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Case Report

Invasive mole presenting as abnormal uterine bleeding: a case report and review of literature

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ABSTRACT

Invasive mole is a type of gestational trophoblastic neoplasia (GTN). It usually occurs after a molar or non-molar pregnancy. Here we would like to present a 47-year-old nulligravida lady who does not give any history of antecedent pregnancy. She had symptoms of abnormal uterine bleeding (AUB) and came to the causality with heavy flow. Beta hCG was very high and MRI showed uterine tumor. She underwent total abdominal hysterectomy with bilateral salpingoopherectomy which showed invasive mole FIGO stage II. Her WHO prognostic score was 9 and hence she received EMA-CO regimen of chemotherapy. GTN can present in different ways, even without a history of previous pregnancy. In such situations a high level of suspicion and a simple Beta hCG level can clinch the diagnosis.

Keywords: Invasive mole, Gestational trophoblastic neoplasia, Chemotherapy, Case report

INTRODUCTION

Invasive mole is a subtype of GTN. GTN occurs due to malignant transformation of trophoblastic tissue which include choriocarcinoma, invasive mole, placental site trophoblastic tumor and epithelioid trophoblastic tumor. GTN can occur after any pregnancy either molar or non-molar but is more common after a molar pregnancy. The incidence of GTN varies from region to region and is common in Asian women 1 in 120 pregnancies.[1] Here, we would like to present a perimenopausal lady who presented to us as AUB with no history of any antecedent pregnancy and on histopathological examination it turned out to be an invasive mole. This case highlights the chances of GTN denovo without the presence of previous trophoblastic tissue.

CASE REPORT

A 47-year-old nulligravida lady came to our emergency department with heavy menstrual bleeding and passage of clots, generalized weakness and fatiguability for 4 days. Patient had been married for 6 years. She had a history of spotting per vagina for nearly 1 month and developed very heavy menstrual flow associated with clots for past 4 days. On examination her body mass index (BMI) was 20 kg/m^2, pulse rate was 116 beats per minute, BP-80/60 mmHg. She had considerable pallor on examination. Per abdomen no mass was palpable. On speculum examination excessive profuse bleeding with clots was noted, cervix could not be visualized properly due to excessive bleeding. Bimanual examination showed uterus was 10 weeks enlarged and a soft mass felt protruding at external os of cervix of 2×2 cm size probably cervical polyp. Before coming to us patient had approached another hospital for spotting per vagina 10 days back. She had following reports with her which were done outside in that hospital–Haemoglobin (Hb)-8.6 g/dl, beta human chorionic gonadotropin (beta hCG) - 1,73,300 mIU/ml (normal -<5), Ca-125-81.7 U/ml (normal -<35), carcinoembryonic antigen (CEA)-1.68 ng/ml (normal 0-3), CA-19.9-35.9 U/ml (normal-upto 39), lactate dehydrogenase (LDH) 169 U/l (normal 120-246), alpha-fetoprotein (AFP)-2.08 IU/ml (normal-upto 7.2), magnetic resonance imaging (MRI) abdomen and pelvis showing uterus 9×6 cm size with diffuse irregular polypoidal growth of 4.7×2.4 cm arising from fundus reaching upto lower segment. There was no evidence of myometrial

invasion and no pelvic lymphadenopathy. Pipelle endometrial biopsy done there showed trophoblastic tissue. When she came to our hospital, her Hb had drastically dropped to 4.7g/dl due to heavy bleeding, beta hCG was on increasing trend with values of 5,09,303 mIU/ml. Thyroid profile showed transient hyperthyroidism (TSH - 0.03, T4–15.2, T3-1.59). Chest X-ray was normal. We gave tranexamic acid injections to control the bleeding and 3 PRBCs were transfused to stabilize her before posting for hysterectomy. Total abdominal hysterectomy with bilateral salpingoopherectomy was done. Intraoperatively uterus was 10 weeks enlarged with normal adnexal structures. On cut section of uterus, molar tissue was noted in the uterine cavity (Figure 1). Postoperative day 4 beta hCG was 21,083 mIU/ml. Histopathological report (HPR) showed uterine tumor size of 10.5×4.5×2.5 cm invasive mole invading 1.5cm of myometrium and fallopian tube suggestive of FIGO stage II (Figure 2, 3). Authors have known invasive mole should occur after a molar or non-molar pregnancy but in this case we could not history or confirmation of an antecedent pregnancy.

