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Cervical twin ectopic pregnancy: case report and systematic review of literature

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ABSTRACT

Background. Ectopic twin cervical pregnancy is a very rare condition with a high risk of heavy bleeding. Since currently no standard treatment guidelines are available, each case is approached individually based on patient preference, physician experience, and resource availability.

Case presentation. A 34-year-old nulliparous Caucasian woman at 5 weeks gestational age presented with slight vaginal bleeding for several days. Transvaginal ultrasound on admission revealed two cervical gestational sacs containing a yolk-sac. The patient underwent removal of the cervical ectopic pregnancy with dilatation and curettage ultrasound-guided, as well as an ultrasound-guided intracervical Foley balloon. The bleeding subsided, and 48 hours later the Foley was removed.

Conclusions. Twin cervical heterotopic pregnancy is a very rare event that almost universally results in life-threatening conditions. Conservative management may be adopted, but it involves a high risk of failure. The present systematic review aimed to increase awareness of clinical characteristics and treatment methods.

INTRODUCTION

Cervical ectopic pregnancies account for less than 1% of all ectopic pregnancies [1, 2]. Risk factors include uterine and cervical anomalies, prior uterine curettage or caesarean delivery, smoking, tubal-factor infertility, and IVF treatment [3]. Because of the risk of heavy bleeding, cervical pregnancy is a dangerous and life-threatening pathologic condition, whose incidence is reported to vary between 1:18,000 to 1:1,000 of all pregnancies [4]. Ectopic twin pregnancy is quite uncommon in the cervix. The disorder can be a life-threatening condition because of the severe haemorrhage risk. First-trimester ultrasound examination is useful for the diagnosis [5]. There are currently no standard treatment guidelines, and each case is approached individually based on patient preference, physician experience, and resource availability [6]. Here we report our successful experience of a cervical twin pregnancy that was diagnosed by transabdominal and transvaginal ultrasound. The patient presented with first-trimester bleeding and pelvic pain was managed successfully.

CASE PRESENTATION

Anamnesis

A 34-year-old nulliparous woman was referred to our hospital for vaginal bleeding and pelvic pain after a positive pregnancy test. According to her last menstrual period, she was 5+3 weeks pregnant on admission. She conceived spontaneously, she had no history of previous ectopic or twin pregnancies, and she underwent neither previous surgery on uterus nor hysteroscopy. Her medical history was unremarkable. Pelvic examination revealed a nulliparous cervix with no signs of bleeding, a uterus typical for a 6-weeks pregnancy, no tenderness of adnexa, and a soft abdomen. Abdominal and transvaginal ultrasound scans showed two gestational sacs located in the cervico-isthmic portion with two yolk sacs, an empty uterine cavity, and no free fluid in the cul-de-sac (Figures 1, 2). Twin cervical pregnancy was confirmed also with a 3D ultrasound examination (Figure 3). Quantitative β -human chorionic gonadotrophin (β -hCG) concentration was 4,783 IU/L on admission. Complete blood count, liver function tests, creatinine levels and coagulation tests were normal.

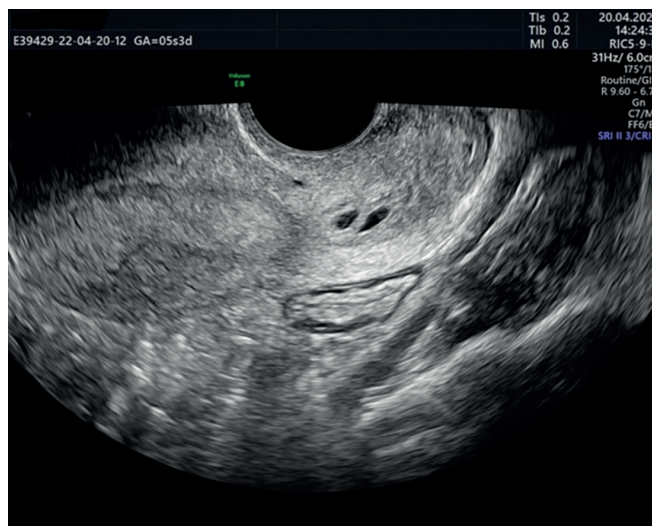


Figure 1. Ultrasound image of cervical twin pregnancy.



