The Journal of Emergency Medicine, Vol. ■, No. ■, pp. 1–5, 2017

0736-4679/$ - see front matter

http://dx.doi.org/10.1016/j.jemermed.2017.06.011

Clinical Communications: OB/GYN

DELAYED DETECTION OF SPONTANEOUS BILATERAL TUBAL ECTOPIC PREGNANCIES AFTER METHOTREXATE TREATMENT

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□ **Abstract—Background: Bilateral tubal ectopic pregnancies are a rare subset of ectopic pregnancy that can pose a diagnostic dilemma for clinicians. There is no distinct clinical presentation for bilateral tubal ectopic pregnancies, although they are typically associated with assistive reproductive techniques. In addition, there is no single diagnostic feature to help clinicians delineate bilateral tubal ectopic pregnancies from other types of ectopic pregnancy prior to passing the discriminatory zone (such as heterotopic pregnancy or twin ectopic [two gestational sacs in one tube]). Diagnosis is typically made via direct visualization intraoperatively and therefore treatment is usually surgical. Case Report: We present a case of spontaneous bilateral tubal ectopic pregnancies diagnosed 7 days apart via transvaginal ultrasound. The patient presented to the emergency department with pelvic pain on the contralateral side of her previously diagnosed ectopic pregnancy and vaginal spotting. Bilateral adnexal masses were visualized on ultrasound and her serum beta–human chorionic gonadotropin level had a 5.9% decline from day 4 to day 7 after methotrexate administration 7 days prior; gynecology was consulted. The patient was successfully treated with an additional dose of intramuscular methotrexate without any complications. Why Should an Emergency Physician Be Aware of This?: The implications of this case suggest that diagnosis of bilateral tubal ectopic pregnancies requires clinicians to have a high level of suspicion in any pregnant female with a suspected or known ectopic pregnancy who presents with pelvic pain regardless of prior diagnosis or treatment.**

□ **Keywords—bilateral; ectopic; methotrexate; pregnancy; spontaneous; tubal**

INTRODUCTION

Ectopic pregnancy accounts for 1.4% of all pregnancies (1). Even though rare, ectopic pregnancies are the leading cause of maternal death in the first trimester, with an incidence of death of 1 per 1000 pregnancies, necessitating prompt identification and intervention (1–3). Risk factors for ectopic pregnancy include a history of ectopic pregnancy, history of a sexually transmitted infection (particularly *Chlamydia trachomatis*) or pelvic inflammatory disease, tobacco use, prior tubal or pelvic surgery, use of infertility treatments, and in utero exposure to diethylstilbestrol (3,4). In addition, although rates of pregnancy are significantly decreased when an intrauterine contraceptive device is in place, if a pregnancy does occur it is more likely to result in an ectopic pregnancy compared to women not using any form of contraception (5). However, the majority of those diagnosed with an ectopic pregnancy have no identifiable risk factors (3).

Bilateral tubal ectopic pregnancies have an estimated incidence of 1 in 750 to 1 in 1580 ectopic pregnancies

Reprints are not available from the authors.

Received: 20 July 2016; Final submission received: 1 February 2017;
Accepted: 28 June 2017

and are typically the result of assisted reproductive techniques (2,6). Spontaneous bilateral tubal ectopic pregnancies are the rarest form of ectopic (heterotopic and twin ectopic [two gestational sacs in one tube] are more common) and are considered spontaneous when no fertility treatments are involved (2,7). Diagnosis typically happens at time of surgery with direct visualization (7,8). The most common treatment is bilateral salpingectomy (9). There are few reported cases of preoperative diagnosis of bilateral tubal ectopic pregnancies with most literature reporting no prior cases (2,10,11). There have been no reports of successful treatment of bilateral tubal ectopic pregnancies with methotrexate (7). This case report describes an instance of spontaneous bilateral tubal ectopic pregnancies diagnosed via ultrasound and treated with methotrexate.

