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Postpartum choriocarcinoma complicated by uterine perforation: A case report and literature review

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ABSTRACT

Choriocarcinoma is a rare, aggressive gestational trophoblastic disorder with metastatic potential, often presenting with abnormal bleeding and increasing levels of beta-human chorionic gonadotropin (b-hCG). Diagnosis is confirmed through histopathologic examination after curettage, and treatment typically involves stage-dependent chemotherapy. This case report concerns a 25-year-old woman with heavy postpartum bleeding, later diagnosed with choriocarcinoma. Despite initial single-agent chemotherapy, disease progression led to uterine perforation and hemoperitoneum, requiring emergency surgery. Following recovery, multi-agent chemotherapy resolved her symptoms. Choriocarcinoma's rarity and varied presentation make diagnosis challenging, with lung metastases common. Levels of b-hCG indicate treatment response, and prompt management combining chemotherapy, monitoring, and surgery is crucial for positive outcomes.

1. Introduction

Choriocarcinoma is a rare and aggressive tumor characterized by trophoblastic differentiation [1]. It occurs in approximately 1 in 50,000–100,000 pregnancies [2] and can develop following a partial mole, complete mole, miscarriage, ectopic pregnancy or normal pregnancy [3]. The primary clinical presentations of this condition are abnormal uterine bleeding and increased levels of beta-human chorionic gonadotropin (b-hCG) [6]. Less frequently, patients may exhibit hemoptysis, dyspnea, coughing, or pleuritic chest pain. In the absence of timely intervention, the disease has the potential to metastasize, leading to severe complications such as cerebral hemorrhage and hepatic hematoma [4]. Diagnosis is confirmed through histopathologic examination of the placenta or endometrial tissue obtained via curettage [5]. Treatment typically involves chemotherapy, with the selection of appropriate drugs based on the tumor's stage and histology. Following successful treatment, women can generally expect favorable pregnancy outcomes, comparable to those in the general population, although with slightly increased risk of stillbirth [6].

In this report, we present a case of a 25-year-old pregnant woman who presented with heavy postpartum bleeding and was diagnosed with choriocarcinoma. Chemotherapy was successful.

This case has been reported in line with SCARE criteria [7].

2. Case Presentation

A 25-year-old woman, gravida 2, para 2, presented to hospital 5 weeks after an uncomplicated vaginal delivery of a healthy newborn, complaining of passing large clots (measuring up to 2.5 cm × 3 cm) for two weeks. The clots passed once every 4–6 h, between which she would have light, fresh-colored vaginal bleeding. Associated symptoms, such as abdominal pain, fever, chills, dizziness, dysuria, or bad odors, were denied. The patient had no medical conditions or previous surgeries and did not use tobacco or alcohol. She had normal findings on general examination. On abdominal examination, the uterus was not palpable, there was no tenderness or other palpable masses, and there were no vaginal or cervical abnormalities on speculum examination. Ultrasound showed an intrauterine hyperechoic, well-circumscribed 2 × 2 cm mass originating from the endometrium. Laboratory results showed a b-HCG level of 13,611 mIU/mL, a hemoglobin level of 10.1 g/dL, and normal white blood cell count, platelet count, liver, and kidney function tests. She was admitted on the same day for a diagnostic dilation and curettage (D&C) procedure, which was done with no complications, and a biopsy was taken.

A week before presenting to hospital, the patient had attended an outpatient clinic with the same complaint. On initial workup, ultrasound showed an endometrial thickness of 1.1 cm in the lower segment. She

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was diagnosed with retained products of pregnancy and was primarily managed with misoprostol (200 μg oral tablets, three times daily) for five days. However, she did not show improvement, and the clots were still present, so she was eventually referred to hospital.

The histopathological results showed features consistent with choriocarcinoma. She was initially managed with single-agent chemotherapy (methotrexate 50 mg). The patient was not compliant; she took the first dose but did not attend clinic to receive the remaining recommended doses despite continuing symptoms (vaginal bleeding with clots). The patient was in denial of having a serious medical condition and was scared of receiving chemotherapy, so she went to another doctor in a private clinic looking for a different diagnosis. She claimed that he told her that one dose of methotrexate was enough and that the only follow-up care she required was monitoring of her b-hCG levels. She did so at a facility in her village, which reported the following results (units: mIU/mL): 1st day 41,650; 4th day 44,256.6; 7th day 32,314; 10th day 22,802.3; 13th day 12,936; 16th day 66,299.7. She did not show the results to her doctor or return to the hospital for follow-up. When she was later asked why she chose to do this she said she was in a depressed mood and did not accept the idea of having "cancer".

