Tanzania Journal of Health Research
Volume 20, Number 2, April 2018
Doi: http://dx.doi.org/10.4314/thrb.v20i2.11

CASE REPORT

A recurrent gestational choriocarcinoma case complicated by a silent postpartum ruptured uterus: a unique presentation

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Abstract
Gestational trophoblastic diseases comprise of potentially malignant conditions arising from defective proliferation of trophoblastic tissue. Among the different types, gestational choriocarcinoma constitutes a malignant form with significant cure rate and minimal sequela if treated adequately and followed up consistently. In this case report, we describe a patient who previously had history of choriocarcinoma and was treated with six courses of combination chemotherapy and was not followed up consistently and 14 months later conceived and delivered a live 1.3 kg female baby at 31 weeks of gestation. Two weeks post-delivery she was diagnosed with ruptured uterus. Long term complication following choriocarcinoma is a rare event. Moreover, coexistence of choriocarcinoma with normal pregnancy and a subsequent ruptured uterus two week after delivery constitutes an atypical presentation. Complications and challenges described in this report highlight some of the difficulties encountered in managing gestational trophoblastic neoplasia in limited resource setting of Tanzania.

Keywords: choriocarcinoma, recurrence, gestational trophoblastic, neoplasia, Tanzania

Background

Gestational trophoblastic diseases consist of benign and malignant interrelated conditions which originate from abnormally proliferative trophoblastic tissues. The magnitude of this condition varies across the globe. In North America the documented rates of gestational trophoblastic disease is 2 per 1000 pregnancies (Palmer, 1994; Tham *et al.*, 2003). The highest reported prevalence is in Japan of 3 per 1000 pregnancies (Palmer, 1994). No available data on the magnitude of gestational choriocarcinoma in Tanzania, but a prevalence of 12.8% of related condition, hydatidform mole among women with incomplete abortion has been reported in northwest region of Tanzania (Kitange et al., 2015).

Remission rate after completion of chemotherapy regime is more than 90% (Flam & Lundstrom, 1989). Documented recurrence rates varies and a proportion of 0.7-1% of molar pregnancy has been reported to recur in subsequent pregnancy (Lorigan *et al.*, 2000; Eagles *et al.*, 2015). To ensure complications associated with gestational trophoblastic disease are captured and treated early, continual human chorionic gonadotropin hormone (β-HCG) monitoring and effective contraceptive usage is vital. The capability to optimally monitor these patients varies depending on the location, and laboratory facility available (Kennedy, 1995). As a substitute for serum beta human chorionic gonodotrophin (β-HCG) monitoring, urine for pregnancy test is offered in majority of health facility in Tanzania.

Here in we present a case of previously choriocarcinoma patient who was treated with six courses of combination chemotherapy but not followed up and 14 months later conceived and delivered a live 1.3 kg female baby at 31 weeks of gestation. Two weeks later, she was found to have ruptured uterus.

Case report

A 32 years old lady who had 4 living children presented Kilimanjaro Christian Medical Centre (KCMC) in Moshi in northern Tanzania being a referral from a nearby Mawenzi Regional Referral Hospital due to minimal vaginal leakage of liquor for two days and difficulty in breathing at a

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gestational age of 31 weeks. She described the liquor discharge to be of an acute onset, clear coloured and odourless and dripping through her legs. Accompanied with this complaint she also presented with history of bilateral pleuritic chest pain and with occasional difficulty in breathing with no obvious relieving or aggravating factors.

On the review of her medical history it was noted that on her previous pregnancy she presented at a gestational age of 18 weeks at KCMC and was diagnosed with molar pregnancy. This was 14 month before this current admission. As part of management of molar pregnancy she was adequately evacuated by suctioning under regional block and later discharged on combined oral contraceptive. She was then followed up for a period of one month with weekly urine for pregnancy test as an alternative follow up for serum β-HCG. Four weeks after evacuation on her follow up visit she presented with a complain of chest pain and coughing. A chest X-ray was done that showed a well circumscribed lesion on the upper lobe of the right lung. Based on radiologist, an impression of choriocarcinoma metastatic lesion was reached. She was then started on a six course of combination chemotherapy consisting of methotraxate, actinomycin D, and cyclophosphamide (MAC). She completed the entire course and recovered, however she was lost on follow up immediately after completion of chemotherapy (4 month after evacuation).

