Gestational choriocarcinoma at Juba Medical Complex and Juba Teaching Hospital: five case reports

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Introduction

Gestational choriocarcinoma (GCC) is the most malignant of the four gestational trophoblastic diseases. The others are: invasive mole, placental site trophoblastic tumour, and epithelioid trophoblastic tumour.[1,2,3,4,5,6] We report five cases of GCC managed at the Juba Medical Complex and Juba Teaching Hospital since 2011. The purpose is to draw attention to this condition with its complex presentations, need for early diagnosis and potential for cure. Recurrent vaginal bleeding in the presence of a pregnancy of unknown location and a positive pregnancy test should make the clinician suspect GCC. A woman of childbearing age with disseminated malignancy of unknown primary cause should have a pregnancy test.[1,2,3,6]

Case 1

A 28-year-old lactating woman (para 3+0) presented on 11/12/2011 with heavy vaginal bleeding. She was restless, sweaty, with cold extremities and severe pallor. Her temperature was 36.5 C, pulse 120/min and BP 80/50mm Hg, A pelvic examination revealed vaginal blood clots and products of conception plugged in the cervix. The uterus was equivalent to 10-12 weeks gestation, freely mobile with no adnexal masses.

After a diagnosis of an incomplete miscarriage, placenta-like tissue was evacuated from the uterus and sent for histology. Hb was2.8 g/dl and the patient transfused with two units of blood.

She delivered a full-term male baby at home 8/8/2011. She had continued bleeding for the subsequent two months. She had had an ultrasound scan (USS) and an evacuation was done for retained placental tissue. She was discharged on haematinics with a diagnosis of retained piece of placenta.

However, bleeding continued and admitted again on 22/12/2011 with vaginal bleeding and collapse: pulse of 130 min. BP 60 /40 mmHg, and the vagina full of clots. Cervix was closed, bulky uterus, no adnexal masses. A gestational trophoblastic neoplasia was suspected. A urinary pregnancy test was strongly positive.

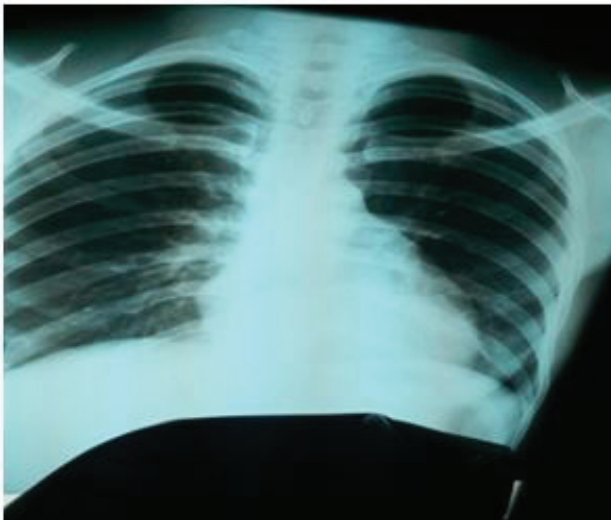

Figure 1. Case 1 chest x-ray (Credit: Kizza Paul and Paula Nuer)

Her Hb was 2.5 g/dl, so she was transfused with two units of blood. Her chest Xray was normal (see Figure 1). USS showed normal abdominal organs. Histology of the vaginal products confirmed

