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SEVERE DISEASE PROGRESSION OF POSTMOLAR GESTATIONAL NEOPLASM IN A VIETNAMESE YOUNG FEMALE PATIENT AFTER TREATMENT REFUSAL: INSIGHTS FROM A CASE REPORT AND LITERATURE REVIEW

Choriocarcinoma is characterized as the most aggressive malignant alternation of gestational trophoblastic neoplasm; however, this illness is a curable malignancy. Although a rarity, this disease affects a female patient's life and causes a fatal condition. Choriocarcinoma is a life-threatening disease since it is initially insidious and can rapidly lead to masive hemorrhage, even death. Choriocarcinoma should be suspected in childbearing-age women with the high-risk scores according to FIGO. The study aims to report a severe case of widespread metastatic choriocarcinoma to optimize the treatment with multiagent chemotherapy and a multidisciplinary cooperation at our center. A G1P0 20-year-old woman was referred to the hospital for suspicion of metastatic choriocarcinoma after self-stopping chemotherapy because of the COVID-19 pandemic. During hospitalization, the tumor metastasized and presented profuse intraabdominal hemorrhage. The patient underwent immediate surgical intervention to control bleeding, and a definitive diagnosis was accurately established by the histopathological examination. After surgery, the EMA/CO regimen was administered as the first line of treatment, despite the patient being in a coma and requiring a ventilator machine. After 6 cycles of the EMA/CO regimen, her serum β-hCG level decreased to 8 mUI/mL, however, her β-hCG concentration was not down to a negative value. Thus, the patient received paclitaxel/cisplatin alternating with paclitaxel/etoposide (TP/TE regimen) for complete remission following 2 cycles. The delays in choriocarcinoma treatment are prognostic factors for worse outcomes, whereas chemotherapy may be considered a suitable treatment even in a patient's coma, thus improving a prognosis substantially.

Keywords: choriocarcinoma, chemotherapy, EMA/CO, multidisciplinary team, surgery.

Gestational trophoblastic disease (GTD) represents a variety of conditions that encompass hydatidiform moles, invasive moles, choriocarcinomas, placental site trophoblastic tumors, and epithelioid trophoblastic tumors. Among them, choriocarcinoma is usually associated with either non-gesta-

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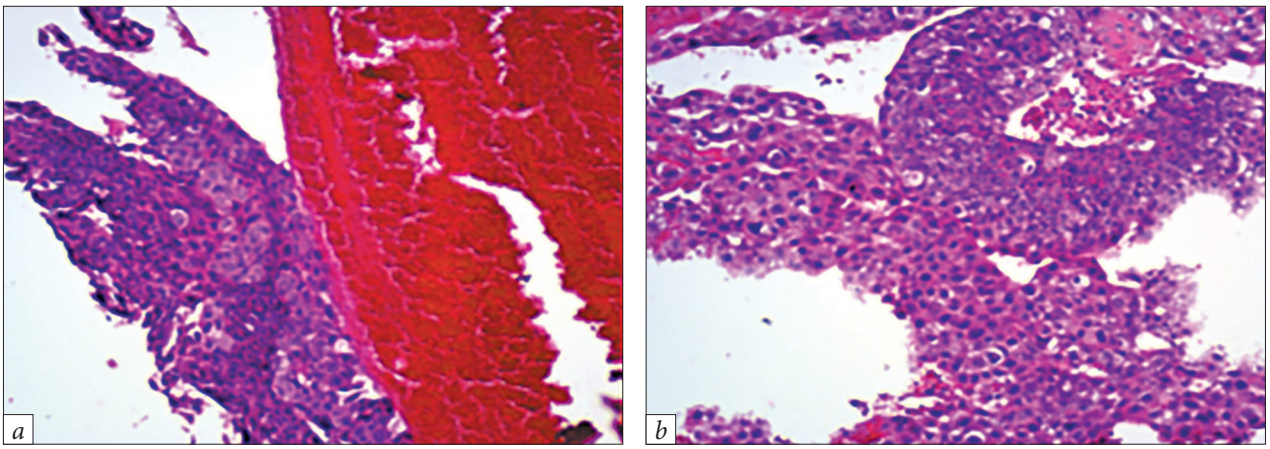

Fig. 1. Histopathological results confirming choriocarcinoma, panel (*a*) x10, panel (*b*) x40

tional events or any gestation molar pregnancy and secretes beta-human chorionic gonadotropin (β-hCG) [1, 2]. Choriocarcinoma is a very rare neoplasm with varied incidences worldwide. In Southeast Asia, 9.2 in 40,000 pregnant women and 3.3 in 40 patients with hydatidiform moles will subsequently develop choriocarcinoma. Another risk factor is a prior complete hydatidiform moles [3]. Choriocarcinoma progresses rapidly and metastasizes through a hematogenous route primarily to distant sites such as the lungs, liver, and brain. Unfortunately, it is often widespread at the time of diagnosis [4].

After treatment, the negative β-hCG levels should be checked monthly for one year [5]. Accordingly, this pathology must be treated with chemotherapy to prevent morbidity and mortality caused by uterine perforation, hemorrhage, or infection [4]. High-risk gestational choriocarcinoma patients have 91% to 93% survival after the completion of treatment utilizing multi-agent chemotherapy with or without radiation and surgery, but mortality still occurs from recurrent chemoresistant tumors [6].

Gestational choriocarcinoma with multi-organ metastases after hydatidiform mole is a rare event-not described frequently in the literature. Herein, we present a case of successful and satisfactory recovery of a young patient with metastatic choriocarcinoma treated timely by a multidisciplinary board (initially via surgical resection with following urgent chemotherapy in the state of coma), along with a brief review of the literature.

