

# Successful management of heterotopic pregnancy after fetal reduction using potassium chloride and methotrexate

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## ABSTRACT

Heterotopic pregnancy, the presence of two gestational sacs simultaneously, is a rare event but with the advent of Assisted Reproductive Technology, it is now an increasingly common complication. The reported incidence of a heterotopic pregnancy in a spontaneous cycle is quoted as 1 in 30,000. We report the case of a 38-year-old primigravida who was referred to our center at 11 + 2 weeks gestation with a diagnosis of heterotopic pregnancy for further management. A non-surgical intervention comprising of transvaginal ultrasound-guided potassium chloride and methotrexate into the cervical pregnancy resulted in a successful outcome. As an obstetrician, a high index of clinical suspicion and an early scan is mandatory to make a diagnosis of a heterotopic pregnancy and manage accordingly.

**KEY WORDS:** Assisted reproductive technology, cervical pregnancy, heterotopic pregnancy

## INTRODUCTION

Heterotopic pregnancy can have a multifactorial etiology. The reported incidence of a heterotopic pregnancy in a spontaneous cycle is quoted as 1 in 30,000.<sup>[1]</sup> The direct increase in the incidence is related to the number of embryos being transferred in an *in-vitro* fertilization (IVF) cycle.<sup>[2,3]</sup> Tubal damage including scarring, tubal epithelium or cilium damage and stenosis of the tubal lumen still remains the most important risk factor.<sup>[4]</sup> There is a 6-fold rise of an ectopic pregnancy in the presence of any pathological changes in the fallopian tubes.<sup>[5]</sup> In Assisted Reproductive Technology (ART) the embryos that are placed in the endometrial cavity do not implant immediately onto the endometrium. They may drift towards the tubes and under the influence of the *corpus luteum*, return later to embed in the cavity.<sup>[2]</sup> However, in the presence of an existing damaged tube, this journey may be interrupted increasing the chances of an ectopic pregnancy and with a higher order of embryos being placed in the womb predispose to a heterotopic pregnancy. The other contributing factors are an excess of

culture media or a misplaced catheter tip or pressure while injecting the embryos.<sup>[6]</sup>

The cervix is not an ideal place for an embryo to implant, and if it does implant, surgical evacuation is notoriously hazardous. A cervical pregnancy does not continue beyond 20 weeks and a miscarriage occurs because the cervical epithelium is composed of a single layer, which does not thicken to continue a pregnancy till term. It requires a surgical evaluation and may, at times, present as an emergency due to torrential bleeding.<sup>[7,8]</sup> The situation may even warrant a hysterectomy to prevent a maternal mortality from occurring. There is associated morbidity with heterotopic pregnancy in case of an incomplete evacuation of a cervical pregnancy where the chorionic tissue left behind may bleed and lead to ascending infection with subsequent development of chorioamnionitis.

The diagnosis of a heterotopic pregnancy is varied. The patient can remain asymptomatic or present with an abdominal pain, which is easily confused with ovarian hyper stimulation syndrome, especially after an IVF procedure.<sup>[1]</sup> Serum b-hCG levels can be

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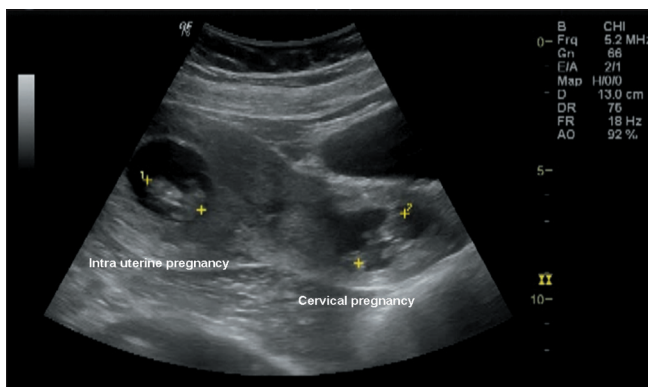
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confusing in a heterotopic pregnancy. The levels are found to be normal or even higher due to the presence of two gestational sacs, one intrauterine and the other extrauterine in its location.<sup>[1]</sup> A transvaginal ultrasound helps in making an early diagnosis of a heterotopic pregnancy.

