

# Hemorrhagic Shock From a Ruptured Ectopic Pregnancy in a Patient With a Negative Urine Pregnancy Test Result

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Ectopic pregnancy has been increasing in frequency over the past 2 decades. The sudden rupture of a fallopian tube caused by ectopic pregnancy can lead to hemorrhagic shock and death if not diagnosed and treated in a timely fashion. The emergency physician is often the health professional that is called on to make the diagnosis and coordinate timely and effective intervention. The first step in the diagnosis of ectopic pregnancy is demonstration of pregnancy by means of a rapidly performed and sensitive qualitative urine test for the  $\beta$ -subunit of human chorionic gonadotropin ( $\beta$ -hCG). A negative urine pregnancy test result will generally be used to exclude ectopic pregnancy from further consideration. The following is a report of a patient presenting to an emergency department with hypovolemic shock in conjunction with 2 negative urine  $\beta$ -hCG analysis results and a quantitative serum  $\beta$ -hCG level of 7 mIU/mL, a value less than the lower limit of detection for the highly sensitive qualitative urine and serum tests. This case report demonstrates the importance of further consideration of the diagnosis of ectopic pregnancy in the setting of a negative urine pregnancy test result.

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## INTRODUCTION

The frequency of ectopic pregnancy has been increasing over the past 2 decades. In 1992, the Centers for Disease Control and Prevention reported an ectopic pregnancy rate of 19.8 per 1,000 pregnancies compared with a rate of 3.7 per 1,000 pregnancies in 1980.<sup>1,2</sup> Although early diagnosis and modern management techniques have contributed to a marked decline in mortality, ectopic pregnancy remains one of the leading causes of maternal morbidity and mortality.<sup>3</sup> Undiagnosed ectopic pregnancy can result in rupture of the fallopian tube with intra-abdominal bleeding, leading to hemorrhagic shock and death. The most common manifestations of ruptured ectopic pregnancy are abdominal pain, lightheadedness, and vaginal bleeding, which collectively can be of moderate sensitivity but low specificity.<sup>4</sup> The first essential branch point in the majority of guidelines for the management of ectopic pregnancy includes a sensitive qualitative urine  $\beta$ -subunit of human chorionic gonadotropin ( $\beta$ -hCG) assay. A negative test result is used to exclude the diagnosis of pregnancy and thereby a possible ectopic gestation.<sup>5-8</sup> The following case is a rare emergency department presentation of a patient with hemorrhagic shock caused by ruptured ectopic pregnancy in the setting of a repeatedly negative urine pregnancy test result and a very low quantitative  $\beta$ -hCG level.

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## CASE REPORT

A 44-year-old woman presented to the ED by paramedic ambulance after a syncopal episode. The emergency medical technician reported that the patient had sudden onset of severe abdominal pain while eating lunch in a restaurant. She had a single episode of emesis, followed by a transient loss of consciousness. Vital signs at the scene included palpable blood pressure of 80 mm Hg and pulse rate of 65 beats/min. Out-of-hospital management included oxygen administered through a nasal cannula and two 0.5-L fluid challenges of intravenous normal saline solution. On arrival in the ED, the patient

was observed to be pale and diaphoretic and was complaining of severe and diffuse abdominal pain, along with fatigue and generalized numbness. She denied vaginal bleeding but reported her last menstrual period to be approximately 6 weeks previous. Vital signs in the ED were blood pressure 72/40 mm Hg, pulse rate 59 beats/min, respiratory rate 28 breaths/min, temperature 34.4°C (94°F), and oxygen saturation 100% on 15 L of oxygen. Physical examination revealed normal heart and lungs, and an abdominal examination was remarkable for diminished bowel sounds, as well as diffuse tenderness to palpation, with guarding and rebound. No vaginal bleeding was noted. Laboratory test results included a hemoglobin and hematocrit level of 8.8 g/dL and 25.2%, respectively. Two sequential, highly sensitive, qualitative urine  $\beta$ -hCG assay (Quidel cards QS urine/serum HCG screen, Quidel Corporation, San Diego, CA) results were negative on different samples. A chemistry panel was normal, with the exception of a potassium level of 2.6 mEq/dL and a glucose level of 212 g/dL. The arterial blood gas on 15 L of oxygen was pH 7.29,  $P_{CO_2}$  was 31 mm Hg,  $P_{O_2}$  was 327 mm Hg, and base deficit was 11.8. A quantitative serum  $\beta$ -hCG assay (Bayer Advia Centaur, Bayer, Leverkusen, Germany) was sent from the ED on initial presentation, but results were not available for several hours.

