

CASE SERIES

SERIE DE CASOS

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Cervical ectopic pregnancy. A case series and literature review

Embarazo ectópico cervical: serie de casos y revisión de la literatura

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ABSTRACT

Objective: To describe a case series of nine patients diagnosed with cervical ectopic pregnancy. **Design:** Descriptive retrospective study of the clinical records of nine consecutive cases of women diagnosed with cervical pregnancy attended at the Instituto Nacional de Perinatología, Mexico City. **Results:** 448 ectopic pregnancies were attended from January 2011 through June 2018. They represented 2.2% of all pregnancies during the period studied. Of these, nine were cervical pregnancies (2% of all ectopic pregnancies). Five of these patients were admitted because of vaginal bleeding. All nine patients were diagnosed with cervical pregnancy by ultrasonography. Eight patients were initially offered pharmacological treatment with resolution of the ectopic pregnancy confirmed by hCG in two patients. Six patients required surgical intervention, and fertility was preserved in five cases. **Conclusions:** Cervical ectopic pregnancy is a risk factor for extreme maternal morbidity. It can present as an unexpected massive hemorrhage that commonly leads to hysterectomy and even death. Nowadays, there is no universal algorithm for treatment as it is performed in a regional and non-standardized manner, and in many cases, fertility preservation is not contemplated. Prospective studies are needed to issue recommendations on the management of these patients.

Key words: Pregnancy, ectopic.

RESUMEN

Objetivo. Describir una serie de casos de nueve pacientes con diagnóstico de embarazo ectópico cervical atendidas. **Metodología.** Estudio retrospectivo descriptivo, con revisión del expediente clínico de nueve casos consecutivos de mujeres con diagnóstico de embarazo ectópico cervical entre enero 2011 y junio 2018, en el Instituto Nacional de Perinatología de Ciudad de México. **Resultados.** Se halló un total de 448 embarazos ectópicos, que representaron 2,2% del total de embarazos, de los cuales, 9 (2% de los ectópicos) resultaron cervicales. Clínicamente, 5 pacientes presentaron sangrado transvaginal, 3 cursaron con dolor cólico y 2 estuvieron asintomáticas. La edad gestacional promedio fue 7,5 semanas. El diagnóstico de embarazo cervical fue mediante ultrasonografía de segunda dimensión. Con respecto al tratamiento, a 8 de las 9 pacientes se les ofreció inicialmente tratamiento farmacológico; solamente dos de las pacientes mostraron resolución de la hCG (gonadotropina coriónica humana) con la terapia farmacológica; el resto requirió alguna intervención quirúrgica. Se logró tratamiento preservador de la fertilidad en 5 pacientes. **Conclusiones.** El embarazo ectópico cervical es un factor de riesgo de morbilidad materna extrema. Puede presentarse con hemorragia masiva inesperada, que comúnmente conduce a la histerectomía e incluso a la muerte. Actualmente no existe un algoritmo universal de tratamiento; se realiza de forma regional y no estandarizada y, en muchos casos, no se contempla la preservación de la fertilidad. Se requiere estudios prospectivos para poder emitir una recomendación sobre el manejo de este grupo de pacientes.

Palabras clave. Embarazo, cervical, ectópico, Fertilidad.



BACKGROUND

Cervical pregnancy results from the implantation of the blastocyst in the endocervix, below the internal cervical orifice. Less than 1% of ectopic pregnancies are implanted in the cervical canal⁽¹⁾.

There are predisposing factors such as cervical manipulations (instrumented uterine curettage, manual endouterine aspiration). Risk is specially increased in patients with in vitro fertilization, with prevalence of 0.1% of all pregnancies achieved through this reproduction technique^(2,3). While the etiology of this implantation is still uncertain, it is attributed to the underlying factors mentioned, as endometrial manipulation would damage the decidua basalis, promoting implantation and growth of the trophoblast in the cervical myometrium. The low incidence of this type of pregnancy has not allowed to correlate pathology with physiopathological causes^(3,4).

Clinically, it tends to simulate a threatened miscarriage. It presents with transvaginal bleeding after a cycle of amenorrhea and only one third of the patients experience pelvic pain⁽⁵⁾. In advanced pregnancies, it can be accompanied by abdominal pain⁽⁶⁾.

In 1959, Paalman and McElin established diagnostic criteria for cervical pregnancy that remain valid today: 1) uterine bleeding after a period of amenorrhea in absence of typical colic pain, 2) enlarged cervix (equal or larger than the uterine fundus), so called "hourglass uterus", 3) products of conception confined solely and firmly to the endocervix, 4) closed internal cervical orifice, and 4) partially open external cervical orifice⁽⁷⁾.

