Case Report

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Varied presentations of gestational trophoblastic disease in Asian women: one year follow up

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ABSTRACT

Gestational trohoblastic tumors are rare tumors which constitute less than 1% cancers of female reproductive system. They have varied presentations of which hydatidiform mole is most common. The incidence is higher in Asia and South America as compared to the rest of the world. We present a total of 5 cases of Gestational trophoblastic disease (GTD) constituting 12.2% of admissions in Gynaecology ward of a tertiary care hospital over one year. There are various risk factors which predispose to GTD include maternal age less than 20 years or more than 35 years, prior GTD, prior miscarriages, Asian ethnicity and blood group A. Commonly the woman presents with vaginal bleeding in first trimester. Sonography and β -hCG are decisive in establishing the diagnosis and further management. Follow up of the patient is very crucial. Early diagnosis and timely management results in good prognosis.

Keywords: Choriocarcinoma, β-Hcg, Invasive mole, Molar pregnancy

INTRODUCTION

Gestational trophoblastic disease (GTD) comprises of a heterogeneous group of tumors arising from abnormal proliferation of trophoblasts in the placenta. GTD accounts for less than 1% of female reproductive system cancers and its incidence varies greatly between different parts of the world. Incidence of GTD in Asia and South America is higher than reported in Europe and North America. ²⁻⁴

It can present itself any of the five clinicopathological forms: hydatidiform mole (complete and partial), invasive mole, choriocarcinoma, placental site trophoblastic tumour and epitheloid trophoblastic tumors. The last four constitute the gestational trophoblastic neoplasia.

The hydatidiform mole is the most common form, representing 80 percent of cases of GTD. Complete hydatidiform moles are diploid and have no fetal tissue

and no maternal DNA while, partial hydatidiform moles are triploid and have somefetal tissue. The incidence of partial moles is 3:1000 and complete mole is 1:1000 of normal pregnancies.⁵

Invasive mole is a hydatidiform mole characterized by the presence of enlarged hydropic villi invading into the myometrium, vascular spaces or into extrauterine sites. In 10% to 15% of cases, hydatidiform moles may develop into invasive moles.⁶

Choriocarcinoma is characterized by abnormal trophoblastic hyperplasia and anaplasia, absence of villi, hemorrhage and necrosis, with direct invasion into myometrium and vascular invasion resulting in its spread to distant sites. Relatively it is an uncommon condition. The incidence varies from 1 in 500 (India) to 1 in 50,000 pregnancies (Western countries).

Placental-site trophoblastic tumor (PSTT) is a very rare form of GTD that develops where the placenta attaches to

the lining of the uterus. More than 200 cases have so far been reported all over the world.⁸

Epithelioid trophoblastic tumor (ETT) is an extremely rare type of gestational trophoblastic disease that can be hard to diagnose as its cells mimic choriocarcinoma cells under the microscope. It can also sometimes be confused with cervical cancer.

We hereby report a series of five cases of gestational trophoblastic disease with varied presentations. They constituted 12.2% of admissions in the Gynaecology ward over a period of one year.

CASE REPORT

Case 1: Complete mole

A 35-year old G2P1L1 presented to Gynaecology emergency at 10 weeks period of gestation with complaint of bleeding per vaginum. On examination, her vitals were found to be stable. Abdominal and pelvic examination, however, revealed enlargement of uterus reaching about 16 weeks of gestation. Ultrasound evaluation showed uterine cavity filled heterogeneous mass with anechoic spaces of varying size and shape (snowstorm appearance) and with normal bilateral adnexa (Figure 1). Maternal serum β-hCG levels were raised (1,00,234mIU/ml). Haemogram, liver function test, TSH and chest X ray were normal. Suction evacuation was performed and products of conception were sent for histopathological examination. The report described marked proliferation of villous trophoblast associated with hydropic swelling of the chorionic villi with no fetal parts and it was finally diagnosed as a case of complete mole. Post evacuation patient β-hCG levels returned to normal range within three weeks.



Figure 1: An ultrasound picture showing heterogeneous mass with anechoic spaces of varying size and shape (snowstorm appearance).

Case 2: Partial mole

A 26-year old primigravida with 18 weeks period of gestation presented to emergency with complaints of irregular bleeding per vaginum for one month. Her

general physical condition and blood pressure was normal except for tachycardia. On abdominal examination, the size of uterus was corresponding to 26 weeks which was more than the period of gestation with increased liquor. Per speculum examination revealed healthy cervix and vagina with slight bleeding through the cervical os. All haematological investigations were found to be within normal limits except thyroid profile (FT₃-9.98; FT₄-40.8; TSH-<0.005) which showed a hyperthyroid picture. β-hCG level was 1791 mIU/ml. Ultrasound revealed a single live intrauterine fetus corresponding to the age of gestation with scalp oedema and a normal looking placenta on the anterior wall of uterus along with an echogenic mass with multicystic spaces appearing to be a molar tissue of size 2×3 cm (Figure 2a and 2b). Propanolol 40mg twice daily was started for tachycardia. During the hospital stay patient had an episode of bleeding and subsequently spontaneously aborted the fetus, the molar tissue and placenta. No gross congenital anomaly was seen in the fetus. Molar tissue and placenta were sent for histopathology. On pathological examination brown soft tissue showing grape like vesicles with markedly enlarged chorionic villi with hydropic change, cistern formation and marked circumferential trophoblastic proliferation was established (Figure 3). Final diagnosis was partial mole. Follow up with serial β-hCG at weekly intervals showed a fall of one log. After one year of follow the woman was disease free.



