Case Report

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Primary vaginal gestational trophoblastic neoplasia treated with uterine angiographic embolization and chemotherapy

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Abstract:

Gestational trophoblastic neoplasia (GTN) in itself is an uncommon condition, much so is a primary extrauterine GTN. The incidence of GTN in the Philippines is at 22.4/40,000 pregnancies. However, no report has been made for primary extrauterine GTN. Only two cases of primary vaginal choriocarcinoma are reported in the literature. This is a case of a 26-year-old gravida 1 para 0 (0010) who came in for profuse vaginal bleeding. Serum beta-human chorionic gonadotropin (β-hCG) was elevated and ultrasound showed a hypervascular vaginal mass and an empty uterus. A primary vaginal GTN was considered, and the patient was treated with etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMACO) regimen. During the course of chemotherapy, there was a note of profuse vaginal bleeding, which was controlled by angiographic uterine artery embolization. A normal β-hCG level was achieved after six cycles of EMACO. The patient was able to have three successful pregnancy outcomes thereafter. Primary vaginal GTN is a rare condition that requires a high index of suspicion. In a nulliparous patient complicated with profuse vaginal bleeding, angiographic embolization is an effective fertility-sparing procedure that can manage the said complication.

Keywords:

Angiographic embolization, extrauterine gestational trophoblastic neoplasia, vaginal gestational trophoblastic neoplasia

Introduction

Gestational trophoblastic neoplasia (GTN) encompasses the malignant end of the spectrum of gestational trophoblastic disease. The incidence of GTN varies in different regions of the world. An incidence of 1 in 40,000 pregnancies was reported in Europe and North America and 3.3–9.2 in 40,000 pregnancies in Southeast Asia.[1] In the Philippines, the incidence of GTN remained to be almost constant at 22.4/40,000 pregnancies.[2] However, the incidence of primary extrauterine GTN has not been reported. To date, only two cases of primary vaginal choriocarcinoma are reported in the literature. Profuse vaginal bleeding as a complication of GTN can be catastrophic and even fatal when not managed promptly. Patient's desire to preserve fertility leads to the utilization of innovative procedures to address both life-threatening hemorrhage and patient's chance for future pregnancy.

Case Report

This is the case of a 26-year-old gravida 1 para 0 (G1P0) (0-0–1-0) with a chief complaint of profuse vaginal bleeding 3 months after having a complete abortion. A consult was

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initially done in Guam where she underwent workup. Complete blood count showed anemia (hemoglobin 7.6 g/dl) which was corrected with transfusion of 3 units packed red blood cells (hemoglobin 11.4 g/dl). Elevated serum beta-human chorionic gonadotropin (β-hCG) at 320,279 mIU/ml was noted. The patient underwent pelvic ultrasound which revealed a heterogeneous, globular, highly vascular mass in the area of the vagina. Uterus was normal in size with thin endometrium. No lesion was seen in the uterus. Initial consideration at that point was GTN. The patient opted to continue her medical care in the Philippines; hence, she was discharged after 2 days with a repeat hemoglobin of 11.4 g/dl and repeat β-hCG of 465,000 mIU/ml and was transferred to a tertiary hospital in the Philippines. With the history of profuse vaginal bleeding and an ultrasound finding of highly vascular vaginal mass, speculum examination and internal examination were not performed to avoid manipulation of the said lesion. A repeat β-hCG was still elevated at 513,551 mIU/ml. The patient underwent careful transvaginal ultrasound which revealed an irregular vascular vaginal mass located caudal to the cervix, measuring 5.6 cm × 4.9 cm × 3.7 cm. Uterus was normal in size, with no lesions. With these findings, diagnosis of primary vaginal GTN (II: 8) was made. The patient was then referred to a GTN specialist. Combined chemotherapy in the form of etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMACO) was started. On the fifth day of the first cycle of chemotherapy using EMACO, the patient experienced profuse vaginal bleeding in which hemodynamic stabilization was done. An attempt to control the bleeding with vaginal packing was unsuccessful; hence, a referral to interventional radiologist was made, who then considered doing pelvic angiography. Angiography showed a hypervascular vaginal mass mainly supplied by the dilated and tortuous bilateral uterine arteries [Figure 1]; hence, a bilateral uterine artery angiographic embolization was performed [Figure 2]. The procedure was completed uneventfully and was tolerated well by the patient. Vaginal bleeding was completely controlled by the procedure. Chemotherapy with EMACO was continued. Serial monitoring of β-hCG was done until a normal result was achieved after six cycles of EMACO, and after three clean up courses, the patient achieved complete remission [Table 1]. Doppler ultrasound of the mass done after EMACO I [Figure 3] was compared with that done after EMACO VIII (clean up course II), which showed significant decrease in the size of previously noted complex mass at the upper vagina [Figure 4].