With transvaginal ultrasound, especially three-dimensional ultrasound and sometimes two-dimensional ultrasound, this type of implantation is easily identifiable. It shows an empty uterus and a gestational sac in the isthmic-cervical area invading the anterior and posterior wall of the cervix. Doppler color scan can be used to identify peri-trophoblastic blood flow. If diagnosis cannot be performed with ultrasound, nuclear magnetic resonance could be required⁽³⁾. Histologically, trophoblastic tissue erodes through the endocervix and the conceptus grows in the fibrous wall of the cervix; a hemorrhagic mass surrounds the trophoblastic structures^(8,9).

This disease is associated with high rates of morbidity and mortality, with risk of secondary hemorrhage from erosion of the cervical blood vessels that may require hysterectomy. Therapeutic options can be divided into 5 categories: compression with Foley catheter, reduction of blood flow, surgical resection of the trophoblast, intraamniotic feticid and systemic chemotherapy⁽⁷⁾. Viable options for hemorrhage control include curettage, Foley catheter compression, local prostaglandins, cerclage, ligation of hypogastric or uterine arteries, and hysterectomy⁽¹⁰⁾.

METHODS

This is a descriptive retrospective study of nine consecutive cases of women with diagnosis of first-trimester cervical ectopic pregnancy attended from 2011 to 2018 at the Instituto Nacional de Perinatología (INPer), a third level reference center from Mexico City. The project was approved by the institutional review board.

RESULTS

A total of 448 ectopic pregnancies were attended from January 2011 through June 2018, representing 2,2% of all pregnancies during this period of study; 9 were cervical pregnancies (2% of the ectopic pregnancies).

Patient's general characteristics are presented in Table 1. Most of the 9 patients had risk factors consisting in previous cesarean section (3), in vitro fertilization (3), former diagnosis of uterine leiomyomatosis (3), uterine curettage (2), and cone biopsy secondary to human papilloma virus infection (2). As individual factors, a cervical polyp was found in one patient. Only one patient did not have an apparent risk factor (Table 2).

On admission, 5 patients presented vaginal bleeding, 3 manifested colic type pain, and 2 were asymptomatic. The average gestational age was 7.5 weeks. Diagnosis of cervical pregnancy was by two-dimensional ultrasonography.

Eight of the 9 patients were initially offered pharmacological treatment, in 4 cases methotrexate (MTX) as first line drug, either intramuscular, intravenous, and/or intrasaccular. Patients received pharmacological treatment for 9 days average, usually through more than one route, and remained hospitalized for 13 days. One patient



TABLE 1. GENERAL CHARACTERISTICS OF PATIENTS WITH CERVICAL ECTOPIC PREGNANCY.

ID	Age	G	P	A	C	Gestational age (weeks)	hCG pre treatment (mUI/mL)	Symptoms	Risk factors
01	30	3	0	0	2	6.0	8 125	Spotting	2 previous cesarean section
02	43	2	0	1	0	6.3	33 618	Pelvic pain	Laser vaporization /Uterine curettage
03	44	3	0	1	1	7.3	14 033	Spotting	Uterine leiomyoma 1 previous cesarean section IVF
04	31	2	0	0	1	7.1	45 527	Spotting	Uterine leiomyoma 1 previous cesarean section
05	37	5	1	3	0	4.6	6 954	Pelvic pain	3 uterine curettage
06	37	1	0	0	0	5.2	22 143	Asymptomatic	IVF
07	29	1	0	0	0	11.5	76 123	Asymptomatic	None
08	23	1	0	0	0	8.5	1 344	Transvaginal bleeding	Cervical polyp
09	43	2	1	0	0	11.5	5 111	Spotting Pelvic pain	IVF Conization of cervix Uterine leiomyoma

G: gestations, P: vaginal births, A: abortions, C: cesarean sections, hCG: human chorionic gonadotropin, IVF: in vitro fertilization

was treated with one dose of mifepristone 200 mg, and two more received combined treatment, either with methotrexate and mifepristone or methotrexate and misoprostol. Only two of the patients showed hCG resolution and the rest required some surgical intervention (Table 3).

Concerning the surgical interventions, 6 were indicated due to failure of the pharmacological treatment and 1 was performed on arrival due

to hemorrhage and hemodynamic instability. Three patients required hysterectomy (two abdominal and one laparoscopic) (Table 4), and conservative treatment was achieved in 5 patients using different approaches (Table 5).

DISCUSSION

Ally Murji et al. performed a retrospective study of cervical pregnancies diagnosed between January 2002 and July 2014 in a third-level center in Canada, with the objective of evaluating the safety and effectiveness of conservative management with methotrexate. Less frequent interventions were uterine arteries embolization, cervical arteries ligation, dilation and curettage with or without vasopressin, and tamponade with Foley catheter. Of the 27 cervical pregnancies included, all approaches were successful.

