

## CASE REPORT

Obstetrics and Gynecology

# Hook effect in gestational trophoblastic disease: An emergency department case presentation

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Email: [jlang@ept911.com](mailto:jlang@ept911.com)**Funding and support:** By JACEP Open policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see [www.icmje.org](http://www.icmje.org)). The authors have stated that no such relationships exist.**Abstract**

Gestational trophoblastic disease is a process that affects  $\approx 1$  of 1000 pregnancies. If left untreated, this can progress to potentially life-threatening complications with malignancy such as choriocarcinoma. The emergency physician must be aware of the presentation and complications of this disease process, including the difficulties in diagnosis. In this case presentation, the authors discuss the presentation and diagnostic process of a patient in the emergency department as well as the phenomenon known as the hook effect, which may complicate the decision-making process.

**KEYWORDS**

beta HCG, gestational trophoblastic disease, hook effect, molar pregnancy, point of care ultrasound, pregnancy complication

## 1 | INTRODUCTION

A 23-year-old woman presented to the emergency department with complaints of possible dehydration. When interviewed initially by the resident, she was unable to verbalize much, but she pulled up Facetime on her phone so her brother, with whom she lived, could provide most of the history. He reported that she had 3 days of headache, nausea and vomiting, and loss of appetite and was concerned about dehydration, so he asked her to go to the hospital. There were no old records available, and she did not report any significant past medical history. Her initial vital signs were temperature of 98.5°F, pulse 107, blood pressure 138/73, saturation of 98% on room air, and weight of 40.8 kg. Her physical examination was significant for thin in appearance, tachycardia, and decreased bowel sounds. The patient had no gross motor deficits, but her speech was very limited in nature, albeit clear, and was quoted as saying "Um, OK, molar," and nodded "yes" when asked if she had a molar pregnancy. Her laboratory work showed a white blood cell (WBC) count of 10.7 K/ $\mu$ L, hemoglobin of 14.2 g/dL, and a chemistry panel that was unremarkable except for glucose of 109 mg/dL and chlo-

ride of 95 mmol/L. Her urine pregnancy was negative, but her urinalysis did have a high specific gravity of 1.031, serum ketones of 80 mg/dL, glucose of 50 mg/dL, and a urine toxicology screen that was positive for cannabinoids. A normal saline infusion of 1000 mL was started for presumed dehydration.

Shortly thereafter, she had a 15-second generalized tonic-clonic seizure. She was given lorazepam intravenously, and a bedside ultrasound was performed showing a uterine mass that was concerning for a molar pregnancy (Figure 1) despite her negative urine pregnancy test. An emergent head computed tomography (CT) (Figure 2) and radiology-performed pelvic ultrasound were done, and a serum beta human chorionic gonadotropin (HCG) was sent. The head CT was significant for "3.6  $\times$  3.3  $\times$  3.8 cm left frontal lobe intraparenchymal hemorrhage with significant surrounding vasogenic edema and left to right midline shift." Neurosurgery was remotely consulted, and the patient was started on 3% normal saline at 30 cc/h and given 1000-mg levetiracetam intravenously. Arrangements were made for an emergent transfer to a tertiary care hospital. The radiology-performed pelvic ultrasound returned with "complex hypervascular structure in uterine body/fundus. Multiloculated cystic structure in right adnexa." After transport to the receiving hospital, her serum beta

Supervising Editor: Prasanthi Govindarajan, MBBS, MAS.

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**FIGURE 1** Point of care transabdominal ultrasound image of uterus showing gestational trophoblastic diseases

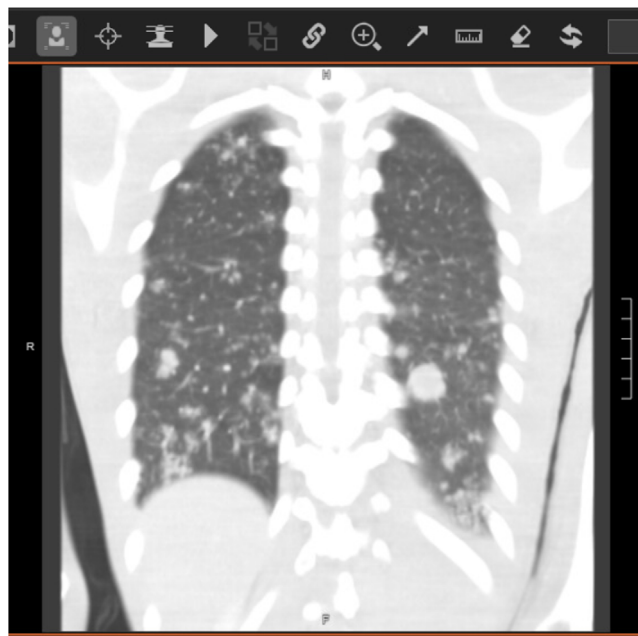


**FIGURE 2** Axial computed tomography scan image of brain showing frontal mass with cerebral edema and midline shift. L, left; R, right

