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■ Case Report

Perforated Uterus and Intestinal Metastasis Resulting from Choriocarcinoma In A 29-Year-Old Nullipara, A Case Report

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ABSTRACT

Background: Uterine rupture following choriocarcinoma is rare and this can increase morbidity and mortality in a condition that has over 90% curative rate. This was the first case of uterine rupture and intestinal metastasis resulting from choriocarcinoma that was managed in our facility. **Case Presentation**: A 29-year-old P^{0+1} lady who presented at our facility on 21/3/2019, with abdominal pain, distension and ultrasound report suggestive of molar pregnancy. Her last menstrual period was on 18/2/2019. She had a history of spontaneous miscarriage about four months prior to presentation. Quantitative beta-human chorionic gonadotropin (B-HCG) was 131,106.17miu/ml and chest x-ray revealed multiple intrapulmonary masses most probably metastatic lung disease. She was scheduled for suction evacuation, but further evaluation revealed signs of haemoperitonium necessitating exploratory laparotomy with finding of extensive molar uterine invasion, ragged uterine rupture and dilated 180^0 twisted small intestinal loops containing blood with areas of mesenteric ischaemia and friable seedlings on the ileum serosa that adhered to the uterus. A total abdominal hysterectomy and mesenteric untwisting were done. She received 6 courses of chemotherapy with Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Oncovin (EMACO) regimen due to high-risk prognostic score of 8. The qB-hCG normalized after the 3rd course of chemotherapy. She had been followed up with monthly qB-hCG for one year with no recurrence. **Conclusions:** This is to emphasize the need for histology of products of conception following miscarriages. It is also pertinent for any woman within the reproductive age presenting with bleeding to have at least one B-hCG assay to ensure that metastatic gestational trophoblastic neoplasia is excluded.

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INTRODUCTION

Gestational trophoblastic diseases (GTD) or neoplasia (GTN) are a heterogeneous group of pregnancy-associated tumours, that arise from placental villous and extravillous trophoblast cells and it covers a spectrum of benign and malignant conditions[1]. Choriocarcinoma is at the end of this spectrum and is the most aggressive form. Choriocarcinomas are

malignant trophoblastic tumours comprising of syncytiotrophoblast, cytotrophoblast and intermediate trophoblast with the absence of chorionic villi [2]. It may accompany or follow any form of pregnancy, with about 50% arising from a complete molar gestation, 25% following a normal pregnancy, and 25% after a spontaneous miscarriage or ectopic pregnancy [3, 4]. Choriocarcinoma is rare, being reported in 2-5% of all cases of gestational trophoblastic neoplasia [3]. It is rapidly invasive with early haematogenous metastasis; however, it is curative in about 90- 95% of cases [2]. It has been advocated that any woman within the reproductive age group presenting with bleeding or tumour in any organ should have at least one B-hCG assay to ensure that metastatic gestational trophoblastic neoplasia is excluded [3].

CASE PRESENTATION

A 29-year-old P^{0+1} lady presented to the gynaecology clinic on the 21/03/2019 with complaints of persistent severe abdominal pain and distension, an accompanying ultrasound scan with features suggestive of gestational trophoblastic disease and a positive serum β HCG test. There was no associated history of bleeding per vaginam, passage of vesicles, weight loss or vomiting. She was initially managed for peptic ulcer disease. She had a previous spontaneous miscarriage four months prior to presentation at about 5-weeks gestational age which was managed medically, and the expelled products of conception was not sent for histology. Following the miscarriage, she had been menstruating for 4-days in a regular 26-day cycles up until her last menstrual period on 18/02/2019.

Examination findings revealed a young lady, conscious and alert, not pale and well hydrated. Vital signs were all normal. However, an abdominal examination revealed a bulky uterus of about 20-week size, tender and doughy. A vaginal examination showed a tubular, closed cervix approximately 3cm long. No bleeding was detected.

An assessment of gestational trophoblastic disease was made, and the instituted plan was to admit, do an urgent quantitative β HCG test, a full blood count (FBC), clotting profile, a chest X-ray and to group and crossmatch at least 2 pints of blood with the aim of carrying out a suction evacuation thereafter. The result revealed βHCG of 131,106.17mm/ml; Chest X-ray (Figure 1) showed multiple intrapulmonary masses most likely metastatic lung disease; FBC, electrolyte/ urea/creatinine, clotting profile and viral markers were normal. An assessment of gestational trophoblastic neoplasia to rule out choriocarcinoma was made.

