Choriocarcinoma of the colon: A rare case*

By Jannah A. Tapodoc, MD and Lynnette R. Lu-Lasala, MD, FPOGS, FPSSTD
Department of Obstetrics and Gynecology, Southern Philippines Medical Center

ABSTRACT

Gestational trophoblastic neoplasia is a group of tumors which includes invasive mole, choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor, all of which develop after a recognized pregnancy. Choriocarcinoma is a highly invasive and metastatic neoplasm which arises in women of reproductive age. Local spread is reported at 15% while distant metastasis at 4%. Of the 4% of cases having distant metastasis, 60% goes to the lungs, 30% to the vagina, and 10% to other sites. Less than 5% of patients with metastatic gestational trophoblastic neoplasia have involvement of the gastrointestinal tract. This is the case of a 47-year-old multigravid patient who came in with an enlarging abdomen 8 years after she had a hydatidiform mole. Work-ups were done which revealed metastases to the colon, liver and lungs. The plan of management was to give multiple agent chemotherapy.

Keywords: Choriocarcinoma, Gestational Trophoblastic Neoplasia, Hydatidiform Mole, Gastointestinal tract

INTRODUCTION

Gestational trophoblastic neoplasia (GTN) represents the malignant end of the gestational trophoblastic disease spectrum and includes invasive mole, choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor.[1] GTN usually develops following a recognized pregnancy, especially after a hydatidiform mole. Diagnosis is made clinically, supported by persistently elevated serum beta human chorionic gonadotropin levels (BhCG) and findings of a highly vascular mass lesion within the uterus.

Local spread is reported at 15% while distant metastasis occurs in 4% of cases. Of the 4% of cases having distant metastasis, 60% goes to the lungs, 30% to the vagina, and 10% goes to other sites. Less than 5% of patients with metastatic GTN have initial involvement of the gastrointestinal tract.[2]

This case was written to highlight the clinical characteristics and incidence of GTN with colonic metastasis. The importance of early recognition for the timely administration of the appropriate management plan is likewise emphasized in order to have a good treatment outcome.

CASE REPORT

This is the case of a 47-year-old G4P2 (2022) who was admitted for the first time at a tertiary government hospital due to a gradually enlarging abdomen. She had a molar pregnancy eight years prior to this admission, for which she underwent an emergency total abdominal hysterectomy with right salpingooophorectomy (TAHRSO) due to a perforated uterus. Histologic diagnosis revealed hydatidiform mole. She had a repeat serum BhCG one week after the procedure then monthly for 2 months. She achieved normal BhCG titers during this time but was lost to follow up.

Three months prior to admission, she noticed a gradually enlarging abdomen, with a sharp, non-radiating hypogastric pain, associated with dysuria and changes in bowel movement. There was no fever, vomiting, tenesmus, and melena. She tolerated the symptoms and did not seek consultation.

A month prior to admission, there was persistence of the signs and symptoms prompting consultation with her previous attending physician. Urinary tract infection was considered since urinalysis showed presence of numerous red blood cells in the urine. Creatinine level was normal and the kidney-urinary-bladder (KUB) ultrasound was unremarkable. She was given unrecalled antibiotics which she took with good compliance.

Three weeks prior to admission, the above symptoms persisted hence urine culture was requested. Organisms found were pure isolates of Escherichia Coli. Laboratory tests such as CA-125, CEA, SGPT, creatinine, Hepatitis B antigen, and 12 L echocardiography showed normal results. The computed tomography (CT) scan of the whole abdomen revealed an irregular isodense peripherally enhancing abdominopelvic mass measuring 10.37 x

*Poster Presentation at the XX World Congress on Gestational Trophoblastic Diseases, October 20-23, 2019, Toronto, Canada

8.57 x 12.83 cms, which appeared to have replaced the uterus and with extension to the sigmoid colon. Consideration was an ovarian tumor. There was also note of bilateral hydronephrosis and hydroureter, non-obstructing nephrolithiasis as well as pulmonary and hepatic metastases. Chest x-ray was done, which revealed pulmonary masses on both upper lobes measuring 3.6 x 3.6 cms and 3.6 x 3.8 cms, respectively. Consideration was pulmonary metastases.

She was then referred to a gynecologic-oncologist for further evaluation and co-management. Serum BhCG was requested, which revealed 211,990 mIU/ml. She was referred to a trophoblastic disease specialist who requested for a cranial CT scan which showed normal findings. The patient was subsequently admitted for further management.

