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CASE REPORT

Ectopic pregnancy treated with Methotrexate, case report

Embarazo ectópico tratado con Metotrexato, reporte de un caso

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ABSTRACT

Introduction: ectopic pregnancy is defined as the implantation of a fertilized egg outside the uterus, representing a potentially life-threatening condition. The most common location is the fallopian tube, although other sites such as the cervix or cesarean scars are also possible. Despite diagnostic and therapeutic advances, disparities in access to care persist. The condition has significant physical, emotional, and reproductive consequences. Diagnosis has improved with transvaginal ultrasound and β-hCG measurement, and treatment has evolved from open surgery to medical options like methotrexate.

Case report: a 29-year-old woman presented with pelvic pain, metrorrhagia, and mild hemodynamic instability. Transvaginal ultrasound and β-hCG levels confirmed a tubal ectopic pregnancy. Intramuscular methotrexate was administered, followed by clinical and hormonal monitoring. The patient showed favorable progression, with decreasing β-hCG levels and complete resolution without complications. She received reproductive counseling and emotional support.

Conclusions: methotrexate proved effective in an uncomplicated ectopic pregnancy. Proper patient selection, strict follow-up, and a comprehensive approach that includes emotional care are key to successful management. Evidence supports this conservative medical treatment as a safe and effective alternative.

Keywords: Ectopic Pregnancy; Methotrexate; Treatment.

RESUMEN

Introducción: el embarazo ectópico se define como la implantación del óvulo fecundado fuera del útero, siendo una condición potencialmente mortal. La localización más común es la trompa de Falopio, aunque también puede ocurrir en otras zonas como el cuello uterino o cicatrices de cesárea. A pesar de los avances diagnósticos y terapéuticos, persisten desigualdades en el acceso a la atención. El impacto emocional y psicológico es significativo, y las consecuencias reproductivas dependen del tratamiento y del estado de las trompas. El diagnóstico ha mejorado gracias a la ecografía transvaginal y la medición de β-hCG, y el tratamiento ha evolucionado desde la cirugía abierta hacia opciones médicas como el metotrexato.

Presentación del caso: paciente femenina de 29 años de edad que fue atendida por presentar dolor pélvico, metrorragia y signos de inestabilidad leve. La ecografía transvaginal y los niveles de β-hCG confirmaron un embarazo ectópico tubárico. Se administró metotrexato intramuscular y se realizó seguimiento clínico y hormonal. La paciente evolucionó favorablemente, con disminución progresiva de β-hCG y resolución completa sin complicaciones. Se ofreció orientación reproductiva y apoyo emocional.

Conclusiones: el tratamiento con metotrexato resultó eficaz en un embarazo ectópico no complicado. La selección adecuada de pacientes, el seguimiento estricto y el abordaje integral que incluya la salud emocional son claves para un manejo exitoso. La evidencia respalda este enfoque como una alternativa segura y conservadora.

Palabras clave: Embarazo Ectópico; Metotrexato; Tratamiento.

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INTRODUCTION

Ectopic pregnancy is defined as the implantation of a fertilized egg outside the uterine endometrial cavity and represents a potentially life-threatening obstetric condition that affects approximately 1–2 % of all pregnancies in Europe and North America. This condition constitutes a time-sensitive medical emergency that can result in tubal rupture and potentially fatal hemorrhage, accounting for 2,7 % of pregnancy-related deaths in the United States.[1]

In the context of Cuba, ectopic pregnancy is a priority challenge for the Maternal and Child Care Program (PAMI). Although the country has universal health coverage and a robust primary care system that facilitates early detection, this condition remains among the leading causes of maternal morbidity and death from hemorrhage during the first trimester. Between 2000 and 2021, at least one death from this cause was reported each year, resulting in a total of 98 maternal deaths. In the period from 2012 to 2018, this pathology ranked fourth among the causes of maternal death, with more than 3 500 surgeries performed annually for this condition, reaching a total of 4 706 cases in 2013. According to epidemiological data, the most affected provinces were Havana, Santiago de Cuba, Camagüey, and Villa Clara (in that order).[2]