A month after the last b-hCG lab result, the patient presented to the emergency room complaining of dizziness associated with minimal vaginal bleeding and diffuse abdominal pain. She was unstable, hypotensive (85/42), and tachycardic (pulse 122 bpm). Laboratory tests showed a hemoglobin level of 5 g/dL. Ultrasound showed free fluid reaching Morrison's pouch and a 3 × 3 cm intrauterine mass. An emergent laparotomy was performed, which revealed approximately 3000 cc of blood filling the abdominal cavity, reaching the subdiaphragmatic area and Morrison's pouch. A perforation was found in the fundus near the right cornua of the uterus, approximately 2 cm in size (Fig. 1). The uterus was filled with blood and clots, and a friable mass was found. Owing to the patient's desire for fertility, the doctors excised whatever they could from the mass, and a hysterectomy was not done. Then the perforation was repaired (Fig. 2). She received six units of PRBCs, eight units of FFP, six units of CRYO, and six units of platelets during and after the procedure. Her b-hCG level was 223,226.22 mIU/mL two days after the procedure.

The patient was referred to an oncology center to receive multi-agent chemotherapy, where she was reevaluated three weeks following her recovery and given a diagnosis of stage III gestational trophoblastic neoplasia based on staging scans that showed two lung nodules.

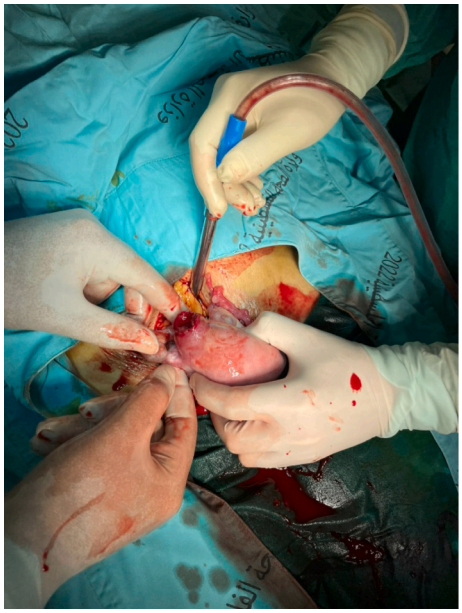

Fig. 1. The perforation can be seen on the right of the posterior wall.

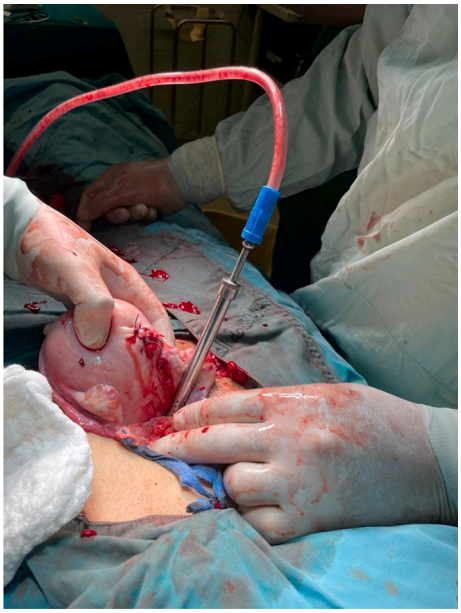

Fig. 2. The patient's uterus after repair.

However, she did not complain of any respiratory symptoms, and there were no abnormalities upon chest or general examination (there was no hemoptysis, dyspnea, coughing, or pleural pain). The EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) protocol was initiated. She completed five cycles with no complications. Her last b-hCG test showed a zero level, and the scans were normal, with the disappearance of the lung lesions, indicating the success of the treatment.

3. Discussion

Choriocarcinoma is characterized by trophoblastic tissue invading the myometrium and has a high likelihood of metastasizing [4]. Rarely, as in the reported case, it can occur after normal intrauterine pregnancy, with an incidence following full-term births that some have stated as 1 in 160,000 [6]. Women of childbearing age are most susceptible, typically within 12 months of a preceding pregnancy. Some publications also document an exceptionally rare occurrence of choriocarcinoma in postmenopausal women, with a long latent period before presentation, as it may develop years after the last pregnancy [10].

