



Second-Trimester Cervico-Isthmic Pregnancy after Donor Egg *In Vitro* Fertilization, Complicated with Placenta Accreta – Case Report

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Abstract

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BACKGROUND: Cervical gestations are rare potentially life-threatening conditions. Although these can cause massive hemorrhage, most of them abort during the first trimester without having been diagnosed. However, cervico-isthmic pregnancies are more likely to persist to an advanced gestation in the second and third trimester owing the need for hysterectomy due to defect placentation.

CASE PRESENTATION: We presented a rare case of cervical pregnancy after donor egg *in vitro* fertilization procedure, with no previous pregnancies, medical, and surgical history. Our patient rejected early termination of pregnancy at 5 gestational weeks. Pregnancy continued until 16 weeks when she was hospitalized and terminated due to medical grounds with curettage. Post-operative period was uneventful until day 20, when she was admitted with suspicion of retained placental tissue and endometritis. A hysterectomy was done with blood transfusion due to excessive blood loss. Histologic examination confirmed placenta accreta spectrum disorder.

CONCLUSION: Cervical pregnancy can be treated conservative if timely diagnosed by early ultrasound, which can reduce the chances of severe life-threatening hemorrhage necessitating hysterectomy or blood transfusion.

Introduction

Cervical ectopic pregnancy is a potentially life-threatening condition that accounts for 0.1% of pregnancies from assisted reproductive technologies and 3.7 % of total *in vitro* fertilization (IVF) ectopic pregnancies. The incidence after spontaneous conception is between 1:2,500 and 1:12,000 of clinical pregnancies [1]. Cervical ectopic pregnancy is associated with a high risk of profuse hemorrhage due to marked vascularization of lower uterine segment, especially with advancing gestation. In the past, hysterectomy was the only treatment option. Ultrasonography is essential to confirm early cervical pregnancy, significantly increasing the possibility of preserving the reproductive capacity of the woman. True cervical pregnancy is defined by its location completely within the cervical canal, with no placental tissue above the internal os, and an intact part of cervical canal between the gestational sac, distally, and the uterine decidua, proximally [2], [3]. In cervico-isthmic implantation, the gestational sac is located more cranially, and the gestational sac is located between

the cervix, distally, and the decasualized functional endometrium, cranially. Although an ectopic pregnancy, a cervical pregnancy is also an extreme form of a placenta previa. There is no consensus on the best approach for treatment [4], [5], [6].

Case Report

A 46-year-old nulliparous woman after IVF with donor eggs was diagnosed with low implantation of gestational sac in the isthmo-cervical region at 5 gestational weeks (Figure 1). Her medical and surgical history was irrelevant.

According to the diagnosis and since the patient was nulliparous, an inpatient conservative approach was proposed with expectant management and follow-up examination after 7 days. A diagnosis of cervico – isthmic pregnancy was confirmed. Despite counseling regarding the poor outcome, woman wished to be re-scanned on a follow-up examination after

another 7 days. Unfortunately, there was no information about the case until 16 gestational weeks when she was hospitalized with the lower abdominal pain and vaginal bleeding. The following ultrasound findings were documented:

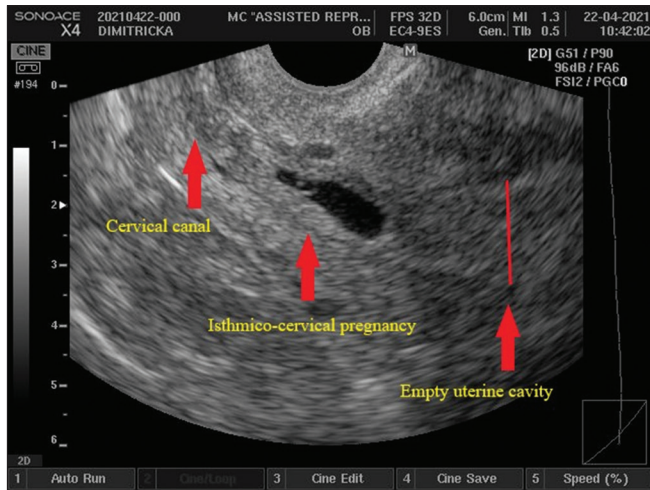


Figure 1: Transvaginal ultrasound (sagittal plane) - Decidual reaction in the empty uterine cavity, gestational sac with yolk sac in the isthmico-cervical region and closed cervical canal

A viable fetus in 16 gestational weeks, located in the isthmico-cervical region of the uterus and pseudoseptation, separating the empty uterine cavity from the isthmico-cervical segment was diagnosed (Figure 2). The length of the cervical canal was 1.7 cm with posterior low-lying placenta covering the cervical canal, suspected for placenta accreta spectrum disorders (Figure 3).