The most common location for ectopic pregnancy is the distal portion of the fallopian tube, where 93 - 97 % of all cases occur. Other less common locations include the interstitial portion of the tube, previous cesarean scar, cervix, ovary, and abdominal cavity. In recent years, the prevalence of uterine ectopic pregnancies has increased, particularly among those implanted in cesarean scars, which has led to the development of new terminology and classification for these variants.[3]

The impact on women's physical health is considerable, as the risk of hemorrhage in patients with untreated ectopic pregnancies can reach 50 % or more. Historically, until the 1970s, 15 % of patients with ectopic pregnancy presented with hypovolemic shock. Although mortality has decreased dramatically to 0,15 deaths per 1 000 ectopic pregnancies because of diagnostic and therapeutic improvements, significant racial disparities persist: African American women are nearly seven times more likely to die from this condition than white women are in the United States, highlighting inequities in access to early pregnancy care.[1]

The emotional and psychological impact of ectopic pregnancy has recently been recognized as a critical component of comprehensive care. Contemporary studies show that this experience has substantial psychological consequences that require specific clinical attention, including manifestations of anxiety, depression, and uncertainty. Posttreatment management should include attention to family planning and the patient's mental health.[1,3]

Reproductive consequences vary depending on the treatment received and the condition of the fallopian tubes. Patients with a previous ectopic pregnancy have an 8 - 15 % risk of another ectopic pregnancy. Conditions that result in inflammation and tubal scarring, such as pelvic inflammatory disease, previous tubal surgery, and previous ectopic pregnancy itself, significantly increase the risk of recurrence. Subfertile women are at increased risk because impaired tubal integrity or function contributes to both conditions. Approximately half of patients with ectopic pregnancy have no identifiable risk factors.[4]

The historical evolution of the diagnosis and treatment of ectopic pregnancy has been remarkable. Until the 1970s, treatment consisted mainly of open laparotomy and salpingectomy, with alarming rates of presentation in hypovolemic shock. The incidence of ectopic pregnancy increased sixfold between 1970 and 1992 but has remained stable since then. The most significant change has been the ability to diagnose the condition before tubal rupture, which has dramatically reduced associated mortality.[4,5]

The development of modern diagnostic techniques has revolutionized management. The introduction of the widespread use of serial levels of human chorionic gonadotropin beta subunit (β-hCG) and advances in ultrasound technology have enabled earlier and more accurate diagnoses. Transvaginal ultrasonography has become the primary diagnostic method, allowing visualization of the absence of intrauterine pregnancy and the presence of an adnexal mass. The concept of the "discriminatory level" of β-hCG, the value above which an intrauterine pregnancy should be visualized by transvaginal ultrasound (1 500 mIU/mL), is fundamental to the diagnostic algorithm.[5]

Therapeutic options have evolved significantly. Whereas in the past, the treatment was exclusively laparotomy, there are now three main modalities: surgical management (laparoscopic salpingectomy or salpingostomy), medical management with intramuscular methotrexate, and, in selected cases, expectant management. Laparoscopic surgery is now recognized as the best and safest surgical treatment for extrauterine ectopic pregnancies. The development of medical treatment with methotrexate has provided a nonsurgical alternative for small, unruptured ectopic pregnancies in hemodynamically stable patients.[3]

The discovery of methotrexate in the 1940s marked a milestone in the treatment of ectopic pregnancy. Originally used as a chemotherapeutic agent in cancer treatment, this drug was found to have unique properties that could induce resorption of trophoblastic tissue in selected cases of ectopic pregnancy. This medical approach has revolutionized the way these cases are managed, allowing women to avoid invasive surgical interventions and preserve their future fertility.[1]

This article aims to describe a case of ectopic pregnancy treated with methotrexate, analyzing not only the clinical and therapeutic aspects but also the emotional and social implications faced by women diagnosed with this condition.

CASE REPORT

A 29-year-old female patient who was Caucasian and nulliparous and had no previous pregnancy and a history of pelvic inflammatory disease two months prior to admission, presented to the emergency department with a five-day history of persistent pelvic pain (rated 7 - 8/10 on the visual analog scale [VAS]), ranging from moderate to severe, and was located in the right iliac fossa and radiating to the lumbar region and ipsilateral thigh. The pain was sharp, intermittent, and intensified with movement and deep palpation. The symptoms were accompanied by light metrorrhagia, for which the patient did not soak a dark brown daily pad, which the patient described as "different from her usual menstruation" in terms of both quantity and duration.

