

Bilateral internal pudendal artery angiographic embolization of labial metastasis from gestational trophoblastic neoplasia*

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ABSTRACT

Patients with Gestational Trophoblastic Neoplasia commonly experience bleeding from metastatic sites in the vulvovaginal area. Digital pressure and early institution of chemotherapy usually achieve control of the hemorrhage, but massive hemorrhage ensues in some cases. This paper documents the case of a 48 year-old Gravida8 Para7 (7017) who previously underwent total hysterectomy for endometrial mass. On histopathologic examination, it was diagnosed as Choriocarcinoma. Patient was then advised multiagent chemotherapy indicated for high-risk metastatic gestational trophoblastic neoplasia. Chemotherapy was discontinued due to intermittent, profuse, vaginal bleeding that rendered the patient anemic, a contraindication to starting another cycle of chemotherapy. Despite direct pressure on the vulvar mass, the bleeding became intractable, rendering the patient hypotensive and hooked on ionotropes for hemodynamic stability. The only option remaining for the patient was emergency embolization.

This paper documents the first embolization to be done in the Philippines for labial metastasis from gestational trophoblastic neoplasia.

Keywords: Choriocarcinoma, embolization, gestational trophoblastic neoplasia, emergency angiographic embolization, massive hemorrhage, vulvovaginal metastasis

INTRODUCTION

Gestational trophoblastic neoplasia (GTN) represents a spectrum of highly invasive trophoblastic tumors, which range from invasive mole to choriocarcinoma.

Metastatic gestational trophoblastic neoplasias are highly responsive to chemotherapy. However, complications from their metastatic sites pose significant therapeutic dilemmas. For example, vulvovaginal metastasis occurs from 30% of metastatic GTN; their friable and hypervascular nature renders them prone to significant hemorrhage. There are several ways to alleviate hemorrhage in vaginal metastasis, but for acute, life-threatening hemorrhage, transcatheter angiography with subsequent embolization proves a safe, quick, and recommended procedure.

CASE REPORT

This is a case of a 48 year-old, Filipino, G8P7 (7017) Roman Catholic from Legaspi City, who was admitted at a tertiary government hospital for the first time for vaginal bleeding. Past medical and family medical histories were unremarkable. Patient is a housewife, a high school graduate, with no known vices. She has had two non-promiscuous sexual partners with first coitus at 22 years of

age. Her 3rd pregnancy was a hydatidiform mole for which suction curettage was done. The rest of her pregnancies were carried to term and delivered vaginally with no complications.

History started eight months prior to admission when patient was brought to a provincial hospital due to increasing abdominal girth. Ultrasound showed a hypervascular endometrial mass, and patient was diagnosed with Gestational Trophoblastic Neoplasia stage I. A total hysterectomy with bilateral salpingoophorectomy was subsequently performed, with chemotherapy advised. Patient however refused chemotherapy and decided to be discharged against medical advice. She was subsequently lost to follow-up.

Three months prior to admission, patient noted vaginal bleeding, using 1 adult diaper per day, and an enlarging mass at the right labia. Patient was transfused with two units of packed red blood cells and subsequently discharged. One month prior to admission, there was recurrence of profuse vaginal bleeding, this time consuming four diapers per day. Patient was then brought to a district hospital and transfused with ten units of packed red blood cells. Patient was subsequently started with multiple agent chemotherapy in the form of Etoposide, Methotrexate, Actinomycin, Cyclophosphamide and Oncovin (EMACO). Due to lack of funds, patient opted transfer to a tertiary public hospital.

On arrival at the admitting section, patient had stable vital signs with blood pressure of 100/70 mmHg and a heart rate of 88 beats per minute. Patient was awake,

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alert, and not in cardiorespiratory distress. Systemic physical examination was unremarkable, except for a 5x5 cm cystic, non-tender purplish-to-bluish mass at the right labial area with a 1 cm point of rupture (Figure 1). There were minimal blood clots and vaginal bleeding within. On internal examination, the vagina was parous and the vaginal stump was intact. Transvaginal ultrasound revealed also an intact vaginal stump with no appreciable masses. Transperineal ultrasound, however, revealed an irregular heterogenous mass occupying the right labia majora measuring 6.8 x 3.6 x 5.6 cm. Color flow mapping of the mass showed moderate vascularity which, on Doppler interrogation, revealed high resistance indices (Figure 2).