Figure 2. Cervical twin pregnancy with yolk sacs.



Figure 3. Ultrasound 3D examination of cervical twin pregnancy.

Operative decision

After discussing with the patient and her husband regarding the therapeutic options, including systemic or local methotrexate injection or dilatation and curettage, we decided to perform cervical dilatation and curettage. Interventional radiology service was also alerted and available in case of the need for uterine artery embolization for massive bleeding. Suction curettage was performed without any complications under abdominal ultrasound guidance. To reduce the haemorrhagic risk after this surgical procedure, a Foley balloon catheter was placed in the cervical canal for 48 hours. The estimated blood loss for the procedure was 150 cc and the patient was given intraoperative antibiotic prophylaxis with amoxicillin 2 g.

Post-operative follow-up

The patient was monitored strictly for the following hours. No haemorrhage, complications or other adverse effects were seen after the procedure. The patient was discharged on the second postoperative day, after balloon removal, in good health, with a postoperative haemoglobin level of 11.6 g/dL. Pathologic examination of the tissue removed from the cervix confirmed the presence of chorionic villi.

DISCUSSION

Cervical pregnancy is defined according to the following ultrasound criteria: an empty uterus, a barrel-shaped cervix, a gestational sac present below the level of the internal cervical os, the absence of the 'sliding sign' and blood flow around the gestational sac using colour Doppler [7]. In the present case, no predisposing cervical or tubal factors were found, and no abnormality of the cervical canal was noted. Early detection of an ectopic pregnancy is vital, and laboratory investigation has limited use. When an ectopic pregnancy ruptures, the resulting hemoperitoneum, a rapid accumulation of blood under pressure within the peritoneum, is an emergency condition that can lead to hemodynamic instability and that requires urgent surgery [8]. Cases of cervical pregnancy typically present with vaginal bleeding, with or without abdominal/pelvic pain. In addition to a thorough physical examination, sonographic de-

tection and final diagnosis of an ectopic pregnancy are the most difficult steps of the management process. Transvaginal ultrasonography (US) is the gold standard method to diagnose cervical pregnancies, with a better sensibility compared to the transabdominal sonography [9, 10]. Currently, conservative treatment includes ultrasound-guided local potassium chloride injection, systemic or local methotrexate injection, or preoperative uterine artery embolization before dilatation and curettage, with the aim to preserve future reproductive potential [11-14]. Methotrexate injection either local or systemic is one of the widely used and successful strategies in the treatment of cervical ectopic pregnancy [4, 15, 16].

The main problem with conservative treatments that have been offered is life-threatening haemorrhage after pregnancy evacuation. Uterine artery embolization is one of the possible measures to control bleeding after evacuated cervical pregnancy [17, 18]. According to literature, gestational age less than 12+0 weeks, absence of foetal cardiac activity and lower serum β -hCG levels are associated with more successful conservative management [19, 20].

Cases of twin cervical ectopic pregnancies are even more uncommon than singleton cervical pregnancies. Therefore, no guidelines are available to recommend treatments in this particular scenario. In this case, we decided to perform a dilatation and curettage because we hypothesized a higher risk of failure with methotrexate injection compared to singleton 6-weeks cervical pregnancies.

We performed a Medline search for studies published in all languages from the beginning to April 1, 2022. We used the key words "twin", "ectopic", "cervical pregnancy". We screened titles and abstracts of all citations for potentially relevant papers. Pertinent additional manuscripts were recognized from reference lists of reviews and editorials. Records selection observes the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [21]. We considered all the publications (original articles, systematic reviews, case reports) that reported cases of cervical ectopic twin pregnancy. Reports about already published cases of ectopic pregnancy were excluded. Data describing the management and complications of these pregnancies were reported.

