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# Choriocarcinoma Syndrome Is a Potentially Fatal but Curable Condition

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## ABSTRACT

**Background**: Choriocarcinoma syndrome is rare and challenging in practice. The condition is fatal if it is associated with uncontrolled bleeding. **Objectives**: The current study aimed to present our experience managing a case of choriocarcinoma syndrome, which complicated a gestational trophoblastic disease.

**Patients and methods**: A case of 35-year-old female with a history of molar pregnancy that was missed and diagnosed with choriocarcinoma stage 4. The patient suffered from a life-threatening gastrointestinal (GIT) bleeding.

**Results**: The patient was managed by intensive transfusion protocol and chemotherapy [EMA-EP protocol (etoposide, methotrexate, actinomycin D, etoposide, cisplatin) and intercaecal methotrexate]. Severe life threating bleeding stopped after 72 hours of active management and blood transfusion. Following six cycles of this protocol, BHCG level returned to normal level with marked improvement of metastatic lesions. **Conclusion**: Choriocarcinoma syndrome is a life-threatening condition that requires intensive management. Cure-rate index is high if the condition is appropriately managed.

**Keywords:** Choriocarcinoma syndrome, Gestational trophoblastic disease, ovarian choriocarcinoma, Case report, Sohag University.

## INTRODUCTION

Gestational choriocarcinoma is a rare neoplasm affecting women between the ages of 25 and 45 [(1)]. Although the disease is aggressive, the cure rate is high when proper systemic treatment is used. An uncommon but potentially fatal complication known as choriocarcinoma syndrome, which was originally identified in 1982, may appear in patients with advanced choriocarcinoma [(2)]. Serious hemorrhagic metastasis signs make up the choriocarcinoma syndrome. Patients with a high tumour burden, numerous metastases, increased tumour markers, and other characteristics of germ cell cancers are at a high risk [(3)]. Choriocarcinoma syndrome can arise spontaneously in advanced disease without any connection to the treatment, which is considerably less common, or it can occur within a few hours of the start of combination chemotherapy, which is more common [(4)]. The invasion of the blood arteries by the tumour may be related to the pathogenesis [(5)]. The prognosis for this disease is considered to be poor, especially in patients with hCG (human chorionic gonadotropin) levels exceeding 50,000 IU/L [(6)].

A shorter course of chemotherapy and a lower dose of induction chemotherapy prior to a full-dose chemotherapy regimen may be reasonable effective approaches in patients with advanced disease [(6)]; nevertheless, there is currently a paucity of information addressing the best course of treatment. Referring patients to tertiary facilities and giving induction chemotherapy in an intensive care setting may both enhance the effectiveness of treatment. In this manuscript, we present our experience in managing one of these cases and propose specific recommendations regarding the disease.

## CASE REPORT

A 35-year-old female referred to our department (Medical Oncology) from Obstetrics and Gynecology Department of Sohag University Hospital (Egypt). The patient was diagnosed with choriocarcinoma complicating missed molar pregnancy. Metastatic workup shows a huge uterine mass associated with extrauterine large pelvic mass infiltrating the intestine, innumerable large metastatic hepatic focal lesions, bilateral large metastasis to the lung and early metastatic disease to the brain with shooting BHCG level (46230 mIU/ml).

Upon admission to our department, she had marked pallor, dyspnea and tachypnea, high liver enzymes and bilirubin level. We decide to start low dose weekly chemotherapy (etoposide, cisplatin) for fear of rapid disease break down and sever bleeding (choriocarcinoma syndrome) Informed consent was discussed with the lady, who approved starting the therapy. After the 1st week chemotherapy, the hemoglobin level markedly decreased without any prove of bleeding and the condition was managed with blood transfusion but after the 2nd week the patients had sever hematemesis affecting her vital signs with very low blood pressure (systolic blood pressure below 60), week thready pulse and hemoglobin level decreased to critical levels with bleeding (4 mg /dl). Supportive measures started immediately with antihemorrhagic measures, nasogastric tube insertion and intensive hemorrhagic protocol. The sever active bleeding continue for 3 days and we couldn't establish the source of bleeding, imaging investigations couldn't detect the source of bleeding and surgical evaluation shows no indication for surgical intervention as no peritoneal collection or surgical abdomen on examination. CT angiography and upper GIT endoscopy



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were done and showed only large gastric hematoma but the source of bleeding couldn't be detected.

We suspect that the source of bleeding might be from the abdominal mass which infiltrate the intestine and bleeding occurs as a result of tumor break down once chemotherapy started or the source might be from the liver metastasis which was the most aggressive in this lady with bleeding got out from the ampulla of vater to the duodenum. Any way radiotherapy, surgery versus interventional radiology couldn't be done in this case as there is no evidence about the bleeding source. And we continue on the extensive supportive measures and scheduled chemotherapy on time.

