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Case Report

Cervical Ectopic Pregnancy, a Case Report and Literature Review

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Abstract: Cervical ectopic pregnancies (CEP) are rare, comprising less than 1% of ectopic pregnancies with an incidence of one in 2500 to one in 18000, and 1 to 2.0% of all pregnancies. Due to the rich cervical vascularity and the incompatibility of the cervix to hold an advancing pregnancy, there is a marked increase in the potential of hemorrhage leading to mortality, morbidity, and infertility experienced by the implicated women. There is a divergence of preferences among health care providers for CEP management which ranges from non-surgical methods to hysterectomy. However, a timely diagnosis increases the likelihood of implementing more conservative methods and retaining patients' fertility. New improvements in high-resolution ultrasonography made earlier diagnosis possible, which lead to the development of many conservative treatment approaches that avoid the need for a hysterectomy and preserve fertility. A high index of suspicion, combined with a detailed review of clinical and radiological findings, is essential to make an accurate diagnosis of cervical pregnancy. Our case presents early diagnosis made of a cervical ectopic pregnancy treated medically with the avoidance of surgical intervention and its associated risks. Early diagnosis is essential as it decreases the risks of future infertility and decreases the risk of fatal complications associated with such pregnancies.

Keywords: Cervical Ectopic Pregnancy, Medical Versus Surgical Treatment, Preservation of Fertility, Radiological Findings in Cervical Ectopic Pregnancy

1. Introduction

Ectopic pregnancies comprise 2% of all clinically recognized pregnancies. These pregnancies occur when a fertilized ovum implants outside the uterine cavity most commonly in the fallopian tubes [1]. Cervical ectopic pregnancies are rare, comprising less than 1% of ectopic pregnancies with an incidence of one in 2500 to one in 18000 [2] and 1 to 2.0% of all pregnancies [3, 4]. Diagnosing EP can be difficult due to its unusual location thus leading to serious health risks to pregnant women [5, 6]. A misdiagnosis or a missed diagnosis of cervical ectopic pregnancy and a consequent delay in treatment could pose a serious threat on pregnant women with a resultant high morbidity and mortality. Cervical ectopic pregnancies have a potential for massive hemorrhage which could lead to a hysterectomy and even death [7, 8]. Ectopic pregnancy accounts for 31.9 pregnancy-related deaths per 100,000 pregnancies in the United States [9] therefore early diagnosis and management is crucial for safe outcomes. Due to the rich cervical vascularity and the incompatibility of the cervix to hold an advancing pregnancy, there is a marked increase in the potential of hemorrhage leading to mortality, morbidity, and infertility experienced by the concerned women [10].

Cervical ectopic pregnancies are due to implantation of a fertilized ovum in the endocervical canal below the level of

internal os [3, 4] with several radiologically defined criteria for diagnosis (discussed later on). Predisposing factors include: trauma to the endometrium after curettage or chronic endometritis, cervical stenosis, leiomyoma, intrauterine devices, in vitro fertilization and primary embryo anomalies. However, the rare incidence of CEP has prevented the publication of retrospective studies, and its association with all these factors remains weak [11-13].

There is a divergence of preferences among health care providers for CEP management which ranges from non-surgical methods to hysterectomy. However, a timely diagnosis increases the likelihood of implementing more conservative methods and retaining patients' fertility [14].

2. Case Presentation

This is a case of a 37 year old Lebanese woman G3P1011 (previous NVD) BG Opos presented to our Emergency Department at 5 weeks and 5 days pregnant with vaginal spotting, mild campy pelvic pain, but otherwise no other reported symptoms.

Patient reports a history of inherited thrombophilia diagnosed earlier, for which she took aspirin during her previous pregnancy but no other medical problems. Her past surgical history consists of one D&C and a Rhinoplasty. She denies any known allergy to any drug or medication. She also denies any history of cigarette smoking, alcohol or illicit drug use during or outside of pregnancy. She only took her prenatal vitamins and aspirin (stopped same day of presentation to ED). Her review of systems was negative for any fever, chills, abnormal vaginal discharge, and nausea or vomiting.

