

# Successful Preoperative Treatment by Plasmapheresis of Hyperthyroidism with Hydatidiform Mole

## Molar Gebelik Sonucu Gelişen Hipertiroidizm Olgusunda Plazmaferez Tedavisi

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### ABSTRACT

We recently encountered the case of an 18-year-old female complaining of abdominal pain, fatigue, nausea, vomiting, tremor of the hands, and vaginal bleeding. Her blood test revealed highly elevated human chorionic gonadotropin (hCG) levels, suppressed thyroid-stimulating hormone (TSH) levels, and increased free thyroid hormone levels. Molar pregnancy and hyperthyroidism were suspected based on highly elevated hCG levels and suppressed TSH levels with the co-existence of ultrasonographic findings of the uterus and thyroid Doppler images. Her symptoms and thyroid hormone levels responded well to plasmapheresis. Subsequently, the patient underwent dilatation and curettage for hydatidiform mole. Histopathology of the products verified the diagnosis of complete hydatidiform mole with no invasion. The patient is currently stable, and her hCG and thyroid hormone levels are within normal reference ranges.

**Keywords:** Hydatidiform mole, hCG, hyperthyroidism, plasmapheresis

### ÖZ

18 yaşında kadın hasta karın ağrısı, yorgunluk, bulantı, kusma, ellerde titreme ve vajinal kanama şikayeti ile başvurdu. Laboratuvar tetkiklerinde artmış human chorionic gonadotropin (hCG), baskılanmış tiroid stimulan hormon (TSH) ve artmış serbest tiroid hormon düzeyleri görüldü. Laboratuvar tetkikleri ile birlikte tiroid doppler ve uterus ultrasonografi incelemesi sonucunda molar gebelik sonucu gelişen hipertiroidizm tanısı düşünüldü. Plazmaferez tedavisi ile hastanın semptomların da düzelme ve serbest tiroid hormonlarında normal düzeye gerileme sağlandı. Plazmaferez tedavisi sonrası hastaya dilatasyon ve küretaj tedavisi uygulandı. Histopatolojik incelemede non-invaziv mol hidatiform tanısı doğrulandı.

**Anahtar Kelimeler:** Mol hidatiform, hCG, hipertiroidizm, plazmaferez

### Introduction

Hydatidiform mole (HM) is the most frequently encountered form of gestational trophoblastic disease and fetal developmental defect, where abnormal trophoblast cells develop inside the uterus following conception (1). The incidence rate ranges from 1 in 500 to 1 in 1500 pregnancies in western developed countries (1). The high hCG levels induced by HM may also induce hyperthyroidism caused by accelerated synthesis of thyroid hormones; typically, patients present with vaginal bleeding (2). The objective of this report is to present a case in which plasmapheresis was administered to control thyroid hormones in hyperthyroidism with a hydatidiform mole.

### Case Report

An 18-year-old woman presented to the gynecology and obstetrics service with abdominal pain, nausea, vomiting, and vaginal bleeding for 2 days. Her last normal menstrual period was a month prior and she had an unremarkable medical history. She was married with no children and reported no tobacco use. Physical examination revealed that she was tachycardic (110 bpm), dehydrated, experienced tremor of the hands, and had a normal blood pressure of 112/66 mmHg. Cardiac assessment yielded normal values of echocardiographic measurements, except for sinus tachycardia yielded on

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electrocardiography. The uterus size was consistent with that associated with a 16-week gestation. Ultrasound revealed that the uterine cavity was significantly extended and filled with an echogenic soft-tissue mass that had small cystic components, most compatible with complete molar pregnancy.

Her hCG levels were over 250,000 mIU/mL, thyroid-stimulating hormone (TSH) level was 0.013  $\mu$ IU/L (0.27-4.2  $\mu$ IU/L), free thyroxine (fT4) was 3.4 ng/dL (0.93-1.7 ng/dL), and free triiodothyronine (fT3) was 8.1 ng/dL (2.0-4.4 ng/dL). Other blood tests, such as hemogram, leukocytes, and renal and liver function tests, were normal. The patient was transferred to an endocrinology department for diagnosis and treatment of hyperthyroidism before uterine curettage with general balanced anesthesia.

