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Challenges of Diagnosis and Management of Postpartum Choriocarcinoma In Resource Limited Settings: A Case Report from a Tertiary Hospital of Western Kenya

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ABSTRACT

Choriocarcinoma is a rare occurrence in pregnancy. It is a highly curable malignant tumour that arises from trophoblastic cells within the uterus. However, the timely diagnosis of choriocarcinoma following birth is challenging, especially in low resource settings because most clinicians are not aware about the existence of the disease following uneventful pregnancy and birth. This report discusses the case of a 28 years old patient, para 2, diagnosed with choriocarcinoma two months after uneventful vaginal delivery at term. She underwent a total abdominal hysterectomy, followed by chemotherapy treatment; and succumbed to her disease. It highlights difficulties encountered on diagnosis and management of postpartum choriocarcinoma in particular context of resource-limited settings.

Keywords

Postpartum, Choriocarcinoma, Metastasis, Tissues, Hysterectomy, Chemotherapy.

Introduction

Gestational trophoblastic neoplasia affects women of reproductive age. It includes an interrelated group of diseases originating from placental tissue with potential to invade normal tissue and metastasize. It is uncommon in postpartum mothers, with a global incidence of 1 in 50,000 live births [1].

In low resource settings, the diagnosis of choriocarcinoma, in postpartum women, can be delayed as the clinical presentation is often misdiagnosed as secondary postpartum bleeding. Although there are several studies that report a high cure rate among affected patients, there are few studies investigating the challenges of diagnosing and managing the condition, in particular context of a resource-limited settings.

Case Report

A 28 years old female patient para 2+0, had a normal vaginal delivery on 02/11/2016 to a live male infant who scored well with a birth weight of 3600grams after an uncomplicated pregnancy and labour. She had persistent vaginal bleeding compared with her previous delivery. At the postnatal clinic, she was incorrectly prescribed antibiotics for postpartum infection. By the end of November, the vaginal bleeding increased in amount (8 soft pads/day). In December 2016, she decided to return to the public hospital where she had delivered. Although she was admitted and treated with antibiotics for two weeks, she was not reviewed by the doctors because they were on industrial action at the time. Other history including medical conditions, family and drug history were not noted, except that she had a primary education level and did not have health insurance.

Initial physical examination was unremarkable. The initial abdomino-pelvic ultrasound done on 29th December 2016 showed retained placental tissue. The plan for uterine evacuation was

made; however, the patient could not afford the fees at private hospital. The subsequent ultrasound, performed on 5th January 2017 at the second private hospital showed an intracavitary uterine mass with increased peripheral vascularization without ascites; this was suggestive of choriocarcinoma. The elevated serum β-hCG titre, 84,000 IU/ml correlated with ultrasonographic findings confirmed the diagnosis. The haemoglobin (Hb) was 6g/dl, blood group B rhesus positive. The chest x-ray was not performed. Total abdominal hysterectomy was performed on 11th January 2017, as alternative of uterine evacuation plus chemotherapy after counselling about the mode of treatment. Anaemia was also corrected before surgery; however, there was no confirmation that the disease was confined into the uterus at time of surgery. She was discharged on 16/01/2017. The gross pathology of the uterus at hysterectomy was sent for histopathology analysis, which showed sheets of atypical trophoblastic and syncytiotrophoblast cells without chorionic villi, features suggestive of choriocarcinoma (written report). She was then scheduled to start chemotherapy, which she could not afford the cost at that time and was lost to follow up.

She presented a year later with complaints of abdominal pain and distension at the public health facility. She was at a poor performance status and noted to be jaundiced. The abdomen was distended with a palpable fixed and tender mass in right upper quadrant, extended to the epigastric region and umbilicus. The vaginal examination was normal. Abdomino-pelvic ultrasound of 14th January 2018 showed a mass compressing gut, involving the liver with presence of ascites. The abdominal CT scan of 18th January 2018 showed features of liver and gastrointestinal tract (GIT) metastatic lesions. The Hb was3.8g/dl, and serum β-hCG 1,843,000 IU/ml. Liver function tests (LFTs) were 237.6 µm/l and 209.6 µm/l for total and direct bilirubin respectively. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 65.2 U/l and 23.5 U/l. The total albumin level was 18.50 g/l; Urea, electrolytes and creatinine (UEC) were unremarkable. Thyroid function tests (TFT) were not performed. The brain CT scan and chest x-ray were reported to be normal.

The first cycle of chemotherapy treatment consisting of dactinomycin, methotrexate, and Etoposide was started on 19th January 2018 after transfusion. She was referred to tertiary hospital; the regimen was changed to Etoposide100 mg/m², methotrexate 100 mg/m² mg IV, actinomycin-D 0.5 mg mg/m² IV, cyclophosphamide 600 mg/m², vincristine 1 mg/m² IV (EMA-CO), and folinic acid IM 15 mg every 12 h. Unfortunately, she succumbed at tertiary hospital, 20 hours after receiving the second cycle of adjusted chemotherapy treatment. Postmortem was not done to determine the possible cause of sudden death.

