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Choriocarcinoma After Full-Term Pregnancy: A Case Report and Review of the Literature

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ABSTRACT: GTN usually follows hydatidiform mole. Post molar GTN develops approximately 15-20% of patients after a CHM and 5% after PHM. GTN can follow abortions, normal pregnancies, ectopic pregnancies, irregular bleeding following an abortion or delivery. We present a very rare case of a 24-year-old lady, admitted with a five-month history of vaginal bleeding after a normal pregnancy. The human chorionic gonadotropin (hCG) was at level of 74991. A pelvic ultrasound scan revealed an endometrial thickness of 6 cm and the presence of an intra-uterine mass measuring 60 × 53 × 45 mm, heterogeneous echogenicity with vesicles and snowstorm appearance. WHO scoring was 6 (low risk GTN), FIGO stage II and we proceeded to refer the patient to the dept of Medical Oncology in view of GTN. She was started on single agent MTX (methotrexate-folinic acid regimen). She received 10 cycles of chemotherapy and was discharged with 5-year annual follow-up. Choriocarcinomas after full-term pregnancies are a rare entity. Even when they happen, they are usually associated with pregnancy complications in the ante-natal period. The prognosis is usually very good, if prompt diagnosis and referral to a specialized center is made. The diagnosis of choriocarcinoma might be proven challenging even for experienced clinicians. Women should be informed that the prognosis is usually excellent if they receive the right and timely treatment.

KEYWORDS: Choriocarcinoma, methotrexate, GTN, hydatidiform mole

INTRODUCTION:

Gestational trophoblastic disease (GTD) envelops a variety of diseases, from the pre-malignant conditions of complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM), to malignant invasive mole, choriocarcinoma (CC) and more rarely, placental site trophoblastic tumor (PSTT) or epithelioid trophoblastic tumor (ETT). Collectively, the malignant forms are referred to as gestational trophoblastic neoplasia (GTN). The incidence of molar pregnancies (CHM/PHM) is reported to be 0.2-1.5 per 1000 births in Europe [1] and one in 714 in the U.K [2]. GTD in most cases is related to molar pregnancies, and the incidence after a full-term pregnancy is rare. In particular, the incidence of CC after a full-term pregnancy is reported in some literature to be as rare as one in 160,000 [3]. To rule out GTN any women presenting with AUB/respiratory/neurological/abdominal symptoms after any pregnancy in the past should be evaluated. Diagnostic criteria for GTN (FIGO 2021)- HPE-invasive mole/choriocarcinoma, plateauing or rising hCG and signs of metastases (CNS, lungs, and GIT).

CASE PRESENTATION:

A 28-year-old P2L2 female presented to a tertiary medical hospital (SKMCH, Muzaffarpur) with a five-month history of heavy postpartum bleeding. She reported having passed large clots in the preceding few days, prompting attendance to a GP practitioner. She was admitted, evaluated, and received two transfusions in view of low hemoglobin. A usg pelvis was done and uterine AV malformation was suspected. The general practitioner then proceeded to prescribe norethisterone pills which controlled her bleeding to minimal extent.

The index pregnancy was normal, with no associated complications. A healthy baby was born vaginally and was being exclusively breastfed. There had been no reported nausea, vomiting, cough, abdominal or pelvic pain, nor loss of consciousness associated with persistent bleeding. There was no notable family history. In view of persistent vaginal bleeding, patient was then referred to Dept of Obstetrics and Gynaecology in a tertiary hospital, in Eastern India.

The general examination was largely unremarkable, with no abdominal tenderness; uterus was anteverted, normal size, mobile, non-tender, left forniceal fullness present, no forniceal tenderness. Rectal mucosa was free. Normal vulva and vagina, with some large clots and blood noted in the vaginal canal. The cervical os was closed. There were no focal neurological signs nor other signs of any potential metastatic disease. One gram of tranexamic acid was administered, which slowed the bleeding. Blood results demonstrated haemoglobin of 6 gm/dl and a beta-human chorionic gonadotropin (b-hCG) of 32462 mIU/ml.

A trans-vaginal ultrasound scan demonstrated a thickened endometrium measuring 60 mm and a large mixed echoic mass in the cavity measuring 60 × 53 × 45 mm with some vascularity (Figure 1. “a” & “b”). A chest x-ray (CXR) was performed to rule out any early pulmonary metastases; this was clear. An MRI scan of the head was also performed, and that showed normal intracranial appearances and no visible metastases. CT angio/pelvis was done that showed no AV malformation, a left adenexal mass 6x5 cm was seen (Figure 2).

