



## Advanced gestational trophoblastic disease: A case report of medical management prior to surgical intervention

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### ABSTRACT

**Background:** Gestational trophoblastic disease (GTD) is a rare developmental form of proliferative trophoblastic tissue. Sparse literature exists regarding the optimal management of patients with advanced GTD, but the definitive treatment is urgent surgical intervention.

**Case:** A 48-year-old woman presented advanced GTD. She was medically managed for hypertension and hyperthyroidism prior to surgical intervention in order to minimize the risk of anesthetic and surgical complications. **Conclusion:** Advanced GTD is rare. Undetected GTD can result in complications such as thyrotoxicosis, which poses substantial risks in the peri-operative period. Appropriate identification and management of this clinical problem are essential to prevent complications as well as subsequent malignant sequelae.

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### 1. Introduction

Gestational trophoblastic disease (GTD) is a spectrum of disorders that may develop following abnormal fertilization [1]. The ultimate treatment for GTD is surgical evacuation of the proliferative trophoblastic tissue [2]. In cases of advanced GTD, patients must be evaluated for hyperthyroidism, and their hypermetabolic status and thyroid function must be optimized prior to surgery to prevent intraoperative complications [3].

As advanced GTD is rare in developed countries, little research has been done on the optimal time and means needed for management of thyrotoxicosis secondary to GTD [2]. This case report discusses the medical optimization of a patient with advanced GTD prior to surgical intervention.

### 2. Case

A pregnant 48-year-old gravida 6 para 3 woman was referred to the outpatient OB-GYN office at 11 weeks' gestation for suspected molar pregnancy. At presentation, the patient complained of a three-day history of headache, right-sided abdominal pain, epistaxis, vaginal bleeding, nausea and vomiting. She was hypertensive (148/98) and was noted to be anxious and mildly diaphoretic.

The outpatient records indicated that the patient's serum beta human chorionic gonadotropin ( $\beta$ -HCG) level measured 8 days previously was 954,143 mIU/L. Pelvic ultrasound performed 3 days earlier revealed an 11 cm complex cystic structure and solid endometrial structure, most consistent with GTD [Fig. 1]. The patient was referred to the Emergency Department (ED) with suspicion of molar pregnancy and possible preeclampsia.

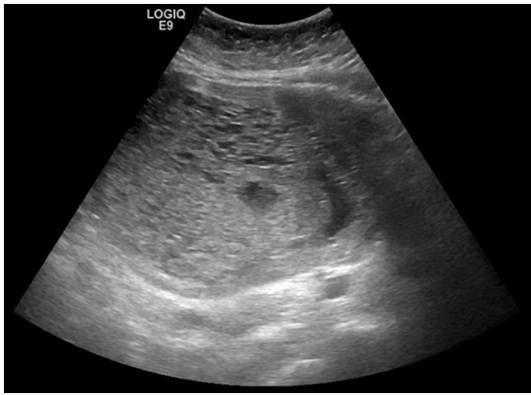
In the ED, the patient's blood pressure was further elevated, at 177/79 mmHg. Laboratory results were: serum  $\beta$ -HCG 1,771,640 mIU/L, urine protein 30 mg/dL (neg), alanine transaminase (ALT) 116 (4–36) IU/L, aspartate transaminase (AST) 80 (8–33) IU/L, thyroid stimulating hormone (TSH) 0.07 (0.34–5.6) u[lu]/mL, T4 25 (6.0–12.0) ug/L, T3 291 (87–188) ng/mL, free T4 4.09 (0.82–1.77) ng/dL, and free T3 9.7 (2.0–4.4) pg/mL.

The patient was admitted to the telemetry unit and placed on intravenous labetalol drip, and started on stress dose steroids, propylthiouracil and potassium-iodide for prophylaxis against thyroid storm. She required administration of multiple courses of intravenous hydralazine to stabilize her blood pressure. By hospital day 4, the patient remained hypertensive. After imaging revealed possible metastatic disease, she was transferred to another institution for further management. She underwent a dilation and curettage without complications and is doing well postoperatively.

