Persistent Invasive Mole: A Case Report

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ABSTRACT

Gestational trophoblastic disease is a group of interrelated lesions arising from the trophoblastic epithelium of placenta after abnormal fertilization. It is a disease of women with pregnancy related tumors. Invasive mole, a common manifestation of gestational trophoblastic disease is characterized by villi accompanying trophoblastic overgrowths and invasion which penetrate deep into the myometrium sometimes involving peritoneum or vaginal vault. Here we present a case of persistent invasive mole in a patient who underwent dilation and curettage twice with persistent vaginal bleeding and elevated serum β-human Chorionic Gonadotropin levels. Investigations revealed enlarged uterus with adnexal pathology, Histopathological examination of Dilation and Curettage showed presence of villi and trophoblastic tissue, increased serum β-hCG levels. The patient is successfully treated and managed with methotrexate chemotherapy. This study is focused on the significance of follow-up of the patient as there are more chances of recurrence associated with gestational trophoblastic disease.

Key words: Gestational trophoblastic disease, Invasive mole, β-hCG levels, Chemotherapy, Methotrexate.

INTRODUCTION

Gestational trophoblastic disease (GTD) is the term used for the group of pregnancy related tumors. GTD is defined as heterogeneous group of interrelated lesions arising from the trophoblastic epithelium of placenta after fertilization which is abnormal. It is a disease of women in reproductive age with several forms of manifestations ranging from pre-malignant lesions which includes hydatidiform mole (partial and complete mole) to malignant lesions (gestational trophoblastic neoplasm) comprising invasive mole, choriocarcinoma and placental site trophoblastic tumor (PSTT).

Human Chorionic Gonadotropin (hCG) is produced by this neoplasm and acts as sensitive tumor marker that is in consonance with clinical outcome of all GTD types except PSTT.

Risk factors associated with developing GTD include maternal age (> 40 and < 20 years), history of prior molar pregnancy or miscarriage, ectopic pregnancy, multiparity, endogenous oestrogens, high beta carotene diet, high animal fat diet, ethnicity, A and AB blood groups, use of oral contraceptives, environmental toxins, smoking, alcohol consumption and herbicide exposure. Early detection of GTD is important as it is mostly chemotherapy responsive and highly curable. This study is focused on the significance of follow-up of the patient as there are more chances of recurrence associated with gestational trophoblastic disease.

CASE REPORT

A 36-year-old woman was referred to our hospital Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India with gravid 3 para 2 live child 2 (Cesarean) abortion 1 (G3P2L2A1) and with a history of dilation and curettage. On examination, she was afebrile, uterus was tender and enlarged.

Primary management of her problem was carried out in another hospital (D and C) then the serum β-hCG levels were >10,000mIU/ml. Vaginal bleeding persisted and visited another hospital after a month with reports of serum β-hCG 5412 mIU/ml and MRI of Pelvis which revealed collection noted within the endometrial...
cavity, hypo intense lesion noted in the anterior wall of the lower body, adherent to the scar region and multilocular cystic lesion noted in the left adnexa and a left ovarian complex cyst. She was examined and a lap scar ectopic resection was done. Bilateral tubectomy and then second curettage was done. Left side ovarian cyst wall excision was done and samples sent for biopsy. D&C sample for HPE revealed extensive areas of blood with organized areas having villi and trophoblastic cells. Biopsy report of left ovarian cyst tissue revealed a corpus luteal cyst.

She presented to our hospital with the reports from the previous curettage. She was not monitored for weekly determination of $\beta$-hCG level. Work up for malignant trophoblastic disease (or) persistent GTN was done because of high $\beta$-hCG level (28,931mIU/ml). Ultrasonography revealed multiple cystic spaces noted at the inner myometrium and endometrial junction and multiple tortuous dilated noted at the adnexa and parametrial region. Chest X-ray was done which did not reveal any abnormality. The liver and renal function tests were normal. MRI of the abdomen revealed a lower uterine segment scar along the anterior wall. Endometrial thickness was around 6mm with cystic areas. There was a well-defined cystic lesion on the right ovary and multiple follicular cysts in the left ovary. A D&C sample was sent again for HPE which showed predominantly areas of hemorrhage, fibroses villi and trophoblastic tissue with degenerative changes. The final diagnosis was Persistent invasive mole (Stage II:3).

The patient was advised to undergo hysterectomy to prevent the relapse, but she didn’t consent for the procedure. She was then treated with a single-agent chemotherapy (CT): Methotrexate (MTX) 100mg in 250 ml normal saline IV weekly once until the completion of 30 cycles. She was also given Inj. Calcium Leucovorin 50mg after two days of each chemotherapy cycle to minimize the toxic effects of MTX on normal cells. The patient was also monitored regularly for $\beta$-hCG levels during chemotherapy after every two cycles (Figure 1). After the final cycle of chemotherapy, the $\beta$-hCG levels were <5mIU/ml. $\beta$-hCG titer was later tested monthly after that the patient was free of tumor and the $\beta$-hCG was negative.

