Published online 2020 January 27.

Case Report



A Report of Three Consecutive Recurrent Ectopic Pregnancies in Two Patients

Nayereh Ghomian ^{1,*} and Zahra Rastin ¹

Received 2019 June 26; Revised 2019 October 17; Accepted 2019 December 08.

Abstract

Introduction: Ectopic pregnancy (EP) is a life-threatening pregnancy complication and can cause maternal morbidity and mortality and early fetal death with the incidence rate of approximately 2% of all pregnancies. The rate of recurrence of EP increases in patients with a past history of EP. We present here two cases that have had three consecutive recurrent EPs during one year with different management.

Case Presentation: Case 1: A 27-year-old woman gravida 3 Ep2 with 6 weeks gestational age was referred with abdominal pain. She had a history of two consecutive ectopic pregnancies 9 and 4 months ago that were treated with methotrexate (MTX) and right salpingectomy. Transvaginal ultrasonography showed left tubal ectopic pregnancy with intra-abdominal bleeding. Left salpingectomy was performed. Case 2: A 34-year-old women gravid 3 with a history of 2 consecutive Ep 11 and 6 months ago that were treated with left salpingectomy and MTX, was referred. She was treated with two doses of MTX.

Conclusions: The rate of recurrent EP considerably rises in patients with a history of the previous EP and considering this medical history is highly recommended in future pregnancies for early diagnosis.

Keywords: Ectopic Pregnancy, Methotrexate, Salpingectomy

1. Introduction

Ectopic pregnancy (EP) is one of the main complications of pregnancy in the first trimester and can cause maternal morbidity and mortality and early fetal death (1). Ectopic pregnancy is defined as the implantation of an embryo outside of the endometrial cavity, which occurs in the fallopian tube in 98% of cases (2). After spontaneous pregnancy, the incidence rate of EP is 1% - 2% and after assisted reproduction technology treatment, the incidence rate is 2% -5% (3). Despite the effort of primary prevention, the incidence of EP has steadily increased each year. History of a previous EP increases the risk of recurrent EP. The rate of recurrent EP is 15% and this rises two-fold after two EPs (4-8).

Abnormal fallopian tube anatomy is a risk factor for many cases of tubal ectopic pregnancy. Tubal surgeries confer the highest risk. The previous history of Ep increases the chance five-fold. The past medical history of sexually transmitted diseases (STDs) which can distort normal tubal anatomy is a major risk factor for EP (4-8).

After using methotrexate (MTX) for the treatment of EP, the incidence rate of recurrent EP is between 10% - 18%. The chance of a subsequent intrauterine pregnancy after

an EP changes from 38% to 89% (9). The incidence of EP has increased markedly in the recent 30 years because of the higher prevalence of pelvic inflammatory diseases, the use of assisted reproduction technology and rising of maternal age (2). Other risk factors of EP are tubal surgery, history of intrauterine diethylstilbestrol exposure, pregnancy with a current intra-uterine device (IUD), tubal damage and multiple sexual partners (3).

We present two cases of three consecutive recurrent ectopic pregnancies which occurred during one year, because of the interesting history, its rarity and different management which was due to their different presentations.

2. Case Presentation

2.1. Case 1

A 27-year-old woman gravida 3 EP2, admitted with abdominal pain from one week earlier. She had 6 weeks of amenorrhea. She had not used any contraceptive methods. Her previous menstrual cycles were irregular. The patient had a history of two consecutive EPs. The first one

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

^{*}Corresponding author: Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: ghomiann@mums.ac.ir

was a right tubal ectopic pregnancy 9 months ago and was treated with methotrexate. The second one was detected on the right fallopian tube 4 months ago and she had undergone a salpingectomy by laparotomy because of massive abdominal hemorrhage. She had no history of the pelvic inflammatory disease and pelvic surgery except the previous salpingectomy.

In spite of being advised of using contraception, after 4 months of right-sided salpingectomy, a new EP occurred in the left fallopian tube. On her physical examination, abdominal tenderness in the left lower quadrant was present. Her pulse rate was 100 beats/min and her blood pressure was 100/90 mmHg. The transvaginal ultrasonography revealed an empty uterine cavity and a gestational sac with the size of 4cm in the left fallopian tube without fetal cardiac activity (Figure 1). Also, there was marked intraabdominal free fluid. Laboratory tests was as follows: hCG level = 3346 mIU/mL, Hct = 28%, and Hb = 9mg/dL. Laparotomy was performed, findings at surgery were hemoperitoneum with the volume of 1000 cc and perforated ampullar Ep with active bleeding, and therefore salpingectomy was performed. The postoperative course was uneventful and she was discharged on the third postoperative day. She was counselled for the other pregnancy she should refer to the in vitro fertilization center. Pathology of the left tube showed immature chorionic villi and fetal parts.