### 3. Discussion

GTD comprises a spectrum of premalignant and malignant diseases, including hydatidiform mole (complete or partial), placental site

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**Fig. 1.** Pelvic ultrasound of uterus, revealing no fetus and characteristic vesicular pattern of multiple echoes and holes within placental mass.

trophoblastic tumor, choriocarcinoma and gestational trophoblastic neoplasia. Hydatidiform mole (also known as molar pregnancy) is the most common form of these [4].

GTD classically presents with a combination of symptoms such as uterine enlargement greater than gestational dates, vaginal bleeding, hyperemesis, pregnancy-induced hypertension and hyperthyroidism. Clinical diagnosis is based on history, physical examination, pelvic ultrasound and serum  $\beta$ -HCG quantification ( $>100,000$  mIU/mL). Treatment is urgent surgical evacuation and curettage, and pathologic examination of the curettage specimen confirms the diagnosis [5].

In North America, there is a 0.1% incidence of molar pregnancy in all pregnancies; in Asia, it is up to three times higher [6]. It is even more rare to encounter advanced GTD in the modern era, due to earlier diagnosis by serum  $\beta$ -HCG quantification and pelvic ultrasound, as well as effective means of uterine evacuation [5]. This patient's presentation of gravely advanced GTD, evidenced by an exceptionally high  $\beta$ -HCG level, can be attributed to a number of causes. It is likely that her lower socioeconomic status impeded earlier detection and medical treatment [7].

The patient's complaints on initial presentation can be explained by hyperthyroidism, secondary to high secretion of  $\beta$ -HCG from the trophoblastic tissue. There is well-documented evidence of molecular mimicry between the hCG and TSH subunits; hCG acts directly on the TSH receptors in the thyroid. At extremely high levels of hCG, there is an increased level of thyroid hormones T3 and T4 and decreased TSH levels, which induces a hyperthyroid state [4, 8]. Symptoms of a hyperthyroid state include hypertension, weight loss, anxiety, diaphoresis, palpitations, tremor and tachycardia, of which the patient presented with hypertension, anxiety and diaphoresis [9].

Preeclampsia was considered as a potential contributing factor to the patient's presentation, particularly her hypertension, proteinuria and transaminitis. Preeclampsia (defined as hypertension in association with either proteinuria, thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances occurring after 20 weeks' gestation) is a well-established cause of hypertension during pregnancy, albeit through incompletely understood mechanisms. There are many risk factors for developing preeclampsia, of which the patient had several, including previous preeclampsia and age over 40 years. However, development of preeclampsia prior to 20 weeks is extremely rare and ultimately magnesium sulfate (the standard pharmacologic treatment of preeclampsia) was not administered [10].

The definitive treatment of GTD is surgical evacuation of the uterus. Dilation and curettage was considered for the patient; however, there were significant perioperative risks. There are several reports of intraoperative thyroid storm and cardiac failure due to thyrotoxicosis. Untreated thyroid crisis is known to be fatal in the perioperative period, particularly in the setting of emergency surgery [2–3, 11]. Thus, it was

decided that control of her hypermetabolic state and thyroid status prior to anesthetic administration and surgical intervention would minimize the risk of these complications, and result in a better long-term outcome than immediate surgical intervention [3]. If the patient had presented with a less advanced stage of GTD and was clinically stable, dilation and curettage would have been performed urgently and without preceding medical management.

There is inadequate research into a definitive length of time for medical management prior to surgical intervention to prevent thyrotoxicosis complications. Ultimately, surgical treatment was delayed until the patient could be further stabilized via medical management. It is hoped that future research will examine the optimal length of time to postpone surgical evacuation to achieve medical optimization, while maintaining safety for patients.

#### 4. Conclusion

Hyperthyroidism is a serious complication associated with GTD. Due to the low prevalence of advanced GTD in developed countries, there is sparse literature discussing the optimal medical management of these patients. When a patient presented with advanced GTD, it was determined that medical management of her hypertension and hyperthyroidism took priority over immediate surgical therapy in order to minimize the risk of anesthetic and surgical complications.

#### Contributors

Ann Lehto participated in acquisition of data and drafted the article. Kyle Hitscherich participated in acquisition of data and critical revision of the article for important intellectual content.

Olga Argeros participated in critical revision of the article for important intellectual content.

All authors saw and approved the final version.

#### Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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#### Patient consent

Written informed consent was obtained from the patient for the publication of this case report.

#### Provenance and peer review

This case report was peer reviewed.

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