**DISCUSSION**

Gestational Trophoblastic Neoplasia occurs when the usual regulatory mechanism to control the spread and invasiveness of trophoblastic tissue is lost. These are rare and constitute less than 1% of all gynecologic malignancy. They are characterized by a distinct tumor marker $\beta$-hCG and have varying tendencies toward local invasion and distinct metastasis. Vascular invasion and metastasis rarely occur in Invasive moles. Demonstration of myometrial vascular mass without the evidence of fetal material on USG is in the context of an elevated $\beta$-hCG is highly suggestive of GTN (Invasive Mole). The incidence of gestational trophoblastic disease varies greatly in different parts of the world, with 0.4 per 1000 births in United States of America to 12.5 per 1000 births in Taiwan. There are wide geographical variations in the incidence of gestational trophoblastic disease as a result of differences in methodology, classifications of mole, case detection. The management of gestational trophoblastic disease depicts one of the success stories of modern medicine. Not all but majority of gestational trophoblastic diseases are potentially curable with the retention of reproductive function, once the diagnosis is made and treatment is commenced early enough. The ultimate treatment for GTD is surgical evacuation of the proliferative trophoblastic tissue. Surgical techniques include dilation and curettage and hysterectomy. After surgical intervention, either single or multiple agent chemotherapy is planned based on the disease risk which is scored according to the FIGO staging for GTD. An average of four cycles of chemotherapy was given. Chemotherapy was given till the three consecutive values of $\beta$-hCG levels were normal. The age of the patient in our study was 36 years which is supported by a study conducted by Jin-Sung Yuk et al. in which the mean age of presentation of disease is 35.4±0.7 years. As enlarged uterus being one of the risk factors, gynecologic examination revealed an enlarged uterus which is complimentary to a study by H.R. Franke et al. and showed a sign of adnexal pathology which is in contrast to a study by Budiana and Pemayun. Histopathologic examination of D&C sample showed villi and trophoblastic tissue which is similar to a study by Barber et al. In our study, patient was presented with vaginal bleeding with marked elevations in serum $\beta$-hCG levels which is complimentary to a study by Shaaban et al. Diagnosis include urine and blood levels of hCG (which are elevated during pregnancy) may give good indication, in most of the cases the levels are elevated, ultrasound (which shows a heterogeneous mass with no fetal development and theca-lutein ovarian cysts) and imaging tests (x-rays, magnetic fields, or radioactive substances) that help find out whether a tumor is present and to learn how far it may have spread. Diagnosis is made based on measurement of serum $\beta$-hCG levels and USG findings as in a study conducted by Akhavan et al. and Shaaban et al. In this case, GTD diagnosis as made primarily based on elevated serum $\beta$-hCG and pathologic examination confirmed our findings. The staging of the disease and a score is allotted to the patients by assessing
the risk factors based on the FIGO anatomical staging and WHO prognostic Scoring System (Table 1).

Management of an invasive mole includes treatment with chemotherapy as well as continued monitoring of β-hCG. Patients with GTN should be followed with weekly quantitative β-hCG levels until normal for three consecutive weeks, then monthly for 12 months.  

In the same way, the patient is being monitored. Ultrasound and Color Doppler have also been shown to be an effective tool in predicting the resolution or persistence of GTN post treatment.  

Dilatation and curettage are not recommended due to the risk of uterine perforation.

With methotrexate, complete remission is achieved in most non-metastatic and low risk cases.
CONCLUSION

This report emphasizes the importance of strict follow-up of all patients with molar pregnancy as the disease is associated with high chances of recurrence. In conclusion, we suggest that monitoring strategy using both serum and ultrasound should always be implemented, to exclude unexpected tumor progression and is also of great value for early diagnosis as well as in follow-up to trace the effects of chemotherapy.

Hysterectomy may be a preferred option for women who do not wish to preserve fertility and patients with extensive uterine tumor, although the development of effective chemotherapy has resulted in improved survival of the patients with GTD.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

GTD: Gestational trophoblastic disease (GTD); D&C: Dilation and Curettage; HPE: Histopathological examination; β-hCG: Beta- Human Chorionic Gonadotropin; MRI: Magnetic resonance imaging; PSTT: Placental site trophoblastic tumor; CT: Chemotherapy; MTX: Methotrexate; GTN: Gestational trophoblastic neoplasia; USG: Ultrasonography; FIGO: The International Federation of Gynecology and Obstetrics; WHO: World health organization; IV: Intravenous.

REFERENCES