Figure 2a: An ultrasound picture showing scalp edema in the fetus.

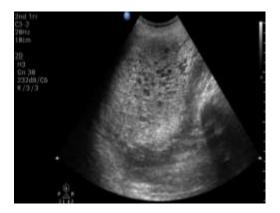


Figure 2b: Placental tissue showing cystic spaces.

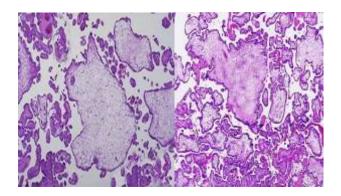


Figure 3: Histopathological examination showing dilated villi lined by attenuated trophoblastic cells.

Case 3: Choriacarcinoma

A 34-year old P2L2 woman with history of normal vaginal delivery six years back presented to Gynaecology emergency with complaint of amenorrhoea for one year and abdominal pain, cough, loss of appetite and weight loss for the last one and a half months. On examination, her general condition was poor with severe anaemia and basal crepitations in both the lungs. Abdominal examination revealed a firm mass corresponding to 18 weeks uterine size. On vaginal examination, the mass appeared to be uterine in origin, firm with restricted Haematological investigations mobility. haemoglobin as 5gms and β-hCG level as 2,25,000 mIU/ml and rest all other investigations were normal. Chest X- ray showed a cannon ball appearance. Ultrasound showed a 10x10x8 cms lesion involving uterine cavity and also involving myometrium and perimetrium with few dilated vessels (Figure 4) CT scan revealed 11x8 cms mass in pelvic cavity with nodular enhancement, merging with the uterus. Both ovaries could not be separately defined. Fat planes along the sidewalls were intact with no free fluid or lymphadenopathy. Final diagnosis was Stage III choriocarcinoma. Four units of blood were transfused and chemotherapy (EMACO regimen) was started. The patient was kept under follow up showed marked improvement with fall in β-hCG levels. Her last β-hCG was 0.5 IU/ml.



Figure 4: Ultrasound picture of choriocarcinoma showing increased vascularity.

Case 4: Recurrent mole

A 28-year old woman, belonging to a lower middle socioeconomic class, married since 11 years came to OPD with complaints of two and a half months amenorrhea followed by bleeding per vaginum and pain in abdomen for the past 7 days. She had a history of four previous pregnancies all of which did not continue beyond the first trimester. The first pregnancy was molar, the second was a blighted ovum and the last two were missed abortions. The patient had no other significant past history besides two units of blood transfusions four years ago following molar evacuation. The patient was undergoing treatment for infertility and had conceived after intrauterine insemination with husband's semen. On per speculum examination, the patient had bleeding per vaginum, a bulky uterus of 12 weeks gestational age and non-tender fornices. She was admitted and ultrasound revealed excessive choriodecidual reaction occupying most of the gestational sac with a few cystic areas in between. The features were suggestive of a hydatiform mole. Her haemoglobin was 7.6 gm% and β-hCG 500,000 IU/L. After cross-matching, suction and evacuation was carried out and products of conception were sent for histopathology. Post operatively, the patient was transfused one unit of packed cells and was monitored with serial β-hCG levels. After the first 48 hours post operatively, the β -hCG levels dropped to 40,188. Histopathology of the products confirmed the diagnosis of hydatidiform mole. The woman was advised karyotyping of both partners which was not done because of financial constraints. She was advised to conceive with IVF using donor sperms and donor ova. The woman however opted for adoption of the baby of a first degree relative. Currently she is asymptomatic with normal β hCG level.

Case 5: persistent gestational trophoblastic disease

A 45-year old woman, G5P3L1 with 5 months amenorrhoea was diagnosed as a case of gestational diabetes mellitus and was admitted for blood sugar monitoring. Her blood sugars were borderline raised on treatment and blood pressure was in the range of 140/90 to 150/106. On examination uterine size was more than the period of gestation. Laboratory investigations (haemogram, liver function test, kidney function test and profile) were normal. Serum β hCG >2,25,000mIU/mL. Chest X ray also showed normal picture. On USG, complete uterine cavity was found to be filled with hyperechoic cystic spaces giving a snowstorm appearance diagnostic of molar pregnancy.

As she was 45 years old with one living child with chronic hypertension and GDM, she was counselled for hysterectomy with mole in situ, for which the couple agreed. Hysterectomy was done at 22 weeks pregnancy. Intra-operative and postoperative period was uneventful. Histopathology report confirmed molar pregnancy.