On the day of admission, she was awake, alert, ambulatory, conscious, coherent, and not in respiratory distress. Her blood pressure was 120/70, tachycardic at 114 beats per minute, respiratory rate of 20 and was febrile at 39.1 degrees Celsius. She had pale conjunctivae, anicteric sclerae, pale lips and with diminished breath sounds on both lung fields. The abdomen was globular, with normoactive bowel sounds, tympanitic in all quadrants, soft with tenderness upon deep palpation on all quadrants.

Speculum examination revealed an intact vaginal stump with whitish mucoid vaginal discharge. On internal examination, the introitus admitted 2 fingers with ease. There was a 15 x 12 cm movable, slightly tender mass on the hypogastric area. The adnexae and corpus were not palpated. On digital rectal examination, there was an irregular, firm, intraluminal mass approximately 4 centimeters from the anal verge. Blood was noted per examining finger.

The initial plan was to complete the diagnostic work-up which include an upper gastrointestinal (UGI) endoscopy and colonoscopy, with possible biopsy of the colonic mass. Baseline laboratory results showed hemoglobin of 115 g/L, WBC of 22.02 x 10^3/uL with neutrophilic predominance of 85%, and platelet count of 423 x 10^3/uL. The urinalysis result was unremarkable. Creatinine level as well as SGPT were normal. Sodium was slightly low at 133.4mmol/L. Other electrolytes were normal.

On the second day of admission, UGI endoscopy and colonoscopy were done. Endoscopic findings were normal. On colonoscopy, a rectosigmoid mass, with irregular borders, located approximately 20 cms from the anus was seen. Biopsy was done which revealed metastatic Choriocarcinoma (Figure 1). Upon the suggestion of the Pathology department, immunostain for hCG was done, which showed the syncytiotrophoblast to be strongly positive for beta hCG (Figure 2) confirming the diagnosis of Choriocarcinoma. Based on the FIGO 2000 Anatomic Staging System (Table 1) and WHO Prognostic Scoring

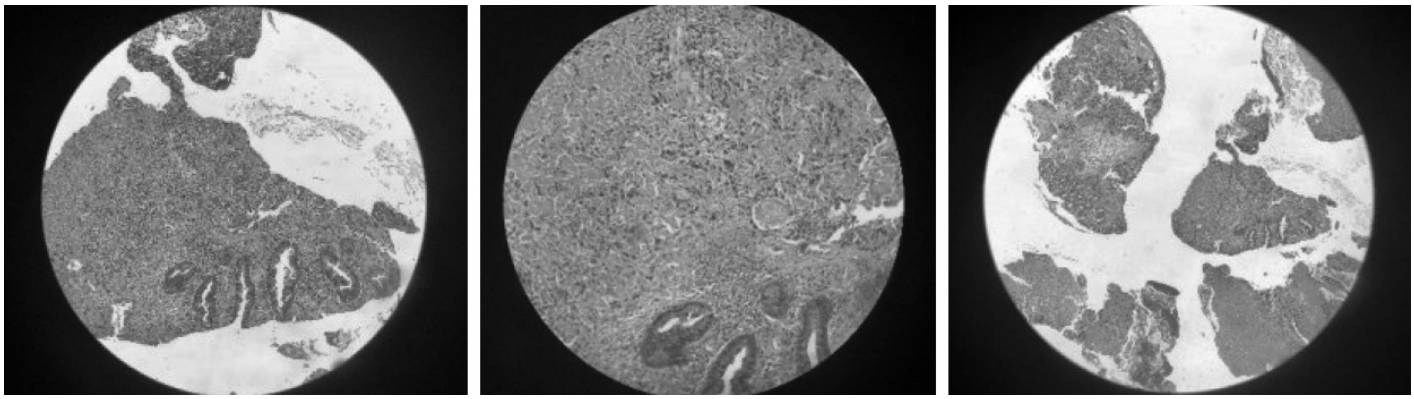

Figure 1. Scanning view of the biopsy specimen showing masses and sheets of trophoblastic cells that invaded the surrounding tissue and permeated vascular spaces

