International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Rafiq S et al. Int J Reprod Contracept Obstet Gynecol. 2024 Jul;13(7):1837-1841
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20241784

Case Report

Silent ovarian ectopic pregnancy: a case report

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Received: 14 May 2024
Accepted: 04 June 2024

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ABSTRACT

In clinical practice, an ovarian pregnancy is considered one of the most challenging diagnoses faced by an obstetrician/gynecologist. In this article, we report a 31-year-old Asian-Pakistani female, who presented to the ObsGynae clinic with 8 weeks of amenorrhea, a positive urine pregnancy test, and very high serum β-hCG levels. Transvaginal ultrasonography ruled out a tubal pregnancy, and the patient was sent for repeat β-hCG levels. The patient was hemodynamically stable and displayed no characteristic signs and symptoms of an ectopic pregnancy. Upon repeat scans and β-hCG levels, a diagnosis of ovarian ectopic pregnancy was made. The patient was managed on medication; a single dose of I/M 50 mg/m^2 methotrexate was administered and the resultant decline in β-hCG levels proved the success of conservative treatment in this case. An ovarian ectopic can present as a life-threatening condition, and a high index of suspicion can prevent morbidity as well as mortality. Ovarian pregnancy, without any alarming signs despite very high β-hCG levels, as reported in this case, is one of the rarest clinical cases observed.

Keywords: Ectopic pregnancy, methotrexate, β-hCG

INTRODUCTION

Ectopic pregnancies are found to occur in only 1-2% of pregnancies worldwide, making it a rare diagnosis. Of these, ovarian implantations account for only about 0.5-2%.[1] Due to the increased vascularization of the ovarian tissue, an ovarian pregnancy typically ends in a rupture in the first trimester often leading to internal bleeding and hypovolemic shock.[2] Studies suggest performing a diagnostic laparoscopy with consequent histopathology to confirm the diagnosis of an ovarian ectopic pregnancy.[3]

Here, we report a case of a silent ovarian ectopic pregnancy presented to the gynecology clinic at 8+6 weeks of gestation with a positive urine pregnancy test and extremely high serum β-hCG levels. Our patient, 31 years of age, had one previous missed miscarriage 7 months ago, for which she underwent manual vacuum aspiration (MVA). She had no known risk factors for ovarian ectopic pregnancy. Despite being hemodynamically stable, the absence of an intrauterine sac warranted further investigation. After sequential ultrasonography scans, a diagnosis of ovarian ectopic pregnancy was confirmed. As the patient was vitally stable with no signs and symptoms of an 8-week ectopic pregnancy, a conservative approach was adopted with the couples' consent. The patient was managed on methotrexate, and the subsequent declining serum β-hCG levels nullified the need for a laparoscopy/surgical intervention.

CASE REPORT

A 31-year-old Pakistani woman was referred to our clinic with amenorrhea and an absent intrauterine sac on ultrasonography with no other signs and symptoms of an ectopic pregnancy. She had a regular menstrual cycle of 28 days. In her medical history, there were no known risk factors such as an intrauterine contraceptive device, ovulation induction, endometriosis, or pelvic inflammatory disease.

The patient had a history of a missed miscarriage at eight weeks gestation seven months ago. Ultrasound and β-hCG levels at that time confirmed intrauterine pregnancy with a positive fetal pole and negative fetal cardiac activity for which she underwent MVA. A subsequent histopathological report confirmed that the sample contained products of conception.

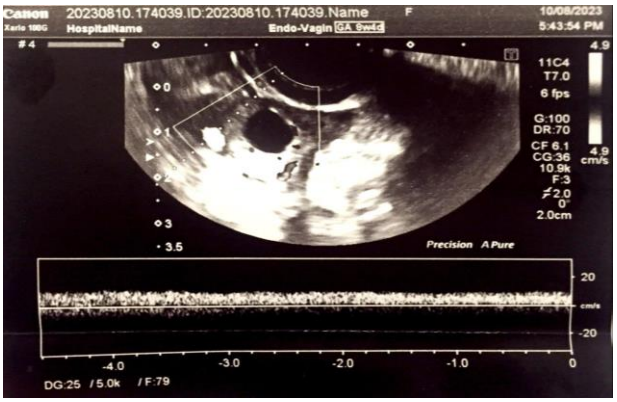

Figure 1: USG image showing a complex left adnexal cyst.

