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## ECTOPIC PREGNANCY IMPLANTED IN A PREVIOUS CESAREAN SECTION SCAR: EXPERIENCE IN THE BRAZILIAN EXTREME NORTH

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### ABSTRACT

**Introduction:** Ectopic pregnancies (EP) are challenges in obstetric practice due to the potentially fatal complications, especially massive hemorrhage and uterine rupture. Although in most cases of EG the blastocyst implants in the uterine tube, it is possible to have implantation in several places in the body - called extra-tubal ectopic, occurring implantation in the abdomen, ovary, cervix, peritoneal cavity, among other possibilities. A rare site of implantation is the scar tissue from previous cesarean sections - also called cesarean section pregnancy (CSP) and it represents an incipient concern in our environment because the increase in cases is closely related to the increase in cesarean sections performed. Diagnosis and treatment protocols are not unanimous among medical authorities and there is a scarcity of case reports on this condition and its management, justifying the development of this study. **Objective:** To report a case of ectopic pregnancy by implantation in the uterine scar of a previous cesarean section, attended in a medical service in Macapá (AP), Brazil. **Method:** From data collected by consulting the patient's medical records, the case report is structured in order to present and discuss it based on the reading of scientific publications on the same theme.

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## INTRODUCTION

Cesarean section pregnancy (or CSP), possibly due to blastocyst implantation into a scarred or fibrous uterine wall, is a rare presentation with an incidence of 1/800 to 1/2500 globally. However, with increasing rates of cesarean sections and reproductive assisted pregnancies (such as in vitro fertilization), it is likely to present more frequently in clinical practice (FYLSTRA, 2002; GONZALEZ *et al.*, 2017). Therefore, it is imperative for the women's health professional to consider it as a differential diagnosis whenever presenting with early pregnancy disorders or complications. When diagnosed early, there are conservative treatment options or less invasive treatments with satisfactory clinical results (GONZALEZ *et al.*, 2017). In contrast, if the condition is not identified, complications - such as uterine rupture and massive bleeding, may require extensive surgical interventions (NAGI *et al.*, 2007). The present paper aims to report the case of a patient seen at the Maternity Hospital Mãe Luzia,

located in the capital of the state of Amapá, Macapá. The pregnant woman was diagnosed with ectopic pregnancy that was later identified as being of scar implantation. The report is justified by the rarity of the occurrence and its relevance in the current clinical context.

## METHODS

The study design is structurally characterized as follows: primary research (original research), observational (without direct interference of the authors in the sample, non-participant observation) of the case report type, based on data from a patient seen in a public health care network. The participant is a pregnant woman admitted to the study site and diagnosed with ectopic pregnancy, later identified as implanted at the site of a previous cesarean section. The present research had as its study area the Mãe Luzia Women's Hospital (HMML), a public foundation subordinated to the State Health

Department (SESA) and located in the city of Macapá, capital of the state of Amapá, belonging to the Brazilian North Region, geographically and socioeconomically contextualized in the Amazon Region. The aforementioned institution currently represents the largest referral center in gynecological and obstetric care in the state, meeting the demand of the Amapá public and often populations of the surrounding areas of Pará. It plays a fundamental role in maternal-fetal health care, offering procedures of various complexities, performing an average of 950 deliveries per month, both normal and cesarean deliveries, with approximately 25% of these being premature deliveries considered high-risk. HMML also plays a fundamental role in the technical and scientific development of the region's health professionals. The data were collected from the documents referring to the patient's case, filled out correctly by the health professionals who attended her at the Maternity Hospital Mãe Luzia. Complementary information was obtained in interviews and questionnaires directly with the patient, to clarify the facts in order to enrich the scientific quality of the case report. This study was approved by the Research Ethics Committee of the Federal University of Amapá (UNIFAP). All ethical principles were respected, such as confidentiality of information identifying the participants, as well as obtaining the consent of the study site and the consent of the Medical Archive and Statistics Service (SAME) for the collection of data in medical records.