Figure 1. Sonographic findings of the first case

2.2. Case 2

A 34-year-old woman, gravida 3, EP 2, who was visited at the gynecological clinic with a one-week history of colicky lower abdominal pain and spotting after 6 weeks of amenorrhea. Previously, she had regular menstrual cycles without dysmenorrhea. The patient had a history of two consecutive EPs. The first one was left tubal EP which was managed by salpingostomy by laparotomy 11 months be-

fore. The second one was detected on the right adnexa and treated with methotrexate 6 months before.

The vital signs were normal. She had tenderness on right lower quadrant of the abdomen. Transvaginal ultrasonography showed an empty uterine cavity and a mass with the size 34*33mm in the right adnexa, without fetal cardiac activity (Figure 2). No intra-abdominal free fluid was detected. Laboratory tests showed that the hCG level was 343 mIU/mL. During serial measurement of β hCG within 10 days, it was raised to 1540 mIU/mL, however, the ultrasonic finding did not change. Endometrial curettage was performed and no chorionic villi were reported by a pathologist. The diagnosis of EP was confirmed. Occlusion of the tubes and preparing for an in vitro fertilization procedure was offered but the patient did not accept. A singledose protocol of methotrexate (50 mg/m²) was administered intramuscularly on day 1, and the hCG level was 3200 mIU/mL and 4100 mIU/mL on days 4 and 7, respectively. The second dose of methotrexate was administered and after that, the levels of hCG were decreased in the following tests.



Figure 2. Sonographic findings of the second case

The Ethical Committee of Mashhad University of Medical Sciences had approved this study in their session held on "Jun 20, 2017". Reference number: IR.MUMS.REC.1396.93.

3. Discussion

We reviewed two rare cases of EP who suffered from three recurrent EPs. Ectopic pregnancy is one of the most important emergencies of gynecology. It is a lifethreatening complication occurring in approximately 2% of all pregnancies. The classic symptoms of EP are abdominal pain, amenorrhea and vaginal bleeding that only 50 percent of patients present with this triad. Physical examination is often nonspecific at unruptured EPs. Ultrasound and serial measurements of hCG are the main tools for correct diagnosis. Early diagnosis is possible with measurement of hCG and transvaginal ultrasonography, and most importantly, clinical suspicion and careful risk factor assessment (10).

The risk of recurrent EP is much higher than primary EP: incidence rate ranges from 6% - 18% after having a history of the first EP. This is raised to 30% following two ectopic pregnancies. There are several treatment options for EP according to clinical presentations and hemodynamic status like expectant management, medical treatment, and surgical approach (laparotomy or laparoscopy).

Expectant management can be used for patients with low (< 1000 IU/L) or declining hCG levels. Patients who are hemodynamically unstable, heterotopic pregnancy with a viable intrauterine pregnancy, do not have access to a medical institution for management of tubal rupture, contraindications to methotrexate and failed medical therapy are the indicated cases for surgical treatment (11). On the other hand, patients who are hemodynamically stable, able to comply follow-up after treatment, have hCG concentration $\leq 5000 \text{ mIU/mL}$, with no fetal heart rate in gestational sac are suitable candidates for medical treatment with methotrexate (12).

In case 1 because the patient was hemodynamically unstable, laparotomy and salpingectomy were performed but case 2 underwent medical treatment. The early diagnosis and management of ectopic pregnancies can increase the successfulness of medical treatment.

Janbakhishov and coworkers reported a case of recurrent EP in the ipsilateral salpinx after ovulation induction and intrauterine insemination treated by laparoscopy (13). Faleyimu and colleagues reported an unusual case with ipsilateral ectopic pregnancy occurring in the stump of a previous ectopic site treated with salpingo-oophorectomy (14). Samiei-Sarir and Diehm reported two cases of recurrent ectopic pregnancy located within the remnant tube following ipsilateral salpingectomy that was finally treated with laparoscopic intervention (15). Adelusi and colleagues reported a 25-year-old woman that had three times of recurrent ectopic pregnancy. In the first EP, a salpingostomy was performed and the second EP was treated with MTX and three months later hysterosalpingography (HSG) was performed. A new ectopic pregnancy occurred one month after HSG, which was treated with MTX (16).

Women treated for EP should be consulted that they have a higher risk for recurrence of EP compared to other women without a history of EP. They should be advised to have an early pregnancy ultrasound scan in any future pregnancies.

3.1. Conclusion

Ectopic pregnancy is one of the most important differential diagnoses in the acute abdomen and must be considered in every woman with abdominal pain and delayed menses. History of ectopic pregnancy is very important and the risk of recurrent EP in these patients is fivefold compared to the general population. Early diagnosis can help to prevent dangerous complications such as fallopian tube rupture and hemoperitoneum. The early detection of EP is confirmed with transvaginal ultrasonography and serial measurement of hCG.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Acknowledgments

The authors would like to thank the patients for their consent for publication of this report. The support of Mashhad University of Medical Sciences is also appreciated.

