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Choriocarcinoma presenting as late postpartum hemorrhage in a 21-year-old primipara

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Abstract:

INTRODUCTION: Obstetrical hemorrhage remains to be one of the most common causes of maternal morbidity and mortality. Postpartum hemorrhage occurs after delivery and is usually secondary to uterine atony, genital tract lacerations, and retained placental fragments.

CASE: A case of a 21-year old, primipara, presented with profuse vaginal bleeding and hemoptysis at 3 weeks' postpartum. A clinical diagnosis of gestational trophoblastic neoplasia was established after an elevated serum beta human chorionic gonadotropin was obtained and an intrauterine mass was seen on ultrasonography, including metastasis to the lungs and liver seen through imaging studies.

DISCUSSION: Chemotherapy with etoposide, methotrexate, actinomycin D, cyclophosphamide and oncovin (EMACO) is the mainstay treatment for Stage IV disease. However, complications such as hemorrhage and tumor rupture are best managed surgically. Although rare, a diagnosis of choriocarcinoma should be considered in patients with persistent bleeding after a normal pregnancy to institute proper management and avoid associated complications of tumor progression.

Keywords:

Choriocarcinoma, gestational trophoblastic neoplasia, postpartum hemorrhage

Introduction

Obstetrical hemorrhage is one of the most common causes of maternal morbidity and mortality. It is subdivided into antepartum and postpartum. Antepartum hemorrhage occurs during pregnancy while postpartum hemorrhage occurs after delivery and may be due to uterine atony, genital tract lacerations, and retained placental fragments.[1] Rare cases of postpartum hemorrhage secondary to gestational trophoblastic neoplasia (GTN) are also documented in literature.

GTN constitutes the malignant spectrum of gestational trophoblastic diseases. It includes invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. Fifty percent of GTN follows a molar pregnancy. It is usually identified in patients undergoing postevacuation surveillance. Twenty-five may occur after an abortion or an ectopic pregnancy and another 25% after a term or preterm pregnancy.

Choriocarcinoma is the most common histologic type that follows a term pregnancy.[1] In Southeast Asia and Japan, choriocarcinoma occurs in 3–9 per 40,000 pregnancies.[2] The development of choriocarcinoma may occur from weeks to months from antecedent pregnancy. In a review done by Nugent *et al*., the average time of diagnosis was at 7 weeks' postpartum following a term pregnancy.[3]

Case Report

A 21-year-old primipara presented at the emergency room with profuse vaginal

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bleeding, hemoptysis, and generalized body weakness at 3 weeks' postpartum. Previously, she delivered through spontaneous vaginal delivery with no fetomaternal complication at a local hospital.

The patient had persistent vaginal spotting postpartum. She also developed a cough with hemoptysis which was treated as pneumonia at a local health center a week after delivery. Three weeks postpartum, she had profuse vaginal bleeding with associated generalized body weakness. She was brought to a local hospital where blood transfusion of 4 units packed red blood cells were given and postpartum curettage was done. A preliminary ultrasound before the curettage was not facilitated. Despite uterotonics and curettage, the patient had persistent vaginal bleeding necessitating transfusion of additional 3 units of packed red blood cells postoperatively. Hence, a transvaginal scan was performed which revealed an enlarged uterus with an irregular, heterogeneous mass measuring 8.8 cm × 8.4 cm × 9.7 cm (volume 340 mL), with cystic spaces containing low-level echo fluid within. The mass appears to invade the full thickness of the myometrium from the posterior midcorpus up to the fundus. Color flow mapping shows minimal central vascularity and absent vascularity within the cystic spaces. Impression of retained placenta with increta versus GTN was considered. Serum beta-human chorionic gonadotropin (hCG) was obtained with a level of >1,500,000 mIU/mL. Chest X-ray revealed the presence of a round opacity in the left lower lobe, overlying the cardiac shadow, approximately measuring 5.0 cm × 5.0 cm and small round opacities were also identified in the right lung, with the largest measuring 2.0 cm × 1.5 cm on the lower lobe. The presence of a homogeneous enhancing mass on the liver measuring 1.3 cm × 1.8 cm was seen on the whole abdominal computed tomography scan. The patient was transferred to a trophoblastic disease center for definitive multiagent chemotherapy as a case of GTN IV: 16.