Further review of the patient with the result of the investigations while on admission by the gynaecologist revealed her to be in respiratory distress, moderately

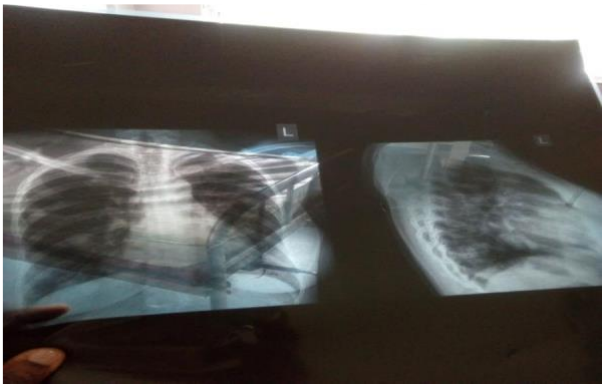


Figure 1: Chest X-ray

pale, with a respiratory rate of 44c/min, a pulse rate of 118b/min and BP 90/60mmhg. Abdominal findings revealed a uniformly distended abdomen, tender, with paracentesis revealing non-clotted blood. An assessment of haemoperitoneum of unknown cause to rule out invasive mole was made and patient was counselled and consent obtained for an emergency exploratory laparotomy.

The findings at the exploratory laparotomy (shown in figures 2 and 3) were:

Haemoperitoneum about 2.0 litres, multiple ragged looking defects on the uterine fundus; multiple moles on the serosal surfaces of the uterus extending from the fundus to the posterior surface of the uterus with friable muscle layer; and dilated 180^0 twisted small intestinal loops containing blood with areas of mesenteric ischaemia. They were friable seedlings on the part of ileum serosa that adhered to the uterus.

Figure 2: dilated intestinal loops containing blood with areas of ischaemia

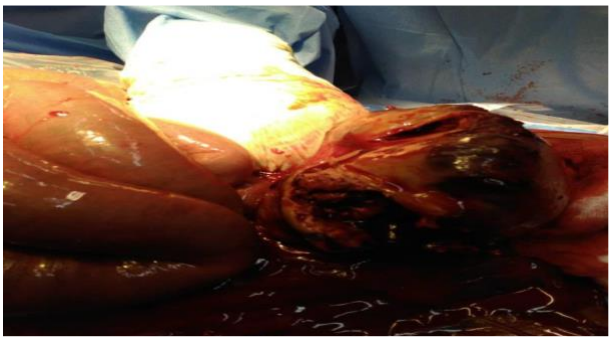
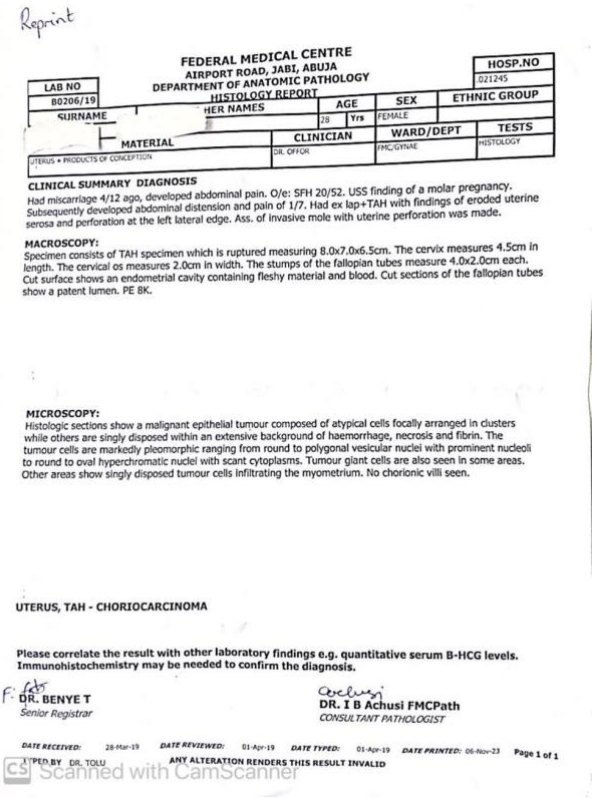


Figure 3: multiple ragged uterine invasion and perforation

The patient subsequently had a total abdominal hysterectomy (TAH) with the general surgeons in attendance to untwist the small bowel and circulation was restored with a warm pack. The specimen was sent for histology. She was transfused with 4 units of blood, was on nil per oral for 3 days, antibiotics and potassium correction. The immediate post-operative state was satisfactory, however, by the 2nd day post-operation, she started passing bloody stool till the 4th day. Post-surgery quantitative B-HCG was done on day 2 and value was 72, 6190.081miu/ml. By the sixth day, a WHO prognostic scoring system assessment classified her as high risk with a value of 8 and the histology report confirmed choriocarcinoma as shown in figure 4.

