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Successful Management of Cervical Ectopic Pregnancy with Multimodal Intervention: A Case Report

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Abstract

Cervical ectopic pregnancy is a rare obstetric complication that can result in significant risk of life-threatening hemorrhage, necessitating prompt diagnosis and treatment. It accounts for less than one percent of all extra-uterine pregnancies; it poses unique challenges due to the absence of established management guidelines. Despite its rarity, the incidence of cervical ectopic pregnancies is increasing due to *in vitro* fertilization and increasing in cesarean delivery. A high index of suspicion, along with clinical and radiological correlation, particularly in cases with previous uterine scars, can aid in preoperative detection.

We present the case of a 35-year-old para II both cesarean delivery mother, who presented with minimal, bright red, and painless vaginal bleeding at 7+3 weeks' gestation from the reliable last normal menstrual period. With an initial serum beta HCG level of 79,918 mIU/ml and positive fetal cardiac activity, a multimodal intervention strategy was employed, including multiple-dose systemic methotrexate, local potassium chloride injection, and cervical dilation and curettage. This approach successfully treated the cervical ectopic pregnancy while preserving the patient's fertility. Our case underscores the importance of early diagnosis and multimodal management in optimizing outcomes for cervical ectopic pregnancies. To preserve fertility in the management of cervical ectopic pregnancy with high serum β-HCG, clinicians could consider a combination of strategies.

Keywords: Cervical ectopic pregnancy; Methotrexate; Fertility preserving treatment; Potassium chloride injection; Dilation and curettage

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Introduction

Cervical Ectopic Pregnancy (CEP) represents a rare form of ectopic gestation wherein the fertilized ovum implants within the endocervical canal, accounting for less than 1% of all extra uterine pregnancies [1]. Ectopic pregnancies in general pose a significant risk to maternal life if undiagnosed or improperly managed, with CEP particularly feared due to its association with life-threatening transvaginal hemorrhage [2]. Historically, emergency hysterectomy was often required to manage extensive hemorrhage, posing a risk to the patient's fertility [3]. However, advancements in high-resolution transvaginal sonography have improved the accuracy of CEP diagnosis [4], enabling earlier detection in asymptomatic patients and facilitating conservative medical treatments such as Methotrexate (MTX) or Potassium Chloride (KCl) administration [5]. Nevertheless, no gold standard treatment exists, especially for advanced CEP cases.

Therapeutic options for CEP include surgical and medical interventions, with traditional management prioritizing maternal hemorrhage risk and often resorting to hysterectomy, potentially compromising fertility [3]. Methotrexate, an effective first-line therapy for early CEP in hemodynamically stable patients, is associated with complications necessitating alternative surgical remedies in case of failure [6]. Embryo reduction has emerged as a viable alternative for preserving reproductive potential when medical treatments fail, demonstrating success in resolving CEP cases without complications [7]. Optimal management remains debated, with multimodal interventions are essential for successful outcomes. We present a rare case of CEP where medical treatment with dilation and curettage is successful management for those with positive cardiac activity and serum β-HCG greater than 10,000 mIU/mL with preserving fertility.

Case Presentation

A 35-year-old gravida III, para II (both early neonatal deaths), mother, whose gestational age from reliable last normal menstrual period was 7+3 weeks, presented to the gynecologic emergency department with a complaint of minimal, painless, and bright red vaginal bleeding of 2 weeks'

Figure 1: Transvaginal ultrasound indicating a cervical ectopic pregnancy at 7 weeks and 6 days gestation, exhibiting positive cardiac activity prior to treatment.

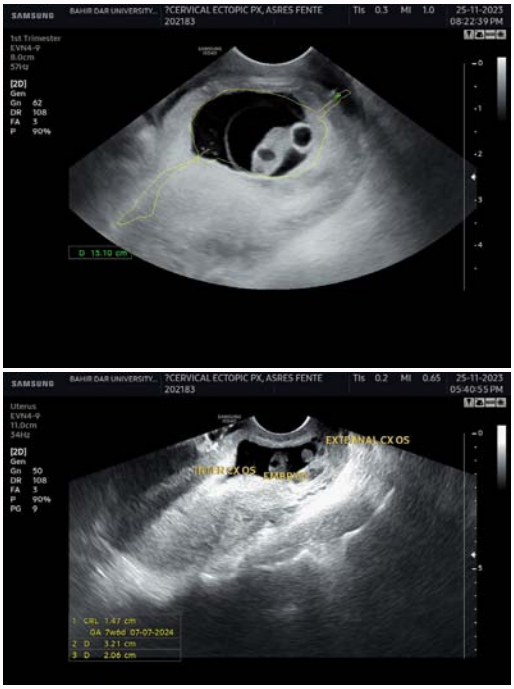

Figure 2: Figures A and B from transvaginal ultrasound revealing an empty uterine cavity with a closed internal os, while displaying products of conception within the intracervical canal.

duration. Previous deliveries were both through cesarean delivery.

