

Case Report

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Cesarean Scar Pregnancy: Conservative Treatment with The Combination of Methotrexate and Mifepristone: A Case Report and Comprehensive Review of Medical Treatment

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Abstract

Cesarean scar pregnancy (CSP) has become more frequent as a direct consequence of the increased number of Cesarean deliveries and the advances in imaging, indeed, it represents 0.04%-0.05% (1/1,800 to 1/2,216) of all pregnancies in 2023 with a frequency of 6.1% in women who had ≥ 1 prior cesarean section (CS). Unrecognized CSP has the potential to cause both fetal and maternal morbidity and mortality several therapeutic options are possible, including medical treatment, however, there is no agreement on the best management. We report the case of a 37 years old women; with a biscalred uterus and who consults for pelvic pain in a context of 7 weeks amenorrea, subsequent explorations showed trophoblastic retention on the scar which was managed by drug treatment: combination of methotrexate and mifepristone. This case suggests that combining mifepristone and systemic methotrexate can be an effective approach and emphasizes the need for clinicians to consider this alternative in the management of certain cases of cesarean scar pregnancy.

Keywords: cesarean scar pregnancy; diagnosis; medical treatment; combination methotrexate; mifepristone

Introduction

Cesarean scar pregnancy (CSP) is considered as one of the rarest types of ectopic pregnancy with an incidence of 6.1% among women who experienced ectopic pregnancy in 2023 [1]. It was first reported by Larsen and Solomon in 1978 [2] and since there has been a substantial increase in its incidence due to an increase in the number of cesarean sections worldwide. Although some cases of cesarean scar pregnancy (CSP) resolve on their own, if left unrecognized or poorly managed, CSP can result in severe maternal and fetal complications. These may include hemorrhage, uterine dehiscence, or rupture in the second or third trimester, caused by the deep implantation of the blastocyst into the fibrous tissue of the lower uterine segment scar [1]. The most common symptoms of cesarean scar pregnancy are lower abdominal pain and vaginal bleeding, although some individuals may be asymptomatic during the first trimester. The preferred diagnostic method for cesarean scar pregnancy is transvaginal ultrasound, often used in combination with a transabdominal scan for a more complete assessment. If the diagnosis remains uncertain, magnetic resonance imaging (MRI) can be used to confirm or rule out the presence of CSP [1]. Although there are several management

strategies for cesarean scar pregnancy (CSP), there is no global consensus or standardized guidelines on the most effective treatment. The choice of treatment depends on factors like the patient's hemodynamic stability, embryo size, residual myometrial thickness, and future fertility plans. Treatment options include both surgical approaches (such as laparoscopy, laparotomy, hysteroscopy, and dilation and curettage) and medical therapies (like methotrexate and mifepristone) [3]. We present a case of a successful conservative treatment of a cesarean scar pregnancy; using a combination of methotrexate and mifepristone; through it we will highlight therapeutic features of this condition.

Case Presentation

Mrs. NO, a 37-year-old patient, she had a history of two cesarean deliveries in the past and 3 curettages for voluntary termination of pregnancy. Her last cesarean section was two years ago. Her menstrual cycles were regular, and she had no significant past, personal, or family history. She presented in our emergency ward with persistent pelvic pain for 8 days in a context of 7-week amenorrhea. On clinical examination, hemodynamics was stable, abdominal palpation revealed no tenderness, and speculum examination

showed a congestive cervix with no bleeding of endouterine origin. Vaginal touch combined with abdominal palpation revealed no latero-uterine mass or signs of peritoneal irritation and a long-closed posterior cervix. A transvaginal ultrasound was done showing a heterogeneous hyperechoic mass of 3.5cm*

2.5cm; vascularized on Doppler at the level of the cesarean scar niche with a total loss of the opposite myometrium: trophoblastic retention at the level of the cesarean scar [Figure 1-2]. A beta-human chorionic gonadotropin (β -hCG) level of 62487 mIU/mL.