The patient had regular follow-up and serial β-hCG monitoring which remained to be normal. Fertility of the patient was preserved as evident in her succeeding obstetric history. She had a total of three pregnancies thereafter, all of which were carried to term, delivered vaginally without fetal and maternal complications encountered. Following chemotherapy and uterine

Table 1: Serial Beta Human Chorionic Gonadotropin showing a significant decreasing trend in the values of the patient from the time of consult until the end of the third clean up course

Timing	Serum Beta Human Chorionic Gonadotropin (mlu/ml)
Baseline	513, 551
After EMACO I and post Embolization	26, 043
After EMACO II	231.1
After EMACO III	42.3
After EMACO IV	8.5
After EMACO V	5.4
After EMACO VI	3.6
After EMACO IX (Clean up Course III)	1.4

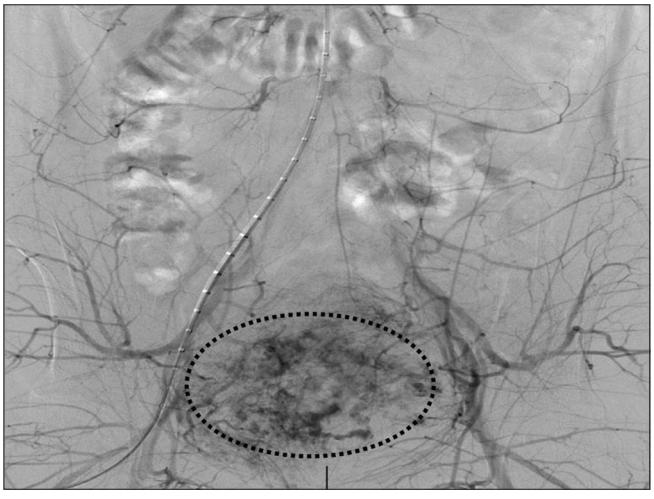

Figure 1: Pelvic angiography: Dotted lines outline the hypervascular vaginal mass mainly supplied by the dilated and tortuous bilateral uterine arteries

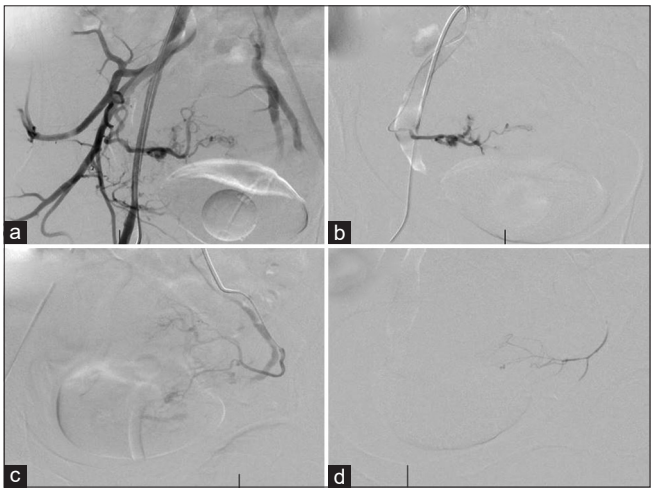

Figure 2: Uterine artery angiographic embolization, (a) tortous right uterine artery before embolization. (b) Right uterine artery showing complete embolization after the procedure. (c) Tortous left uterine artery before embolization. (d) Left uterine artery showing complete embolization after the procedure

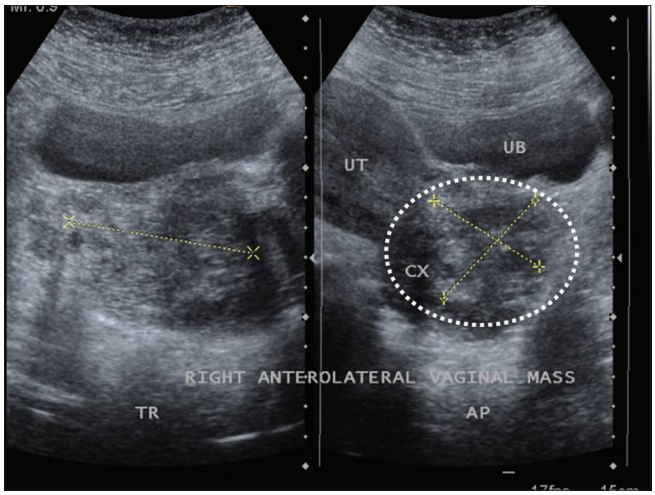

Figure 3: Sonographic image of the vaginal mass (marked by dotted circle) measuring 4.2 cm × 6.5 cm × 4.5 cm after the first cycle of EMACO, EMACO: Etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine

