

Uterine choriocarcinoma: A gynaecological masquerader case report and review of the literature

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Received 9 July 2013; revised 15 August 2013; accepted 1 September 2013

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ABSTRACT

Background: Choriocarcinoma is a rare clinical condition, and its diagnosis may be difficult, especially in resource-limited settings. **Case Presentation:** A 38-year old para 2 woman is with a 4-month history of intractable vaginal bleeding and offensive vaginal discharge, but without antecedent pregnancy. She had previously been managed at various tertiary medical institutions where several pelvic ultrasound scans and even histology of endometrial curette could not clinch the diagnosis. The diagnosis of choriocarcinoma was made by a serial strip-based pregnancy testing, which was still positive at 1:200 dilutions. She was treated with chemotherapy involving Adriamycin, Cyclophosphamide, Methotrexate and Folinic acid. **Conclusion:** The diagnosis of choriocarcinoma may be difficult especially when it develops *ab initio* without preceding abortion, molar or term pregnancy. In settings where serum hCG assay may be not available, the simple strip-based pregnancy test in dilution could be helpful in its diagnosis and treatment monitoring.

Keywords: Choriocarcinoma; Chemotherapy; Human Chorionic Gonadotropin; Resource-Limited Settings

1. INTRODUCTION

According to the World Health Organization Science Group in 1983 [1] on histopathological and clinical terminology, gestational choriocarcinoma is a carcinoma arising from the trophoblastic epithelium that shows both cytotrophoblastic and syncytiotrophoblastic element. It may arise from conceptions that give rise to a live birth, a still birth, and abortion at any stage, an ectopic pregnancy or

a hydatidiform mole, or it may arise from *ab initio*.

Gestational trophoblastic diseases (GTD) comprise a variety of biologically interrelated conditions which form a clinical spectrum consisting of four distinct clinical pathological entities namely, molar pregnancy, invasive mole, placental site trophoblastic tumours, and choriocarcinoma [2-4]. Serum human chorionic gonadotropin (hCG) assay has remained the main stay of diagnosis, prognosis and monitoring of the condition.

The purpose of this report is to illustrate how difficult the diagnosis of choriocarcinoma could be and to show how a simple and “technology free” pregnancy test could still be relevant in its diagnosis and treatment in resource-poor settings.

2. CASE PRESENTATION

A 38-year old para-2 Nigerian woman was presented in our centre with 4 months history of intractable vaginal bleeding. The bleeding was said to be heavy and was associated with passage of big blood clots. It was associated with offensive vaginal discharge, weight loss, fever and antecedent menorrhagia. It was not however associated with any history of amenorrhea, termination of pregnancy, lower abdominal swelling, post-coital or contact bleeding. Her last confinement was four years prior to presentation. There was no history of cough, hemoptysis, jaundice, unusual behaviour, convulsion, urinary or gastro-intestinal symptoms. Prior to her presentation at our center, the patient had been managed at the various tertiary hospitals (both in northern and south-eastern Nigeria), where various abdominal ultra-sound scan report suspected uterine fibroids, cervical cancer and endometrial cancer respectively. A histopathological report from one of the centres queried chronic endometritis. There was no definite diagnosis, but she had been transfused with many units of blood.

Initial evaluation revealed severe anaemia, with high grade fever, tachycardia (120 beats/minute) and low

blood pressure (80/50 mmHg). Her chest was clinically clear, while she had suprapubic tenderness and offensive vaginal discharge associated with altered blood and cervical excitation tenderness. There was no suburethral or cervical lesion. Due to her previous conflicting investigation reports, the patient was booked for examination under anesthesia, where she had torrential bleeding that was coming from uterine cavity. Thus, a pregnancy test was ordered that led to the diagnosis of choriocarcinoma. Although a titrated serum hCG could not be done, an analysis of urine hCG was positive at 1:200 dilution. Her blood group was B⁺, while her husband's was O⁺. Her PCV on admission was 12% and her total white blood cell count, platelet count, serum electrolytes and urea were within normal limits.

She was successfully resuscitated with antibiotics and massive blood transfusion (20 units). Further evaluation did not show any evidence of lung, liver or brain metastases. Meanwhile, prognostic scoring of the patient was uncertain as she was not "pregnant" and the serum hCG could not be assayed, but she was placed at clinical stage I (tumour confined to the uterus). She was then commenced on cancer chemotherapy.

Therapy was instituted using **Methotrexate** 50 mg on days 1, 3, 5 and 7; **Folinic acid** 7 mg on days 2, 4, 6 and 8; **Cyclophosphamide** 650 mg daily for 5 days (in saline), and **Adriamycin** 75 mg stat on day 1. Following the first course of chemotherapy, the bleeding ceased and the patient made tremendous clinical improvement. The course was repeated on day 21, while the patient was consistently monitored for signs of toxicity. Pregnancy test became negative at the end of the second course. She was scheduled to receive one more course of chemotherapy but she defaulted due to high cost of the cytotoxic drugs and the apparent relief of her symptoms. She presented three months later with relapse and features of metastasis and died.