Figure 1: transvaginal ultrasound showing trophoblastic retention of 37*32 mm at the cesarean scar.

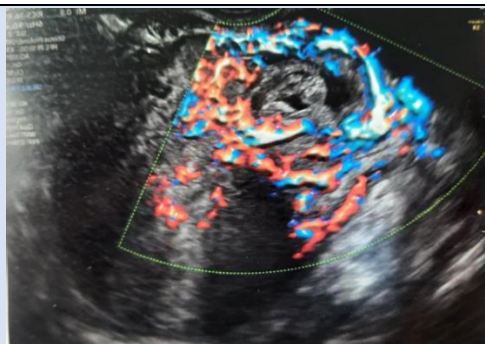


Figure 2: Doppler study by transvaginal ultrasound showing peripheral vascularization in the crown.

Ultrasonography findings were confirmed using MRI which showed an aspect in favor of an ectopic pregnancy on a cesarean section scar without visible

myometrial wall creating a 25mm deep pocket coming into contact with the bladder with doubt about left anterolateral accretization [Figure 3].

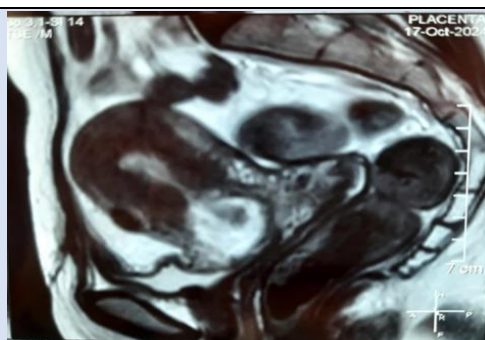


Figure 3: MRI showing an accretization of an ectopic pregnancy on the cesarean section scar.

Given these findings, the patient was initially given 600 mg of mifepristone in single dose along with one injection of MTX (J0), then another dose of MTX was admitted at J 4 and one last one at J 7. The rate of bhcg was controlled before every injection of MTX and then once a week. After two weeks of the last

injection; an aspiration and intracavitary evacuation under echographic control was done; carrying a trophoblast tissue. The bhcg rate was controlled until negativization [Figure 4] and an ultrasound was done after the aspiration showing an empty uterus.

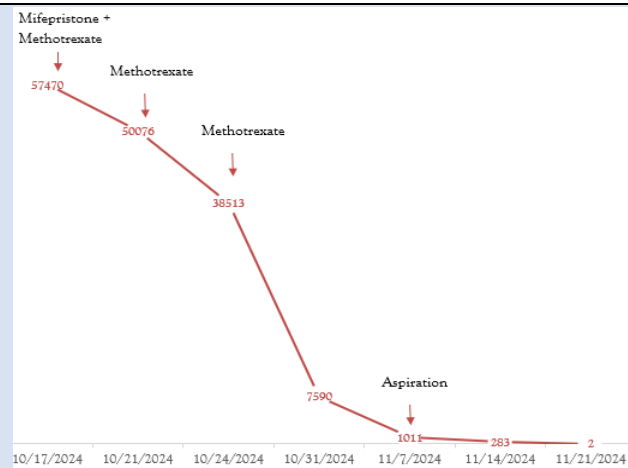


Figure 4: Curve of evolution of the rate of Bhcg.

Discussion

Caesarean scar pregnancy is a very uncommon and potentially fatal form of abnormal implantation of a gestational sac. It delineates a variant of ectopic pregnancy where the gestational sac implants entirely or partially beyond the confines of a prior cesarean scar situated in the lower uterine segment. It corresponds to only 6.1% of ectopic pregnancies in 2023 [1,3,7,21]. The identified risk factors are similar to those for placenta accreta and include: the number of previous cesarean sections (with two or more prior C-sections associated with a higher risk of this condition), an interval of less than two years between the current pregnancy and the most recent C-section, and the indications for previous cesarean sections, which also influence the occurrence of CSP [4,5]. Additional risk factors include endo-uterine procedures (like curettage and manual uterine revision), other uterine surgeries (such as myomectomy), having more than two induced abortions, being over the age of 35, smoking, and retroversion of the uterus. [7,9,11] Finally, it was found that in vitro fertilization (IVF) techniques involving embryo transfer have also been implicated. The less-stimulated and less-mature lower segment may not support optimal healing, thereby increasing the risk of ectopic implantation of the embryo [13,14,16]. Although the exact pathogenesis of CSP is not fully understood, it is believed that the mechanism involves a blastocyst implanting within a microscopic dehiscence tract in the scar from a previous cesarean delivery. Due to the fibrous nature of the scar tissue, these inherently deficient implantation sites are at risk for dehiscence, placenta accreta spectrum, and hemorrhage as the pregnancy advances.