The patient now presented with 8 weeks of amenorrhea with a positive urine pregnancy test, after spontaneous conception. She was hemodynamically stable with good vital signs: blood pressure 120/80 mmHg, pulse 82 beats/min, temperature 37 degrees Celsius. Her physical and speculum examination was unremarkable and there was no abdominal tenderness or per-vaginal bleeding.

Transabdominal ultrasonography (TAU) done at her initial checkup showed a partially filled bladder with an empty uterine cavity and a complex left adnexal cyst (Figure 1). She was, therefore, suspected of a tubal ectopic pregnancy and was referred to our specialist clinic. Upon performing a repeat TAU and transvaginal ultrasonography (TVS) in the gynecology clinic, intrauterine and tubal ectopic pregnancy were both ruled out. She was, therefore, referred to a radiologist for a Doppler TVS.

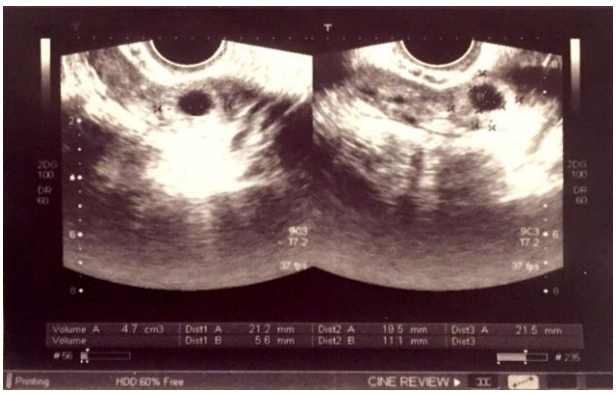

Figure 2: USG image showing small left adnexal ectopic gestation with no signs of rupture in the pelvic cavity.

The first TVS revealed an oval-shaped nodule measuring 2.4×1.5×2.0 cm (vol: 3.5 cm^3) in the left adnexa with a central cystic component (14.0 mm in diameter) encased by a rim of soft tissue of 4.0-7.0 mm in thickness. The embryonic pole or yolk sac was not visualized. Her β-hCG had risen to 32389 I/l. Since the patient remained vitally stable, she was advised to have a repeat scan after two days for confirmation of the suspected diagnosis (Figure 2).

Two days later, with a β-hCG level of 34,111 IU/l, an ectopic gestational sac was confirmed at the inferomedial aspect of her left ovary on TVS. The fetus and fetal heartbeat were not detected. Vascular proliferation called 'ring of fire,' which is typical for ectopic ovarian pregnancy, was seen around the gestational sac. The TVS revealed a normal-sized anteverted uterus with an absent intrauterine gestational sac and an endometrial thickness of 11.0 mm. Her right ovary and tubal structures appeared normal. A final diagnosis of ovarian ectopic pregnancy was made.

Laboratory analysis showed a white blood cell count (WBC) of 11,600/mm^3, hemoglobin (Hb) of 12.3 g/dl, and normal urine RE results. Her TSH level was 1.07 (normal), her HbA1C was 5.0% (normal), and non-reactive serum HbsAg and serum anti-HCV.

The decision to adopt a more conservative approach was taken in cohort with the radiologist and the pathologist in accordance with international guidelines. She was hemodynamically stable, with an unruptured ovarian ectopic pregnancy, and without any embryonic cardiac activity, making her a good candidate for medical management. Moreover, the absence of any known contraindications to MTX further solidified the rationale for its administration. The couple was apprised of the situation and thus, medical management was initiated after obtaining their full informed consent. They were advised to arrange 2 units of red cell concentrate (RCC) after group and save sampling, in case clinical deterioration warranted emergency surgical intervention. The patient was also counselled to increase her liquid intake.