Her calculated body surface area was 1.50 $\underline{m^2}$ and she commenced chemotherapy after medical oncologist input with the EMACO regimen: etoposide 150mg infusion on day 1 & 2, methotrexate 150mg on day 1, actinomycin 0.5mg on day 1 & 2, cyclophosphamide 900mg and vincristine (oncovin) 1.5mg on day 8 with 15mg folinic acid on day 2-4. The chemotherapy courses were preceded with premedication using dexamethasone 8 mg stat and ondansetron 8mg after ensuring that Electrolytes/Urea/Creatinine, Liver Function Test, clotting profile and Full blood count were within normal limits. An interval of 14 days was given in between the courses. She had weekly quantitative βHCG done and 3 normal results were noted after the 3rd course of chemotherapy. She received a total of six courses of EMACO regimen due to the chest x-ray finding of residual disease after the 3rd course. The repeat chest x-ray after the 6th course was normal. She was followed up with monthly B-hCG for 1 year and the B-hCG and other parameters had remained normal. She was subsequently reviewed at 2 years with no evidence of recurrence. Other fertility options were discussed with her, and she opted for surrogacy.



Reprint

FEDERAL MEDICAL CENTRE
AIRPORT ROAD, JABI, ABUJA
DEPARTMENT OF ANATOMIC PATHOLOGY
HISTOLOGY REPORT

LAB NO	HOSP.NO			
B0206/19	021245			
SURNAME	HER NAMES	AGE	SEX	ETHNIC GROUP
		28 Yrs	FEMALE	
MATERIAL		CLINICIAN	WARD/DEPT	TESTS
UTERUS + PRODUCTS OF CONCEPTION		DR. OFFOR	FMC/GYNAE	HISTOLOGY

CLINICAL SUMMARY DIAGNOSIS
Had miscarriage 4/12 ago, developed abdominal pain. O/e: SFH 20/52. USS finding of a molar pregnancy. Subsequently developed abdominal distension and pain of 1/7. Had ex lap+TAH with findings of eroded uterine serosa and perforation at the left lateral edge. Ass. of invasive mole with uterine perforation was made.

MACROSCOPY:
Specimen consists of TAH specimen which is ruptured measuring 8.0x7.0x6.5cm. The cervix measures 4.5cm in length. The cervical os measures 2.0cm in width. The stumps of the fallopian tubes measure 4.0x2.0cm each. Cut surface shows an endometrial cavity containing fleshy material and blood. Cut sections of the fallopian tubes show a patent lumen. PE 8K.

MICROSCOPY:
Histologic sections show a malignant epithelial tumour composed of atypical cells focally arranged in clusters while others are singly disposed within an extensive background of haemorrhage, necrosis and fibrin. The tumour cells are markedly pleomorphic ranging from round to polygonal vesicular nuclei with prominent nucleoli to round to oval hyperchromatic nuclei with scant cytoplasms. Tumour giant cells are also seen in some areas. Other areas show singly disposed tumour cells infiltrating the myometrium. No chorionic villi seen.

UTERUS, TAH - CHORIOCARCINOMA

Please correlate the result with other laboratory findings e.g. quantitative serum B-HCG levels. Immunohistochemistry may be needed to confirm the diagnosis.

DR. BENYE T
Senior Registrar

DR. I B Achusi FMCPath
CONSULTANT PATHOLOGIST

DATE RECEIVED: 28-Mar-19 DATE REVIEWED: 01-Apr-19 DATE TYPED: 01-Apr-19 DATE PRINTED: 06-Nov-23 Page 1 of 1
TYPED BY DR. TOLU ANY ALTERATION RENDERS THIS RESULT INVALID

Figure 4: The histology Report.