Based on this physiopathogenesis, two different types of CSPs were described [11]:

Type I or on the scar, in which the amniotic sac is implanted on a cesarean scar and progresses into the cervical-isthmic space and uterine cavity. Type II or in the niche, when the CSP is implanted within the scar defect, resulting in deep invasion and progression to the bladder and abdominal cavity. A cesarean scar ectopic pregnancy often presents without symptoms and is typically discovered incidentally during an ultrasound. However, some women may experience vaginal bleeding or pelvic pain [11]. Transvaginal ultrasound (TVUS) with color Doppler assessment is generally considered the gold standard for diagnosing CSP. The diagnostic criteria for identifying cesarean scar implantation on TVUS include: an empty uterine cavity, a gestational sac or solid trophoblastic mass located anteriorly, positioned at the site of the previous cesarean section scar in the lower uterine segment, a thin or absent myometrial layer between the gestational sac and the bladder, evidence of prominent trophoblastic/placental circulation on Doppler (as observed in our case), and an empty endocervical canal [23]. Magnetic Resonance Imaging (MRI) can be used as a second-line diagnostic tool when the diagnosis is unclear. It provides detailed information about the anatomical relationships, the extent of trophoblastic invasion into the myometrium, potential involvement of the serosa or bladder, and the exact positioning of the gestational sac [11,13,21]. The primary goal in managing scar pregnancy is to avoid massive hemorrhage and conserve the uterus for future reproductive and overall health benefits.

Currently, there are no standardized guidelines for the treatment of CSP. Expectant management is generally not advised due to the risk of serious

complications. At present, no formal recommendations exist regarding specific treatment approaches [14,16,21]. Treatment, whether medical or surgical, is typically conservative, unless there is therapeutic failure. Medical treatment in hemodynamically stable patients is feasible for many teams [15]. Methotrexate (MTX) is the most widely used chemotherapeutic agent and is recognized as an effective non-surgical treatment for certain ectopic pregnancies. It can be administered either locally (through an injection at the site, potentially guided by ultrasound or clinical techniques), systemically, or as a combination of both, with a standard dose of 1 mg/kg [14]. Methotrexate functions as a folic acid receptor antagonist, competitively inhibiting the enzyme dihydrofolate reductase, and thereby impeding the conversion of dihydrofolate to tetrahydrofolate ultimately interfering with trophoblastic cell replication [15,20]. The main side effects of methotrexate typically include nausea, vomiting, mucosal ulcers, loss of appetite, and skin rashes. Higher doses can cause more severe and potentially life-threatening complications, such as hair loss, fatigue, infections, fever, gastrointestinal bleeding, pancreatitis, bone marrow suppression, renal failure, and malignancies like lymphoproliferative disorders [15,16]. Thus, additional drugs may also be used along with medical management with systemic methotrexate such as mifepristone or potassium chloride [5,18]. Indeed, the findings suggest that the combination therapy of mifepristone with methotrexate shows superior curative effects [1,4]. This approach was associated with improvements in cure rates, a reduction in β -hCG levels, a decrease in mass size, and relief from symptoms like abdominal pain and bleeding, all without worsening toxic side effects. Mifepristone, a steroidal anti-progesterone, works by inhibiting progesterone release, which ultimately leads to cell degeneration. [17,18,19].

