A Case of Misdiagnosed Gestational Trophoblastic Neoplasia with Brain and Lungs Metastasis; Complications and Modified Treatment: A Case Report

**Abstract**

**Introduction**
Timely diagnosis of gestational trophoblastic neoplasia (GTN) is essential for successful management of the condition and preservation of fertility. The aim of the present study was to describe a case of misdiagnosis GTN with brain and lungs metastasis.

**Patient information**
The present case study was conducted in Imam Khomeini hospital, Tehran, Iran, in 2017. A 35-year-old woman presented with acute headaches and left hemiplegia one month after the conclusion of her term pregnancy. The patient was previously diagnosed as a case of subarachnoid hemorrhage and inferior sagittal sinus thrombosis and was unsuccessfully treated with anticoagulant drugs leading to worsening signs and symptoms. Her initial β-hCG at admission to the hospital was 22,000,000IU/L, which lead to diagnosis of GTN with extensive metastatic lesions in the lungs and brain. Due to extensive intracranial hemorrhage, the patient was first treated with whole brain radiation therapy for 10 sessions daily (Total Dose=3000cGy). EMA-EP treatment was initially withheld due to concern for bleeding during concurrent radiation therapy. Following the brain radiation therapy, the chemotherapy was started for the patient. Upon completion of 3 cycles of EMA-EP, the patient’s hCG was lowered to 5IU/L. The treatment was continued for 5 more cycles and resulted in hCG reading of under 2IU/L at her last visit.

**Conclusion**
This case highlights the variable presentation of GTN which might easily cause misdiagnosis and delayed treatment and shows excellent response to treatment despite late treatment and massive tumor burden with some modifications to plan of treatment.

**Keywords**
Gestational Age; Trophoblastic Neoplasms; Neoplasia; Diagnose; Therapeutics

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**Citation Links**

[1] Chemoresistant gestational trophoblastic neoplasia: A case report
[3] Unusual clinical presentation of disseminated gestational trophoblastic neoplasia
[5] Current chemotherapeutic management of patients with gestational trophoblastic neoplasia
[6] Update on the diagnosis and management of gestational trophoblastic disease
[8] Immunoassay of human chorionic gonadotropin, its free subunits, and metabolites
[9] False negative urine pregnancy testing with complete molar Pregnancy: An example of the hook effect
[10] Current management of gestational trophoblastic disease
**Introduction**

Gestational Trophoblastic Disease (GTD) is a trophoblastic disease of women in reproductive age with several forms of manifestations ranging from benign partial or complete hydatidiform mole to aggressive invasive mole, choriocarcinoma, and placental site trophoblastic tumor (PSTT) [1, 2]. Gestational trophoblastic neoplasia (GTN) refers to the aggressive form (Invasive mole, choriocarcinoma, and PSTT), which has the capability for independent growth and metastases [2, 3]. GTN might appear following the evacuation of a molar pregnancy, normal term or preterm pregnancy, abortion, and ectopic pregnancy and show different pathologic behavior regarding local invasion and metastases [2]. GTN might occur in a pregnant woman of any age, but it is more common in teenagers and in women of advanced maternal age (40 to 50 years) [2, 4]. Early detection of GTN is important as it is one of the most chemotherapy responsive and highly curable cancers [1, 2]. The aim of the present study was to describe a case of misdiagnosis GTN with brain and lungs metastasis.

**Patient Information**

The present case study was done in Imam Khomeini Hospital, Tehran in 2017. A 35-years-old woman G3P1Ab1Mol1 (Gravida, Para, Abortion, Molar Pregnancy), was referred to the center with a suggested diagnosis of GTN one month after the conclusion of her term pregnancy. On admission, she complained of an acute headache and her pulse rate was 80 per minutes, her respiratory rate was 16 breaths per minutes and her blood pressure was 110/60mmHg. Other laboratory findings were Hb equal 9g/dl, normal differential count, total platelet count 270,000/ml and normal blood sugar level. Also, renal and liver function tests were all within normal limit. Her respiratory and cardiovascular examinations revealed no abnormality. On abdominal palpation, abdomen was soft, non-tender and there was no organomegaly. In vaginal exam uterine size was normal with no sign of vaginal bleeding. The coagulation tests (Prothrombin Time or PT; International Normalized Ratio or INR) were in upper normal limit range. In her brain Magnetic resonance imaging (MRI) examination, a patient had signs of a metastatic choriocarcinoma (Figure 1) and her lung computed tomography (CT) scan revealed multiple metastatic lesions.

The patient had a history of the first in vitro fertilization (IVF) in May 2015 resulting in spontaneous abortion in the fifth week of gestation and a second IVF procedure in March 2016 resulting in a partial mole extraction using curettage. Interestingly, after her second pregnancy resulting in molar abortion, the patient was not followed with recommended serial checking of human chorionic gonadotropin (hCG) levels following a molar pregnancy. She then underwent a third IVF procedure in October 2016 resulting in her third pregnancy. Then at the end of this third pregnancy, the patient developed headache, nausea, and vomiting. These symptoms were contributed to probable pre-eclampsia, but this was ruled out based on patient’s normal blood pressure and lack of proteinuria. Since signs were not subsided the patient was referred to a neurologist. The MRI conducted at this time was reported as subarachnoid hemorrhage and inferior sagittal sinus thrombosis.

