

# Gestational Trophoblastic Neoplasia with Brain Metastasis Presented with Initial Presentation of Dyspnea: A Case Report

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## Abstract

**Background:** Choriocarcinoma is the most aggressive kind of gestational trophoblastic neoplasms. Although the risk of brain metastasis in GTN is rare, in patients with choriocarcinoma the incidence of brain metastasis is 11%. We have reported a case of choriocarcinoma with brain metastasis which was successfully treated with EMACO regimen.

**Case presentation:** A 34-year-old woman was presented with vaginal bleeding, dyspnea and moderate abdominal pain. She had menstrual delay of about two weeks. She had a primary  $\beta$ -HCG of 132,600 mIU/ml. In lung CT scan, a metastatic lesion with a size of 68×50 mm was observed in the lower lobe of the left lung. The patient underwent D&C which revealed choriocarcinoma. Brain MRI also showed a small metastatic mass with a size of 7 mm at right occipital lobe. The patient was started on chemotherapy with EMACO regimen. The patient's  $\beta$ -HCG decreased continuously and it was negative after 4th cycle and 6 sessions of radiotherapy. It also remained negative 6 months after chemotherapy. The final examinations of the patients had no abnormal findings.

**Conclusion:** Brain metastasis may be relatively asymptomatic in patients with choriocarcinoma and it should be considered by physicians even when there are no neurological symptoms. Also, EMACO regimen seems to be an appropriate regimen for treatment of metastatic choriocarcinoma.

**Keywords:** Gestational trophoblastic neoplasm; Metastasis; Pleural effusion; Dyspnea

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## Introduction

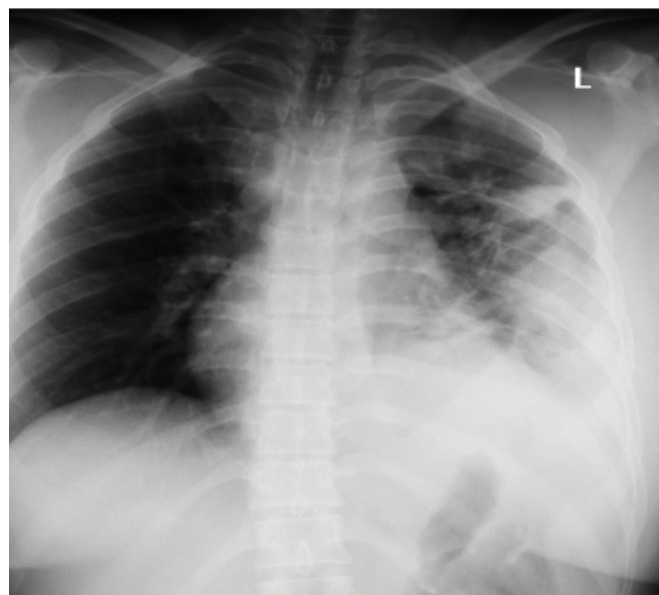
Gestational trophoblastic disease (GTD) refers to group of malignant or benign conditions [1]. Gestational trophoblast neoplasia (GTN) is a term of malignant tumors that consist of invasive moles, choriocarcinoma, placental site trophoblastic tumors (PSTT), and epithelioid trophoblastic tumors (ETT) [1]. Choriocarcinoma is the most aggressive malignant tumor with an incidence of

0.18 per 100,000 women and 1 to 9 in 40,000 pregnancies between the ages of 15-49 years in the united states [2,3]. Although the risk of brain metastasis in GTN is rare and it is approximately 2-3 cases per million pregnancies, in patients with choriocarcinoma the incidence of brain metastasis is 11%

