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Management of cesarean scar pregnancy with methotrexate. A case series of combined systemic and percutaneous therapy in a tertiary center in Colombia.

Pacientes con embarazo en cicatriz de cesárea tratadas con metotrexato. Serie de casos de terapia combinada sistémica y percutánea en un centro de tercer nivel de Colombia

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Abstract

OBJECTIVE: To report a scheme of non-surgical care in patients with cesarean scar pregnancy, in the context of a low-resource health system. Additionally, we aimed to describe the tolerance, monitoring, evolution, and outcome of each patient treated with the scheme under study.

MATERIALS AND METHODS: Descriptive study of a case series of patients who, between May 2020 and March 2023, attended the emergency room of a tertiary care institution in Barranquilla, Colombia, because of obstetric symptoms, or were referred to the institution with a diagnosis of cesarean scar pregnancy, confirmed with ultrasound. Study parameters: Measurement of sociodemographic, obstetric, clinical evolution, and maternal complication variables. A descriptive analysis of the data was made.

RESULTS: Eleven patients were documented, resulting in an incidence of 1.85 cases per 5000 pregnancies. Pelvic pain and vaginal bleeding were the most common symptoms. Five patients had two or more cesarean sections, the rest only one, and five more had a history of obstetric curettage. Nine of the eleven patients were treated at less than 8 weeks gestation. The success rate was 100%, with a mean beta-hCG negativity of 38.7 days. There were no major complications, and no surgical intervention was required.

CONCLUSIONS: We described the implementation of a combined systemic and local scheme with methotrexate. The scheme was safe and effective, with preservation of fertility.

KEYWORDS: Pregnancy; Methotrexate; Cesarean section; Cicatrix; Fertility preservation; Curettage; Pelvic pain; Colombia.

Resumen

OBJETIVO: Describir un esquema de atención no quirúrgica en pacientes con embarazo en cicatriz de cesárea en el contexto de un sistema de salud con bajos recursos. Además, describir la tolerancia, vigilancia, evolución y desenlace de cada una de las pacientes tratadas con el esquema propuesto.

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MATERIALES Y MÉTODOS: Estudio retrospectivo, descriptivo de serie de casos de pacientes que acudieron al servicio de Urgencias de una institución de tercer nivel de atención en Barranquilla, Colombia, entre los meses de mayo de 2020 a marzo 2023 debido a síntomas obstétricos o fueron remitidas a la institución con diagnóstico, confirmado por ultrasonografía, de embarazo en cicatriz de cesárea. *Parámetros de estudio:* medición de variables sociodemográficas, obstétricas, de evolución clínica y complicaciones maternas. Se efectuó el análisis descriptivo de los datos.

RESULTADOS: Se documentaron 11 pacientes que dieron una incidencia de 1.85 casos por cada 5000 embarazos. El dolor pélvico y el sangrado fueron los síntomas más prevalentes. Cinco pacientes tuvieron dos o más cesáreas, el resto una sola previa y cinco antecedente de legrado obstétrico. Nueve de 11 pacientes se atendieron con menos de 8 semanas de embarazo. La tasa de éxito alcanzada fue en las 11 pacientes, con negativización de la beta hCG a los 38.7 días en promedio. No se registraron complicaciones severas ni requerimiento de atención quirúrgica.

CONCLUSIONES: Se describió la implementación de un esquema combinado sistémico y local con metotrexato que resultó seguro y efectivo, con preservación de la fertilidad.

PALABRAS CLAVE: Embarazo; metotrexato; cesárea; cicatriz; preservación de la fertilidad; legrado; dolor pélvico; Colombia.

BACKGROUND

A cesarean scar pregnancy is an early, anomalous implantation of the pregnancy in the myometrium, due to a previous C-section.[1] Unlike an ectopic pregnancy, the cesarean scar pregnancy is located within the uterine cavity. As such, this last type of pregnancy could continue and culminate in the birth of a new being, alive and in good conditions. The main challenge is to establish a timely diagnosis to facilitate an adequate treatment, without neglecting the risk of a potentially severe maternal morbidity, which could ensue in the eventuality of a complication, such as uterine rupture, or placenta accreta.

