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Case Report

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Postpartum metastatic choriocarcinoma. Keys for diagnosis and early treatment

Abstract

Choriocarcinoma is a rare pathology but potentially fatal if left untreated. It is included within gestational trophoblastic neoplasms, a group of highly invasive, metastatic and highly vascularized malignant tumors. Its presentation after a full-term pregnancy carries a worse prognosis than after an abortion or a hydatidiform mole because it reflects a delay in diagnosis and treatment.

Clinical case: Patient who went to the emergency service, referring pleuritic pain and fever of 6 days of evolution after a normal delivery a month ago. Clinical manifestations, Doppler ultrasound, β-hCG levels, and imaging tests were sufficient to diagnose postpartum choriocarcinoma. Early treatment with polychemotherapeutic agents allowed a favorable evolution of the patient.

Conclusion: This type of pathology represents a difficult diagnostic challenge. Early diagnosis is essential in order to avoid delays in potentially curative treatment.

Keywords: gestational trophoblastic disease, human chorionic gonadotropin, choriocarcinoma, pregnancy, metastasis

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Introduction

Gestational trophoblastic disease is defined as a rare complication of pregnancy characterized by abnormal proliferation of trophoblastic tissue. It includes a wide spectrum of clinical-pathological entities that range from benign trophoblastic disease (Complete Hydatidiform Mole and Partial Hydatidiform Mole) to malignant pathologies (Invasive Hydatidiform Mole, Choriocarcinoma, Placental Site Tumor and Epithelial Trophoblastic Tumor) also known as Gestational Trophoblastic Neoplasia.[1] All of them are characterized by their great invasive capacity, due to a failure in the mechanism regulating the invasion of the trophoblastic tissue into the decidua and their rich vascularization, which determines their extension via the vascular system.[2,3]

The incidence of malignant trophoblastic disease is difficult to establish with certainty, it depends on the geographical area and data on the incidence of pregnancies and trophoblastic events are not available in most countries.[4] Specifically, the incidence of choriocarcinoma in Europe and North America is estimated at 3/100,000 pregnancies, while in Asia these values rise to 5-200/100,000 pregnancies. These differences have been associated with the use of different histological classifications, diet or genetic conditions.[5]

The main clinic is metrorrhagia, both in the initial stages of pregnancy and postpartum. The determination of β-hCG is used as a diagnostic, prognostic, response and tumor activity marker related to the progression, persistence and cure of the disease.[3]

We present the clinical case of a choriocarcinoma diagnosed one month after an eutocic delivery at term without complications and with a favorable evolution after treatment.

Clinical case

38-year-old patient, with no history of interest. Three previous pregnancies to term without complications. The course of the pregnancy was normal.

She was admitted at 37+5 weeks of gestation in the active phase of labor. After an eutocic delivery without incident, she was born a healthy female fetus. Neonatal weight of 2980g, Apgar 8/10, pH 7.30 of umbilical artery. The delivery was directed, with a macroscopically normal placenta and no abnormal uterine bleeding observed. Discharged 48 hours after delivery with hemoglobin analysis of 13.8g/dL.

Two weeks after delivery, she presented to the emergency department of a private center for persistent vaginal bleeding. Transvaginal ultrasound revealed intracavitary remains, so Methergin was administered in One month after delivery, she went to the Emergency Department of our hospital due to pleuritic pain predominantly at night and fever of 6 days of evolution, where a chest x-ray was performed that showed a typical image of balloon release (Figure 1). Given her findings, the patient was transferred to the gynecology emergency department for a directed study and performance of the following complementary tests:

a. **Gynecological examination:** Hematic remains not malodorous. Active bleeding less than normal. Patent cervix, not painful on mobilization. Uterus well involuted to the touch.

b. **Vaginal ultrasound:** Hyperrefringent image with imprecise contours and approximately 26x24mm, which covers from the middle third of the myometrium to the intracavitary space. Abundant vascularization in Doppler study (Figure 2).

c. **Analytics:**

   i. LDH 313. CRP 60.3mg/dl. normal rest

   ii. Hb 12.1g/dL, Hct 36.2%, Platelets 242,000, Leukocytes 6700 (N 55.4%)

   iii. Normal coagulation

   iv. β-hCG: 59631

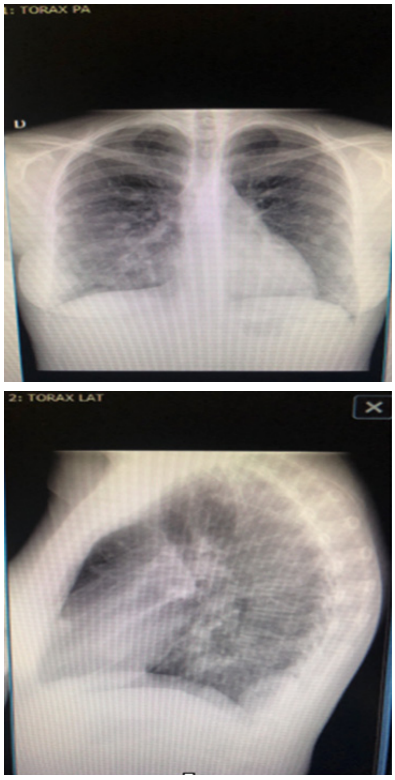

Figure 1 RX chest PA and lateral.