DISCUSSION

Uterine rupture resulting from choriocarcinoma is rare due to early detection and prompt management in modern gynaecology, but when this occurs, it can be a cause of maternal near miss (as in this case) and mortality. Choriocarcinoma is usually preceded by hydatidiform mole in 50% and spontaneous miscarriage in 25% [4]. Other risk factors implicated in choriocarcinomas include extremes of maternal age, long- term oral contraceptive use, low socio-economic status, women of Asian, American Indian and African American descent and highest risk in women of blood group A married to men of the same blood group [5]. This patient had a miscarriage 4-months prior to presentation and was of African descent.

Pathophysiologically, choriocarcinomas have been seen to produce high levels of angiogenic growth factors that are able to remodel the uterine vasculature which can lead to haemorrhage[6]. it is also rapidly invasive with early hematogenous metastasis to the

lungs and other organs [7]. Moreover, due to their syncytiotrophoblast contents, they cause elevated blood levels of B-hCG [8]. All these manifested in this patient. Deep myometrial invasion, tumour size, tumour stage, and site of metastases also influence the outcome of patients with choriocarcinoma [9-11].

The clinical manifestations most often include irregular vaginal bleeding, enlarged uterus, cough, haemoptysis, headache, and vomiting [12-14]. It has been recognized that women with malignant gestational trophoblastic disease following non-molar pregnancies may have subtle signs and symptoms of disease, which make the diagnosis difficult [5], as in this case who presented with persistent abdominal pain and enlarged uterus. Also, untreated choriocarcinoma characteristically presents with early haematogenous metastases to the lung, brain, liver, kidney, and bowel and often presents with massive haemorrhage. This patient had a chest X-ray evidence of lung metastasis, haemoperitoneum, friable seedling on the part of ileum that adhered to the uterus, twisted and distended small bowel loops containing blood, mesenteric ischaemia and gastrointestinal bleeding. Patients can also have symptoms due to hypersecretion of B-hCG, which include hyperplasia of endocervical glands, decidual reaction, Arias-Stella phenomenon, bilateral enlargement of the ovaries by theca lutein cysts and hyperplasia of mammary lobules.

The Standard treatment options for GTN depend on the type and stage of disease and include chemotherapy, suction evacuation, hysterectomy, or a combination of these [11]. Hysterectomy was done for this patient due to the ragged uterine rupture and severe haemorrhage found at exploratory laparotomy. Other indications for hysterectomy include patients > 40 years of age, those who are desirous of sterilization, those with resistant disease or those with severe infection and uncontrolled bleeding [2, 8, 11.]

Intestinal metastasis was said to be rare and occur in approximately 5 % of patients with choriocarcinoma and may manifest with vomiting, abdominal pain and lower gastrointestinal bleeding [15]. This patient was initially managed for peptic ulcer disease following abdominal pain and the intra-operative findings of mesenteric ischaemia, twisted and distended small bowel loops containing blood, friable seeding at the ileum adherent to the uterus and subsequent passage of bloody stool for four days were pointers to intestinal metastasis. Histologic diagnoses of the specimen which is the gold standard was done for the hysterectomy sample and this confirmed choriocarcinoma.

Based on International Federation of Gynecology and Obstetrics (FIGO) / WHO prognostic score[16] which was calculated using the following variables: age ≥ 40, antecedent pregnancy, interval months from index gestation, pretreatment B-hCG levels, largest tumor size, site and number of metastases and previous failed chemotherapy; patients are classified into low risk (≤ 6) and high risk (≥ 7). Low risk (single chemotherapeutic agent with methotrexate or actinomycin); High risk: (intensive combination chemotherapy) and Cranial metastasis (radiation therapy). This patient had a high-risk score of 8 and was given multi-agent chemotherapy in addition. Chemotherapy has been noted to offer a cure rate of about 90-95% [8].

It was advocated to continue chemotherapy until B-hCG values have normalized, followed by at least 2 or 3 courses of maintenance chemotherapy with the hope of eradicating all viable tumours [5]. This was done for this patient. There was no need for salvage therapy since the patient responded well to the EMACO regimen. It was observed that despite the use of sensitive B-hCG assays and maintenance chemotherapy, up to 13% of patients with high-risk disease will develop recurrence after achieving an initial remission [17,18]. This patient was followed up with monthly B-hCG for one year and was reviewed again at two years without any sign of recurrence.
Fertility option was also discussed with her, and she opted for surrogacy. The prognosis for choriocarcinoma is good especially in young women as in this case.

CONCLUSION

This report was to emphasize the need for any woman within the reproductive age presenting with bleeding or tumour in any organ to have at least one B-hCG assay to ensure that metastatic gestational trophoblastic neoplasia is excluded.

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