



# A Rare Case of Ruptured Ectopic Pregnant Woman Present With Double Negative Pregnant Test

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The urine pregnancy test is one of the most useful methods for initially excluding pregnancy emergencies in the emergency department (ED). Although most urine pregnancy tests are regarded to be up to 99% accurate, false-negative results may lead ED physicians toward considering incorrect diagnoses, mask critical conditions, and even influence patient safety. Therefore, blood pregnancy tests (quantitative measurements) are clinically used for second-line screening. A double false-negative result from two pregnancy tests is very rare and has scarcely been reported for life-threatening ruptured ectopic pregnancy patients. In this report, for the first time, we describe a rare case of a 32-year-old female who suffered a life-threatening ruptured ectopic pregnancy and who had a double pregnancy test (both urine and blood) that was a false negative.

**Key words:** *ectopic pregnancy, pregnancy test, false negative*

## Introduction

An ectopic pregnancy occurs in approximately 1.9% of all pregnant women and has a high mortality rate (up to 10%) in the first trimester, especially in those with silent intra-abdominal hemorrhaging or even delayed diagnosis.<sup>1-3</sup> The classical symptoms of ectopic pregnancy are well known and include lower abdominal pain, vaginal bleeding, shoulder tip pain, and a palpable adnexal mass.<sup>4</sup> However, atypical presentations are also not infrequent and challenge primary physicians. In the emergency department (ED), the urine pregnancy test is globally used before radiological imaging studies; furthermore, it is recommended to rule out pregnancy-associated disease (i.e., ectopic pregnancy), especially when an intrauterine pregnancy has not been confirmed. Additionally, blood pregnancy tests (quantitative measurements) are

clinically used for second-line screening.<sup>5,6</sup> A double false-negative result from two pregnancy tests is very rare and has never been reported in life-threatening ruptured ectopic pregnancy patients. In this report, for the first time, we present a rare case of a 32-year-old female who suffered a life-threatening ruptured ectopic pregnancy and who had a double pregnancy test (both urine and blood) that was a false negative.

## Case Report

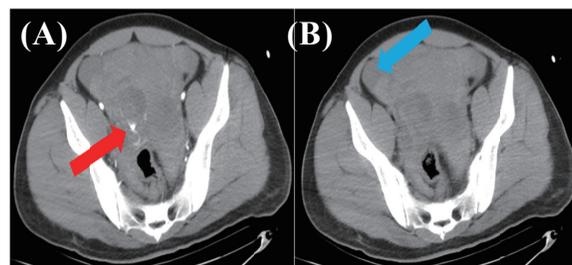
A 32-year-old female, Gravida 2 Para 1, was sent to our ED by ambulance after suffering sudden onset syncope at the train station. According to the prehospital emergency medical service records, she did not suffer trauma, a seizure attack, or a hypoglycemic episode. Her consciousness returned before arriving at our ED. In the ED triage, her Glasgow coma

Received: September 17, 2019; Revised: January 6, 2020 (2nd); Accepted: January 31, 2020.

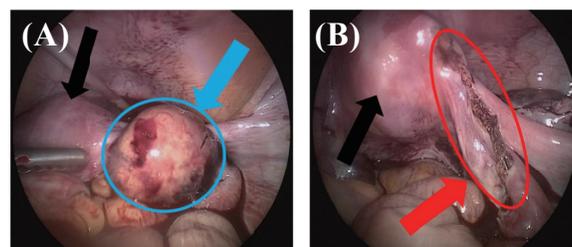
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scale score was E4M6V5. At the time of presentation, her skin color was pale, and her blood pressure was only 64/47 mmHg with a heart rate of 115 beats per minute (bpm). Her major complaint was progressive abdominal pain accompanied by cold sweating four hours previously.

