beta-subunits of hCG and TSH can account for the thyroid-stimulating activity of hCG.¹³ This activity of hCG is further illustrated by the inverse relationship between TSH and hCG during the latter's peak at about 10-12 weeks of pregnancy.¹⁴

While uncommon, clinical hyperthyroidism has been reported to occur in patients with complete hydatidiform mole, with a prevalence of around 25 to 64%.^{3,4} Higgins and co-workers reported that clinical symptoms of hyperthyroidism become apparent when hCG levels are above 300,000 mIU/mL.¹⁵ Our patient had partial hydatidiform mole with the clinical presentation of severe hyperthyroidism, and a β -hCG titer of >10,000 mIU/mL. Determination of β -hCG was performed using the ARCHITECT Total β -hCG assay, a two-step immunoassay to determine the presence of β -hCG in serum and plasma using chemiluminiscent microparticle immunoassay technology with flexible assay protocols. Specimens with β -hCG levels greater than or equal to 25 mIU/mL are read as "positive" and values exceeding 10,000 mIU/mL are flagged with the code ">10,000 mIU/mL." In our case, the lower serum level of β -hCG detected was probably due to the limitation of the machine to detect a much higher β -hCG level. Another possible explanation is the high-dose hook effect, which can occur in the presence of a very high concentration of antigen that causes incomplete antibody-antigen complexes to form.¹⁶

The elevated FT4 and suppressed TSH in this patient demonstrated the thyroid response to the excess level of β -hCG. Though palpitations and weight loss may be part of nonspecific symptoms associated with early pregnancy, the presence of hyperdefecation along with findings of elevated FT4 and suppressed TSH were likely due to hyperthyroidism.

Thyroid storm, while known to occur rarely, was previously reported in partial hydatidiform molar pregnancies.^{5,6} In these reports, patients were admitted due to clinical manifestations of thyroid storm, which improved after evacuation of the molar tissues. In contrast, our patient went into thyroid storm after surgical evacuation of the molar tissues. The precipitating factors identified in this case were stress from surgical intervention combined with unrecognized thyrotoxicosis from excess serum β -hCG levels and anemia from blood loss.¹⁷ These aggravated the hyperthyroidism pushing the patient into high-output cardiac failure and thyroid storm.

Return to undetectable levels of serum β -hCG following termination of pregnancy can vary widely from 7 to 60 days; in situations following evacuation of complete or partial molar pregnancy, the average time to normalization is 99 and 59 days, respectively.^{18,19} The marked elevation of β -hCG levels in molar pregnancy can be accounted for by its longer half-life, resulting to longer exposure to its thyroid stimulating activity.¹¹ Another complication that might occur in patients with molar pregnancy is pulmonary embolization of trophoblastic cells, causing tachypnea, tachycardia, cough and diffuse rales.²⁰

Early detection of signs and symptoms of hyperthyroidism in any pregnant woman is essential. Any patient suspected

with molar pregnancy must undergo early determination of serum β -hCG levels, with subsequent monitoring of the titer as recommended.²¹

Learning Points

The importance of a complete history and physical examination cannot be over emphasized in patients with suspected molar pregnancy. Thyroid hormone screening is warranted for patients with hydatidiform mole. Hyperthyroidism secondary to molar pregnancy warrants prompt diagnosis prior to any procedure to avoid thyroid storm.

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