

Case Report

Ruptured Ectopic Pregnancy with a Negative Urine Pregnancy Test

Urgent message: Ectopic pregnancy must be considered in women of childbearing age who present with abdominal pain—even if ‘ruled out’ by a negative hCG test.

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Introduction

The incidence of ectopic pregnancy is estimated to be 19.7 per 1,000 pregnancies and is responsible for 9% of pregnancy-related deaths.¹ Ectopic pregnancy is always near the top of the differential diagnosis for abdominal pain in women of childbearing age, but is generally considered to be ruled out by a negative urine human chorionic gonadotropin (hCG) level.

Standard urine hCG tests are able to detect β hCG levels as low as 20 mIU/mL. This case report shows that an ectopic pregnancy can exist and be large enough to rupture at β hCG levels below the threshold detectable by urine pregnancy screening tests. Considering the mortality and morbidity associated with a ruptured ectopic pregnancy, this case report emphasizes the necessity of confirming a negative serum quantitative hCG before ruling out ectopic pregnancy.

[*Note: While this case report concerns a patient who presented in an ED setting, abdominal pain is a common presenting complaint in urgent care. The teaching points are highly relevant to the urgent care practitioner.*]

Case Report

A 36-year-old female gravida 0 prima 0 whose last menstrual period was two months prior presented to the emergency department with the chief complaint of severe abdominal pain that awakened her from sleep. She described the pain as 10 out of 10 in severity (i.e., the worst pain imaginable in the patient’s estimation); the pain was greatest in the left lower quadrant, and became worse with any motion.

The review of systems was pertinent for the pres-

ence of vaginal spotting and right shoulder pain, and for the absence of chest pain, shortness of breath, syncope, or fever.

The patient’s past medical history was significant for infertility, fibroids, and irregular menses. She had no prior surgical history, took no medications, and had no allergies. She had no risk factors for ectopic pregnancy: no history of sexually transmitted diseases or pelvic inflammatory disease, no prior gynecological surgery, no intrauterine device use, and she was not taking fertility medications.

Her initial vitals were as follows:

- **BP** 90/52
- **Heart rate** 103
- **Respiratory rate** 24
- **Temperature** 36.7 C (98.1°F)
- **Pulse oximetry** 100% on room air

The patient was clearly uncomfortable, but not in acute distress. Cardiac exam revealed a regular rate and rhythm. Pulmonary exam was clear to auscultation bilaterally. Abdominal exam revealed positive bowel sounds, soft without guarding but extremely tender to palpation, with diffuse rebound and a positive pelvic shake. Pelvic exam was notable for cervical motion tenderness and bilateral adnexal region tenderness; uterine and adnexal size were difficult to assess secondary to pain.

The urine hCG was negative. Intravenous access was obtained, and a complete blood count, chemistry panel, blood type and cross, and serum quantitative hCG were sent to the laboratory. The patient was given intravenous fluids and the ob/gyn service was promptly consulted.

The ob/gyn physician performed a bedside ultrasound, which showed free fluid and a left adnexal mass; the patient was taken immediately to the operating room with the presumptive diagnosis of a ruptured hemorrhagic ovarian cyst.

In the operating room, she was found to have one liter of free blood and a ruptured left tubal pregnancy.

A left salpingectomy was performed. The patient did well and was discharged home on postoperative day 2.

The serum quantitative hCG was eventually reported as 13mIU/mL.

Discussion

β hCG is produced by the trophoblasts of both intrauterine and ectopic pregnancies.¹ Using modern assays that can detect serum β hCG levels as low as 5 mIU/mL, the hormone may be detected in the serum as early as one week postconception.¹

β hCG levels in normal intrauterine pregnancies double every 1.4 to 2.1 days; therefore, urine pregnancy tests which can detect β hCG levels as low as 20 mIU/mL to 25 mIU/mL are usually positive by the first day of the next expected menstrual period. Even in a normal intrauterine pregnancy, false negative urine pregnancy results may occur if the urine is very dilute.

Four theoretical mechanisms have been proposed to explain unusually low or undetectable β hCG levels in ectopic pregnancies:²

- Trophoblast degeneration with resultant decrease or absence of hormone production (more likely to occur in chronic ectopic pregnancies)
- Very small volume of trophoblastic tissue, likely due to the slow growth of an improper implantation
- Defective β hCG synthesis by ectopic trophoblasts; cases have been documented by immunohistochemical stains
- Rapid clearance of β hCG from the serum, possibly related to defective hormone synthesis causing a modified molecule with a higher rate of clearance

A negative urine hCG does not definitively rule out ectopic pregnancy, regardless of the date of the last menstrual period. If suspicion of pregnancy exists, a serum quantitative β hCG should be obtained.

Because β hCG levels do not rise normally in ectopic



pregnancies, ectopic pregnancies can be large enough to rupture at very low β hCG levels.

An article by Brennan notes that 10% of ectopic pregnancies with a quantitative β hCG <100 mIU/mL were ruptured, and that 7% of all ectopic ruptures occurred at levels <100 mIU/mL.³

Furthermore, Galstyan, et al, found the range in serum β hCG between ruptured and unruptured tubal ectopic pregnancies to be broad and non-significant.⁴ A low β hCG level should not be considered reassurance that rupture is unlikely.

It is commonly accepted that one should not expect to see ultrasonographic findings consistent with an intrauterine pregnancy with a quantitative β hCG of less than 1200 mIU/mL.⁵ However, this discriminatory threshold does not apply to ectopic pregnancies; it would be a dangerous error to forego ultrasound to rule out an ectopic on the basis of a low serum hCG. One study demonstrated that 56% of ectopic pregnancies confirmed by ultrasound had serum hCG levels below 500 mIU/mL.⁶

Teaching Points

This case highlights several important points:

- A negative urine hCG does not rule out pregnancy.
- Even at very low β hCG levels, ectopic pregnancies can (and do) rupture.

“Negative screening tests may lull the busy practitioner into a false feeling of security.”

- A β hCG below the accepted discriminatory range for normal pregnancies does not preclude the utility of ultrasound in ectopic pregnancies.

Conclusion

Ectopic pregnancies that present to an acute care setting may be large enough to rupture at β hCG levels below the threshold detectable by urine pregnancy screening tests or the discriminatory range of serum β hCG levels.

While similar cases have been reported in the past,⁷⁻⁹

they are infrequent; thus, a similar presentation with negative screening tests may lull the busy practitioner into a false sense of security.

This case serves to emphasize the importance of obtaining an ultrasound, irrespective of urine and/or serum hCG levels any time an ectopic pregnancy is suspected. ■

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“Search others for their virtues, thyself for thy vices.”

Benjamin Franklin (1706-1790), American author, diplomat, inventor, printer, scientist, and Founding Father

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