



## AN AGGRESSIVE FORM OF CHORIOCARCINOMA ANURADHA PRASANAN

Department of Obstetrics and Gynaecology, SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES

**Abstract :** Gestational choriocarcinoma may occur as a sequel to any type of pregnancy. Choriocarcinoma is a rare trophoblastic tumor occurring approximately 50 percent after term pregnancy, 25 percent after molar pregnancy and the remainder after other gestational events. We present a case of a 22 year old lady presenting with abnormal uterine bleeding, who had a term vaginal delivery 6 months back. Evacuation was done as USG showed features suggestive of molar pregnancy. The Beta hCG levels were 20,000 mIU/ml. Although the levels of Beta hCG were abnormally low, the histopathology surprisingly revealed features suggestive of choriocarcinoma. The tumour then aggressively progressed to stage III within a week, but still the Beta hCG levels were around 20,000 mIU/ml. This case merits reporting, as in spite of its aggressive nature, low levels of Beta hCG were documented which is highly unusual in cases of post term choriocarcinomas (where the pretreatment levels are usually 1,00,000 mIU/ml).

**Keyword :** choriocarcinoma, Gestational trophoblastic disease, GTD, Gestational trophoblastic neoplasia, GTN, Beta HCG

### Introduction:

Gestational trophoblastic disease is the term used to describe the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblasts. Benign lesions consist of hydatidiform mole, complete and partial mole, whereas malignant lesions consist of invasive mole, placental site trophoblastic tumour and choriocarcinoma. The malignant lesions are called gestational trophoblastic neoplasias (GTN). Although (GTN) commonly follow molar pregnancy, they can occur after any gestational event including induced or spontaneous abortion, ectopic pregnancy or term pregnancy<sup>1</sup>. Choriocarcinoma follows a normal term pregnancy in 1 per 150,000-160,000 normal pregnancies and it is associated with an unfavorable outcome. GTD after a normal pregnancy is always choriocarcinoma. Choriocarcinoma usually invades and metastasizes early. Berkowitz reported an incidence of 4.1% choriocarcinoma

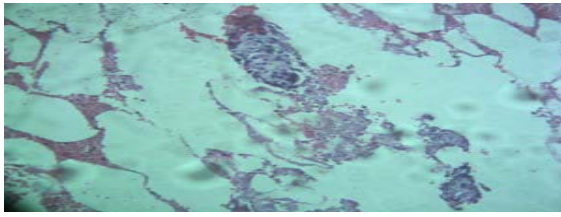
after term delivery, in 366 cases of GTD<sup>2</sup>. Post term gestational choriocarcinoma has a propensity for more extensive metastatic spread, particularly liver and brain. Remission rates, in patients to conventional chemotherapy was lower than other forms of GTD (Remission rate = 61.5%)<sup>3</sup>

### CASE

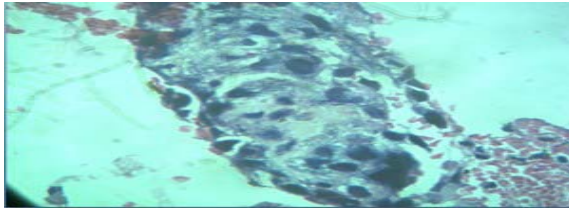
A 22 year old lady presented with continuous bleeding P/V since 1 ½ months and associated lower abdominal pain. She also gave a history of high grade intermittent fever for past 1 week. She was a P1 L1 with h/o a full term vaginal delivery 6 months back. Before the episode of abnormal uterine bleeding, she had two normal regular cycles. A Cu-T was inserted on the 6th day of menstruation; 40 days post partum. In view of the abnormal uterine bleeding, the Cu-T was removed 3 months after its insertion. Even after removal, she had persistent and excessive bleeding P/V. She also gave a history of weight loss of 5 kg over the last 6 months. On admission she was pale, temp was 101°F, Pulse -98/min, BP-100/60 mmHg. P/A – suprapubic tenderness was present, uterus was just palpable per abdomen. L/E - bleeding P/V++. No suburethral nodule was present. Pelvic examination done revealed - cervix soft admitting 1 finger, uterus enlarged to 12 weeks size, and no adnexal masses were present. All other systems were normal. USG showed enlarged uterus, 12x8.5x6.3 cm with a heterogeneous area of 7.5x4.5 cm in the endometrial cavity, with features suggestive of hydatidiform mole. Both ovaries were normal. Preevacuation hCG (28/5/14) was 18,450 mIU/ml.