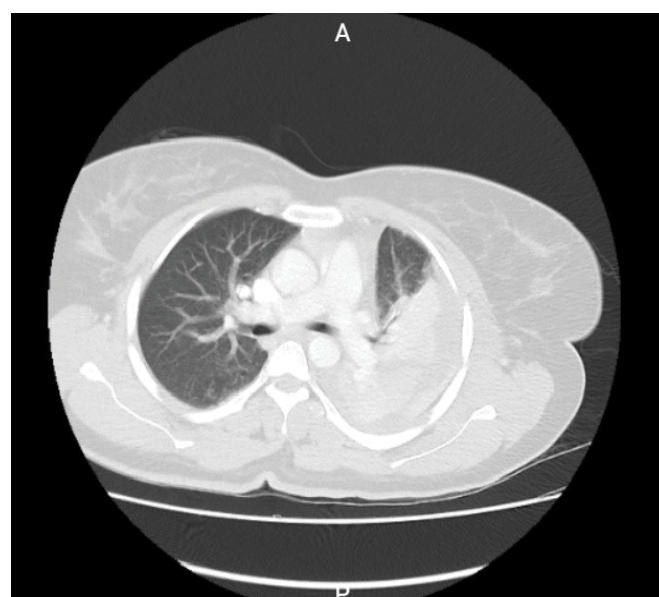
[3,4]. Due to FIGO (International Federation of Gynecology and Obstetrics) anatomic staging, patients with brain metastasis are classified at disease stage IV (2). According to this staging system, FIGO stages II–III: score >7 and Stage IV are considered as high-risk GTN and are treated with multiple chemotherapy regimens [5]. EMACO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) is used as a most common option. In brain metastases cases, an increase in the intravenous methotrexate to 1 g/m<sup>2</sup> will help better drug permeation into blood-brain barrier [6,7]. In this case report we aim to present a case of choriocarcinoma with brain metastasis with unusual initial presentation of dyspnea which was successfully treated with EMACO regimen.

## Case Presentation

A 34-year-old (gravida 5, para 3, abortion 2) presented to Gynecological Emergency Department, Motahari Hospital, Urmia, Iran with vaginal bleeding, dyspnea and moderate abdominal pain. She had menstrual delay of about two weeks. The patient's blood pressure was 90/60 mmHg, and pulse and respiratory rates were 120 and 26 per minute, respectively. The fundal height was about 8 weeks. Primary laboratory data showed a  $\beta$ -Human Chorionic Gonadotropin ( $\beta$ -HCG) of 132,600 mIU/ml and hemoglobin (Hb) of 5. The patient underwent abdominal and pelvic ultrasonography which showed a uterus larger than normal with completely heterogenic myometrium and several hypo- and hyper-echoic regions which was consistent with molar pregnancy. The endometrium thickness was also 4 mm and there was no free fluid in pelvis. The ultrasonography of abdomen and ovaries was normal. The patient also underwent chest radiography which showed pleural effusion in the left hemithorax (**Figure 1**). Three units of packed cells were given and a chest tube was inserted in the left hemithorax.  $\beta$ -HCG of pleural fluid was 64,000 mIU/ml. Then, the patient underwent a dilation and curettage (D&C). The final pathology of D&C revealed choriocarcinoma. So, the patient was transferred to Gynecology-Oncology Department for further oncologic management. The patient also underwent spiral computed tomography (CT) scan of lungs and peritoneum with and without contrast which demonstrated moderate pleural effusion in the left hemithorax. Also, collapse of left lung in the inferior regions was seen. There was no abnormality in the right lung, heart, and the large vessels of mediastinum. Finally, a round lesion with a size of 68 × 50 mm was observed in the inferior lobe of the left lung which was consistent with metastasis due to patient's history of choriocarcinoma (**Figure 2**). The patient's respiratory symptoms were mostly resolved after chest tube insertion and she underwent further chest radiography (**Figure 3**) and spiral CT scan of lungs and mediastinum (**Figure 4**) which showed a very mild pneumothorax near the tip of chest tube in the posteroinferior region of left hemithorax in the shape of a 60×60 mm loculation with air-fluid level. Collapse consolidation was also seen in the base of left lower lobe. Three days later, the patient became disoriented and neurology consultation was requested. The patient underwent brain CT scan due to neurology consultation which showed no abnormality, but brain magnetic resonance imaging (MRI) was recommended for further assessment. She underwent brain MRI which showed small mass with a size of 7 mm at right occipital lobe with several vasogenic edema which was consistent with brain metastasis. The patient was started on chemotherapy with etoposide, methotrexate (MTX), and actinomycin alternating with cyclophosphamide and vincristine (EMACO) regimen [8]. It included actinomycin 0.5 mg IV bolus, etoposide 100 mg/m<sup>2</sup> IV infusion (30 minutes), and MTX 1000 mg/m<sup>2</sup> IV infusion (24 hours) for the 1st day. It also included actinomycin 0.5 mg IV bolus, etoposide 100 mg/m<sup>2</sup> IV infusion (30 minutes), and leucovorin calcium 15 mg orally every 8 hours for nine doses starting 32 hours after start of MTX for the 2<sup>nd</sup> day. Finally, the 8th day consisted of vincristine 1.0 mg/m<sup>2</sup> IV bolus, and cyclophosphamide 600 mg/m<sup>2</sup> IV infusion. She underwent a total of four cycles and during each cycle, 2 vials of