CASE REPORT

A 32-year-old G5P1031 (gravida: 5 pregnancies including current pregnancy, para: 1 full-term delivery, 0 preterm deliveries, 3 abortions [2 spontaneous abortions and 1 prior ectopic pregnancy treated with methotrexate, side unknown], and 1 living child) with a right ectopic pregnancy diagnosed 7 days prior presented to the emergency department with vaginal bleeding and pelvic cramping. At time of diagnosis of right ectopic pregnancy, the patient had a serum beta–human chorionic gonadotropin (β-hCG) level of 2484 mIU/mL without an intrauterine pregnancy visualized on ultrasound and a visible 13 × 9 × 10 mm right adnexal mass with architectural pattern consistent with ectopic pregnancy. The patient's only risk factor for ectopic pregnancy was her history of previous ectopic pregnancy. After consultation with gynecology, the patient received intramuscular methotrexate (single dose regimen of 50 mg/m^2) and was scheduled for outpatient follow-up and β-hCG level on day 4 after methotrexate administration (level was 2526 mIU/mL on day 4).

The patient stated after she received the methotrexate she had intermittent cramping that was initially moderate and located diffusely to the pelvic region, however, 48 h prior to arrival at the emergency department pain shifted to the left side of the pelvis and became more intense. Patient also noted interval resolution of vaginal bleeding after methotrexate administration; however, on the day of presentation to the emergency department she had onset of vaginal spotting.

The patient's temperature was 36.1°C (96.9°F), her heart rate was 76 beats/min, her blood pressure was 113/72 mmHg, her respiration rate was 16 breaths/min, and her O_2 saturation was 100% on room air. Her abdominal examination revealed bilateral lower quadrant tenderness to palpation mostly in the pelvic region without guarding, rigidity, or rebound tenderness. Pelvic examination was deferred given known tubal ectopic pregnancy on right. She had a β-hCG level of 2377 mIU/mL, indicating a 5.9% decline from day 4 to day 7 after methotrexate administration. Repeat pelvic ultrasound demonstrated the previously visualized adnexal mass on the right measuring 21 × 13 × 14 mm, consistent with patient's previously diagnosed ectopic pregnancy (Figure 1). In addition, the ultrasound demonstrated a new left adnexal mass measuring 20 × 16 × 14 mm with architectural pattern consistent with an ectopic gestation (Figure 2). Gynecology was consulted for management recommendations. Ultimately, the patient received an additional dose of intramuscular methotrexate (50 mg/m^2) in light of the patient's clinical and hemodynamic stability. In addition, the patient highly desired medical management as opposed to surgical management with possible resulting sterility. The patient's β-hCG level was followed until complete resolution without further incident.

DISCUSSION

A suspicion of ectopic pregnancy is based on the presence of abdominal or pelvic pain and vaginal bleeding in a female patient with a history of amenorrhea and a positive urine or serum pregnancy test (12). Although risk factors strengthen the likelihood of the diagnosis, the lack of risk factors should not prompt a clinician to rule out the condition because >50% of patients with an ectopic pregnancy have no risk factors (3). The diagnosis of ectopic pregnancy is based on quantitative serum β-hCG measurement and transvaginal ultrasonography, although it is sometimes diagnosed intraoperatively if the patient is hemodynamically unstable or has hemoperitoneum.

Typically, evidence of an intrauterine gestation will be visualized on a transvaginal ultrasound when the β-hCG level is between 1500 and 2000 mIU/mL; this is classically referred to as the "discriminatory zone" (3). If the β-hCG level is >2000 mIU/mL and there is no evidence of an intrauterine gestation, this raises concern for ectopic pregnancy (3). The caveat to this scenario is with a gestation containing multiple pregnancies (i.e., twins, triplets) where the β-hCG level may be >2000 mIU/mL before there is evidence of an intrauterine gestation on transvaginal ultrasound (3,13). For this reason, it has been suggested that the level of the discriminatory zone be increased to at least 3000 mIU/mL to account for the possibility of multiple gestations and avoid inappropriate administration of methotrexate to a potentially viable pregnancy (13). When the β-hCG level is <1500 mIU/mL and there is no evidence of an intrauterine gestation on ultrasound, there are several outcomes. If β-hCG is <1500 mIU/mL and transvaginal ultrasound