Patient was subsequently admitted with an impression of GTN I:13 with tumor progression (Choriocarcinoma), status post THBSO (July 17, 2014), status post EMACO I (September 17, 2014), status post suction curettage for hydatidiform mole (1995, Legaspi). Hemoglobin was 87 and hematocrit was 0.24%. Baseline serum beta human chorionic gonadotropin (β hCG) was at 232,600 mIU/mL (Table 1). Plan for the patient was to continue EMACO chemotherapy.

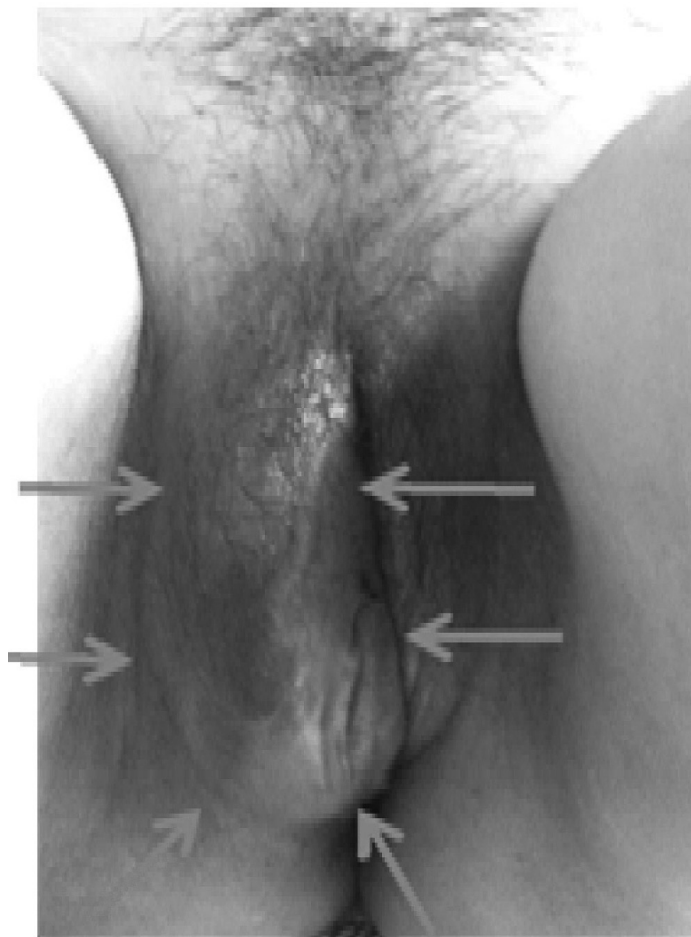


Figure 1. Arrows showing metastatic right labial mass measuring 5.0 x 5.0 centimeters, from gestational trophoblastic neoplasia, on admission



Figure 2. Ultrasound of the labial mass A) Yellow arrows border the anteroposterior view of the mass. B) Yellow arrows border the transverse view of the mass. C) Color flow mapping of the labial mass showing moderate vascularity.

Table 2. Trend in patient's serum beta human chorionic gonadotropin.

	Serum Beta human chorionic gonadotropin (mIU/mL)
Baseline	232,114
After EMACO Cycle 1	81,130
After EMACO Cycle 2	9512
After EMACO Cycle 3	1456
Post Emobilization	362
After EMACO Cycle 4	90/98
After EMACO Cycle 5	64.32
Current	16.26

During admission, patient had intermittent bouts of profuse vaginal bleeding, requiring multiple blood transfusions which inhibited regular administration of chemotherapy. On her 40th hospital day, after receiving only one cycle of EMACO chemotherapy, there was massive hemorrhage from the 1 cm point of rupture at the labial mass; this was unresponsive to digital pressure or vaginal packing. Hemoglobin dropped from 109 to 43 mg/L, and patient became hypotensive, requiring norepinephrine infusion. The patient was referred to interventional radiology for further treatment.