In this index pregnancy she presented with several episodes of vaginal bleeding in first trimester. She was kept on bed rest as a case of threatened abortion. Clinically she was not very ill looking, not wasted, not pale; her blood pressure (BP) was 130/90mmhg and a pulse rate of 86 breath per minute, with an axillary temperature (37.2°C) with oxygen saturation of 92% in room air during admission. She had a respiratory rate of 32 breath per minute with good air entry bilaterally with no crepitation. Her fundal height was consistent with 32 weeks of gestation with longitudinal lie and cephalic presentation, foetal heart rate was 135 beats per minutes. Speculum examination revealed a ruptured membranes with cervical dilatation of 4 cm. A diagnosis of preterm labour with premature rupture of membrane and acute respiratory distress with differential of pulmonary embolism and pneumonia was entertained.

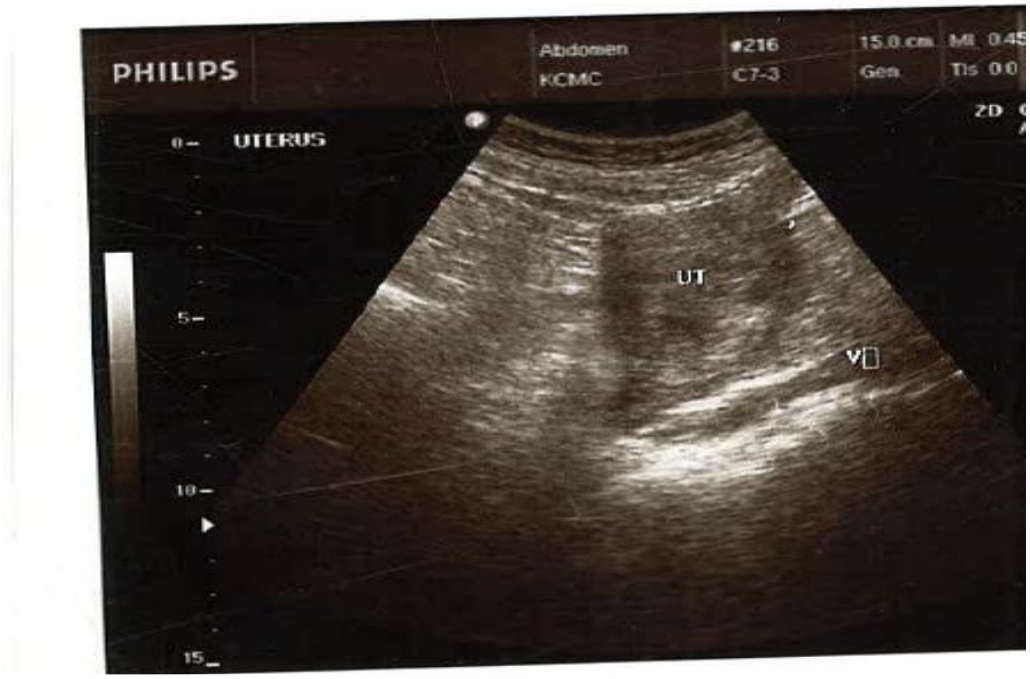

Figure 1: Ultrasound of the pelvis showing hypoechoic areas in the uterus with fluid in the pouch of Douglas

The chest X-ray and electrocardiogram (ECG) revealed normal findings. Random blood glucose was 17.8g/dl, haemoglobin level of 11.1g/dl, HIV status was checked due to respiratory symptoms and as part of routine care and was found to be negative. A full blood picture was

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unremarkable. She was then started on routine management of preterm premature rupture of membrane with ampicillin 1 g intravenously (IV) 8 hourly and metronidazole 500 mg IV 12 hourly. Moreover dexamethasone 6 mg IV 12 hourly was also commenced for foetal lung maturation. Placement of nasal prongs for oxygen administration of 2 litres per minutes was also done. Uterine contractions on admission were two per ten minutes lasting for 15 seconds. An administration of oxytocin 2.5 IU was started at rate of 15 drops per minutes to facilitate labour progress. Four hours after admission she delivered a 1.3 kg female baby with an Apgar score of 3, 6, 9 in the first minute fifth minute and ten minutes, respectively. Rescutitation was done and the baby recovered and was transferred to neonatal intensive care unit due to prematurity and prolonged ruptured of membranes. She was then seen regularly at the postnatal ward while she was kept on antibiotics for duration of one week. But on the second day post-delivery she presented with complaints of generalized abdominal pain and extreme fatigue on ambulation. She was then empirically ordered to be started on Lasix 40 mg once a day and Aldactone 12.5 mg twice a day for pulmonary oedema with ferrous sulphate 200mg orally twice a day and folic acid 5 mg and ceftriaxone 1 g IV twice a day metronidazole 500 mg IV three times a day, gentamycin 80 mg IV bid due risk of endometritis as result of prolonged rupture of membranes.

