Successful rescue hysteroscopic resection of a cervical ectopic pregnancy previously treated with methotrexate with no combined safety precautions

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Summary

Background: Cervical pregnancy (CP) is a life-threatening condition that represents less than one percent of all ectopic pregnancies. Transvaginal sonography (TVS) is the gold standard for an accurate diagnosis. For hemodinamically stable women the available treatments involve a medical therapy, alone or in combination with interventional measures (hysteroscopy, angiographic embolization or laparoscopic ligation of uterine arteries). *Materials and Methods:* The authors describe a CP unsuccessfully treated with methotrexate (MTX), but resolved with hysteroscopy. *Case Report:* A nulliparous woman arrived with low abdominal pain without vaginal bleeding at six weeks of amenorrhea. TVS revealed a gestational sac implanted in the isthmic cervical region, with a serum β-hCG of 1,100 mUI/ml, that raised to 4,274 mUI/ml in a week, despite one intrasaccular-MTX injections and two systemic doses. The authors arranged for a hysteroscopic resection with no previous dilatation of the cervix. They did not adopt any safety precautions to their procedure. *Conclusion:* It is difficult to define the exact role of hysteroscopy regarding CP. Despite some authors dispute on its complementary function to MTX, the authors believe that it could be used as a rescue method in case of MTX failure. The final aims of a proper management are to minimize the risk of haemorrhage and preserve women's fertility.

Key words: Cervical ectopic pregnancy; Methotrexate; Hysteroscopy; Fertility.

Introduction

Ectopic cervical pregnancy (CP) is a rare life-threatening condition with the incidence varying from 1:1,000 to 1:18,000 reported pregnancies [1,2], and represents almost less than one percent of all ectopic pregnancies [3]. There is a growing frequency of CP that could be due to an improved incidence in patients who undergo assisted reproductive technology procedures for infertility treatment. Other risk factors are the use of intrauterine device, previous abortion, uterine curettage, and previous cesarean section. In the past, an emergency hysterectomy was often the only available choice because of profuse hemorrhage that accompanied the attempts of removal of a suspected incomplete abortion. Advances in ultrasonography (US) technology and the availability of quantitative beta-human chorionic gonadotropin (β-hCG) have made diagnosis of CP possible at an early gestational age. According to a recent review, a CP could be diagnosed on sonography if the following criteria are fulfilled: 1) an empty uterus, 2) a barrel-shaped cervix, 3) a gestational sac present below the level of uterine arteries, 4) absence of the sliding sign (when pressure is applied to the cervix using the probe, the gestational sac slides against the endocervical canal in a miscarriage, but does not in an implanted cervical pregnancy) and 5) blood flow around the gestational sac on color Doppler [4]. Available treatments usually consist of a combination of medical measures, such as methotrexate (MTX), misoprostol, mifepristone, and interventional measures, for example the US-guided injection of MTX or potassium chloride (KCl) directly in the gestational sac, curettage and tamponade, and needle aspiration of the products [5, 6]. Other authors have reported the use of laparoscopic surgery, hysteroscopic excision, and angiographic uterine artery embolization, with a high degree of success and minimal morbidity [3, 7-10].

In the present report the authors describe a case of a CP unsuccessfully treated with MTX (both intrasaccular and systemic), but resolved with a hysteroscopic resection of the gestational sac.

Case Report

A 40-year-old pregnant nulliparous woman with a history of salpingectomy for pelvic inflammatory disease, who conceived following in vitro fertilization-embryo transfer (IVF-ET) and freezing blastocyst transfer, was referred to the present center with a recent history of low abdominal pain without vaginal bleeding. The gestational age, according to her last menstrual period, was six weeks. Transvaginal sonography (TVS) revealed the possible diagnosis of a CP on the basis of the presence of a gestational sac located in the cervical canal, below the internal os, and an empty uterine cavity; there was no embryonic heart rate (EHR) and the initial serum β-hCG was 1,100 mUI/ml. The patient was hemodinamically stable for two days, with an increased serum β-hCG (2,023 mUI/ml) and was counselled about possible options and

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Figure 1. — Transvaginal ultrasound showing the gestational sac implanted in the cervical-isthmic region.

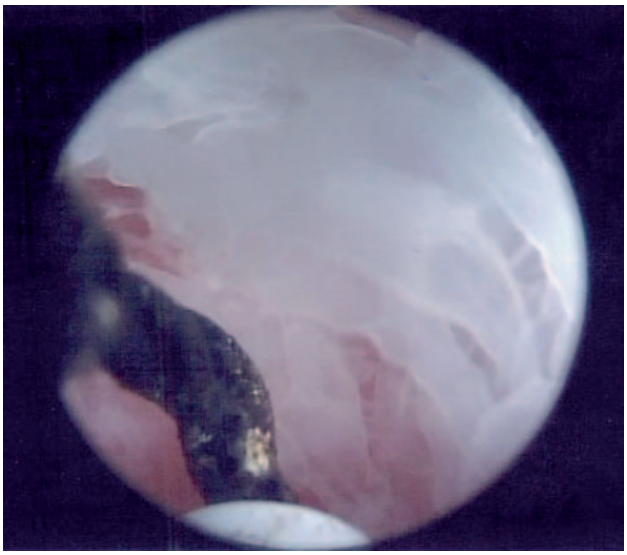

Figure 2. — The cervical canal vision from the five-mm Bettocchi hysteroscope, right before the resection of the cervical pregnancy.