### Routine investigations:-

Blood group: B positive, Hb-10.1gm/dl, Total counts-13,800cell/cumm, DC- P77L20E1 RBS-103mg/dl HIV, Hbsg, VDRL – negative Suction evacuation was done and an aspirate of about 60 c.c. was obtained. No macroscopic evidence of molar tissue or chorionic villi was present. The post evacuation hCG (29/5/14) was 9719mIU /ml. The histopathology report, showed - no villous pattern, only scanty necrotic tissue, nests of uninucleated trophoblastic cells with enlarged hyperchromatic nucleus.



**Fig 1:**Nests of trophoblastic cells absent of villous pattern and necrotic tissue



**Fig 2:** uninucleated trophoblasts with enlarged hyperchromatic nucleus

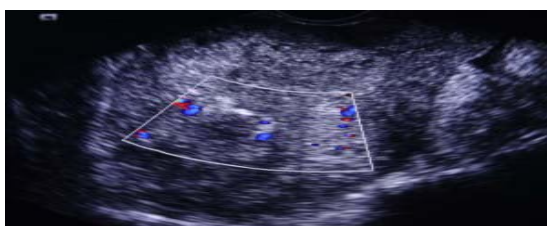
But the hCG after 4 days (2/6/14) showed an abnormally low value of 9636mIU/ml.

28/5/14(Pre evacuation)	18,450mIU/ml
29/5/14(Postevacuation)	9719mIU/ml
2/6/14(Follow up)	9636mIU/ml
9/6/14(Follow up)	20,810mIU/ml
ON ADMISSION TO RCC	
18/6/14	30,299mIU/ml

The patient did not come back for follow up. She was traced within a week. The repeat hCG on 9/6/14 was 20,810 mIU/ml .At this time, patient had complaints of persistent bleeding P/V, cough and hemoptysis. Repeat USG showed enlarged uterus, 12 x 7x5cm with evidence of a complex heterogenous area in the anterior and left lateral wall of the uterus with irregular hypo and anechoic areas within. Doppler showed evidence of vascularity in the lesion. Both ovaries appeared normal.



**Fig 3** USG showing bulky uterus with heterogenous areas in the endometrial cavity and myometrium



**Fig 4 -doppler** showing evidence of vascularity within

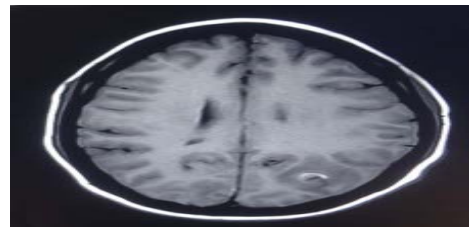


**Fig 5: Chest radiograph P-A view - appears normal**  
Chest radiograph was normal. As she was symptomatic CT-chest was done which revealed multiple subcentimetric nodular soft tissue density lesions in both lungs suggestive of metastasis.

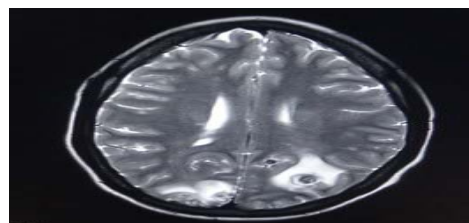


**Fig 6: CT Chest** showing multiple, well defined, nodular subcentimetre soft tissue density lesions

CT - Brain showed no evidence of any metastasis. She was referred to the regional cancer centre (RCC) immediately. On admission to RCC ,the hCG was 30,299m IU/ml and CT chest showed lung metastasis. She was put on chemotherapy. There she was given two cycles of the EMACO regime. Then she did not report back. 2 months later she came to us with complaints of severe headache, nausea and vomiting. She had features suggestive of raised Intracranial tension. MRI brain revealed multiple 1-1.3 cm hemorrhagic metastases in the brain.