WHO prognostic score came upto 9–high risk (age >40=1point, past pregnancy – not sure, interval from index pregnancy–not sure, largest tumor size >5 cm =4 points, beta hCG >105=4 points). Positron emission test (PET) scan was done and no active lesions were noted. Patient was given etoposide, methotrexate, adriamycin-cyclophosomide, oncovin (EMA-CO) regimen till beta hCG levels became normal and two more cycles after beta hCG came to normal to prevent relapse. Total 4 cycles of EMA-CO regimen were given. Presently beta hCG levels are normal and are followed up every month for past 3 months now. We plan to keep a close follow up and monitor beta hCG levels upto 2 years.

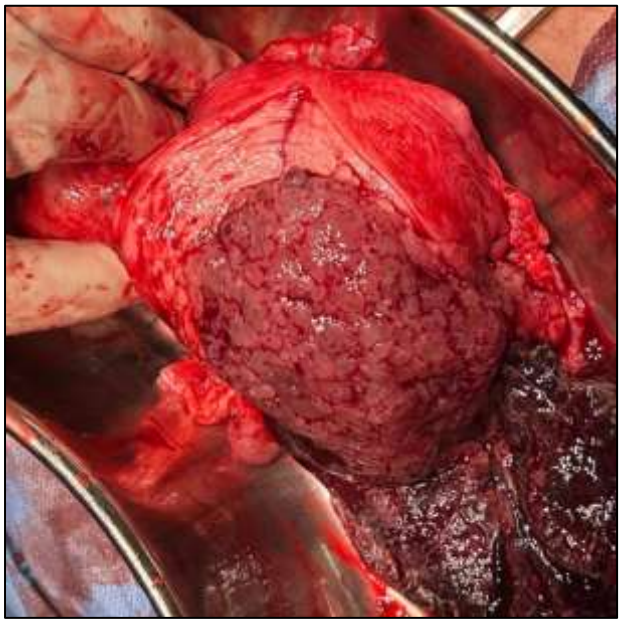

Figure 1: Uterine gross specimen with molar tissue in the cavity.

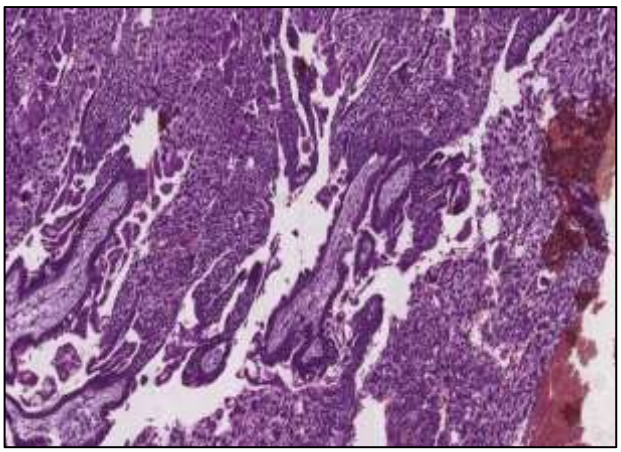

Figure 2: Histopathology showing molar tissue with villi and decidual tissue.

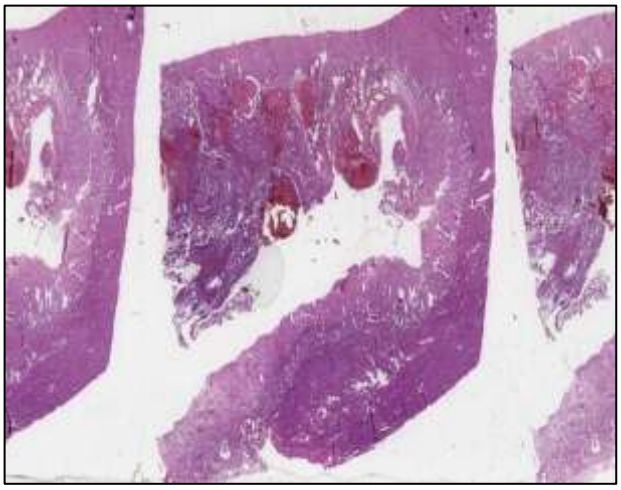

Figure 3: Histopathology showing molar tissue invading the tubal wall.

DISCUSSION

Invasive mole is a gestational trophoblastic disease which arises from abnormal growth of placental tissue. It is characterized by invasion of edematous trophoblastic tissue and hydropic chorionic villi to uterine musculature with or without invading vessels and sometimes extending beyond uterus.