Case presentation

A 20-year-old female patient (gravida 1, para 0, complete hydatidiform mole –1), whose last pregnancy resulted in hydatidiform mole (interval from HM 16 months). She was referred to our hospital from a local hospital for presumed choriocarcinoma. Thus, she underwent the first evacuation, followed by the second curettage due to residual tissue. Histopathological evidence demonstrated complete HM (Fig. 1). During treatment, the patient was informed about the risk of malignant trophoblastic tumors after HM evacuation. Consequently, the patient was planned to receive the MTX-FA regimen (50 mg MTX intramuscularly on days 1, 3, 5, and 7 with folic acid 15 mg orally 24 h after MTX on days 2, 4, 6, and 8) over 8 days and repeated every 2 weeks. However, the patient denied the continuation of treatment, stopped at the fourth dose of MTX, and did not return to the hospital for monitoring over one year due to the COVID-19 pandemic quarantine. At that time, her β-hCG levels plateaued and continued to rise after therapeutic cessation. The serum β-hCG level resurged highly at 8,700 mUI/mL, and the patient was diagnosed with gestational trophoblastic neoplasm (GTN) stage 1 (Fig. 2).

Upon the arrival at our center, the patient's general condition was clinically unstable. On admission, the patient complained of feeling dizzy and weak with nausea and vomiting. The patient was noted to be in an unstable condition, including a tachycardia rhythm with a pulse of 120 bpm, a blood pressure of 100/60 mm Hg, a respiratory

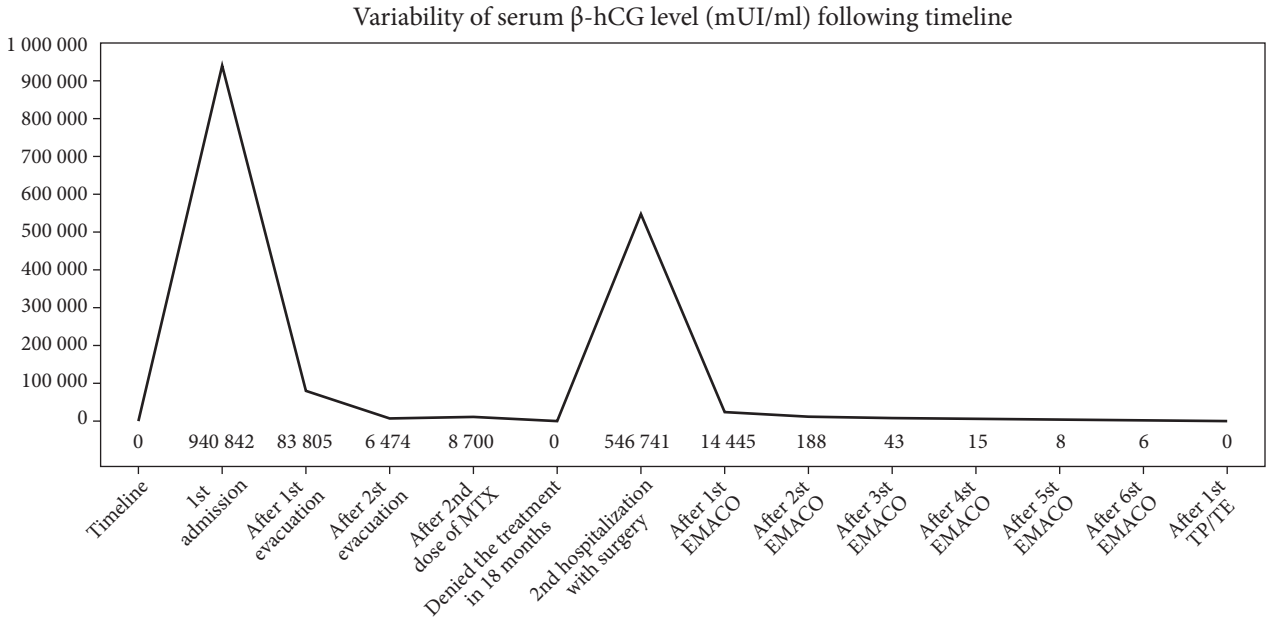

Fig. 2. Variabilities of the β-hCG levels following timeline from the onset to negative values of β-hCG