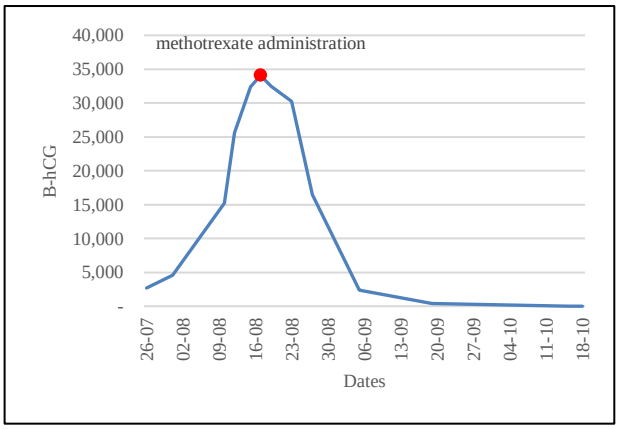

Figure 3: Rising β-hCG levels and fall after methotrexate administration

The patient was admitted to the hospital and a single dose of 50 mg/m^2 intramuscular MTX was administered. She remained stable and β-hCG after 24 hours showed declining levels. She was discharged after 48 hours with advice for clinical follow-up. The patient was advised to get quantitative serum β-hCG measurements on day 4, and day 7. A decline of >45% between day 4 (32,446 IU) and day 7 (16,433 IU) was observed proving the success of a single-dose regimen. Subsequently, weekly β-hCG levels were checked to monitor her progress. In the eighth week following MTX treatment, her β-hCG level dropped to 2.6 IU (nonpregnancy level). The patient was counselled on various contraceptive methods and advised to strictly avoid a pregnancy in the next 3-6 months (Figure 3).

DISCUSSION

An ectopic pregnancy is defined as the implantation of a fertilized ovum anywhere outside the uterus. Ectopic pregnancies account for 0.5-2% of all pregnancies. The most common location for an ectopic pregnancy is the ampullary region of the fallopian tube. Ovarian ectopic pregnancies are rare and account for less than 1% of all ectopic pregnancies.[1] They can either be primary (in the cortex) or secondary (on the surface of the ovary).[4]

Risk factors for ectopic pregnancy include pelvic adhesions (due to prior abdominal, pelvic, or fallopian tube surgery, pelvic inflammatory disease, or endometriosis), and ovulation induction treatments such as IVF and letrozole.[4-6] With the increasing use of intrauterine contraceptive devices and assisted reproductive technology, the incidence of ectopic ovarian pregnancy is also on the rise.[5] IUCDs prevent 99.5% of all intrauterine and 95% of tubal pregnancies, however, they do not play any role in preventing ovarian ectopic pregnancies.[7] 57-90% of all ovarian pregnancies have been found to be associated with IUCD usage.[8]

Diagnostic modalities like ultrasonography (USG) have enabled earlier detection of ectopic pregnancies, allowing for timely management. An important surgical diagnostic criterion for ovarian ectopic pregnancy was established by Otto Spiegelberg in 1878. According to the Spiegelberg criteria, the following requirements must be fulfilled for the diagnosis of ovarian ectopic pregnancy: The ipsilateral fallopian tube, including the fimbriae, must be intact and clearly demarcated from the ovary; the gestational sac must definitively occupy the normal anatomic position of the ovary; the sac must be attached to the uterus via the utero-ovarian ligament; ovarian tissue must be present in the wall of the removed pregnancy specimen.[9] Important differentials to consider in this case are corpus luteal cyst, hemorrhagic cyst, and molar ectopic pregnancy. These differentials make the diagnosis challenging for both surgeons and radiologists alike. This is because the presence of a cystic mass and a positive pregnancy test in the setting of an absent intrauterine gestational sac could also represent the corpus luteum of an early or nonviable intrauterine pregnancy.[10]

Women with ovarian pregnancies most commonly present in the first trimester with acute abdominal pain and bleeding per vagina. Ovarian rupture occurs in around 91% of women in the first trimester, who present with hemodynamic instability and signs of peritoneal irritation.[11] The thin-walled structure and decreased elasticity of the ovarian cortex are the main contributing factors to the rupture of the ovary; increased vascularity of the ovary leads to massive internal hemorrhage.[8] At this point, USG can no longer differentiate between a ruptured ovarian and a ruptured tubal pregnancy. An ovarian ectopic pregnancy rarely presents without any characteristic signs and symptoms. The absence of an intrauterine pregnancy, hence, necessitates that further investigation be done to rule out intratubal or ovarian ectopic pregnancy.