The bleeding was severe and the patient developed disseminated intravascular coagulopathy (DIC) which complicated the condition severely and required a more meticulous approach of packed RBCs, fresh frozen plasma, cryoprecipitate and platelet transfusion.

The 3rd week low dose chemotherapy started, while the patient on bleeding (after 2 days of active bleeding). After 24 hours, the condition gradually improved, and the patient's general condition and vital signs became more stable with stoppage of bleeding. As the patient had early brain metastasis our multidisciplinary team (MDT) decided that EMA-EP with intercaecal methotrexate is an appropriate protocol for her condition, after 6 cycles the imaging shows marked reduction of the size of the widespread metastasis, and the b-HCG level became 4 mIU/mL.

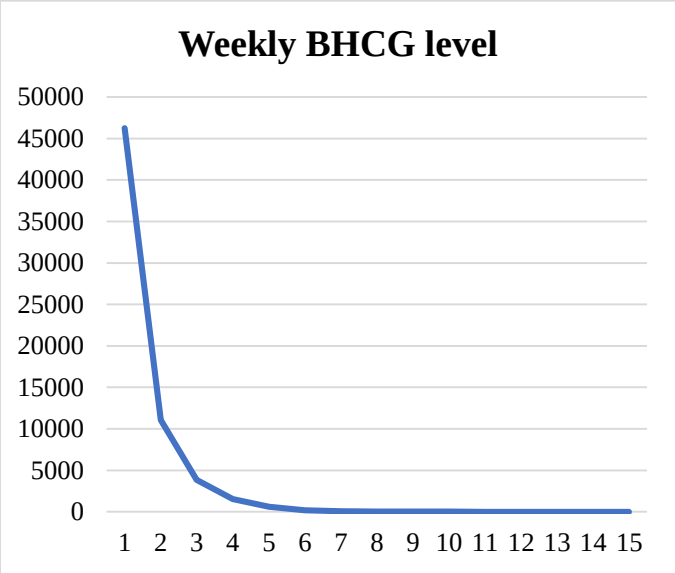


**Figure 1: Weekly B-HCG level decreased from 46230 mIU/ml to 0 within 4 months.**

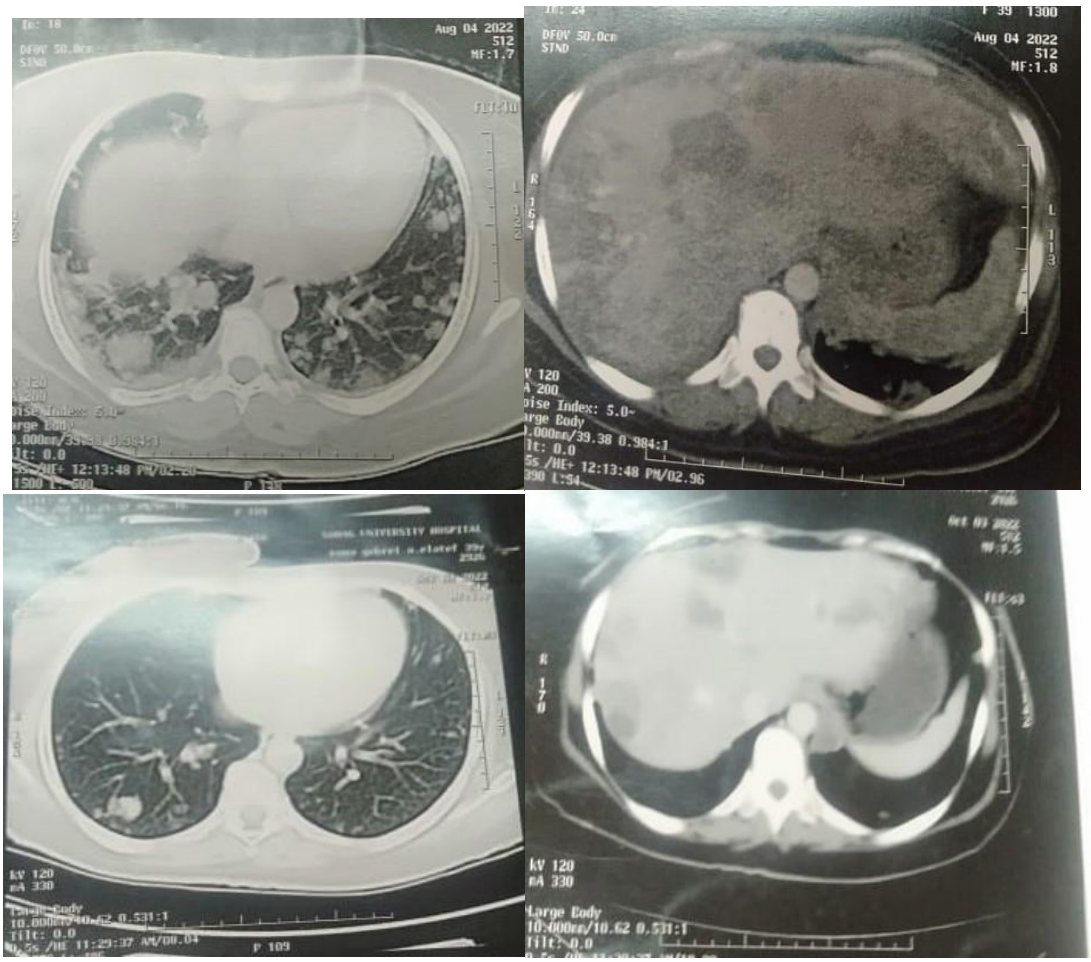

**Figure 2: Marked improvement of lung and liver metastasis after 3 cycle chemotherapy.**

**Ethical consent:** The Academic and Ethical Committee of Sohag University approved the study. The patient signed an informed written consent for the acceptance of the treatment. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

## DISCUSSION

Rapid proliferation, invasiveness, vascularity, and a propensity to overrun its blood supply with subsequent tumour necrosis are all characteristics of choriocarcinoma [(7)]. Both haematological and lymphatic spreads occur early in case of choriocarcinoma affecting the lymph nodes, lungs, liver and brain [(8)]. Patients with gestational trophoblastic disease have a known tendency to haemorrhage; choriocarcinoma syndrome is a serious and life-threatening consequence of the disease [(1)].

The biological behaviour of choriocarcinoma cells, which directly enter, erode, and damage blood vessels, can explain this complication. Additionally, some tumour cell byproducts are thought to intensify blood vessel damage without directly causing it [(9)]. Choriocarcinoma syndrome's primary cause is likely chemotherapy-induced extensive tumour lysis. No effective preventive precaution is present against the development of such life-threatening complication. In this case, we started with EP rather than EMA/EP to decrease the risk of developing choriocarcinoma syndrome. Although the complication occurred, the condition could be managed successfully with extensive supportive care and the patient completed subsequent more extensive treatment