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Case Report

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Case Report: Intracranial Hemorrhage as Initial Manifestation of Metastatic Trophoblastic Disease

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ABSTRACT

Background: Gestational trophoblastic disease is a heterogeneous group of epithelial tumors that arise in placental trophoblastic tissue following abnormal fertilization and are related to a pregnancy event (miscarriage, extrauterine or term/preterm pregnancy). Choriocarcinoma is the most aggressive histologic type, as it shows early vascular invasion and blood metastases. It can manifest itself through hemorrhages originating in the most frequent metastatic foci of choriocarcinoma, which are usually the lung (80%), vagina (30%), brain and liver (10%).

Clinical Case: 22-year-old female patient, who presented to the emergency department secondary to neurological deterioration with initial evaluation Glasgow 3 points, with presentation of Fisher IV subarachnoid hemorrhage, which merited neurosurgical treatment (decompressive craniectomy), with diagnosis of choriocarcinoma, with result of chorionic gonadotropin beta fraction 91114 mIU/ml, uterine choriocarcinoma in posterior wall of uterus, metastasis to lung and splenic and right renal infarction.

Conclusion: Choriocarcinoma is a highly aggressive trophoblast pathology, due to its great capacity for angioinvasion, which facilitates its dissemination and favours the development of pulmonary, cerebral, hepatic and other organ metastases. This increases mortality, since diagnosis and treatment is usually not carried out early, or is incomplete.

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Introduction

The first description of gestational trophoblastic disease was made by Hippocrates around 400 BC. However, it was not until 1895 that Félix Marchand discovered the association between pregnancy and gestational trophoblastic disease [1].

Gestational trophoblastic disease is a heterogeneous group of epithelial tumors that originate in the placental trophoblastic tissue after abnormal fertilization and are related to a pregnancy event (miscarriage, extra uterine or term/preterm pregnancy) [2].

It can be classified into two groups according to whether it is metastatic from the beginning or non-metastatic. Within the non-metastatic ones, we find the two most frequent which are complete and partial hydatidiform mole while the metastatic ones are globally called gestational trophoblastic neoplasms [3].

Etiology

Trophoblasts, the first cells to differentiate from the fertilized egg, supply nutrients to the embryo and eventually form the fetal portion of the placenta. These placental trophoblasts are the origin of molar pregnancies and gestational trophoblastic neoplasms. Specifically, cytotrophoblasts and syncytiotrophoblasts create hydatidiform moles and choriocarcinomas [4].

The trophoblast shows limited histolytic, angiotropic and invasive power, not exceeding the thin decidua basalis of the myometrium. Chorionic neoplasms, which are histologically similar to chorionic villi, have invasive morphologic and proliferative attitudes [5].

Epidemiology

Gestational trophoblastic neoplasia after a non molar pregnancy occurs in about 2 to 200 per 100,000 pregnancies (according to global reports) and is typically a choriocarcinoma.6 After pregnancy loss it occurs in 1 in 15,000 cases; And in a full-term pregnancy it occurs in 1 in every 150,000 cases [6,7].

Globally, it is estimated that gestational trophoblastic neoplasms arise in 50% after molar pregnancy, 25% after spontaneous abortions or tubal pregnancies, and 25% after full-term pregnancies or premature births. The most frequent histologic type is invasive mole (15%), followed by choriocarcinoma (5%) [8].

Choriocarcinoma

They are malignant human chorionic gonadotropin (HCG)-releasing epithelial malignant tumors with central necrosis and a characteristic biphasic structure. Intraplacental choriocarcinomas may also occur and are probably responsible for metastatic disease after term pregnancies. Most neonatal choriocarcinomas are the result of metastatic spread of intraplacental choriocarcinomas [9].

Histologically, post molar and non-molar choriocarcinomas are characterized by invasion of the myometrium, but unlike invasive hydatidiform mole, there is absence of chorionic villi, abnormal syncytiotrophoblast and cytotrophoblast, necrosis, and hemorrhage.