Based on these findings the termination of pregnancy was suggested and the patient underwent a Cesarean section at the 36th week of her pregnancy in July 2017. Then the patient was treated using anticoagulant therapy, but the overall condition of the patient did not improve after this treatment. At this point, an hCG examination was conducted with a reading of 22,000,000 IU/L and the patient was referred to the center for further management with a probable diagnosis of GTN with brain metastasis in August 2017. Based on the history as well as laboratory and imaging findings and the very high reading of hCG, the patient with GTN stage IV was diagnosed. Due to extensive intracranial hemorrhage, the patient was initially treated with whole brain radiation therapy for 10 sessions daily to address extensive metastatic lesions in the brain (Total dose: 3000cGy). Upon completion of initial radiotherapy treatment, the patient’s brain hemorrhage subsided and subsequently, the patient underwent 3 cycles of etoposide methotrexate and actinomycin-D/etoposide and cisplatin (EMA-EP) resulting in her hCG reading dropping to under
5IU/L. The treatment was continued for 2 more cycles with EMA-EP and then because of the patient becoming neutropenic and thrombocytopenic due to bone marrow suppression caused by methotrexate, three more treatment cycles were performed using paclitaxel plus carboplatin.

In total 8 courses of chemotherapy were performed which resulted in hCG reading of under 2IU/L at the patient’s last visit. At the end of chemotherapy, the patient’s neurologic signs improved and the remission of metastatic signs was confirmed in lungs and brain CT scan (Figure 2). Also following the treatment and physiotherapy the patient showed improved motion in her extremities and her speech ability. The HCG level did not increase in a follow-up 6 months after the termination of treatment.

Figure 2) Brain CT scan after radiation treatment showed right periventricular hypodense lesions

Discussion

The aim of the present study was to describe a case of misdiagnosis GTN with brain and lungs metastasis.

In the present study, a case of misdiagnosed GTN due to the absence of recommended serial checking of hCG levels following a molar pregnancy was reported (Following the second IVF in the present patient). According to the result of the present study, the importance of these serial hCG readings to confirm the normal levels of hCG since the molar pregnancy has been reported to be one of the frequent predisposing conditions for gestational trophoblastic diseases including GTN [5, 6].

It is interesting that despite this history of molar pregnancy with the start of symptoms namely headache and initial MRI findings the GTN was not considered as a differential diagnosis and patient underwent anticoagulant therapy with a diagnosis of brain infarct. It should be noted that even in presence of hCG tests a "hook effect" caused by saturation of antibodies used in pregnancy tests at hCG levels above 500,000IU/mL, resulting in false negative reading, so the probability of GTN diagnosis should be considered in all patients with a history of molar pregnancy even in absence of high hCG levels [7-9].

Another interesting aspect of this patient was the modified treatment used in the patient due to the presence of severe intracranial hemorrhage. The routine treatment for stage IV of GTN with brain metastasis is a concurrent whole brain radiation therapy (WBRT) of brain lesions and high dose etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine (EMA-CO) [10]. In the present case due to severe intracranial hemorrhage and concern for bleeding and presence of severe and progressive neurologic defects such as left hemiplegia, right hemianopia, and aphasia, it was decided to delay the chemotherapy treatment and start the treatment with WBRT alone. Upon completion of initial radiotherapy treatment, the patient subsequently underwent 3 cycles of EMA-EP resulting in her hCG reading dropping to under 5IU/L. In the present study of literature, only one similar patient reported by Girda in 2016 was found [9]. Their case was a 35-year-old woman with acute limb ischemia secondary to malignant obstruction of bilateral femoral arteries, as well as extensive intracranial, pulmonary, hepatic, splenic and cardiac metastasis two years after a first-trimester spontaneous abortion, with an initial β-hCG level of 1,228,233IU/L. Similar to the present approach, they treated their patient initially with whole WBRT for two weeks with concurrent weekly etoposide and cisplatin to address extensive metastatic disease and initially withheld chemotherapy treatment (In their case EMA-CO) due to concern for bleeding with concurrent radiation. The present success in controlling the intracranial bleeding and subsequent success in treating other metastatic masses using EMA-EP cycles reaching an hCG reading of under 2IU/L, showed that the routine concomitant therapy for stage IV patients can be successfully modified to accommodate for specific patient’s conditions.

The present case highlights the variable presentation of GTN which might easily cause misdiagnosis and delayed treatment and reiterates excellent response to treatment despite late treatment and massive tumor burden with some modifications to plan of treatment.

The limitation of this study was hard access to the patient’s first medical information and it suggests to perform a new chemotherapy method for the treatment of GTN stage 4 in cases of ovaries.

Conclusion

This case highlights the variable presentation of gestational trophoblastic disease, which might easily cause misdiagnosis and delayed treatment and shows excellent response to treatment despite late treatment and massive tumor burden with some modifications to plan of treatment.
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Ethical permissions: This case study was approved by the ethics committee of Tehran University of Medical Sciences and informed consent was obtained from the patient before reporting the case.

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