

CASE REPORT

Case of rupture ectopic pregnancy with emergency contraception levonorgestrel 0.075 mg in a lactating woman

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Abstract

Levonorgestrel emergency contraception (LNG-EC) tends to make uterus unfavorable for implantation but does not prevent embryo implantation. Emergency contraceptives pills should be used with caution among lactating women who at the same time should be monitored closely for ectopic pregnancy.

KEYWORDS

contraceptives, ectopic, lactation, LNG-EC, pregnancy

1 | INTRODUCTION

Ectopic pregnancy (EP) is defined as extrauterine ovum implantation. After fertilization, the embryo must reach the uterus after travelling through the fallopian tube. In most cases, EP occurs in the fallopian tubes and rarely in the cervix, intramural, ovaries, or abdominal region.¹ There are even reports of coexistent EP and intrauterine pregnancy.² Regardless of the implantation site, EP is a life-threatening condition that accounts for 10% of early pregnancy-related mortality.³ The exact etiology of the disease remains unknown, but the main reason is the abnormal tubal motility and changes in the microenvironment leading to arrest of the embryo in the fallopian tube and early implantation.³ Studies have shown that there are few main factors that increase the risk of EP. The most common risk factors that are associated with EP are previous EP,⁴ uterine/Fallopian tube

instrumentation or procedures,⁵ pelvic inflammatory disease,² and use of intrauterine contraceptive devices.⁶

For over 20 years, emergency contraception methods have been widely used to prevent undesired pregnancy after unprotected coitus.⁷ The most commonly used emergency contraception is Levonorgestrel emergency contraction (LNG-EC; 0.075 mg; two tablets, stat dose), which is a synthetic progesterone derivative. Various clinical trials have shown its efficacy and safety over a long period.⁸ The mechanism of action includes inhibition of ovulation and making the uterus unfavorable for implantation. To avoiding conception, it has to be taken within 72 hours of coitus. It works better if taken 2-3 days before the luteal surge in the cycle. However, using Levonorgestrel before or after the ovulation period has an unclear effect, and it also increases the risk of EP. Noe et al reported 100% prevention of clinical pregnancy when LNG-EC was used in the preovulation period, while LNG-EC was less

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effective in preventing pregnancy and did not prevent implantation when taken on the day of ovulation or after the ovulation period.⁹ Not much information is available about the safety of emergency contraception pill (ECP) use among breastfeeding women. Here, we report the case of a patient with a ruptured EP following LNG-EC administration in a lactating mother.

2 | PATIENT INFORMATION

A 39-year-old woman with a high education level, who was married for 12 years, and gravida 7, para 3, abortion 3 presented to the emergency department with severe abdominal pain. She was lactating for the previous 14 months. Frequency of lactation was four to six times a day, and the maximum duration between feeds was 3 hours. Her social history was negative for smoking, alcoholism, or drug abuse. The patient was seen in March 2019.

2.1 | Main concerns and symptoms

The main symptoms were acute onset severe pain in the right lower quadrant that was associated with nausea, cold sweats, and feeling dizzy. The patient had intermittent pain in the right lower abdomen for the past week, for which she was taking acetaminophen tablets, and the pain resolved with rest and medication. The patient was not sure if she was pregnant on presentation to the emergency department. She had an episode of vaginal bleeding with pain 3 days before the current episode. She soaked one normal pad and bleeding was more like normal menstrual bleeding, and no clots or heavy bleeding was reported. The patient thought that it was dysmenorrhea related to a normal menstrual cycle, so she ignored the pain and bleeding and did not seek any medical advice for her complaints. She also assumed that she was not pregnant because she had taken LNG-EC (0.75 mg, two tablets, stat dose) 18 hours after unprotected coitus. She took the ECP around 20 days before the current presentation.

