

## CASE REPORT

# Gestational Choriocarcinoma with Varied Clinical Presentation and Treatment Outcome: A Case Series

<sup>1</sup>Tshering Tamang, <sup>2</sup>Ugyen Tshomo

## ABSTRACT

Gestational choriocarcinoma is a highly malignant form of gestational trophoblastic neoplasia often seen with local and distant metastasis. It can arise from any type of pregnancy and presents with varied clinical signs and symptoms. Here, we present gestational choriocarcinoma cases diagnosed at Jigme Dorji Wangchuck National Referral Hospital with a variety of clinical presentation and the treatment outcomes. Six cases were confirmed in 2 years. Two cases presented with lung metastases; one with hemoptysis and the other with a chronic cough and lung mass. Three had large pelvic masses and abnormal vaginal bleeding. One patient had persistent uterine bleeding after a miscarriage. Two of the six patients had failed to follow-up after the diagnosis of molar pregnancy. Multiagent chemotherapy with selective hysterectomy and beta-hCG surveillance led to favorable outcomes.

### Teaching points:

- A high degree of clinical suspicion is necessary for early diagnosis and appropriate treatment
- Strict adherence to follow-up after molar pregnancy is important to avoid complications

**Keywords:** Choriocarcinoma, Gestational trophoblastic neoplasia, Molar pregnancy.

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## BACKGROUND

Gestational choriocarcinoma is a rare variety of gestational trophoblastic neoplasia. Its highly malignant nature is due to early vascular invasion causing widespread

metastases. Histologically, abnormal trophoblastic hyperplasia is seen with anaplasia and absence of chorionic villi. Hemorrhage and necrosis are common. The reported incidence in Europe and North America is about 1 in 40,000 pregnancies and 1 in 40 hydatidiform moles; whereas in Southeast Asia and Japan, the rates are higher at 9.2 and 3.3 per 40,000 pregnancies respectively.<sup>1</sup> It can follow any pregnancy. Clinical presentations vary according to the extent of disease and location of metastases. Following a molar pregnancy, beta-hCG may be persistently elevated, or symptoms like abnormal uterine bleeding and pelvic pain or pressure due to the growth of a tumor may be present. However, after a normal pregnancy, the features are usually due to metastases. Chemotherapy forms the primary treatment after classification into risk groups as defined by the International Federation of Obstetrics and Gynecology (FIGO) staging and scoring system. Here, we present six cases of gestational choriocarcinoma with heterogeneous clinical presentation and treatment outcomes that were diagnosed in JDW hospital in two years.

## CASE REPORTS

### Case 1

A 26-year-old G3P2+0 woman, after a one-year history of a dry cough, chest pain, and dyspnea, presented with fever and respiratory distress and was treated for acute pneumonia. However, a chest X-ray revealed a right pleural effusion and left lung mass, and on computer tomography (CT) scan imaging, there was a left lung circumscribed mass. The patient was admitted to the medical ward and referral to India was arranged for the evaluation and treatment of suspected lung carcinoma. Meanwhile, a gynecology consultation was requested for abnormal vaginal bleeding and a positive urine pregnancy test with a normal pelvic ultrasound.

The patient's last child had been delivered uneventfully 7 years previously, and she was using depot medroxyprogesterone acetate for contraception. Four months prior to this admission she reported with a one-year history of irregular vaginal bleeding and was managed as having a complete miscarriage. However, the bleeding had continued. At the time of gynecology assessment, the initial serum beta-hCG was negative, but a second report was 92,640 mIU/mL. Gestational

<sup>1</sup>Resident, <sup>2</sup>Professor

<sup>1,2</sup>Department of Obstetrics and Gynecology, Khesar Gyalpo University of Medical Science, Thimphu, Kingdom of Bhutan

**Corresponding Author:** Tshering Tamang, Resident, Department of Obstetrics and Gynecology, Khesar Gyalpo University of Medical Science, Thimphu, Kingdom of Bhutan, e-mail: tsering3113@gmail.com

trophoblastic neoplasia stage III was diagnosed and chemotherapy initiated with etoposide, methotrexate, actinomycin-D, cyclophosphamide, oncovin (EMACO) multi-agent regimen. After six cycles she improved dramatically, but by CT imaging of the lung mass remained unaltered in size. For a second opinion, the patient was referred to Kolkata Cancer Hospital and three additional cycles of EMACO were administered. Monthly beta-hCG levels were followed for two years and remained in the normal range indicating a complete cure.