successfully. In case of high risk of developing choriocarcinoma syndrome (extensive metastasis and high tumour burden), starting with non-full dose chemotherapy as reported in our case would probably avoid the risk of choriocarcinoma syndrome, or at least lessen the severity [(10)]. The most typical choriocarcinoma syndrome presenting symptom is acute haemorrhage in the pulmonary metastasis with respiratory failure, which is usually deadly and connected to acute respiratory distress syndrome (ARDS) [(10)]. Although intrabdominal and gastrointestinal (GIT) bleeding presentations of choriocarcinoma syndrome have been recorded, they are significantly less common than haemorrhage into pulmonary metastases, which can cause bleeding issues in any organ with a high burden of metastatic choriocarcinoma [(10)]. Early detection and quick multimodal treatment are required for choriocarcinoma syndrome in order to save patients' lives. Concerning the treatment of choriocarcinoma syndrome, there is no agreement. The challenge of clinical disposition is brought up by this pressing predicament. Since patients are in such critical condition, intensive chemotherapy is rarely possible. Delaying chemotherapy, as with other extremely malignant germ cell tumours, would make the condition worse. Such efforts would produce a fair prognosis because choriocarcinoma is extremely sensitive to the appropriate chemotherapy [(11)]. We present this case of a female patient who had advanced-stage choriocarcinoma with intraperitoneal deposits and brain metastases. The patient developed severe GIT bleeding (choriocarcinoma syndrome) upon start of chemotherapy. The rapid response to chemotherapy was associated with more bleeding, especially in the first cycles. The situation even went further when disseminated intravascular coagulopathy was diagnosed. Intensive supportive measures were taken, and the patient was lucky to achieve complete remission. Unfortunately, there are no precise recommendations for managing Choriocarcinoma syndrome. It is unknown if chemotherapy precipitates the bleeding [(4)].

## CONCLUSION

Choriocarcinoma syndrome is a life-threatening consequence of gestational trophoblastic disease and is characterized by profound hemorrhage from metastatic sites. Therefore, a high index of suspicion and early recognition is needed. Choriocarcinoma syndrome should be suspected when the patient presents with a tormenting bleeding attack, augmented by radiographic evidence of metastatic lesions.

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