

Case Report

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This Paper Provides a Description of a Rare Case of a Gestational Trophoblastic Tumor of The Choriocarcinoma Type That Has Metastasized to The Brain, Lung and Kidney

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Abstract

Introduction: Choriocarcinoma is a type of gestational trophoblastic tumor, with approximately 20% of patients requiring treatment for malignant sequelae after the evacuation of a hydatidiform mole. Therefore, rigorous follow-up with quantitative levels of human chorionic gonadotropin (hCG) is essential. This type of tumor occurs in around 1 in every 20,000 to 40,000 pregnancies, with a 2-3% risk following a complete mole.

Case Report: A clinical case is described of a patient with metastatic choriocarcinoma to the brain, lungs, and kidney, the latter being of low prevalence. The patient did not receive medical follow-up after a complete hydatidiform mole and was diagnosed due to neurological symptoms. Thus far, she has experienced a favorable evolution under hCG level monitoring, although with complications secondary to acute hemorrhages in disseminated organs, such as the brain.

Discussion: Gestational trophoblastic diseases are proliferative disorders of the placental trophoblast, including premalignant conditions or true neoplastic gestational trophoblastic tumors. Choriocarcinoma tends to spread widely via hematogenous route and is associated with distant metastasis. It has been reported to commonly metastasize to the lungs and vagina, and less frequently to the liver, brain, kidneys, and gastrointestinal tract. Symptoms of metastatic lesions are usually secondary to acute hemorrhages in the organ to which they spread, as in the case of the patient.

Conclusion: The optimal management of this disease depends on the type of specialized center, pathology review, and evidence-based treatment guidelines. Given the rarity of trophoblastic tumors, as well as the associated diagnostic challenges, it is crucial to follow up on hydatidiform moles to prevent metastasis, as in the case of this patient.

Keywords: gestational trophoblastic tumor; choriocarcinoma; brain metastasis; human chorionic gonadotropin hormone; lung metastasis; high risk choriocarcinoma

Introduction

Choriocarcinoma, categorized as a gestational trophoblastic tumor, poses a notable risk, as evidenced by the fact that 20% of patients experience malignant complications post-evacuation of a hydatidiform mole. Therefore, diligent follow-up through quantitative hCG level monitoring becomes imperative. This particular tumor manifests in approximately 1 in 20,000 to 40,000 pregnancies, with a 2-3% risk post-complete mole (0.1-0.5% in incomplete mole) [1]. It stands out as the most common trophoblastic tumor, exhibiting a diverse range of presentations, typically emerging around the age of 30. Choriocarcinoma can originate from

various gestational, with statistics indicating 50% occurrence after a full-term pregnancy, 25% following a molar pregnancy, and another 25% after different types of pregnancies [2].

While uterine bleeding emerges as the predominant symptom, extrauterine events may serve as the initial indicators in cases of extrauterine dissemination. As observed in the reported patient's case, metastasis to the lung, central nervous system, and, less frequently, the kidney occurred. Uterine bleeding is the most frequent symptom, but extrauterine events can be the first presentation in a patient with extrauterine dissemination, as in the case of the patient reported, with metastasis to the lung, central nervous system, and kidney, the latter being reported with less

frequency. Effectively managing choriocarcinoma hinges on the specialized center's expertise, thorough pathology reviews, and evidence-based treatment aligned with management guidelines. This approach significantly influences the prognosis. Given their rarity, trophoblastic tumors present considerable diagnostic challenges due to the extensive array of differential diagnoses and the diagnostic uncertainties associated with their precursor lesions [3].

Case Presentation

A 38-year-old female patient was admitted to the emergency room with an altered state of consciousness, seizure from focal motor to bilateral tonic-clonic onset lasting 3 minutes with recovery of consciousness and a new similar episode during the assessment. The postictal period was 15 minutes. Treatment was started with levetiracetam (500 mg every 12 hours) with an adequate response. During the evaluation, the patient presented with vaginal bleeding, with a report of positive qualitative beta subunit chorionic gonadotropin. Family members reported that she had metrorrhagia for one month.

The last pregnancy was 10 months prior, with evidence of a molar pregnancy, and was carried out for curettage, with pathology revealing gestational trophoblastic disease type complete hydatidiform mole. The patient was lost to follow-up and did not receive control treatment. In the 2 weeks prior to admission, she presented intense headache, changes in behavior due to aggressive and irritable behavior, and seizures.