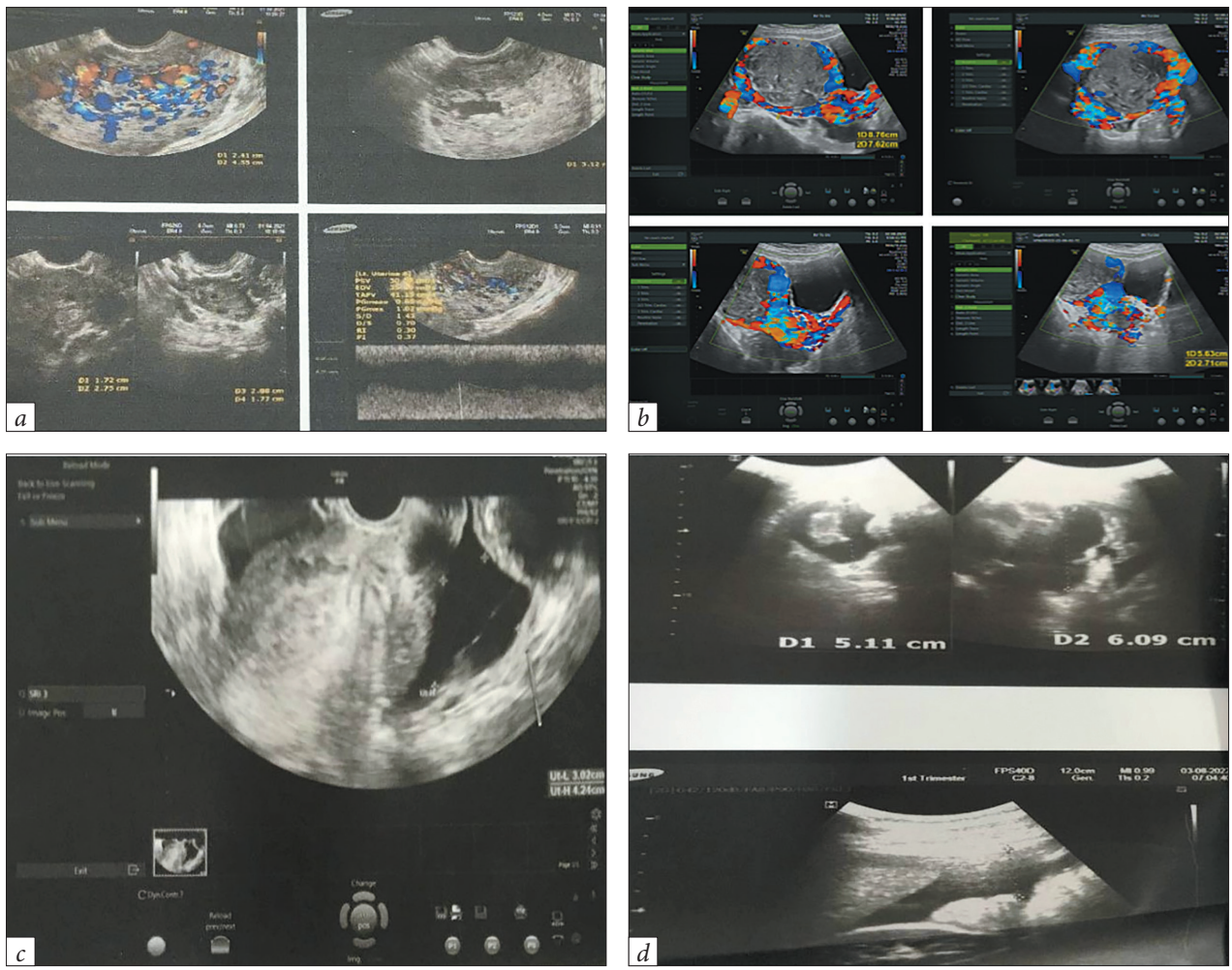

Fig. 3. Ultrasound scan showed: (*a*) Proliferative vascular corresponding to hydatidiform mole at the first admission. (*b*) Hypervascularity surrounding uterus was revealed corresponding to GTD at the second admission. (*c*) Free fluid was observed in the pelvis and cul de sac. (*d*) Fluid collection filled in the abdominal cavity

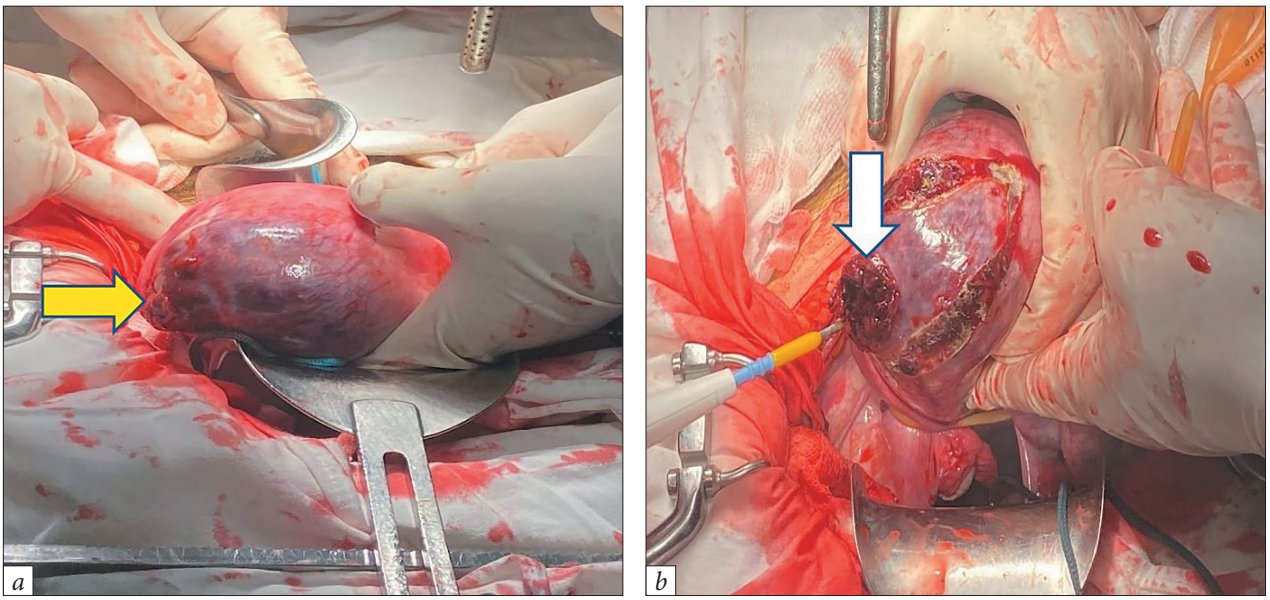

Fig. 4. Intraoperative image showed (*a*) A hypervascular focal lesion (yellow arrow) invaded to the serosal layer leading to the rupture at the left posterior fundus of the uterus and (*b*) The mass lesion (white arrow) was totally resected and hemostatic procedure was performed by electrocoagulation

frequency of 48 times/min, a saturation of peripheral capillaries at 92% with pale skin. She was determined to be in an acute respiratory distress, although both her lungs were clear, as well as rales and pleural friction sounds were not heard. No palpable enlargement of the lymph nodes or lumps beneath the skin were observed. At the gynecologic examination, the cervix was closed and the uterine size corresponded to 10 weeks. At the speculum, a bleeding spot was observed. No violet hematoma was found in the vaginal tract.