### Case 2

A 50-year-old, G7P5+1 whose last term delivery was 15 years ago, followed by spontaneous miscarriage two years ago presented with heavy vaginal bleeding after a period of amenorrhea of unknown duration and positive urine pregnancy test. After an emergency uterine evacuation in a local hospital, she continued to have vaginal bleeding for which a second uterine evacuation was performed. A serum beta-hCG was 14698 mIU/mL was obtained before the second evacuation, and histopathology of the uterine content reported as 'suspicious choriocarcinoma.' Post-evacuation beta-hCG level was rising from 3803 to 4538 mIU/mL and referral to our center was made. A pelvic ultrasound revealed an echogenic mass of 2 × 2 centimeters in the endometrial cavity extending into the myometrium. She underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO) at which time the tumor was found in the endometrial cavity invading into myometrium without extension to serosa or vagina. Choriocarcinoma was confirmed by pathologic evaluation. The patient received adjuvant EMACO chemotherapy with remission after

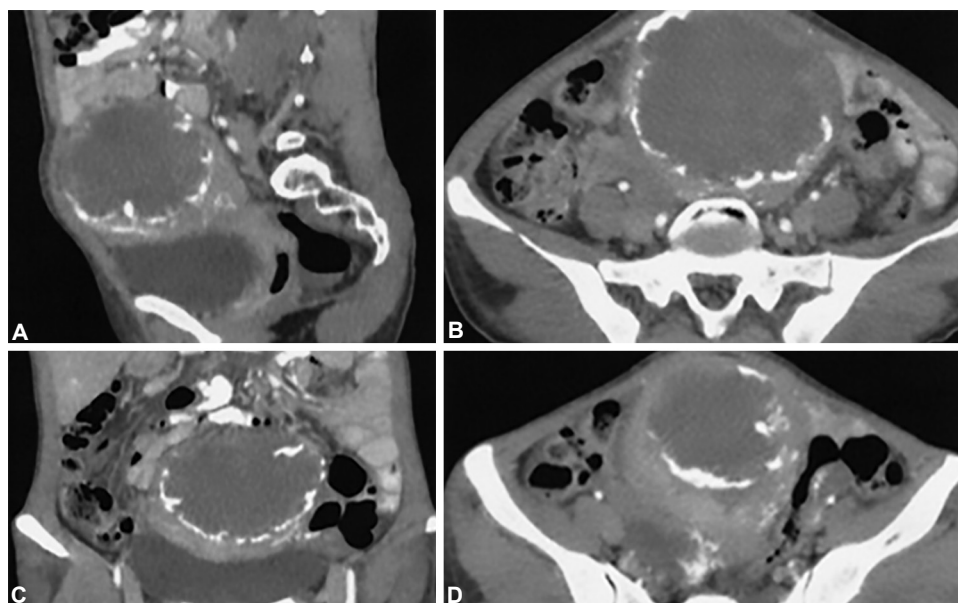
three cycles. Follow-up beta-hCG monthly for 2 years remained normal level and cure achieved.

### Case 3

A 48-year-old G7P6016 female presented with abdominal pain, a large pelvic mass, and 6 months of irregular vaginal bleeding for which she was referred to JDWNRH from a district hospital. The patient gave a history of her last term delivery occurring 6 years previously. Two years ago she was diagnosed with a molar pregnancy after which she developed gestational trophoblastic neoplasia. She received three cycles of chemotherapy before being lost to follow-up. At the time of the JDWNRH referral, a firm, 20-week size pelvic mass was palpated. Evaluation included a beta-hCG level of 137,450 mIU/mL, and an ultrasound revealed a large, mixed-echoic area, measuring 9.6 × 8.8 centimeters, with increased peripheral vascularity within the uterus (Fig. 1). A highly vascular growth in the uterus and thrombus in the inferior vena cava (IVC) were seen on abdominal CT (Fig. 1). MRI of the brain was normal. The patient has diagnosed with stage III choriocarcinoma and underwent a TAH+BSO. No metastases were noted in the adnexa or vagina, and choriocarcinoma was confirmed by surgical pathology. Postoperative EMACO chemotherapy was commenced and remission seen with six cycles and negative hCG level after one-year follow-up.

