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Failed Methotrexate Therapy in Tubal Ectopic Pregnancy: A Case Requiring Left Partial Salpingectomy

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Introduction

- An ectopic pregnancy is a rare clinical condition that is characterized by the implantation of a fertilized egg outside of the uterus¹
- Ectopic pregnancies affect about 1-2% of all pregnancies and is a leading cause of morbidity and mortality in pregnant individuals^{2,3}
- The most common location for an ectopic pregnancy to occur is the ampulla of the fallopian tube, however the implantation can also occur in the ovary, cervix, and abdomen⁴
- Risk factors for developing an ectopic pregnancy include:⁵
 - Prior ectopic pregnancy
 - Prior cesarean section
 - Previous tubal surgery
 - Previous genital infection (e.g., pelvic inflammatory disease)
 - Active or previous tubal pathology
- The most common presenting symptoms of an ectopic pregnancy include amenorrhea, abdominal pain, and first-trimester vaginal bleeding⁶

Imaging

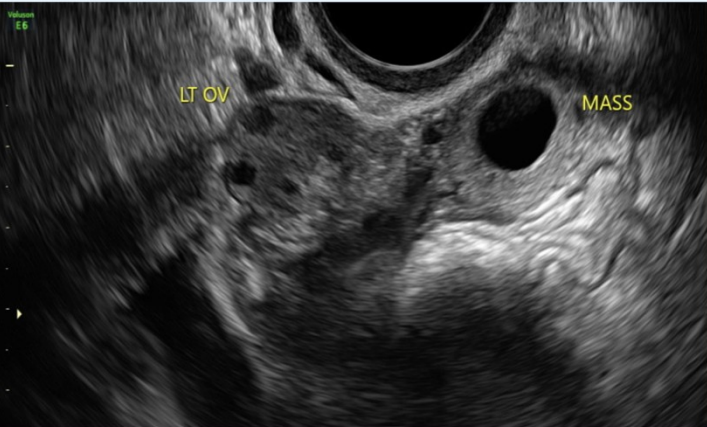


Figure 1

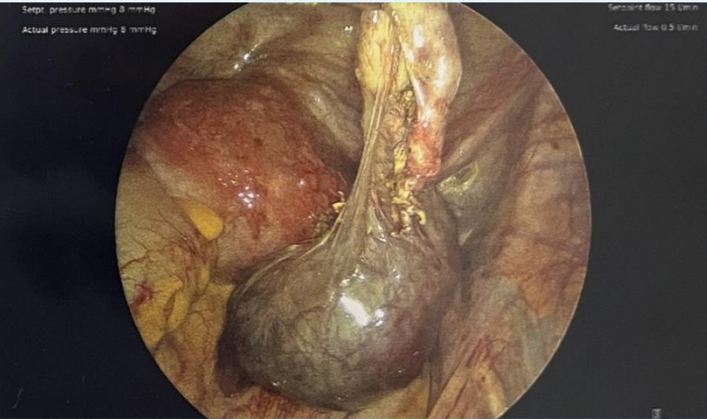


Figure 2

Case Description

History of Present Illness

- **Office visit 1 (initial evaluation)**
 - 39-year-old G2P1001 female presented to the OB/GYN clinic with one day of left lower abdominal pain and light vaginal bleeding
 - She had a positive urine β -hCG result two weeks prior
 - She denied fever, chills, dizziness, nausea, vomiting, or urinary symptoms
- **Office visit 2 (8 days after initial evaluation)**
 - The patient returned to the office for repeat transvaginal ultrasound due to inappropriately decreasing quantitative β -hCG values between days 4 and 7 of methotrexate therapy
 - She had worsening left lower quadrant pain that she described as “increasing pressure”
 - She denied fever, chills, dizziness, nausea, vomiting, urinary symptoms, or vaginal bleeding
- No past medical history
- No past surgical history
- No medications or allergies
- Family and social history non-contributory

