Journal of Obstetrics, Gynecology and Cancer Research | ISSN: 2476-5848

A Case Report of Ruptured Ectopic Pregnancy with Negative HCG -beta Test

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Article Info

10.30699/jogcr.9.5.587

Received: 2023/10/07;
Accepted: 2024/02/02;
Published Online: 18 Aug 2024;

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ABSTRACT

Background & Objective: Although 1% to 2% of all pregnancies are ectopic, ectopic pregnancy (EP) is the most frequent obstetrical disease leading to maternal mortality and morbidity in the first trimester. The basic diagnostic method for EP is the human chorionic gonadotropin (HCG) test and transvaginal ultrasound. There are some rare EP cases with a negative HCG -beta test.

Case presentation: A 31-years-old woman was referred to the emergency department with hypogastric, periumbilical, right upper quadrant intermittent pain, vaginal bleeding, and prior history of EP 7-months ago that was treated with methotrexate and her intrauterine device had been removed at that time. Her last menstrual period was undetermined. Although the qualitative HCG- betatest was negative (2.08 IU /ml), the ultrasound examination showed an 43×53 mm echogenic, heterogenic complex solid mass in the left adnexa and a large amount of echogenic fluid demonstrating hemoperitoneum. Surgery because of the exceeded abdominal pain, revealed active bleeding in the left salpinx due to a ruptured EP.

Conclusion: Management of patients suspected of EP with a negative HCG-beta test is difficult. In these uncommon cases in an emergency, computed tomography, ultrasound and diagnostic laparoscopy or laparotomy can improve the prognosis of the patient.

Keywords: Ectopic Pregnancy, HCG-beta, Shock, Transvaginal Ultrasound

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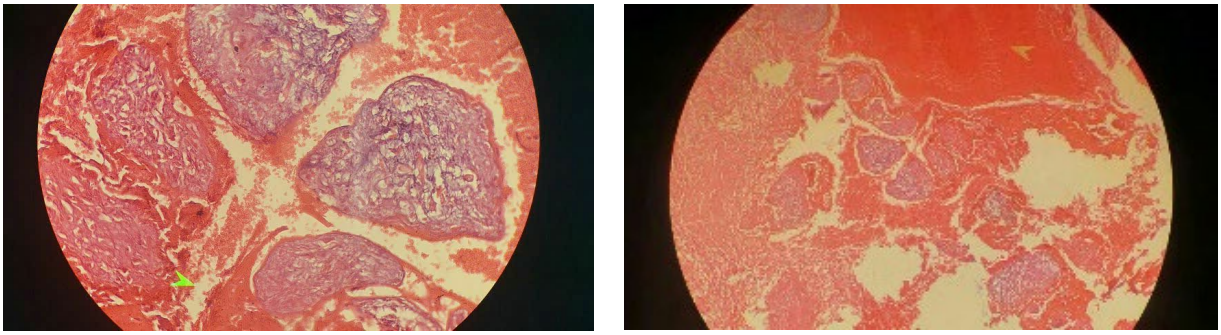
Introduction

When a blastocyst implants in another site of the endometrial cavity, EP occurs. Although only 1% to 2% of all pregnancies are ectopic, it is one of the important obstetrical complications, which leads to serious maternal mortality and morbidity. A study of a single large health network from 1997 to 2000 demonstrated a rate of 20.7 per 1000 pregnancies **(1)**. Complications from EP and the related treatment procedures may cause recurrent EP and future infertility. Among pregnant women referring to an emergency department in the first -trimester with bleeding and/or pain, the range of EP is 6 to 16 percent **(2)**. EP is the most common obstetrical cause of maternal mortality in the first trimester of pregnancy and accounts for 4 to 10 percent of all pregnancy-related deaths. In older women, the risk of EP increases **(3)**. The location of EP in 96 percent of cases is the fallopian tube. Rupture of tubal EP can lead to hemorrhagic shock, and then the early diagnosis of EP is critical. Before rupture, an EP is diagnosed based on laboratory and ultrasound findings. The primary laboratory test is the HCG - beta test- quantitative. HCG is a pregnancy hormone, which is detectable in body fluids within a short time after embryo implantation. The presence of HCG in urine is the basis for a home pregnancy test. A variety of isoforms of HCG which are detectable in urine, contain intact HCG, nicked forms, free α and free β subunits of HCG, also the β-core fragment of HCG (βcf-HCG; this breakdown product of HCG found in urine only) **(4, 5)**. There are some rare EP cases reported with a negative HCG - beta test. Therefore, the negative HCG - beta test can lead to missed diagnosis of EP. In these cases, tubal rupture and hemoperitoneum, and shock can occur.

Case Presentation

A 31-year-old woman was referred to the emergency ward with hypogastric, periumbilical and right upper quadrant intermittent pain, nausea, and vomiting started from the morning of admission, and also vaginal bleeding (spotting) from one week ago after discontinuing oral contraceptive pills which had