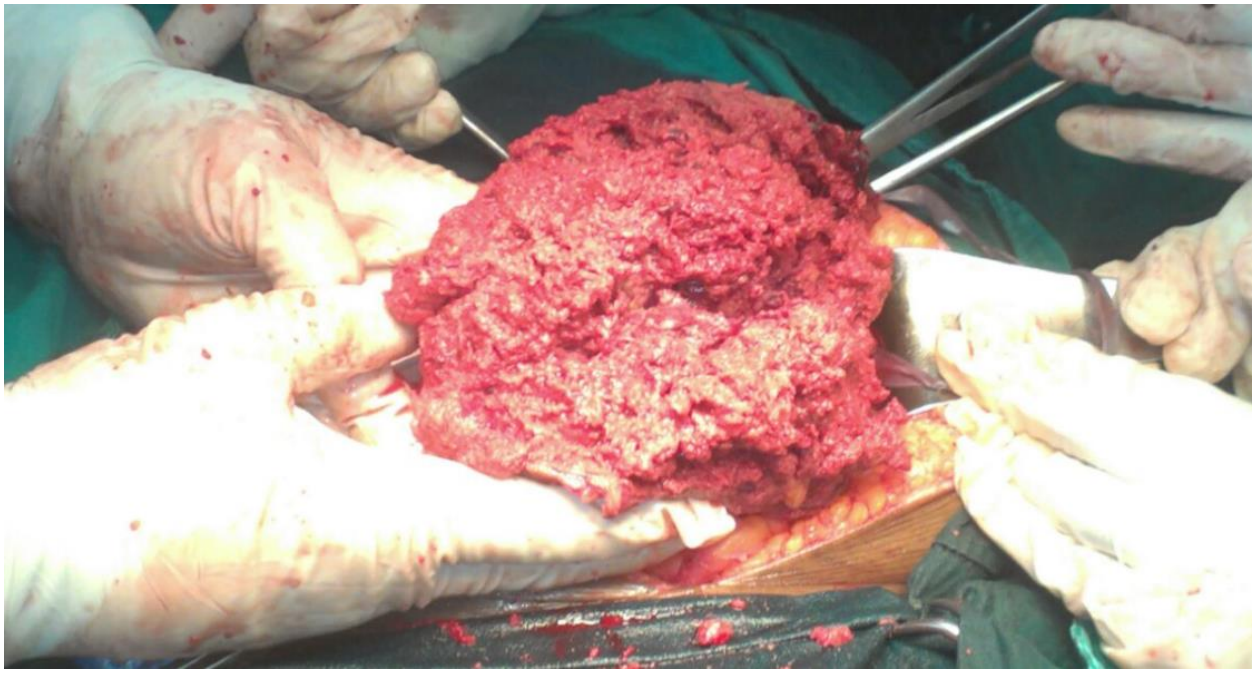

Figure 2: An inverted ruptured uterus exposing the endometrium (Uterine wall friable and tumour mass invade full thickness of myometrium to the serosa)

For the first week after delivery her conditions was not stable due to continuous abdominal pain with occasional dyspnoea. On day 13 post-delivery a pelvic ultrasound was done that revealed a bulky uterus with linear hypoechoic areas on the fundus with significant amount of fluid in the abdomen (Figure 1). The ultrasonographer suggested a diagnosis of perforated uterus with significant haemoperitoneum. This necessitated a prompt laparatomy to be done. The preoperative evaluation revealed (vital signs, pulse rate=96 pbm, respiratory rate =28 breath per minute, 02 saturation, then haemoglobin of 7.5g/dl, BP 100/60mmhg, oxygen saturation of 94% on room air. Two units of whole blood were prepared as standby for the operation.