On arrival at the emergency room, immediate assessment and resuscitation was rendered. The patient came in frail and in respiratory distress. On physical examination, she had bibasal crackles and decreased breath sounds on the right basal lung field. The abdomen was globular, with a pelvoabdominal mass approximately measuring 12.0 cm × 10.0 cm, with no tenderness appreciated. On pelvic examination, the vaginal walls were smooth, with no vaginal mass. The cervix was open, with moderate vaginal bleeding. The uterus was enlarged comparable to an 18-week size gravid uterus. No adnexal tenderness was appreciated.

A repeat transvaginal ultrasound revealed an endomyometrial mass measuring 10.9 cm × 10.4 cm × 7.4 cm with full-thickness myometrial invasion at the posterofundal portion of the uterus, highly considering a GTN, with bilateral theca lutein cyst [Figures 1 and 2]. Repeat serum beta hCG was >3,000,000 mIU/mL. Induction chemotherapy with etoposide and cisplatin was the initial plan for the patient. However, the patient developed abdominal pain and had persistent vaginal bleeding. Hence, an emergency exploratory laparotomy with bilateral internal iliac artery ligation and hysterectomy was done. Intraoperatively, there was 250 cc hemoperitoneum. The uterus was enlarged and highly vascular, with a 0.5 cm point of rupture at the left fundal area [Figure 3]. The rest of the uterine serosa was intact. The right ovary was enlarged to 5.0 cm × 4.0 cm with multiple points of rupture and area of hematoma. The left ovary measured 3.0 cm × 2.0 cm with a single point of rupture and area of hematoma. Evacuation of hematoma and ligation of bleeders were done on both adnexa. On the cut section of the uterus, there was a 10.0 cm × 8.0 cm × 7.0 cm solid mass, with areas of necrosis and hemorrhage, attached to the posterofundal area with full-thickness myometrial invasion [Figure 4]. Histopathology was consistent with choriocarcinoma [Figure 5].

During the postoperative period, the patient had persistent hemoptysis and progressive dyspnea, with decreased breath sounds. Chest radiograph revealed near total opacification of the left hemithorax with a