### Case 4

A 27-year-old G3P2012 woman reporting two uneventful pregnancies with the last delivering 6 years previously was referred from a district hospital with an adnexal mass and irregular menses. On examination, an 18-week size



**Figs 1A to D:** Computed tomography abdomen showing large uterine mass with peripheral increased vascularity

mass was palpated, which was confirmed by ultrasound. The mass measured 17 × 12 centimeters and had features suggestive of hydatidiform mole. A beta-hCG level was 141,460 mIU/mL, but when no tissue was obtained upon dilatation and uterine evacuation. The patient was discharged from the hospital for hysterectomy planned on a later date. However, soon thereafter she was readmitted with peritonitis and sepsis. An urgent abdominal CT was obtained, and the images were suggestive of an invasive mole (Fig. 2). An emergency laparotomy and total abdominal hysterectomy (TAH) were performed. Surgical findings included foul-smelling, dark-colored peritoneal fluid, a large fleshy growth on the uterus, and apparent uterine perforation. Postoperatively, the patient was monitored closely in the intensive care unit. Fever and signs of sepsis persisted prompting a second laparotomy with peritoneal lavage. She then recovered without further problems. Choriocarcinoma was confirmed upon pathologic evaluation, and the EMACO regimen was started. After three cycles the beta-hCG level dropped to 10 mIU/mL. The patient has since been lost to follow-up.

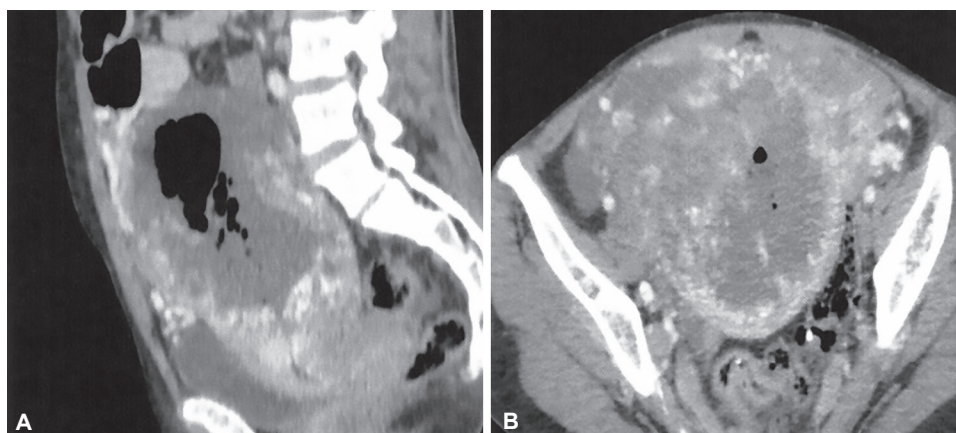
**Case 5**

A 28-year-old G2P1011 woman delivered at term 3 years ago which was followed by a molar pregnancy 18 months

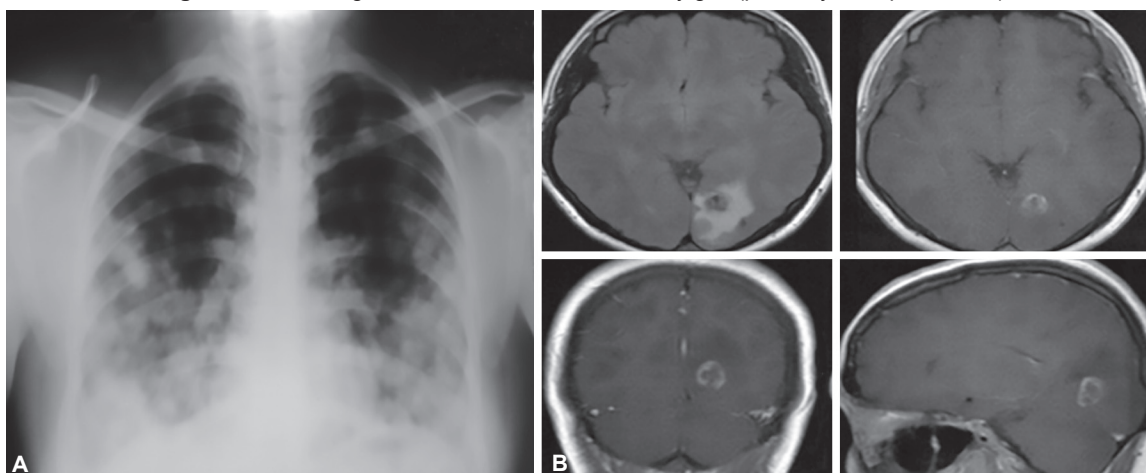
later. However, she was lost to follow up until she presented to a district hospital with a two-week history of a productive cough, breathlessness, and frank hemoptysis. Investigations were done with the presumptive diagnosis of tuberculosis prior to transfer. Upon arrival at JDWNRH, the patient was in respiratory distress and was treated with intravenous antibiotics for acute pneumonia while further evaluation was pursued. Bilateral cannon balls were visible on chest X-ray (Fig. 3), and serum beta-hCG was 143,800 mIU/mL even though a urine pregnancy test had been negative. She was managed as stage III gestational trophoblastic neoplasia (GTN) with lung metastases with the EMACO regimen. After six cycles, remission was noted, but she relapsed with brain metastasis (Fig. 3) and referred to India. She underwent high dose chemotherapy and brain radiation which had brought successful remission. Currently, she is following up with monthly beta-hCG.