Transfemoral, lower aorta, and bilateral internal iliac angiograms were done using non-ionic contrast media, which showed a hypervascular mass in the inferior pubic area that correlated to the position of the labial mass (Figures 3A and 3B). Feeding arteries to the vulvar mass were shown to arise from branches of both pudendal and right obturator artery. Catheterization of the bilateral pudendal arteries was done. Once identified, the vascular supply was embolized with polyvinyl alcohol followed by gel foam particles until the blood flow ceased. Post-embolization angiograms showed absence of flow to both internal pudendal artery branches and right obturator artery branches. The patient tolerated the procedure well and without any complications (Figures 3C and 3D). The lesion regressed in size over the course of one week, and the chemotherapy was resumed. Currently, the patient is on her sixth cycle of EMACO chemotherapy with serum β hCG levels as low as 16.26 mIU/mL. There has been no

recurrence of vaginal bleeding with near disappearance of the labial mass (Figure 4A and 4B).

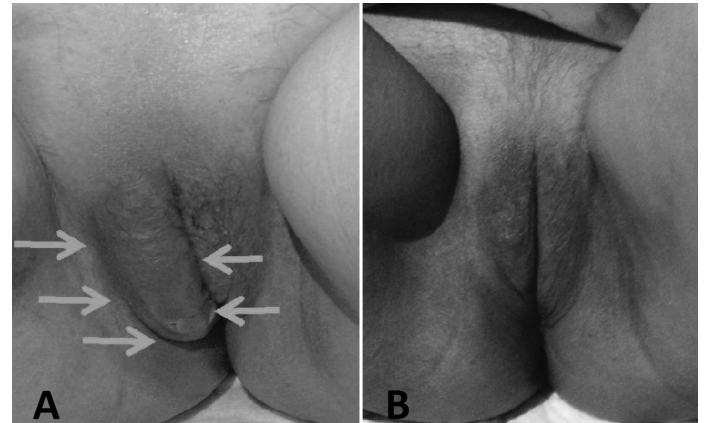


Figure 4. Post-Embolization. A) Arrows metastatic labial mass one week post-embolization. B) No visible lesion three months post-embolization.

DISCUSSION

Gestational trophoblastic neoplasia (GTN) is composed of four neoplastic entities: invasive hydatidiform mole, choriocarcinoma, placental site trophoblastic tumors (PSTT), and epitheloid trophoblastic tumor (ETT). All are highly malignant with a high propensity for local invasion and hematogenous spread.¹

Around fifteen percent of metastatic gestational trophoblastic neoplasias spread to local structures by local invasion. Only 4% tend to have distal metastases; spread to distal areas is via hematogenous route. Common sites of metastasis include the lung (60%), vulvovaginal (30%), liver (10%), and brain (10%).²

Metastasis in the vulvovaginal area, with 30% occurring in those with distal metastasis, is often misleading at first glance, especially in the vulvar area. As with our index patient, antecedent pregnancy does not usually arouse suspicion in the clinician. The patient had a molar pregnancy twenty years ago and has had five term pregnancies since. Commonly, recent vulvovaginal swelling and bleeding are the only presentation. The clinician may easily misdiagnose such a case, especially when the vulvovaginal mass does not present as usual, with the blue to purplish hue of metastatic choriocarcinoma.

The clinician should have a high index of suspicion and take an accurate clinical history along with a thorough pelvic examination, to avoid misdiagnosis and possibly fatal hemorrhage. The diagnosis should also be correlated with the serum β hCG titer.