On physical examination, the patient's abdomen was soft and non-tender, with an old suprapubic scar. Initial vital signs were blood pressure 110/70 mmHg, respiratory rate 20 breaths per minute, temperature 36.6°C, and pulse rate 80 beats per minute. A sterile speculum exam showed a cystic anterior cervical mass with the cervical os pushed posteriorly. Transvaginal ultrasound revealed a thickened endometrium, closed internal and external cervical os, an embryo in the cervical os with positive cardiac activity which was surrounded by hypervascularity on Doppler and it is below the level of uterine artery insertion, and the gestational age by crown-rump length was determined to be 7+6 weeks (Figures 1-3). All hematological values were within normal limits. The baseline serum beta-Human Chorionic Gonadotropin (HCG) level was 79,918 mIU/mL. After discussing with the patient on management options and possible complications, medical management was decided. The patient received an intramuscular injection of methotrexate 50 mg/m^2 BSA on days 1, 3, 5, and 7, and a folinic acid injection of 0.1 mg/kg on days 2, 4, 6, and 8.

Apart from clinical and hematological monitoring, the effect of medical management was assessed with transvaginal ultrasound and serial serum β-HCG measurements that were determined every two days. After the first dose of methotrexate and folinic acid administration, serum β-HCG was increased to 94,147 mIU/mL from baseline. The second dose of methotrexate and folinic acid was given, and beta HCG was determined to decrease to 52,054 mIU/ml from baseline. Even though serum beta HCG has been decreased by 35% from baseline, fetal heartbeat remained positive. Intra-amniotic potassium chloride injection was performed, and multiple doses of methotrexate were continued. After the third dose of methotrexate and on the second post-procedure day of potassium chloride injection, β-HCG decreased to 32,929 mIU/mL, and transvaginal

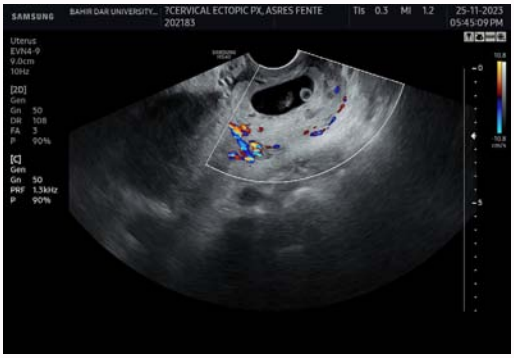

Figure 3: Color Doppler imaging revealing blood flow around the trophoblast layer.

ultrasound showed a decreased gestational sac, decreased coelomic activity, decreased vascularity, and no cardiac activity (Figure 4). Following multiple doses of methotrexate and a single dose of potassium chloride, serum β-HCG levels decreased serially. Dilation and curettage and a balloon tamponade insertion were done due to persistently high levels of serum β-HCG after a full course of multiple doses of methotrexate. Finally, the patient was discharged with stable vital signs on the third post-procedure day and was followed with ultrasound and serial serum HCG measurements (Table 1 and Figure 5). Biopsy taken during dilation and curettage showed abundant fibrino-hemorrhagic material consisting of scattered chorionic villi along with trophoblastic cells, concluding cervical ectopic pregnancy.

Discussion

Cervical Ectopic Pregnancy (CEP) is a rare form of ectopic gestation wherein the fertilized ovum implants within the endocervical canal, accounting for less than 1% of all extrauterine pregnancies [1]. Nowadays, the incidence of CEP seems to be rising, attributed not

Figure 4: Ultrasound images showing cervical ectopic pregnancy following administration of the third dose of methotrexate and 48 h post-potassium chloride injection.

Figure 5: Pelvic ultrasound image obtained during follow-up after undergoing multiple doses of methotrexate, potassium chloride injection, and dilation and curettage.

only to assisted reproductive technologies but also to improved access and accuracy of transvaginal ultrasound scanning [8].

Several risk factors increase the likelihood of individuals developing CEP (Cervical Ectopic Pregnancy). These include undergoing *in-vitro* fertilization, experiencing endometrial injury due to pelvic inflammatory disease, encountering post-surgical trauma like cesarean section or uterine curettage, having a history of abortions, using intrauterine contraceptive devices, developing intrauterine adhesions, having benign growths such as myomas, and having structural uterine anomalies [9]. Our case involved a patient with a history of two previous cesarean sections, which is a significant risk factor for CEP.

The most common symptom of CEP is painless vaginal bleeding following a period of amenorrhea [9], as observed in our case. Diagnostic criteria proposed by Paulman and McEllin (1959) involve amenorrhea, uterine bleeding without abdominal pain, an hourglass-shaped cervix, and the absence of placental tissue upon endometrial curettage.