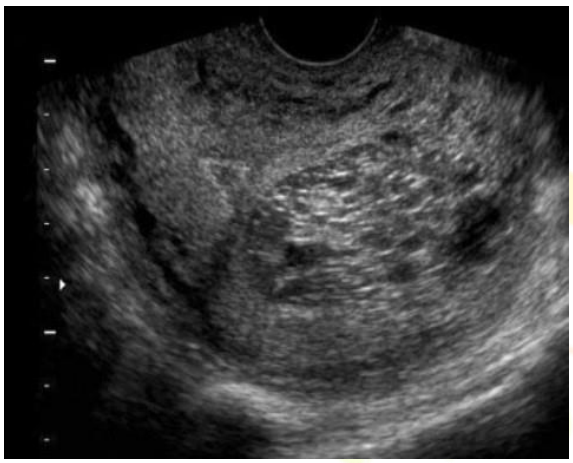

Fig 1. “a” TVS showing 6x5 cm intrauterine mass

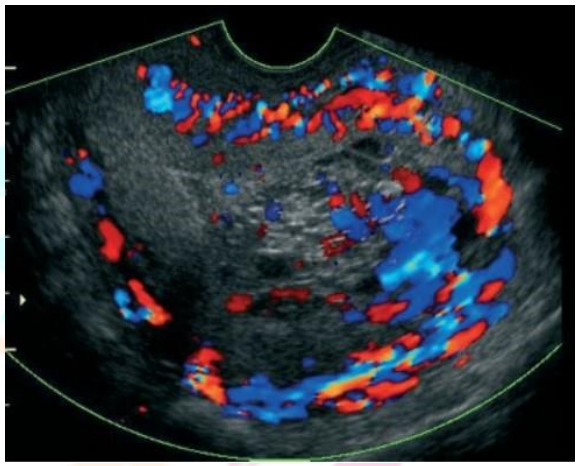

Fig 1. “b” Increased colour flow on doppler

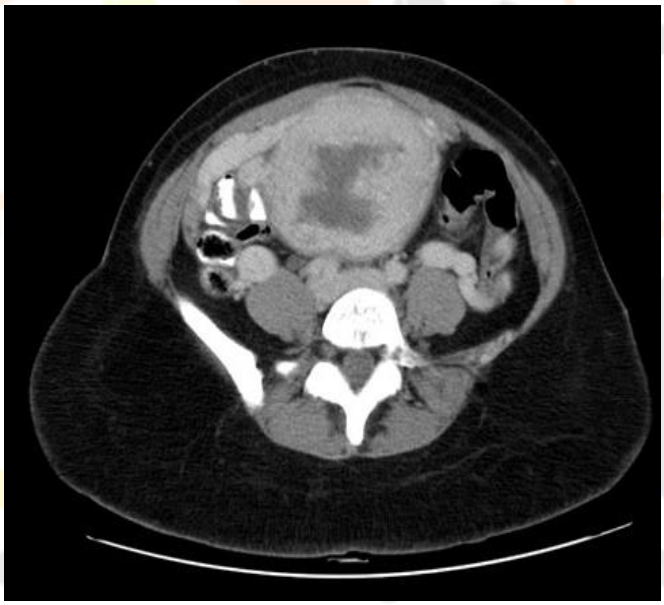

Fig 2. A left adnexal mass 6x5 cm was seen

Her International Federation of Gynaecology and Obstetrics (FIGO) score was 6 (low risk) (Age<40=0, antecedent pregnancy=1, duration from event (5 months) =1, pretreatment bhCG (>1000) =2, largest tumor size (6x5 cm) =2, no. of mets=0, size of mets=0, no. of failed chemotherapy=0.)

The case was discussed with Oncology Department. and it was agreed that the most likely differential was that of post-partum choriocarcinoma. The patient then proceeded to a surgical evacuation of the uterus on the. Products of conception (POC) were obtained and sent for histological analysis. Peri-operatively, the patient lost an estimated 1.5 l of blood and received two units of packed red cells. The POC were felt to be friable on palpation and likely molars.

Histology demonstrated macroscopically a sac weighing 40.6 g, with no obvious vesicles nor fetal parts. Microscopically, it was comprised of large areas of hemorrhage with some necrosis and viable cells. The viable cells were in the form of atypical mononuclear intermediate trophoblastic cells in sheets that were surrounded by multinucleate syncytiotrophoblast tumour cells. There was no myometrial invasion, nor were chorionic villi visualised. The pattern was consistent with a diagnosis of choriocarcinoma.

The patient was transferred to the local GTD centre with the diagnosis of post-partum choriocarcinoma, and she received 10 cycles of chemotherapy (MTX-Folinic acid). She responded very well to chemotherapy and was advised that she could try to conceive again after one year. She will be followed-up in the tertiary centre for 5 years. Her b- hCG results are demonstrated in Figure. 3.

