Abstract:
Determining pregnancy status is vital in the approach to adolescent females with abdominal pain or vaginal bleeding. The prognosis of extrauterine pregnancies and gestational trophoblastic disease depends greatly on the ability to make an early diagnosis. Urine qualitative β human chorionic gonadotropin (β-hCG) tests are routinely used in emergency departments for pregnancy screening. However, point-of-care testing can be misleading in molar or late first-term pregnancies when β-hCG levels are extremely high. We report a case of an adolescent female presenting with a molar pregnancy in which point-of-care pregnancy testing was falsely negative due to the "high-dose hook effect." The "hook effect" affects almost all current qualitative assays and highlights the dangers of reliance on a single laboratory test.

Keywords:
molar pregnancy; false-negative; urine pregnancy test; point-of-care testing; hook effect

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Presented at the Section on Emergency Medicine Emergi-Quiz Case Competition, held at the American Academy of Pediatrics National Convention & Exhibition, San Diego, CA, October 2014.

1522-8401
Published by Elsevier Inc.

A 14-Year-Old Female With Abdominal Pain and Vaginal Bleeding

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A 14-year-old previously healthy Burmese girl with no significant medical history was brought to the regional pediatric emergency department by ambulance for acute onset of lower abdominal pain and vaginal spotting. The pain began 12 hours before arrival, and she denied pain before the day of presentation. She described the pain as sudden, sharp, and different from her normal menstrual pain. The patient denied fever, dysuria, or diarrhea and recent weight loss or weight gain. Her review of systems was otherwise negative. She stated that she was gravida 0, para 0, and her last menstrual cycle was reported to be 3 weeks before presentation. Menarche was described as starting 6 months previously, and all periods were described as light flow. She denied recent trauma or sexual intercourse.

Her medical history was unremarkable. She had no previous surgeries. She was taking no medications and had no drug allergies. Her immunizations were current. Her family medical history was negative for dysmenorrhea, bleeding disorder, or malignancy. She lived with her father and had no siblings. They emigrated from Burma to the United States 1 year ago. She was a freshman in high school and speaks English as a second language. She does not participate in after school programs or sports. She denied personal or family history of mental health disease. She denied sexual activity to multiple care providers. The history was obtained with the assistance of a Burmese interpreter with her father both present and absent from the examination room.

On examination, she was a pale adolescent female in visible distress, lying on her side with legs curled into her abdomen. Vital signs included a temperature of 38.0° C, heart rate of 110 beats per minute, blood pressure of 122/78 mm Hg, respiratory rate of 29 breaths per minute, and pulse oximetry of 99% on room air. Her weight was 50 kg (49th percentile) and height, 63 inches (45th percentile). She was tachycardic, without murmur, rub or gallop, and had good pulses. Her abdomen was diffusely tender with voluntary guarding throughout, with pain greatest in the lower abdomen. Bowel sounds were absent. There was no organomegaly. The external genital examination revealed scant vaginal bleeding with no evidence of trauma. The remainder of her physical examination was unremarkable.

Point-of-care testing included a negative β human chorionic gonadotropin (β-hCG) qualitative test and venous blood gas with a pH of 7.44; P_{CO_2} 19; base deficit −6; hemoglobin level 8.5; potassium 4.0; and sodium 138. Initial formal laboratory testing was significant for normal serum chemistry and liver function studies. A urinalysis revealed 2+ protein and 3+ blood, with a specific gravity of 1.023 and was negative for glucose, ketones, leukocyte esterase, and nitrates. C-reactive protein was 6 mg/dL; and the white blood cell count was 20.3 cells/mm^3 (75% neutrophils); hemoglobin level 7.8 g/dL; hematocrit 25; and platelet count was 343 000/mm^3. A 2-view abdominal radiograph was ordered and revealed no evidence of obstruction or free air. An additional bedside diagnostic study was performed, and a confirmatory laboratory test supported the presumptive diagnosis. Consultants were contacted, and arrangements were made for a transfer to the operating room.

DIFFERENTIAL DIAGNOSIS

The patient's most notable examination findings were her pale appearance, diffuse abdominal tenderness in the lower abdomen, and scant vaginal bleeding. Abdominal pain and vaginal bleeding are a presentation associated with several life-threatening conditions. A measured approach to this patient should focus on the girl's menstrual and pregnancy status. The pregnant patient is at risk for an extrauterine/ectopic pregnancy, molar pregnancy, or complication of an intrauterine pregnancy.[1] Blood loss from an ectopic or intrauterine pregnancy complication can lead to hypovolemic shock and ultimately death if not treated. Delayed diagnosis of molar pregnancy cannot only lead to worsening blood loss but also increases the risk of developing choriocarcinoma.[2] Given the importance of establishing this diagnosis, it is important to note the limitation of qualitative β-hCG testing. False-negative results can occur with faulty test cartridges, incorrect interpretation of results, levels below test threshold (<30 mIU/mL), or with excessively dilute urine samples (Table 1).[3] If the clinician has determined that the patient is not pregnant, then the broader differential is considered (Table 2).[4]

Dysmenorrhea is a common medical condition defined by pain during menstruation that interferes with daily activities. This can be caused by normal menses or specific anatomic pathology, such as ovarian cysts or uterine fibroids. An intact or ruptured ovarian cyst, hemorrhagic cyst, and uterine or cervical malignancy may also be considered in the differential. Vaginal foreign bodies are also an important consideration in the female presenting with bleeding and pain and no concern for pregnancy. Menorrhagia is characterized by heavy and prolonged menses and can be painful in cases of endometriosis. Blood thinners, antiplatelet agents, and bleeding disorders such as hemophilia or von Willebrand disease should be considered in cases of prolonged bleeding and pain. Pelvic inflammatory disease can present with bleeding and severe lower abdominal pain. This condition can be associated with tuboovarian abscess and septic shock. Sexual abuse can lead to cervical or vaginal lacerations, which can be associated with hemodynamically significant blood loss. Abortions performed in the clinic or outside the medical system can lead to uterine trauma or retained products. Endometritis is a concern in these patients who undergo post-spontaneous or planned abortions.

CASE PROGRESSION AND DIAGNOSIS

The degree of pain and diffuse guarding led to a bedside transabdominal ultrasound being performed by the pediatric emergency medicine fellow. No free fluid was seen on the focused assessment with sonography for trauma examination, but the uterus was noticed to be enlarged with echogenic,

TABLE 1. Causes of falsely negative or low β-hCG testing.

"High-dose hook effect" or "hook effect"
High levels of β-hCG fragment
β-hCG level below test threshold
Inappropriate interpretation
Expired of faulty cartridge
Overdiluted urine