2.2 | Past medical and obstetric history

The patient had no surgical or medical history of any chronic illness. She had a bad obstetric history with severe postpartum hemorrhage after spontaneous vaginal delivery during her first childbirth. In the second childbirth, the patient had a history of antepartum hemorrhage, and induced labor ended with vaginal delivery. This was followed by three consecutive abortions all within 35–40 days of conception with levels of β -human chorionic gonadotropin

(HCG) not exceeding 300–400 mIU/mL. Her treating doctors indicated that this was a chemical pregnancy because no intervention was needed, and the patient recovered with conservative management. The last childbirth was an uncomplicated full-term vaginal delivery at 40 weeks. The patient had no history of EP, and no history of irregular cycles, with the duration of menstrual cycles ranging from 24 to 27 days and bleeding for up to a maximum of 6 days. After the last childbirth, she had lactational amenorrhea for 8 months followed by a normal cycle until the current episode of EP. She was not sure of the exact date of her last menstrual period (LMP) at the time of presentation to the hospital. In the patient record, β -HCG at 25 days before this event was available, and this test was completed before performing an X-ray of the lower limbs. Thus, the current EP was not more than 25 days. Patient was not using any regular contraceptive method.

2.3 | Clinical findings

The patient presented to the emergency room and was admitted for further investigation because her urine dipstick test was positive for pregnancy. According to the facility's protocol, a urine dipstick test is performed during vital sign assessment for each childbearing married woman who is unsure of pregnancy. Therefore, the patient was admitted with a working diagnosis of unexplained pain and pregnancy. On examination, the patient was well oriented, and her vital signs were stable. The palpation test was positive for guarding and rebound tenderness. Pressure in the left lower quadrant caused pain in the right lower quadrant. The rest of the abdominal and pelvic exam was unremarkable. There was no per vaginal bleeding or spotting at the time of presentation. The patient's pregnancy status was confirmed using a serum β -HCG test, which showed an elevated β -HCG level of 40,000 mIU/mL.

2.4 | Diagnostic assessment

For the initial assessment, all the routine investigations were performed including complete blood chemistry (CBC) tests and routine urine examination to rule out urinary tract infection or appendicitis. Renal and liver function tests were also performed. Initial transabdominal ultrasound was performed and showed empty uterine cavity with right sided undifferentiated mass. Investigation of an ovarian cyst on abdominal ultrasound was later confirmed to be a corpus luteal cyst of pregnancy. The diagnosis of an EP was confirmed using transvaginal ultrasound, which showed an anteverted uterus with an empty cavity. The patient had a history of mild bicornuate uterus, which

was observed as a slight dimple in the middle of the fundus, but no complete septation was noted. Both ovaries had several small follicles and one clear cyst (corpus luteal cyst of pregnancy), and positive blood flow was observed. There was a small amount of free fluid in the pouch of Douglas. There was a heterogeneous mass at the right adnexa lateral and anterior to the right ovary, which measured $3.7 \times 2.6 \times 2.3$ cm. A hypochoic structure was seen within the mass, but no obvious fetal pole was observed. All the blood chemistry tests including the CBC tests, renal function test, coagulation profile, liver profile, and serum electrolytes were performed, and the results were unremarkable.

After the diagnosis of an EP was confirmed, the initial management plan was to discharge the patient home on medical treatment with methotrexate and follow-up on the β -HCG levels. After 9 hours in the ER, the patient's blood pressure was consistently slightly low and based on the high levels of β -HCG above 40 000 units mIU/mL and no visible fetal parts that were detected on the ultrasound, the management plan was switched to laparoscopic removal of the EP. After the patient was prepared for surgery and general anesthesia, it was discovered that the EP had ruptured and the patient had internal bleeding. Almost 850 mL of blood was drained though the suction from the pelvic cavity. The bleeding site was the right tube, which was secured, followed by a right salpingectomy and removal of the EP. The right ovary was preserved and hemostasis was secured. The pregnancy was confirmed on the histopathology report, and it showed decidual and chorionic villi. The site of rupture was 1.5 cm from the fimbriated end and 6 cm from the stapled end. No fetal parts were identified on biopsy. The patient was stable after surgery, and she was given supportive postsurgical treatment and discharged in stable condition. A follow-up appointment was made to discuss long-term alternative contraceptive methods.

