Metastatic Gestational Choriocarcinoma Mimicking an Incomplete Abortion: a Diagnostic Challenge Resolved with the EMA-CO Regimen

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Coriocarcinoma Gestacional Metastático Simulando um Aborto Incompleto: um Desafio Diagnóstico Resolvido com o Esquema EMA-CO

Coriocarcinoma Gestacional Metastásico Simulando un Aborto Incompleto: un Reto Diagnóstico Resuelto con Esquema EMA-CO

Ruperto Esteban Guerrero-Quiroz[1]; Carlos Zehir Cárdenas Ramírez[2]; Lorena Garcia Agudelo[3]; Sandra Y. Leguizamón-Martínez[4]

ABSTRACT

Introduction: Choriocarcinoma is a rare disease of trophoblastic origin that is usually aggressive. Its monitoring and prognosis are based on constant measurements of human chorionic gonadotropin beta subunit, and early treatment has a significant influence on prognosis and survival. **Case report:** A 23-year-old female was admitted for vaginal bleeding. A transvaginal ultrasound was performed, which revealed endometrial thickening and significantly elevated beta-hCG. She was subsequently admitted with fever and suspected post-curettage endometritis, for which antibiotic treatment was initiated. However, given the persistence of signs suggestive of trophoblastic disease, a pelvic MRI was requested, which revealed a large expansive lesion. **Conclusion:** Choriocarcinoma is a highly malignant disease that requires timely and aggressive diagnosis and treatment. The treatment consisted in surgical excision of the tumour and chemotherapy.

Key words: Uterine Hemorrhage; Choriocarcinoma; Chorionic Gonadotropin; Uterine Neoplasms.

RESUMO

Introdução: O coriocarcinoma é uma doença de origem trofoblástica que se apresenta de forma pouco frequente, sendo geralmente uma patologia agressiva. Seu acompanhamento e prognóstico baseiam-se em medições constantes da subunidade beta da gonadotrofina coriônica humana, e seu tratamento precoce influencia significativamente o prognóstico e a sobrevida. **Relato do caso:** Mulher de 23 anos, internada por sangramento vaginal. Foi realizada uma ecografia transvaginal, que evidenciou um espessamento endometrial e um bHCG significativamente elevado. Posteriormente, ela foi internada com síndrome febril e suspeita de endometrite pós-curetagem, pelo que foi iniciado o tratamento com antibióticos. No entanto, diante da persistência de sinais sugestivos de doença trofoblástica, foi solicitada uma ressonância magnética da pelve, que evidenciou uma lesão expansiva de grande tamanho. **Conclusão:** O coriocarcinoma é uma doença altamente maligna que requer diagnóstico e tratamento oportunos e agressivos. O tratamento incluiu a extirpação cirúrgica do tumor e quimioterapia.

Palavras-chave: Hemorragia Uterina; Coriocarcinoma; Gonadotrofina Coriônica; Neoplasias Uterinas.

RESUMEN

Introducción: El coriocarcinoma es una enfermedad de origen trofoblástico que se presenta de forma poco frecuente, suele ser una patología agresiva. Su seguimiento y pronóstico se basan en mediciones constantes de la gonadotropina coriónica humana subunidad beta, y su pronto tratamiento influye de manera significativa en el pronóstico y la sobrevida. **Informe del caso:** Femenina de 23 años, ingresó por sangrado vaginal. Se realizó una ecografía transvaginal, la cual evidenció un engrosamiento endometrial y una bHCG significativamente elevada. Posteriormente, ingresó con síndrome febril y sospecha de endometritis post legrado, por lo que se inició manejo antibiótico. No obstante, ante la persistencia de signos sugestivos de enfermedad trofoblástica, se solicitó una resonancia magnética de pelvis, la cual evidenció una lesión expansiva de gran tamaño. **Conclusión**: El coriocarcinoma es una enfermedad altamente maligna que requiere un diagnóstico y tratamiento oportunos y agresivos. El tratamiento incluyó la extirpación quirúrgica del tumor y la quimioterapia.

Palabras clave: Hemorragia Uterina; Coriocarcinoma; Gonadotropina Coriónica; Neoplasias Uterinas.