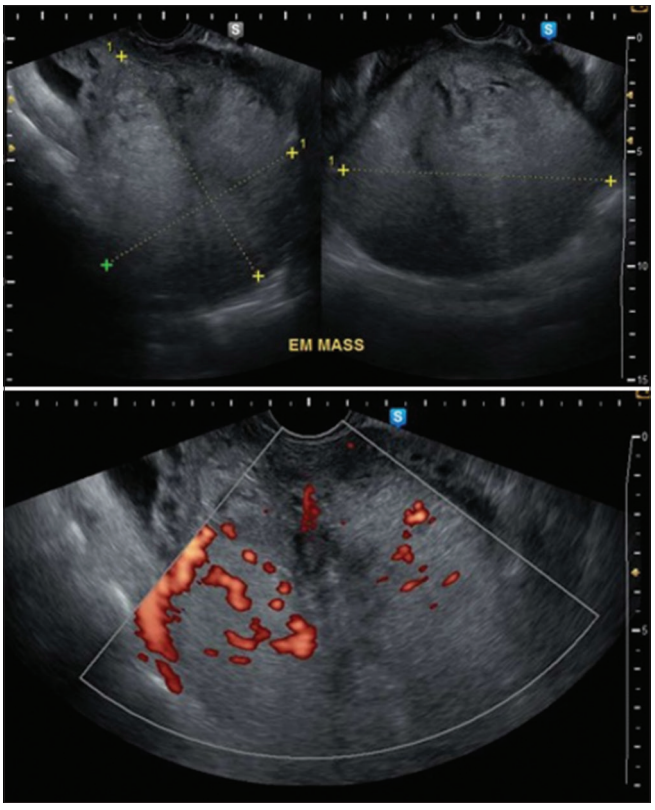

Figure 1: Endomyometrial mass on transvaginal ultrasound

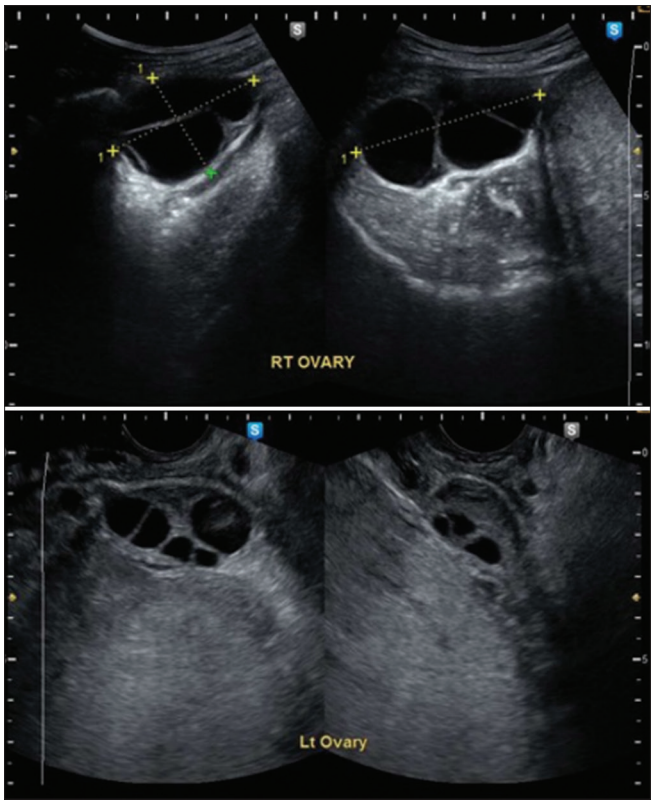

Figure 2: Bilateral theca lutein cysts in transvaginal ultrasound

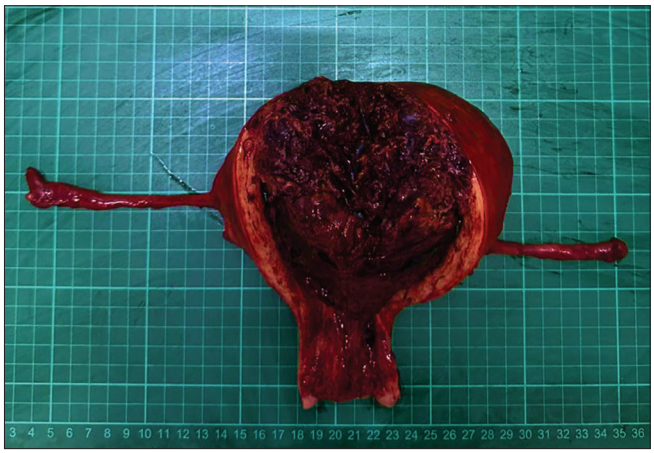

Figure 4: Cut section of the uterus

contralateral deviation of the mediastinal structures [Figure 6], and a 700 cc pleural effusion on the left lung was visualized on chest ultrasound. Chest tube thoracostomy was done and evacuated 700 cc serosanguinous fluid. Antibiotic was also given concurrently.

The patient was started on induction chemotherapy with etoposide and cisplatin, given for two cycles with 1-week interval. Multiple agent chemotherapy with etoposide, methotrexate, actinomycin D, cyclophosphamide and oncovin (EMACO) was given thereafter. It showed an adequate response with decreasing serum beta hCG

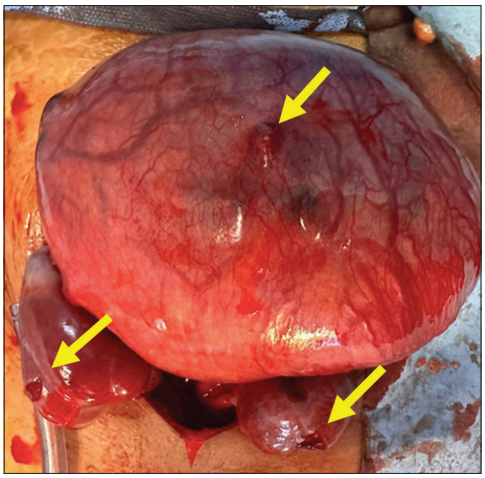

Figure 3: Intraoperative findings Yellow arrows: point of rupture on the left fundal area of the uterus, multiple points of rupture on the right ovary and point of rupture on the left ovary

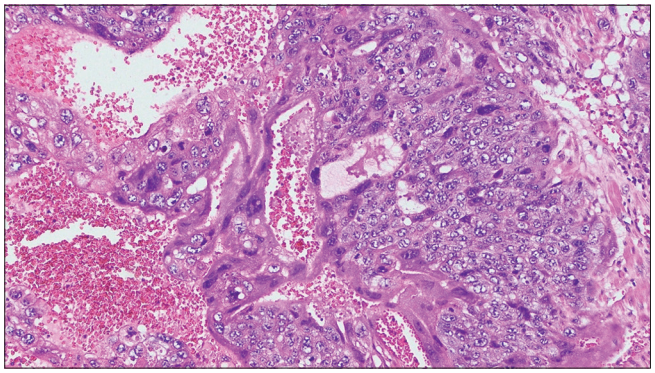

Figure 5: Photomicrograph of choriocarcinoma

levels [Figure 7]. The patient completed a total of 8 cycles of EMACO, including 3 consolidation courses.