A presumptive diagnosis of hypovolemic shock as a result of intra-abdominal bleeding was made, and the patient was treated with an infusion of 6 L of normal saline solution and 2 units of packed RBCs over 45 minutes. An emergency surgical consultation was obtained. Although an ectopic pregnancy was strongly considered on the basis of the patient's age and clinical presentation, this diagnosis was not readily accepted because of the negative urine pregnancy test results. A bedside ultrasonogram was obtained, which revealed a large amount of free intraperitoneal fluid and a 2.8-cm cystic pelvic mass interpreted as a likely ectopic gestation. A repeat hematocrit level measured 45 minutes after presentation was 12%. Systolic blood pressure remained at or less than 90 mm Hg throughout the patient's stay in the ED. Arrangements were made for an emergency lapar-

omy, and RBC infusions were continued. The time from ultrasonography to laparotomy was approximately 50 minutes.

An open laparotomy was performed that revealed a ruptured right ectopic pregnancy with a free intraperitoneal blood volume estimated at 3,000 mL. A right salpingectomy was performed, and the patient was stabilized with further transfusion of packed RBCs and crystalloid solution. She had an uncomplicated postoperative course and was discharged home 4 days after admission. The quantitative serum  $\beta$ -hCG value obtained in the ED was subsequently reported at 7 mIU/mL approximately 2 hours after the test was ordered.

## DISCUSSION

Ectopic pregnancy continues to be one of the leading causes of death in women of childbearing age.<sup>3</sup> Most management guidelines use a sensitive qualitative urine  $\beta$ -hCG test as the first step in the evaluation of possible ectopic pregnancy.<sup>5-8</sup> A negative test result generally eliminates further consideration of this diagnosis. It is estimated that up to 1% of ectopic pregnancies will be associated with  $\beta$ -hCG values of less than 20 mIU/mL and will therefore escape detection by most urine  $\beta$ -hCG assays, which promote sensitivities of greater than or equal to 25 mIU/mL urine.<sup>9-14</sup> Ectopic pregnancies associated with such low  $\beta$ -hCG values are generally early or very small. An ectopic gestation sufficient to result in fallopian tube rupture and hemorrhagic shock would be expected to produce sufficient  $\beta$ -hCG to yield a positive urine test result.

There are 4 proposed mechanisms to account for low or absent serum and urine  $\beta$ -hCG values in ectopic pregnancies: (1) trophoblast degeneration with cessation of hormone production; (2) a very small mass of villi producing the hormone; (3) defective biosynthesis of  $\beta$ -hCG hormone production; and (4) enhanced circulatory clearance of the hormone.<sup>14</sup> An alternative explanation may relate to aggressive crystalloid hydration, which may dilute the urine to a degree sufficient to result in a false-negative urine  $\beta$ -hCG assay result.<sup>15</sup> However, in this scenario, it would be expected that the

serum  $\beta$ -hCG assay results should remain positive. The patient described in this case report, although the recipient of significant amounts of intravenous crystalloid before urine sampling, had a coincident quantitative  $\beta$ -hCG level that would not be expected to yield a positive qualitative urine test result.

An extensive review of the literature has revealed false-negative urine and serum  $\beta$ -hCG test results of less than 1%; however, only a single report of hemorrhagic shock from a ruptured ectopic pregnancy with a low or undetectable level of  $\beta$ -hCG was identified.<sup>11</sup> Reports of 2 patients with ruptured chronic ectopic pregnancies and hemoperitoneum without overt shock have also been reported. Chronic ectopic pregnancies present similarly to acute ectopic pregnancies, except that the symptoms are generally longer in duration, and the pain is more gradual in onset.<sup>16</sup> In the patient presented here, the repeatedly negative urine pregnancy test results contributed to a delay in surgical intervention because of a reluctance to accept a diagnosis of ruptured ectopic pregnancy. This case demonstrates the importance of continued consideration of the diagnosis of ectopic pregnancy, despite a negative urine test result and even a very low quantitative serum  $\beta$ -hCG measurement. In addition to an ectopic pregnancy, a ruptured corpus luteum cyst should be considered as an alternative diagnosis. Although it is unusual for a ruptured corpus luteum cyst to present with massive hemoperitoneum and hemorrhagic shock, cases with this presentation are noted in the recent medical literature.<sup>17-19</sup>

In conclusion, an ectopic pregnancy large enough to result in fallopian tube rupture and hemorrhagic shock can occur in the setting of very low quantitative serum  $\beta$ -hCG levels and negative sensitive qualitative urine test results. Although screening for ectopic gestation with a sensitive qualitative urine  $\beta$ -hCG test remains a very valuable and generally reliable tool, it is essential that in an appropriate clinical setting the diagnosis of ectopic pregnancy not be discounted on the basis of negative pregnancy test results. In patients without overt shock but significant pain and a negative  $\beta$ -hCG assay result, adjunct radiographic studies, such as computed tomography or ultrasonography, may be useful in

determining the cause of the patient's symptoms. Emergency laparotomy is indicated for patients with presumed hypovolemic shock.