Figure 2: Transabdominal ultrasound. A pseudo-septum was visualized, separating the isthmico-cervical region (a*) and uterine cavity (b*)

After discussing the risk for continuing the pregnancy with possible complication of life-threatening hemorrhage, she was admitted for therapeutic abortion

on medical grounds. Medical abortion was induced with application of a hygroscopic dilator, 6 h before the manipulation and subsequent curettage in the operating room.



Figure 3: Transvaginal ultrasound. Posterior low-lying placenta with free floating placental structure, observation for placenta accreta spectrum disorders

Post-operative period was uneventful and patient was discharged on day 3. Twenty days later, she was hospitalized again with fever, vaginal bleeding, and abdominal pain, suspected for residual placental tissue and endometritis. Hysterectomy was performed and a diagnosis of placenta accreta with endometritis was confirmed (Figure 4).

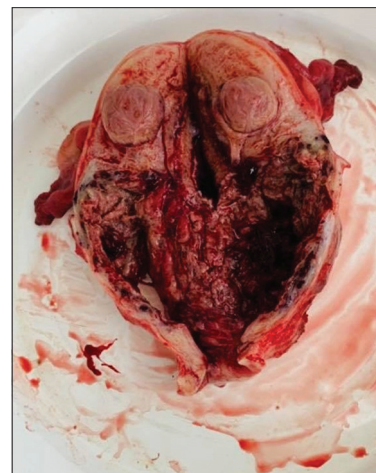


Figure 4: Macroscopic section of the uterus with residual placental tissue in the cervical region and evidence for placenta accreta spectrum disorders

Discussion

The incidence of cervical pregnancy after IVF is between 0.9% and 2%. Low implantation is associated with embryo transfer technique, but few studies have shown that this is the only factor. Other possible causes are: Ovarian hyperstimulation, multiple

embryo transfer, secondary infertility, and treatment for endometriosis [7], [8]. It is considered that cervical gestation is related to the exacerbation of contractions of the junctional zone of the uterus in luteal phase, affected by the elevation of progesterone, producing a similar effect on the tubal motility [4].

Risk factors for cervical ectopic pregnancy are the same as ectopic pregnancy at all: Pelvic inflammatory disease, induced abortion, uterine anomalies, fibroids, Asherman syndrome, uterine or cervical surgery, intrauterine device use, previous cesarean delivery, previous pelvic surgery, smoking, previous ectopic pregnancy, IVF, and diethylstilbestrol exposure [9]. Majority of women with cervical pregnancy have a low parity [10].

Cervical pregnancy combined with placenta accreta spectrum disorders can be explained by the absence of protective decidua basalis in the cervical stroma, which results in trophoblastic invasion into the cervical tissue [11]. Placental involvement of the cervix can cause erosion of the uterine arteries and massive bleeding when placental removal is attempted.

Cervical ectopic pregnancy can be misdiagnosed on ultrasound examination with similar pathologies like: Low implantation of normal uterine pregnancy, incomplete abortion, cesarean scar pregnancy, cervical mass, nabothian cyst, and heterotopic pregnancy. Due to the differences in the management and the outcome an accurate diagnosis is of a great importance. Regarding ultrasound features, the difference with scar pregnancy is that cervical pregnancy is located below the internal os, while scar pregnancy is located above, at the level of the cesarean scar incision. Cervical pregnancy can also be widely misdiagnosed as an ongoing abortion. The best way to distinguish the two situations is by the sliding sign, which means that when gentle pressure is applied on the cervix with the probe, the implanted cervical pregnancy does not slide, and unlike the gestational sac of the abortion [12].

There are strict sonographic criteria for the diagnosis as follows: (1) Intra-cervical localization of the ectopic gestation; (2) closed internal os; (3) trophoblastic invasion in the endocervical tissue; (4) empty uterine cavity; (5) hourglass-shaped uterus; (6) intra-cervical peritrophoblastic blood flow; and (7) diffuse amorphous intrauterine echoes [13]. Color Doppler is an important diagnostic marker for differentiating peritrophoblastic blood flow in cervical pregnancy and its absence in incomplete abortion localized in the cervical canal [14].

In our case, two ultrasonographic findings supported the diagnosis of cervico-isthmic pregnancy. First, the implantation of the gestational sac occurred near the sonographic internal cervical os and the cervical canal was preserved and closed, thus ruling-out cervical pregnancy. Second, more than half of the

uterine cavity above the sac was not involved by the sac implantation.

The main clinical manifestation was found to be painless heavy vaginal bleeding in the first trimester. Paalman *et al.* defined five clinical signs for diagnosing cervical ectopic pregnancy:

- a. Painless bleeding after a period of amenorrhea;
- b. Softened and disproportionately enlarged cervix, with a size equal to or larger than the size of the uterine body (hourglass-shaped uterus);
- c. Products of conception localized in the endocervix;
- d. Closed internal cervical orifice
- e. Partially open external cervical canal orifice.