We detected hypervascularization of the thyroid gland on Doppler ultrasound examination. Based on power Doppler sonographic findings and thyroid hormone levels, she was diagnosed with hyperthyroidism. She received methimazole at a dose of 40 mg daily and was initiated with  $\beta$ -receptor antagonist therapy and dexamethasone treatment. To rapidly displace the thyroid hormones from the body for better hormonal control, plasmapheresis was administered to the patient prior to surgery. One session of plasmapheresis was administered to the patient on the first day, which lasted for approximately 3 h. No complications developed during or after the procedures. During plasmapheresis, 3,000 mL of plasma was collected from the patient, and the same volume of fresh frozen plasma was given to the patient. At the time of surgery, on the second day after admission, her serum fT4 and fT3 levels were 2.3 ng/dL and 5.1 ng/dL, respectively.

Subsequently, the patient underwent dilatation and curettage for evacuation of the mole. There were no complications during surgery or postoperatively. At 36-48 hours postoperatively, her hCG levels decreased to 77.724 mIU/mL. Histopathology of the products verified the diagnosis of complete hydatidiform mole with no invasion. The patient is currently stable, and her hCG and thyroid hormone levels are within normal reference ranges. Written informed consent was obtained from the patient.

## Discussion

HM with hyperthyroidism is a rare clinical condition, but thyroid hyperstimulation by highly elevated hCG may have triggered the cardiopulmonary system (3). Most people with HM do not have hyperthyroidism; however, women with HM have an increased risk of developing hyperthyroidism (2). In a retrospective study, biochemical hyperthyroidism was 7% and clinical hyperthyroidism was only 2% in 196 female patients with HM (4). HM occasionally co-exists with markedly elevated hCG levels, as can be observed in our patient, who had an hCG level of approximately half a million mIU/mL (5). Markedly elevated glycoprotein hormone, hCG, is the primary diagnostic indicator of HM (5). The similarity between

hCG and TSH can induce cross-reactivity in their receptors. This similarity between hCG and TSH molecules can cause hyperthyroidism (6). Glinoer reported that for every 10,000 mIU/mL upregulation in serum hCG, fT4 increases by 0.1 ng/dL and TSH reduces by 0.1 mIU/mL (7). When gestational trophoblastic disease causes a significant upregulation in hCG levels, it may produce hyperthyroidism that requires urgent treatment. Elective surgery and treatment should be postponed until the patient becomes euthyroid. In instances of emergency surgery, such as in the present case, it may not be possible to wait 1 week for the thyroid hormone levels to stabilize. As expected, hyperthyroidism resolves with curettage for evacuation of the mole and normalization of hCG levels (2). However, lack of preoperative control of the thyrotoxic state considerably increases the risk of thyroid storm. The thyroid storm associated with surgery can manifest intraoperatively but is more likely to occur 6-18 hours postoperatively (8). Untreated hyperthyroid crisis (thyroid storm) is typically fatal. The mortality rate of the thyroid storm is currently approaching 30% despite early recognition and adequate treatment (8).

While HM can be eradicated by simple curettage, untreated molar pregnancies the incidence of acute respiratory complications increased to 27% (9). In the literature survey, we found that unaddressed hyperthyroidism with HM can induce acute respiratory insufficiency, a known complication of molar pregnancies occurring in 8-11% of cases and up to as many as 50% (10). Untreated HM with hyperthyroidism is typically fatal (10, 11). Because the subsequent prolongation of thyroid function impairment could induce respiratory insufficiency and in molar pregnancy with hyperthyroidism, patients have encountered acute cardiopulmonary distress following suction evacuation under general anesthesia and massive trophoblastic embolism, death may occur (10, 11).

Antithyroid medications are frequently used to treat hyperthyroidism (12). However, antithyroid drugs cannot achieve complete control of thyroid hormone levels rapidly and typically require at least 3 weeks to reduce thyroid hormone levels (12). To avoid the risk of thyroid storm and respiratory insufficiency because of both of these diseases, plasmapheresis was selected before surgery.

## Conclusion

In the literature survey, four case reports (13-15) showed that plasmapheresis was used to treat hyperthyroidism with hydatidiform mole. We suggest that plasmapheresis management be considered a suitable choice when life-threatening hyperthyroidism is encountered in women with HM.

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