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Case Report

INVASIVE MOLE CAUSING UTERINE PERFORATION: A CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

An invasive mole causing uterine perforation is a rare occurence. Although an invasive mole is generally less malignant than choriocarcinoma, it may be associated with fatal metastases, the uterine perforation and hemoperitoneum that adds the risk of morbidity and mortality.When it occurs early in pregnancy it mimicks other pregnancy related complications such as ectopic pregnancy as seen in our patient. In the case reported here, the woman presented with acute abdomen in early pregnancy.There was loss of contour of uterus and hemoperitonium on ultrasound and with features of shock at 8 weeks of pregnancy. The emergency exploratory laparotomy saved the woman's life from this potentially fatal complication.Since the accurate diagnosis was made only on laparotomy in this case if diagnosed earlier or before perforation the uterus could have been saved as well. This article is expected to increase awareness regarding invasive mole causing uterine perforation so that such complication could be detected on time and proper management can prevent hysterectomy in young individuals.

Keywords: Molar pregnancy, Uterine perforation, Hemoperitoneum, shock

INTRODUCTION

A hydatidiform mole is a neoplasm of the trophoblast which involves both epithelial layers, cytotrophoblast and syncytiotrophoblast, in different proportions in different cases. [1] Gestational trophoblastic disease (GTD) comprises a spectrum of interrelated tumours, including complete and partial hydatidiform mole, placental site trophoblastic tumour and choriocarcinoma. [1,2,3] Invasive mole is a condition where molar pregnancy it may be a partial hydatidiform mole or complete hydatidiform mole invades the wall of the uterus. They are characterized by persistence of edematous chorionic villi with trophoblastic proliferation. The presence of villi in the trophoblastic tissue differentiates an invasive mole from chorionic carcinoma. [4]

In Europe and North America, trophoblastic disease complicates 1 in every 1000-2000 pregnancies. The incidence is as high as 1 in 200-300 live-births in South- East Asia. Women aged over 40 are particularly susceptible to complete mole and are responsible for at least one-third of all cases. [1,2]

The high incidence of molar pregnancy in some populations has been attributed to nutritional and socioeconomic factors. Areas with a high incidence of molar pregnancy also have a high frequency of vitamin A and folic acid deficiency. Dietary factors, therefore, may partly explain regional variations in the incidence of complete mole. Maternal age older than 35 years has consistently been shown to be a risk factor for complete mole. Ova from older women may be more susceptible to abnormal fertilisation. Blood groups also play some part. [1,2,3]

The blood group A woman mated with a group A man is at least risk; and the woman whose blood group is AB is at greatest risk. Paternal aetiological factor is strongly suggested by the fact that it is not uncommon for more than one wife of the same man to die from choriocarcinoma. Considering the rarity of the disease this must be more than a chance occurrence. [1,2]

Trophoblastic tumours may be categorized into three broad groups.

1. Benign hydatidiform mole. It may be a complete or a partial mole. The tumour sometimes invades the wall of the uterus and the surrounding structures, when it is called invasive mole.
2. Persistent trophoblastic disease (PTD) also known as residual trophoblastic disease (RTD) includes invasive mole.
3. Choriocarcinoma. This is truly a malignant tumour and was earlier known as chorioepithelioma. It could be a non-metastatic (NMTD) or metastatic (MTD) trophoblastic disease [1,2]

While these have varying behaviour regarding local invasion and metastasis, even those with widespread dissemination can be cured completely [1,2,3]

Pathological features which characterise the partial mole as distinct from the complete mole are the presence of foetal or embryonic tissue, focal changes of hydatidiform swelling of chorionic villi and trophoblastic hyperplasia, marked scalloping of chorionic villi and prominent trophoblastic stromal inclusions. [1,2]

Although the histological picture varies, the typical complete diffuse mole shows proliferation and pleomorphism of epithelial cells whose nuclei are hyperchromatic and actively mitotic. The stroma of each villus is at first oedematous but soon the whole central core, including most of the vessels, is destroyed. The villus then swells to form a rounded cyst filled with watery fluid. The chorion thus becomes converted into a mass of grape-like structures each attached by a fine stalk. The cysts vary in size from a pin head to a cherry. No foetal tissue can be identified. [1,2,3]

In partial hydatidiform mole, persistent tumour develops in approximately 4 per cent of patients. The majority of these have a triploid karyotype. The disease is usually non-metastatic in nature.