Diagnosis and management of a heterotopic pregnancy remains a challenge even in the hands of a skilful obstetrician. The extrauterine pregnancy needs to be terminated using minimally invasive technique and without disturbing the intrauterine gestation sac. Although systemic medical therapy like methotrexate is contraindicated, we used it successfully in our patient combined with intracardiac instillation of potassium chloride.

## CASE REPORT

A 38-year-old primigravida who conceived after IVF-ET and a day 3 transfer of 3 embryos. A scan at 6 weeks at the IVF unit confirmed a viable intra-uterine pregnancy. Her next scheduled visit for a follow-up scan was at 10 weeks, which was missed by her. She eventually reported with vaginal bleeding at 11 weeks to the IVF unit when a suspicion of heterotopic cervical pregnancy was made. She was referred to our hospital at 11 + 2 weeks period of gestation when the diagnosis of Heterotopic pregnancy was confirmed. She was hemodynamically stable, and her medical history revealed a tubal reconstructive surgery in the past. A transvaginal ultrasound demonstrated a live intrauterine pregnancy with a crown rump length (CRL) of 4.53 cms corresponding to 11 + 2 weeks of pregnancy. In addition, there was a cervical pregnancy with embryonic heart activity, CRL 4.28 cms corresponding to 11 + 1 weeks [Figure 1]. The patient was counseled about the potential hemorrhage and other risks involved with a cervical pregnancy expulsion, more so at an advanced gestation of 11 + 2 weeks. It was her desire to continue with the intrauterine pregnancy. After a written consent, decision was taken for instillation of potassium chloride and methotrexate into the sac. Adequate blood was cross-matched in case of an emergency transfusion.



**Figure 1:** Coexisting intrauterine and cervical pregnancy

Potassium chloride 5 ml (2 meq/ml) was injected and within 1 minute resulted in asystole and feticide. Local methotrexate in a dose of 50 mg was injected for trophoblast destruction. A transvaginal ultrasound 48 hours later showed a collapsed cervical gestational sac while the intrauterine one was still viable. Fortunately, there was no hemorrhage, and the patient was discharged a week later without any complications. She had a regular antenatal follow-up and at every visit, the cervix was carefully inspected. Follow-up scans revealed resorption of the sac present in the cervix. A healthy male child weighing 2.3 kgs was delivered by cesarean section at 36 + 4 in view of impending eclampsia. There was profuse hemorrhage from the cervical canal, probably due to inadvertent bleeding from the cervix provoked by vaginal toileting, which required packing and the bleeding was controlled.

## DISCUSSION

A remote but possible event is the presence of a coexistent cervical and intrauterine heterotopic pregnancy, especially with widespread use of assisted reproductive techniques. However, a live birth with a heterotopic intrauterine and cervical pregnancy is a rare event. The signs and symptoms of a heterotopic pregnancy as described by Reece include abdominal pain, adnexal mass, peritoneal irritation in the presence of an enlarged uterus.<sup>[1]</sup> A careful evaluation of the clinical situation is mandatory. In order to avoid a catastrophic event, it is imperative to treat the cervical pregnancy and preserve the intrauterine one. An ideal situation would be to evacuate the cervical pregnancy without disturbing the intrauterine one. This is a rather difficult situation and the risk of trauma, torrential hemorrhage, and infection remain. Recently, a non-surgical approach with a limited medical armamentarium is being used in such cases. A few of these conservative methods for termination of cervical pregnancy include uterine artery embolization, cervical dilatation followed by curettage and aspiration and even tamponade with Foley catheter to secure hemostasis.<sup>[9]</sup> Another conservative approach described in literature for cervical pregnancy consists of evacuation of pregnancy after applying transvaginal ligatures (with absorbable sutures) of the cervicovaginal branches of the uterine arteries at the 3 and 9 o'clock positions of the uterine cervix.<sup>[10]</sup>

Potassium chloride (KCl) injections have been widely used for selective reduction in multiple pregnancies and this has found favor with heterotopic pregnancies as well. Goldstein *et al.* reviewed 11 cases of heterotopic pregnancies treated with potassium chloride injection and reported that 6 of the 11 cases failed to respond to treatment and required a surgical intervention.<sup>[11]</sup> In a case report by Cheng *et al.* treatment of a cervical pregnancy by potassium chloride injection resulted in delayed bleeding for which

a cervical stay suture was applied.<sup>[12]</sup> Monteagudo *et al.* and Kiri *et al.* have the largest experience of conservative management of heterotopic pregnancy by injecting either potassium chloride intracardiac or in the gestation sac or methotrexate systemically.<sup>[13,14]</sup> The intervention carried out by them resulted in successful pregnancy termination without any major complications. In only 1 patient, a second dose of methotrexate along with blood transfusion and uterine embolization was required in view of secondary hemorrhage 14 days post-treatment.