During the current evaluation, on ultrasonography, an enlarged uterus was found, and multiple endometrial cystic foci configured a mass with a snowstorm pattern, measuring 108x66x70 mm and having a volume of 264 cc; these findings are suggestive of molar pregnancy (Figure 1). On physical examination, she was febrile and drowsy and required invasive mechanical ventilation and vasopressor support. Respiratory sounds with bilateral rhonchi and abundant mobilization of secretions were observed. Her chorionic gonadotropin concentration was 219181 mIU/ml in her blood (Table 1). Her obstetric curettage revealed an enlarged uterus (11 cm), a curettage product with scant ovular remnants, and difficult bleeding control.

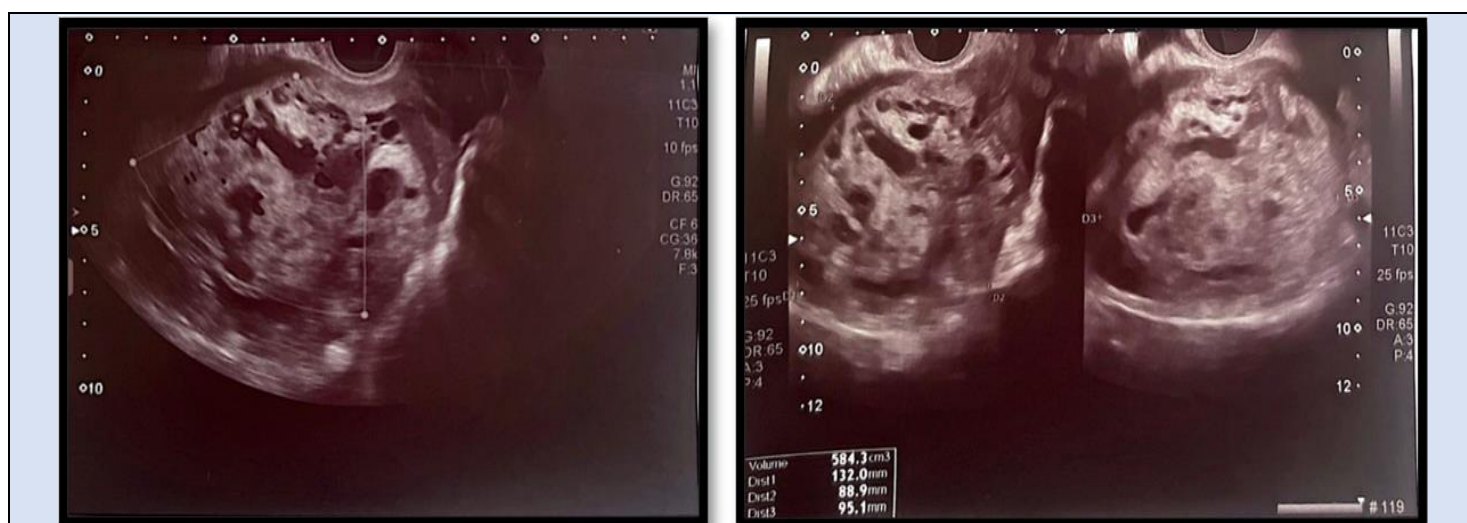


Figure 1: Ultrasonography. Patient ultrasonography revealed multiple endometrial cystic foci configuring a mass with a snowstorm pattern measuring 108x66x70 mm and with a volume of 264 cc, suggesting molar pregnancy.

Table 1: Paraclinical.

Gravindex	Positive	
Calcium	8.06	mg/dl
Chlorine	105	mEq/L
Potassium	3.12	mEq/L
Sodium	137	mEq/L
Bun	6.8	mg/dl
Creatinine	0.60	mg/dl
H.B.	11.7	
HTO	31.1	
Neutrophils	5420	uL
Lymphocytes	4.1	%
Neutrophils	80.4	%
BHCG	219181	mUl/ml
Total, Bilirubin	0.59	mg/dl
Direct Bilirubin	0.42	mg/dl
Indirect Bilirubin	0.17	mg/dl
TGO-AST	27	U/L
TGP-ALT	15	U/L
PTT	30.4	sec
PTT	10.8	sec
INR	1.07	
Lactate	0.68	mmol/L

Magnetic resonance imaging of the brain was performed (Figure 2) and revealed an intra-axial lesion in the deep white matter of the left frontal lobe measuring 5 mm and was oval, with peripheral contrast enhancement, which is associated with extensive vasogenic edema (thickness up to 12 mm). Moreover, in ferromagnetic sequences, bleeding within the lesion is evident. Without ruling out neuro

infection, paraclinical tests are performed, with a complete blood analysis revealing anemia and mild hypokalemia, as well as metabolic acidosis partially compensated for by mild oxygenation disorder. Lumbar puncture showed no signs of an infectious process; however, there was a report of elevated hCG in the CSF. (Table 2).