Analysis of the sex chromatin pattern of hydatidiform moles has revealed that the majority are female. [1,2]

This is due to the *complete* or *classical* mole possessing a dual set of paternal genes and none of maternal origin (due to the development of an ovum under the influence of the nucleus of a spermatozoon but with the usual nucleus of the ovum being absent or inactivated). Even in the 10 per cent which have a 46, XY karyotype, the chromosomes appear to be of paternal origin. The *partial* mole, which has hydropic villi interspersed among normal villi and is associated with a foetus, has chromosomal abnormalities which are triploid in the majority of cases, the extra haploid set of chromosomes generally being derived from the father. [1,2,3] It is postulated that there is no transition from partial to complete moles and malignant change is very rare in partial moles. [1]

In practice, the biological activity and clinical behaviour of the tumour are better indices of prognosis

CASE REPORT

A 21-year-old woman was referred from a local hospital to the Paropkar Women's and Maternity hospital in Kathmandu as a case of early pregnancy with pain abdomen and spotting per vagina since last night (19 hours). She was married for the past 5 years, had 2 pregnancies and 2 live children. Both were home deliveries with no known complications. This pregnancy was the 3rd which she conceived after 1-year of the last childbirth. The eldest child was 4-year-old whom she conceived within first year of her marriage. She had amenorrhea of 2 months. She had no history of bleeding per vagina or passage of vesicles. There was no suggestive family or past history. No history of any surgeries in the past including dilatation and curettage. On examination, she had a severe degree of pallor, afebrile, thready pulse-92 beats/minute, blood pressure - 100/70 mmHg. Abdominal examination revealed distension/ tense abdomen with tenderness and guarding Bimanual examination was avoided as she was suspected to have ectopic pregnancy. Urgent ultrasound revealed hemoperitoneum and possibility of ruptured ectopic pregnancy was considered.

Serological investigations Investigations revealed:

Blood group A +ve; Hemoglobin: 5.8 g%; Platelets: 3.3 lakhs;

Bleeding time: 2 min 16 sec; Clotting time: 3 min 30 sec

Random blood sugar: 87 mg%; Renal parameters: Blood urea: 40 mg%

Serum creatinine: 0.8 mg%; Serum electrolytes: Sodium: 137 mEq/l
Potassium: 3.5 mEq/l; Chloride: 103 mEq/l; HIV: Non-reactive

She was admitted in the hospital due to acute abdominal pain. An emergency ultrasound done reveals that massive hemoperitonium. Urinary β hCG test positive. On examination she was palor (+++), hypotensive and vague tenderness all over the abdomen. Uterine size could not be delineated. Emergency resuscitative measure taken and emergency laparotomy done under general anesthesia with a provisional diagnosis rupture ectopic pregnancy, using sub umbilical midline incision. Laporotomy findings -Hemoperitoneum of about 2 L, uterus of the size of 10-12 weeks size, after clearing the abdominal cavity,it was found that a complete form of molar pregnancy perforating the uterine fundus. One of the perforation was on anterior surface of uterus above the attachment of round ligaments with vesicles protruding out and another on posterior surface near the fundus of uterus with vesicles protruding, myometrium was thinned out on the anterior side below perforaton site. Both of the ovaries were enlarged and cystic. Subtotal hysterectomy was done.Intraoperatively 3 units blood transfusion given. During post-operative period another 2 units' blood transfusion given and proper antibiotic coverage given and she had uneventful recovery.

The pathological diagnosis was invasive molar pregnancy and complete form with infiltration into the myometrium. Post-operative follows up for metastasis done including serial quantitive β hCG, chest X-ray, upper abdominal ultrasound did not show any signs of metastasis. Post-operative β hCG was 162 mIU/ml and it falls rapidly to 24 mIU in the first week and <5 mIU/ml 4 weeks following surgery. Subsequent β hCG level were negative on regular follow up visit.

DISCUSSION

Invasive moles occur in about 20% of molar pregnancies but are more common in complete molar pregnancies than in partial molar pregnancies. Invasive moles can develop both before and after treatment by dilatation and curettage (D & C) [4,5]

Invasive mole follows approximately 10 to 15 percent of complete hydatidiform moles. They are characterised by the persistence of edematous chorionic villi with trophoblastic proliferation invading into the myometrium. [6]

The literature suggests that in the UK, most women with hydatidiform mole present with vaginal bleeding or suspected miscarriage in early pregnancy, which prompts pelvic ultrasonography, although in one observational study of 41 women with confirmed hydatidiform mole, 40% were asymptomatic, and the disorder was detected after routine ultrasonography in early pregnancy. Most presented with vaginal bleeding; only 2% reported hyperemesis, and no other systemic symptoms were reported. [7] The initial diagnosis is therefore likely to be threatened abortion and, in approximately 50 per cent of cases, the mole is not suspected until it is expelled in part or whole, or the patient undergoes ultrasonography to check for foetal viability. [1]
In our case the patient was asymptomatic till 8 weeks of pregnancy then presented with pain abdomen and vaginal bleeding.

Vaginal bleeding is common in early pregnancy and often not important, but it should prompt an early ultrasound examination.