Discussion

Choriocarcinoma is a potentially curable malignant tumour, rarely diagnosed in postpartum mothers. Histologically, it is characterized by the presence of syncytiotrophoblast and cytotroblast, and affects women of reproductive age at any time or following any gestational event including induced or spontaneous abortion, ectopic pregnancy, or term pregnancy [2]. Persistent vaginal bleeding is the most common symptom of choriocarcinoma following miscarriage, medical termination of pregnancy, uterine evacuation of molar pregnancy, and during the postpartum period [3]. However, because of the similar clinical presentation of choriocarcinoma and secondary postpartum haemorrhage, it is often a challenge diagnosing the disease in an early stage. In line with this, Nugent D et al., found the mean time until diagnosis was 7 weeks postpartum (range, 0-60 weeks) [4]. For the current case, the diagnosis was made after 8 weeks postpartum. Another challenge is lack of clinicians' awareness about the possible existence of choriocarcinoma in the early postpartum period, because literature has described the condition to be extremely rare following birth [4]. The presented case showed that lack of awareness as the patient was incorrectly managed with antibiotics and limited laboratory investigations and/or imaging. There is however a need for clinicians working in reproductive health field to remain aware and vigilant in patients with persistent postpartum vaginal bleeding. In addition, authors acknowledge that some of key investigations such as serum β-hCG titre and ultrasound are not routinely done, and mostly not available in resource constrained settings of sub-Saharan Africa. This is related to precarious health systems in most of developing countries [5].

There was no documented information on the macroscopic aspect of uterus of the presented case; however, the microscopic findings are similar to what described by Travassoli et al. [5]. With regards to treatment of postpartum choriocarcinoma, the initial treatment of the case report was total abdominal hysterectomy. Several factors could have influenced the decision of hysterectomy, including poor understanding of the disease and the curative treatment options because of low patient education level. It is also possible that the patient and her partner thought that surgical treatment alone could radically cure her condition. In line with this, authors acknowledge patient involvement in decision making is crucial and respectful. However, they doubt that there was enough clarification from the doctor regarding the effectiveness of chemotherapy treatment as the only option to cure the disease. Studies have shown that in low-risk patients with non-metastatic disease, the remission rate approaches 100% and remains the privilege and first line treatment for patients with GTN [6]. In addition, there was no confirmation that the tumour was confined to the uterus, even if patient seemed have completed her family size. The current literature supports surgical treatment for molar pregnancy (uterine evacuation) and placental site trophoblastic tumour (hysterectomy). However, those patients who receive surgical treatment ought to be followed up with serial serum β-hCG and human placental lactogen (hPL) respectively. Appropriate therapy should be instituted as soon as there are signs of persistence of the disease. In contrast, hysterectomy as a primary treatment option cannot cure choriocarcinoma even in the absence of metastasis. Moreover, Lana de Lourdes Aguiar lima and co-workers (2017) recommend hysterectomy as an adjuvant to minimize the possibility of metastatic induction by tissue manipulation to reduce the length of hospital stay and the number of chemotherapy cycles [6]. It is indicated if bulky and haemorrhagic tumour is present and/or in patients who did not

respond to chemotherapy regimen first [6]. In case of metastatic disease, the role of surgery remains controversial and may even increase morbidity among affected patients [6].

With regards to prognosis, Nugent et al., found that the prognosis of postpartum choriocarcinoma is related to the site or extension of the disease and not the antecedent [4]. For example, brain metastasis of choriocarcinoma may be associated with fatal outcome. Thus, the authors divide these patients in three groups: non-metastatic, metastatic low-risk and metastatic-high risk. Similarly, the International Federation of Gynaecologists and Obstetricians (FIGO) classified choriocarcinoma based on the site or progress of the disease in four stages: stage I: disease confined to the uterus, stage II: disease limited to the genital tract, stage III: metastasis to the lung, and stage IV: other metastases. This classification in our point of view shows the extension of the disease and may predict the response to treatment, as well as the prognosis of the disease [7]. Fortner et al reported 10% of patients with metastatic disease, who had involvement of the liver, occurred only in patients who delayed treatment [8]. Zong et al., found that the disease with liver metastasis has relatively poor prognosis [9] as is shown in our case. In addition, Bratila et al found the pre-treatment serum β-HCG level >30,000 IU/ml was associated with a poor prognosis [10] again consistent with a poor outcome in our patient. Although, patients with liver, brain, spleen and gastrointestinal tract metastases, should be considered as special subgroup of high risk category, with WHO risk score of 13 or greater. In line with this, recent studies found that starting treatment of those patient with standard chemotherapy may cause sudden tumor collapse with severe bleeding, metabolic acidosis, myelosuppression, septicemia, and multiple organ failure, which can result to sudden deterioration of the patient's condition and death [11]. This could probably explain the sudden death of the presented case. However, for those very high-risk patients, Ahamed E et al., found that another more intensive regimen rather than EMA-CO, may reduce the rates of sudden complications [11, 12]. Induction etoposide 100 mg/m^2 and cisplatin 20 mg/m^2 on day 1 and 2, repeated weekly for 1-3 weeks, before starting normal chemotherapy regimen has been used to eliminate sudden death [13]. This finding is valuable, and may improve the management outcome.

Conclusion

This case report emphasizes the importance of early diagnosis and chemotherapy as the first line treatment of patients with choriocarcinoma. Hysterectomy should be considered as adjuvant therapy, even for patients who had completed their family size. Although there is indication of hysterectomy, there should be evidence that the disease is still confined to the uterus prior to hysterectomy. The advantage of chemotherapy in a particular context of resource-limited areas is that it is cheap and effective for patients with low socio-economic level.

Ethics Approval and Consent to Participate

We obtained a formal approval from Moi University-Moi Teaching and Referral Hospital Institutional Research and Ethics Committee (IREC).

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