3 | DISCUSSION

We present the case of a multigravida lactating woman with a ruptured EP. The unique features in the case were the presence of high β -HCG levels of 40,000 mIU/mL, no identifiable fetal parts, and a history of taking ECP. In cases of normal pregnancy with β -HCG levels $> 10,000$ mIU/mL, there is usually a gestational sac and an embryo is clearly visible.¹⁰ The high β -HCG level in early pregnancy is associated in the literature with multiple gestations, abnormal pregnancy such as hydatidiform mole, and chromosomal abnormalities. However, no specific abnormality could be confirmed at any stage during the surgery or the histology examination in our patient.

The patient conceived irrespective of use of LNG-EC and ended up with an EP. There are two common oral regimens that are used for emergency contraception: the Yuzpe regimen and Levonorgestrel only pills.¹¹ The Yuzpe regimen is a method that uses a combination of 0.1 mg of ethinyl estradiol and 0.5 mg of Levonorgestrel at 12-hour intervals while the other includes only Levonorgestrel.¹² Both regimens are effective if taken within 72 hours after unprotected sexual intercourse. Trials have also shown that ECP can be effective even up to 120 hours after the first dose. However, the efficacy is lower compared to the 72-hour timeframe. In our case, the patient took the Levonorgestrel within 18 hours. The chances of conception were very low, but our patient still conceived, which is contrary to what is reported in the literature.¹¹ One possible explanation could be that the patient took the medication on or during the postovulatory period. The literature shows that ECP, if taken during the postovulatory period, is less effective for preventing pregnancy.⁹

The exact mechanism of EP remains unknown, but numerous risk factors have been proposed that increase the likelihood of EP. Some of the most common risk factors that have been reported are adnexal or pelvic surgery, previous cesarean section, pelvic infections, and previous EP.¹³ None of the commonly reported risk factors were present in our patient. ECP works in numerous ways to prevent pregnancy. According to Croxatto et al, the processes that are affected by ECP are sperm survival and transfer, ovulation, fertilization, embryo tubal transfer, and implantation, and thus, the theory of defective tubal mortality resulting in implantation in the tube during embryo transfer cannot be overlooked.¹⁴ In our patient, there was no other mechanism that could have hindered tubal motility, as would be expected in the case of a previous surgery or pelvic infection. The patient had no previous history that had a connection to the occurrence of EP. The literature shows that ECP should be taken 2-3 days before the luteal surge for its maximum effectiveness.¹⁵ Our patient was most likely to have taken the medication at time of ovulation. This may be the reason for the EP because if ECP is taken before ovulation, then pregnancy is not possible because it prohibits ovulation.

The use of contraception methods postpartum helps to improve the health of both the mother and her offspring. Longer birth intervals prevent dangerous complications such as death, anemia, and third-trimester bleeding, and they help women to avoid psychological and financial issues after delivery.¹⁶ However, in lactating women, the choices of contraception methods are limited. Because most hormonal contraception affects the quality and quantity of milk, progesterone only pills and an intrauterine contraceptive device (IUCD) are the most effective methods that are used in the first 6 month postpartum.¹⁷ In our case, the patient had a history of uterine abnormalities, and the use of IUCD was contraindicated for her.

More research is needed to test the efficacy of IUCDs among women with uterine abnormalities.

Although the safety of ECP has been well studied and established to help in preventing unwanted pregnancies, cases have still been reported with EP linked to its use. Since 2002, several cases of EP after the use of ECPs were reported. However, some evidence suggests that the rate of EP following the use of LNG-EC is not greater than that in the general population.¹⁸ There is a dearth of knowledge about the safety of ECP among lactating women, and future research is needed to bridge this gap and establish the cause-and-effect relationship between ECP use and EP.

This study has some limitations. This is a single case report and causality cannot be directly linked to the use of ECP that was taken to prevent pregnancy based on this case. Additionally, there is little information in the context of lactating women. The manufacturers of the medications and the prescribing information that comes with the dispensed pack also do not indicate that breastfeeding is a contraindication to the use of ECP. This limits the generalizability of the claim from this report, but in situations of unprotected sex, the most suitable approach toward prevention of unwanted pregnancy is administration of ECP. However, contraception strategies among lactating women must be improved to avoid the need for ECP.