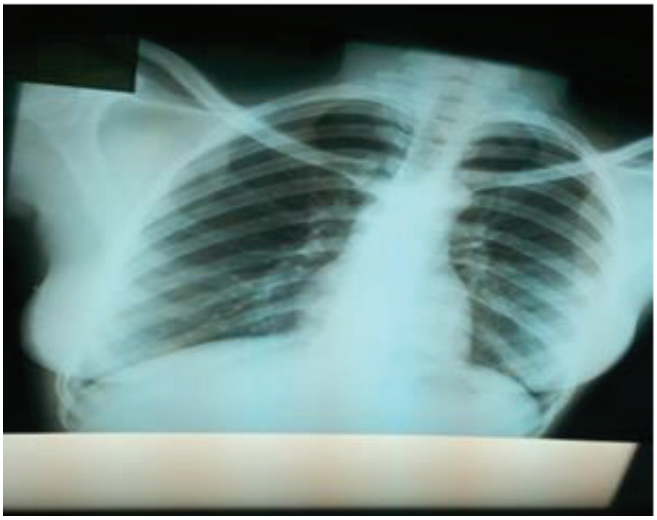

Figure 2. Case 2. Normal chest X-ray

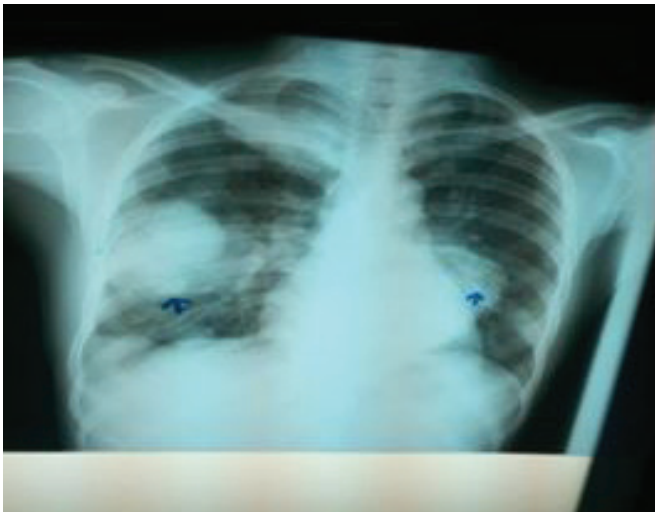

Figure 3. Case 3. X-ray showing three cannon ball masses balls in lungs (Credit: Kizza Paul and Paula Nuer)

a choriocarcinoma. She was graded as a low risk choriocarcinoma and for low risk chemotherapy.

After two cycles of chemotherapy the urine pregnancy test was negative. After the 4th cycle she absconded but returned six weeks later due to vaginal bleeding. The pregnancy test was positive. High risk chemotherapy was started. She completed six cycles on 5/10/2012. βhCG was normal. Two months later, she had miscarriage at six weeks pregnancy. βhCG was normal two weeks later.

Case 2

A 22-year old woman (para 3+1) presented on 4/7/2012 with recurrent vaginal bleeding following miscarriage of an abnormal pregnancy ten months earlier. Pulse was 86/min, BP 120/70 mm Hg. The uterus size was equal to a 12 weeks pregnancy. A pelvic examination was normal.

Hb was 9.1 g/dl, pregnancy test was positive, chest X-ray was normal, (see Figure 2); USS showed a distorted heterogeneous mass 12x1.6x6 cm in the endometrium partially attached to the uterus. Curettage produced necrotic tissue. A missed abortion was considered the most likely diagnosis. She was discharged the following day with a plan for histology to be checked in three weeks.

Three weeks later, she was readmitted with heavy vaginal bleeding. A pregnancy test was strongly positive. Low risk choriocarcinoma was suspected clinically and confirmed histologically. The chemotherapy was started immediately. After four cycles of chemotherapy the urine pregnancy test was negative and βhCG remained low.

Seven months later, an USS showed a 12-week old foetus and she delivered a normal 3.2kg baby at term.

Case 3

A 28-year-old woman (para 6+1), presented with recurrent vaginal bleeding following spontaneous vaginal delivery in

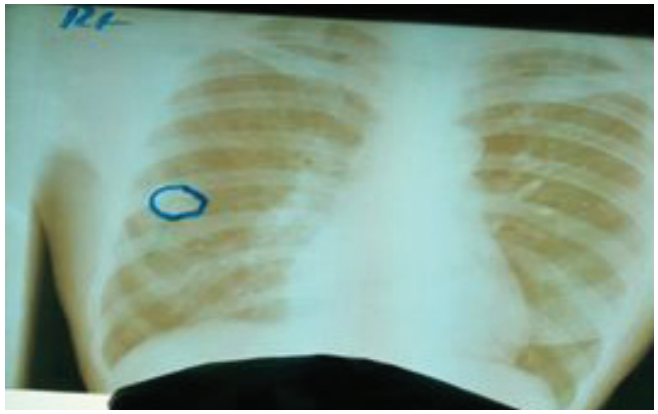

Figure 4. Case 3. X-ray with remaining coin like lesion (Credit: Kizza Paul and Paula Nuer)

October 2012. She had had three evacuations of retained products of conception. The vaginal bleeding persisted with abdominal pain but no cough or haemoptysis.

Examination revealed severe pallor, Hb of 5.5 g/with pulse 98/min, BP 90/60 mm Hg. The size of the uterus was equivalent to a 12–14-weeks pregnancy. Pelvic examination was normal apart from blood oozing from the cervical os and a chest X-ray showed cannon ball metastases (Figure 3).