Invasive mole is a type of persistent trophoblastic disease which may need further treatment with chemotherapy. About 10-15% of complete mole and 0.5% of partial mole develop into invasive mole.[2] Locally invasive form occurs in 15% and metastatic form occurs in 4% following hydatidiform mole.[3] In our case it is a locally invasive mole with infiltration to the myometrium and fallopian tube. Overall incidence is 1/15,000 pregnancies.[4] It usually occurs in reproductive age group but there are few cases seen in postmenopausal women as well.[5] Risk factors to develop persistent trophoblastic neoplasia is extremes of maternal age, antecedent complete molar pregnancy, beta hCG levels >1,00,000 mIU/ml, uterus enlarged more than

gestational age, theca luteal cyst >6 cm. The commonest symptom of invasive mole is persistent vaginal bleeding following evacuation of molar pregnancy. Other symptoms include pain abdomen. Other ways to suspect is subinvolution of uterus, persistent theca lutein cyst and persistent high beta hCG levels. But to suspect invasive mole without any history of antecedent pregnancy is tough. In this case it was difficult to suspect GTN. MRI showed intrauterine vesicular growth, so beta hCG was done which turned out to be very high. Still, it does not mean it is GTN, it could be a simple complete mole. Here, since we went ahead with hysterectomy, we could clinch the diagnosis. There are few case reports where in ectopic pregnancy (tubal and cornual pregnancy) specimens have shown invasive mole in histological examination. Hence, diagnosis of GTN is difficult in a non-molar pregnancy and needs high level of suspicion.[8]

Invasive mole is commonly locally invasive as it invades uterine myometrium but extrauterine metastasis to lungs (hematogenous spread) is seen in 5% only. Other common sites of metastasis include vagina, vulva and brain. Though invasive mole is locally invasive, tumor mortality rate is 15%.[9] Chorionic villi tissue in invasive mole is maintained as benign form but it has the ability to invade. It can invade uterine musculature and cause uterine perforation and hemoperitoneum or it can invade surrounding tissue and vessels as well.[10] While in choriocarcinoma there is atypia with proliferation of the trophoblastic tissue and absent chorionic villi and hematogenous spread is quite common to lungs, gastro intestinal tract and brain.

Depending on WHO prognostic score and FIGO staging, patients fall into either low-risk category (FIGO stage I-III, score <7) or high-risk category (FIGO stage II-III SCORE >7 or FIGO stage IV). For low-risk single agent chemotherapy is sufficient with 100% cure rate and high-risk category requires multi-agent chemotherapy with 90% cure rate. Chemotherapy is given till beta hCG becomes normal and 2 to 3 extra cycles are given once beta hCG becomes normal to prevent recurrence.

Hysterectomy is done when patient has uncontrolled bleeding per vagina just like in our case, uterine rupture with intra-abdominal bleed, placental site trophoblastic tissue, chemo-resistant tumor and sepsis. Hysterectomy does not prevent metastasis. Hence, after looking at the prognostic score, chemotherapy should be considered. The need for total number of chemotherapy doses reduces following hysterectomy as the bulk of the tumor reduces. In younger patients with uterine rupture, fertility sparing surgeries like excision of the lesion followed by chemotherapy are to be considered. In a case report, they have even tried conservative management in a case of uterine rupture with active intraperitoneal bleed where in uterine artery embolization was done and methotrexate 35mg was injected into each uterine artery to stop the acute bleeding followed by EMA-CO regimen.[11]

Our case presents few unusual features like no history of past pregnancy to develop an invasive mole, patient had features of abnormal uterine bleeding and was difficult to suspect GTN, but a simple test of beta hCG helped to think in terms of GTN, and hysterectomy was done as patient was unstable with severe bleeding and to save her life. Especially women in reproductive age group presenting as AUB, we should suspect pregnancy related complications and always get a beta Hcg done. The ideal treatment is chemotherapy but hysterectomy can be done in certain circumstances to save the patient. Further research is required to identify whether GTN can develop de-novo without any prior pregnancy and to understand pathological mechanism for the contributory factors and transformation to GTN. This case also highlights the difficulty faced in diagnosing GTN without any substantial history of GTDs.

CONCLUSION

Gestational trophoblastic neoplasia can present in different ways. Diagnosis following a molar pregnancy is common and easier to clinch. Invasive mole can present as abnormal uterine bleeding without any antecedent pregnancy. One should have a high level of suspicion and a simple beta hCG level is very useful to diagnose the condition.

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