The simultaneous use of methotrexate accelerates the dissolution of trophoblastic cells more effectively than systemic methotrexate alone. [1,4,9,20,21]. The combined regimen of mifepristone and methotrexate was evaluated against a single dose of methotrexate. The findings indicated that the combination therapy significantly lowered the risk of treatment failure in the medical management of CSP [22]. The most frequently used surgical treatment for both live and failed CSPs is suction evacuation with or without ultrasound guidance after the medical treatment.

Overall suction evacuation has relatively low complication rate: 4.5% of clinically significant blood loss (defined as loss of ≥ 1000 mL), 3.1% can cause a RPOC (tissue from the conception persisting after the pregnancy has ended), 0.5% may occur a deep vein thrombosis, 0.5% sepsis, and 0.5% can cause a bladder injury (0.5%) [23]. Our case suggests that this type of combination treatment can be considered, whereas its success with a considerable decrease in the level of Bhcg.

Conclusion

CSP is a growing health concern, largely due to the increasing maternal age, the rise in cesarean sections, and the higher prevalence of medically assisted reproduction, all of which contribute to abnormal pregnancy implantation. The management of CSP is complicated by its rarity, the absence of clear guidelines, and the mixed results from various treatments reported in the literature. A combination of mifepristone and systemic methotrexate may offer more effective medical treatment for CSP, but its use depends on the specific case and patient adherence, and further research is needed to confirm its efficacy.

Declarations

Conflicts of Interest

The authors declare no conflicts of interest.

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Data Availability

No data is associated with this article.

References

1. Stabile, G., Vona, L., Carlucci, S., Zullo, F., Laganà, A. S., et al. (2024). Conservative Treatment of Cesarean Scar Pregnancy with The Combination of Methotrexate and Mifepristone: A Systematic Review. *Women's Health*, 20:17455057241290424.
2. Larsen, J. V., Solomon, M. H. (1978). Pregnancy in a Uterine Scar Sacculus-An Unusual Cause of Postabortal Haemorrhage. A Case Report. *South African Medical Journal*, 53(4):142-143.
3. Mollo, A., Alviggi, C., Conforti, A., Insabato, L., De Placido, G. (2014). Intact Removal of Spontaneous Twin Ectopic Caesarean Scar Pregnancy by Office