An USS showed normal ovaries and an intrauterine heterogeneous mass with no clear demarcation between the mass and myometrial wall. βhCG was 31,537mlu/ml. High-risk choriocarcinoma was diagnosed and the patient was started on high-risk chemotherapy. After the 9th cycle, the lung masses had markedly shrunk (Figure 4) and βhCG was normal

Case 4

A 42-year old woman (para 7+0), having had her last delivery five years previously, presented on 15/06/2012 with recurrent vaginal bleeding and haemoptysis. On

examination she was very pale with a blood pressure of 110/70 mmHg and a clear chest on auscultation. Pelvic examination revealed dark blood from the cervical os and a uniformly enlarged uterus consistent with a 12 – 14 weeks pregnancy. Her Hb was 5.0g/dl and she was transfused with three units of blood.

An USS showed in intrauterine mass with associated fluid. A dilation and curettage produced necrotic tissue and histology confirmed a choriocarcinoma.

A chest X-ray showed lung deposits (Figure 5). Due to her age, bleeding, and difficulty in obtaining drugs and blood, she underwent a hysterectomy. Subsequently, high-risk chemotherapy was given and after two cycles the urine pregnancy test was negative. She completed five cycles and the βhCG remained normal.

Case 5

A 26-year old woman (para 5 + 0) was referred with persistent vaginal bleeding and a diagnosis of metastatic endometrial carcinoma. Her background included previous normal deliveries and excision of a vaginal tumour at another hospital.

On examination she was pale (Hb 3.5 g/dl). There was a bleeding vaginal ulcer and uterus size was consistent with a 14-weeks pregnancy. Bilateral adnexal masses were felt.

An USS showed a mass in the endometrial cavity and bilateral adnexal cystic masses with normal liver and spleen. A pregnancy test was positive. She was transfused with five units of blood and a hysterectomy was performed.

Her recovery was complicated by a bleeding vaginal ulcer and severe wound sepsis. Due to financial constraints, high risk chemotherapy could not be procured. Low risk chemotherapy was started to control the bleeding. At the end of first cycle, bleeding and sepsis were clearing. Histology confirmed choriocarcinoma and the patient received two further units of blood

After the 5th cycle of chemotherapy the βhCG was normal. She requested to visit her children over Christmas and return after a week. She returned four months later with right hemiplegia and a high βhCG. A Chest X-ray revealed a coin lesion in the right lower lung zone (Figure 6.). A brain metastasis was considered the most likely cause of the hemiplegia. She died before medication could be obtained.

The operative specimens are shown in Figures 7 and 8. The endometrium was hypertrophied with a friable cavity mass, the cervix distorted and the ovaries were polycystic.

Histologically the tumour consisted of sheets of markedly pleomorphic malignant trophoblastic cells with prominent macro-nucleoli and prominent mitotic activity. There was myometrial invasion and numerous foci of necrosis.

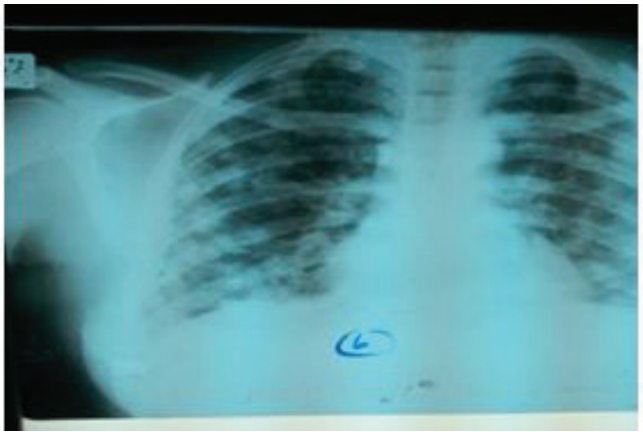

Figure 5. Case 4. X-ray showing TB like deposits in lungs in patient with haemoptysis after hysterectomy (Credit: Kizza Paul and Paula Nuer)