Very few cases of simultaneous heterotopic intrauterine and cervical pregnancy are reported in literature, ours being the 27<sup>th</sup> case. Of these, 2 conceived naturally and the rest had received some form of infertility treatment. The pregnancies were diagnosed by an ultrasound examination between 5 to 13 weeks of gestation. A successful pregnancy outcome was achieved in 12 of these cases. In 4 patients, potassium chloride was injected into the amniotic cavity of the cervical pregnancy while 7 patients had some form of evacuation for cervical pregnancy. In only 1 patient, potassium chloride and methotrexate were used resulting in a healthy newborn at 30 weeks. Honey *et al.* described the termination of an 8 week heterotopic pregnancy with profuse vaginal bleeding that was controlled by uterine artery embolization. Subsequently, selective cervical fetal reduction was done using ultrasound-guided intra-cardiac potassium chloride injection. The patient was readmitted at 9 weeks with features of chorioamnionitis, intrauterine fetal demise, and torrential bleeding, which warranted an abdominal hysterectomy.<sup>[15]</sup> Ginsberg *et al.* described a patient at 6 weeks with an intrauterine pregnancy and a twin cervical pregnancy where an embolization of the uterine and internal iliac arteries was done to control the vaginal bleeding followed by cervical dilatation and evacuation of both gestation sacs.<sup>[16]</sup>

In our patient, although embryo transfer was performed under ultrasound guidance through the cervical canal into the uterine cavity, a heterotopic pregnancy resulted probably due to a reflux of embryos into the cervical or trauma to the cervix during the procedure itself. The management of our case was challenging because the patient presented at an advanced gestation of 11 + 2 weeks of gestation and no data exists regarding the behavior and outcome of concomitant use of injecting cervical pregnancy with potassium chloride intracardiac and methotrexate into the sac at such a gestation. The rationale behind using methotrexate and potassium chloride was considering the advanced gestation of the cervical pregnancy in our patient where one treatment modality would not suffice for resorption of the relatively larger gestational sac. Our main aim was to maintain the viable intrauterine pregnancy while preserving the reproductive function of the woman with minimal invasive and aggressive treatment. The use of a single dose, local

injection of methotrexate in our case avoided not only the continued effects of the drug on the intrauterine pregnancy but also the adverse chemotherapeutic effects of systemically-applied methotrexate.<sup>[17]</sup> However, methotrexate hastens the absorption process and obstetricians are aware of its widespread use in cases of placenta accreta.<sup>[18,19]</sup> The use of methotrexate alone or when combined with cervical curettage or tamponade has been found effective in ectopic pregnancies less than 12 weeks of gestation.<sup>[20]</sup> Sijanovic *et al.* have described a successful perinatal outcome following the use of methotrexate in local treatment of cervical heterotopic pregnancy.<sup>[21]</sup> As the numbers of cases reported are few, one cannot formulate a treatment algorithm for treatment of a heterotopic pregnancy. Each case needs management on an individual basis keeping in mind a pregnancy-preserving approach with a subsequent live birth.

## CONCLUSION

- With better diagnostic modalities, an early and precise diagnosis of a heterotopic pregnancy is now possible.
- In a hemodynamically stable patient, after evaluating the risks and benefits, the aim should be to continue the intrauterine pregnancy while treating the one in an ectopic site.
- To avoid multiple pregnancies, it is advisable to limit the number of embryos to be transferred to one or two as per HFEA guidelines.
- When a heterotopic cervical and intrauterine pregnancy is diagnosed, it is wise to keep blood concentrate prepared and anesthetists informed in the event of an emergency surgical intervention.
- A non-surgical approach is safe and effective in patients who are hemodynamically stable.

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