On the first day of hospitalization, the laboratory workup indicated that hemoglobin levels, platelet count, and C-reactive protein levels were 52 g/L, 85×10^9/L, and 83.3 g/L, respectively. The pretreatment serum β-hCG level was highly yielded at 546,741 mUI/mL. The coagulation disorders were slightly noticeable. The liver and kidney tests were normal. Her blood group was A Rhesus positive (A+). Abdominal ultrasound showed a heterogeneous echo of uterus about 87 × 76 × 84 mm in size without intrauterine gestational sac, the vascular proliferation spread out to the cervix, and hypervascularity structure closer to the uterus with an irregular borderline, measured approximately 56 × 27 × 42 mm (Fig. 3). The peritoneal fluid in high volume was well-defined in the abdominal cavity, up to the liver and kidney. The bilateral ovaries were normally visualized. A chest X-ray showed a pleural effusion and secondary like lesion as pulmonary metastases and also revealed a visible focal change from 13 to 80 mm in diameter, located in the left lung area. These findings were interpreted as consistent with metastatic lung disease from the choriocarcinoma (Fig. 4).

According to the FIGO staging system, the patient was classified as stage III high-risk GTN leading to the rupture of chorion mass and causing hypovolemic shock. Subsequently, the patient underwent laparotomy to promptly control the massive bleeding and lesion mass removal. Upon laparotomy, the abdominal cavity contained diffusely 1600 ml of blood, including clot and brown blood, at the bottom of the uterus reaching the left cornus, and a lesion mass of about 6 cm × 7 cm × 8 cm in size was seen and caused continuously active bleeding with a perforative point of about 1 cm × 1 cm (Fig. 4). The surgeon performed uterine tourniquet by Foley-12, opened the capsule, removed the nucleonic mass of choriocarcinoma tumor, and performed some hemostatic sutures in macroscopically bleeding sites, then placed an abdominal drain in the right iliac fossa. Totally, the patient received a total of 6 units of packed red blood cells (RBC) for acute anemia (350 mL/unit), 13 units of platelet packs (40 mL/unit), as well as fresh frozen plasma and concentrated coagulation factors.

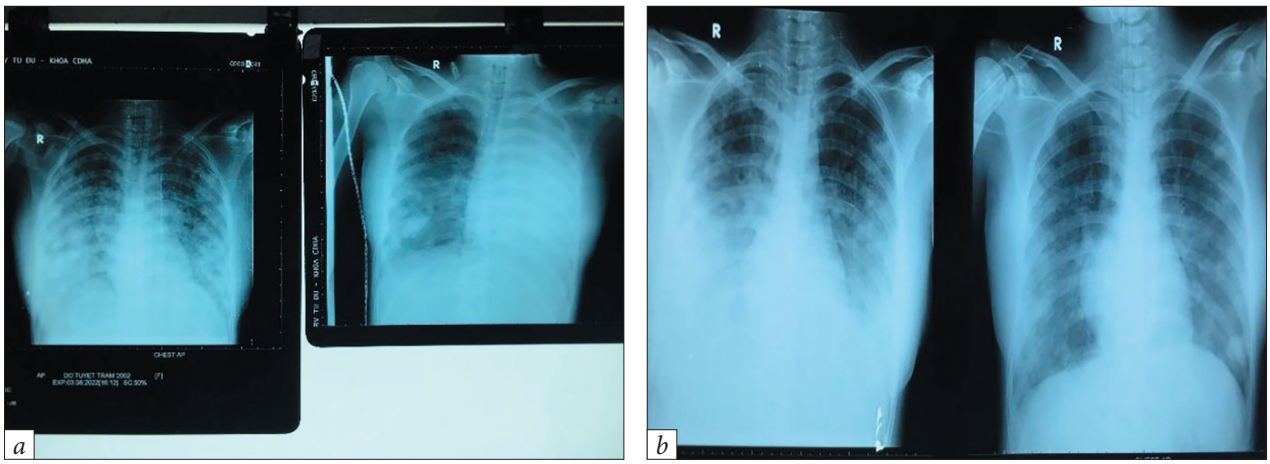

Fig. 5. Chest X-rays revealed: (*a*) Small diffused nodules, some with ground glass halos, scattered throughout both lungs compared as flaky, patchy, or cotton-like lesions along with pleural effusion. (*b*) Pulmonary lesions disappeared gradually after treatment

After surgery, she was immediately followed up in the intensive care unit (ICU) for two weeks. On the postoperative course, the patient's condition was unstable, and she suffered disorders of coagulopathy, severe anemia, electrolyte disturbance, pneumonia, sepsis, multiorgan failure, hypertension, and coma. Her consciousness state was deteriorated and the Glasgow Coma Scale was evaluated at $E_2V_2M_4$. She underwent machine ventilation, a tracheostomy, sedative drugs, antihypertensive drugs, and muscular relaxers. At this stage, the patient received additional transfusion of 6 units packed RBC (350 mL/unit), 3 units of frozen plasma (200 mL/unit), 6 packs of platelet transfusion (40 mL/unit), and 3 packs of cryoprecipitate.

Unfortunately, due to the presence of coma and supported machine ventilation, pneumonia was progressive and the tracheal liquid culture was obviously positive for *Candida spp.,* and her urine culture showed *Candida tropicalis*. The team also excluded pulmonary tuberculosis by laboratory testing since Vietnam is an epidemic area of tuberculosis. In addition, the findings suggested severe infection with a high increase of white blood cells up to 27,000/mm^3 and a CRP of 85.3 mg/dL (Table 1). Thus, she was given intravenous broad-spectrum antibiotics for 14 days.

Although the site and number of metastases were unidentified due to the lack of imaging evidence, the patient was classified as high-risk following the FIGO score (modification from the World Health Organization scoring system based on prognostic factors) (Table 2).

After multidisciplinary counseling among obstetricians, anesthesiologists, gynecological oncologists, nutritionists, and clinical pharmacists, multiagent chemotherapy was scheduled. The patient received the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine) regimen as the first line chemotherapy (Table 3).