In several studies, a history of term pregnancy is considered a prognostic risk factor in patients with choriocarcinoma [10].

Choriocarcinoma after term delivery has been reported to account for 16.2 to 22.5% of choriocarcinomas.

Postpartum choriocarcinoma is divided into two subgroups: short interval groups (4 months), according to the time interval between the onset of the disease and the previous pregnancy [11].

Among all trophoblastic neoplasms, choriocarcinoma is the most aggressive histological type, presenting early vascular invasion and metastasis via the bloodstream, which can manifest itself through bleeding originating in the most frequent metastatic foci of choriocarcinoma, which are usually the lung (80%). vagina (30%), brain and liver (10%) [12].

The current FIGO prognostic scoring system was adapted from the WHO classification. (Table 1) The FIGO prognostic score is based on individual risk factors that have been shown to predict resistance of gestational trophoblastic neoplasia to single-agent chemotherapy [13].

Table 1

Score	0	1	2	4
Prognostic Factor				
Age in Years	< 40	>= 40	-	-
Pregnancy Antecedent	Molar Pregnancy	Abortion	Pregnancy at Term	-
Interval Since Pregnancy Index in Months	< 4	4-6	7-12	> 12
Pre-Treatment HCG (mIU/mL)	< 1000	1000 – 10, 000	10,000 – 100,000	>=100,000
Largest size of the Tumour Including the Uterus in cm.	< 3	3 - 5	> 5	-
Metastatic Sites	Lung	Spleen, Kidney	Gastrointestinal	Brain, Liver
Number of Metastases	0	1-4	5-8	>8
Previously Failed Chemotherapies	None	None	Single Drug	2 or more Drugs

Low-risk gestational trophoblastic disease has a total prognostic score of less than 7 and high-risk has a total prognostic score of 7 or more [14].

In patients with postmolar gestational trophoblastic neoplasia, evaluation involves a detailed clinical history, physical examination including a pelvic examination, pelvic ultrasound, and imaging including chest radiograph and/or computed tomography (CT) scan of the chest, abdomen, and pelvis. If there is no extrauterine disease, single-agent treatment is appropriate. In the case of extrauterine disease, the stage and Federation of Gynecology and Obstetrics (FIGO) prognostic score should be determined to assess whether the patient is at low or high risk for persistent or recurrent disease. Studies have reported a recurrence rate of 2.9% in patients with nonmetastatic disease and up to a 9.1% recurrence rate in patients with metastatic disease [15].

The metastatic disease score is used to determine treatment. In low-risk metastatic disease (prognostic score <7), single-agent methotrexate or dactinomycin is appropriate. Between 10% and 30% of low-risk patients will develop resistance after single-agent chemotherapy, while up to 50% of patients with high-risk metastatic disease will develop resistance. Patients who develop resistance to the initial single drug will generally respond to an alternative single drug, and only 5% to 10% of patients will require multidrug therapy [16,17].

Multiagent chemotherapy is indicated in high-risk metastatic disease (prognostic score ≥7) and guidelines recommend etoposide, methotrexate, and actinomycin D alternating with cyclophosphamide and vincristine. However, up to 40% of patients with high-risk metastases may fail to respond or relapse [18]. Most patients present to tertiary care units with advanced disease, often due to late diagnosis and suboptimal prior treatment [19].

Associated mortality is significantly high in low- and middle-income countries and women with WHO scores ≥13 are at increased risk of death and, in particular, premature death. Late diagnosis, late presentation at advanced stages of disease, late treatment, healthcare limitations, and social and economic barriers are thought to be predictors of mortality [20].

The aim of this paper is to present the report of a clinical case of choriocarcinoma after term pregnancy, with presentation of endocranial hypertension syndrome and pulmonary metastasis at the Zumpango Regional High Specialty Hospital, State of Mexico, in order to collaborate in the diagnosis and treatment of this pathology.