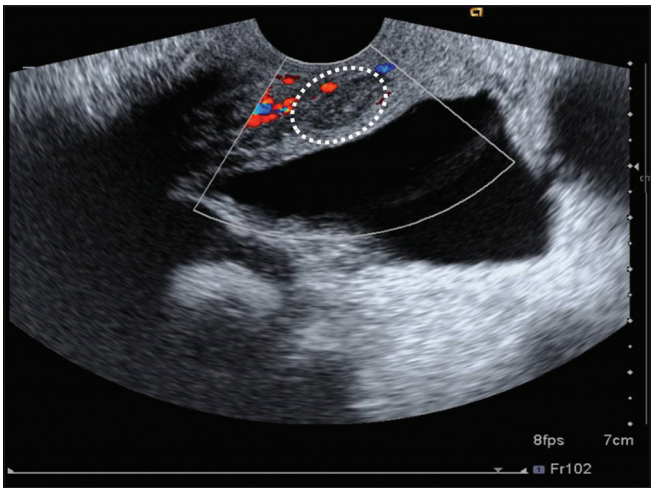

Figure 4: Sonographic image of the vaginal mass (marked by dotted circle) measuring 1.7 cm × 1.0 cm × 0.7 cm after the eighth cycle of EMACO, EMACO: Etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine

artery embolization performed, succeeding pregnancies were delivered as follows: first pregnancy was delivered 2 years and 4 months after, second was delivered 4 years and 9 months after, and third was delivered 6 years from chemotherapy and uterine artery embolization.

Discussion

Clinical presentation

Extremely rare cases of primary extrauterine GTN, with cervix as the most identified site of lesion, are reported in the literature.[3] Some theories suggest that it may have arisen from a uterine cavity tumor that spontaneously regress after it spreads to other site.[4] Clinical manifestations of GTN differ according to the site affected by the disease, with vaginal bleeding being the most common initial symptom. In rare cases of primary GTN outside the uterus, clinical signs and symptoms are more nonspecific as it may mimic other more common diseases considered in the site of the lesion. Vaginal metastasis may have the same manifestation as that of primary vaginal GTN. Both can present as a bluish cystic vaginal mass which has deep pelvic anastomosis; hence, biopsy should never be attempted since it can cause intractable bleeding. There were two cases of primary vaginal choriocarcinoma published in the literature. First case was that of a postmenopausal woman reported by Sonobe *et al*., who presented with atypical vaginal bleeding 23 years after her last pregnancy.[5] Second case was that of a 33-year-old woman who presented with lower abdominal pain and urinary retention who on workup was noted to have elevated β-hCG and an anterior vaginal mass.[6]

In the case presented, the only attributable risk factor that could predispose her to develop tumor is the history of spontaneous abortion. The patient presented with profuse vaginal bleeding with associated vaginal mass and increased β-hCG. Based on the criteria made by Saito in their extensive survey on extrauterine GTN,[7] we considered this case as a primary ectopic GTN. The criteria include (1) absence of focus of choriocarcinoma in the uterine corpus as the sonographic imaging of the patient showed normal-sized uterus without note of any mass or lesion and (2) exclusion of extrauterine choriocarcinoma coexisting with hydatidiform mole or intrauterine pregnancy. Further, a part of the criteria is that an intramural choriocarcinoma in the uterine corpus should not be considered as ectopic choriocarcinoma, which was not present in the patient. The last criterion is a histopathological diagnosis confirmed as choriocarcinoma. However, this could not be done in the index case because biopsy of the vaginal mass was not performed to avoid possible intractable hemorrhage.

Diagnosis

Diagnosis of GTN is based on the clinical presentation, hormonal assay, and imaging studies. Histopathological diagnosis is not always possible, as with the index patient wherein further manipulation of the vaginal mass is avoided to prevent further intractable hemorrhage. In other cases, these factors contribute to the difficulty in making accurate clinical diagnosis and eventually may lead to delayed appropriate management. The most important factor in the recognition of GTN is a high index of suspicion and consideration for its possibility. In the case presented, to denote the extent of the disease, as that of primary uterine GTN, the International Federation of Obstetrics and Gynecology (FIGO) anatomical staging and WHO scoring system were applied.