TABLE 2. RISK FACTORS IDENTIFIED IN PATIENTS PRESENTING CERVICAL ECTOPIC PREGNANCY IN THIS STUDY.

Cervical manipulation	4 (44%)
Assisted reproduction techniques	3 (33%)
Previous cesarean section	3 (33%)
Uterine leiomyomata	3 (33%)
Cervical polyp	1 (1.1%)
None	1 (1.1%)

TABLE 3. CHARACTERISTICS OF MEDICAL MANAGEMENT IN THIS SERIES.

ID	Total dosage	Treatment days	Days of hospital admission	Average days of resolution using hCG	Additional drugs (dose)	Need for surgical intervention
01	Methotrexate 186 mg IM	6	8	No resolution	None	Yes
02	Mifepristone 200 mg	5	6	No resolution	None	Yes
03	Methotrexate 968 mg IV	10	13	31	None	No
04	Mifepristone 200 mg Methotrexate 117 mg iv	4	6	No resolution	None	Yes
05	Methotrexate 50 mg IS	3	14	No resolution	None	Yes
06	Methotrexate 500 mg IS Methotrexate 164 mg IM Methotrexate 330 mg IV	20	23	No resolution	None, CEFM	Yes
07	Misoprostol 8 000 mg VB	26	29	No resolution	MTX 640 mg IV MTX 80 mg IS	Yes
09	Misoprostol 2 800 ug VV	2	30	30	None	No

CEFM: Espinosa Flores Modified cerclage, IM: intramuscular, IV: intravenous, IS: intravascular, VB: per os, VV: vaginal route, MTX: methotrexate



TABLE 4. TYPE OF SURGICAL MANAGEMENT.

ID	Intervention	Days of hospital admission	Additional interventions	Conservative management	Histopathology
01	Laparoscopic total hysterectomy + bilateral salpingo-oophorectomy	8	None	No	Isthmocele, decidual reaction, chronic cervicitis
02	Abdominal total hysterectomy + right cystectomy	7	None	No	Chorionic villi, benign decidua, corpus luteum
03	None	13	None	Yes	Not applicable
04	Abdominal total hysterectomy	10	None	No	Chronic cervicitis
05	Surgical hysteroscopy with intravascular methotrexate	14	Espinosa Flores modified cerclage	Yes	Not applicable
06	McDonald cerclage and intravascular methotrexate by hysteroscopy	23	Hydrodissection with hysteroscopy and vasopressin	Yes	Chorionic villi and thrombohematoma
07	Hysteroscopy with intrasaccular methotrexate	29	Manual vacuum aspiration	Yes	Chorionic villi with necrosis
08	Surgical hysteroscopy + uterine curettage	3	None	Yes	Chorionic villi with acute deciduitis

TABLE 5. CONSERVATIVE MANAGEMENT OF THE CERVICAL ECTOPIC PREGNANCY.

Initial intervention	Additional interventions	Interval between treatments
Medical treatment	None	Not applicable
Espinosa Flores modified cerclage and intrasaccular methotrexate by hysteroscopy	None	Not applicable
McDonald cerclage and intravascular methotrexate by hysteroscopy	Hydrodissection with hysteroscopy and vasopressin	19 days
Hysteroscopy with intravascular methotrexate	EMA	21 days
Hysteroscopy and uterine curettage	None	Not applicable

EMA: endouterine manual aspiration

In a retrospective study, Donald L et al. reviewed 13 consecutive cervical pregnancies from 1995 to 2014 at the University of South Carolina. All cases were treated surgically with the same technique: the cervical stroma was injected in a circumferential way (around the cervical pregnancy) with 20 mL of diluted vasopressin in 50 mL of saline solution; this was followed by placement of a cervical suture as prophylactic McDonald technique (without tying the sutures), curettage of the trophoblast through suction, and a compression balloon was immediately placed in the cervical canal (Foley catheter) with 30 mL of saline solution, leaving the tamponade for 24 hours before slowly deflating it. Of the 13 patients studied, none presented hemorrhage after the procedure. Furthermore, the cerclage sutures never required tying, but rather stayed in place until after the curettage, and were removed following aspiration and placement of the tamponade⁽¹⁾.

In our group of patients treated conservatively, the approaches were: placement of cerclage as measure of bleeding compression, application of intrasaccular methotrexate, and hydrodissection by hysteroscopy, all of them successful.

Among the limitations of the study that could influence the results, it is retrospective in nature and with a reduced number of patients. This is a hypothesis generator study, prospective type, as well as multicenter. Further studies will be required to achieve an adequate number of patients to identify the best treatment scheme.

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