Authors identified 57 records, of which there were 9 reported cases of twin cervical ectopic pregnan-

cy [2, 5, 12, 22-27]. Characteristics of cervical twin pregnancies reported in literature, including the present case, are summarized in **Table 1**. All the reported twin cervical pregnancies were diagnosed in the first trimester of pregnancy. Of the 10 pregnancies, 8 were twin cervical pregnancies [2, 5, 12, 23, 24, 26, 27], while 2 were triplet pregnancies with 1 gestational sac in utero and 2 gestational sacs in the cervico-isthmic region [22, 25]. 5/10 pregnancies were conceived after IVF [12, 22, 25, 26, 27], while 7/10 pregnancies (70%) presented with vaginal bleeding [2, 12, 23, 24-26]. B-hCG levels at diagnosis ranged from 4,783 UI/L to 133,675 UI/L. Medical treatment included US-guided injection of methotrexate in each gestational sac [12], uterine artery catheterization with local methotrexate injection and subsequent embolization [22], US-guided intraamniotic injection of potassium chloride and subsequent uterine arteries embolization [24], transvaginal US-guided aspiration of the gestational sacs [26], oral mifepristone and systemic methotrexate [2, 27], systemic methotrexate [5, 23], and dilatation and curettage [25]. In 5/7 cases (71.4%) [2, 12, 23, 24, 27] dilatation and curettage were required after conservative medical therapy with methotrexate [12, 23], methotrexate plus mifepristone [2, 27] or potassium chloride [24]. Notably, 2 women required blood transfusion and these cases were associated with the highest β -hCG levels at diagnosis (83,465 UI/L and 133,673 UI/L) [2, 12]. These data are in contrast with success rates of conservative management with methotrexate for singleton non-tubal ectopic pregnancies reported in literature. Krissi *et al.* reported 25 cases of non-tubal ectopic pregnancies (10 cervical, 9 interstitial, and 6 caesarean scar pregnancies) treated with uterine artery embolization plus systemic methotrexate, with a success rate of 96% [28]. Hunt *et al.* reported 60 cases of non-tubal ectopic pregnancies (34 cornual, 14 caesarean section scar, nine cervical and three cervical involving previous caesarean scar) and 38 patients received medical therapy with single or multidose methotrexate with a success rate of 87% [29]. Recent evidence has pointed out also the possible role of laparoscopic reversible uterine arteries occlusion in cases of ectopic pregnancies with high risk of haemorrhage [30]. This difference may be due to the different pharmacological response to classic methotrexate regimen for twin ectopic pregnancies, with a higher risk of treatment failure and subsequent need of

surgical treatment. Data from our review point out how management of twin cervical pregnancies requires a personalized approach due to the higher risk of response failure to pharmacological treatment and of excessive bleeding requiring blood transfusion, in particular for twin cervical pregnancies associated with high β -hCG levels at diagnosis. It is therefore imperative to provide extensive counselling for the patient because there is no evidence to support the use of any therapeutic method.

This is the first literature review provide an overview of the clinical characteristics and medical management of a rare but challenging type of ectopic pregnancy. The review was limited by the small number of published cases, preventing a consensus on definitive success rates or treatment recommendations. No data are available on the fertility and reproductive outcome according to different managements for twin cervical pregnancies. There is no consensus on the best management in cases of ectopic pregnancies; recent evidence has shown that scar pregnancies can benefit from a laparoscopic approach [31], and also in cases of heterotopic pregnancies, the laparoscopic treatment is safe for both the woman and the in-utero pregnancy [32, 33]. Data from literature showed that, in cases of tubal ectopic pregnancies, expectant management may have better reproductive outcomes compared to women who underwent surgery, with the shortest time to achieve a subsequent intrauterine clinical pregnancy [34, 35]. Moreover, observations are biased because negative treatment outcomes are less likely submitted or accepted for publication. In addition, the paucity of reported cases does not allow to establish a standard approach, *i.e.*, surgical *versus* medical. New approaches for the treatment of cervical pregnancies have been recently evaluated, including the systemic and local methotrexate therapy combined with hysteroscopic resection, but further evidence is needed [36]. Since 50% of reported twin cervical pregnancies were from IVF pregnancies, it would be interesting to evaluate whether different methods of embryo transfer would be more associated with cervical pregnancies and negative outcomes. A recent meta-analysis on the ultrasound-guided embryo transfer showed no difference in incidence of ectopic pregnancy in transvaginal ultrasound guided IVF *versus* the trans-abdominal approach, but data were based on low-quality studies [37].