On admission her vital signs were stable. BP 100/70, HR 84, afebrile. Physical exam showed mild suprapubic tenderness.

Routine labs including CBC, PT/PTT, LFTs, creatinine levels, and BHCG were taken on Emergency Department admission. These showed the following values:

Hb: 15.2g/dl, Hct: 46%, Wbc: 7700/mm^3, Plts 268000/mm^3, Pt INR: 1.5, Ptt: 38.3 seconds, GGT: 9 U/L, SGOT: 15 U/L, SGPT: 12 U/L, Alk phos: 50, creatinine: 0.58 with a serum BHCG of 2270 mIU/ml.

An official pelvic ultrasound was ordered and showed: "cervical ectopic pregnancy located at the cranial aspect of the endocervical canal".

Decision was made to give an intramuscular methotrexate injection (82.2mg based on Body Surface Area) and to repeat BHCG levels on days 4 and 7 after treatment.

On day 4, Patient presented to our ED with severe vaginal bleeding, having passed multiple blood clots at home with uncontrollable heavy bleed changing a pad every 30 min in addition to having menstrual cramps.

On admission patient vitals were stable: BP was 100/70 mmHg and HR 80 bpm. She was afebrile and physical exam done showed mild pelvic pain.

The ultrasound was followed by a speculum exam showing small blood clots around the cervix and a small (around 1 cm) cyst like structure that was sent to pathology. The Pathology specimen diagnosis came out a few days later as chorionic villi that could constitute the sac previously present in the cervix.

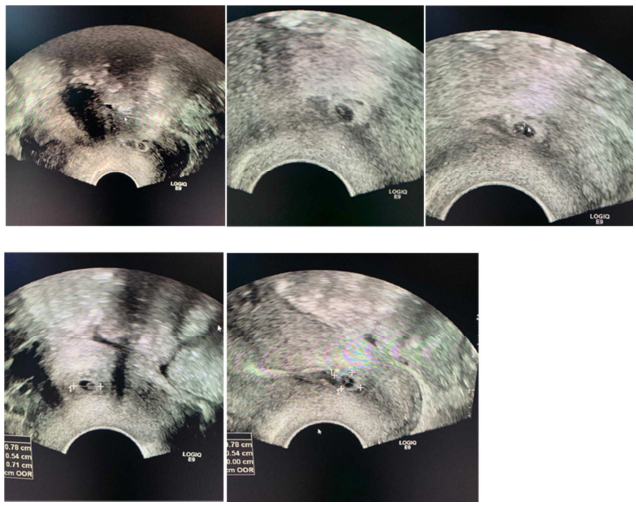

Figure 1. *Images of CEP on day 0 methotrexate.*

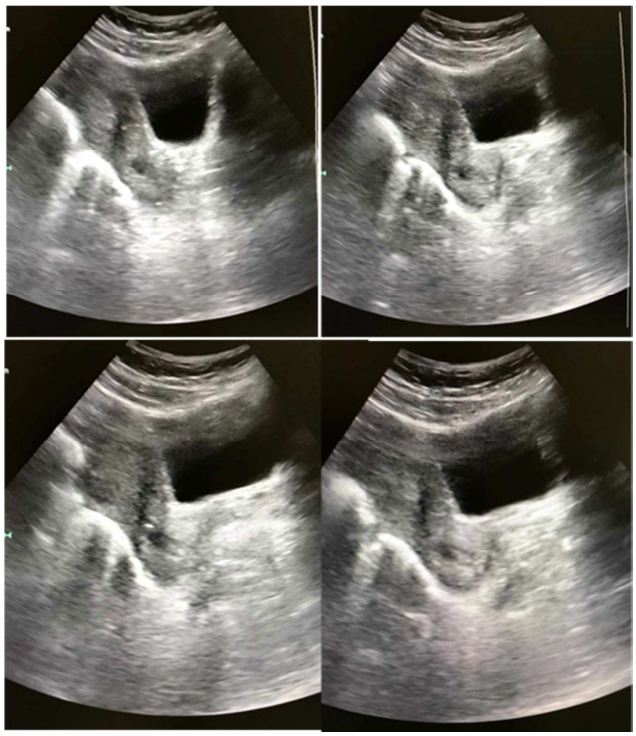

Figure 2. *Images of CEP on day 4 methotrexate by pelvic ultrasound (abdominal approach).*

A count of pads was started to keep monitoring her bleeding from admission. Bleeding progressively decreased from admission to become streaks. Patient was given 1g of Tranexemic acid slowly over 1 hour in 1L hydration fluid to keep the bleeding to a minimum.