The real incidence of cesarean scar pregnancies is unknown due to inaccurate documentation. Regardless, it is estimated that the incidence rate is parallel to that of C-sections. At a global scale, it is calculated that it grew from 5 to 32%,[2] with variations in some regions of Latin America and the Caribbean, where the incidence has reached up to 42.8%.[3] The known incidence of cesarean scar pregnancy is of 1 case per 1800 to 2500 pregnancies with a previous C-section. A low rate of detection and registration has been detected, despite broader access to ultrasound and other technological resources which aid in the diagnosis.[4]

Certain previous uterine surgeries, such as a C-section, lead to a thin or non-existent basal decidua on the myometrium wall, in the lower uterine segment. This myometrium defect allows for the pregnancy to set in the uterine cavity, the trophoblast grows within this space, and remodels all the vascular bed to allow a low resistance and high speed system that feeds the growing embryo.[5,6] The pattern of implantation shows two types of pregnancies, type I, or endogenous, which sets on the cesarean scar, and grows towards the uterine cavity, and type II, or exogenous, which sets on the niche, and grows towards the bladder or the uterine cavity.[7] Patients with a pregnancy implantation on the "cesarean scar " have a substantially better outcome than the ones with a "niche" implantation.[8]

The risk factors for cesarean scar pregnancy are: one or more C-sections with a defect in the uterine myometrium, which favors the implantation of a pregnancy with growth in the scar or the niche. These factors can be related with hysterorrhaphy, the incision location, the wound cicatrization, and the uterine retroflexion.[9,10]

Regarding the clinical manifestation of the patients with cesarean scar pregnancy, it is usually within the first trimester, with variable clinical pictures that range from uterine bleeding, to uterine rupture, or hemoperitoneum. There are also many descriptions of asymptomatic cases. An ultrasound is the only way to establish a diagnosis.[11]

An ultrasound evaluation is the first-choice test to diagnose a pregnancy with an anomalous implantation. The initial finding of a gestational sac with anterior, low implantation, in patients with a history of C-section, should raise suspicions of the likelihood of a cesarean scar pregnancy. An incorrect diagnosis will lead to serious complications.[12]

The transvaginal ultrasound procedure is optimal for the evaluation of this type of pregnancy, given the higher resolution of its results, with the recommendation of gray scale evaluation, additional to Doppler color evaluation.[13] One approach suggests the following ultrasound criteria to diagnose cesarean scar pregnancy, without necessarily meeting all of them: an empty uterine cavity and endocervix; placenta, gestational sac, or both, embedded in the hysterotomy scar; a triangular, rounded, or oval-shaped gestational sac filling the "niche" of the scar; a thin or missing myometrium layer between the gestational sac and the bladder; an abundant or prominent vascular pattern in the area of the cesarean scar; a fetal pole, or yolk sac, or both, with or without fetal cardiac activity.[4]

Given that the risk of maternal morbidity is severe, the only collective recommendation, founded on the main studies and consensus, is to not expect gestation, because the reported rates for complications and pregnancy interruption right after diagnosis, are over 50%.[1] Multiple schemes are reported in the literature, which can be pharmacological, minimally invasive, and surgical, and they can be used in combination or as a single scheme. The described modalities for treating a cesarean scar pregnancy include: hysteroscopy, laparoscopy, laparotomy, open surgery, transvaginal surgery, curettage (including sharp aspiration and vacuum techniques), uterine artery embolization, methotrexate (by guided local injection or by systemic administration), direct potassium chloride injection, needle-guided sac decompression, high-intensity focused ultrasound, balloon catheters, and a combination of these methods.[14,15]

The pharmacological treatment for patients with cesarean scar pregnancy with local intra-gestational methotrexate injection, with or without systemic accompaniment, is one of the first choice approaches, due to its efficacy, simplicity, and lower risk of complications, besides being the recommended approach when fertility is wished to be preserved.[1,16] The single administration of systemic or intramuscular methotrexate is not recommended, given its low effectivity.[17,18] A decrease of gestational mass has been observed with the pharmacological treatment, which can last weeks or months as observed with ultrasound follow-up, with a mean of 88 days, approximately, besides a transient increase in beta-hCG, and a decrease afterwards.[19,20]