Labial mass may be easily misdiagnosed as a dilated Bartholin's cyst, the most common large cyst of the vulva. This condition is managed by marsupialization or excision of the cyst, but if the mass is actually a metastatic GTN

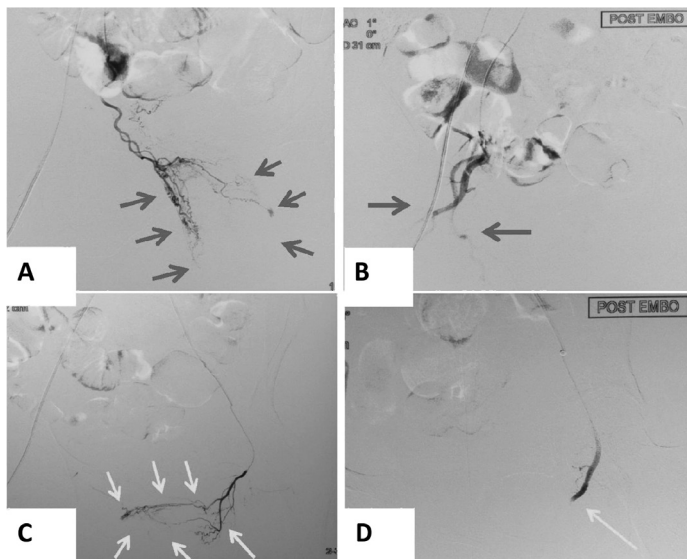


Figure 3. A) Red arrows showing labial mass being supplied by the right internal pudendal artery and obturator artery pre-embolization. B) Obliteration of right internal pudendal artery and obturator artery post-embolization. C) Yellow arrows showing labial mass being supplied by the left internal pudendal artery and obturator artery pre-embolization. D) Obliteration of left internal pudendal artery and obturator artery post-embolization.

mass, these procedures may precipitate life-threatening hemorrhage. Bhattacharyya *et al.*³ documented such an incident, where the vulvar mass presented as swelling measuring 4x3 cm, which appeared only two months prior to consultation. The associated swelling was tense, tender, cystic, and appeared infected. Upon excision of the mass, the physicians unexpectedly encountered profuse and intractable hemorrhage, which was controlled by deep mattress suturing; this initially relieved the bleeding, but it later recurred. Noticing a bulky uterus, they finally diagnosed this case as gestational trophoblastic neoplasia. In our case, it was fortunate that the patient already had undergone total hysterectomy with bilateral salpingo-oophorectomy and had a histologic result of choriocarcinoma, thus raising our index of suspicion of the labial mass to be metastatic choriocarcinoma.

Treatment of GTN, in general, is based on the FIGO 2000 staging and WHO prognosis scoring system. Metastatic high-risk patients are usually treated with EMACO chemotherapy, with good remission rate⁴. Surgery, particularly total hysterectomy in GTN is an adjuvant procedure; it decreases the tumor load, therefore decreasing the cycles of chemotherapy required. In some patients, chemotherapy also controls hemorrhage and removes resistant/persistent disease. Our patient, however, initially refused chemotherapy. This led to a total hysterectomy of the patient by a private physician. Evidence shows that although hysterectomy clearly has a place in the management of metastatic GTN, it is not often indicated as a primary management of patients with widely metastatic disease⁴. When controlling profuse uterine bleeding, bilateral internal iliac artery ligation is another effective surgical technique. Pelvic structures do not lose their blood supply after this procedure, as collaterals to the pelvic area are abundant.

The vascularity and fragility of metastatic vulvovaginal GTN puts a patient at severe risk for significant hemorrhage, one of the most common complications. Although bleeding may be controlled by digital pressure, packing, and sometimes local excision, angiographic embolization is an emerging safe and successful procedure which can be applied to metastatic lesions⁶. Local excision has been associated with many complications and a high morbidity rate. Angiographic embolization may prevent such catastrophic hemostatic morbidity when applied early in the course of clinical disease. In our case, digital pressure proved unsuccessful, and packing of the bleeding vulvar mass was not possible, as the mass was located on the labia. Local excision and oversewing were not considered, as additional manipulation and surgical procedure might incur additional bleeding and may have proven to be fatal. In this case, the only option was angiographic embolization of the artery feeding the labial mass.