[1,2]Hospital Regional de la Orinoquía, Departamento de Investigación. Yopal, Colombia. E-mails: rupertoguerrero601@gmail.com; czcardenas05@gmail.com. Orcid iD: https://orcid.org/0009-0002-0420-6308; Orcid iD: https://orcid.org/0009-0004-0504-5934
[3]Hospital Regional de la Orinoquía. Yopal, Colombia. E-mail: dr.lorenagarcia29@gmail.com. Orcid iD: https://orcid.org/0000-0001-9557-0900
[4]Hospital Regional de la Orinoquía, Departamento de Ginecología y Obstetricia. Yopal, Colombia. E-mails: drasandraleguizamon3@gmail.com. Orcid iD: https://orcid.org/0000-0001-6607-6225
Corresponding author: Ruperto Esteban Guerrero Quiroz. Calle 15, 07-95. Yopal, Colombia. E-mail: rupertoguerrero601@gmail.com

INTRODUCTION

Gestational trophoblastic disease encompasses a heterogeneous group of lesions caused by the abnormal trophoblastic proliferation where the choriocarcinoma represents the most aggressive histological variant and with high malignancy potential[1]. It is a low incident neoplasm in the West, with estimated occurrence of one case in 40,000 pregnancies; its frequency rises significantly post molar gestations and pre-delivery or full-term delivery obstetric events[2].

Clinically, it presents a highly invasive biological behavior, primarily manifesting as abnormal uterine hemorrhage. However, due to its early hematogenous spread, the initial manifestations can arise from metastatic remote compromise of lungs, central nervous system, gastrointestinal tract or placenta, sometimes provoking critical complications such as massive fetomaternal hemorrhage or acute abdomen[3,4].

The basic diagnostic consists in the correlation between clinical suspicion, high resolution imaging and serial serum quantification of the subunit beta-human chorionic gonadotropin (beta-hCG), that acts as a serum marker of choice to monitor the tumor load and the therapeutic response[5]. In despite of its chemosensitivity nature, the metastatic choriocarcinoma is frequently classified as a high-risk disease according to the criteria of the International Federation of Gynecology and Obstetrics (FIGO), requiring intensive polychemotherapy regimens such as the protocol EMA-CO[2,5,6].

Although this regimen attains high rates of cure, the development of chemoresistance and coexistence with other epithelial somatic malignancies of the uterine corpus entail complex therapeutic scenarios[7,8]. In light of the failure of conventional treatments, target therapies and immune therapy based on immune checkpoints inhibitors currently appear as strong salvage alternatives for refractory trophoblastic tumors[6,9,10].

The objective is to report a case of a young patient diagnosed with choriocarcinoma, detailing the diagnostic approach, the clinical response and biochemical remission reached with the chemotherapy protocol EMA-CO and bring updated evidences about the successful management of this pathology.

CASE REPORT

23-year-old female patient with the following history: four pregnancies, three vaginal deliveries, had no C-sections, three living children and one abortion. Sought medical care due to moderate vaginal bleeding for one month exacerbated five hours prior to admission, becoming abundant, followed by diaphoresis, lipothymia and adynamia. At initial physical examination, reported moderate abdominal pain in deep palpation without signs of irritation and expected cervix for a multiparous patient with moderate vaginal bleeding with clots.

A transvaginal ultrasound revealed a 25mm endometrial thickening as single abnormal finding raising the suspicion of an incomplete abortion, the beta-hCG was positive. Later, a complementary study was performed showing quantitative beta-hCG above 200,000 mUI/ml, reason for which the additional possibility of trophoblastic disease as differential diagnosis was considered. The patient was submitted to dilation, curettage and extraction of hematic remains; a sample was shipped to pathology and she was discharged without complications.

Four days later, she was readmitted due to three days of fever (40ºC), asthenia, adynamia, occasional coughing, left otalgia and diaphoresis. Pain persisted in the right iliac fossa without signs of peritoneal irritation. The control transvaginal ultrasound was unaltered, the acute phase reactants were elevated and a CBC has shown anemia. A possible endometritis post-curettage was considered, and antibiotic management was initiated.

Along the evolution, the control beta-hCG was declining, in the third day after readmission, the follow up CBC revealed anemia with transfusion criteria which was performed without complications. Due to the persistence of the pain, a MRI of the pelvis showed a large expansive lesion (Figure 1).

The pathological report indicated the presence of a trophoblastic neoplasia consisting in trophoblast with a dual population, marked atypia that includes the differential diagnosis of choriocarcinoma (Figure 2).

The patient was readmitted for oncologic management, staging TNM and FIGO T3NxMx FIGO II > 7, being initiated protocol EMA-CO in the following schedule: Week 1: Phase EMA (days 1 and 2). Day 1: Etoposide, Methotrexate and Actinomycin D. Day 2: Actinomycin D, Etoposide and Folinic Acid. Follow-up with proper hematologic control.