There is no consensus in the literature for the treatment of patients with cesarean scar pregnancy. The only clear recommendation, based on reports of series of cases, is the recommendation for not following a conservative approach. The early diagnosis and treatment are decisive to prevent the consequences of a significant morbidity, which could result in a late complication of a C-

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section. The main goal of the study was to report a scheme of a non-surgical treatment for patients with cesarean scar pregnancy, in the context of a low-resource health system. Another goal was to describe the tolerance, monitoring, evolution, and outcomes of every one of the patients treated with the scheme under study.

MATERIALS AND METHODS

Descriptive study of a case series of patients who attended the emergency service of a tertiary level institution in Barranquilla, Colombia. The patients were admitted because of obstetric symptoms, or were referred to the institution with a diagnosis of cesarean scar pregnancy confirmed by ultrasound, between the months of May 2020 and March 2023. The criteria of the Society for Maternal-Fetal Medicine,[1] and the inclusion criteria were applied. A consecutive convenience sampling was made, and there were no exclusion criteria.

Patients who attended the institution, during the established period, and met the selection criteria, were identified. The inclusion criteria were reviewed by the Maternal-Fetal Medicine group. A maternal-fetal medicine specialist made an ultrasound to complete the diagnosis. The patients confirmed with cesarean scar pregnancy, received pharmacological treatment in a combination of systemic and local methotrexate, after signing the informed consent form. Sociodemographic and obstetric variables were reviewed, patients were followed up for clinical evolution and complications, and a descriptive analysis of the data was made. Next is a step-by-step description of the methodology, and the technique used with patients who chose the combined pharmacological management scheme.

Patients with a confirmed diagnosis of cesarean scar pregnancy were treated in-hospital, and received counseling about treatment options. The informed consent was signed before starting the systemic methotrexate administration. All the patients had paraclinical studies to evaluate renal and liver function, and coagulation. Patients with results within normal parameters initiated the systemic treatment. The dosage was 50 mg/m2 (as per body surface), in a single intramuscular dose. Twenty-four hours after the methotrexate administration, the intrasaccular local medical treatment was performed, guided by a transvaginal ultrasound. Before starting the procedure, an ultrasound scan was made to verify the location of the gestational sac, the embryonic structures, and the possibility of embryocardia, which defined the additional action of local potassium chloride.

The technique consisted of a spinal anesthesia **(Figure 1)** and a transvaginal ultrasound to assess and confirm the ultrasound characteristics of the cesarean scar pregnancy **(Figure 2)**. Then, a Spinocan-20 needle was attached to the transducer and guided by ultrasound, a transvaginal puncture was performed, at the level of the anterior cervical fornix. Upon entering the gestational sac **(Figure 3)**, its contents were vacuumed (2 cc). In cases of embryocardia, potassium chloride (KCl) (2 cc= 2mEq/mL) was administered to induce the embryonic asystole. Afterwards, a single intrasaccular dose of methotrexate (23 mg) was administered **(Figure 4)**. The ultrasound findings were reviewed again **(Figure 5)**, and the vaginal transducer was withdrawn. Upon ending the procedure, the hemostasis of the vaginal cavity was verified. To follow up on β -hCG concentrations, a control was made after 48 hours, and this was taken as baseline. Further β -hCG measurements were taken every week until negative results, which was considered a successful treatment. Instructions were given to patients to attend medical services immediately upon vaginal bleeding, fever, or any other symptom related to the treatment, which was considered unsuccessful when β-hCG concentrations had plateaued or increased.