A full lab workup was repeated including a CBC, PT/PTT, LFTS, creatinine, and a serum BHCG (same time as day 0 and in the same lab) with the following values:

Hb: 13.4 g/dl, Hct: 40.7%, Wbc: 5130/mm^3, Plts 253000/mm^3, PT INR: 0.93, PTT: 28.42 seconds, GGT: 8 U/L, SGOT: 19U/L, SGPT: 13U/L, Alk phos: 48, creatinine: 0.59

BHCG in serum day 4: 1484

Repeat BHCG on day 7: 294.82

BHCG day 10: 94.67. By this day bleeding was very minimal.

BHCG day 17: 8.63

No further workup was needed to treat her CEP as her BHCG became negative upon follow up after a single dose of methotrexate IM.

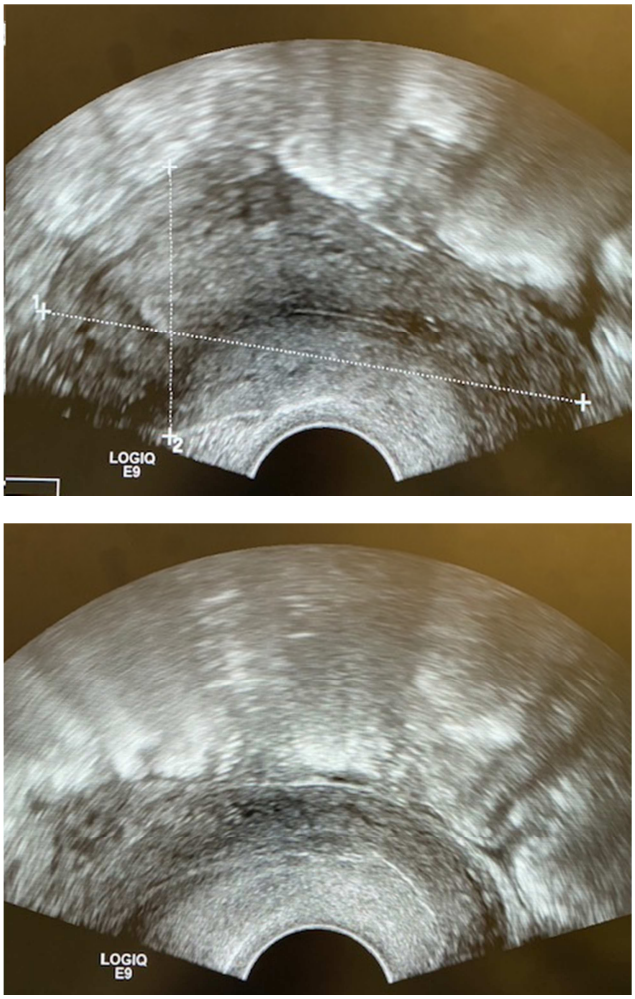

Figure 3. *Images of CEP one month post methotrexate by pelvic ultrasound (vaginal approach).*

3. Discussion

New improvements in high-resolution ultrasonography made earlier diagnosis possible, which lead to the development of many conservative treatment approaches (medical or surgical) that avoid the need for a hysterectomy and preserve fertility.

Diagnosis (Clinically, Ultrasound, MRI) [advantage of early diagnosis]

3.1. Clinical Diagnostic Criteria

Painless vaginal bleeding is the most common presentation. Only one third of women present with massive hemorrhage. In 1959, Paalman and McElin [15] offered *5 clinical signs to establish the diagnosis:*

(1) Uterine bleeding without cramping pain after a period of amenorrhea.