## CASE REPORT

Female patient, 38 years old, G2D1A1. First cesarean delivery 6 years ago and abortion 2 years ago. She sought medical attention for menstrual delay (LMD: 08/14/2021), with no other complaints. Transvaginal ultrasonography (USG) was performed, no gestational sac was identified and the patient was requested follow-up. According to the patient's report, she later sought the emergency service of the Santana Hospital after presenting vaginal bleeding in appearance of "coffee grounds" and mild colic pain. At the hospital, a new transvaginal USG was performed, indicating the presence of placental remnants in the uterine cavity and the need to investigate incomplete abortion. Then, after guidance and initial therapy, the patient sought a private service to perform manual intrauterine aspiration (MIA), performed on 10/12/2021. The anatomopathological and histological study of the aspirated content, on 10/13/21, revealed partially necrotic placental and decidual remains amidst blood clots. Patient reports that, after the procedure, there was pain relief and cessation of bleeding. However, on 11/14/2021, the patient presented sudden and intense pelvic colic, irradiating to the lumbar region. She also reported heavy and intermittent vaginal bleeding. On 12/13/2021, the patient underwent a new transvaginal USG. On this occasion, the image described a uterus with normal dimensions and regular contours, containing heterogeneous, predominantly solid material, but with several permeable vesicular areas, with no definition of the endometrial limits. The presence of a heterogeneous mass was also described in the region of the left appendages, measuring 80 x 76 x 79 mm, with an approximate volume of 258 mm<sup>3</sup>. Gestational trophoblastic disease was questioned, among other differential diagnoses. A complementary laboratory study performed on 12/15/2021 showed the following noteworthy values: hemoglobin 9,00 g/dL, hematocrit 32.6%, leukocytes 6,500/mm<sup>3</sup> (segmented 64%; typical lymphocytes 26%), platelets 308,000/mm<sup>3</sup>. The quantitative measurement of human chorionic gonadotropin showed beta hCG = 31,950.0 mUI/mL. On 12/16/2021, the metrorrhagia mentioned by the patient reappeared, accompanied by large clots and high intensity colic pain. The patient then sought emergency care at the Santana Maternity Hospital. At the institution, she received blood transfusion for clinical stabilization. Consecutively, a pelvic magnetic resonance imaging (MRI) with contrast was performed on the same day - 12/16/2021. The uterus was observed measuring in its greatest transverse axes about: 13.4 x 6.2 x 9.36 cm, with an estimated volume of about 401 cm<sup>3</sup> and heterogeneous content, distending the uterine endometrial cavity, with the left cranial portion being impregnated by the venous contrast. The content measured around 3.3 x 2.9 cm, neither infiltrating the endometrium-myometrium junctional zone, nor

the uterine myometrium. The endometrium-myometrium junctional zone presented preserved thickness (< 1 cm), inferring a low probability of adenomyosis. The observed cervix had the usual anatomical morphology and intensity of signs, except for a grossly oval lesion infiltrating the anterior portion of the uterine cervical stroma, measuring about 4.2 x 4.0 cm. This finding could correspond to hematic content inside a hypertrophic cesarean section scar, but the possibility of other differential diagnoses such as placental accretism and molar gestation in this topography have not been ruled out. Other aspects evaluated by MRI did not demonstrate remarkable alterations, observing appendages, bladder, lymph nodes, rectum and perirectal fat in usual conditions. The patient was referred to the Mãe Luzia Women's Hospital, where she underwent curettage on 12/22/2021 (collected material submitted to biopsy, but the results were not available in time). After the procedure, she was referred for follow-up at the Capuchinhos outpatient clinic. Patient reports that after the curettage there were no new episodes of vaginal bleeding, however, the pain persisted, with continuous cramps that led her to seek frequent medical attention.

Laboratory tests on 01/26/2022 showed erythrogram, leukogram and coagulogram at standard values; urea, creatinine and AST/ALT were unchanged. A transvaginal pelvic USG performed on the same day documented an uterus with increased dimensions (9.2 x 6.1 x 6.4 cm; volume of 188.1 cm<sup>3</sup>), irregular contours and heterogeneous myometrial echotexture. Additionally, presence of a heterogeneous mass with vesicles inside, located in the isthmic region and measuring 54 x 39 x 46 mm. Due to the unclear uterine mass, hydatidiform mole was questioned. She underwent routine urine examination and sedimentoscopy on 02/02/2022, and hematuria (RBCs 9-12/field) and pyuria (4-7/field) were evident. On February 10, 2022, the patient was again admitted to the Mãe Luzia Women's Hospital due to her clinical condition. The main suspicion until that moment was hydatidiform mole. A new transvaginal USG was performed, and identified uterus dimensions 90 x 48 x 59 mm - volume: 136.9 cm<sup>3</sup> and heterogeneous cystic mass with thick echogenic wall on the topography of the uterine cervix, with peripheral flow at Doppler, measuring 49 x 40 x 35 mm, volume: 37.1 cm<sup>3</sup>. After this examination, the main suspicion became ectopic pregnancy in a previous cesarean section scar. After dialoguing with the medical team and explaining the situation to the patient, a joint decision was made to perform a hysterectomy on February 12, 2022. A total hysterectomy with bilateral salpingectomy was chosen. Due to the difficulty in completely visualizing the specimen, the uterine body and cervix were removed at different times in a row. However, there were no intercurrences during the surgery. The patient recovered uneventfully. The patient returned for postoperative follow-up reporting improvement of pain symptoms and no new complaints. Abdominal palpation revealed no masses and a painless abdomen.