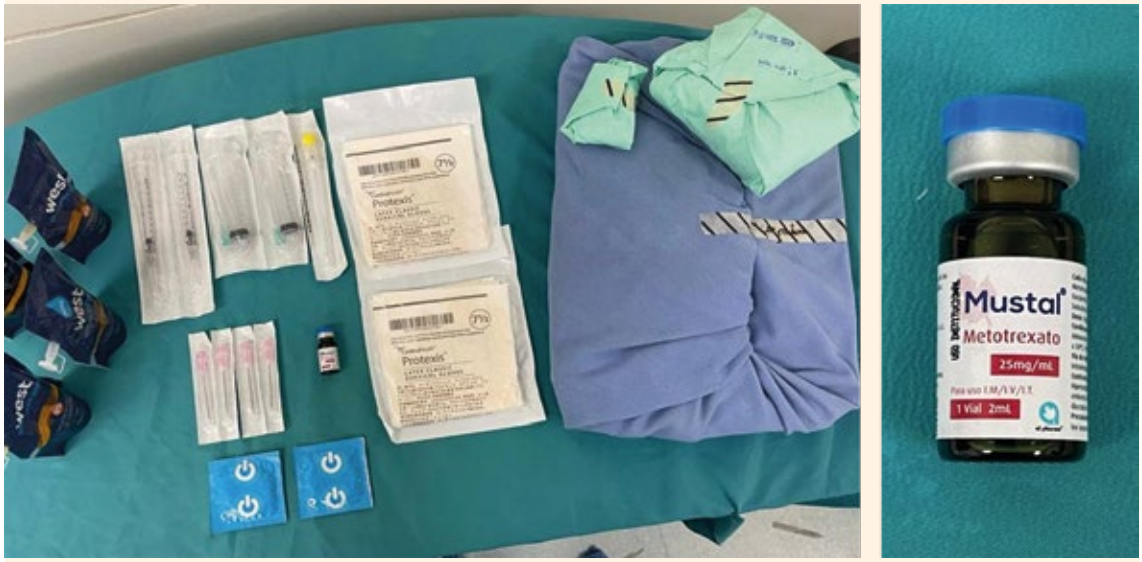


Figure 1. Supplies used in the procedure: intrasaccular injection in ectopic pregnancy in cesarean scar. Source: Study archive.



Figure 2. IUltrasound image of cesarean scar gestation. Source: Study archive.

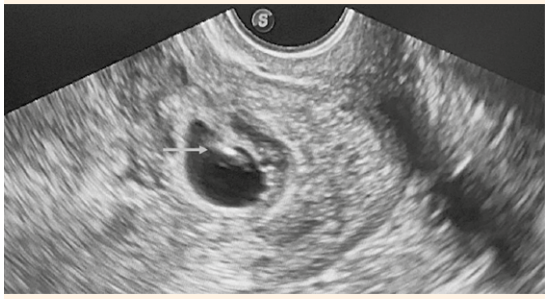


Figure 3. Ultrasound study of gestational sac with evidence of intrasaccular Spinocan 20 needle tip (long arrow). Source: Study archive.

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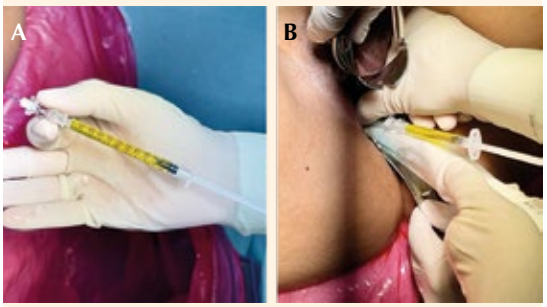


Figure 4. (A) 25 mg dose of methotrexate. **(B)** Intrasaccular methotrexate administration guided by ultrasound. Source: Study archive.

Measured variables. Age, origin, parity , deliveries, C-sections, abortions, gestational sac, yolk sac, and embryo measurements, the existence, or lack of, embryocardia, weeks of pregnancy, hospital admissions, symptoms upon admission, β-hCG concentrations at admission, β-hCG remission time in days, systemic methotrexate treatment dosage, intrasaccular methotrexate local administration dosage, intrasaccular potassium chloride dosage, and complications.

Statistical analysis. A database with quantitative and qualitative variables data was made on SPSS v. 24. The data was analyzed with descriptive statistics measuring frequency, central tendency, and dispersion.

Ethical considerations. For the analysis and publication of the present case series, the patients were informed of their diagnosis, and they signed the informed consent, where they granted authorization to access their clinical records, and taking and publishing pictures of the procedures. Their personal information remains strictly confidential.