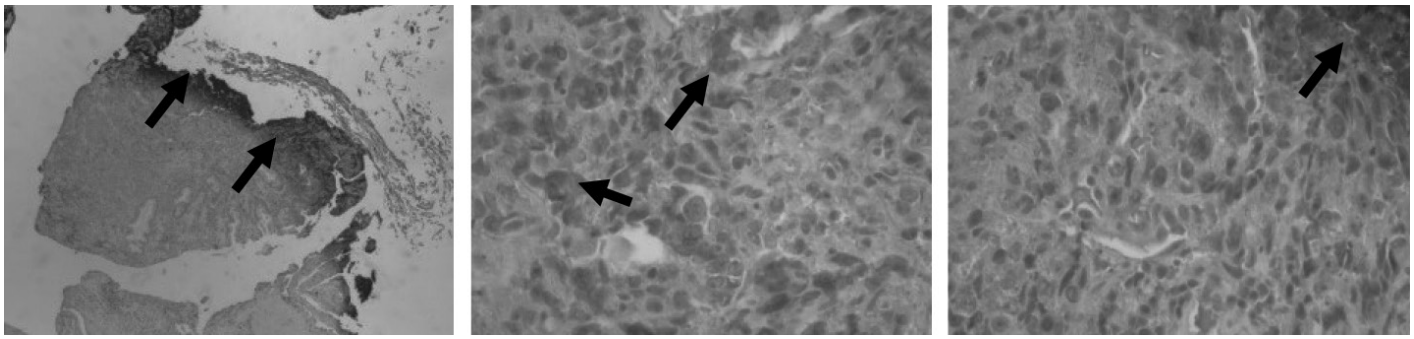

Figure 2. Immunostaining for hCG showing strongly positivity for beta hCG

System (Table 2), patient had a stage IV disease and a score of 16 (Table 3).

The patient had melena around 3-4 times a day, amounting to approximately 50-100 ml per episode. This was associated with diffuse, mild crampy abdominal pain. She also had febrile episodes with maximum temperature of 40.1 degrees Celsius. She underwent blood transfusion and was referred to the Section of Infectious Diseases (IDS) for co-management.

Hepatic artery embolization was contemplated due to the hepatic metastases. A triphasic CT scan was done but upon reviewing the result, the Section of Interventional Radiology noted that the hepatic mass was small, and it could not be possible to perform the procedure. The plan at this time was to initiate multiple agent chemotherapy using the EMACO regimen composed of Etoposide, Methotrexate, Actinomycin, Cyclophosphamide and Vincristine.

The patient continued to have episodes of melena occurring around 4-5 times a day amounting to around 50-100 cc per episode. Despite aggressive blood transfusion, her hemoglobin continued to drop making it impossible to start the chemotherapy. Additionally, she continued to have febrile episodes despite antibiotic treatment with Meropenem given intravenously at 1 gram every 8 hours. Naproxen Challenge test was done as suggested by the Infectious Diseases Section, however, there was no resolution of fever.

On the 40th hospital day, the patient developed dyspnea, which may be due either to the pulmonary metastasis or the progressive anemia. She was appraised regarding the need for intubation; however, the patient did not consent.

She eventually expired on the 42nd day of admission. The final diagnosis was Multiorgan Failure secondary to Gestational Trophoblastic Neoplasia Stage IV:16 (Pulmonary, Hepatic and Gastrointestinal metastases); G4P2 (2022); Status Post Cesarean Section II for Cephalopelvic Disproportion (1996 – SPMC, 2007 – LIMSO); Status Post Total Abdominal Hysterectomy with Right Salpingooophorectomy for Hydatidiform Mole (2010-LIMSO); Anemia, Severe, Secondary to Chronic Blood Loss; Complicated Urinary Tract Infection.

Table 1. FIGO 2000 Staging System

FIGO anatomical staging
I Disease confined to uterus
II GTN extending outside of the uterus but limited to the genital structures
III GTN extends to the lungs with or without genital involvement
IV Extension to the other sites of metastasis (brain, kidneys, liver, etc.

Table 3. Prognostic Score of the patient

PARAMETERS	SCORE
Age	1 (>40)
Antecedent Pregnancy	0 (Mole)
Interval from index pregnancy, months	4 (>12months)
Pretreatment hCG (miu/ml)	4 (211,990miu/ml)
Largest tumor size inc. uterus, cm	2 (>5cm)
Site of metastasis inc. uterus	4 (liver, lung, GI)
Number of metastasis identified	1 (3)
Previous failed chemotherapy	0

CASE DISCUSSION

Gestational trophoblastic neoplasia (GTN) is the malignant end of the gestational trophoblastic disease (GTD) spectrum. This disease entity includes invasive mole (IM), choriocarcinoma (CC), placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic

Table 2. WHO Prognostic Scoring System

FIGO/WHO scoring system based on prognostic factors.