Clinical Case

Female patient, 22 years old, native and resident of Tlaxcala, marital status unmarried, occupation housewife, with no personal or family history to highlight. Her obstetric history includes menarche at 14 years of age, four pregnancies, four cesarean sections, and four months after the last cesarean section, with a diagnosis in the last pregnancy of hypertensive disease of pregnancy in management with calcium channel antagonist, with resolution of pregnancy at term, without apparent complications, discharged without antihypertensive drugs and without medical follow-up. Her last menstrual period was May 23, 2024.

She presented to the emergency department on May 25, 2024 due to headache of a month and a half of evolution, oppressive type pain, with progression of intensity up to 10/10 in analog

pain scale, accompanied by nausea and emesis of gastro biliary content, right hemiparesis, tonic clonic movements in hands with loss of alertness for 2 minutes, self-medicated with acetylsalicylic acid and aspirin, without improvement, so she was transferred to the unit.

On admission with blood pressure record of173/90 mmHg, and neurological deterioration with non-traumatic Glasgow coma scale of 7 points, so advanced airway management is performed, with subsequent taking of simple cranial tomography with report of: Fisher IV subarachnoid hemorrhage with intraparequimatous extension of left parito-occipital location with dimensions of 50x34x30 mm in ventro dorsal axes, caudal and lateral medial face, with approximate volume of 26 cc, with perilesional vasogenic edema and discrete adjacent intraparenchymal hemorrhagic areas measuring 13x11x9 mm and another of 12x9x10 mm, subarachnoid hemorrhage in right parietal, bilateral hemispheric cerebral edema that conditions midline deviation 12 mm to the right. Compression of the left lateral ventricle with obliteration of the posterior horn, as well as compression of the third ventricle, sulcal herniation as shown in figure 1 and 2.

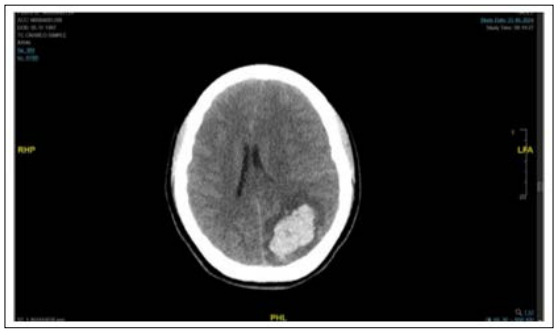

Figure 1

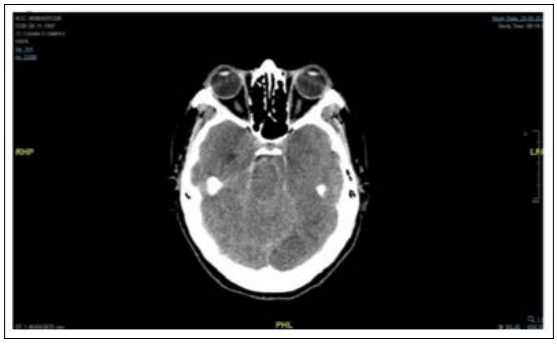

Figure 2

It was deserved surgical intervention by the neurosurgery service that performed a left tempura parietal decompressive craniectomy.

She was admitted to the adult intensive care unit, neurologically maintained under sedation in goals maintaining RASS -5, with adequate analgesia, hypertonic solutions are administered and neurocritical patient care is maintained according to GHOST CAP, THE MANTLE, hemodynamically with vasopressor support to maintain average blood pressure for cerebral perfusion, achieving goals at this time of 90-110 mmHg, at respiratory level with minimal parameters for alveolar protection, oxygen saturation between 90-94%, normocapnia, without imbalance acid base at this time, renal hydric with preserved renal function, with urinary flows in goals, hematoinfectious with thrombocytopenia classified as severe, platelet transfusion was performed, hemoglobin reported between 8-12 mg/dl.