Angiographic embolization is a minimally invasive procedure, in which guide wires and catheters are inserted into a large vein, and contrast material is injected to visualize the blood supply. Digital subtraction angiography (DSA) locates the artery or vein which is supplying the pathology. Once the vessel is identified, artificial embolus is placed, and another set of DSA images are taken to ensure an adequate deployment. This procedure prevents blood flow to the targeted area, and is effective at shrinking tumors and blocking aneurysms.

Since the development of new catheters and embolic materials, angiographic embolization has served as primary therapy for lower gastrointestinal bleeding.⁵ Recently, it has gained attention in the fields of obstetrics and gynecology, and is seeing more and more use in the specialty. The most common gynecological indication is uterine fibroids, based on the theory that reduction of myometrial arterial blood flow will cause infarction of the fibroids, which leads to a decrease in size.

Angiographic embolization has been used to treat massive hemorrhage in patients with gestational trophoblastic neoplasia. Keepanasseril's study⁶ documented seven women who underwent angiographic embolization due to massive hemorrhage. In this series, two were done in bilateral iliac arteries, four were in the bilateral uterine arteries and one was in bilateral internal iliac artery and hepatic artery, with a success rate of 85.7%. This study concluded that transcatheter embolization is a safe and quick procedure, and should be considered in GTN patients with acute hemorrhagic life-threatening complications.

Complications occur in approximately 6-9% of obstetric and gynecologic transcatheter embolization⁷. Some of the more serious complications include nephrotoxicity and hypersensitivity reactions to the contrast load, bleeding, thrombosis or hematoma around the puncture site, and the rarest, ischemic plexopathy. The complications enumerated here occur in less than 1% of the procedures. Fifty percent (50%) of patients experience postembolization syndrome, which includes pain, fever, nausea, and leucocytosis immediately after the procedure⁸. This is relieved by analgesic and anti-inflammatory medications. With the advancing knowledge and practice of embolization, these risks are considered minimal compared the highly malignant nature of the disease.

Unfortunately, angiographic embolization is very costly and may not be a feasible option for all patients who merit the procedure. Cost-effectiveness must be weighed in patients with very limited funds prior to proceeding. Still, this is a safer and more cost-effective measure compared to the cost of multiple blood transfusions, with the associated prolonged hospital stay and expensive

medications to stabilize the patient. If the patient has no funds, more affordable measures may be tried, but if all other measures to combat hemorrhage have been exhausted, angiographic embolization should be done to save the patient's life. Additional benefits include ischemia of the lesion, which allows fewer courses of chemotherapy than would otherwise be necessary.

Chemotherapy in gestational trophoblastic neoplasia is highly effective and is still the management of choice. In low-risk metastatic GTN and non-metastatic GTN, single agent methotrexate achieves complete response rates ranging from 48-74% after five cycles of chemotherapy⁹. High-risk metastatic GTN requires multiple chemotherapy agents, usually in the form of Etoposide, Methotrexate, Vincristine, and Cyclophosphamide. In these patients, complete response rate was 71%, with overall survival rate reaching 91%¹⁰.

Considering the success and effectivity of chemotherapy to GTN, one dilemma posed is whether to instill chemotherapeutic agents, in the form of methotrexate or etoposide, to the area identified in angiography, prior to embolization. Due to the lack of evidence and case reports on this, instillation of any chemotherapeutic agent was

deferred. There was no available literature on the type and dose of chemotherapeutic agent, or on the result of the instillation. Collaterals to the labial mass were visualized during the angiograph, and it was concluded that even if the main blood supply of the mass was blocked, systemic chemotherapeutic agent would still reach the labial mass through the collaterals and small feeding vessels. In this decision, the Hippocratic adage *Primum non nocere* was upheld.

SUMMARY

This is the first case of angiographic embolization in bilateral internal pudendal artery branches and obturator artery branches in our country and probably the world, based on the absence of literature documenting such a procedure.

Angiographic embolization is a safe and fast procedure which can be primarily employed in massive and profusely bleeding vulvovaginal masses from gestational trophoblastic neoplasias. It bears only minimal risk and proves to be a cost-effective technique in controlling hemorrhage. ■

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