Discussion

Postpartum hemorrhage remains to be the leading cause of maternal mortality in the country. It is classified as early postpartum hemorrhage when it occurs immediately after delivery, and late postpartum hemorrhage when bleeding happens 24 h–12 weeks after delivery.[1] At 3 weeks' postpartum, our index case had profuse vaginal bleeding with associated cough and hemoptysis. Initial impression of retained placental fragments was entertained and the hemoptysis was attributed to an upper respiratory tract infection. Such misdiagnosis is common in reported cases of postpartum choriocarcinoma as the condition is rare with a reported incidence of 1 in 50,000 full-term pregnancies.[4]

Vaginal bleeding remains to be the most common presenting symptom of postpartum choriocarcinoma. It is often associated with bleeding from metastatic sites, as in the index patient. Irregular scanty bleeding observed postpartum is usually dismissed as a normal occurrence.

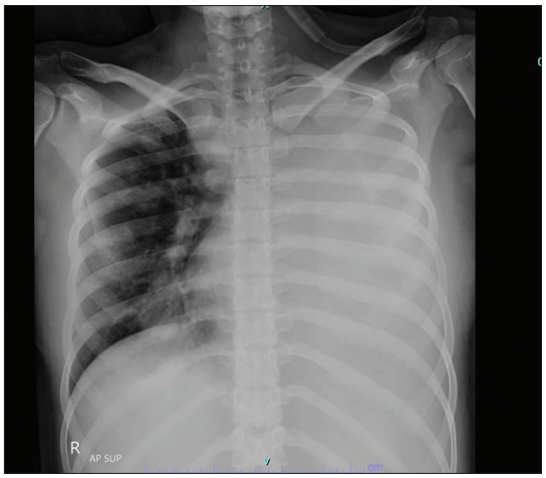

Figure 6: Multiple pulmonary nodules on chest radiograph

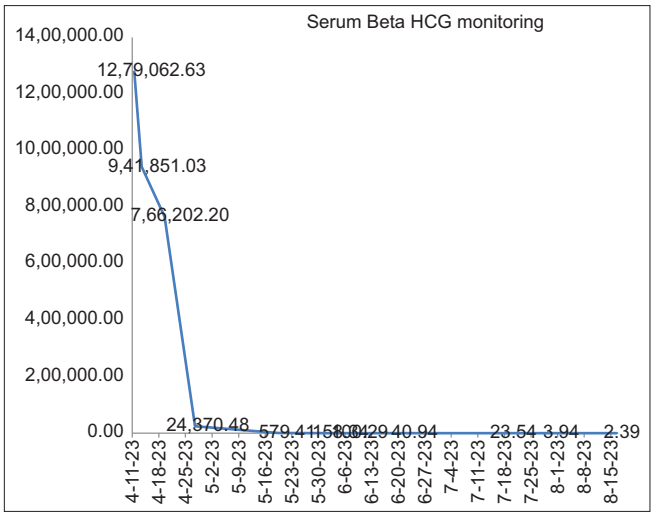

Figure 7: Serum beta human chorionic gonadotropin curve

In such cases, diagnosis and management are delayed causing disease progression and even death. In the study by Guo *et al.* in 2019, most patients with postpartum choriocarcinoma presented with vaginal bleeding, with an incidence of 93.1%.[4] Other patients were reported to manifest with symptoms referable to the metastatic sites like hemoptysis from pulmonary metastasis as in the index patient, intracranial bleeding and neurologic deficits from brain metastasis, and intra-abdominal bleeding from metastatic lesions in the liver. The lungs are still the most frequent site of metastasis, followed by the brain, liver, and the vagina. Postpartum choriocarcinoma has been reported to have a propensity to present with more extensive metastasis in 86.7% of cases and thus, it is associated with a poorer prognosis.[5]

A high index of suspicion is imperative in the diagnosis of postpartum choriocarcinoma as this would lead the clinician to request appropriate tests that would verify the diagnosis. The presence of vaginal bleeding, cough, and hemoptysis, with an endomyometrial mass on sonography, including lung and liver metastasis on imaging studies, and an elevated serum beta hCG in the index case was highly suggestive of GTN. The combined FIGO 2000 Anatomical Staging and WHO Prognostic Scoring System [Tables 1 and 2] are used to determine the extent of the tumor and possible resistance to single agent chemotherapy. The index patient, with lung and liver metastasis, was diagnosed as FIGO Stage IV with a risk score of 16 (stage IV: 16), and therefore classified as ultra-high risk. This is associated with poor prognosis, higher disease burden and higher incidence of resistance.[6]