Management

GTN is unique compared to other malignant tumors since treatment can be initiated even without a histologic

confirmation. Just like in cases of primary uterine and metastatic GTN, the cornerstone in the treatment of this patient's vaginal GTN is chemotherapy. However, due to the highly vascular nature of the tumor, hemorrhage can persist and worsen even with the initiation of chemotherapy, as what transpired with the index patient. In a young and nulliparous patient such as this case, an innovative procedure such as angiographic embolization can address both a life-threatening hemorrhage and a patient's chance for future pregnancy.

Due to the rarity of the condition of interest, there is a scarcity of studies on the relationship of uterine artery angiography and succeeding fertility among patients who had GTN treated with the said procedure. McGrath *et al*. reviewed 19 GTN patients with bleeding vaginal metastases who underwent polyvinyl alcohol particle-based radiological embolization via femoral artery approach at Charing Cross Hospital in London from 2000 to 2009. Control of hemorrhage was achieved in 18 out of 19 patients while only one patient necessitated surgical intervention. Pelvic pain requiring opiate administration was the most common morbidity of the procedure. Out of the 19 patients reviewed, nine had successful pregnancy outcomes.[8] A study conducted by Keepanasseril *et al*. in 2011 included eight women diagnosed to have GTN who presented with massive vaginal hemorrhage. All women underwent angiography, and embolization was performed in seven of the eight patients. Bilateral internal iliac artery embolization was done to two patients, bilateral uterine artery embolization was done to four patients, and one patient underwent bilateral uterine and hepatic artery embolization. In 85.7% of the patients, embolization was successful in managing massive hemorrhage. Chemotherapy was administered to all patients. Five out of the eight patients were in remission while three succumbed to the disease. Out of the two who tried to get pregnant, one delivered a term infant while the other had a miscarriage.[9] A case report by Silva *et al*. in 2021 presented a 23-year-old G1P0 (0010) with GTN III: 7 complicated by severe vaginal hemorrhage whose uterus was rescued by utilizing uterine artery embolization.[10] These cited cases and reports showed that angiographic embolization, with low short-term toxicity, is a safe procedure that could be considered among patients with GTN who present with massive vaginal hemorrhage and are still desirous of getting pregnant since the procedure showed no obvious detrimental effect on future fertility. The first reported angiographic embolization utilized in a GTN patient in the Philippines was reported by Yap *et al*. in 2016.[11] Angiographic embolization was done in the bilateral internal pudendal artery branches and obturator artery branches of a choriocarcinoma patient with metastasis to the labia.

In the index patient, percutaneous right transfemoral 5F Cordis pigtail catheterization of the lower abdominal aorta was performed for the aortoiliac study, and 5F Impress Berenstein and 3F Terumo Progreat selective and superselective catheter-contrast examination of the bilateral common iliac, internal iliac, and uterine circulations was done. The procedure revealed a hypervascular vaginal mass mainly supplied by the dilated and tortuous bilateral uterine arteries. Minor collateral blood supplies were noted to be coming from the adjacent pelvic vessels. The rest of the visualized internal iliac circulations showed normal intimal outline and branching pattern. Sequential superselective catheterization of the left and the right uterine arteries facilitated embolization using Boston Contour polyvinyl alcohol particles. This provided complete resolution of the profuse vaginal hemorrhage.

GTN is a rare tumor, much so is a primary extrauterine GTN, in the case presented, a primary vaginal GTN. To date, this is the first case of primary vaginal GTN reported in our country and third in the world. Although staging and prognostication seem to be the same for primary vaginal GTN and metastatic GTN to the vagina, primary vaginal GTN is still worth reporting as it may raise the index of suspicion of the attending physician in diagnosing GTN in the absence of uterine lesion or mass. Knowledge of such case may lead to proper diagnosis and in turn prompt and appropriate management of GTN patients who are presented with extrauterine mass and normal empty uterus.

The angiographic embolization presented in this paper is the first reported case performed in a clinically diagnosed primary vaginal GTN with a purpose of sparing fertility. Angiographic embolization is a life-saving procedure in managing acute hemorrhage in a GTN patient who is still desirous of future pregnancy.

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.

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Conflicts of interest

There are no conflicts of interest.

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