In rare cases, a gynecological examination may reveal a cystic lesion of PVCU, which is a trophoblastic invasion of the cervical stroma.

Cervical pregnancy treatment is a challenge depending on the time of diagnosis and the availability of future reproductive plans. The main problem is the prevention of a life-threatening hemorrhage due to the implantation of the gestational sac in the underdeveloped muscles of the isthmico-cervical region. Some authors rarely adopt expectant management, monitoring throughout the development of the cervical pregnancy, as some cases can spontaneously resolve itself. Patients with early cervical pregnancy with no cardiac activity and low and declining serum beta-human chorionic gonadotropin (hCG) concentrations are candidates for this type of management. Titers of beta-hCG lower than 1500 mIU/ml and declining indicate a high possibility of spontaneous involution [15].

Ushakov *et al.* proposed some criteria for initiating conservative treatment, including the following: having a reliable diagnosis of cervical ectopic pregnancy; a hemodynamically stable patient with mild or no bleeding; gestational age of <10 weeks based on last menstruation period; normal platelet count; normal liver; and renal function [16]. Options for conservative treatment are: Systemic or topical administration of methotrexate (MTX) (single or regimen), KCL, mifepristone with topical or systemic prostaglandin, topical intracervical injection of vasopressin, and intrauterine instillation of 3.5% H₂O₂. Intramuscular MTX is effective in 80–90% of cases of early cervical pregnancy. Selection criteria include: a hemodynamically stable patient and the presence of a gestational sac up to 3 cm in size. In more advanced pregnancies with cardiac activity, combination treatment with a multi-dose MTX regimen and intraamniotic and/or intrafetal administration of KCL is preferred [17], [18].

MTX treatment continues to be the conservative treatment most frequently described in the international literature [19]. Hung *et al.* describes some criteria for multiple-dose MTX regimen: hCG

>10,000 mIU/ml, gestational age of more than 9 weeks, presence of embryonic or fetal heart activity; and a crown-rump length of more than 10 mm on transvaginal ultrasound [18], [20].

Surgical treatment includes vacuum aspiration curettage, cervicotomy, and hysteroscopic resection to maintain fertility. A literature review of 130 titles in 2020 found that there were no studies in which dilatation and curettage (D and C) was used as the only treatment. In only two cases a D and C plus Foley catheter balloon tamponade was used [21]. If a life-threatening hemorrhage occurs or failure/contraindications from the previous procedures, hysterectomy is the method of choice. In 2014, Fylstra reported 13 cases of cervical pregnancy in the first trimester, successfully treated with vacuum curettage without complications and the need for subsequent hysterectomy. A key point in curettage is not to start with dilatation of the cervical canal, but directly with the application of a vacuum cannula of appropriate size. Dilatation can disrupt implantation and lead to heavy vaginal bleeding. Following the procedure, Foley balloon tamponade and application of prostaglandin F_{2α} are recommended to reduce bleeding [22].

In a hemodynamically stable patient, uterine artery embolization may be performed to prevent blood loss in addition to curettage or hysteroscopic resection [23]. Zakaria *et al.* proposed the following criteria for selection of combination therapy with embolization: Beta-hCG values >34,000 mIU/mL and contraindications to MTX .

Ortiz *et al.* reported in May 2021 three cases of successful treatment of cervical pregnancy by embryo reduction to preserve fertility. Hysteroscopy, alone or in combination with MTX, is an effective method of treatment for future reproductive plans, in addition to reducing hospital stays and recovery time before subsequent pregnancy attempts [5]. The risk of severe hemorrhage can be reduced by preoperative measures such as transvaginal ligation of the cervical branches of the uterine arteries, cerclage - by the method of Shirodkar, and angiographic embolization of the uterine arteries [24].

A review of the literature in 2009, reported 403 cervical pregnancies with 162 resulting in term deliveries, most of them requiring abdominal hysterectomy and high risk for maternal death [25]. There are available data in the literature for life-birth after cervico-isthmic pregnancy, followed by hysterectomy. More data need to be analyzed to understand the strong criteria in which conservative management can be proposed as a last option for having a child, like in our case, with counseling stressing on the importance of the risk of hysterectomy at delivery.

Conclusion

Isthmic-cervical pregnancy is a rare form of ectopic pregnancy. Proper and timely diagnosis is a challenge for the obstetrician-gynecologist and often leads to delayed treatment due to misdiagnosis of the condition as incomplete abortion. Vacuum aspiration without prior dilation of the cervical canal is recommended as the first choice of treatment for pregnancies in the first trimester. After cervical pregnancy, the incidence of cervical insufficiency and premature birth is increased. Even if the expectant treatment can be a valid option, it is often associated with an emergency hysterectomy due to postpartum massive bleeding.

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