The grape-like or hydropic change occurs mainly in the second trimester, and ultrasonography shows a classic snowstorm-like appearance. However, most women develop vaginal bleeding in the first trimester and undergo uterine evacuation around 10 weeks' gestation in the UK. At this time, minimal hydropic change is present, which makes early sonographic diagnosis less reliable. Two recent retrospective studies identified molar pregnancy by ultrasonography in the first and early second trimester in only 40-60% of cases. In the largest study of 1000 patients, 40% of cases (80% of complete moles and 30% of partial moles) had a sonographic diagnosis suggesting molar pregnancy. The sonographic diagnosis was mostly simple miscarriage, with the diagnosis of hydatidiform mole being dependent on subsequent routine histological examination of the products of conception. [7]

A blood test which measures the amount of the pregnancy hormone human chorionic gonadotrophin (hCG) may also raise the suspicion that you have a molar pregnancy. Usually, the levels of this hormone are much higher than would be expected in a healthy pregnancy.A molar pregnancy may be found after what is suspected to be a miscarriage.[1,8]

Complete hydatidiform mole is the typical mole which, although tending to invade the myometrium more than does a normal placenta, generally has a benign behaviour. Fragments remaining in the uterine wall after its removal usually atrophy and only give rise to local uterine invasion in 15 per cent and metastases in 4 per cent of cases.The risk is highest if the serum hCG level at presentation is >100 000 mIU/ml, the uterus is excessively enlarged or the theca lutein cysts are >6 cm in diametre. In these women the chance of subsequent choriocarcinoma maybe 10 per cent. Older women are also at a higher risk of developing persistent tumour. [1,7]

The diagnosis of invasive mole rests on the demonstration of complete hydatidiform mole invading the myometrium or the presence of villi in the metastatic lesion. Myometrial invasion is difficult to document on pelvic ultrasound and also in uterine curettings unless there is a sufficient myometrium to demonstrate the invasion [6,8].

Per operative discovery made of a profuse haemorrhage from the uterine isthmus and the perforated area resembled trophoblastic tissue were determinent to suspect invase mole. [6] Heavy and prolonged vaginal bleeding superimposed on pre-existing malnutrition leads to anaemia in half these women. [1] Human chorionic gonadotrophin has an alpha subunit identical to that of TSH and therefore has an inherent capacity to stimulate the thyroid. The thyrotoxicosis disappears dramatically when the mole is removed, but may be severe enough to require treatment with beta-adrenergic blockers before operation or the patient can have a thyroid storm. [1,2] Dilatation and curettage is advocated as soon as this condition is diagnosed. [1,7] Severe bleeding is an indication for chemotherapy to reduce haemorrhage, even if the hormone concentration is falling. [7,8]

Chemotherapy regimen for high risk patients with gestational trophoblastic disease.

Drugs Dose- Regimen 1

Day 1:

Etoposide 100 mg/m2 by intravenous infusion over 30 min

Dactinomycin 0.5 mg intravenous bolus

Methotrexate 300 mg/m2 by intravenous infusion over 12 h

Day 2:

Etoposide 100 mg/m2 by intravenous infusion over 30 min

Dactinomycin 0.5 mg intravenous bolus

Folinic acid rescue (starting 24 h after beginning the

methotrexate infusion)

15 mg intramuscularly or orally every 12 h for 4 doses

Regimen 2

Day 8:

Vincristine 1 mg/m2 intravenous bolus (maximum 2 mg)

Cyclophosphamide 600 mg/m2 intravenous infusion over 30 min

The two regimens alternate each week.

The protocol for surveillance after hydatidiform mole include-

Two weekly serum and urine samples until human chorionic gonadotrophin concentrations are normal.

Then when hormone concentrations are normal:

If 56 or fewer days after evacuation, measure urine concentrations monthly for six months from evacuation date.

If more than 56 days after evacuation, measure urine concentrations monthly for six months after values become normal [7]

To determine if treatment is working. HCG levels should drop to normal after treatment and to detect GTD that has come back after treatment is especially important to monitor HCG levels during treatment and follow-up- to make sure the disease is going or has gone away, or has not returned. The HCG test is generally very accurate. In rare cases, patients may have abnormal substances (antibodies) in their blood that interfere with the HCG test. When these patients' blood samples are tested, the HCG levels appear higher than they really are, a situation known as phantom HCG. In some cases, women have been diagnosed with GTD when it is not actually present. A sign of phantom HCG is having high blood levels of HCG, but normal urine levels (because the abnormal antibodies are not present in urine). If doctors notice that the blood (or serum) levels of HCG are high but the urine levels are not, they can order special tests to distinguish between truly elevated HCG levels and phantom HCG. [9]

Molar disease may occasionally be reactivated after a subsequent pregnancy, even several years later, so hormone concentrations should be monitored at six and 10 weeks after any further pregnancy ends.

Following a molar pregnancy, the risk of the next gestation being a hydatidiform mole rises to one in 80. Thus most women can expect to have a normal pregnancy. [7,8]

CONCLUSION

Emergency laparotomy helps in saving the life of the patient presenting with perforating mole. If we diagnose it early and evacuate early, we can prevent the patient from landing up in a life-threatening complication. Therefore, I insist that all women should have an early scan almost mandatory at 5-6 weeks of gestation. In this case, the woman had an ultrasound only after she developed symptoms of an abdominal catastrophe. Had she been diagnosed earlier she would not have had to lose her uterus.

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