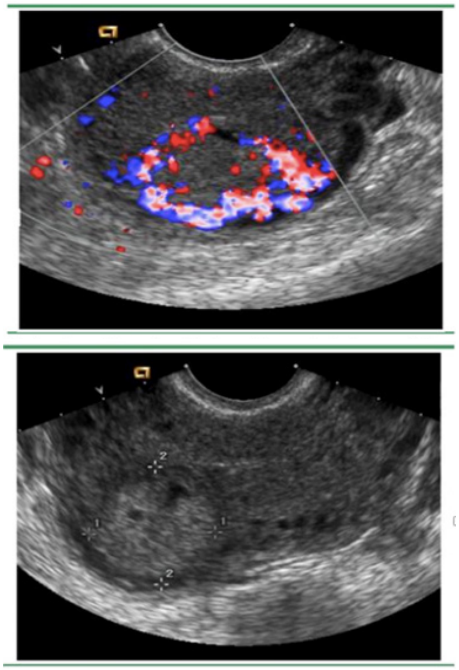

Figure 2 gynecological doppler ultrasound.

Given the findings and suspicion of choriocarcinoma, the patient was admitted to complete the study and start early treatment.

A. CT TAP: Bilateral lung metastases of up to 4.8 cm in LID with a necrotic center (Figure 3).

B. NMR: Heterogeneous tumor with hyper- and hypointense areas located in the myometrium measuring 5.2x4cm in APxT that protrudes into the endometrial lumen and does not protrude from the external uterine contour (Figure 4).

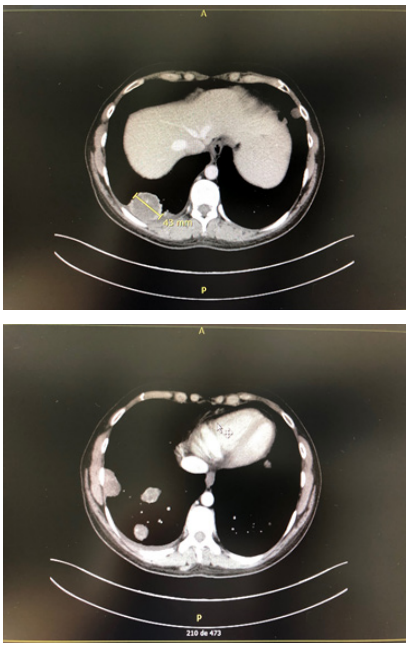

Figure 3 TAC total body.

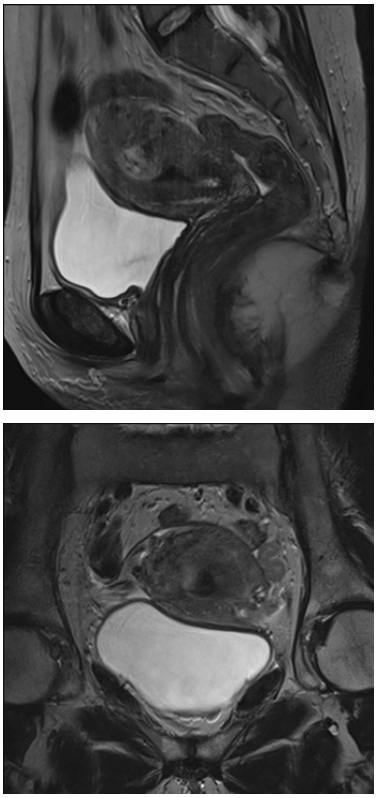

Figure 4 RMN.

The patient was transferred to the oncology service to start treatment three days after admission. Choriocarcinoma stage III (pulmonary metastases on chest X-ray, with or without uterine, pelvic or vaginal involvement) was classified as high risk (FIGO Risk Score 9) and polychemotherapeutic treatment was started with a 1st-line scheme EMA/CO (Etoposide, Methotrexate, Actinomycin/ Cyclophosphamide and Vincristine). Seven cycles were administered, repeated every 14 days.

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After being stabilized, prior to starting treatment, a hysteroscopic biopsy was performed (Figure 5) on a scheduled basis in order to obtain a biopsy that would be useful for targeted treatment. During it, moderate atony occurred that required the placement of a Cook balloon and embolization of the uterine arteries by the interventional radiology service after its withdrawal at 24 hours due to persistent bleeding.

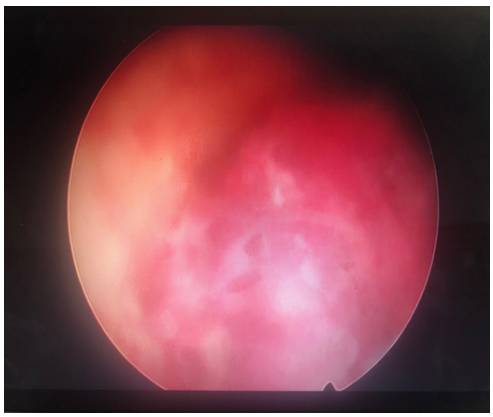

Figure 5 Hysteroscopy.