**Case 6**

A 35-year-old G3P2012 female had a miscarriage six months ago and underwent uterine evacuation with normal findings upon pathologic inspection. Irregular vaginal bleeding continued, and the patient presented in a local hospital when the bleeding became heavy. An ultrasound revealed a uterine mass suggestive of



**Figs 2A and B:** Huge uterine mass with intracavitary gas (probably from perforation)



**Figs 3A and B:** Cannonball appearance of lungs and focal brain metastasis in the right occipital lobe

hydatidiform mole. A suction curettage was attempted but discontinued due to profuse bleeding. The patient was transferred to JDWNRH for an urgent uterine evacuation and blood transfusion. A beta-hCG was 95,240 mIU/mL, and her hemoglobin was 8.9 g/dL after transfusion. The CT imaging revealed a large growth in the uterus invading the myometrium and possible pulmonary and hepatic metastases (Fig. 4). A TAH was performed. Postoperatively there was a fall in beta-hCG to 6,094 mIU/mL. Adjuvant EMACO regimen was given, and remission achieved after six cycles. Currently, the patient is being followed monthly, and hCG levels have remained normal for one-year follow-up.

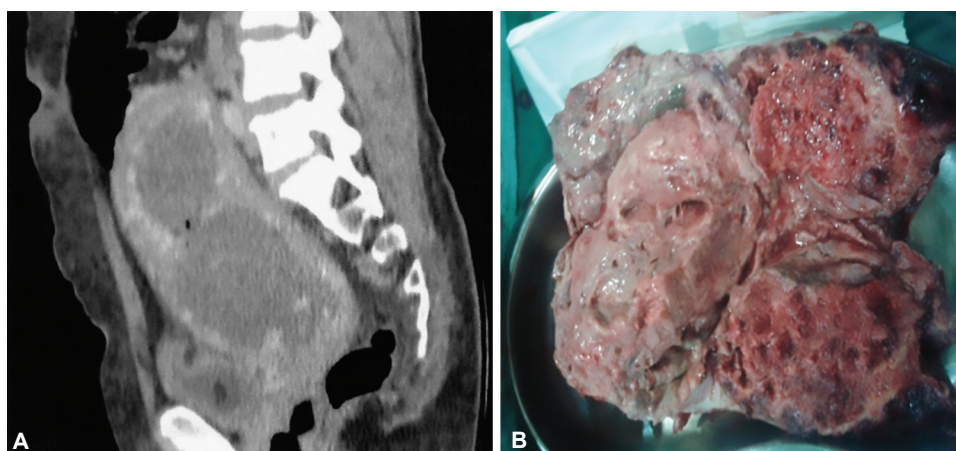
## DISCUSSION

Gestational choriocarcinoma is a highly malignant and aggressive trophoblastic tumor. About 50% of GTN arise from hydatidiform moles, 25% from the term or preterm pregnancies and another 25% from abortions or tubal pregnancies. Only 2–3% of molar pregnancies progress to choriocarcinoma.<sup>1</sup> After evacuation, around 15–20% of complete mole and 1–5% of the partial mole may progress to GTN including choriocarcinoma.<sup>2</sup> In our cases, two patients had preceding molar pregnancies, two normal pregnancies, and two miscarriages. The interval from antecedent pregnancy was 6 months to 7 years.