She also reported morning sickness, abdominal distension, and generalized fatigue, which she initially attributed to work-related

stress. In the past two days, she began to experience episodes of dizziness when standing up, cold sweats, and palpitations, which prompted her to seek medical attention. She denied fever, vomiting, or diarrhea. She had no history of chronic diseases or previous surgeries, although she mentioned having had a pelvic infection treated approximately one year ago.

Physical examination revealed a patient with pained expression, pale skin, signs of mild hypotension (BP 90/60 mmHg), and tachycardia (HR 108 bpm). The abdomen was soft but tender to deep palpation in the hypogastrium and right iliac fossa, with no signs of peritoneal irritation. Vaginal examination revealed a normal-sized uterus, with pain associated with cervical mobilization and a right adnexal mass that was firm and painful to palpate.

A urine pregnancy test was positive. Serum β-hCG quantification was requested, with a concentration of 2 800 mIU/mL. Transvaginal ultrasound revealed no intrauterine gestational sac and the presence of a 3 cm heterogeneous image in the right adnexal region, which is consistent with tubal ectopic pregnancy. No signs of hemoperitoneum were observed at that time. No free fluid was observed in the Douglas pouch.

Given the patient's hemodynamic stability, the absence of active bleeding, the size of the mass (3 cm), the absence of a fetal heartbeat, the confirmation that the pregnancy had not ruptured because of the absence of free fluid in the Douglas pouch, and the quantification of serum β-hCG concentration at 2 800 mIU/mL, medical treatment with a single dose of 50 mg/m² was initiated under a follow-up protocol with serial β-hCG checks and close clinical monitoring. The patient weighed 68.5 kg and was 164 cm tall. According to Mosteller's formula, her body surface area is 1.76 m²; thus, she was administered 90 mg of methotrexate.

During the days following the administration of methotrexate, the patient was monitored on an outpatient basis under a strict follow-up protocol. She was instructed to rest, avoid sexual intercourse and sun exposure, and refrain from taking nonsteroidal anti-inflammatory drugs. The importance of seeking immediate medical attention at any sign of alarm was explained to her in detail.

On the third day after treatment, the patient returned for her first follow-up appointment. She reported a slight improvement in pelvic pain (4/10 according to the VAS), although she still felt heaviness in her lower abdomen. She also mentioned an isolated episode of heavier vaginal bleeding, which she described as "similar to heavy menstruation," quantified as 3 to 4 sanitary pads filled in 24 hours, accompanied by moderate cramping. She had no fever or signs of infection. On physical examination, she was hemodynamically stable, with vital signs within normal parameters and no signs of peritoneal irritation. The β-hCG level slightly increased from the initial value (3 100 mIU/mL), which was considered within the expected range at this stage of the protocol. A new check was scheduled for the seventh day.

At the next visit on the seventh day, the patient reported a progressive decrease in pain (2/10 according to the VAS) and bleeding to less than one pad per day. She felt more energetic, although still fatigued. The β-hCG concentration significantly decreased (2 400 mIU/mL), indicating a favorable response to treatment. The need to continue weekly check-ups until the hormone test was completely negative was reinforced.

During the following weeks, the β-hCG concentration continued to decline steadily (1 500 mIU/mL on day 14 and 800 mIU/mL on day 21). The patient had no complications, and her general condition improved noticeably. Finally, after four weeks of follow-up, hormone levels became negative (β-hCG concentration <5 mIU/mL), confirming the complete resolution of the ectopic pregnancy.

The patient was referred to a gynecologist for evaluation of her reproductive health and family planning. Emotional aspects of the process were addressed, and psychological support was offered. The patient expressed gratitude for the support she received and expressed her desire to receive guidance for a safe future pregnancy.

DISCUSSION

The clinical case presented is an exemplary illustration of the application of medical treatment with methotrexate in an uncomplicated tubal ectopic pregnancy, on the basis of clinical, biochemical, and ultrasound criteria well established in the current scientific literature. Notably, the presence of pelvic inflammatory disease two months earlier was a risk factor for ectopic pregnancy.