3. DISCUSSION

Gestational trophoblastic disease most commonly follows molar pregnancy and may also occur following normal or ectopic pregnancies and spontaneous or therapeutic abortions. Its incidence varies with figures as high as 1 in 120 pregnancies in some areas of Asia and South America, compared to 1 in 1200 in United States [5]. In the United Kingdom, it has a calculated incidence of 1 in 714 live births [3]. Metastatic gestational trophoblastic disease occurs in 4% patients after local management of Hydatidiform mole [5]. The incidence of choriocarcinoma after complete hydatidiform mole is about 1000 times greater than after a normal pregnancy. It may occur *ab initio* as in the case presented [1,6]. Choriocarcinoma is a rare tumour. In western countries, the incidence is 1 in 45,000 to 50,000 pregnancies [5,7]. Higher

incidence is reported from, Africa, Asia and South America [8]. Majority of cases occur in women aged less than 35 years of age [5].

Choriocarcinoma is suspected when there is persistent or irregular uterine haemorrhage, following abortion or hydatidiform mole. However, as illustrated in this case, it could also be suspected in cases of undiagnosed vaginal bleeding, even in the absence of pregnancy. Rapid growth and haemorrhage make the tumour a gynecological emergency. Metastasis may occur in lung, pelvis and vagina. Rare sites include gastrointestinal tract, spleen, and kidney. The central nervous system is seldom involved in the absence of pulmonary metastasis [2]. Metastatic disease occurs in 4% of patients after local management of hydatidiform mole and very rarely after term pregnancies or abortions [1]. Sometimes they may be combined with malignant germ cells components; and it may be difficult to differentiate a primary tumour from a metastasis. For females in non reproductive age group, the tumours may arise from ovarian germ cells, which is histologically similar to gestational uterine choriocarcinoma [6].

Hitherto, serum hCG assay has remained the key factor in diagnosis and monitoring of the progression of the disease. This has made clinical prognostic scoring easy and objective, as the serum hCG provides a sensitive and reliable indicator of the body burden of the tumour, its progression and regression in response to treatment [1]. However, in resource-limited settings, like ours, serial dilution test for urine hCG has also proven to be a useful diagnostic tool. The emphasis, however, should be to correlate the urine titers with serum values. This will enhance prognostication of patients for appropriate chemotherapy. According to I.A. McNeish *et al.* [9], proper classification of patients (as low risk) did not compromise outcome, but rather prevented undue exposure to potentially carcinogenic chemotherapy.

Traditionally, patients with uterine choriocarcinoma have been categorized as low risk (score of 0 to 5), medium risk (score of 6 to 9) and high risk (score > 9), using the prognostic scoring system [1]. This enables rational use of chemotherapy with emphasis on the risk of developing resistance. However, I.A. McNeish *et al.* [9] have proposed a new scoring system: Charing Cross scoring system (**Table 1**), which is intended to further reduce the risk of undue exposure to chemotherapy. This new system proposes the use of Methotrexate-Folinic acid regimen for low risk disease (score 0 - 8), while EMA/CO (Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Oncovin) is reserved for high risk disease (score > 8). An algorithm (**Figure 1**) has also been developed to enhance case management.

Initial treatment for those with low-risk disease was Methotrexate (MTX) (50 mg intramuscularly on days 1,

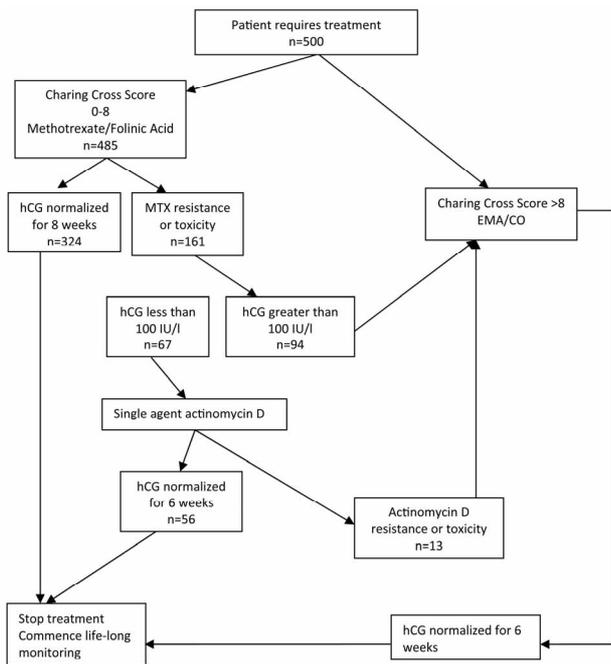


Figure 1. Treatment pathway for low-risk gestational trophoblastic disease.