Intraoperatively, a subumbilical midline incision was done, an old haemoperitoneum was noted ~ 150 ml and omentum completely adhered to the anterior uterine wall. A uterus was ruptured (7-10cm) at the fundus with necrotic edges (Figure 2 and 3I). Both right and left adnexae and ovaries appeared normal. Total abdominal hysterectomy was done and the specimen was

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submitted for histology. No complication was encountered during surgery. The histology result revealed a uterine choriocarcinoma. Post operatively the patient recovered within 3 days. She was discharged fourth day after laparatomy with her blood pressure was 128/70mmhg, pulse rate=82 beats per minute. After that she was referred to Ocean Road Cancer Institute for further management.

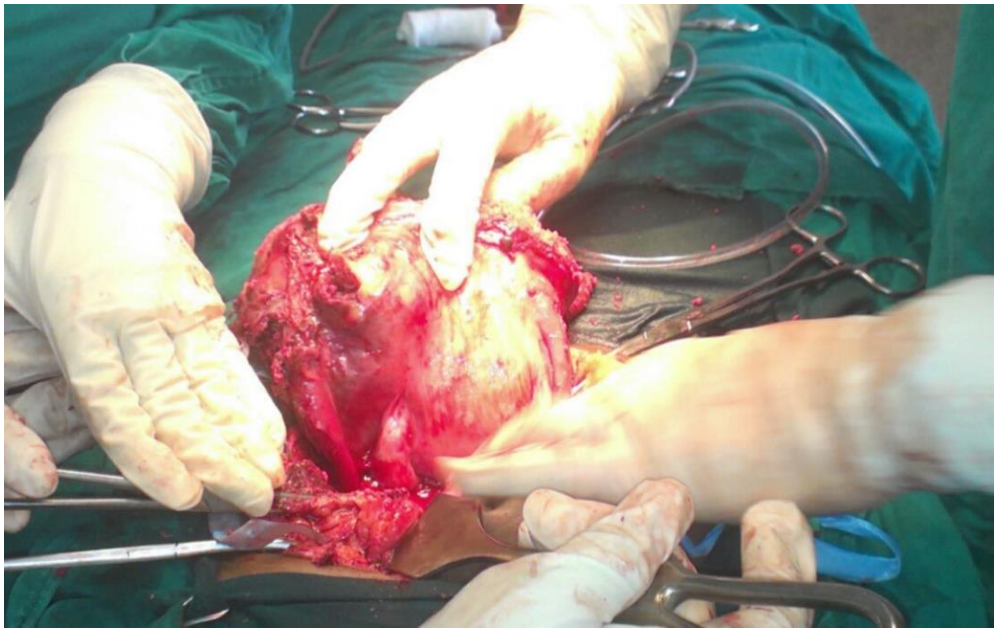

Figure 3: Uterine rupture with haemoperitoneum (thumb inserted in the ruptured plane of the uterine wall)

Discussion

Gestational trophoblastic diseases constitute a spectrum of conditions resulting from defective proliferation of trophoblastic tissue with potential malignant transformation. Hydatidform mole, invasive mole, and choriocarcinoma are the commonly described gestational trophoblastic disease types (Berkowitz & Goldstein, 2009). Choriocarcinoma is a malignant form of gestational trophoblastic disease that is curable with 78% remission rate if detected and treated early (Bower *et al.*, 1997). Universally, suspected cases of gestational trophoblastic diseases are managed with uterine evacuation, serial beta human chorionic gonotrophin (β-HCG) level, effective contraception and chemotherapy (Berkowitz & Goldstein, 2009; Seckl *et al.*, 2010). There are significant differences in different part of world in the capability to monitor, treat and ensure adherence to the proposed follow up and treatment regime (Kennedy, 1995). Recurrence of gestational choriocarcinoma in pregnancy is a very rare event (Peng *et al.*, 2014). Moreover, co-existence of gestational choriocarcinoma in pregnancy and a distinctive complication of silent rupture uterus without overt clinical features noted in this particular case in our opinion represents a peculiarity that has not been documented before. Only a few reports of coexistence of pregnancy with gestational trophoblastic neoplasia have been documented elsewhere (Makary *et al.*, 2010; Luna Russo *et al.*, 2015). Documented reports of uterine rupture following invasive uterine choriocarcinoma are mainly as a result of failure to adhere to strict follow-up regime (Bruner et al., 2013). Majority of uterine ruptures arise within 6 month after diagnosis of molar pregnancy (Luna Russo *et al.*, 2015). To our knowledge recurrence resulting in rupture 14 month following a live pregnancy is an extremely rare event.