Ultrasound imaging is essential for diagnosing CEP (Cervical Ectopic Pregnancy), relying on specific criteria including the absence of an intrauterine pregnancy, the presence of a gestational sac below the level of the internal cervical os, the absence of a sliding sign, and the detection of flowing blood around the gestational sac using Doppler technology [10]. However, it's crucial to distinguish CEP from other conditions such as incomplete abortion and large Nabothian cysts [8]. Concerning ultrasound features, cervical pregnancy can be

Table 1: Quantitative serum beta HCG levels.

Date	B HCG mIU/mL
16/3/2016 E.C	79918
18/3/2016 E.C	94147
20/3/2016 E.C	52054
22/3/2016 E.C	59901
28/3/2016 E.C	32929
1/4/2016 E.C	19346
3/4/2016 E.C	9580
8/4/2016 E.C	2458
25/4/2016 E.C	19
2/5/2016 E.C	5.4

mistakenly identified as scar pregnancy. The key difference lies in the location: cervical pregnancy is situated below the internal os, whereas scar pregnancy occurs above, typically at the level of the cesarean scar incision. Additionally, cervical pregnancy may often be misdiagnosed as an ongoing abortion. The most effective method to differentiate between the two scenarios is by observing the sliding sign. This entails applying gentle pressure on the cervix with the ultrasound probe; in cervical pregnancy, the implanted gestational sac does not slide, unlike the gestational sac in abortion cases [11].

The exact etiology and pathogenesis of CEP remain unclear, with hypotheses suggesting damage to the uterine cavity impairs normal implantation in the endometrium [12].

Therapeutic approaches for CEP aim to preserve fertility and may include systemic or intra-amniotic methotrexate injection, local intra-sac potassium chloride injections, or cervical canal vacuum evacuation followed by Foley catheter tamponade. In cases where medical treatment fails or is contraindicated, fertility-sparing surgical methods such as excision of the trophoblast *via* curettage/aspiration or surgical hysteroscopy may be considered [13]. During managing cervical ectopic pregnancies, it is important to take into account factors such as patient stability, β-hCG level, pregnancy size, and fetal cardiac activity [14]. A planned multimodal approach is often beneficial, which may involve the use of medications such as methotrexate, mifepristone, and misoprostol, usually combined with interventional measures. Methotrexate is the most effective medical treatment, administered either systemically *via* intramuscular single or multiple doses and/or locally *via* intra-amniotic injection. Systemic methotrexate treatment may fail when the serum β-hCG level exceeds 10,000 m IU/mL, the crown-rump length surpasses 10 mm, or fetal heartbeat is present [8]. In such cases, combined therapy with intra-amniotic methotrexate can enhance treatment effectiveness. When a fetal heartbeat is detected, intra-amniotic administration of potassium chloride for embryocide or feticide is recommended [15]. If medical treatment fails or is not feasible, fertility-sparing surgical methods such as trophoblast excision *via* curettage/aspiration or surgical hysteroscopy may be considered [11].

However, due to the absence of smooth muscle tissue in the cervical region, there is a risk of significant bleeding during dilatation and curettage, often necessitating emergent hysterectomy to control hemorrhage [8]. Therefore, adjuvant measures to reduce blood loss post- or pre-procedure are recommended, including tamponade with a Foley balloon catheter, reduction of blood supply by vasopressor/prostaglandin cervical injections, cervical cerclage, surgical ligation

of cervical/uterine/internal iliac arteries, and arterial embolization [15]. In cases where serum hCG levels exceed 10,000 IU/mL and fetal heartbeat is present, multiple-dose systemic methotrexate injection and single-dose intraamniotic potassium chloride injection was preferred in this case. Regardless of the chosen treatment, follow-up until complete resolution, defined by negative serum hCG values, is necessary [11]. Due to the substantial risk of potential hemorrhage, the patient underwent close monitoring in the hospital for 29 days. Dilation and curettage were performed, and a balloon tamponade insertion was carried out due to persistently high levels of serum hCG after completing the full course of multiple doses of methotrexate. Subsequent follow-up continued until serum beta hCG levels dropped below 5 mIU/mL.

In an effort to avoid major surgical interventions that could negatively affect fertility, a personalized treatment approach combining minimally invasive procedures and medical therapy was devised for our case. This approach effectively controlled the elimination of the pregnancy while preserving the patient's fertility. Finally, considering the teratogenic effect of methotrexate, classified as pregnancy category X by the FDA [13], a reliable contraceptive method should be prescribed for at least three months after methotrexate therapy. In our case, she was given combined oral contraceptive pills for three months.

Conclusion

In summary, a personalized combination of various techniques tailored to individual circumstances can effectively preserve fertility in patients with cervical pregnancy. While this approach may carry a higher risk of complications, personalized medicine incorporating conservative treatments presents a viable option for patients seeking to maintain their reproductive potential. Successful outcomes in our case were attributed to a multimodal management approach including multiple dose systemic methotrexate, intra-amniotic KCL injection, and dilatation and curettage. It is essential for treating physicians to recognize the rarity of cervical ectopic pregnancies and the critical nature of timely diagnosis and individualized intervention to prevent life-threatening complications.

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