**Figure 1&2. Extracted uterine body and cervix mass, with dimensions of 13.5 x 8 x 2.5 cm**

Histopathological examination of the mass removed during surgery revealed fragments of endometrial mucosa with extensive areas of decidual transformation of the stroma, which has permeated blood clots and chorionic villi of loose stroma, externally lined by a double

layer of well constituted trophoblast. Partially necrotic placental and decidual remnants in the midst of blood clots - confirming the hypothesis of ectopic pregnancy in the topography of a previous cesarean section scar.

## DISCUSSION

The incidence of EP globally is difficult to determine, however, it appears to have increased steadily since the mid-20th century to reach a plateau in the 1990s. According to a survey conducted by the Centers for Disease Control, the reported prevalence of ectopic pregnancy increased from a total of 17,800 cases in 1970 to 108,800 cases in 1992, a five-fold increase. Currently, ectopic pregnancy accounts for about 2% of all recognized pregnancies in the United States, with the highest rate concentrated in the 35 to 44 age group. Despite improvements in health care, tubal ectopic pregnancies still account for an alarming 6% of maternal deaths in the country (LEHNER *et al.*, 2000; MARION *et al.*, 2012). The reasons for the increase in cases are complex and multifactorial, highlighting the increased incidence of pelvic inflammatory disease (PID), access to improved diagnostic techniques that result in earlier identifications not possible in the past, and the growing demand for assisted reproductive treatments (MARION *et al.*, 2012). Although the etiology spans different elements, about 50% of patients with EP have no identifiable risks. The widely accepted risks for ectopic pregnancy are not necessarily independent of each other, and the recognized risks show variable rates depending on the population studied. Therefore, the mechanisms underlying the risk of extrauterine implantation remain unclear (HENDRIKS *et al.*, 2020; TONG *et al.*, 2015). Ultimately, conditions that delay or prevent the passage of the embryo through the tube into the uterine cavity may lead to ectopic implantation. The etiopathogenesis correlates strongly with anatomic obstruction, abnormalities in tubal motility or ciliary function, abnormal conception, and chemotactic factors that stimulate tubal implantation (LEHNER *et al.*, 2000; CARUSI *et al.*, 2019).

Other risk factors include smoking, in utero exposure to diethylstilbestrol and fertility treatments. The occurrence of GE is markedly increased in women undergoing assisted reproductive technology, occurring in about 1.5% to 2.1% of patients who have undergone in vitro fertilization. Specific risk factors in this subgroup include infertility due to tubal factor, transfer at the blastocyst stage, higher number of embryos transferred, decreased endometrial thickness, variation in culture media, and fresh embryo transfer. However, the scientific literature is still scarce and divergent regarding the risk factors for ectopic pregnancy in the context of assisted reproduction (MARION *et al.*, 2012; LEHNER *et al.*, 2000). Furthermore, the use of an intrauterine device (IUD) is often mentioned as a risk factor for EP, but the interpretation of this relationship should be cautious. Although the risk of pregnancy is low with IUD in general, if pregnancy is identified with the device in situ correctly positioned, the risk of extrauterine implantation is much higher - about 5% of such pregnancies are ectopic (SCIBETTA *et al.*, 2019). The most frequent site of ectopic implantation is the uterine tube (up to 95% of cases). The ampullary portion of the tube is unquestionably the most common site and is involved in 70% of cases. The rest of tubal pregnancies are evenly distributed between the fimbria (11%) and the isthmus (12%). Less commonly, we can observe implantation in the interstitial portion of the uterine tube, fallopian tube, within the myometrium in the horn (3%) (CARUSI *et al.*, 2019; OLIVER *et al.*, 2007).