RESULTS

Eleven patients with confirmed diagnosis of cesarean scar pregnancy were identified **(Figure 6)**; which resulted in an accumulated incidence, at the end of the period of study, of 1.85 cases per 5000 pregnancies. The sociodemographic variables and obstetric history are shown in **Table 1**. The mean age of the patients was 32 years. Seven of the 11 patients had 3 pregnancies or more,

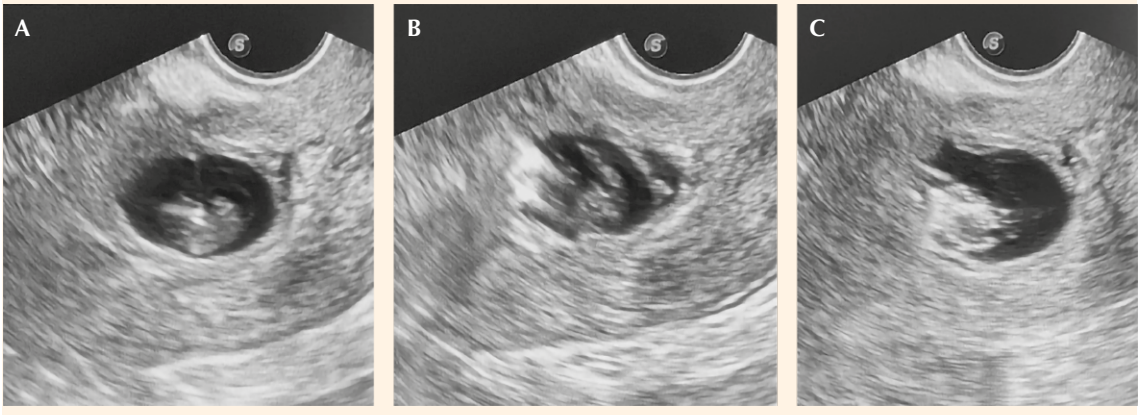


Figure 5. (A) Methotrexate intrasaccular injection. The intrasaccular hyperechogenic needle is evidenced. **(B)** Liquid is seen to enter the gestational sac cavity, where it fills and deteriorates the embryonic image. **(C)** Final ultrasound image, where a clear image of the embryo is missing, filled with the previously injected medication. Source: Study archive.

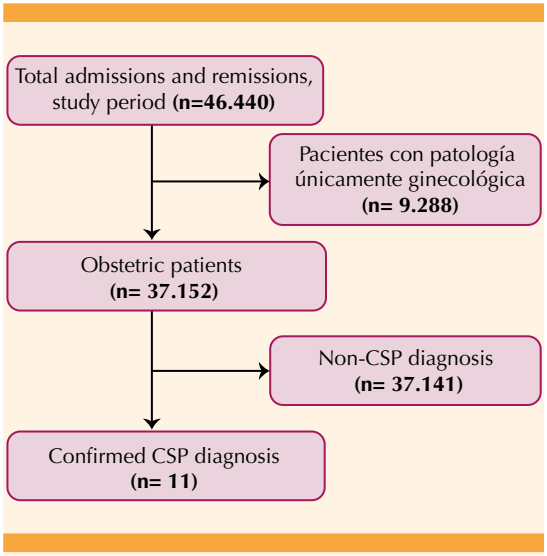


Figure 6. Flow chart of the study patients' choice. CSP : ectopic pregnancy implanted on previous cesarean scar. Source: Made for study.

and all of them had at least one C-section. Five patients had a history of 2 C-sections.

Upon reviewing the clinical records of the patients, we found that 5 patients had a history of abortion with curettage, 3 of them in the group of 2 previous C-sections, and 2 more with one previous C-section.

All the patients with cesarean scar pregnancy diagnosis had a transvaginal ultrasound made upon admission, as part of the diagnosis procedure. Among the ultrasound findings **(Table 2)**, we found that all the patients were admitted in the first trimester of pregnancy, with less than 8 weeks of gestation. All the patients had ultrasound findings of a gestational sac with adequate ultrasound characteristics, and present embryonic structures, both yolk sac, and embryo. Eight patients had positive embryocardia before the intervention.