Following the first regimen, the chemotherapeutic effect was remarkable, as evidenced by the shrinkage of metastatic foci and the gradual fall

Table 2. **Blood count follow-up in intensive care unit (ICU)**

Blood count	2/8	3/8		4/8			5/8	7/8	8/8	9/8
		Morning	Afternoon	Morning	Afternoon	Evening				
WBC	16.83	21.24	11.39	13.45	12.12	27	24	14.57	16.8	124
Hb	5.2	6.9	6.7	7.3	6.2	8.5	8.6	6.9	7.5	7.8
PLT	85	71	58	46	94	84	104	100	141	123

Notes: Hb — hemoglobin; PLT — platelets; WBC — white blood cells.

of serum β-hCG levels. Following 3 days of the EMA/CO regimen, the patient recovered in a healthy condition. After six days, she opened her eyes and communicated with the staff. At that time, her blood analysis revealed WBC of 12,400 cells/mm^3, Hb of 7.8 g/dL, and PLT of 123,000/mm^3.

Two weeks later, the patient was transferred to the Gynecologic Oncology Department for the continuation of treatment. She recovered quickly, walking and eating normally. After two courses of EMA/CO, her serum β-hCG level dropped to 14,445 mUI/mL. Thus, the patient was discharged

Table 2. **WHO scoring system based on prognostic factors**

WHO risk factor scoring with FIGO staging	First hospitalization	Score	Second hospitalization	Score
Age (years)	19	0	20	0
Antecedent pregnancy	Absence	0	Complete hydatidiform	0
Interval from index pregnancy, months	1 month	0	16 months	4
Pretreatment β-hCG (mIU/ml)	940,842	4	83,805	4
Largest tumor size including uterus (cm)	9.5	2	8.7	2
Site of metastases including uterus	Absence	0	Lung*	0
Number of metastases identified	Absence	0	Unidentified	—
Previous failed chemotherapy	None	—	Denied treatment	—
Total score (points)		6 (Low-risk)		At least 10 (High-risk): Stage III

Note: Brain metastasis was unknown since the MRI and CT scan were not performed in coma condition at the ICU.

Table 3. **Multi-agent chemotherapy with EMA/CO and TP/TE regimens**

EMA/CO		TP/TE	
DAY 1		*DAY 1*	
Etoposide	100 mg/m^2 intravenous infusion over 30 min	Paclitaxel	135 mg/m^2 in 250 ml NS over 3 h iv
Actinomycin D	0.5 mg intravenous bolus	Cisplatin	60 mg/m^2 in 1 L NS over 3 h iv
Methotrexate	100 mg/m^2 intravenous bolus 200 mg/m^2 intravenous infusion over 12 h		
DAY 2		*DAY 15*	
Etoposide	100 mg/m^2 iv infusion over 30 min	Paclitaxel	135 mg/m^2 in 250 ml NS over 3 h i.v.
Actinomycin- D	0.5 mg iv bolus	Etoposide	150 mg/m^2 in 1 L NS over 1 h iv
Folic acid rescue	15 mg intramuscularly or orally every 12 h for four doses (starting 24 h after beginning the methotrexate infusion)		
Regimen 2			
DAY 8			
Vincristine	1 mg/m^2 iv bolus (maximum 2 mg)		
Cyclophosphamide	600 mg/m^2 iv infusion over 30 min		

Notes: NS — normal saline, iv — intravenous.

home for a week and then returned to complete the course of chemotherapy. Chemotherapy was continued until serum β-hCG values were normalized and followed by at least two to three courses of consolidation chemotherapy to eradicate all viable tumors. Before the third course of EMA/CO, the β-hCG level was 43 mUI/mL. After 6 cycles of intravenous EMA/CO, the pulmonary lesions vanished completely and the serum β-hCG level fell to 6 mIU/mL (Fig. 5). However, it did not completely decrease to negative values. Thus, the patient received paclitaxel/cisplatin alternating with the paclitaxel/etoposide schedule (alternative TP/TE regimen) for a complete remission. Her body mass index was 16.2 kg/m^2. Her body surface area was 1.5 m^2 when using the EMA/CO regimen and 1.36 m^2 when using the TP/TE regimen, respectively. After two cycles of TP/TE chemotherapy, her β-hCG concentration remained consistently below detectable levels for 6 months, thus the chemotherapy was ceased completely. During chemotherapy, the patient was observed without remarkably severe complications except for anemia and a decreased WBC count. Subsequently, she received 2 units of red blood cell packs and granulocyte colony-stimulating factors (G-CSFs) for bone marrow-stimulation.

The patient felt satisfied with the treatment, and her family was grateful to the hospital for saving her life in a severe condition where "it hangs by a thread". Before discharging, the girl wrote a handwritten letter with notes of gratitude to the doctors and nurses who helped her revive from death and preserve her reproductive function. Following the treatment, she has been monitored for one year without complications. Today, she is in good condition, and regular follow-up has been uneventful afterward.

Discussion and literature review

Etiology. Gestational choriocarcinoma is a rare malignant disease that develops from an abnormal trophoblastic proliferation during hydatidiform mole, a normal pregnancy, or, most commonly, a spontaneous abortion. As compared with the hydatidiform mole, which accounts for 80% of all GTD cases, choriocarcinoma is relatively rare [7]. Choriocarcinoma is part of the spectrum of disorders of gestational trophoblastic neoplasms, and it commonly occurs in women of childbearing age. Rarely, it occurs in the younger female population, coexisting with a live fetus, or in postmenopausal women [8—10]. Despite the rarity, by the report of Argawal et al. [11], 76/13960 (<1%) patients with hydatidiform moles have persistently high β-hCG concentrations of above 5 UI/6 months after evacuation. Thus, we postulated a previous molar pregnancy without strict follow-up as the cause of choriocarcinoma in our patient.