FIGO/WHO risk factor scoring with FIGO staging	0	1	2	4
Age	<40	>40	–	–
Antecedent pregnancy	Mole	Abortion	Term	
Interval from index pregnancy, months	<4	4-6	7-12	>12
Pretreatment, hCG, mIU/mL	$<10^3$	$>10^3$ - 10^4	$>10^4$ - 10^5	$>10^5$
Largest tumor size including uterus, cm	–	3-4	≥5	–
Site of metastases including uterus	Lung	Spleen, kidney	Gastrointestinal tract	Brain, liver
Number of metastases identified	–	1-4	5-8	>8
Previous failed chemotherapy	–	–	Single drug	Two or more drugs

tumor (ETT).[1] GTN may occur following any type of pregnancy but has an increased incidence following a molar pregnancy. Approximately 1 in 40,000 normal pregnancies and 1 in 40 hydatidiform moles progress to gestational choriocarcinoma.[3] Around fifty percent of choriocarcinoma cases are preceded by molar gestation, 25% by spontaneous abortions, 22.5% by normal pregnancy, and 2.5% by ectopic pregnancy.[4] Because of the high propensity for development of GTN following a molar gestation, patients are advised strict post-evacuation BhCG monitoring. The Philippine Society for the Study of Trophoblastic Diseases recommends a repeat BhCG titer a week after molar evacuation followed by BhCG monitoring every two weeks until 2 normal determinations. Patients are then advised monthly BhCG monitoring for six months during which pregnancy must be avoided. In addition, patients who become pregnant within 6 months before completing BhCG follow up has been reported to have increased risk of abnormalities including spontaneous abortions, fetal demise and repeat molar pregnancy.[1] The index case underwent TAHRSO 8 years prior to admission. She followed up with her attending physician after a week, still with increased BhCG. However, she was able to achieve normal BhCG within 2 months after her surgery. In a study by Gueye et al, the risk of relapse after achieving a nondetectable serum BhCG is very low at <1%.[5]

Diagnosis of GTN is commonly made clinically. Vaginal bleeding is the most common symptom but presentation may vary depending on the site of metastasis. This patient presented with symptoms referable to the gastrointestinal tract, the most prominent of which were hypogastric pain and melena.

Choriocarcinoma is a highly malignant tumor with propensity for local invasion and metastasis. Metastasis is thought to occur primarily by hematogenous dissemination and the invasiveness of trophoblastic tissue is enhanced by its ability to breach end-arterial networks.[6] Hematogenous metastasis develops in the early stages of the disease leading to a high metastatic rate (30%) at presentation. The most commonly involved sites are the lungs (80%), vagina (30%), pelvis (20%), liver (10%), and the brain (10%).[4] Metastatic sites of GTN are highly vascular and frequently result in local bleeding complications. It is believed that the high affinity of trophoblastic cells towards blood vessels with disruption of normal vascular architecture leads to bleeding.[7]

Gastrointestinal involvement is present in less than 5% of cases.[2,8] Proper localization is achieved through an endoscopy and therapy of these lesions can be achieved by chemotherapy coupled with angiographic embolization or surgery.[8] Despite being a highly curable malignant disease, the occurrence of gastrointestinal bleeding worsens prognosis.[9] The index patient had metastasis to the colon, particularly in the rectosigmoid area.

Risk factors for colonic metastasis is not known; however, it is theorized that previous uterine perforation is associated with colonic recurrence.[2] The patient underwent TAHRSO in 2010 due to perforated uterus, which could already be an invasive mole. Proper metastatic work-up and institution of chemotherapy at that point may have already been done.

Following the diagnosis of GTN, patients are scored using the FIGO 2000 Staging System (Table 2) and classified as low risk or high risk using the modified WHO prognostic scoring system. A score of less than 7 is classified as low risk while a score of 7 or more is considered high risk.[9] Treatment is then based on the patient's stage and score.

Chemotherapy is the main treatment modality for GTN.[1,9] Patients with low risk disease generally respond well to single-agent chemotherapy, with Methotrexate and Actinomycin being the most commonly used agents.[1,9] On the other hand, patients with metastatic, high risk disease are unlikely to be cured with single agent therapy. Therefore, these patients are treated with combination chemotherapy. Currently, the EMACO regimen, composed of Etoposide, Methotrexate, Actinomycin, Cyclophosphamide and Vincristine, is the most widely accepted first line regimen used to treat high risk GTN due to its high effectiveness with acceptable toxicity profile.[1,9] For the case presented, combination chemotherapy in the form of EMACO was ideal since she was classified as having a metastatic, high risk disease.

This patient was diagnosed to have liver metastasis based on CT scan findings. It is known that there is an increased risk of hemorrhage from the main tumor as well as from the metastatic sites upon initiation of chemotherapy.[10] Thus, a transcatheter angiographic embolization was planned in anticipation of this occurrence as this modality is very useful in controlling severe hemorrhage in metastatic.[1,10] However, in this case, the procedure was deferred because the hepatic mass was small and therefore did not warrant embolization.