- Hysteroscopy: Case Report and Literature Review. *Reproductive BioMedicine Online*, 29(5):530-533.
4. Fu, P., Sun, H., Zhang, L., Liu, R. (2024). Efficacy and Safety of Treatment Modalities for Cesarean Scar Pregnancy: A Systematic Review and Network Meta-Analysis. *Ameri Jour of Obste & Gynecol MFM*, 101328.
 5. Timor-Tritsch, I. E., Monteagudo, A., Santos, R., Tsybal, T., Pineda, G., et al. (2012). The Diagnosis, Treatment, And Follow-Up of Cesarean Scar Pregnancy. *Ameri Jour of Obste & Gynecol*, 207(1):44-e1.
 6. Huo, S., Shen, L., Ju, Y., Liu, K., Liu, W. (2023). Treatments for Cesarean Scar Pregnancy: 11-Year Experience at A Medical Center. *The Journal of Maternal-Fetal & Neonatal Medicine*, 36(1):2162818.
 7. Li, Y., Hua, C. (2023). Is High-Intensity Focused Ultrasound Superior to Uterine Artery Embolization in Cesarean Scar Pregnancy and Subsequent Pregnancy Outcomes? A Meta-Analysis of The Chinese Population. *Journal of Mini Inv Gynec*, 30(3):180-191.
 8. Liu, Y., Wang, L., Zhu, X. (2023). Efficacy and Safety of High-Intensity Focused Ultrasound Compared with Uterine Artery Embolization in Cesarean Section Pregnancy: A Meta-Analysis. *Inv Gynec*, 30(6):446-454.
 9. Patel, M. A. (2015). Scar Ectopic Pregnancy. *The Journal of Obstetr and Gynecology of India*, 65(6):372-375.
 10. He, C., Zheng, F., Lin, J., Chen, S., Yang, W., et al. (2023). A Nomogram to Predict the Risk of Scar Pregnancy After Caesarean Section. *Journal of Obstetrics and Gynaecology*, 43(1):2142767.
 11. Agten, A. K., Jurkovic, D., Timor-Tritsch, I., Jones, N., Johnson, S., et al. (2024). First-Trimester Cesarean Scar Pregnancy: A Comparative Analysis of Treatment Options from The International Registry. *American Journal of Obstetrics and Gynecology*, 230(6):669-e1.
 12. Jordans, I. P. M., Verberkt, C., De Leeuw, R. A., Bilardo, C. M., Van Den Bosch, T., et al. (2022). Definition and Sonographic Reporting System for Cesarean Scar Pregnancy in Early Gestation: Modified Delphi Method. *Ultra in Obste & Gynec*, 59(4):437-449.
 13. Alfiya, R., Sabu, S. T., Dharan, S. S. (2020). A Detailed Study of Methotrexate Treatment in Ectopic Pregnancy. *Int J Res Hosp Clin Pharm*, 2:85-92.
 14. Chande, N., Wang, Y., MacDonald, J. K., McDonald, J. W. (2014). Methotrexate for Induction of Remission in Ulcerative Colitis. *Cochrane Database of Systematic Reviews*, 8.
 15. Kremer, J. M., Petrillo, G. F., Hamilton, R. A. (1995). Pharmacokinetics and Renal Function in Patients with Rheumatoid Arthritis Receiving a Standard Dose of Oral Weekly Methotrexate: Association with Significant Decreases in Creatinine Clearance and Renal Clearance of The Drug After 6 Months of Therapy. *The Journal of Rheumatology*, 22(1):38-40.
 16. Su, Q., Feng, H., Tian, T., Liao, X., Li, Y., et al. (2022). The Efficacy of Mifepristone Combined with Methotrexate for The Treatment of Ectopic Pregnancy: A Systematic Review and Meta-Analysis. *Annals of Medicine*, 54(1):3268-3284.
 17. Perdu, M., Camus, E., Rozenberg, P., Goffinet, F., Chastang, C., et al. (1998). Treating Ectopic Pregnancy with The Combination of Mifepristone and Methotrexate: A Phase II Nonrandomized Study. *Ameri Jour of Obstetrics and Gynecology*, 179(3):640-643.
 18. Ghezzi, F., Laganà, D., Franchi, M., Fugazzola, C., Bolis, P. (2002). Conservative Treatment by Chemotherapy and Uterine Arteries Embolization of a Cesarean Scar Pregnancy. *Europ Journal of Obstetrics & Gynecology and Reproductive Biology*, 103(1):88-91.
 19. Sabiri R., Said H., El-Hachami FZ., Zein M., Assal A., et al. (2024). Pregnancy On Caesarean Scar: Conservative Treatment: In A Case and Literature Review, *Interna Jour of Clini and Surgi Pathol*. 1(2):1-5.
 20. Stabile, G., Vona, L., Carlucci, S., Zullo, F., Laganà, A. S., et al. (2024). Conservative Treatment of Cesarean Scar Pregnancy with The Combination of Methotrexate and Mifepristone: A Systematic Review. *Women's Health*, 20:17455057241290424.
 21. Salvi, P., Gaikwad, V., Bhadoriya, A., Ponde, S. (2024). Medical Management of Cesarean Scar Ectopic Pregnancy: A Unique Approach. 16(3).
 22. No, G. T. G. (2016). Diagnosis and Management of Ectopic Pregnancy.
 23. Agten, A. K., Jurkovic, D., Timor-Tritsch, I., Jones, N., Johnson, S., et al. (2024). First-Trimester Cesarean Scar Pregnancy: A Comparative Analysis of Treatment Options from The International Registry. *American Journal of Obstetrics and Gynecology*, 230(6):669-e1.

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