Other reported sites for extra uterine pregnancies are the abdomen, ovary, cervix, peritoneal cavity, rudimentary uterine horns (also known as cornuals), and cesarean section or cervical removal scar region - all considered to be rare circumstances. Abdominal pregnancy has been associated with higher morbidity and mortality than other types of ectopic pregnancy. In exceptional cases, post-hysterectomy pregnancies have been described. Non-tubal EP poses a difficult diagnostic challenge, often falsifying the hormone levels

used in the early identification of pregnancy (PARKER *et al.*, 2016; SHAN *et al.*, 2014). Among the possible sites of implantation in an ectopic pregnancy, cesarean section pregnancy (CSP) has been highlighted in recent years. This is a relatively new type of ectopic pregnancy. Although the cesarean incision usually heals without any complications, the increase in reports of scar ectopic pregnancies in the medical literature may be due to a high rate of cesarean sections worldwide in recent years, as well as the modernization of imaging examinations in obstetrics and gynecology (GONZALEZ *et al.*, 2017; FYLSTRA, 2002). Currently, it represents 6% of all ectopic pregnancies in women with at least one anterior incision of the lower uterine segment. Although the lack of accuracy in its diagnosis may hinder estimates, its incidence is speculated to be 1 case for every 1,688 pregnancies, with 1/3,000 in the general obstetric population and about 1/2,000 of all cesarean deliveries (GADEEB *et al.*, 2019).

CSP is subdivided into 2 types: type I, or endogenous, when there is progression to the cervicoisthmic space or uterine cavity, and type II, or exogenous, when there is deep scar tissue invasion with progression to the bladder and/or abdominal cavity. In ectopic implantations that evolve endogenously, it is possible that the pregnancy is viable, but with a high risk of bleeding at the placental site. In turn, pregnancies of the exogenous type may complicate with uterine rupture and bleeding in the first trimester (GONZALEZ *et al.*, 2017). Early diagnosis and treatment are essential for better outcomes, therefore, considering the resources available in each service, some authors suggest that all pregnant women with a history of cesarean section should be screened early in pregnancy. Ultrasonography and Doppler imaging are the tests of choice for diagnosis. MRI can facilitate the exact localization of ectopia, when necessary. It should be emphasized that the examiner should differentiate pregnancies with a cesarean section scar from cervical and cervico-isthmic pregnancies (KUMARI *et al.*, 2021). There are still no unanimous treatment guidelines for pregnancies with cesarean section scar due to the rarity of this event; however, it is reinforced that the treatment must be individualized according to the peculiarities of the case such as clinical presentation,  $\beta$ -hCG levels, radiological characteristics and experience of the surgeon in charge (GADEEB *et al.*, 2019; KUMARI *et al.*, 2021). Systemic administration of methotrexate and surgical aspiration of the sac are effective methods of conservative management of a scar pregnancy. Several authors describe systemic treatment with methotrexate as the first approach in early pregnancy; also, cytoreductive therapy is believed to help the gestational sac to protrude into the uterine cavity (KUMARI *et al.*, 2021; FYLSTRA, 2002). In patients treated with methotrexate, residual CSP is possible. In these cases, the condition is often associated with isthmocele (a cesarean scar defect). In cases of isthmocele with a significant defect and the patient's desire for pregnancy, laparoscopic repair may be proposed. Diagnosis and treatment of isthmocele is usually performed after successful treatment of a scar ectopic pregnancy - isthmocele repair can be performed in the same surgical procedure as removal of residual CSP (GADEEB *et al.*, 2019). In the circumstance of an endogenous CSP that has progressed to gestation with a viable fetus, an elective cesarean section should be seriously considered as soon as fetal lung maturity is reached, in order to avoid emergent outcomes such as uterine rupture or massive hemorrhage (GONZALEZ *et al.*, 2017). The pathophysiological mechanism is not yet completely elucidated, however it is speculated that the embryo penetrates the myometrium through a microscopic dehiscence of the scar - previously existing in the maternal uterus (SCHMITT *et al.*, 2017; LAI *et al.*, 1995).

The prevalence of cesarean section defect in a random population of women with cesarean section is up to 84% and is usually asymptomatic. Researchers evaluated the histopathology of uterine wound healing and found different thicknesses of myometrium along the scar with disordered muscle fibers and elastosis. Although its mechanism is still unclear, it appears that impaired healing of the cesarean section incision predisposes to the development of CSP (NAGI *et al.*, 2007; GONZALEZ *et al.*, 2017). Factors that predispose to poor wound healing include inadequate closure of the uterine incision, postoperative infections, and impaired health

conditions such as diabetes or collagen disorders. In addition, decreased blood flow to the affected tissue predisposes to incomplete or delayed healing. Clinically, the short interval between cesarean pregnancy and subsequent pregnancy increases the likelihood of having CSP and accreted placenta. The definition of short interval in this context is unclear (LAI *et al.*, 1995; FYLSTRA, 2002; SCHMITT *et al.*, 2017).

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