While chemotherapy remains to be the primary mode of treatment for GTN, surgery may be beneficial in select cases, such as chemotherapy resistance, tumor perforation, intractable bleeding, and infection not responding to antibiotics.[11] For patients presenting with metastasis in the gastrointestinal tract, bowel resection may be done if the bleeding is massive and could not be controlled by conservative management and chemotherapy. Bowel lesions may require surgery for the following reasons: (1) Severe and persistent bleeding which may be caused by lesions sloughing off and causing bleeding into the bowel lumen; (2) Perforation of the bowel, which may cause peritonitis; (3) Intestinal obstruction caused by extensive intra-abdominal disease.[12] In these cases, excision of the

lesion and reanastomosis is usually effective treatment. Surgical intervention involving resection of the mass may have been an option for the index case in order to stop bleeding. However, persistence of the anemia and infection did not make her a good candidate for surgery.

The prognosis of gestational trophoblastic neoplasia with multiorgan metastases is not as bad compared to other malignancies. The five-year overall survival of patients treated with the EMACO regimen vary from 75% to 90%. Presence of liver metastasis correlated with only 27% long term survival and dropped to 10% when concomitant brain metastasis was present.[13]

The patient presented in this paper was a therapeutic challenge. While chemotherapy was planned out, it could not be started due to the persistence of bleeding. Despite continuous blood transfusion, she remained severely anemic; thus, preventing the institution of chemotherapy. Surgery may have been an option but this was likewise not considered since she was a poor candidate for surgery.

SUMMARY

Colonic metastasis in patients with gestational trophoblastic neoplasia, is a rare occurrence, usually happening in less than 5% of cases. Uterine perforation is associated with colonic metastasis. With the availability of potent chemotherapeutic agents, prognosis of patients with GTN has improved. However, early diagnosis and timely institution of therapy are vital elements for the increased survival rate of patients with metastatic high risk gestational trophoblastic neoplasia. ■

REFERENCES

1. Clinical Practice Guidelines for the Diagnosis and Management of Gestational Trophoblastic Diseases. Philippine Society for the Study of Trophoblastic Diseases, Inc. November 2016.

2. Ju Hyun Ryu, Chel Hun Choi, Tae-Joong Kim et al. Chemo-resistant choriocarcinoma metastatic to colon cured by low-anterior resection. *J Gynecol Oncol*. 2011; 22(3):203-6.

3. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol*. 2010 Dec; 203(6):531-9.

4. Kuyumcuoglu U, Guzel Al, Erdemoglu, M, Celik Y. Risk Factors for Persistent Gestational Trophoblastic Neoplasia. J Exp Ther Oncol. 2011; 9(1):81-84.

5. Gueye M, Kane-Gueye SM, Ndiaye-Gueye MD et al, Gestational trophoblastic neoplasia after achieving a nondetectable serum human chorionic gonadotropin level. *BJOG*. 2014; 121(11):1415-1419.

6. Soo Yeon Park, Da Eun Lee, Hee Jung Park et al. Retroperitoneal nongestational choriocarcinoma in a 25-year-old woman. *Obstet Gynecol Sci*. 2014; 57(6):544-8.

7. Bouchrad-Frtier G and Covens A. Gestational trophoblastic disease. In: Lentz GM, Lobo RA, Gershenson DM, Katz VL (eds): Comprehensive Gynecology 7th Edition. Philadelphia:Elsevier 2017; 787-800.

8. Infante JM, Pedreño B, Noiseux R et al. Gastrointestinal hemorrhage due to metastatic choriocarcinoma with gastric and colonic involvement. *Rev Esp Enferm Dig*. 2004; 96(1):77-80.

9. Gestational Trophoblastic Disease. In: Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL (eds): Williams Obstetrics. 25th Edition. United States. McGraw-Hill Education. 2018; 20:824-839.

10. Lemanska A, Banach P, Katarzyna S et al. Urgent Embolization of hemorrhagic choriocarcinoma liver metastatsis – Case report and review of literature. *Hinekol Pol*. 2015; 86(12):957-61.

11. Kyung Jin Eoh, Yung Shin Chung, Young Tae Kim. Role of surgical therapy in the management of Gestational Trophoblastic Neoplasia. *Obstet Gynecol Sci*. 2015; 58(4):277-83.

12. Barnard DE, Woodward KT, Yancy SG et al. Hepatic Metastases of Choriocarcinoma: A Report of 15 Patients. *Gynecol Oncol*. 1986; 25(1):73-83.

13. Seckl MJ, Sebire NJ, Fisher RA et al. Gestational trophoblastic Disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow up. *Ann Oncol*. 2013; 24 Suppl 6:vi39-50.