Symptoms. Regarding the clinical manifestations, menorrhagia is the most common presentation. Generally, patients with choriocarcinoma may develop corresponding acute symptoms and be misdiagnosed due to multiple organ metastases. GTN is even harder to diagnose if the primary site of metastasis is unknown. Patients with pulmonary metastatic lesions present infrequently with cough, dyspnea, respiratory dysfunction, hemoptysis, or signs of pulmonary hypertension similar to primary pulmonary malignancy [15, 16]. Very rarely, a gum metastasis leading to bleeding gums and a renal metastasis resulting in hematuria were also reported in the literature. Therefore, any signs associated with vaginal bleeding without a clear etiology should be considered a clue to metastatic GTN in the case of an abnormal β-hCG elevation [17, 18]. Cerebral involvement is encountered in patients who have had an antecedent molar pregnancy and a protracted delay in tumor diagnosis. In our case, the patient refused follow-up because of Covid-19, thus extrauterine symptoms progressed seriously. Multi-organ insufficiency and severe coagulopathy as worsening outcomes of GTN metastasis were mentioned in several reports, particularly, in the patients requiring surgical intervention [8, 15].

Diagnosis. Serum The β-hCG concentration is an excellent biomarker of disease progression, response, and subsequent post-treatment surveillance. Plateaued or rising β-hCG levels can occur in 15%—20% and 0.5%—5% of complete and partial hydatidiform mole, respectively [5]. In the present case, serum β-hCG concentration increased highly during the first and the second hospitalization. Moreover, patients with GTN should also undergo a thorough imaging assessment to determine the extent of the disease. The initial evaluation includes a chest X-ray, pelvic ultrasound, and abdominal ultrasound [6]. Exploratory ultra-

sound plays an important role in the diagnosis of lesions associated with hypervascular proliferation. Brain magnetic resonance imaging (MRI) or CT scan with contrast should be performed in any patient with pulmonary metastases or neurologic symptoms [4]. Although the chest X-ray is considered adequate for lung metastasis detection, smaller pulmonary lesions can be missed on conventional radiographs. Meanwhile, a CT scan is recommended to confirm pulmonary metastatic disease and determine the cancer stage [19]. However, chest X-rays were commonly used since this modality is cheaper, reproducible, and available [20]. In our case, the patient could not assess the CT scan as well as MRI workup since she was in a coma condition and required a ventilation machine. Therefore, we did not investigate more for cerebral metastasis.

Choriocarcinoma spreads mainly to the lung, vagina, liver, and central nervous system. Extremely rare, this malignancy can metastasize to the kidney and skin [18]. The most common metastatic site is the lung (80%), and the occurrence of respiratory failure requiring intubation is an independent factor for poor outcome, whereas metastasis to the brain occurs in 10% of patients. Particularly, choriocarcinoma can be present primarily in the lung [16].

The histopathological endpoint accurately verifies this pathology. The histological pattern is characterized by the presentation of cytotrophoblasts and syncytiotrophoblasts without chorionic villi. However, if GTN metastasis is highly suspected, an initial biopsy is not recommended due to the risk of massive hemorrhage. The response to chemotherapy may also support the diagnosis of GTN [17]. As in the present case, the specimen was revealed in the surgery for the purpose of hemostasis.

Treatment. In this context, to avoid adverse complications, a multidisciplinary team involving a gynecologist, a surgical oncologist, and an anesthesiologist is mandatory, thereby reducing the morbidity and mortality rates. A stratified treatment should be administered according to the FIGO staging and WHO prognostic scoring systems. Surgery was immediately performed in an emergency situation due to a ruptured metastasis mass and malignant lesion removal [13]. Great caution is used in attempting excision of any metastatic disease site due to the risk of profuse hemorrhage, except for an emergency condition involving hemodynamic instability and a consequence of disseminated intravascular coagulation. Therefore, metastasis should generally not be resected and ought to be alternately treated by upfront chemotherapy.

Despite the tremendous tendency to metastasize widely, GTN is one of the solid tumors most curable with chemotherapy. These lesions respond relatively well to chemotherapy, and this treatment is associated with good results. Chemotherapy for high-risk GTN includes etoposide, methotrexate, and dactinomycin alternating with cyclophosphamide and vincristine (EMA/CO) [21]. This regimen is well-tolerated and highly effective (83% survival rate and cure rate as high as 100%) for high-risk GTN and should be considered the primary treatment in most circumstances [7]. According to the study of Li et al. [22], for the GTN patient with a FIGO score of 12 or greater, the EMA/CO, etoposide-platinum alternating with the EMA (EP/EMA), and floxuridine actinomycin-etoposide-vincristine (FAEV) were the three most commonly used regimens. The complete response rate was 55.2%, 60.0%, and 63.1% for the EMA/CO, EP/EMA, and FAEV, respectively. In the present case, following 6 cycles of the EMA/CO regimen, serum β-hCG decreased to 6 mUI/mL. However, since the β-hCG concentration remained slowly negative, the team had a precaution of adverse side effects of repeated EMA/CO cycles. Thus, the TP/TE regimen was used to achieve the complete remission. To our knowledge, no evidence has been demonstrated of how many repeated cycles are required to obtain the negative value of the β-hCG concentration.

According to some reports, another treatment option is to start chemotherapy in GTN with massive disease or metastatic sites likely to bleed profusely (such as the liver and brain) with a single or double agent rather than multi-agent treatment. There is also a probability of systemic toxicity and recurrence. Furthermore, chemotherapy has limited effects on recurrent tumors due to their chemoresistance. It is imperative to overcome these problems in order to effectively treat the tumors at the metastatic site [7]. Recently, although some data have been reported on the role of immunotherapy in GTN resistant to classical chemotherapy regimens; the patient also follows

the treatment strictly to avoid the chemoresistance. Brain metastases are treated by radiotherapy along with chemotherapy. The primary target of radiation is to reduce the incidence of spontaneous intracranial bleeding during or, more commonly, after chemotherapy [23].

