

## Uterine artery embolization with methotrexate infusion as treatment for cesarean scar pregnancy. Case report.

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### Abstract

Cesarean scar pregnancy is a rare form of ectopic pregnancy. It is associated with many complications, including a high risk of massive bleeding and hysterectomy under unfavorable conditions. Conservative treatment with systemic methotrexate (MTX) has been used preferentially with the aim of allowing the patient to have a reproductive future. However, cases of complex ectopic masses in a cesarean scar with guarded prognosis demand techniques that are more effective, such as uterine artery embolization (UAE) in association with intra-arterial MTX infusion. We describe the case of a 35-year-old patient in the 8th week of pregnancy who was referred to us because of genital bleeding and suspected ectopic pregnancy in the cesarean scar. After confirmation of the diagnosis, an initial attempt at systemic treatment with MTX was made. This was abandoned due to the elevation of the hepatic transaminase level. In addition, because of the complexity of the mass and the patient's desire to preserve her reproductive capacity, it was decided to perform UAE with local MTX infusion. The procedure was performed successfully and the patient's fertility was preserved.

**Keywords:** cesarean scar pregnancy, ultrasound, magnetic resonance imaging, methotrexate, embolization.

### Introduction

Ectopic pregnancy in a cesarean scar was described for the first time in 1978 [1]. Its incidence is around 1:2,000 pregnancies and it presents high risk because of the possibility of catastrophic complications such as extensive vaginal bleeding and uterine rupture. It may result in compromising the patient's reproductive future in cases of hysterectomy [2]. Over the years, there have been improvements in diagnostic resources, particularly with regard to ultrasonography: when this is allied with

Doppler velocimetry, it enables early detection and treatment [3]. In turn, clinical treatment may be expectant or drug-based, in which systemic methotrexate (MTX) is used and the beta fraction of human chorionic gonadotropin (B-HCG) is assayed [4]. Surgical approaches with exploratory laparotomy have led to high mortality and the possible need for emergency hysterectomy.

For this reason, other treatment techniques have been proposed for ectopic pregnancy, and especially for such pregnancies located in the cesarean scar, such as use of local MTX, local resection of the mass, uterine artery embolization, and aspirative curettage [2].

Use of uterine artery embolization (UAE) has been described in some case reports as being an effective treatment. However, more recent articles, also in small numbers, have made reference to the UAE technique used in association with intra-arterial MTX infusion [5-7].

We report a case of complex ectopic pregnancy in a cesarean scar that was treated with UAE in association with local MTX infusion. We describe the propaedeutics used and highlight the intervention procedure and patient evolution.

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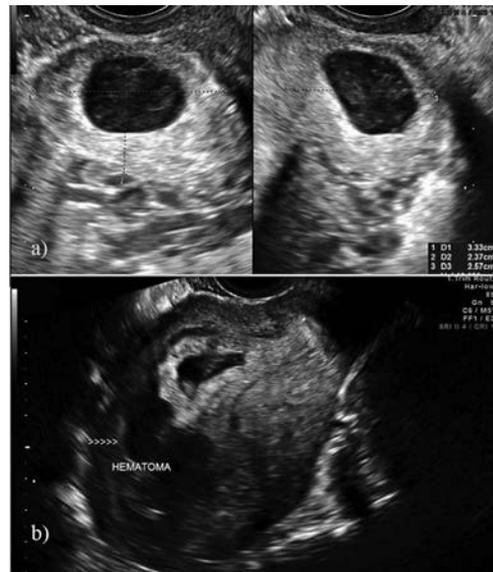
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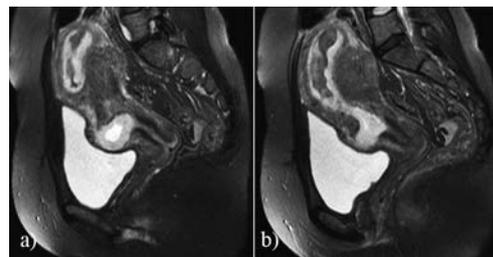
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### Case report