(2) Softened and disproportionately enlarged cervix equal to or larger than the corporal portion of the uterus (an hourglass-shaped uterus).

(3) Products of conception entirely confined within, and firmly attached to, the endocervix.

(4) A snug internal os.

(5) A partially opened external os.

3.2. Ultrasound & Doppler

The hallmark ultrasonographic image by color Doppler is an empty uterus and a gestational sac within the cervix, protruding the anterior or posterior wall of the cervix with a peri-trophoblastic blood flow [13].

The combination of transvaginal and transabdominal ultrasonography with high-resolution transducers establishes a diagnosis in most of the cases in the first trimester. It is essential because only cases diagnosed before twelve weeks, where the trophoblast has not infiltrated too deeply into the cervical wall, are amenable to conservative treatment.

In 1978, Raskin [16] *suggested 4 sonographic diagnostic criteria:*

(1) Enlargement of the cervix

(2) Uterine enlargement

(3) Diffuse amorphous intrauterine echoes

(4) Absence of intrauterine pregnancy

In 1996, Jurkovic et al [17] added two diagnostic criteria to differentiate between an intrauterine pregnancy that is aborting and present at the level of the cervix and a cervical ectopic pregnancy:

(1) The "sliding sign" detected on transvaginal ultrasound examination when the gestational sac of an abortus slides against the endocervial canal after gentle pressure on the cervix with the vaginal probe. This sign is not seen in an implanted cervical pregnancy.

(2) The presence of peritrophoblastic blood flow shown by color flow Doppler which is not present in a nonviable sac passing through the cervix.

Three-dimensional transvaginal ultrasonography is also used in obese women and in the presence of a retroverted uterus which promotes a detailed analysis of the endometrial cavity.

The impression of a cervical pregnancy while performing ultrasonography is exact in 87.5% of cases of true cervical ectopic pregnancies.

3.3. MRI

MRI is used when an ultrasonographic impression is inconclusive while facing unusual or complicated cases. Magnetic resonance imaging (MRI) is also used as a supplementary method [18]; It can be used to differentiate between a cervical and cervical-isthmic pregnancy. The combination of both the ultrasonographic and MRI techniques allows better view of disease evolution and early diagnosis [13, 18].

There is little evidence about the sensitivity and specificity

of imaging modalities in the diagnosis of cervical Ectopic pregnancy.

4. Treatment

Many factors should be considered for each patient when considering treatment options including but not limited to: controversial medical and surgical CEP management strategies, gestational age, hemodynamic status of the patient, fertility preservation, and physician expertise.

Different medical and surgical therapies are reported:

4.1. Medical Treatments Include

Single or multidose systemic methotrexate (MTX), local intraamniotic sac injection (with either MTX, potassium chloride or absolute ethanol), or a combination of these treatments [19, 20].

4.2. Surgical Treatments Include

Uterine artery embolization (UAE) [21], dilation and curettage with balloon insertion [22], hysteroscopy [23], and hysterectomy in uncontrolled hemorrhage or failed medical management. Case reports of cervical cerclage are successfully reported for the management of CEP especially in heterotopic pregnancies [24, 25]. Foley catheter placement in the cervix, d evascularization of the uterus, internal iliac artery ligation, uterine artery embolization and needle aspiration of the gestational tissue are also used [26]. The local or systemic administration of MTX, later followed by hysteroscopic resection, seems to minimize the risks for patients and preserve fertility [27].

Cerclage methods are also used in specific cases when medical therapy or UAE contraindications are present or when hysteroscopies are not available.

Early detection of a CEP and treatment medically or in combination with minimally invasive methods to preserve fertility, is widely used as a conservative method [28]. MTX is very successful at early gestational ages mainly before 12 weeks gestation. MTX is very successful at early gestational ages mainly before 12 weeks gestation. 15% decrease in serum βHCG is needed when comparing days 4 and 7 to attain a successful MTX treatment. Most commonly after MTX treatment people experience nausea, vomiting, stomatitis, diarrhea, and elevated liver function tests but are mild symptoms. Rarely do they experience nephrotoxicity, interstitial pneumonitis, and alopecia dermatitis.