Table 1. Characteristics of included studies.

Study	Year	Patient age (years)	Parity	Type of pregnancy	GA at diagnosis	Mode of conception	Symptoms	B-hCG levels	Treatment	Complications
Pascual <i>et al.</i> [12]	2001	39	G1	Twin cervical	5 w	IVF	Vaginal bleeding	83,465 IU/L	US-guided injection of 50 mg MTX in each gestational sac + D&C	Blood transfusion required
Nitke <i>et al.</i> [22]	2007	45	G3P0	Triplet (one in utero and two in the cervix)	7 w	IVF	no	61,596 IU/L	Selective uterine artery catheterization, local MTX injection (50 mg/m ²) and subsequent embolization	No
Trojano <i>et al.</i> [23]	2009	36	G1	Twin cervical	6 w	Spontaneous	Vaginal bleeding and pelvic pain	52,000 IU/L	MTX i.m. (50 mg/m ²) + D&C (after prophylactic ligation of cervical branches of uterine arteries)	No
Cetin <i>et al.</i> [5]	2010	40	G9P7	Twin cervical	7 w	Spontaneous	no	7,676 UI/L	Multiple-dose regimen consisting of MTX i.m. (1 mg/kg) on days 1, 3, 5, and 7, and folic acid i.m. (0.1 mg/kg) on days 2, 4, 6, and 8	No
Ben Farhat <i>et al.</i> [24]	2010	41	G2P1	Twin cervical	11 w	Spontaneous	Vaginal spotting and dizziness	N/A	US-guided intraamniotic injection of potassium chloride, uterine arteries embolization and D&C	No
Vitner <i>et al.</i> [25]	2011	47	G2P1	Triplet (one in utero and two in the cervix)	6 w	IVF	Vaginal bleeding	1,0000 UI/L	D&C	No
Aboulfoutouh <i>et al.</i> [26]	2011	26	G1	Twin cervical	5 w	IVF	Vaginal bleeding	489.49 UI/L	Transvaginal US guided aspiration followed by single dose 50 mg MTX i.m.	No
Saroja <i>et al.</i> [2]	2011	30	N/A	Twin cervical	9 w	Spontaneous	Vaginal bleeding	133,675 UI/L	Mifepristone 200 mg per os and MTX i.m. (50 mg/m ²) 48 h later for 2 routes. Uterine artery embolization followed by US-guided D&C	Blood transfusion required
Anev <i>et al.</i> [27]	2013	41	G1	Twin cervical	6 w	IVF	no	18,470 UI/L	Oral mifepristone and MTX i.m. + D&C	No
Conte <i>et al.</i> (current study)	2023	34	G1	Twin cervical	6 w	Spontaneous	Vaginal bleeding and pelvic pain	4,783 UI/L	D&C and intracervical Foley balloon	No

IVF: *in vitro* fertilisation; MTX: Methotrexate; D&C: dilatation and curettage; i.m.: intramuscular.

CONCLUSIONS

In conclusion, cervical ectopic pregnancy is a very uncommon event with a high risk of massive haemorrhage. When the clinician faces with a twin cervical ectopic pregnancy, the patient’s status and wishes should be assessed, as well as the physician experience and availability of resources. Fertility-sparing management appears to be an option, without compromising the patient’s reproductive

capacity. Transvaginal ultrasound appears to be an accurate and safe methods of detecting hemoperitoneum and to correctly localize the site of implantation of the pregnancies. Conservative management may be an option but with an apparent high risk of failure. In our case, dilatation and curettage, followed by the placement of intracervical Foley balloon, successfully terminated the pregnancies, and preserved the patient’s fertility, without any other complications.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

A.S.: Conceptualization. A.C.: Data curation: G.P.: Formal analysis. A.S.: Methodology. P.P.: Supervision. L.C.: Validation, visualization. A.C.: Writing – original draft. A.S.: Writing – review & editing.

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N/A.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

N/A.

Informed consent

Patients mentioned in the present manuscript read and agreed written informed consent for the publication of their personal data anonymized.

Data sharing

Data are available under reasonable request to the corresponding author.

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