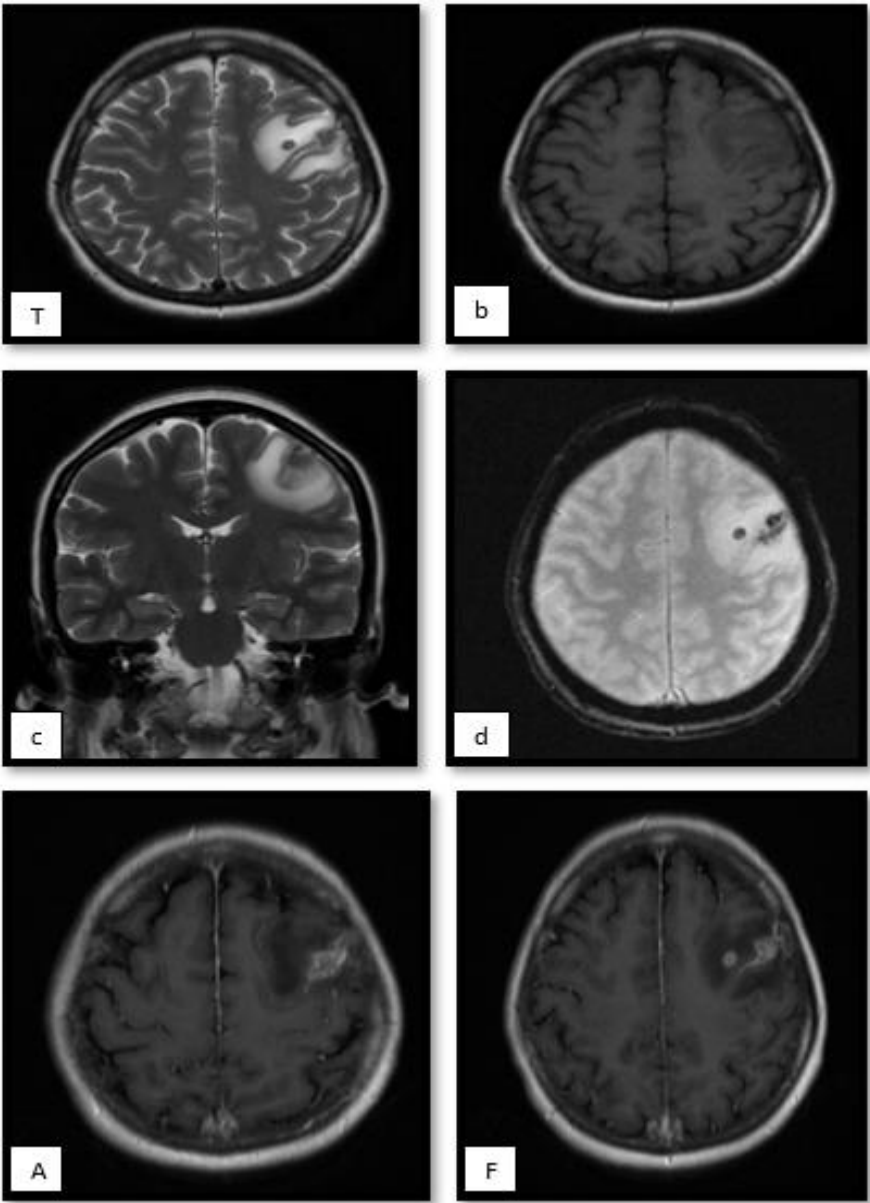


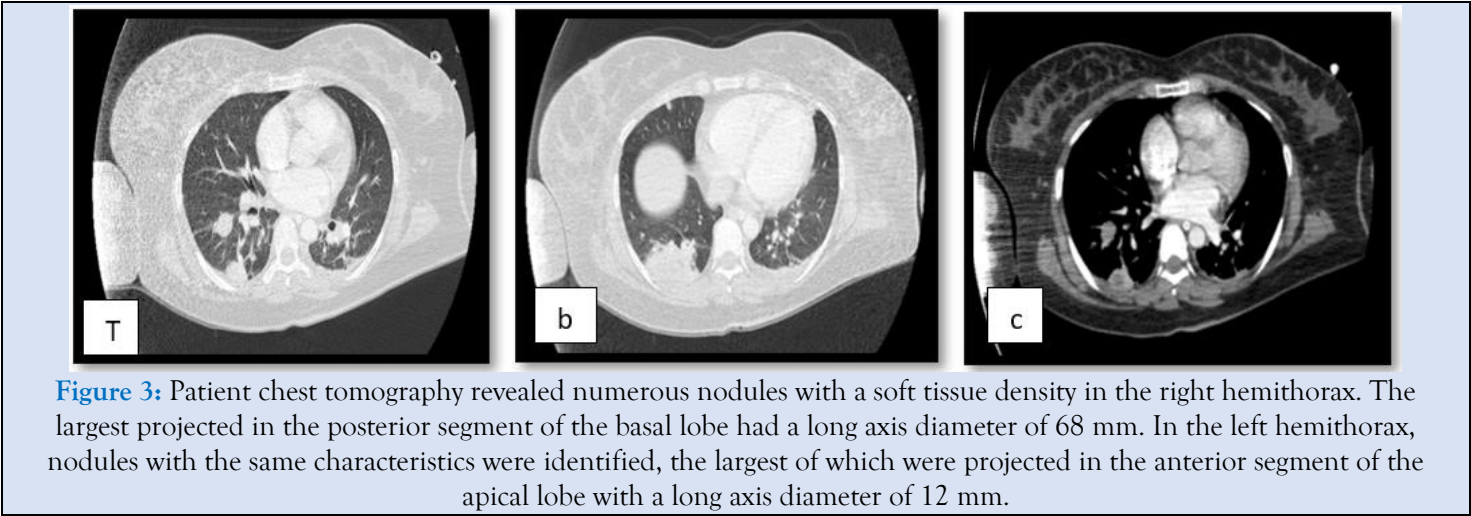
Figure 2: Magnetic resonance imaging of the brain. Patient magnetic resonance imaging of the brain showing intra-axial lesion in the deep white matter of the left frontal lobe that measures 5mm, oval, isointense on T1 (B), hypointense on T2 (AC), which is associated with extensive vasogenic edema (thickness up to 12mm). and in ferromagnetic sequences, bleeding within the lesion is evident, characteristic of these. With peripheral contrast enhancement (F).

Table 2: CSF.

CSF		
Glucose	67	
Total Proteins	14	
VDRL Serology	NR	mg/dl
White	0	
Red	2	
Neutrophils	0	
Lymphocytes	0	%
Fresh Erythrocytes	100	%
Created Erythrocytes	Either	
Crop	Negative	
Chinese Ink	Negative	
hCG	747	
Gram	Negative	mUl/ml

Chest tomography (Figure 3) showed evidence of bilateral pleural effusion predominantly on the right. Numerous nodules with soft tissue density were identified in the right hemithorax. The largest projected in the posterior segment of the basal lobe

had a long axis diameter of 68 mm. In the left hemithorax, nodules with the same characteristics were identified, the largest of which were projected in the anterior segment of the apical lobe with a long axis diameter of 12 mm.



Given these findings, an extension of the search for lesions was carried out via neck tomography, revealing numerous lymph nodes in different spaces of the neck, the largest of which were projected to left station III with a diameter of 12 mm in the short axis. In addition, in the bone system, a small lytic lesion projected on the vertebral body of C5. On

tomography of the abdomen and pelvis (Figure 4), in the middle third of the left kidney, an ill-defined hypodense image of 34 × 33 mm with soft tissue density and a central uterus with a thick endometrium of 31 mm of heterogeneous content were observed. The other tumor markers were reported (Table 3).