The medication schema for the second week was: Day 8: Vincristine and cyclophosphamide. Later, hematologic control from day 9 to day 14 with normal reports and declining curve of beta-hCG, based on which the cycle was reinitiated. The patient received four cycles of EMACO reaching a beta-hCG <5 m UI/mL for three consecutive weeks. Currently, after a 12-month follow up, the patient continues asymptomatic and in clinical-biochemical control with no evidence of relapse.

The Ethics Committee of "*Hospital Regional de la Orinoquía*", according to the Notes of Meeting number 010 of 2026, approved the study, in compliance with the

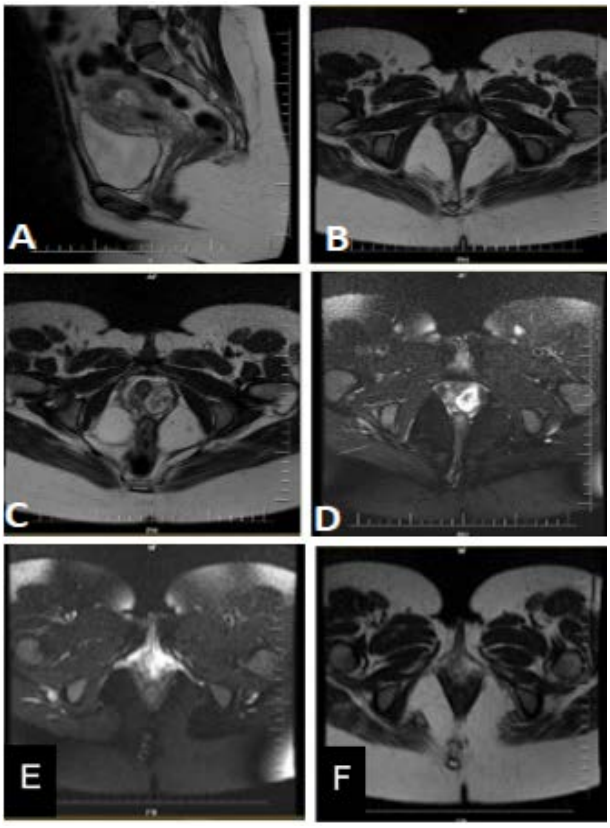

Figure 1. Magnetic resonance of the pelvis with contrast. **A.** Sagittal section in T2 showing enlarged uterus. **B** and **C.** Axial sections in T2 and T1 with contrast, respectively, showing left heterogeneous expansive corpus lesion (49 x 61 x 52 mm), compromising the full myometrial thickness, transposition of the serosa and extension to the ipsilateral parametrium; presents intense heterogeneous enhancement compatible with solid hypervascular mass. **D.** Axial sequence showing congestion and enhancement of the left gonadal vein, suggestive of vascular invasion. **E** and **F.** Axial sections identifying a metastatic/satellite lesion on the side wall of the lower third of the vagina (32 x 25 x 32 mm), heterogeneous in T2 and isointense in T1, intense peripheral enhancement and hypocaptant center that protrudes toward the introitus and compromises the vaginal canal

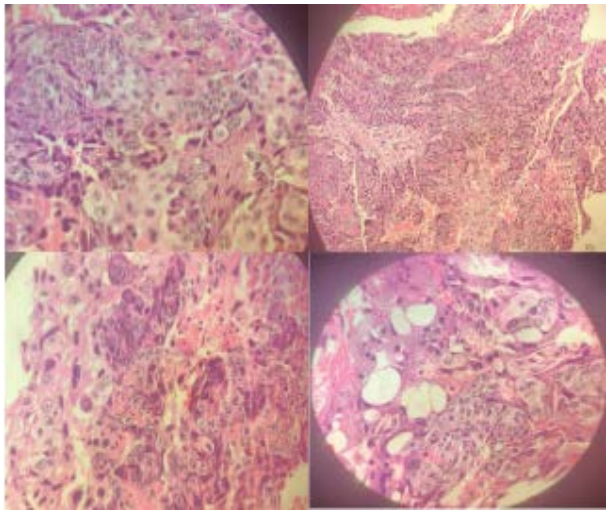

Figure 2. Histopathology. The sections show atypical trophoblast with multiple mitoses, hyperchromatic pleomorphic nuclei, enlarged size and trophoblastic neoplasia consisting of trophoblast with a dual population with marked atypia. The differential diagnosis includes choriocarcinoma

Declaration of Helsinki 2024[11] and the current legislation for research with human subjects[12]. The informed consent form was signed by the patient encompassing the review of her clinical history and publication of data and images, ensuring the confidentiality and anonymity of her identity.