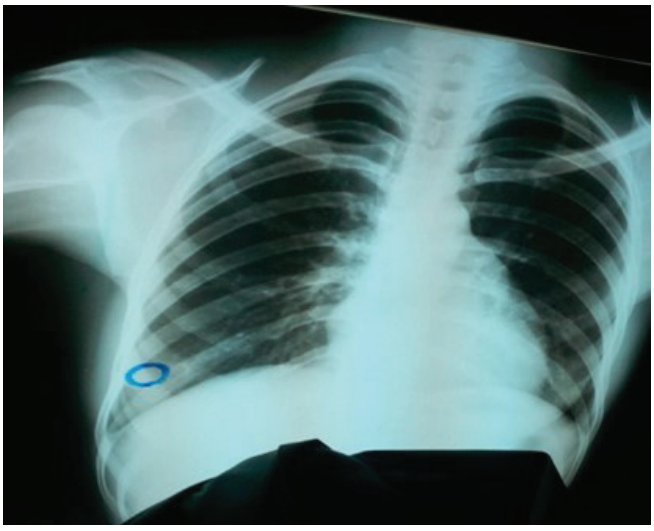

Figure 6. Case 5. X-ray. Coin like lesion in right lung (Credit: Kizza Paul and Paula Nuer)

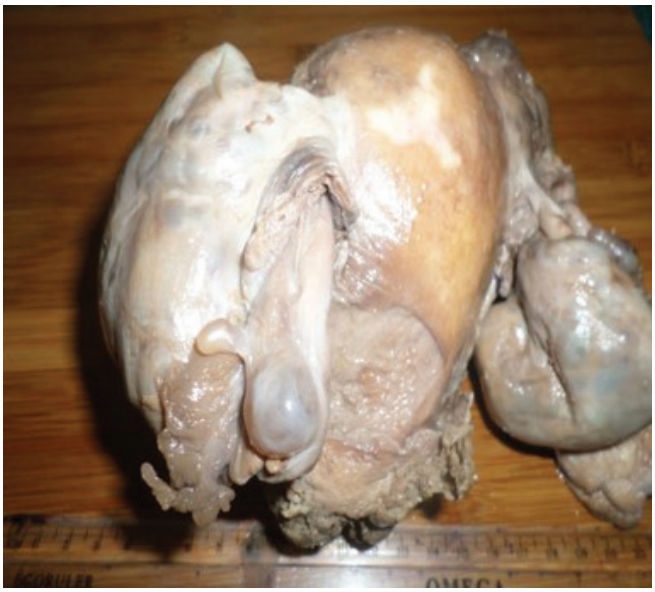

Figure 7. Case 5. Hysterectomy specimen with GCC and cystic ovaries (Credit: Changkel Banak)

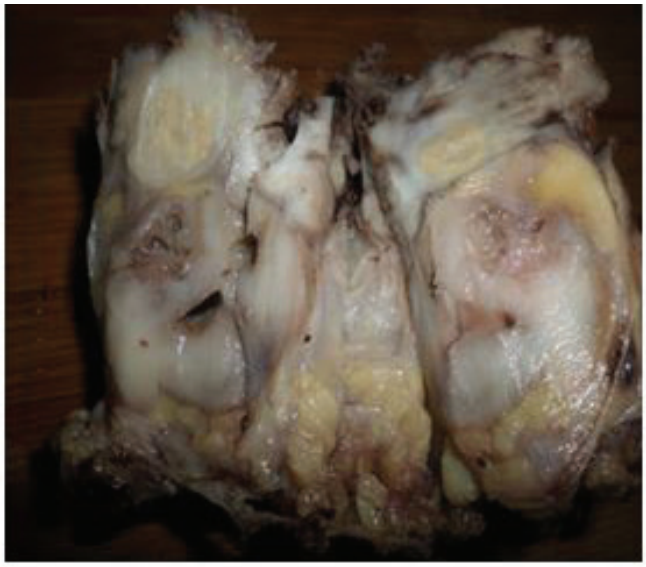

Figure 8. Case 5. Opened specimen showing GCC in endometrial cavity (Credit Changkel Banak)

Discussion

Five patients with GCC are reported. Four of these patients are in remission, two resumed their fertility and one delivered a normal female baby, another had a miscarriage and their βhCG are normal. This pattern has been reported elsewhere. [2,3,6] The fifth died from probable brain metastases leading to her hemiplegia.[7]

GCC is a malignant tumour arising from the placenta. Histologically it shows sheets of anaplastic cytotrophoblast cells, vascular necrosis and vascular invasion but chorionic villi are absent. When in the uterus, it invades the endometrium then myometrium which may perforate. Metastasis occurs early and in most cases GCC is a systemic disease.[1,2,3,6] GCC is highly sensitive to chemotherapy; urinary or serum βhCG is a useful monitoring tool.[4,5,7] Untreated GCC mortality is 100%, but with current chemotherapy, over 98% of patients achieve remission even without surgery.[1,2,3,7,8]