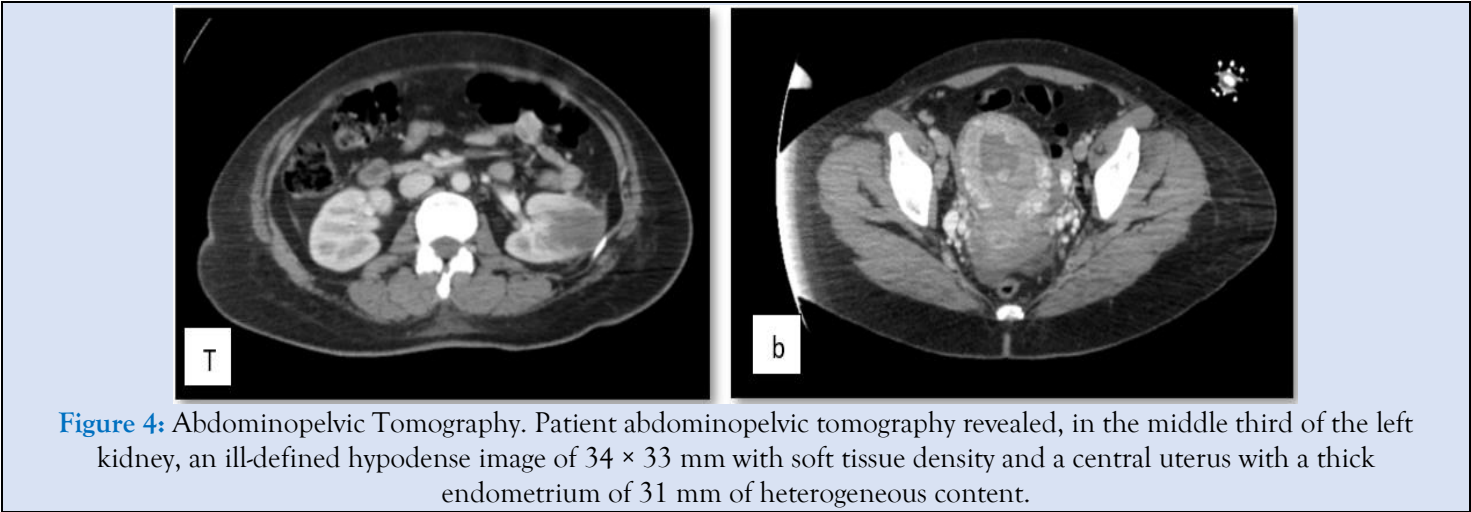


Table 3: Tumor Markers.

Tumor Markers		
ANTIGEN 19-9	10.22	U/mL
LDH	434	U/L
AC 125	21.30	U/ml
Carcinoembryonic GA	3.54	ng/ml
Serum Alpha-Fetoprotein	2.66	ng/ml
Alpha-Fetoprotein in CSF	<0.5	UI/mL
BHCG IN CSF	747.90	mUI/ml

Progressive weaning of vasopressor support and ventilation was initiated due to clinical and hemodynamic stability. If metastatic lesions are suspected, a biopsy of the lung lesion is performed. Pathology revealed a lower left segmental lobectomy: a violet-brown lobectomy product measuring 3.5x1x1 cm and a violet-colored nodular lesion measuring 0.6x0.6x0.6 cm in apparent contact with the pleura. With respect to the evidence of involvement by choriocarcinoma, immunohistochemistry studies have shown reactivity in the population affected by HCG, CKAE1/AE3, P63, PLAP, MUC4, INHIBINA and SALL4. P53: 50%. KI67: 70%. Pathology of the obstetric curettage material revealed atypical cells that suggested gestational tumors, with reactivity in the population with GATA-3, PLAP, CKAE1/AE3 or HCG. There was patchy reactivity with SALL4, INHIBIN and MUC4. No reactivity with P63. P53: NEGATIVE. KI67: 30%. A report of choriocarcinoma was available. Patient ventilatory and hemodynamic stability were successfully achieved. With symptomatic improvement.

Finally, given the diagnosis of FIGO IV gestational trophoblastic neoplasia of the choriocarcinoma type, treatment with chemotherapy was chosen to manage the high-risk trophoblastic neoplasia that the patient presented (cyclophosphamide, etoposide, methotrexate, vincristine, and dactinomycin in combination with folic acid, dexamethasone, and pegfilgrastim for complete the diagram). During the course of chemotherapy, in the second cycle, secondary intracranial hemorrhage was documented as a lesion already described in the brain MRI, clinically with evidence of right hemiplegia and focal motor crises in the right upper limb; thus, the dose was increased. of levetiracetam with seizure resolution. In addition, supplemental oxygen must be provided at low flow to maintain perfusion oxygenation. The values of the patients who underwent follow-up with hCG are shown in Figure 4.