Several publications describe successful intraamniotic MTX administration in monofetal or multifetal CPs as a single approach or combined with other conservative methods [29]. These combinations have a success rate of almost 90%. Systemic administration of MTX in multiple doses has been described as one of the methods of treatment of CEP, recommending its use in cases of low gestational age fetuses and in the absence of fetal viability.

According to the most recent literature, conservative management of CEP with MTX (systemic or local or both) has success rates of 92.7% for multi-dose treatment and 88.1% for single-dose treatment, respectively [27]. In some cases, curettage was used as a complementary treatment in combination with MTX [29]. Curettage is a blind method which is why there is a high risk of injury to the cervical gestation, and a higher risk of uncontrollable bleeding which makes is why this method of treatment is rarely used.

The dose regimens of systemic methotrexate varies. Single dose (50 mg/m^2 intramuscularly IM) with monitoring of serum hCG levels on days 4 and 7 was described. If the difference in serum hCG levels is 15% or greater, the test is repeated weekly until it becomes undetectable. If the difference is less than 15%, methotrexate dose should be repeated, and new day 1 is begun. Multiple-dose regimens are used as well such as the 1 mg/kg on days 1, 3, 5, 7, and 9 IM either with or without the folinic acid rescue dose on the days in between. There should be at least a 1 week period before being able to use more than 5 doses of methotrexate. In 2009, an alternative high-dose regimen of methotrexate was suggested by Song et al [30] in the form of a single course of 100 mg/m^2 in addition to 200 mg/m^2 in 500 mL of normal saline given intravenously with a 0.1 mg/kg rescue dose of folinic.

Methotrexate can also be used intracervically or intra-sac in a dose of 50 mg/m^2. This method might lead to active bleeding after the injection due to the rupture of the intra-amniotic membrane. Unfortunately, the present data are too limited and inconsistent to compare the efficacy of different regimens [31].

Follow up after methotrexate and the resolution time of cervical pregnancy after chemotherapy, as determined by serum hCG levels, varied from 2 to 5 weeks and, by sonographic appearance of the cervix, varied from 2 to 12 weeks. An issue that might be faced with methotrexate use is the possible occurrence of severe bleeding due to atony and involution of the cervix after having shed the trophoblastic tissue.

Current literature review showed that 49% of viable cervical pregnancies have required an additional operative procedure to eradicate the aberrant trophoblastic tissue.

Unsatisfactory results of primary methotrexate treatment might occur due to many prognostic factors present including an elevated serum hCG level (10,000 mIU/mL or greater), a gestational age of 9 weeks or later, presence of a heartbeat, or a crown-rump length of more than 10 mm.[31].

5. Risks and Future Feritility

Historically, CEPs were difficult to diagnose and were identified at later gestational ages [27]. Because of profuse vascularization and strong blood flow of cervical tissue, CEP was often associated with massive hemorrhage, which often led to life-threatening complications and necessitated emergency hysterectomy. Early diagnosis is associated with decrease in morbidity, because treatment options are capable of preserving the uterus and subsequent fertility [18].

According to the literature there is no consensus for

treatment. Cervical pregnancy is often associated with significant morbidity and devastating effects on future fertility. This can be due to the deep rooting effect of the trophoblast into the cervical walls and the uterine blood supply. 70% of reported cases of CEP required hysterectomy due to massive blood loss [32]. The maternal mortality was reported to be 0% to 6% [33, 34].

The effect of cervical pregnancy on future fertility is largely unknown because of the rarity of this condition and the infrequent observation after treatment. The rarity of theses cases makes it difficult to predict as well if the risk of their recurrence is elevated. This is why it is recommended to council women of the possible recurrence of an ectopic pregnancy or a pregnancy loss in the second trimester, and possibly need ing a prophylactic cerclage.

6. Conclusion

A high index of suspicion, combined with a detailed review of clinical and radiological findings, is essential to make an accurate diagnosis of cervical pregnancy. The success of conservative treatment options and avoidance of surgical intervention depends mainly on early diagnosis. Early diagnosis is essential as it decreases the risks of future infertility and decreases the risk of other fatal complications associated with such pregnancies.

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