Upon admission in the emergency service **(Table 3)**, all patients showed hemodynamic stability, and no signs of abdominal irritation that indicated the need for an immediate and invasive intervention. Seven patients were admitted in emergencies with symptoms of mild pelvic pain, vaginal bleeding, and amenorrhea. Pelvic pain and vaginal bleeding were the two most frequent symptoms.

Table 1. Summary of case reports. Sociodemographic variables and obstetric history

Case	Age	Origin	Parity	N. of Deliveries	N. of C-sections	N. of Abortions
1	31	Urban	G3C1A1E1V1	0	1	1
2	30	Rural	G4C2A1E1V2	0	2	1
3	34	Urban	G3C2E1V2	0	2	0
4	27	Urban	G3C2E1V2	0	2	0
5	29	Urban	G2C1E1V1	0	1	0
6	27	Urban	G2C1M1E1V0	0	1	0
7	27	Urban	G2C1E1V1	0	1	0
8	35	Urban	G5C2A2E1V2	0	2	2
9	35	Rural	G5P2C1A1E1V3	2	1	1
10	38	Rural	G5C2A2E1V2	0	2	2
11	39	Rural	G5C1A3E1V1	0	1	3

Source: Made for study.

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Table 2. Summary of case reports. Ultrasound findings upon admission

Case	Gestational sac size (mm)	Yolk sac size (mm)	Embryo size (mm)	Embryocardia	Gestational age (weeks)
1	25	4,4	5,7	yes	6,6
2	18	2,4	2,5	no	5,5
3	35	3,2	18,6	yes	8,2
4	19	1	2,2	yes	5,5
5	13	4	4,6	yes	6,1
6	10,7	3	2	no	4,1
7	26	1,4	11	no	7
8	26,5	2	13	yes	7,2
9	27,4	3,3	14,1	yes	7,5
10	24	4,1	7,3	yes	6,4
11	54	4,4	6	yes	6,3

Source: Made for study.

Table 3. Summary of case reports. Clinical data and follow-up

Case	Admission	Symptoms at admission	B-hCG level at admission (mIU/ml)	B-hCG remission time (days)	IM systemic methotrexate management (mg)	Intrasaccular local methotrexate management (mg)	Intrasaccular local potassium chloride management (cc)	Complications
1	Emergency	Vaginal bleeding	37.662	43	56	25	2	None
2	Emergency	Pelvic pain and Vaginal bleeding	6.935	42	100	25	-	None
3	Referral	-	16.206	29	82	25	-	None
4	Emergency	Pelvic pain and Vaginal bleeding	117.718	67	79	25	-	Vaginal hemorrhage
5	Emergency	Pelvic pain and Vaginal bleeding	21.639	28	90	25	-	None
6	Emergency	Amenorrhea	2.108	28	90	25	-	None
7	Emergency	Pelvic pain and Vaginal bleeding	588	49	90	25	-	None
8	Emergency	Pelvic pain and Vaginal bleeding	41.432	42	90	25	2	None
9	Referral	-	42.131	28	100	25	2	Post-puncture headache
10	Referral	-	72.702	35	85	25	-	PID
11	Referral	-	18.227	35	78	25	-	None

Source: Made for study.

All the patients received combined systemic and local methotrexate treatment. Of the eight patients who had positive embryocardia upon admission, 5 didn't require potassium chloride administration, because the ultrasound scan before the intrasaccular injection showed a negative embryocardia. Only 3 patients received potassium chloride as embryocardia was still present upon administration of the local methotrexate dose.

Regarding the β-hCG concentrations follow-up **(Table 3)**, the mean, in days, to become negative, was of 38.7. However, there was one case, with an extreme response, showing negative results 67 days after the treatment.