consumed since 3 weeks ago. She was gravida3 para2 EP1 with a history of two natural vaginal deliveries and history of EP 7-months ago that was treated with methotrexate and her intrauterine device had been removed at that time. The HCG -betatest-quantitative was serially checked and the final test was 49 IU/ml six months ago. Her past medical history was renal stones and surgery due to cleft palate in childhood. Physical examination revealed vital signs with blood pressure of 80/60 mm Hg and a pulse rate of 98 beats/minute. Abdominal examination showed tenderness in the right lower quadrant and hypogastric without guarding and rebound tenderness. Laboratory evaluation demonstrated a negative HCG -beta test-qualitative. The Hemoglobin was 9.7 gr/dl and WBC was 13.2 × 10^3 /µl. Six hours later, the abdominal pain increased, especially in the hypogastric and right upper quadrant progressively and blood pressure and pulse rate were 75/60 mm Hg and 110 beats/min. The hemoglobin concentration dropped from 9.7 to 7 gr/dl. Ultrasound examination revealed a 43×53 mm complex solid mass in the left adnexal that was echogenic, heterogenic, and had vascularity and a large amount of echogenic fluid in the pelvic cavity, demonstrating acute hemoperitoneum. During surgery, massive hemoperitoneum and active bleeding in the infundibulum of the left salpinx due to ruptured EP were found and the right salpinx was normal. A left salpingectomy was performed. The HCG -beta test-quantitative was 2.08 IU /ml. The patient was discharged after two days. Pathology results confirmed ectopic pregnancy (Figures 1, 2).



Figures 1, 2. Chorionic villi are present characteristic with ectopic pregnancy

Discussion

EP is the most frequent obstetrical cause of maternal mortality in the first trimester. If we don't consider clinical features, serious mistakes will occur. History of regular menses will cause excluding EP in some cases but not in all. There is a possibility of any menstrual cycle history in EP, amenorrhea less than 4 weeks or greater than 12 weeks was reported in about 15% of cases, including the ruptured EP. Even sexual history is not reliable and may be problematic to exclude pregnancy risk. At least, there is a 10% chance of pregnancy in women reporting normal menses, and in those who reported "there is no chance that they could be pregnant" **(6)**. Historical criteria are not successful in excluding pregnancy in emergency department patients. Transvaginal ultrasound and HCG -beta test are the main diagnostic assays in EP. If we do not check the HCG- beta test, EP will be confused with other diseases, like ovarian torsion, appendicitis, pelvic peritonitis, ovarian cyst, and miscarriage. HCG -beta test with laparoscopy and histological examination differentiate between them. Negative HCG in urine and blood test may cause an incorrect diagnosis of EP. Consequently, the fallopian tube will be ruptured. EP with a negative HCG- beta test is rare. Relatively 1% of ectopic pregnancies have negative urine pregnancy tests and the HCG- beta test is lower than 20 mIU/mL. In intrauterine pregnancy, trophoblasts secrete HCG that during two weeks of fertilization, its blood levels rise 50–300 mIU/mL. When the HCG -beta test is ≥25 mIU/mL, the HCG in urine will be detectable. In intrauterine pregnancy, HCG- beta test-quantitative level doubles relatively every 48–72 hours until 60–90 days after fertilization. This rise occurs in 71% of pregnant women with normal pregnancy and 15% of EP cases. The mechanism of low HCG- beta test levels in EP is degeneration of trophoblasts, small chorionic villi producing HCG, abnormal HCG synthesis, and increased HCG clearance. In abortion cases, HCG -levels decrease relatively one-half in 48 hours and will be zero after several days **(7)**. When there is a high level of βcf-HCG, it can cause false- negativity in point-of-care and over-the-counter pregnancy tests **(8-10)**. The "hook effect" for intact part or free β-HCG is the main cause **(5).** The retrospective study about EPs showed in 25% of patients HCG -beta test-quantitative was less than 1000 mIU/mL while pelvic ultrasound was suspected of EP. Because HCG assays are not sensitive, more diagnostic efforts are needed in unstable cases or highly suspicious patients. In unusual features of EPs, diagnostic laparoscopy or laparotomy may improve prognosis of patients. Ultrasound and computed tomography can help to diagnose hemoperitoneum and adnexal mass.

Conclusion

EP is the most frequent obstetrical cause of maternal mortality in the first trimester of pregnancy. Relatively 1% of EPs have a negative urine pregnancy test and HCG -beta level < 20 mIU/mL **(6)**. The emergency physician should be aware that unexplained intra-abdominal hemorrhage or severe pelvic pain, may be ruptured EP that can present with a negative HCG in urine. Our case shows clinical diagnostic challenges for EP. We should not rule out EPs with negative pregnancy tests. If a pregnant woman has symptoms that may be EP, the HCG -beta test-quantitative cannot help to determine if ultrasound is necessary or not. In one study, in relatively 25% of EPs in the emergency department, the HCG -beta test-quantitative was < 1500 mIU/mL, which was the traditional HCG -betatest level that an intrauterine pregnancy can be detectable on ultrasound. The retrospective study on EPs have found out in 25% of patients HCG- beta test-quantitative was < 1000 mIU/mL, while pelvic ultrasound was suspicious for EP **(7)**. In uncommon cases of EP, ultrasound, computed tomography, and diagnostic laparoscopy or laparotomy can help to save a patient's life.

Acknowledgments

The authors would like to express their appreciation to all the individuals who participated in this study.

Authors' Contribution

Each author participated in data analysis, drafting, and revising of the manuscript, and consented to assume responsibility for all aspects of this project.

Conflict of Interest

The authors declare no conflict of interest in planning, researching, and submitting the manuscript.

Funding

The research was not specifically funded by any public, commercial, or not-for-profit agencies.

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How to Cite This Article:

Talebian, M., Talebi Mazreshahi, Z., Khosravi Mashizi, E., Khalili, N. A Case Report of Ruptured Ectopic Pregnancy with Negative HCG -beta Test. J Obstet Gynecol Cancer Res. 2024;9(5):587-90.

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