The primary factors raising clinical suspicion of choriocarcinoma (CC) are elevated b-hCG levels and postpartum bleeding. However, in certain instances, intuition is clinically supported by symptoms induced by metastasizing lesions [6]. Additionally, in rare cases, suspicious white nodules and infarcted areas may be discovered on the placenta during macroscopic examination at labor, further raising clinical suspicion of CC [11]. Nonetheless, the definitive diagnosis is confirmed only after histopathologic examination of the placenta or endometrial tissue following curettage [6,11]. The lack of routine placental histological examination can lead to a delay in diagnosis, impacting the patient's prognosis by increasing the risk of metastasis and resistance to single-agent chemotherapy. Nevertheless, due to the rarity of the disease following a full-term pregnancy, placental histological examination is not commonly performed, making intrapartum diagnosis challenging [11]. Therefore, CC is typically diagnosed after abnormal postpartum bleeding and curettage, alongside elevated b-hCG levels with or without metastatic symptoms [6,8]. This aligns with how the patient in this case both presented and was diagnosed.

Metastases from choriocarcinoma most commonly occur in the lungs, presenting with symptoms such as hemoptysis, dyspnea, coughing, or pleural pain. Less frequently, metastases may occur in the brain,

pelvis, vagina, and liver [9]. After confirming the diagnosis of choriocarcinoma, a series of tests is conducted to rule out metastatic disease. These include contrast-enhanced abdominal CT, chest X-ray, MRI of the brain and pelvis, and pelvic Doppler ultrasound [10]. In the present patient's case, a CT scan was performed to assess for lung metastases, given their frequent occurrence, and it revealed two lung nodules.

The staging system of the International Federation of Gynecology and Obstetrics (FIGO) for CC aims to evaluate the disease's progression and guide treatment decisions and follow-up. It is outlined in Table 1 [6,12,13].

FIGO evaluation methods are abdominal and pelvic CT scans used to determine the tumor's location, size, characteristics, tumor extension, lymph node involvement, and distant metastases. MRI is useful for accurately identifying tumor extension. Additionally, proper staging of the disease requires the identification of lung metastases, making lung evaluation mandatory. PET scans can also be used to evaluate the tumor's metabolic activity and identify distant metastases [6,13].

The risk of resistance to mono-chemotherapy determines the **FIGO prognosis score**; a score of less than six indicates a low risk, a score of seven or more indicates a high risk [12,14]. These risks are presented in Table 2 [6,12].

The patient in this case was 25 years old, presented less than four months after a term antecedent pregnancy, with a serum β-hCG level of 13,611 mIU/mL and a tumor size of 2 × 2 cm, without initial evidence of metastasis. She was started on single-agent chemotherapy; however, due to denial of her condition and fear of the treatment, she took only one dose. Subsequently, she developed lung metastases, necessitating multi-agent chemotherapy, which increased her prognostic score from 5 to 7. Consequently, she was initially classified as low-risk but was later reclassified into the high-risk group.

Chemotherapy is a foundational treatment for CC. According to the FIGO score, single-agent chemotherapy such as methotrexate is required in the low-risk group, while the high-risk group is treated with multi-agent chemotherapy, such as EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine) [6,12]. The remission rate of this approach is 98–100 % [6].

The duration and number of chemotherapy cycles are customized based on the patient's stage and clinical response, but chemotherapy generally continues with two additional cycles after b-hCG normalization is achieved [6,13]. The present patient was in stage 1 and considered low risk, therefore she had single-agent chemotherapy (methotrexate). However, after regression she progressed to stage 3 (high-risk group) and received five cycles of multiagent chemotherapy.

Both low- and high-risk groups should be followed up by monitoring of b-hCG levels every four weeks for six months after completing treatment, and then every six months for five years after that [12].

After successful treatment of choriocarcinoma with chemotherapy, women should be counseled that they can expect similar pregnancy outcomes to the general population in future pregnancies, although there may be a slightly higher risk of stillbirth. Additionally, it is important to note that menopause may occur earlier than expected in women who have received multi-agent chemotherapy. By the time they reach 40 or 45 years of age, 13 % and 36 % of these patients, respectively, have experienced premature menopause [6]. Regarding recurrence, there is a published case report concerning a patient with a history of choriocarcinoma and premature menopause at the age of 30 who presented 20 years later with a new onset of choriocarcinoma [10].

Other treatment modalities include surgery, especially in cases of significant hemorrhage in highly vascularized tumors, and radiotherapy in the presence of brain metastasis. Hysterectomy is not beneficial for high-risk patients but may be used in women who have decided to end their reproductive plans and are considered low-risk, as it can minimize the duration of chemotherapy [12].