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## REFERENCES

- Centers for Disease Control and Prevention. Current trends ectopic pregnancy—United States, 1990-1992. *MMWR Morb Mortal Wkly Rep.* 1995;44:46-48.
- Lipscomb GH, Stovall TG, Ling FW. Nonsurgical treatment of ectopic pregnancy. *N Engl J Med.* 2000;343:1325-1329.
- Dorfman SF, Grimes DA, Cates W Jr, et al. Ectopic pregnancy mortality, United States, 1979-1980. *Obstet Gynecol.* 1984;64:386-390.
- Aboud E, Chaliha C. Nine year survey of 138 ectopic pregnancies. *Arch Gynecol Obstet.* 1998;261:83-87.
- Brennan DF. Ectopic pregnancy—part II: diagnostic procedures and imaging. *Acad Emerg Med.* 1995;2:1090-1097.
- Buck RH, Gihwala N, Rom L, et al. Detection of urinary human chorionic gonadotropin by rapid immunoconcentration method is the first-line test for suspected ectopic pregnancy. *Fertil Steril.* 1987;48:761-765.
- Kingdom JC, Kelly T, MacLean AB, et al. Rapid one step urine test for human chorionic gonadotrophin in evaluating suspected complications of early pregnancy. *BMJ.* 1991;302:1308-1311.
- ACEP Clinical Policies Committee, Clinical Policies Subcommittee on Vaginal Bleeding. Clinical policy for the initial approach to patients presenting with a chief complaint of vaginal bleeding. *Ann Emerg Med.* 1997;29:435-458.
- Barnes RB, Roy S, Yee B, et al. Reliability of urinary pregnancy tests in the diagnosis of ectopic pregnancy. *J Reprod Med.* 1985;30:827-831.
- Bozoklu S, Bozoklu E, Ciftci A, et al. Ruptured ectopic pregnancy with undetectable  $\beta$ -hCG levels coexisting with acute appendicitis. *Acta Obstet Gynecol Scand.* 1997;76:181-182.
- Lonky NM, Sauer MV. Ectopic pregnancy with shock and undetectable  $\beta$  human chorionic gonadotropin: a case report. *J Reprod Med.* 1987;32:559-560.
- Maccato ML, Estrada R, Faro S. Ectopic pregnancy with undetectable serum and urine  $\beta$ -hCG levels and detection of  $\beta$ -hCG in the ectopic trophoblast by immunocytochemical evaluation. *Obstet Gynecol.* 1993;81:878-880.
- Olson CM, Holt JA, Alenghat E, et al. Limitations of qualitative serum  $\beta$ -hCG assays in the diagnosis of ectopic pregnancy. *J Reprod Med.* 1983;28:838-842.
- Taylor RN, Padula C, Goldsmith PC. Pitfall in the diagnosis of ectopic pregnancy: immunocytochemical evaluation in a patient with false-negative serum  $\beta$ -hCG levels. *Obstet Gynecol.* 1988;71:1035-1038.
- Cartwright PS, Victory DF, Moore RA, et al. Performance of a new enzyme-linked immunoassay urine pregnancy test for the detection of ectopic gestation. *Ann Emerg Med.* 1986;15:1198-1199.
- Brennan DF, Kwatra S, Kelly M, et al. Chronic ectopic pregnancy—two cases of acute rupture despite negative  $\beta$ -hCG. *J Emerg Med.* 2000;19:249-254.
- Sarihan H, Unal M, Ozoran Y. Massive hemoperitoneum due to spontaneous rupture of ovarian cysts in children. A report of 2 cases. *S Afr J Surg.* 1996;34:44-46.
- Hertzberg BS, Kliewer MA, Paulson EK. Ovarian cyst rupture causing hemoperitoneum: imaging features and the potential for misdiagnosis. *Abdom Imaging.* 1999;24:304-308.
- Kayaba H, Tamura H, Shirayama K, et al. Hemorrhagic ovarian cyst in childhood: a case report. *J Pediatr Surg.* 1996;31:978-979.