Table 1: The American College of Obstetrics and Gynecology (ACOG) guidelines.[13]

Contraindicated	Good candidate	Poor candidate
Hemodynamically unstable	Hemodynamically stable	High hCG (>5000 mIU/ml)
Suspected ruptured ectopic pregnancy	Low hCG (<5000 mIU/ml)	Large mass (>3.5 cm)
Sensitivity to methotrexate	Small mass (<3.5 cm)	Embryonic cardiac activity present
Intrauterine pregnancy	Unruptured mass	Significant abdominal pain
Breastfeeding	No embryonic cardiac activity	Intrauterine pregnancy has not been ruled out
Active pulmonary disease	Certainty that there is no intrauterine pregnancy	Questionable ability to return for all outpatient visits
Renal disease	No known sensitivity to MTX	
Chronic liver disease	Willingness for follow-up	
Immunodeficiency		
Peptic ulcer disease		
Preexisting blood dyscrasia		
Unable to come for a follow-up visit		

MTX: methotrexate.

Treatment modalities for ovarian ectopic pregnancy include medical management with methotrexate and/or surgical intervention with laparoscopy. According to the American Society of Obstetrics and Gynecology, indications for medical management include hemodynamic stability, β-hCG levels <5000 mIU/ml, mass diameter of <3.5 cm, unruptured mass, absence of intrauterine gestation, and no embryonic cardiac activity. In addition, the patient must be compliant with follow-up appointments.

Methotrexate (MTX), is a folate antagonist and antineoplastic agent that inhibits proliferation of the ovum and prevents stretching and rupture of the ovary. Furthermore, the use of multi-dose methotrexate as additional therapy to surgery allows for the destruction of any remaining fetal cells. Medical management with methotrexate has the advantage of preserving the ovary and avoiding oophorectomy and its complications such as decreased future fertility, and other surgical complications such as the development of adhesions which increases the risk of future tubal ectopic pregnancy. Side effects of methotrexate include nausea, vomiting, mouth ulcers, rash and immune deficiency.[12]

There are several regimens for methotrexate; single-dose, double-dose, and multi-dose. A single dose of 50 mg/m^2 body surface area (or 1 mg/kg body weight) of methotrexate is given after which hcG levels are checked on days 0, 4, and 7. If hCG levels do not fall by 15% between days 4 and 7, the second dose is administered on day 7. The multi-dose regimen involves 1 mg/kg of methotrexate and 0.1 mg/kg of leucovorin (folinic acid), with each given on alternate days. HCG is monitored on days 0, 1, 3, 5 and 7. Additional doses are administered only if hCG does not drop by 15% from the previous value.[13] If medical management is unsuccessful, surgical treatment is advised.

Our patient, a 31-year-old, asymptomatic, hemodynamically stable woman, with an unruptured ovarian ectopic pregnancy of diameter <3.5 cm and no embryonic cardiac activity made her a good candidate for medical management with methotrexate (Table 1). The criterion for medical management was fulfilled with the exception of the patient's β-hCG levels being 34,111 IU (> 5000 IU). Moreover, the absence of any known contraindications to MTX in our patient further solidified the rationale for its administration. The patient was counseled regarding the potential outcomes and risks associated with both medical and surgical treatments. After multidisciplinary meetings, and keeping the patient's concerns for future fertility in mind, a decision was made to proceed with medical management. Prior to administering methotrexate, the patient's β-hCG levels had already dropped by 1500 IU indicating that the pregnancy was in an early stage of failure. At a β-hCG level of 32,446 IU, our patient was administered a single dose of 50 mg/m^2 methotrexate intramuscularly and kept under observation. β-hCG levels recorded were 30,237 IU on day 4 and 16,433 IU on day 7, indicating a steep decline of more than 45%, hence additional doses were not required in our patient. As the pregnancy was already failing, administration of methotrexate augmented the clearance of fetal tissues from the ovary. Following this, her β-hCG levels gradually declined over eight weeks, finally dropping to below 2.6 IU, proving the success of conservative management and treatment.

CONCLUSION

Ovarian ectopic pregnancy should be kept in mind in women presenting with raised β-hCG levels without an intrauterine gestational sac. The absence of common symptoms, such as abdominal pain and hemodynamic instability, should not be used to rule out the diagnosis. In hemodynamically stable patients, especially those who are young, nulliparous, and without any known risk factors, the use of methotrexate should be considered due to its advantage of preserving future fertility

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Rafiq S, Shakeel S, Tanveer N, Pervaiz Z, Khan T. Silent ovarian ectopic pregnancy: a case report. Int J Reprod Contracept Obstet Gynecol 2024;13:1837-41.