Cranial tomography angiography is requested suspected arteriovenous malformation, the following is reported: Surgical changes due to left temporoparietal decompressive craniectomy associated with external herniation fungus cerebri type of approximately 98 mm, subgaleal hematoma, as well as emphysema and edema of the subcutaneous cellular tissue in that region. Persistent Fisher IV subarachnoid hemorrhage with intraparenchymal extension with perilesional vasogenic edema that deviate the midline structures 2 mm to the right (previous 12 mm). Persistence of subarachnoid hemorrhage in right parietal. Persistence of generalized moderate cerebral edema. Compression of the supratentorial ventricular system persists. Resolution of the subalpine herniation. (Figure 3)

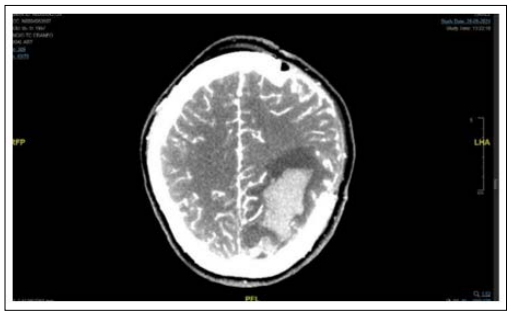

Figure 3

As part of the late puerperium protocol, a qualitative immunological pregnancy test was taken and reported positive. And endovaginal ultrasound is requested with report of: Uterus of usual shape located in retroversion, measuring 50 x 41 x 56 mm, the perimetrium is homogeneous lobulated echogenic, heterogeneous myometrium, by the presence of a rounded echogenic and well-defined image, located in the anterior uterine wall, the central endometrium is regular heterogeneous, predominantly echogenic with a hypoechogenic image towards the fundus, the thickness is 10 mm, without alteration in the vascularity at the application of color Doppler. No gestational sac was observed (Figure 4).

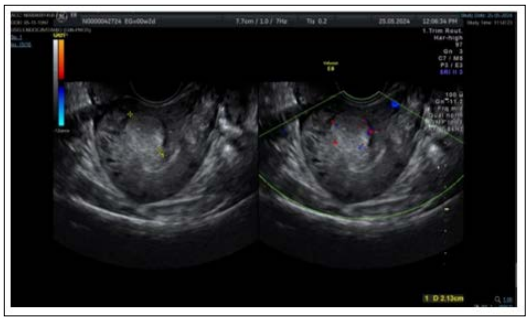

Figure 4

Patient with a positive pregnancy test, and ultrasound without observing gestational sac, so chorionic gonadotropin fraction is requested beta, with a result of 91114 mIU/ml with institutional ultrasound which reports endometrium of 10 mm, by quantification would be expect to observe intrauterine or ectopic gestational sac, However, no adnexal tumors are reported, so as a second diagnosis we have to suspect a probable trophoblastic disease (choriocarcinoma), so a contrasted tomography of the thorax, abdomen and pelvis is taken with the following findings:

Probable uterine choriocarcinoma in posterior wall of the uterus. Uterus in retroversion, with heterogeneous myometrium by hypodense, round image in posterior wall, which contacts the endometrium, which after the contrast medium, maintains

hypodense center, and presents avid peripheral enhancement, with approximate dimensions of 27 x 29 x 24 mm, correlates with endovaginal ultrasound image of 05/25/2024, in which it is observed hyperechogenic, heterogeneous, with high peripheral vascularity, with contact with the endometrium, being determined as diagnostic suspicion of uterine choriocarcinoma (Figure 5).