Fluid resuscitation was activated immediately due to unstable vital signs. Upon initial ED physical examination, she was straight-faced and denied any recent trauma or cardiogenic/systemic/neurological disease history, but she had taken some weight-loss drugs (with unknown components). Her abdomen was soft without obvious tenderness or guarding. However, although her menstrual period was previously regular, this period was delayed for two months. Abdominal sonography was performed by an emergency physician in the ED and revealed abundant hyperechoic fluid collection over the whole abdomen and no evidence of solitary organs or great vessel injuries. Spontaneous hemoperitoneum with hemorrhagic shock was initially suspected, and an emergency blood transfusion was prescribed. Her laboratory data revealed hemoglobin: 14.5 g/dL; platelet count: 270000/uL; prothrombin time: 10.2 seconds; and activated partial thromboplastin time: 25.1 seconds. Since the menstrual period was delayed for two months, ectopic pregnancy was reasonably suspected. However, the initial urine pregnancy test showed a negative result, and the levels of the secondary blood  $\beta$  subunit of human chorionic gonadotropin ( $\beta$ -hCG) were only 7.4 mIU/mL (normal range < 10 mIU/mL). In addition, she denied having a bleeding tendency, and her blood coagulation functions were also normal. Computerized tomography (CT) of the abdomen was performed immediately and demonstrated active bleeding from the adnexa with abundant hemoperitoneum (Fig. 1). After initial resuscitation, her blood pressure returned to 98/66 mmHg, and her heart rate decreased to 88 bpm. After a consultation with the gynecologist, internal bleeding associated with the adnexal mass rupture was suspected, and emergency surgery consisting of laparoscopic right salpingectomy was performed (Fig. 2). Total blood loss was 6000 mL during the operation. After surgery, she was admitted to our surgical intensive care unit and discharged alive on day four after the operation. Finally, the pathology report revealed ectopic pregnancy, degenerated chorionic villi, trophoblasts, and blood clots.



**Fig. 1.** The representative of abdominal computed tomography (pelvic) with and without contrast enhancement in coronal view. (A) Arterial phase image. An active bleeding source was noted with contrast extravasation (red arrow). (B) Non-contrast enhance phase image. A few abundant hemoperitoneum (blue arrow) was noted.



**Fig. 2.** The representative of pictures during operation. (A) Pre-laparoscopic right salpingectomy and hemoperitoneum were noted around the uterus (black arrow) and ectopic sac (blue arrow). (B) Picture of post-laparoscopic right salpingectomy and no active bleeding around the fallopian tube (red arrow) and the uterus (black arrow).

## Discussion

A pregnancy test is recommended for differential diagnosis in the ED if a reproductive-aged female patient suffers from abdominal pain, vaginal bleeding, syncope, or hypotension.<sup>7,8</sup> The accuracy of the pregnancy test is not commonly doubted, especially when excluding the possibility of pregnancy in critical conditions or performing emergency radiation examinations. Some previous studies reported that the false-negative ratio was only 3.1% and 2.6% for urine and plasma  $\beta$ -hCG tests, respectively.<sup>9</sup> Since the goal of a pregnancy test is to detect  $\beta$ -hCG in urine or serum, pregnancy tests in clinical use are typically reported as “positive” when the  $\beta$ -hCG concentration is  $\geq 20$  mIU/mL in urine and  $\geq 10$  mIU/mL in serum.<sup>10</sup> The most common cause of a false-negative result is performing the test too soon after conception. Rarely, false-negative results occur due to a hook effect (an

inaccurately low result, caused by very high concentrations of an analyte or antibody in one-step immunoassays).<sup>11,12</sup>

There have been only nine published cases of ruptured ectopic pregnancies with false-negative tests (both urine and serum) in the past 30 years. Most of their serum  $\beta$ -hCG concentrations did not exceed 10 mIU/mL and were not considered positive results.<sup>13</sup> Among these cases, the major reasons for low detectable  $\beta$ -hCG levels were trophoblast degeneration and cessation of hormone production, followed by enhanced  $\beta$ -hCG hormone clearance, possibly from the presence of anti- $\beta$ -hCG antibodies. Although some previous studies have reported that medications (e.g., methotrexate) might lead to a reduction in the  $\beta$ -hCG concentration,<sup>14</sup> the relationship between the patient's unknown weight-loss drug and her false-negative pregnancy tests could not be determined. In this case, we suspected that fluid resuscitation and stabilized hemodynamics were the first consideration. Because the pregnancy test result was negative, we did not consult a gynecologist for the first time and spent more time preparing for a CT. After the examination, we and gynecologist even thought that it was an unexplained intra-abdominal hemorrhage and did not expect to be a ruptured ectopic pregnancy.

In conclusion, sonography in the ED is useful to quickly demonstrate hemoperitoneum in female patients with a suspicion of ruptured ectopic pregnancy for emergency physicians. Although double false-negative pregnancy tests (urine and blood) might indeed occur simultaneously, we still recommend that clinical assessments (further imaging studies) or emergency exploratory laparotomy be not delayed in critical patients.

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