β-hCG values decreased from the start of treatment, with β-hCG becoming negative from the 4th cycle. The latest imaging tests performed show a clear improvement in the metastatic disease.

I. CT: Significant decrease in the overall size of bilateral lung lesions, many of them being punctate at the present time.

II. NMR: Examination without significant findings.

Currently, the patient continues to be monitored by the gynecological oncology and medical oncology service, with monthly controls of β-hCG.

Discussion

Choriocarcinoma can appear after any type of pregnancy: an abortion, a hydatidiform mole, an ectopic pregnancy or a full-term pregnancy. It can appear even years after a normal delivery, which would be associated with a worse prognosis. Intraplacental choriocarcinomas are rare but usually occur after apparently uncomplicated term gestations.

It has a great affinity for vascular invasion and early lung metastasis in up to 80% of cases, which coincides with our case, which had lung metastases from the time the diagnosis was established. Other frequent sites of metastasis are the vagina and the CNS.[6]

The most common manifestation is persistent postpartum bleeding (74%), either scarce or even producing hemorrhagic shock. Other manifestations of the tumor are uterine subinvolution or symptoms derived from metastases: headaches, neurological alterations, dyspnea, hemoptysis, abdominal pain or hematuria.[7]

Risk factors related to the appearance of choriocarcinoma are maternal age less than 20 years or greater than 39 years and a previous history of trophoblastic disease. Some studies also state that there is an increased incidence when the paternal age is greater than 40 years, regardless of the maternal age, although these results are yet to be confirmed.[5] Multiparity has been associated with an increased risk, but only in those women with more than 5 previous pregnancies. The risk of choriocarcinoma increases from 2.0 to 6.4 in women who have ever used oral contraceptives (OCs), although their use does not increase the risk of following a molar pregnancy. Some studies only affirm an increased risk with OACs when prolonged use is greater than 7 years.[4]

When a choriocarcinoma is suspected or diagnosed, a Doppler ultrasound should be performed, which allows low-resistance indices to be observed, and a chest X-ray to rule out pulmonary metastases, since these are the most frequent. Chest-abdominal-pelvic CT can reveal lung metastases not detected on chest X-ray in up to 40% of malignant trophoblastic diseases.[1] An MRI is recommended to rule out brain metastases in high-risk cases or in the presence of lung metastases.

When a choriocarcinoma is diagnosed, chemotherapy treatment is always indicated and it must be started at the right time to avoid hemorrhagic complications and metastatic spread. Choriocarcinoma is one of the most sensitive tumors to chemotherapy. The cure rate, even for metastatic cases, is close to 90-95%.[1,2]

The FIGO Risk Score classification divides patients into two groups: low risk (0 to 6) and high risk (≥7). The low-risk group will receive monochemotherapeutic treatment, while the high-risk group, in which our patient was included, are candidates for polychemotherapeutic treatment.[4,8]

During treatment, bhCG levels should be monitored weekly until they return to normal.[4]

It is necessary to inform the patient of the importance of avoiding a new pregnancy during the follow-up of ß-HCG. Oral contraceptives will be recommended during follow-up since in these patients there is sufficient evidence that they do not increase the risk of subsequent malignant trophoblastic disease, they may even decrease it, and they have a lower pregnancy rate compared to the use of barrier methods.[4,9]

The importance of this entity lies in the fact that it is a medical emergency, which requires early diagnosis and initiation of treatment to avoid complications and favor the prognosis. It is not a frequent pathology and on many occasions there is a delay in diagnosis after a non-molar pregnancy, since the symptoms and signs are very subtle and β-hCG determinations and histological study of the placenta are not performed routinely . This occurred with our patient, who came to the emergency department with abnormal bleeding and an ultrasound image compatible with intracavitary remnants without suspecting malignant trophoblastic disease. Choriocarcinoma should be suspected in all women of reproductive age with metastases of unknown origin.

As a criticism of our case, it is important to note that, unlike other solid tumors, a tissue diagnosis is not required before treatment.

The clinical presentation is more important to determine and initiate treatment than a precise histological diagnosis, which is why many of these cases are diagnosed without a pathological study. In fact, performing a tumor or metastatic lesion biopsy is not recommended if there is no guarantee of controlling bleeding, as occurred in our case, since these are highly vascularized lesions. In addition, there are published cases in which, after performing a biopsy, it is not diagnostic of choriocarcinoma due to the important necrotic and hemorrhagic component of the tumor.[10]

As a conclusion to this case, it is important to point out that the diagnosis of this pathology is difficult. The relative ignorance of the disease and the prototype of a healthy patient with an uncomplicated delivery is only one of the causes. The delay in the

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diagnosis and treatment of our patient's complications depended on the multidisciplinary approach of several specialists (emergency department, medical oncology service, obstetrics service, and oncology gynecology service.

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Conflicts of interest

Author declares there is no conflict of interest exists.

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