Footnotes

Conflict of Interests: None to be declared.

Ethical Approval: The Ethical Committee of Mashhad University of Medical Sciences had approved this study in their session held on "Jun 20, 2017". Reference number: IR.MUMS.REC.1396.93.

Funding/Support: None to be declared.

References

- Igberase GO, Ebeigbe PN, Igbekoyi OF, Ajufoh BI. Ectopic pregnancy: An 11-year review in a tertiary centre in the Niger Delta. *Trop Doct.* 2005;35(3):175-7. doi:10.1258/0049475054620888. [PubMed: 16105350].
- Farquhar CM. Ectopic pregnancy. Lancet. 2005;366(9485):583-91. doi: 10.1016/S0140-6736(05)67103-6. [PubMed: 16099295].
- Boufous S, Quartararo M, Mohsin M, Parker J. Trends in the incidence of ectopic pregnancy in New South Wales between 1990-1998. Aust N Z J Obstet Gynaecol. 2001;41(4):436-8. doi: 10.1111/j.1479-828x.2001.tb01325.x. [PubMed: 11787921].
- Bhattacharya S, McLernon DJ, Lee AJ, Bhattacharya S. Reproductive outcomes following ectopic pregnancy: Register-based retrospective cohort study. *PLoS Med.* 2012;9(6). e1001243. doi: 10.1371/journal.pmed.1001243. [PubMed: 22723747]. [PubMed Central: PMC3378618].
- Al-Sunaidi M, Tulandi T. Surgical treatment of ectopic pregnancy. Semin Reprod Med. 2007;25(2):117-22. doi: 10.1055/s-2007-970050. [PubMed: 17377898].

- 6. Practice Committee of American Society for Reproductive Medicine. Medical treatment of ectopic pregnancy: A committee opinion. *Fertil Steril.* 2013;**100**(3):638-44. doi: 10.1016/j.fertnstert.2013.06.013. [PubMed: 23849842].
- 7. Arleo EK, DeFilippis EM. Cornual, interstitial, and angular pregnancies: Clarifying the terms and a review of the literature. *Clin Imaging*. 2014;**38**(6):763–70. doi: 10.1016/j.clinimag.2014.04.002. [PubMed: 25156020].
- 8. Gonzalez N, Tulandi T. Cesarean scar pregnancy: A systematic review. *J Minim Invasive Gynecol*. 2017;**24**(5):731–8. doi: 10.1016/i.jmig.2017.02.020. [PubMed: 28268103].
- Cohen A, Bibi G, Almog B, Tsafrir Z, Levin I. Second-dose methotrexate in ectopic pregnancies: The role of beta human chorionic gonadotropin. Fertil Steril. 2014;102(6):1646–9. doi: 10.1016/j.fertnstert.2014.08.019. [PubMed: 25241368].
- Condous G, Okaro E, Khalid A, Lu C, Van Huffel S, Timmerman D, et al. The accuracy of transvaginal ultrasonography for the diagnosis of ectopic pregnancy prior to surgery. *Hum Reprod.* 2005;20(5):1404–9. doi: 10.1093/humrep/deh770. [PubMed: 15695311].
- Paavonen J, Varjonen-Toivonen M, Komulainen M, Heinonen PK. Diagnosis and management of tubal pregnancy: Effect on fertility

- outcome. Int J Gynaecol Obstet. 1985;**23**(2):129–33. doi: 10.1016/0020-7292(85)90057-8. [PubMed: 2862074].
- Tulandi T. Reproductive performance of women after two tubal ectopic pregnancies. Fertil Steril. 1988;50(1):164–6. doi: 10.1016/s0015-0282(16)60025-0. [PubMed: 3384110].
- Janbakhishov T, Dogan S, Dogan E. Laparoscopic treatment of recurrent ectopic pregnancy in the ipsilateral salpinx after ovulation induction and intrauterine insemination. *Taiwan J Obstet Gynecol*. 2013;52(4):568-70. doi:10.1016/j.tjog.2013.10.020. [PubMed: 24411045].
- Faleyimu BL, Igberase GO, Momoh MO. Ipsilateral ectopic pregnancy occurring in the stump of a previous ectopic site: A case report. Cases J. 2008;1(1):343. doi: 10.1186/1757-1626-1-343. [PubMed: 19025603]. [PubMed Central: PMC2599900].
- Samiei-Sarir B, Diehm C. Recurrent ectopic pregnancy in the tubal remnant after salpingectomy. Case Rep Obstet Gynecol. 2013;2013:753269. doi: 10.1155/2013/753269. [PubMed: 24151570]. [PubMed Central: PMC3789312].
- Adelusi B, al-Meshari A, Akande EO, Chowdhury N. Three consecutive recurrent ectopic pregnancies. East Afr Med J. 1993;70(9):592-4. [PubMed: 8181445].