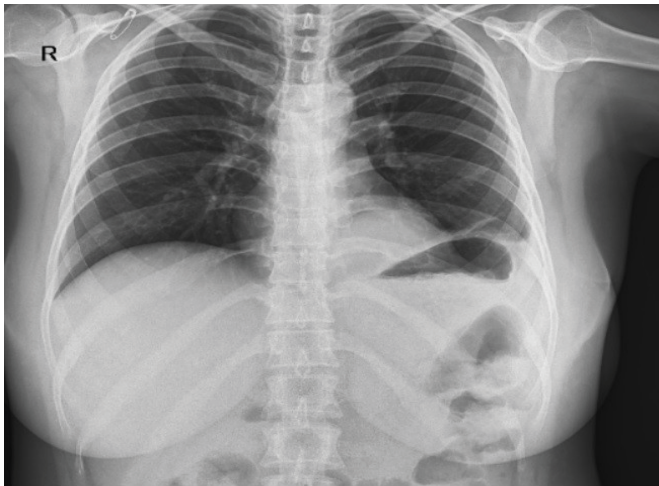


**Figure 1** Primary chest radiography of the patient presented with dyspnea, spotting, abdominal pain and menstrual delay (pleural effusion in the left hemithorax).

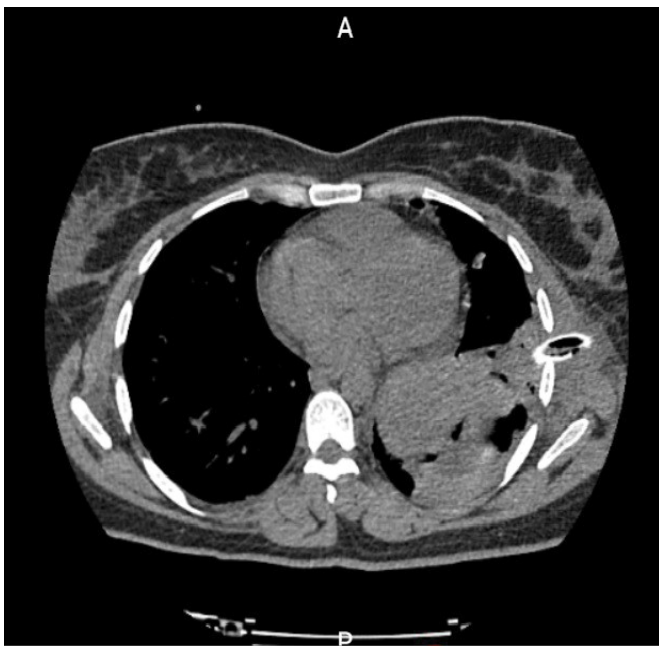


**Figure 2** Primary lung and mediastinum CT scan of the patient (moderate pleural effusion in the left hemithorax, collapse of left lung in the inferior regions, and around lesion with a size of 68×50 mm in the inferior lobe of the left lung).

G-CSF were given every other day. Only during one of the cycles, the patient did not receive G-CSF due to fever (body temperature of 38.2° C axillary), empyema, and white blood cell (WBC) count of 30,000/mm<sup>3</sup>. In that period of time, the patient underwent thoracoscopy and adhesion was observed in left pleural cavity which was resolved during thoracoscopy. It might have been the cause of incomplete drainage of pleural effusion after chest



**Figure 3** Chest radiography of patient after chest tube insertion (a very mild pneumothorax).



**Figure 4** Lung and mediastinum CT scan of patient after chest tube insertion (a very mild pneumothorax in the posteroinferior region of left hemithorax in the shape of a 60x60 mm loculation with air-fluid level and collapse consolidation in the base of left lower lobe).

tube insertion. The cytological study of pleural effusion showed reactive mesothelial cells, red blood cells and hemosiderin laden macrophages. We also administered 2 grams of intravenous ceftriaxone every 12 hours and 900 mg of clindamycin every 8 hours for two weeks. The patient's symptoms recovered after thoracoscopy and antibiotic administration and WBC count was within normal range. During chemotherapy course, patient's  $\beta$ -HCG decreased continuously and it was negative ( $\beta$ -HCG=4 mIU/ml) after 4th cycle. It also remained negative 6 months after chemotherapy. The final examinations of the patients had no

abnormal findings. After treatment, the patient underwent brain MRI and it was negative for lesions and the final chest radiography was also normal.