The common gynecological presentations are abnormal vaginal bleeding and pelvic masses. Non-gynecological presentation occurs due to metastases in the lungs and brain. The sites of metastases are pulmonary (80%), vagina (30%), central nervous system (10%) and hepatic (10%).<sup>3</sup> Symptoms of lung metastasis can be dyspnea, chest pain, cough, hemoptysis, pleural effusion, and respiratory failure whereas vaginal metastases typically present with vaginal bleeding or purulent vaginal discharge. Involvement of the central nervous system presents with headache, neuropathy, dizziness, slurred speech, visual distur-

bances, or hemiparesis due to intracranial haemorrhage or mass. However, non-typical or unusual presentations have been described in the literature. Headache with pituitary metastasis, orbital swelling, and ptosis with lacrimal gland infiltration, uterine perforation with hemorrhage, and postmenopausal bleeding have been described.<sup>4-8</sup> Our cases displayed a variety of unusual clinical manifestation including suspected pulmonary tuberculosis, lung mass, pneumonia, heavy vaginal bleeding, pelvic mass and peritonitis which highlights the importance of having a high degree of clinical suspicion of choriocarcinoma in women of reproductive age.

Gestational trophoblastic neoplasia (GTN) including choriocarcinoma is highly sensitive to chemotherapy. The treatment is guided by FIGO staging and scoring system. Low-risk disease (score <7) responds well to single-agent methotrexate or actinomycin-D, and the cure rate approaches 100%. Patients with high-risk diseases are generally given multi-agent EMACO regimen, and cure rate approaches 80–90%.<sup>2,9</sup> Patients with scores exceeding 13 (ultrahigh-risk), the response rate with etoposide, platinum/etoposide, methotrexate actinomycin-D (EP/EMA) regimen is about 60% of inducing remission.<sup>9</sup> In about 30% of patients, incomplete response to first-line chemotherapy or relapse from remission is expected. When the central nervous system metastases are involved, remission achieved can be 60–80% with whole brain irradiation and/or intrathecal methotrexate infusion along with simultaneous systemic chemotherapy.<sup>9</sup> All our cases were stages I–III with scores of 8–12 falling into the high-risk group; however, EMACO therapy and selective hysterectomy provided beneficial role. Although we do not have the information concerning the patient lost to follow up for chemotherapy, there was no mortality in the other five patients. Mortality is usually seen in nonpulmonary metastatic and chemoresistant type of choriocarcinoma. Higher risk is associated with previous antecedent term pregnancy, long interpregnancy intervals, and higher



**Figs 4A and B:** CT abdomen showing large mass with involvement of cervix and postoperative cut-section of the growth in the uterus

**Table 1:** Summary of patients' characteristic

Age: Years	Antecedent pregnancy	Clinical presentations	Pretreatment $\beta$ -hCG	Stage/score	Treatment
27	P2 term	Cough, SOB, Chest pain, fever, Lung mass	96,240	III/9	• EMACO
50	P5 miscarriage	Amenorrhea Heavy PV bleed	14,698	I/ 8	• TAH+BSO • EMACO
48	P6	Amenorrhea, PV bleeding	137,450	III/11	• TAH+BSO • EMACO
27	P2	Irregular PV bleed	141,460	II/10	• TAH + • EMACO
28	P1 H. mole	Cough, hemoptysis Amenorrhea, PV bleeding	1,43,1800	III/11	• EMACO
35	P2 miscarriage	Irregular PV bleed	95,240	II/12	• TAH + • EMACO

pretreatment beta-hCG level as illustrated in our patients. Death in these patients occurs early as a result of massive hemorrhage; necrosis or side effects of chemotherapy.<sup>10</sup>

Administering three cycles of consolidation chemotherapy after remission which is given every 15 days is standard practice. A negative beta-hCG suggests the number of malignant cell present is  $10^5$  and the body is not completely eradicated of cancer.<sup>11</sup> Except for one who lost to follow-up, all patients were received consolidation therapy in this series.

Post-evacuation surveillance with beta-hCG monitoring is essential for early diagnosis of post-molar GTN and choriocarcinoma. Studies show that GTN rarely occurs after the hCG has spontaneously returned to normal.<sup>12</sup> As seen in two of our cases, who failed to follow-up after molar pregnancy in the past; and subsequently presented with choriocarcinoma which could have been prevented with serial followed-up. The cases and their presentation can be viewed in Table 1.

## CONCLUSION

A variety of clinical signs, symptoms, and complications can be associated with gestational choriocarcinoma. A high degree of clinical suspicion is essential for early diagnosis, and high-risk GTN is uniquely sensitive to multi-drug chemotherapy with a high cure rate and survival.

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