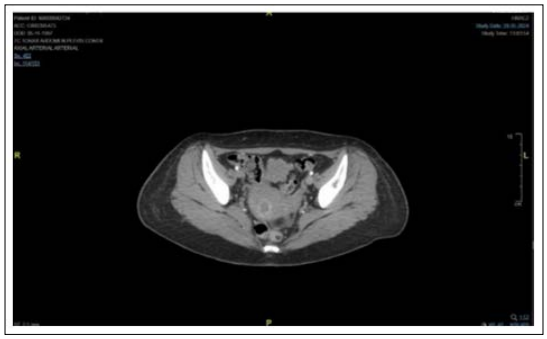

Figure 5

Heterogeneous splenic (peripheral) and right renal (wedge-shaped) enhancement, suggesting splenic and right renal infarction. No vascular filling defects suggesting thrombus are evidenced at the time (Figure 6 and 7).

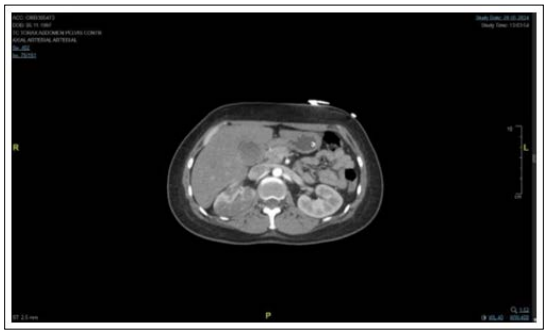

Figure 6

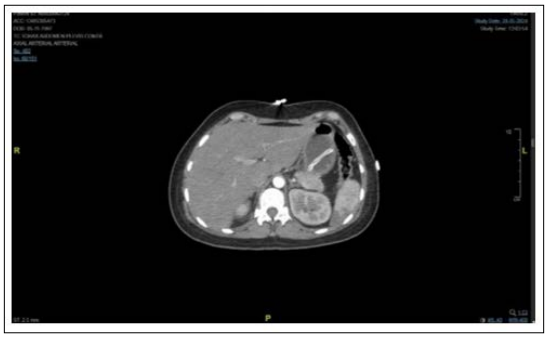

Figure 7

Round subpleural pulmonary nodule (8 mm) with contrast enhancement in the apical segment of the right upper lobe, metastasis is not ruled out. Subpleural pulmonary micro-nodule (2 mm) in the anterior segment of the left upper lobe (Figure 8).

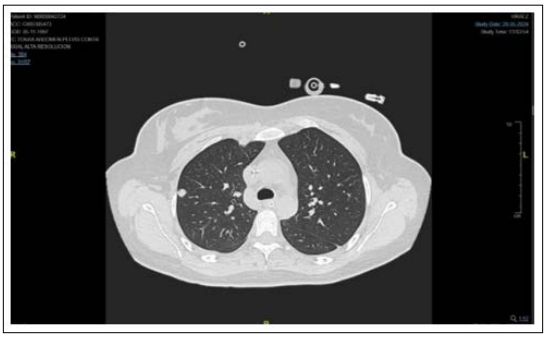

Figure 8

Patient with poor prognosis due to reports of tomographic study with progression of gynecological pathology to posterior uterine wall with pulmonary metastasis, splenic and right renal infarction, classified as stage 3 according to FIGO, with 6 points according to the new FIGO/WHO prognostic scoring system, so support is requested to third level for assessment and management by gynecologic oncology service.

Discussion

Choriocarcinoma is a highly aggressive pathology of the trophoblast, due to its great capacity for angioinvasion, which facilitates its dissemination and favors the development of pulmonary, cerebral, hepatic and other organ metastases. This increases mortality, since diagnosis and treatment are usually not carried out early or is incomplete. Symptomatology appears late due to metastasis to different organs, so it is extremely important to suspect this pathology, completing the diagnostic protocol. Serum quantification of the beta-HCG fraction is extremely important, since it is not only the basis of diagnosis but also establishes the prognosis, unlike what happens with other neoplasms, histological confirmation is not necessary to initiate adequate therapy. Imaging studies as a complement to know the extent of the pathology and thus be able to classify it and determine the appropriate treatment. In the case reported, it complies with what is described in the literature reviewed. Therefore, it was possible to establish a diagnosis and prognosis, and referral to gynecologic oncology to receive appropriate treatment.

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