complications for this pregnancy. The third day a new TVS revealed a six-mm gestational sac implanted in the isthmic cervical region, with yolk sac and still no cardiac activity (Figure 1). After these evidences the authors decided to perform a US-guided intrasaccular MTX injection (50 mg on two ml of NaCl), explaining all the possible complications. During the first postoperative day the patient was stable, but her serum β-hCG increased (2,742 mUI/ml) and a new TVS showed a seven-mm gestational sac with a three-mm yolk sac, with a fetal pole of 1.5 mm, and a discover of EHR. On the third day post-intrasaccular MTX injection, another TVS revealed an hematoma in the inferior pole (probably related to the operative procedure). Moreover, ββ-hCG increased to 3,979 mUI/ml, so they decided to repeat MTX, but with a systemic dose (1.5 mg/kg), since another intrasaccular injection was impossible to perform due to the cervical hematoma. Three days after they decided to perform a second systemic MTX dose (the third, counting the intrasaccular injection) because serum ββ-hCG had increased (4,274 mUI/ml), EHR was still present and the patient became emotionally unstable. The following day serum ββ-hCG slightly decreased (3,979 mUI/ml), but an additional TVS still displayed a 18-mm gestational sac with persistent cardiac activity, so the authors arranged for a hysteroscopic resection of the CP. Under general anesthesia, they inserted into the cervical canal a five-mm Bettocchi hysteroscope, with no previous dilatation of the cervix, using the vaginoscopic approach; they introduced through the operative channel a 5F bipolar electrode, and resected the implantation site under direct visualization of the chorial villi (Figure 2). A second look showed an empty cervical canal. The day after serum ββ-hCG dropped down to 1,566 mUI/ml. The postoperative course was almost uneventful, so the patient was dismissed with a planned follow-up based on TVS examination and ββ-hCG measurements. After two months ββ-hCG was 10 mUI/ml and a TVS exam revealed a small non-vascularized lesion, that was easily removed by an office hysteroscopy. ββ-hCG measurement is now actually negative and the patient is trying to become pregnant.

Discussion

This case report shows that an early CP can be treated with a conservative hysteroscopic resection of the gestational sac after the failure of MTX administrations (local or systemic).

Several studies have reported that MTX therapy has a 91% success rate, but also carries the potential risk of MTX-related disadvantages: the need of adjuvant surgical or endoscopic procedures (34%), a mean longer time for ββ-hCG negativization, a long time to return of menstruation, and a possible leukocytopenia [11]. Moreover, the efficacy of MTX could be related to some conditions that have to be respected: in fact a serum ββ-hCG >10,000 mUI/ml, a gestational age > nine weeks, the presence of EHR or crown-rump length (CRL) > ten mm have been shown to be accompanied by a higher rate of MTX failure and may need additional interventions [12]. MTX can be administrated by two different routes. Although the systemic administration is easier to perform than the local intra-amniotic injection [13], it is less effective, it needs an increased dosage if compared with the intrasaccular procedure, it has more side-effects, and also takes more days for aberrant trophoblast to be eradicated through MTX-induced antimetabolite effects [12].

If MTX can be considered the most conservative approach regarding CP, on the other hand it can be taken into account as conservative procedures all minimally invasive techniques that could preserve women's fertility, such as hysteroscopy, discussed for the first time in 1992 [14]. Since the risk for hemorrhage in a CP is high, all approaches need to be cautious. In fact some authors dispute on the safety of the endoscopic route alone, so several reliable precautions have been described, such as laparoscopic uterine artery ligation [7], or transfemoral uterine artery embolization [9, 10]. It is not clear if all these described safety precautions are necessary and it resulted that the endoscopic route is safer. In fact, Jozwiak *et al.* did not report any complications describing a heterotopic CP treated only with hysteroscopy, without previous dilatation or security

adjustments [15]. In addition, all these safe maneuvers may result in uterine hypoperfusion and possible subsequent hypofertility [16].

The present authors' clinical management initially resorted to conservative MTX therapy, because CP respected the inclusion criteria for a successful pharmacological treatment. Considering that ββ-hCG increased and that EHR was still persistent (despite three MTX doses), they changed their strategy and opted for the hysteroscopic approach. This procedure resulted to be secure and with low operative time. In fact, a previous dilatation could provoke a severe hemorrhage, while the cervical distension is not triggered using a five-mm hysteroscope. For these reasons the authors did not adopt any safety precautions with their hysteroscopy; in their opinion the laparoscopic ligation of uterine arteries is too invasive and takes a long mean operative time, while angiographic embolization requires radiologic facilities with expertise and specialized instrumentation, not available in every center. Moreover it requires to be confirmed whether hysteroscopy could become a secure one-step procedure in selected cases without previous dilatation, surgical or medical precautions.

The final aims of a proper management are to concentrate on minimizing the risk of hemorrhage, eliminating the gestational cervical product, and preserving women's fertility. So an early diagnosis of a CP influences the choice of treatment, that has to be customized based on the women's condition, their clinical manifestations, the availability of different procedures and, finally, the clinician's experience. Considering its small incidence, only prospective randomized multicentric studies will be able to determine its proper management. In conclusion, with this case report the authors would like to suggest a rescue role for hysteroscopy after a MTX failure. This approach could be a safe, simple, rapid, and resolving treatment regarding uncomplicated cervical ectopic pregnancy.

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