Discussion

Gestational trophoblastic diseases are described as proliferative disorders of the placental trophoblast. These may be non-neoplastic proliferations, known as partial and complete hydatidiform moles; which are premalignant conditions; or true neoplastic conditions, such as gestational trophoblastic tumors. Within this group, different pathologies are known,

such as gestational choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and placental site nodule recently added to the guidelines. Collectively referred to as gestational trophoblastic neoplasms, each of these conditions arises from various subtypes of placental trophoblasts with different pathobiology's [1].

It has been noted that tumors may develop following various gestational event, with 50% arising post-pregnancy, 25% after a molar pregnancy, as seen in our patient, and 25% following other types of pregnancies [4]. Approximately 20% of patients undergo treatment sequelae after evacuation of a hydatidiform mole, a condition observed in around 1 in 600 therapeutic abortions and 1 in 1000-1200 pregnancies [5].

The incidence of choriocarcinoma is roughly 1 in 20,000 to 40,000 pregnancies. The risk of choriocarcinoma following a complete mole is 2-3 with a lower but existing risk following an incomplete mole (0.1-0.5%). According to existing literature, the diagnosis of post molar choriocarcinoma is typically made around 13 months after mole evacuation.

While placental trophoblastic site tumors and epithelioid trophoblastic tumors produce various amounts of the HCG, choriocarcinoma is consistently present in all patients. This makes it an excellent biomarker of disease progression. Allowing for early detection of complete or partial hydatidiform mole progression to gestational trophoblastic neoplasia. Proper management based on HCG level monitoring facilitates positive detection, treatment, and follow-up [6].

Serial quantitative determinations of the serum hCG concentration should be performed after molar evacuation; the first sample should be obtained 48 hours after evacuation, every 1 to 2 weeks while elevated, and then at intervals of 1 to 2 months for 6 to 12 months. additional. Monitoring hCG contraception is recommended to reduce recurrent pregnancy during post molar surveillance. Unlike our patient, who did not perform controls and lost follow-up, which is related to the neoplastic proliferation of gestational trophoblastic tumors, this patient was excluded [4].

Gestational choriocarcinomas typically present as uterine masses characterized by hemorrhage and necrosis. Histopathologically, the tumor exhibits proliferating cells resembling chorionic villous trophoblasts with cytotrophoblasts surrounded by layers of multinuclear syncytia trophoblastic cells.

Immunohistochemistry confirms strong and diffuse positivity for HCG and HSD3B1. Our patient's case aligns with this pattern, as intermediate trophoblasts express Mel-CAM, HLA-G, and MUC-4. Additionally, the Ki-67 proliferation index generally exceeds 90% [7].

Choriocarcinoma tends to disseminate hematogenously, frequently leading to distant metastases, commonly observed in the lungs and vagina, and less frequently in the liver, brain, kidneys, and gastrointestinal tract. Symptoms of metastatic lesions typically arise from acute hemorrhages within the affected organs [8].

There are few documented cases of brain metastases due to choriocarcinoma; however, 10-20% of cases have been described. They are highly vascularized tumors and have a propensity to bleed as well as metastasize. The presence of blood products may be evident on MRI as a loss of signal and "blooming" or flowering on T2* and an intrinsically hyperintense signal on T1 [9]. Patients who metastasize hematogenously with the possibility of presenting with aneurysmal lesions and other subdural or intraparenchymal hematomas [10].

The differential diagnosis of choriocarcinoma necessitates differentiation from its non-gestational counterpart of either somatic or germ cell origin, a condition that commonly presents in children and young adults. This category encompasses choriocarcinomas occurring in nulligravids. Characterized by a mixed component of germ cells found in both ovarian and extragonadal sites, distinguishable through histological examination. Moreover, it is imperative to differentiate these tumors from other gestational trophoblastic tumors [11].

The diagnosis was based on the International Federation of Gynecology and Obstetrics (FIGO) 2000 criteria and included four or more stable human chorionic gonadotropin concentrations for three weeks and increasing hCG concentrations for three consecutive weekly measurements for at least one period of 2 weeks or more elevated but decreasing

concentrations of human chorionic gonadotropin for six or more months after molar evacuation, if there was a histological diagnosis of choriocarcinoma [4].