Physical Exam

- **Office visit 1 (initial evaluation)**
 - Vitals: Temp: 98.7 °F, oral | HR: 68 bpm | BP: 101/67, R arm, sitting automatic | RR: 18 breaths per minute | SpO2: 99% on room air
 - General: alert and oriented in no acute distress
 - Cardiovascular: regular rate and rhythm
 - Pulmonary: no wheezing or accessory muscle use
 - Abdomen: soft, no guarding or rebounding. Mild, focal tenderness to deep palpation in the left lower quadrant
 - Vagina: trace of blood noted. No lesions, no erythema, no pooling of blood
 - Cervix: grossly normal, closed cervical os, no discharge or cervical motion tenderness, no active bleeding
 - Uterus: midline, non-tender
 - Adnexa/parametria: no palpable masses, no tenderness. No parametrial tenderness, no adnexal tenderness, no palpable ovarian masses
- **Office visit 2 (8 days after initial evaluation)**
 - Vitals: within normal limits (WNL)
 - Abdomen: soft, non-tender, moderate focal tenderness to deep palpation in the left lower quadrant. No rebounding or guarding
 - Adnexa/parametria: tenderness to bimanual palpation of left adnexa
 - The rest of the physical exam was WNL

Diagnostic Testing

CBC, BMP, Urinalysis and Progesterone level WNL

Transvaginal Ultrasound

Visit 1	<ul style="list-style-type: none">- No evidence of intrauterine pregnancy- Pseudo gestational sac measuring 0.5 cm x 0.24 cm x 0.5 cm- Left adnexa: thick-walled, complex mass with vascularity measuring 1.85 cm x 1.39 cm x 1.6 cm with distinct separation from left ovary
Visit 2	<ul style="list-style-type: none">- No evidence of intrauterine pregnancy- Pseudo gestational sac measuring 0.53 cm x 0.26 cm x 0.15 cm- Left adnexa: thick-walled, complex mass with vascularity measuring 2.39 cm x 1.63 cm x 1.92 cm with distinct separation from left ovary (Figure 1)

Quantitative β -hCG levels

Lab Visit 1	2,649 mIU/mL
Lab Visit 2	3,735 mIU/mL
Lab Visit 3	4,592 mIU/mL – day 1 of methotrexate therapy
Lab Visit 4	11,971 mIU/mL – day 4 of methotrexate therapy
Lab Visit 5	12,235 mIU/mL – day 7 of methotrexate therapy

Differential Diagnosis

Physiologic/implantation bleeding, threatened abortion, ruptured ovarian cyst, urinary tract infection, pelvic inflammatory disease

Final diagnosis: left tubal ectopic pregnancy

Patient Management and Outcome

- Risks, benefits, and alternatives of second methotrexate dose versus surgical management with laparoscopic salpingectomy discussed with patient
- Due to patient’s worsening left lower quadrant pain and inappropriately decreasing β -hCG levels, she elected to proceed with surgical management
- The patient underwent a laparoscopic left partial salpingectomy with removal of an unruptured ectopic pregnancy (Figure 2)
- The patient was discharged home from the hospital the same day of the surgery
- The patient was instructed to follow-up in the office one week later to assess for appropriate decline of quantitative β -hCG levels

Discussion

- The treatment options for an ectopic pregnancy include expectant management, medical management with systemic methotrexate therapy, and surgical intervention⁷
- Methotrexate therapy (including one-dose and two-dose regimens) has a success rate of nearly 90% in treating an unruptured ectopic pregnancy in a hemodynamically stable patient⁸
- Women with lower pre-treatment quantitative β -hCG levels (< 5,000 mIU/mL) have a greater chance of success with medical management⁹
- Patients who require a repeat dose of methotrexate therapy due to an inadequate reduction in quantitative β -hCG levels on day 7 of therapy (< 15% of day 4 levels) are more likely to fail medical therapy and require additional intervention⁹
- The two-dose methotrexate protocol has been found to have a higher success rate than the single-dose protocol¹⁰
- For surgical intervention, salpingectomy is generally preferred over salpingostomy if the patient has a healthy contralateral fallopian tube¹¹
- Management of an ectopic pregnancy with methotrexate therapy increases chances of future fertility compared to surgical management¹²
- There is no significant difference in chance of future intrauterine pregnancy between women who undergo salpingectomy versus salpingotomy¹²