Eight of the eleven patients didn't have symptoms or complications after the procedure, nor during the β-hCG concentration follow-up. There were 3 cases with complications: one with vaginal hemorrhage, another with post-puncture headache, and a third with pelvic inflammation. The vaginal hemorrhage case evolved with no signs of instability. It was described as mild to moderate vaginal bleeding, without clots, and no need for further in-hospital care. The headache case happened three days after the procedure, when the patient was admitted due to a headache secondary to the spinal puncture. She was treated with analgesic and anti-inflammatory medication in-hospital, she was evaluated by the anesthesiologist, and as the clinical symptoms disappeared, she was discharged the same day. In the third case, the patient was admitted in the emergency service a week after the procedure. She had vaginal discharge, and pain on movement of the cervix. She was diagnosed with pelvic inflammatory disease and was prescribed with antibiotics. The patient of the second case had a new pregnancy a year after her cesarean scar pregnancy, and it came to term, without complications.

DISCUSSION

There is no consensus for the treatment of cesarean scar pregnancies. The incidence of pregnancies implanted in the area of a cesarean scar has increased in recent years, in direct association with the growing rates of C-sections. In some regions, such as Latin America and the Caribbean, the C-section rate has reached up to a 42.8% increase. These pregnancies, with anomalous implantation, regardless of the gestation weeks they reach, can lead to severe complications. A timely diagnosis and follow-up, to provide personalized treatment, are fundamental. A delay in the beginning of treatment results in a higher risk of complications. The therapeutic trends aim to keep reproductive function with the application of a systemic or intraamniotic methotrexate injection, intrasaccular local injection of potassium chloride, or the vacuuming of the cervix canal.[21] The local treatment with potassium chloride or methotrexate in combination with the administration of systemic methotrexate has shown lower risk of complications and a higher rate of success.[22]

The current diverse approaches and schemes haven't managed to clarify which one is better in terms of efficacy, safety, and fertility preservation, while all of them can lead to substantial complications.[23] Timor et al. published a review[22] where they evaluated 751 cases with cesarean scar pregnancies, where different successful treatment protocols were applied, and presented with complications. These authors identified that in almost half of the compiled cases, there were emergency treatments: hysterectomies, laparotomies, and uterine artery embolizations, all with the purpose of stopping bleeding. Besides, some first-line single treatment schemes, such as systemic methotrexate, uterine curettage, and uterine artery embolization, led to more complications, with 66.1, 61.9, and 46.9%, respectively. Hys-

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teroscopy and local intrasaccular methotrexate or potassium chloride injection, with additional systemic methotrexate, were more successful, and with fewer complications. These outcomes are confirmed in the present case series where there were no severe complications, nor were additional surgeries necessary. The bleeding case was mild, caused by a hemodynamic affectation of the patient.

When the literature related to single dose systemic methotrexate is reviewed, it is found that it is associated with complication rates as high as 62.1%, especially because additional treatment is required, and the results can take several days, and the embryo or fetus and its vascularization grow.[16] Its failure rate as a single treatment scheme can be caused by its slow action, and its debatable capacity to stop cardiac activity and placental invasion.

The intragestational methotrexate injection approach, with ultrasound guidance, has shown efficacy, with articles that report its successful application. Yin et al. treated 20 out of 34 patients with cesarean scar pregnancy, with gestational sac methotrexate injection, guided by transvaginal ultrasound, without complications.[24] Also, Yamaguchi et al. successfully treated 8 cases of cesarean scar pregnancy with local methotrexate injection, with ultrasound guidance, while 2 patients required additional treatment with systemic methotrexate.[25]

When searching for a medical treatment for cesarean scar pregnancy, the preferred approach is local methotrexate injection, with or without the systemic administration, as a strong recommendation.[1] Cheung et al., found in a literature review, a 73.9% success rate when treating patients with a cesarean scar pregnancy with local methotrexate, reaching 88.5% when combining with systemic methotrexate.[18]

At the Maternal-Fetal Medicine Unit, in Barranquilla, the scheme used for patients with cesarean scar pregnancy is the administration of systemic intravascular and local methotrexate. The main findings in the 11 reported patients were technical and clinical success of 100%, where no patient had severe complications, or required a hysterectomy. Also, as the scheme is based on low-cost and easily accessible elements, it is a replicable strategy that requires easily attainable competencies for most specialists with experience with ultrasound and percutaneous procedures.