Outcomes and follow-up. Overall, the treatment with chemotherapy was uneventful. The serum β-hCG level returned to negative values. No abnormal mass has been revealed on follow-up yet. The metastatic lesions disappeared after two cycles of the multi-agent chemotherapy, and complete remission was achieved after six cycles of EMA/CO and 2 cycles of TP/TE. Serum β-hCG is a sensitive marker for evaluating therapeutic efficacy and follow-up after remission [13]. After plasma β-hCG normalization is achieved, patients with GTN should be managed with serial determinations of the β-hCG levels at 2-week intervals during the first 3 months of remission and then at monthly intervals for at least 12 months [5]. The risk of recurrence after 1 year of remission is less than 1% and is higher for patients with high-risk GTN. Therefore, high-risk patients should receive β-hCG monitoring at 6 to 12-month intervals beyond the first year of remission [24]. At the time of writing this paper, the patient is being monitored and has been in complete remission after 6 months of follow-up.

Prognosis. The prognosis of chemosensitive choriocarcinoma remains good with 90% survival outcomes after 5 years. Importantly, the recurrences occur many years after the complete remission of GTN. The overall recurrence rates after treatment with the EMA/CO regimen has been reported to be approximately 11%—19% [12].

Regardless of the contraception, the oral contraceptives should be used during chemotherapy and the first year of remission after treatment of GTN [5]. Because of the 1%—2% risk for the second molar in a subsequent pregnancy, the ultrasound examination at 8 weeks is recommended during all future pregnancies in addition to histological evaluation of the placenta and post-delivery β-hCG examination but there are no studies detailing the utility of these measures. It has not been reported on increasing the risk of congenital malformations or other complications related to pregnancy in this context [4]. Patients treated with EMA/CO had a 13% risk of menopause at the age of 40 and 36% by the age of 45. The risk of early menopause in this group increased in women treated after the age of 30 [25].

Indeed, an early diagnosis, proper treatment modalities, and chemotherapeutic agents can improve control of the disease and increase the survival rate. The gynecologist should be aware of all possible metastatic sites of GTN. Moreover, the fatal complications relating to this disease should be noticed as early as possible. Therefore, this case report may help less experienced clinicians consider possible combinations of chemotherapy treatment in patients undergoing surgery and complication in multiorgan metastases.

To sum up, a high-risk hydatidiform mole without a follow-up and sufficient chemotherapy can develop rapidly into choriocarcinoma in the absence of proper management. A multidisciplinary team ought to be required to ensure timely and successful management of the clinical condition and for fertility-preserving treatment. Multi-agent chemotherapy should be used for the elimination of choriocarcinoma. EMA/CO regimen can be used to limit the progression of tumor following hemodynamic stabilization in the condition of a ruptured tumor.

Ethical Approval

Ethics approval was naturally waived for case reports by the ethics committee of Tu Du Hospital. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate

Written informed consent was obtained from all participants.

Consent for publication

Written informed consent was obtained from the patient for publication of this study and accompanying images.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests. This manuscript has not been published and is not under consideration for publication elsewhere. Additionally, all of the authors have approved the contents of this paper and have agreed to the journal's submission policies.

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Author's contributions

TNV was involved in patient care, collected the data, and reviewed the final manuscript. PNN organized to collect data and contributed to writing, editing, and revising the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Yu X, Du Q, Zhang X, et al. Pure primary non-gestational choriocarcinoma originating in the ovary: A case report and literature review. *Rare Tumors*. 2021;13:20363613211052506. https://doi.org/10.1177/20363613211052506
2. Yee LS, Zakaria R, Mohamad N, Fong OW. Non-gestational choriocarcinoma of the ovary: A case report. *J Taibah Univ Med Sci*. 2021;16(4):632-636. https://doi.org/10.1016/j.jtumed.2021.01.001
3. Bishop BN, Edemekong PF. *Choriocarcinoma*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535434/
4. Soper JT. Gestational trophoblastic disease: current evaluation and management. *Obstet Gynecol*. 2021;137(2):355-370. https://doi.org/10.1097/AOG.0000000000004240
5. Ngan HYS, Seckl MJ, Berkowitz RS, et al. Diagnosis and management of gestational trophoblastic disease: 2021 update. *Int J Gynaecol Obstet*. 2021;155(S1):86-93. https://doi.org/10.1002/ijgo.13877
6. Feng X, Wei Z, Zhang S, et al. A review on the pathogenesis and clinical management of placental site trophoblastic tumors. *Front Oncol*. 2019;9:937. https://doi.org/10.3389/fonc.2019.00937
7. Kim GS, Hwang KA, Choi KC. A promising therapeutic strategy for metastatic gestational trophoblastic disease: Engineered anticancer gene expressing stem cells to selectively target choriocarcinoma (Review). *Oncol Lett*. 2019;17(3):2576-2582. https://doi.org/10.3892/ol.2019.9911
8. Li XM, Liu XY, Liu ZX. Choriocarcinoma with multiple lung, skull and skin metastases in a postmenopausal female: A case report. *Oncol Lett*. 2015;10(6):3837-3839. https://doi.org/10.3892/ol.2015.3750
9. Shen C, Ai L, Li K, et al. Choriocarcinoma brain metastasis in a patient in the third trimester: a case report. *J Med Case Rep*. 2021;15(1):417. https://doi.org/10.1186/s13256-021-02808-3
10. Ding W, Zhang N, Rao Y, et al. A successfully treated multiple metastatic choriocarcinoma coexistent with live fetus: a case report and literature review. *Front Oncol*. 2021;11:777707. https://doi.org/10.3389/fonc.2021.777707
11. Agarwal R, Teoh S, Short D, et al. Chemotherapy and human chorionic gonadotropin concentrations 6 months after uterine evacuation of molar pregnancy: a retrospective cohort study. *Lancet*. 2012;379(9811):130-135. https://doi.org/10.1016/S0140-6736(11)61265-8
12. Ghaemmaghami F, Karimi Zarchi M. Early onset of metastatic gestational trophoblastic disease after full-term pregnancy. *Int J Biomed Sci*. 2008;4(1):74-77. PMID: 23675070; PMCID: PMC3614675.
13. Song L, Li Q, Yin R, Wang D. Choriocarcinoma with brain metastasis after term pregnancy: A case report. *Medicine*. 2018;97(42):e12904. https://doi.org/10.1097/MD.0000000000012904
14. Reddy R. Rare case of a young female with co-existent hydatidiform mole and pulmonary metastases: an underrecognized entity. *Cureus*. 2021;13(12):e20245. https://doi.org/10.7759/cureus.20245
15. Zhang W, Liu B, Wu J, Sun B. Hemoptysis as primary manifestation in three women with choriocarcinoma with pulmonary metastasis: a case series. *J Med Case Rep*. 2017;11(1):110. https://doi.org/10.1186/s13256-017-1256-9