Ectopic pregnancy is among the leading causes of maternal morbidity during the first trimester, and early diagnosis is crucial for avoiding serious complications such as tubal rupture and massive hemoperitoneum. In this context, the combination of serum β-hCG levels and transvaginal ultrasound has proven to be the most effective diagnostic strategy, allowing early identification even before the onset of severe clinical signs.[6]

The use of methotrexate as a conservative medical treatment has been widely validated in the literature. According to the Stovall protocol, a single intramuscular dose of 50 mg/m² is effective in most appropriately selected cases, with success rates ranging from 80 % to 95 %.[7]

Eligibility criteria for medical treatment included hemodynamic stability, the absence of severe or persistent abdominal pain, a commitment to follow-up until complete resolution, and normal liver and kidney function. Patients with β-hCG concentrations less than 5 000 mIU/mL (the patient had 2 800 mIU/mL), the absence of embryonic cardiac activity, and an ectopic pregnancy size less than 4 cm (the patient had 3 cm) are ideal candidates for methotrexate as alternatives to surgical treatment. Efficacy is inversely proportional to baseline β-hCG levels: when levels are less than 1 000 mIU/mL, the median time to resolution is 20 days but can sometimes extend to 34,5 days when levels exceed 2 000 mIU/mL.[8]

The slight increase in β-hCG observed on the third day after treatment (3 100 mIU/mL in the patient) is an expected phenomenon and should not be interpreted as therapeutic failure. Studies have shown that the peak β-hCG concentration can remain stable or even increase slightly before beginning to decline, with the value on day 7 being the most predictive of therapeutic success (in the patient, it was 2 400 mIU/mL on day 7). In this case, the progressive decrease in hormone levels and clinical improvement corroborate a favorable response to treatment.[1]

From a clinical point of view, the onset of mild abdominal pain and vaginal bleeding after methotrexate administration is also

considered a physiological response to the process of trophoblastic tissue resorption. The literature reports that up to one-third of patients may experience these symptoms without complications.[9]

Methotrexate does not adversely affect ovarian reserve or subsequent fertility, which is particularly relevant for women who wish to preserve their reproductive capacity. In a recent study of nontubal ectopic pregnancies treated with combined methotrexate (intragestational and systemic), 78 % (7/9) of patients who subsequently attempted to conceive achieved pregnancy within the study period.[10]

Resolution time is an important consideration. The median time to complete the resolution of pregnancy (β-hCG concentration <5 mIU/mL) was 22 days in successful cases, although it ranged from 2 - 3 weeks to 6 - 8 weeks when pretreatment β-hCG levels were in the highest range. Approximately 20 % of patients should be informed that they may require a second dose of methotrexate, and 24 % may eventually need surgery.[7,10] In this patient, resolution took 4 weeks, and a second dose of methotrexate was not necessary.

The adverse effects of methotrexate are generally mild and self-limiting, including nausea, vomiting, diarrhea, gastritis, stomatitis, and conjunctivitis, reported in 23 - 31 % of patients depending on the protocol used. Serious adverse events, such as severe neutropenia and alopecia, are rare with short-term use. Patients should discontinue prenatal supplementation with vitamins containing folic acid and any additional folic acid supplements, as this decreases the effectiveness of methotrexate.[1]

Close clinical and hormonal monitoring is a fundamental pillar of medical management. Adherence to the protocol of serial β-hCG checks until negative is essential to confirm complete resolution and avoid recurrence or late complications. In this case, the patient strictly complied with the instructions, which undoubtedly contributed to the successful outcome.[11]

Finally, the comprehensive approach, which included referrals to gynecology for fertility evaluation and the offer of psychological support, reflects a holistic view of reproductive health care. The emotional experience of an ectopic pregnancy can be deeply impactful, and adequate support is as important as medical treatment itself.[11]