The index patient was given two cycles of induction chemotherapy with low-dose etoposide and cisplatin. Studies state that induction chemotherapy reduces the risk of early death among ultra-high-risk GTN patients with larger tumor loads and higher propensity for hemorrhage. Definitive management of Stage IV disease is chemotherapy using multiagent regimen of etoposide, methotrexate, actinomycin, cyclophosphamide, and oncovin (EMACO) which was given to our index case. In a previous study, 21 of 29 patients with postpartum choriocarcinoma were given EMACO and showed no evidence of disease from 2 to 72 months after chemotherapy.[4] The response rate to EMACO as first-line multiagent chemotherapy is reported to be 76.1%, with a survival rate of 89%.[7] Adjunctive surgery on the other hand is reserved for cases of chemoresistance and GTN-associated complications such as hemorrhage and tumor rupture. The index patient had uncontrolled uterine bleeding secondary to erosion of uterine vessels secondary to tumor invasion, with associated tumor rupture. Hence, a hysterectomy with bilateral internal iliac artery ligation was done to control the bleeding. Intraoperatively, ruptured bilateral theca lutein cysts were also noted, and evacuation of hematoma with ligation of bleeders was done on both ovaries. Theca lutein cysts result from overstimulation of hCG and appear as multiloculated cystic mass.[8] It is best left alone unless a complication of rupture or torsion is detected.[1] In patients still desirous of future pregnancies, wherein the size of the tumor is not extensive, a more conservative approach of resection or uterine artery embolization may be done for fertility preservation.[9] Nonetheless, this was not possible in the index patient given the extent of the uterine tumor.

Table 1: FIGO staging

Stage	Description
Stage I	Disease confined to the uterus
Stage II	GTN extends outside the uterus but is limited to the genital structures (adnexa, vagina, broad ligament)
Stage III	GTN extends to the lungs with or without genital tract involvement
Stage IV	All other metastatic sites

GTN: Gestational trophoblastic neoplasia, FIGO: FIGO 2000 Staging

Table 2: World Health Organization prognostic scoring system

Index case	Score	0	1	2	4
21 y/o	Age (years)	<40	>40		
Term	Antecedent pregnancy	Mole	Abortion	Term	
1 month	Pregnancy interval, in months	<4	4-6	>6	
>3,000,000 mIU/ml	Pre-treatment BhCG (mIU/ml)	<1,000	1,000-10,000	10,000-100,000	>100,000
10 × 8 x 7 cm	Largest tumor size	<3	3-5	>5	
Lungs and liver	Site of metastasis	Lungs	Spleen, kidney	Gastrointestinal	Brain, liver
Multiple	Number of metastasis	0	1-4	5-8	>8
None	Previous failed chemotherapy			Single drug	2 or more drugs

Patients with postpartum choriocarcinoma are associated with a poorer prognosis compared to gestational trophoblastic neoplasm after a hydatidiform mole or abortion primarily because of the tendency to present with a more extensive disease. The presence of brain and liver involvement is associated with lower cure rates. It has also been reported that an increased time interval between the onset of disease and the previous pregnancy is associated with worse outcomes.[10] For the index patient, the interval from the normal delivery and the diagnosis was only 4 weeks but the presence of liver metastasis is a poor prognostic factor.

The index patient received a total of 8 EMACO chemotherapy cycles, including 3 consolidation courses, with good response and regressing serum beta hCG levels. Based on guidelines, follow-up is done with monthly serum beta hCG monitoring for the first 6 months then bimonthly to complete 1 year.

Conclusion

GTN, particularly choriocarcinoma, may arise from a term pregnancy. Chemotherapy is the cornerstone of management in GTN. However, complications such as hemorrhage and tumor rupture arising from the disease may warrant surgical intervention. It is the primary objective of this article to increase awareness that postpartum choriocarcinoma should be part of the differential diagnosis in a patient presenting with postpartum hemorrhage to ensure timely diagnosis and immediate management of this highly aggressive but treatable tumor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authorship contributions

Shelyne Rose S. Cruz, MD - Involved in conceptualization, methodology, data curation, writing of original draft, writing review and editing.

Elizabeth K. Jacinto, MD - Involved in conceptualization, methodology, writing review and editing.

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Conflicts of interest

There are no conflicts of interest.

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