16. Rali P, Xie J, Rali G, et al. A rare case of metastatic choriocarcinoma of lung origin. *Case Rep Pulmonol*. 2017;2017:4649813. https://doi.org/10.1155/2017/4649813
17. Jareemit N, Benjapibal M. Gestational trophoblastic neoplasia with gum metastasis: a case study and literature review. *Case Rep Oncol*. 2020;13(2):485-490. https://doi.org/10.1159/000506329
18. Parajuli P, Poudyal S, Chapagain S, et al. Gestational choriocarcinoma presenting with bilateral kidney and lung metastases with unknown primary: An uncommon clinical scenario. *Urol Case Rep*. 2020;33:101433. https://doi.org/10.1016/j.eucr.2020.101433
19. Hong T, Hills E, Aguinaga MDP. Radiographically occult pulmonary metastases from gestational trophoblastic neoplasia. *Radiol Case Rep*. 2017;12(2):292-294. https://doi.org/10.1016/j.radcr.2017.01.007
20. Braga A, Elias KM, Horowitz NS, Berkowitz RS. When less is more: regarding the use of chest X-ray instead of computed tomography in screening for pulmonary metastasis in postmolar gestational trophoblastic neoplasia. *Br J Cancer*. 2021;124(6):1033-1034. https://doi.org/10.1038/s41416-020-01209-5
21. Alazzam M, Tidy J, Osborne R, et al. Chemotherapy for resistant or recurrent gestational trophoblastic neoplasia. *Cochrane Database Syst Rev*. 2016;2016(1):Cd008891. https://doi.org/10.1002/14651858.CD008891.pub2
22. Li J, Yue H, Wang X, et al. Chemotherapy for gestational trophoblastic neoplasia patients with a FIGO score of 12 or greater: A multistudy analysis. *Eur J Obstet Gynecol Reprod Biol*. 2019;238:164-169. https://doi.org/10.1016/j.ejogrb.2019.05.023
23. Tsai J, Vellayappan B, Venur V, et al. The optimal management of brain metastases from gestational trophoblastic neoplasia. *Expert Rev Anticancer Ther*. 2022;22(3):307-315. https://doi.org/10.1080/14737140.2022.2038566
24. Aznab M, Nankali A, Daeichin S. Determination of clinical process and response rate to treatment in patients with gestational trophoblastic neoplasia (GTN) with low and high risk and evaluation of their first pregnancy outcome. *Int J Hematol Oncol Stem Cell Res*. 2018;12(4):291-297. PMID: 30774829; PMCID: PMC6375376.
25. Savage P, Cooke R, O'Nions J, et al. Effects of single-agent and combination chemotherapy for gestational trophoblastic tumors on risks of second malignancy and early menopause. *J Clin Oncol*. 2015;33(5):472-478. https://doi.org/10.1200/JCO.2014.57.5332

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ТЯЖКИЙ ПЕРЕБІГ ГЕСТАЦІЙНОЇ ТРОФОБЛАСТИЧНОЇ НЕОПЛАЗІЇ У МОЛОДОЇ ЖІНКИ З В'ЄТНАМУ ПІСЛЯ ПРИПИНЕННЯ ХІМІОТЕРАПІЇ: АНАЛІЗ КЛІНІЧНОГО ВИПАДКУ ТА ОГЛЯД ЛІТЕРАТУРИ

Хоріокарцинома є найбільш агресивною за проявом гестаційною трофобластичною неоплазією. Тим не менше, вона є виліковною в разі застосування відповідної терапії. Хоча це захворювання є досить рідкісним, воно може призвести до фатальних наслідків. Хоріокарцинома є загрозливим для життя захворюванням, яке на початку може бути безсимптомним, але швидко прогресує, призводячи до масивної кровотечі з можливим летальним наслідком. Її можна підозрювати у жінок дітородного віку з високим ризиком щодо гестаційної трофобластичної хвороби за критеріями FIGO. У цьому повідомленні аналізується тяжкий випадок метастатичної хоріокарциноми і оптимізації лікування хворої завдяки застосуванню поліхіміотерапії і багатопрофільному підходу до терапії. 20-річна жінка зі статусом G1P0 була направлена до клініки з підозрою на метастатичну хоріокарциному після припинення хіміотерапії через пандемію COVID-19. Під час перебування в клініці пухлина метастазувала, що призвело до профузної внутрішньочеревної кровотечі. Для припинення кровотечі було проведено термінове хірургічне втручання. Матеріал, одержаний при втручанні, було піддано гістопатологічному дослдженню, що дозволило точно встановити діагноз. Після хірургічного втручання було призначено поліхіміотерапію за схемою EMA/CO як першої лінії терапії, хоча хвора знаходилась у комі і потребувала штучної вентиляції легень. Після шести циклів EMA/CO рівень сироваткового β-hCG знизився, хоча й тільки до 8 мМО/мл. Для повної ремісії застосовували два цикли чергування паклітакселу/цисплатину та паклітакселу/етопозиду (схема TP/TE). Відтермінування хіміотерапії хворих на хоріокарциному може призводити до тяжких наслідків. У той же час, навіть у стані коми своєчасне застосування хіміотерапії дозволяє суттєво покращити прогноз захворювання.

Ключові слова: хоріокарцинома, поліхіміотерапія, схема EMA/CO багатопрофільний підхід.