CONCLUSIONS

The therapeutic success achieved in this clinical case, with complete resolution within five weeks, confirms that a single dose of methotrexate is a highly effective alternative for the management of tubal ectopic pregnancy in patients with β-hCG levels above the discriminatory threshold but below 5 000 mIU/mL (specifically 2 800 mIU/mL in this patient). The clinical evolution documented using the visual analog scale and the quantification of bleeding made it possible to distinguish pain due to physiological separation from therapeutic failure, validating the strict outpatient follow-up protocol. In the Cuban public health setting, the application of this conservative medical approach not only preserves women's reproductive capacity by avoiding salpingectomy but also optimizes the use of hospital resources through serial biochemical and ultrasound monitoring. The integration of posttreatment psychological support and family planning counseling is crucial for mitigating the emotional impact of pregnancy loss and ensuring a favorable reproductive prognosis.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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AUTHOR CONTRIBUTIONS

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REFERENCES

1. Schreiber CA, Sonalkar S. Tubal Ectopic Pregnancy. New England Journal of Medicine. 19 de febrero de 2025;392(8):798-805. doi:10.1056/NEJMcp2402787

2. Carlos Moya Toneut, Javier Cruz Rodríguez, Miguel Román Sarduy Nápoles, Nubia Blanco Barbeito, Robinson Borges Fernández, Anabela del Rosario Criollo Criollo. Reflexiones acerca de las políticas para la atención del embarazo ectópico. Revista Eugenio Espejo. 15 de abril de 2024;18(2):94-103. doi:https://doi.org/1 0.371 35/ee.04.20.08

3. Farren J, Al Wattar BH, Jurkovic D. The diagnosis and management of extrauterine and uterine ectopic pregnancy. Hum Reprod Update. 8 de octubre de 2025;dmaf024. doi:10.1093/humupd/dmaf024 PubMed PMID: 41061761.

4. Barnhart KT. Ectopic Pregnancy. New England Journal of Medicine. 23 de julio de 2009;361(4):379-87. doi:10.1056/NEJMcp0810384

5. Barash JH, Buchanan EM, Hillson C. Diagnosis and management of ectopic pregnancy. Am Fam Physician. 1 de julio de 2014;90(1):34-40. PubMed PMID: 25077500.

6. Brook OR, Dadour JR, Robbins JB, Wasnik AP, Akin EA, Borloz MP, et al. ACR Appropriateness Criteria® Acute Pelvic Pain in the Reproductive Age Group: 2023 Update. Journal of the American College of Radiology. 1 de junio de 2024;21(6):S3-20. doi:10.1016/j.jacr.2024.02.014 PubMed PMID: 38823952.

7. Davenport MJ, Lindquist A, Brownfoot F, Pritchard N, Tong S, Hastie R. Time to resolution of tubal ectopic pregnancy following methotrexate treatment: A retrospective cohort study. PLoS One. 2022;17(5):e0268741. doi:10.1371/journal.pone.0268741 PubMed PMID: 35609041; PubMed Central PMCID: PMC9129037.

8. Zhang J, Zhang Y, Gan L, Liu XY, Du SP. Predictors and clinical features of methotrexate (MTX) therapy for ectopic pregnancy. BMC Pregnancy Childbirth. 29 de octubre de 2020;20(1):654. doi:10.1186/s12884-020-03350-8 PubMed PMID: 33121473; PubMed Central PMCID: PMC7597060.

9. Wu J, Ludlow JP, De Vries B, Black K, Beale P. Single-dose methotrexate treatment for ectopic pregnancy and pregnancy of unknown location and progesterone as a predictor of success. Aust N Z J Obstet Gynaecol. octubre de 2014;54(5):469-74. doi:10.1111/ajo.12247 PubMed PMID: 25287564.

10. Strug M, Deng J, Monseur B, Alvero R, Aghajanova L. Implementation of a Program for Combined Intra-Gestational and Systemic Methotrexate Injection to Treat Non-Tubal Ectopic Pregnancy: A Report of Outcomes and Feasibility. Reprod Sci. 1 de agosto de 2025;32(8):2685-91. doi:10.1007/s43032-025-01920-9

11. Farren J, Al Wattar BH, Jurkovic D. The diagnosis and management of extrauterine and uterine ectopic pregnancy. Hum Reprod Update. 8 de octubre de 2025;dmaf024. doi:10.1093/humupd/dmaf024