4 | CONCLUSIONS

We report the case of a patient who used ECP but who did not have any identifiable risks for EP. This case report cannot establish an association between the use of ECP and the occurrence of EP. However, based on the existing literature and the lack of clear guidelines for administration of ECP to lactating women, we recommend that ECP should be used with caution among such women. Additionally, the patients need to be strictly monitored for any symptoms of genital bleeding, abdominal pain, or a positive pregnancy test to rule out EP so that similar consequences such as those that are described in this case report can be avoided.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

NM: contributed as a senior member to conception, drafting manuscript and technical revision of the manuscript for purpose of publication. SS: contributed to data extraction, writing the first draft also provided support in literature review.

TB, SK, and FK: contributed equally to writing the first draft also provided support in literature review. All authors have read and approved the final version of the article for submission.

INFORMED CONSENT

Informed consent for the publication was obtained from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Tahmina S, Daniel M, Solomon P. Clinical analysis of ectopic pregnancies in a tertiary care centre in southern India: a six-year retrospective study. *J Clin Diagn Res.* 2016;10(10):qc13-qc16.
2. Anderson J, Patterson C, Riley A. Heterotopic interstitial pregnancy: A case report. *Case Rep Women's Health.* 2018;17:8-10.
3. Abdulaziz A-T. Trends in ectopic pregnancies in eastern Saudi Arabia. *ISRN Obstet Gynecol.* 2013;2013:975251.
4. Pisarska MD, Carson SA, Buster JE. Ectopic pregnancy. *Lancet.* 1998;351:1115-1120.
5. Marchbanks PA, Annegers JF, Coulam CB, Strathy JH, Kurland LT. Risk factors for ectopic pregnancy: a population-based study. *JAMA.* 1988;259:1823-1827.
6. Xiong X, Beukens P, Wollast E. IUD use and the risk of ectopic pregnancy: a meta-analysis of case-control studies. *Contraception.* 1995;52:23-34.
7. Ghosh B, Dadhwal V, Deka D, Ramesan CK, Mittal S. Ectopic pregnancy following levonorgestrel emergency contraception: a case report. *Contraception.* 2009;79(2):155-157.
8. Hamoda H, Ashok PW, Stalder C, Flett GM, Kennedy E, Templeton A. A randomized trial of mifepristone (10 mg) and levonorgestrel for emergency contraception. *Obstet Gynecol.* 2004;104(6):1307-1313.
9. Noé G, Croxatto HB, Salvatierra AM, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. *Contraception.* 2011;84(5):486-492.
10. Connolly A, Ryan DH, Stuebe AM, Wolfe HM. Reevaluation of discriminatory and threshold levels for serum β -hCG in early pregnancy. *Obstet Gynecol.* 2013;121(1):65-70.
11. Allen RH, Goldberg AB. Emergency contraception: a clinical review. *Clin Obstet Gynecol.* 2007;50(4):927-936.
12. Leung VW, Soon JA, Lynd LD, Marra CA, Levine M. Population-based evaluation of the effectiveness of two regimens for emergency contraception. *Int J Gynaecol Obstet.* 2016;133(3):342-346.
13. Lozeau AM, Potter B. Diagnosis and management of ectopic pregnancy. *Am Family Phys.* 2005;72(9):1707-1714.
14. Croxatto HB, Devoto L, Durand M, et al. Mechanism of action of hormonal preparations used for emergency contraception: a review of the literature. *Contraception.* 2001;63:111-121.

15. Sarkar NN. The emergency contraceptive drug, levonorgestrel: a review of post-coital oral and peri-coital vaginal administration for prevention of pregnancy. *J Obstet Gynaecol*. 2011;31(8):703-707.
16. Truitt ST, Fraser AB, Grimes DA, Gallo MF, Schulz KF. Hormonal contraception during lactation. systematic review of randomized controlled trials. *Contraception*. 2003;68(4):233-238.
17. Kelsey JJ. Hormonal contraception and lactation. *J Hum Lactat*. 1996;12(4):315-318.
18. Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. Ectopic pregnancy and emergency contraceptive pills: a systematic review. *Obstet Gynecol*. 2010;115(6):1263-1266.

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