Sometimes the history of a molar pregnancy may be obscured by subsequent pregnancies. In a 1995 study by Fisher et al., the genetic origin of GCC that developed after a full-term normal twin pregnancy was traced to a molar pregnancy that occurred four years before.[1, 2, 6, 10]

GCC is most common in young women. Our patients' ages ranged from 22 to 42 years (mean 29.5 years). Others have reported similarly.[11,12] Early diagnosis is crucial in obtaining the best outcome.[1,2,3,6,8,9] A report from the Netherlands showed a post-term GCC had a median diagnosis interval of 16 weeks. The author ascribes 68% and 28% lung and liver metastases respectively in his patients were due to delayed diagnosis. He recommends that post term GCC be treated as a high-risk disease.[8]

Three of our patients had GCC following normal pregnancies, the time interval to diagnosis ranging from four months to five years and all needed high risk treatment.

Intra-placental GCC develops in a placenta of normal baby; 30 cases have been reported and in 17 diagnosis in the baby lead to the diagnosis of GCC in the mother.[2,8]

The common way in which GCC presents is with bleeding from the uterus or vaginal metastases. A temptation to biopsy bleeding vaginal lesion must be avoided until the pregnancy test is negative. The bleeding vaginal ulcer may be a GCC metastasis which is highly vascular and biopsy will lead to bleeding as happened in case 5.

Most GCC follow molar pregnancy and repeated evacuations for a molar may increase the patient's chances of developing GCC. A second evacuation may be done in selected cases and when βhCG is less 5000IU/L. βhCG should be normal within six months in most cases.[2,4,6,7,15]

Haemoptysis, chest pain and dyspnoea due to lung metastases are other presenting or complicating features. Haemoperitoneum due to bleeding liver metastases or abdominal masses and intestinal obstruction have also been reported.[1,2,6]

A third of GCC patients have no pelvic symptoms and may present with headache, seizures, or hemiplegia due to brain metastases.[2,6]

Investigations to be considered depending on availability are:

- Urine pregnancy test
- USS to show masses in the uterus, liver and spleen and rule out pregnancy.
- Serum βhCG.
- Chest X-ray to look for metastases.
- Biopsy and uterine curettage may lead to severe haemorrhage and uterine perforation. It is not mandatory to have histology for the diagnosis of GCC.[1,2,5,6]
- CT scan to seek metastases in the liver and especially the brain.

The mainstay of GCC treatment is chemotherapy. It is essential that treatment is undertaken by trained staff that follows clear protocol, so enhancing patient safety. It has been shown that mortality of this condition is lower if managed by those who are experienced in handling it.[13, 14] We used Charing Cross Hospital London protocol for GCC chemotherapy.[1,2,6] Brain metastases used to carry poor prognosis. Currently high dose chemotherapy with intrathecal drugs for a patient who has not been previously on chemotherapy carried a good prognosis.

Patients are graded into low risk, high risk and ultra-high risk.[1,2,3,6] Low risk may be treated with a single drug while high risk needs multiple drugs. These drugs are toxic and

if not used properly can be fatal to the patient.

In our environment where blood is hard to obtain, uterine bleeding in a patient of 40 years and above, a hysterectomy may be appropriate. Surgery may be definitive treatment and reduces the duration of chemotherapy.[5,8,13,14,15] It must be remembered that GCC is a systemic disease and so most patients need chemotherapy after surgery.

Role of surgery

Surgery may be used in the following:

- Resecting localised disease that is resistant to chemotherapy e.g. lung, liver, intestinal or brain metastases.
- Reduce tumour mass like a uterus riddled with tumour or a patient who has completed her family.
- Ovaries are usually cystic due to βhCG they must be preserved as these are young women and need their ovarian function.
- Patient with uncontrollable haemorrhage from the uterus or liver, etc.
- A wedge resection of a chemotherapy resistant localised tumour in myometrium for a patient desiring to keep her fertility.

Follow up of these patients may lead to early detection of neoplastic changes and hence good treatment results.

Recommendations

- Set up a treatment protocol for gestational choriocarcinoma in South Sudan.
- Follow up all post-molar pregnancies in treating facilities.
- Explore means of obtaining drugs to expand the availability of treatment more widely.

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