## Discussion

Choriocarcinoma is a highly malignant tumor that is response well to chemotherapy. The clinical presentation of choriocarcinoma is so atypical and varied in the majority of cases making it difficult to diagnose at an earlier stage. Thus patients usually presents in an advanced clinical stage [9].

One of the most common presentations of choriocarcinoma is an abnormal uterine bleeding following ectopic or normal pregnancies and spontaneous or therapeutic abortions or hydatidiform mole [10]. Frequent metastasis sites of choriocarcinoma are lung (80%), vagina (30%), liver and brain (10%). The gastrointestinal tract can also be affected [11-13]. Symptoms of brain metastasis have been various. It is presented in the form of intra or extra axial hemorrhage [14] due to intracranial aneurysm rupture [15], in the form of subdural hematoma and infarction [16]. Daniel, et al. [17] have reported a case of choriocarcinoma in the form of a stroke with right upper limb hemiparesis and right-sided facial nerve palsy [17]. Symptoms of increased intracranial pressure like headache, vomiting, personality change, and sometimes loss of consciousness have been the only presenting symptom in some cases [12].

In this case, the patient first presented with symptoms of vaginal bleeding, dyspnea and moderate abdominal pain secondary to the metastatic lesions, even though the primary site was the uterus. Our case was unique because the patient's dominant symptoms were neither vaginal nor neurologic symptoms, but dyspnea. Thus, it can be concluded that brain metastases may not be symptomatic in patients with choriocarcinoma. Due to relatively high incidence of brain metastases in choriocarcinoma, it is recommended to always consider brain metastases in each patient presented with symptoms of GTN. Especially because the mortality rate in patients with choriocarcinoma with brain metastasis is relatively high. Xiao et al. [18] reported the mortality rate of choriocarcinoma with brain metastasis as 29.7%. While, the overall mortality from GTN is estimated to be only 5%. It shows the significant difference of mortality caused by brain metastasis that accentuates the importance of early diagnosis of brain metastasis in patients presented with GTN symptoms.

For patients with high-risk metastatic choriocarcinoma, several multi-agent chemotherapy regimens have been introduced. These regimens include MAC chemotherapy (methotrexate, actinomycin D and cyclophosphamide), CHAMOCA regimen (cyclophosphamide, hydroxyurea, actinomycin D, methotrexate, doxorubicin, melphalan and vincristine) and EMACO/EMACE (cyclophosphamide vs. cisplatin). In patients treated with MAC therapy, a cure rate of 30-51% has been observed. While, in EMACO therapy, the survival rate has been estimated as about 88%. Also, it has been observed that in 75% of high-risk patients with metastatic choriocarcinoma, there was no evidence of disease after EMACO therapy [19]. As in cases of choriocarcinoma

with brain metastasis, it is required to use high-dose MTX, we have used MTX with high doses in the current patient. Frost et al. [20] has also used the same regimen for their patient with brain, lung, and vaginal metastases. Their patient was successfully treated without brain radiation or intrathecal chemotherapy. In their case, the patient underwent craniotomy with complete excision due to significant focal neurological deficits and concerns for bleeding secondary to hemorrhagic mass. In our case, we did not perform surgery because there were no focal neurologic deficits and the patient only had disorientation. Moreover, the neurological symptoms of our patient were completely cured after using EMACO regimen without performing surgery. Thus, in cases with focal neurological deficits, craniotomy is recommended,

while I patients without these kinds of deficits, we recommend rapid start of chemotherapy regimen.

## Conclusion

We can conclude that brain metastasis may be relatively asymptomatic in patients with choriocarcinoma and it should be considered by physicians even when there are no neurological symptoms. Also, EMACO regimen seems to be an appropriate regimen for treatment of metastatic choriocarcinoma.

## Conflict of Interest

The authors declare that there is no conflict of interests.

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