3, 5, and 7 with Folinic acid (FA) 7.5 mg orally on days 2, 4, 6, and 8, repeated every 2 weeks. [1] Whereas for those with medium-risk disease, the chemotherapy regimen consisted of MTX as above, plus oral Hydroxyurea 1 g on day 1, oral mercaptopurine 75 mg on the same day as the FA, alternating with courses of either intravenous Etoposide 250 mg/m² on days 1 and 3, or courses of intravenous Actinomycin 0.5 mg daily for 5 days. 2 Treatment for high-risk disease was infusional chemotherapy according to the Etoposide, Methotrexate, and dActinomycin (EMA)/Cyclophosphamide and Vincristine (CO) regimen 3 (Table 2) [9].

Our case typically illustrates the frustration associated with cancer chemotherapy in Nigeria and indeed other developing countries where prevalent poverty makes procurement and sustenance of the drugs impossible.

Meanwhile, several complications of both uterine choriocarcinoma and its management have been documented. Being a highly malignant disease, metastases may occur in lung, pelvis and vagina. Rare sites include gastrointestinal tract, spleen, and kidney. The central nervous system is seldom involved in the absence of pulmonary metastasis [5]. There are reports describing

Table 1. Charing cross scoring system for gestational trophoblastic disease¹.

Variable	Charing Cross Scoring System ²			
	0	1	2	6
Age, years	<39	>39		
Antecedent pregnancy	Male	Abortion or unknown	Term	
Interval (end of antecedent pregnancy to start treatment), months	<4	4 - 7	6 - 12	>12
hCG, IU/L	10 ³ - 10 ⁴	<10 ³	10 ⁴ - 10 ⁵	10 ⁵
ABO (male x female)		A x O O x A O/A X unknown	B x A/O AB x A/O	
No. of metastases	0	1 - 4	4 - 8	>8
Site of metastases	Nil or lungs or vagina	Spleen, kidney	GI tract	CNS, liver
Largest tumor mass, cm	<3	3 - 5	>5	
Previous chemotherapy	Nil	Nil	Single agent	Two or more drugs

¹Low risk, 0 to 8; high risk, >8. ²The patient's Charing Cross score is calculated at the start of treatment. All patients are assessed with clinical history, serum hCG, chest radiograph, and uterine ultrasound. If there is evidence of metastatic disease on radiograph, computed tomographic scan of the chest, abdomen and pelvis and a cranial magnetic imaging scan are obtained. The largest tumor mass measurement usually derives from the uterine ultrasound scan.

Table 2. Dactinomycin and EMA/CO chemotherapy regimens.

Regimen	Dosage
Dactinomycin	0.5 mg IV daily x 5 Repeated every 2 weeks
EMA/CO EMA Day 1	Dactinomycin 0.5 mg IV bolus Etoposide 100 mg/m ² over 30 minutes Methotrexate 300 mg/m ² over 12 hours
Day 2	Dactinomycin 0.5 mg IV bolus Etoposide 100 mg/m ² over 30 minutes Folinic acid 15 mg PO bid over 2 days commencing 24 hours after start of methotrexate
CO	Vincristine 0.8 mg/m ² (maximum 2 mg) bolus Cyclophosphamide 600 mg/m ² over 30 minutes EMA and CO alternatively weekly

metastasis to large intestine from choriocarcinoma presenting as pseudo-obstruction and metastasis to stomach. Metastasis to gastrointestinal tract and presentation as perforation of small intestine is very rare [10]. Also, it has been reported that exposure to combination, but not single-agent, chemotherapy is associated with an increased incidence of second tumors, especially myeloid leukemia and colon cancer [11]. In addition, combination chemotherapy, more than single agent Methotrexate, increases the risk of an early menopause [12].

4. CONCLUSION

Although uterine choriocarcinoma, a rare form of gestational trophoblastic disease, usually follows a molar pregnancy, term deliveries or abortions, it can also present *ab initio*. Its diagnosis can often pose a dilemma in resource-limited settings, but a high index of suspicion is helpful. The high cost of cytotoxin, which contributed to the default in treatment and eventual death of the patient, should be revisited. There is a need to make the cytotoxic drugs available and affordable across the world. Finally, although urine hCG assay is not the gold standard for the diagnosis and monitoring of this disease, it is useful in resource-limited settings. Further studies, however, should be done to correlate urine hCG titres with serum hCG levels in order to enhance the diagnosis and management of choriocarcinoma in low-resource settings.

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