DISCUSSION

Choriocarcinoma is a gestational trophoblastic neoplasia characterized by fast myometrial invasion and early hematogenous spread[1-5]. In the present case, the 23-year-old patient underwent a severe abnormal uterine bleeding that initially led to a diagnosis of incomplete abortion, a frequent phenomenon in clinical practice because the initial symptoms mimic regular gestational discharges. According to Moreno-Gomez B, et al.[1] the primary clinical presentation is generally characterized by abundant vaginal bleeding; nevertheless, the presence of expansive myometrial masses with local invasion can change drastically the pelvic anatomy, requiring a high level of suspicion. Sorrentino F, et al.[2] and Stabile G, et al.[3] concur and emphasize that the choriocarcinoma can develop after any prior obstetric event, including the patient's history of abortion and full-term deliveries, occasionally associated with systemic acute hemorrhagic or fetomaternal complications with dismal prognosis if timely intervention does not occur.

The delayed initial diagnosis due to suspicion of endometritis post-curettage emphasized the complexity of this pathology. Although the transvaginal ultrasound had initially revealed only endometrial thickening of 25 mm, the persistence of the pain and aggravation of the symptoms led to the decision of performing a magnetic resonance imaging (MRI) of the pelvis. The MRI was the tool of choice to determine the limits of the left body mass with parametrial extension and metastatic lesion in the lower third of the vagina. This pattern of local and remote spread characterizes the tumor aggressiveness; in fact, Cheng X, et al.[4] reported that metastatic choriocarcinoma can simulate confounding clinical conditions in unusual anatomic sites due to its angiogenic avidity, which requires studies of multimodal imaging extension in face of critically elevated beta-hCG. The monitoring of the serum beta-hCG was critical for the follow-up and confirmation of the response to the treatment, whose initial result exceeded 200,000 mUI/mL. The kinetics of this biomarker determines the success of the therapeutic protocol.

In that regard, Sirimusika N, et al.[5] indicated that the relations and declining curves of serum beta-hCG have not only confirmed the remission, but also that they are indispensable for the timely detection of the resistance to

the protocol EMA-CO in patients with high-risk disease. The patient presented an excellent biological response, achieving negative hormone test result beta-hCG< 5 mUI/mL at the end of the fourth cycle of polychemotherapy.

The management with the schema EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine) applied to this high-risk patient (stage FIGO II) reflects the findings of the international literature. Although the regimen EMA-CO achieves cure rates above 85%, a portion of the patients develop chemoresistance or present complex histological varieties. As reported by Bai L, et al.[7] and Mangla M, et al.[8], there are rare scenarios where the choriocarcinoma coexists with endometrioid adenocarcinoma or presents trophoblastic differentiation in malignant neoplasms of the uterine corpus, which changes radically the response to conventional chemotherapy and reduces global survival.

For the patients who experience therapeutic failures or toxicities to the first-line medications, medical science has evolved to target-therapy. Burkett WC, et al.[9], and the recent reviews of Barcellos MB, et al.[6] and Zeng J, et al.[10] have highlighted that immune checkpoint inhibitors show a promising role to reactivate antitumor immunity in refractory gestational trophoblastic tumors. The disease-free survival after 12-month outpatient follow-up, completely asymptomatic and biochemically stable, validated the high efficacy, safety and effectiveness of the classic protocol EMA-CO when applied within a context of strict hematologic monitoring and correct diagnostic staging.

The clinical documentation, diagnostic precision through neuroimaging and continuous 12-month follow up that confirmed the sustained remission of the patient, are the strong aspects of the present investigation, serving as a referential of the therapeutic success with polychemotherapy. The study limitations, however, are inherent to the study design such as the impossibility of generalizing the conclusions to larger populations.

CONCLUSION

Choriocarcinoma is an extremely aggressive neoplasm, but curable if timely diagnosed. This case shows the effectiveness of the protocol EMA-CO in a high-risk young patient with vaginal metastasis, achieving full clinical and chemical remission in the fourth cycle. The magnetic resonance imaging was essential for correct staging, in addition to maintaining high diagnostic suspicion in face of refractory abnormal hemorrhages, avoiding therapeutic delays that compromise the prognosis of the patient.

CONTRIBUTIONS

All the authors contributed substantially to the study concept and design, acquisition, analysis and interpretation of the data, writing and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the content underlying the text is contained in the manuscript.

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