A very unusual complication of choriocarcinoma is uterine rupture [4]. There is very little literature on this particular scenario. The present case was complicated by uterine perforation and hemoperitoneum one month after the initial diagnosis was made. The patient presented complaining of vaginal bleeding, and acute abdomen with hemodynamic instability, prompting immediate exploratory laparotomy. Although the precise pathophysiology of uterine rupture in choriocarcinoma is unknown [4], some research indicates that hypervascular tumors such as choriocarcinomas, can result in uterine perforation due to myometrial invasion [15]. In the present case, the cause of uterine perforation may be attributed to the extensive invasion of the choriocarcinoma into the myometrium as the chemotherapy treatment was not completed due to the patient's non-compliance. This was evidenced by the rise in serum b-hCG levels to 223,226.22 mIU/mL two days after the uterine repair procedure. This increase followed a period of improvement and declining b-hCG levels, which had occurred when the patient started single-agent chemotherapy. However, the chemotherapy was discontinued, and follow-up of b-hCG levels was also halted after the last recorded level of 66,299.7 mIU/mL.

When a uterine perforation causes an acute abdomen, patients need to be managed aggressively with surgery. The best course of action for females is a total abdominal hysterectomy (TAH). However, conservative surgery is the best choice for female patients whose disease is restricted to the uterus and who wish to maintain their fertility [4,15], as with the present patient.

Levels of b-hCG serve as a valuable tumor marker during chemotherapy, aiding in monitoring the patient's response to treatment and determining the uterine focus of the disease [15]. A negative serum b-hCG result suggests the clinical absence of invasive cytotrophoblasts, as the concentration of trophoblastic tissue is reflected in serum b–hCG [15]. At the last follow-up, the present patient's serum b-hCG reached zero after five cycles of chemotherapy, prompting the cessation of treatment.

A limitation in this case was the initial misdiagnosis as retained products of pregnancy by an outpatient clinic at another hospital, which led to ineffective treatments and delayed the correct diagnosis of choriocarcinoma (CC) and subsequent chemotherapy. This delay

Table 1
The **FIGO anatomical staging** system for CC.

Stage	Description
1	Confined to the uterus.
2	Extends outside the uterus, but limited to genital structure (vagina, broad ligament, adnexa).
3	Metastasis to the lung, with or without genital tract metastasis.
4	Other organ metastasis (brain, kidney, liver).

Table 2
The international FIGO prognosis score for gestational trophoblastic neoplasm.

Score for each risk factor	0	1	2	4
Age	Less than 40 years	More than 40 years		
Antecedent pregnancy	Mole	Abortion	Term	
Interval: months from index pregnancy	Less than 4 months	4 to 7 months	7 to 12 months	More than 12
Preterm serum hCG	Less than 1000	1000 to 9999	10,000 to 99,999	More than 100,000
Size of the tumor	Less than 3 cm	3 to 4 cm	5 or more than 5 cm	
Metastasis site	Lung, vagina	Spleen, kidney	Gastrointestinal, liver, and brain	
Number of metastases	0	1 to 4	5 to 8	More than 8
Prior chemotherapy failure	None	Single	More than two drugs	

increased the risk of complications, including a uterine rupture. Additionally, the absence of a dedicated gestational trophoblastic disease center for patient management, compliance, and follow-up contributed to the issue. The lack of programs for communicating with patients outside hospital also played a role, as poor patient compliance exacerbated the deterioration. Lastly, patient's fertility after chemotherapy was not discussed due to the lack of specialized programs concerning about preservation procedures and oocyte freezing, which could help the patient in case of future early menopause risk.

4. Conclusion

Choriocarcinoma is a rare, aggressive malignancy that presents with a wide spectrum of clinical manifestations, most commonly postpartum hemorrhage and elevated serum beta-hCG levels. Management typically involves individualized chemotherapy protocols, with serial monitoring of beta-hCG levels to evaluate therapeutic response. Surgical intervention may be warranted in cases complicated by uterine perforation or other structural damage. Early identification of choriocarcinoma is essential to ensure timely treatment and to minimize the risk of further complications.

Contributors

Rayan R. Salahaldin, Mais E. Abubaker, Ghada M. Abdalqader, Anas R. Tuqan, Basel A. Zaben contributed to conception of the case report, acquiring and interpreting the data, drafting the manuscript, undertaking the literature review, and revising the article critically for important intellectual content.

Ibaa Barghouthi contributed to patient care, conception of the case report, acquiring and interpreting the data, and revising the article critically for important intellectual content.

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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