Biopsy is a method of confirming gestational trophoblastic neoplasia, but complications can occur depending on the location of the biopsy, causing massive uncontrollable bleeding in the lungs, abdominal-pelvic organs, or brain biopsies, as in our patient. Staging is essential. The American guidelines recommend initial stratification via magnetic resonance imaging (MRI) of the brain and abdominopelvic and computed tomography (CT) of the chest, and the FIGO recommends performing pelvic-transvaginal Doppler ultrasound and a chest X-ray. For patients with metastases larger than 1 cm or doubts about normality in chest X-rays, chest CT and brain MRI should be used in combination [12].

The use of positron emission tomography (PET) has not yet been well established; there are no differences with respect to conventional images, although it could be useful for identifying metastases at unusual locations or for differentiating metastatic nodules from necrotic or hemorrhagic tissue. even after the use of chemotherapy.

The treatment of gestational trophoblastic neoplasia is guided by the International Federation of Gynecology and Obstetrics (FIGO) score; with our patient classified as stage IV and high risk. Therefore, the recommended approach involves combined chemotherapy. Recognizing the high cure rates and acceptable toxicity profiles of OSTs, two regimens-etoposide, methotrexate, dactinomycin, cyclofosamide, vincristine (EMA-CO) and etoposide, methotrexate, dactinomycin, etoposide, and cisplatin (EMA-EP)-are employed. Management of myelosuppression includes the use of granulocyte colony-stimulating factor. Regular monitoring of hCG levels continued until the serum hCG concentration normalized, as outlined in Figure 5 [13]. However, despite the normalization of hCG, the patient presented complications secondary to intracranial hemorrhage, which is the risk of metastasis and high-risk trophoblastic neoplasia.

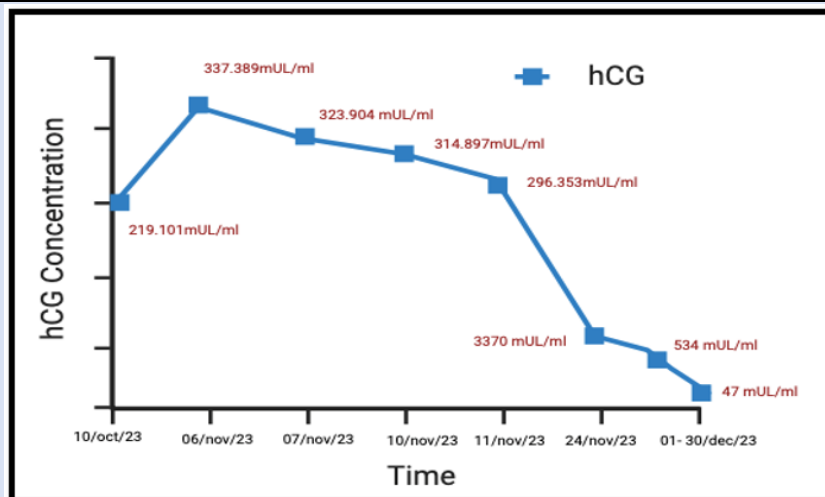


Figure 5: hCG levels over time.

Conclusion

Identifying gestational trophoblastic tumors poses challenges due to their relative rarity and overlap with common gynecologic tumors. Early and accurate diagnosis is essential for determining the appropriate treatment, particularly for patients with gestational choriocarcinoma, known for its favorable response to chemotherapy. Monitoring both complete and partial moles with serum hCG, a key marker in surveillance, is crucial. Choriocarcinoma typically spreads hematogenous, and our patient exhibited metastases to the brain, lung, and kidney, classifying them as ultrahigh risk according to FIGO. Complications, such as acute hemorrhages or intracranial hemorrhage, underscore the importance of adequately controlling molar pregnancies to minimize acute complications and promptly identify malignant sequelae.

Declarations

Authors Contribution

Analida Martínez: Conceptualization, Research, Methodology, Supervision, writing (original draft), Writing (review and editing of the manuscript).

Ignacio Salgado: Research, Methodology, Visualization, writing (review and editing of the manuscript).

Dana Mena: Writing (original draft), Writing (review and editing of the manuscript).

Andres Becker: Visualization, writing (review and editing), Investigation.

Lady Diaz: Writing (original draft), Writing (review and editing of the manuscript), Visualization.

Ethical Considerations

There are no ethical considerations to report in the completion of this manuscript.

Conflicts of Interest

Through this we can assert that none of those present have any conflicts of interest.

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