Management of gestational trophoblastic disease in our setup poses multiple challenges as seen in this particular case. Serum β-HCG follow up for these patients remains logistically challenging due to resource limitation. In this particular case, if serum β-HCG could have been

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done earlier in previous pregnancy could have assisted in detection of deranged levels of serum β-HCG and eventually prevent development of choriocarcinoma. Evidence shows a poor correlation of the urine for pregnancy test and serum β-HCG level especially in patient with low β-HCG titres (Lertkhachonsuk, 2015). This reaffirms the fact that using urine for pregnancy test may represent a missed opportunity to detect residual disease. Moreover patients follow up visits to the clinic are likely not to be adhered due to a poor health seeking attitude in resource-poor settings that is partly attributed to financial constraints. Nonetheless, our hospital monitoring capability may not be optimal to allow early detection of this complication and provide intervention timely. Specifically, more sensitive image technique could have been used and detect a choriocarcinoma early to allow timely intervention.

Combination chemotherapy consisting of Ectoposide, Methotraxate, Actinomycin D, Cyclosphosphamide and Vincristine (EMOC) is the most effective and the most commonly used combination therapy for high risk gestational trophoblastic tumour (Cyriac *et al*., 2011). In our case Methotraxate, Actinomycin D, Cyclophosphamide has been used because it is readily available and it is inherent in the institutional guidelines that have not be reviewed recently. EMOC has been shown to be effective with low recurrence rate and low toxicity (Bower *et al*., 1997). To our understanding no good data is available to evaluate the effectiveness of MAC treatment in high risk patients. The complication encountered in our case could result from use of ineffective combination chemotherapy.

A ruptured uterus could be explained by the invasion of tumour into the muscular portion of the uterine wall. Exact mechanism involved is poorly understood. Speculative theory suggest invasion of the uterine vasculature by the invasive tumour cell and subsequent infarction due to thrombosis and intertumoral bleeding have been documented (Ma *et al*., 2008). It is not known whether the ruptured uterus occurred immediately after delivery or afterwards. Intuitively, uterine rupture immediately after delivery seems not to be the likely explanation as the patient could have not survived that long. Moreover, an insignificant amount of blood loss noted intraoperative may suggest a form of avascular necrosis of the entire uterine wall.

This particular case exemplifies challenges in management of gestational trophoblastic neoplasia in limited resource settings. Alternative urine for pregnancy test follow up regime adopted due to unavailability of the β-HCG reagent likely due to resource limitation in our institution could be the cheaper option but may not be cost-effective. Moreover, poor individual health seeking behaviour inherent in this setting as evidenced by inability of this patient to adhere to the follow up regime may compromise the serial β-HCG follow up and compromised early detection of complication. Additionally clinicians managing a pregnant women with prior history of choriocarcinoma should monitor them closely antenatally, during intrapartum period and in the postpartum period. Moreover, long-term recurrence of choriocarcinoma reported in this case suggests that for patient treated with MAC may have residual malignant cells that can recur overtime and so the importance of conducting follow up cannot be underestimated.

In conclusion, recurrent choriocarcinoma presenting with silent ruptured uterus following successful delivery is a rare presentation. This may poses a serious threat to the mother and the foetus. Choricarcinoma cases needs to be followed up closely to detect early complications and provide timely intervention. A high index of clinical suspicion with vigilance in intrapartum and postpartum care is needed when encountering pregnant women with previous history of choriocarcinoma. From this finding, we recommend further investigation in a longitudinal manner to explore potential long-term complication of uterine choriocarcinoma.

Ethical considerations

Informed written consent was sought from the patient prior to collection of this detailed particulars of the patient and the care obtained in our institutions. An informed written consent

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was obtained from the subject for usage of this information and picture and other detailed information for publication to further research and knowledge.

Authors' contributions

BM managed the case, and has provided significant contribution in the manuscript writing. GM has provided significant contribution in the development of manuscript. PT has provided significant contribution in literature search and managed the patient.

Competing of interest

The authors declares to have no competing interests in writing this article

Acknowledgments

We wish to acknowledge the team of staff in obstetric ward who managed this patient, but also provided necessary information that assisted in development of this article.

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Doi: http://dx.doi.org/10.4314/thrb.v20i2.11

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