**Fig 7: T1 W.I. -** predominantly hypointense lesion in the left parieto occipital region with hyperintense periphery



**Fig 8: T2 W.I. showing** predominantly hypointense lesion in bilateral parieto occipital region with surrounding edema



**Fig 9: Post contrast T1 W.I. - enhancing lesions in bilateral parieto occipital region involving the grey white matter junction suggestive of metastasis**

MRI – abdomen showed metastatic lesions 2-3 cm in the body of the uterus, fallopian tubes, ovaries, broad ligament and vagina. She was immediately referred back to RCC, where she expired one day after admission.

#### DISCUSSION

In the present case, the patient presented with abnormal uterine bleeding erroneously considered to be due to Cu-T. The bleeding persisted even after its removal. She had a full term vaginal delivery 6 months back and she resumed her regular cycles after one month. Evacuation was done as USG was suggestive of Hydatidiform mole. The pre evacuation -hCG was 18,450 mIU/ml. Molar pregnancies present with irregular bleeding P/V (97%), excessive uterine enlargement (50 %), hyperemesis (25%), preeclampsia and hyperthyroidism.<sup>1</sup> They have abnormal high levels of hCG which is responsible for all the symptoms and signs seen. Levels of hCG are usually more than 40,000-50,000 mIU/ml in molar pregnancies.<sup>4</sup> Women are at high risk for trophoblastic neoplasias when hCG levels are more than 1,00,000 mIU/ml, when uterine size is more than normal and when the theca lutein cysts are of 6 cm or more in size. In a study of 70 cases of GTN, Gulia S et. al. reported the median hCG levels to be 50,000 mIU/ml.<sup>5</sup> Miller reported poor prognostic factors in choriocarcinoma after term delivery, that include: Initial human chorionic gonadotropin titer of greater than 100,000 IU/24 hrs; Interval > 4 month between termination of pregnancy to initiation of treatment; Previous failure of chemotherapy; Brain or liver metastasis.<sup>6</sup> Relatively fewer cases with low hCG levels are reported, and they are usually either non gestational, or not post term choriocarcinomas. They are usually not very aggressive and have a favourable outcome. Saydain et. al. reported a case of large solitary invasive lung mass, which later proved to be a metastatic choriocarcinoma. In this case the hCG levels were 8278 IU/L.<sup>8</sup> Fatemeh et. al. reported a case of choriocarcinoma presenting as secondary PPH, 10 days post partum, with hCG levels of 55,000mIU/ml pretreatment which rose to 84,000 mIU/ml when she developed pulmonary metastasis. <sup>9</sup> Mirambo et. al. reported a case of unsuspected uterine choriocarcinoma with lung metastasis in a 27 year old woman who presented to the medical ward with history of respiratory symptoms and the hCG levels were >30,000 IU/L.<sup>10</sup> In the case discussed here considering the choriocarcinomatous range of beta hCG, the pre-treatment hCG levels were very low i.e. 18,450 m IU/ml and post evacuation the levels further dropped to even lower levels of 9719 and 9636 m IU/ml. In spite of this good prognostic factor, the tumour aggressively progressed to stage III within a week and hCG levels were still low; around 20,810 m IU/ml. Here the levels of hCG were misleading and the diagnosis of a neoplasia could only be established by histopathology. The diagnosis of choriocarcinoma should be considered in any women in the reproductive age group presenting with abnormal vaginal bleeding or unexplained systemic symptoms.<sup>11</sup> The presence of a Cu-T misled the primary health care physician and lead to a delay in diagnosis. Choriocarcinoma can develop as soon as 4 weeks to the antecedent pregnancy, late presentations of upto 15 years and even after menopause have been reported. The other form of GTD, after term pregnancy is Placental Site Trophoblastic Tumor (PSTT). This

occurs in 53-78% cases, after a term pregnancy. PSTT also presents with low levels of hCG when compared to the choriocarcinomas.<sup>12</sup> But PSTT is mostly confined to the uterus and metastasize very rarely, in very late cases. Prognosis of metastatic choriocarcinoma after term pregnancy is generally poor, due to early extensive spread of disease, unresponsiveness to chemotherapy, change in the host immune response and due to delayed diagnosis <sup>9</sup>.

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