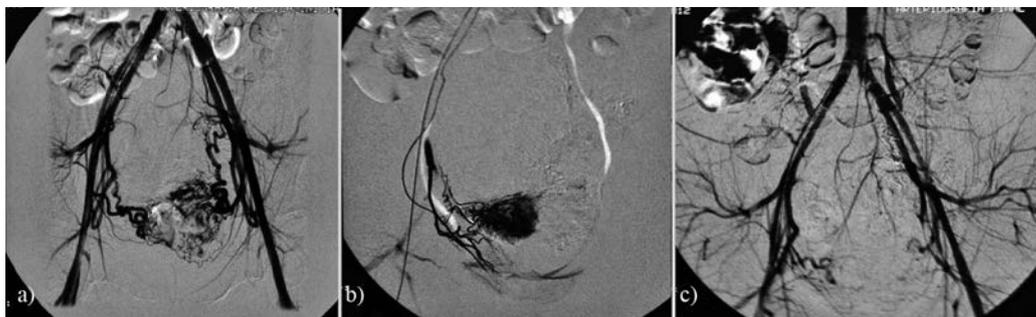
The patient was a 35-year-old uniparous woman in her second pregnancy who was admitted to the obstetrics service of Hospital São Paulo, Paulista School of Medicina, Federal University of São Paulo (UNIFESP), with a complaint of genital bleeding that had started one day earlier and a suspicion of ectopic pregnancy in the cesarean scar, from ultrasonography performed at another clinic. In the examination at the time of admission, she was found to be hemodynamically stable and use of a speculum showed minimal bleeding. Transvaginal ultrasonography was performed, which showed a gestational sac of dimensions 3.3 x 2.3 x 2.5 cm in the region of the uterine scar, without an embryo, and also a subchorionic hematoma measuring 4.2 x 3.6 x 2.4 cm (fig. 1). Magnetic resonance imaging showed a gestational sac in the cesarean scar measuring 5.0 x 3.5 cm with an adjacent placental reaction (fig 2). Initially, it was decided to use systemic MTX treatment with a multiple-dose protocol. However, this was abandoned due to an initial elevation of the hepatic transaminase level. The B-HCG assays before the first and second MTX doses were 280,000 and 140,000 mIU/mL, respectively. Because of the patient's declared desire to preserve her reproductive capacity, the team decided to perform UAE with arterial infusion of MTX (50 mg/m<sup>2</sup> in each embolized uterine artery) after the second MTX dose. The procedure was performed successfully (fig. 3) and was accompanied by a gradual decline in the B-HCG assay over the subsequent days. The patient returned to our service 10 days after the procedure and underwent new ultrasonography and magnetic resonance imaging examinations, for control purposes, which showed that there had been a favorable evolution of the ectopic mass, with diminished size and vascularization, also accompanied by a marked decline in the B-HCG assay.



**Fig 1.** Transvaginal sonogram of the uterus, showing deep implantation of a gestational sac embedded at the site of a previous cesarean scar, without any fetal parts visible in the uterine cavity (a). Hematoma area below the ectopic mass (b).



**Fig 2.** Sagittal T1-weighted magnetic resonance image showing a heterogeneously hypointense mass in the region of the cesarean scar (a). No presence of an embryo can be seen in any of the slices. An adjacent placental reaction can be noted (b).



**Fig 3.** Bilateral uterine angiography before and after uterine artery embolization: a) Uterine arteries were enlarged by means of hypervascular infusion of methotrexate before uterine artery embolization; b) Unilateral occlusion was successfully performed; c) Bilateral arterial occlusion was confirmed after the uterine artery embolization and no extravasation was observed.

## Discussion

Cesarean scar pregnancy is an extremely rare presentation of ectopic pregnancy. The possibilities of complications and treatment failure become increasingly significant with diagnoses that are made at a late stage. Ultrasonography provides great assistance in the propaedeutics, especially when performed in conjunction with appropriate clinical investigation.

Use of systemic MTX continues to be of great value in cases of stable patients who wish to preserve their reproductive capacity [8]. Many authors have described use of multiple dose protocols, local resection of the mass, uterine artery embolization and aspirative curettage as possible treatments that can be chosen [2]. However, the literature seems to be pointing towards use of UAE allied with local MTX infusion as a viable alternative for dealing with ectopic pregnancy, especially in cases in which the initial B-HCG assay is greater than 5,000 mIU/mL [4].

It cannot be denied that countries like Brazil, which has the highest cesarean delivery rate in the world, will be represented by higher rates of cesarean scar pregnancies. Thus, such countries need to acquire knowledge about new targets for effective treatment. The UAE technique used in association with intra-arterial MTX infusion was first described by Yang et al [9]. Their intention was to infuse the chemotherapy through the uterine arteries and not directly into the gestational sac or surrounding endometrium, which could cause scar rupture and extensive hemorrhaging. The objective in this type of treatment is to place the chemotherapy in direct contact with the embryo, thereby reinforcing the ischemia and trophoblastic degeneration that is promoted by embolization. Studies have shown that local MTX infusion can be performed using higher doses of the drug without greater side effects compared to the systemic treatment using the same dose. Moreover, systemic absorption of MTX may be limited by deficient vascularization of the fibrous scar tissue [10-13].

However, it needs to be emphasized that no invasive procedure is risk-free. Case reports on the use of embolization for treating uterine myomatosis have demonstrated occurrences of vaginal necrosis, vesicular fistulae and endometrial atrophy with continual amenorrhea [13,14]. Another associated complication consists of fever and intense painful conditions that appear due to tissue necrosis.

Future fertility is also a focus of concern at centers using this technique. In a prospective randomized study, the spontaneous intrauterine pregnancy rate was 73% after a single dose of MTX and 62% after laparoscopic

treatment [15]. Zhang et al [16] found that the normal menstrual cycle resumed two to four months after performing UAE in association with local MTX, and a normal pregnancy had started in 50% within one year. It has been estimated that once the blood vessel has been embolized, it reopens its course after around two to three weeks, which is advantageous for the ideal of future reproduction [17]. It is important to remember that contraception should be used for at least three months after use of MTX, and patients should be adequately informed about the associated risks, during and after the treatment [18].

In conclusion, although it has been indicated in the literature that UAE with local MTX infusion is a promising form of treatment, randomized controlled studies are still required in order to assess the real advantage of the procedure and to better evaluate the associated complications. There are still some doubts regarding the intra-arterial dose that is recommended for treating ectopic masses in cesarean scars. In addition to making improvements to the new technique, countries should also invest in health-care policies that prioritize reversal of the culture of excessive cesarean delivery rates.

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