Not only a previous C-section has been described as a risk factor for the anomalous implantation of a pregnancy in a cesarean scar; other risk factors have been described, such as a consequence of another uterine surgery, like a myomectomy, the manual extraction of the placenta, obstetric curettage, and even in-vitro fertilization.[26] When analyzing the 11-case series of patients with diagnosis of cesarean scar pregnancy, it was found that 45% of the patients had more than one previous C-section, and that also, 63% of them had a surgical history, and obstetric curettage secondary to early gestation loss. It has been demonstrated that these procedures increase the risk of a cesarean scar pregnancy. While the kind of study, and the number of cases don't allow for an association, it is noteworthy that there were more cases in the group with two previous C-sections and a history of curettage, than in the cases with just one C-section and a history of curettage. This finding should be studied further in more research to explore this association.

As for the clinical manifestations, cesarean scar pregnancies don't have specific symptoms, situation which makes an initial diagnosis by symptoms and physical examination, difficult. Besides, it can be easily confused with the clinical manifestations of spontaneous abortion, low

intrauterine pregnancy, cervical pregnancy, or trophoblastic tumor.[27]

Grechukhina et al. described a case series of 30 patients whose main symptoms were pain and vaginal bleeding, with 33 and 23%, respectively.[28] In the cases described in the present report, 64% of the patients presented with pain and vaginal bleeding. While these findings are often nonspecific, it is important to include cesarean scar pregnancy as part of the differential diagnosis of these patients.

Methotrexate is an antagonist of folic acid widely prescribed for treating tubal ectopic pregnancies.[29] The systemic treatment with methotrexate can cause secondary effects in patients which can include nausea, hair loss, and impaired liver function.[30] The local intrasaccular infusion with methotrexate aims to extend the direct action of the drug, shorten the gestational sac resolution, and accelerate the decrease of B-hCG concentrations, and with it, diminish the secondary effects of the systemic administration. Gromnica et al. reported that 19 of 62 patients with cervical pregnancies, who received systemic methotrexate, had signs and symptoms of toxicity related to the drug during their treatment.[31] None of the 11 cases of the present study with local and systemic methotrexate had secondary effects. Likewise, the authors consider that when applying the intrasaccular and systemic dose, the re-treatment requirements are reduced.

B-hCG concentrations are a very useful laboratory marker when monitoring patients after methotrexate treatment while aiming to preserve fertility.[32] When patients who are treated medically are monitored, the gestational mass, and B-hCG concentrations can increase transitorily. Timor et al. reported a mean time of 88 days (range 26-177) to resolution after a treatment which aimed to preserve fertility, in a group of 22 women.[19] Knowing the post-treatment development can help to minimize additional, unnecessary treatments. In the 11 studied cases, a success rate of 100% was observed, with negative concentrations of B-hCG in a mean of 38.7 days. An extreme result was observed in one patient who reached negative B-hCG 67 days after the combined treatment. Some studies describe a similar behavior of B-hCG concentrations. Levin et al. published a retrospective, cohort study which included patients with cesarean scar pregnancy, who were treated with systemic and local methotrexate. Their results were successful with a 37-day median.[33] Cesarean scar pregnancies are a growing challenge worldwide, and the safest and most efficacious clinical and therapeutic approach is yet to be determined. Until now, the literature supports an interventionist approach, more than a medical one.

While it was not the goal of the study, a case of a successful pregnancy after the intervention was documented, without gestation complications. This reinforces even more the low complication and fertility preservation goals, when choosing this therapeutic option.

CONCLUSIONS

Despite research done about the treatment of cesarean scar pregnancy patients, an optimal treatment has not been determined, because there is no evidence from randomized, controlled studies. The literature reports different surgical and non-surgical options, but despite this, there is still a lack of data for complications in the long and short term after treatment. Thus, the evidence suggests avoiding expecting behavior. The outcomes of the study published here support the combined treatment with systemic and local methotrexate as a good option for patients with diagnosis of cesarean scar pregnancy, considering the therapeutic results shown in every one of the studied cases, with a reduced rate of complications. Also, it is a treatment scheme that can be used by low-resource health systems. Without a doubt, more comparative studies are

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needed, with the different therapeutic modalities, and with a greater casuistry to guide a comprehensive practice, always keeping in mind the independent characteristics of each patient with a cesarean scar pregnancy diagnosis.

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