HCG resulted at  $>1,000,000$  mIU/mL. She was admitted to the intensive care unit (ICU) with a metastatic gestational trophoblastic disease (GTD) diagnosis, underwent surgery for hematoma evacuation, and was started on chemotherapy. She was also noted to have numerous lesions in her lungs (Figure 3), likely metastatic in nature, and was diagnosed with hyperthyroidism. She had a good recovery of neurologic abilities on subsequent evaluations. It was later noted that she was diagnosed with molar pregnancy the year before with elevated beta HCG levels despite undergoing a dilation and curettage but was lost to follow-up. A month before her presentation described previously, she was reported to have a beta HCG of  $>10,000$  mIU/mL.

## 2 | CASE DISCUSSION

The patient's initial presentation was remarkable on an exam for expressive aphasia, likely from the frontal lobe lesion that developed



**FIGURE 3** Coronal computed tomography scan image of the chest showing multiple lung lesions concerning for metastatic disease. L, left; R, right

the hemorrhagic transformation. She was also noted to be tachycardic, and her initial complaint was possible dehydration from vomiting. Her urine was consistent with dehydration, but her renal panel was not abnormal. She was later diagnosed with hyperthyroidism, which is a known, but not well understood, complication of GTD. Interestingly, she had a negative urine pregnancy test, but had a markedly elevated serum beta HCG. This could be laboratory error but could also be from a phenomenon known as the Hook effect. Normally, the beta HCG is supposed to bind to a capture molecule and tracer/signal molecule and form a "sandwich." The excess is then washed away, and the immobilized "captured" molecule with the signal is then read by the assay against a standard concentration curve to read as positive or negative. In the Hook effect, the amount of beta HCG is so high, usually  $>500,000$  mIU/mL, that it overwhelms the capture molecule so that it does not bind with a high enough concentration to cause the test to become "positive." This can be seen with molar pregnancy because of the high levels of beta HCG.<sup>1</sup>

GTD is also known as molar pregnancy. This is often benign and results from an ovum without maternal chromosomes that is fertilized by  $\geq 1$  sperm or a normal ovum that is fertilized by 2 sperm. The incidence is reported as 1 in 1000 pregnancies.<sup>2</sup> The most common form of GTD is a hydatidiform molar pregnancy and can present as complete, partial, or invasive. These are characterized by hydropic villi, and in the case of invasive, can invade the myometrium or other sites. These are often identified by higher-than-expected beta HCG levels and a characteristically abnormal ultrasound, commonly identified as a "snowstorm pattern" or "cluster of grapes" and frequently with theca lutein cysts. GTD is now often identified in the first trimester, and treatment is uterine evacuation or hysterectomy.<sup>3</sup> The diagnosis is confirmed with a

histological evaluation of tissue. Other associated issues from GTD can be preeclampsia and hyperthyroidism, which typically are seen after the first trimester.

After a molar pregnancy,  $\approx 15\%$  of women will develop gestational trophoblastic neoplasia (GTN). This includes invasive molar pregnancy, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. After uterine evacuation,  $\approx 20\%$  of women with a molar pregnancy will have tissue still in the uterus or already have metastases.<sup>4</sup> Beta HCG levels are followed after GTD removal, and if not returning to 0, this indicates the patient has GTN. The large majority of GTN is either invasive molar tissue or choriocarcinoma. Fortunately, both are very responsive to chemotherapy, with a stage II/III disease cure rate of 90% to 100%, and with stage IV complete remission in 60% to 70%. Surgery and radiation may be used as adjuncts to treatment, especially with cerebral metastasis.<sup>3,5</sup>

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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**How to cite this article:** Lang J, Byars D, Martin C. Hook effect in gestational trophoblastic disease: An emergency department case presentation. *JACEP Open*. 2022;3:e12832. <https://doi.org/10.1002/emp2.12832>