Serum β hCG fell to 54,325 mIu/ml 48 hrs after the surgery. Blood pressure was also controlled with Tab amlodipine 5 mg OD. She was discharged on the sixth post-operative day. On day 7 β -hCG was 8426mIU/ml. On 20th post-op day she complained of pain and slight bleeding per vaginum and level of 8540 mIU/ ml. On examination, 4 subcentric nodules were present in posterior vaginal mucosa close to pouch of douglas. In view of the plateauing of serum β hCG values and vaginal nodules, diagnosis of persistent gestational trobhoblastic disease with metastasis was made and metastasis workup was done. CT chest showed multiple nodular metastasis involving both the lungs. All other investigations were within normal limits. She underwent five cycles of EMACO regime and showed complete recovery.

DISCUSSION

GTD occurs in women of childbearing age. Risk factors for GTD include maternal age less than 20 years or more than 35 years, prior GTD, prior miscarriages, Asian ethnicity and blood group A. All the five women belonged to Asian ethnicity thus they were at a higher risk of GTD. Three of the women(complete mole, choriocarcinoma and persistent gestational trophoblastic disease) had age >35 years as an additional risk factor. They usually present with vaginal bleeding in the first trimester or with abnormal routine ultrasonography at 10–12 weeks gestation (reviewed by Sebire and Seckl). Initial treatment involves uterine evacuation, which also enables a histopathological diagnosis. In the vast majority of cases, any residual disease resolves spontaneously over time but in 16% of complete mole and 0.5% of partial mole, persisting disease can develop (Seckl et al). 10

In the present series of five cases we report one women who presented with recurrent mole. She had two risk factors viz previous molar pregnancy and previous miscarriages. Barkut et al also reported a case of recurrent partial hydatidiform mole after an initial normal pregnancy. Also, Okionomidis et al reported recurrence of complete mole eighteen years after a first molar pregnancy.

In case 4, the woman presenting with recurrent mole had conceived after IUI. Chen et al, also reported a case of complete hydatidiform mole (CHM) associated with dizygotic twin pregnancy conceived by intrauterine insemination and concluded that prenatal sonographic diagnosis of placentomegaly with grape-like vesicles should include a differential diagnosis of partial hydatidiform mole , placental mesenchymal dysplasia, and recurrent hydatidiform mole. ¹³

Gestational choriocarcinoma although rare but is the most malignant form of GTD. Fifty percent of cases of choriocarcinoma arise from molar pregnancy, 25 percent from miscarriages or tubal pregnancy, and 25 percent from term or preterm pregnancy. In the present series, one woman presented after six years of a normal live

birth with widespread metastatic disease. Although choriocarcinoma is rare after term delivery but a high index of suspicion should always be kept in women in reproductive age group with features of malignancy. Roy et al also reported a case of choriocarcinoma following a term livebirth. Improvement in the survival may be achieved by both early detection and prompt initiation of therapy. ¹⁶

Diagnosis is established on the basis of raised concentration of β -hCG and appropriate histology. Ultrasonography is the best imaging modality used an adjunct to confirm the diagnosis. Early diagnosis of the condition can lead to remarkable outcome with timely institution of proper chemotherapy. The development of combination chemotherapy for choriocarcinoma has dramatically improved the prognosis in some patients. ¹⁷

Primary management of hydatidiform moles includes surgical evacuation coupled with close monitoring of serial human chorionic gonadotropin values. In women where residual complete mole or partial mole is dying out, the β -hCG concentration in serum and/or urine falls.However, for women who have completed their families and have risk factors for postmolar GTN, hysterectomy offers the advantage of simultaneous evacuation and sterilization. Hysterectomy decreases the overall risk for postmolar GTN to approximately 3.5% from the anticipated 20% following suction and evacuation. Hall patients should be chemically monitored after hysterectomy because it does not completely eliminate the potential for postmolar GTN.

In present case 1 of complete mole the woman was in the reproductive age group with no other comorbidity hence a suction evacuation was carried out in contrast to case 5 where the woman was 45 years old and had associated comorbidities hence hysterectomy was carried out after an informed consent. Although it has been reported that hysterectomy decreases postmolar GTN but in present case 5 post hysterectomy the woman presented with widespread metastatic disease which resolved after chemotherapy. A similar case was reported by Thanikasalm where hysterectomy was done for molar pregnancy in 1985 and women presented five years later with choriocarcinoma having pulmonary and renal metastasis.²¹

CONCLUSION

Women of Asian ethnicity with complicated early pregnancies should be managed with a high index of suspicion for gestational trophoblastic disease. Hydatiform mole can recur following first incident hence women with previous molar pregnancy should report early for investigations at the first possibility of pregnancy. GTN should be considered in the differential diagnosis of women presenting in perimenopausal age group with signs of malignancy. Ultrasound in conjunction with serial β -hCG is the best method of

preventing the morbidity and mortality of untreated disease after early pregnancy loss. A plateaued or rising hCG is an early sign of persisting disease which usually requires chemotherapy, hence β -hCG follow-up is crucial.

It is important to distinguish women who require less intensive therapies from those who need more intensive regimes to achieve a cure. GTD has a good prognosis if diagnosed early with correct regime of management and an assiduous follow-up.

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