Conclusion

- Ectopic pregnancy is a rare complication that can lead to increased morbidity and mortality amongst pregnant patients
- Hemodynamically stable patients with qualifying quantitative β -hCG levels and absent embryonic cardiac activity are often successfully treated with methotrexate therapy
- It is important for clinicians to recognize signs of failed medical management with methotrexate, such as inappropriately decreasing β -hCG levels, worsening pain or vaginal bleeding, and onset of hemodynamic instability
- Management of an ectopic pregnancy should be a shared and informed decision between patient and clinician and should prioritize patient safety and desires for future fertility

References

1. Lee IT, Barnhart KT. What is an ectopic pregnancy? *JAMA*. 2023;329(5):434. doi:10.1001/jama.2022.22941
2. Zhang S, Liu J, Yang L, Li H, Tang J, Hong L. Global burden and trends of ectopic pregnancy: an observational trend study from 1990 to 2019. *PLoS One*. 2023;18(10):e0291316. doi:10.1371/journal.pone.0291316
3. Almutairy S, Aldakhlil LO. Clinical presentation as a predictor of the response to methotrexate therapy in patients with ectopic pregnancy. *Journal of Pregnancy*. 2022;2022:1-6. doi:10.1155/2022/5778321
4. Fan YY, Liu YN, Mao XT, Fu Y. The prevalence of ectopic gestation: a five-year study of 1273 cases. *IJGM*. 2021;Volume 14:9657-9661. doi:10.2147/IJGM.S344648
5. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM. Risk factors for ectopic pregnancy: a meta-analysis. *Fertil Steril*. 1996;65(6):1093-1099. doi:10.1016/S0015-0282(16)58320-4
6. Ray A, Gaur A, Kumari S. Predictors of successful medical management with methotrexate in unruptured tubal ectopic pregnancy. *Cureus*. 2022;14(11):e31923. doi:10.7759/cureus.31923
7. Mullany K, Minneci M, Monjazeb R, C Coiado O. Overview of ectopic pregnancy diagnosis, management, and innovation. *Womens Health (Lond)*. 2023;19:17455057231160349. doi:10.1177/17455057231160349
8. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing “single dose” and “multidose” regimens. *Obstet Gynecol*. 2003;101(4):778-784. doi:10.1016/s0029-7844(02)03158-7
9. Ray A, Gaur A, Kumari S. Predictors of Successful Medical Management With Methotrexate in Unruptured Tubal Ectopic Pregnancy. *Cureus*. 2022;14(11):e31923. Published 2022 Nov 26. doi:10.7759/cureus.31923
10. Alur-Gupta S, Cooney LG, Senapati S, Sammel MD, Barnhart KT. Two-dose versus single-dose methotrexate for treatment of ectopic pregnancy: a meta-analysis. *Am J Obstet Gynecol*. 2019;221(2):95-108.e2. doi:10.1016/j.ajog.2019.01.002
11. Chen L, Zhu D, Wu Q, Yu Y. Fertility outcomes after laparoscopic salpingectomy or salpingotomy for tubal ectopic pregnancy: A retrospective cohort study of 95 patients. *Int J Surg*. 2017;48:59-63. doi:10.1016/j.ijsu.2017.09.058
12. Hao HJ, Feng L, Dong LF, Zhang W, Zhao XL. Reproductive outcomes of ectopic pregnancy with conservative and surgical treatment: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2023;102(17):e33621. doi:10.1097/MD.0000000000003621