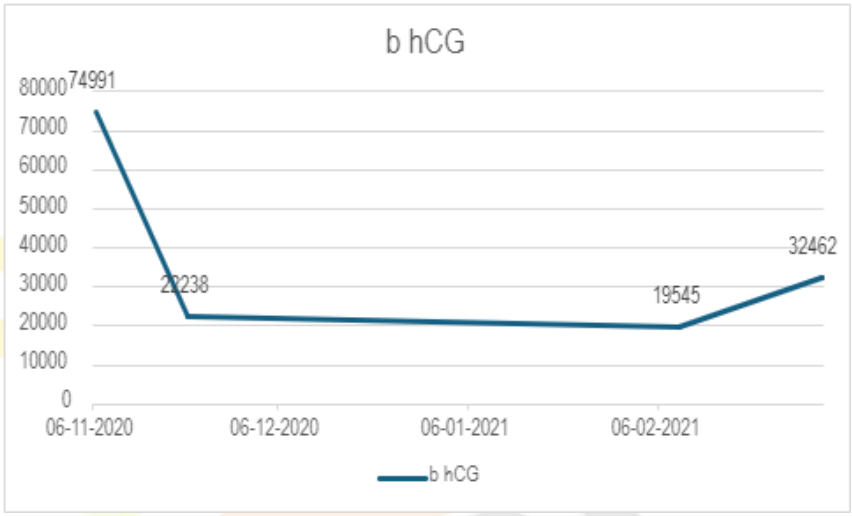

Fig 3. showing trends of b hCG

Discussion:

Choriocarcinoma after term pregnancy is a rare entity [4], with an estimated incidence after a live birth of one in 50,000 [5,6]. Diagnosis is usually prompted by increased levels of hCG in association with postpartum haemorrhage, like in our case. Final confirmation of the diagnosis is established after histological examination of the placenta or endometrial curettings. However, in many cases, the diagnosis is incidentally established after histopathological examination of the placenta [7]. Choriocarcinomas, unlike our case, tend to be associated with pregnancy complications such as hydrops fetalis, fetal-maternal haemorrhage, intra-uterine fatal death, and irregular cardiotocography (CTG) patterns. In our case, the pregnancy was uncomplicated. Maternal complications may include intracranial haemorrhage and pulmonary embolism, thus choriocarcinoma should be considered as a possible diagnosis in women who present with these pathologies, especially in the post-natal period [4]. The prognosis of choriocarcinoma is usually very good, provided that the appropriate referral to a tertiary centre is made and the appropriate chemotherapy regimen is started in a timely manner [8,9]. However, the prognosis might be worse in cases of CC after non-molar pregnancy, probably due to delay in diagnosis or advanced disease [10]. The FIGO prognostic score is widely used to identify high-risk patients and guide treatment regimens [2]. Low-risk patients (FIGO 6 or less) are usually treated with single-agent chemotherapy (methotrexate), whereas high-risk patients (FIGO 7 or more) require polytherapy with etoposide, methotrexate, and dactinomycin being one of the most widely used treatment regimens. The cure rate after successful referral to a tertiary centre is 98-100% in the U.K [2]. High dose chemotherapy with stem cell recovery might be required in rare cases of multi-relapsed disease [11]. Confirming the diagnosis with tissue diagnosis is a matter of debate and discussion, as the diagnosis is often

evident from the history, the clinical picture, and the hCG levels. However, it can sometimes lead to different treatments, in case the placental site trophoblastic tumour is diagnosed. Proceeding to a surgical evacuation of the uterus to confirm the diagnosis of choriocarcinoma is also associated with an increased risk of bleeding [2], as in our case, thus effective communication with the local gestational trophoblastic centre should be maintained.

In regard to the long-term outcomes, these are generally promising, with approximately 80% of women achieving a further pregnancy following MTX treatment or multi-agent chemotherapy [2]. Women, on the other hand, should be warned about the risk of early menopause and the implications for fertility as they approach the age of 40 [12]. Finally, the potential risk of a second cancer is extremely low. One large study [12] has reported no increase in the risk of cancer after MTX or multi-agent chemotherapy treatment.

Conclusions:

In summary, diagnosing CC can be challenging. However, combining the gynaecological history, elevated bhCG levels and USS findings, usually leads to the diagnosis. Biopsy often leads to heavy bleeding,and in cases where the diagnosis is evident, it could be avoided. The overall prognosis is very good if a prompt diagnosis is made, and care is provided in a centre with experience in the management of these cases.

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