Case report

Title: Persistent Gestational Trophoblastic Disease following Ovarian Molar Pregnancy: A Case report of A Rare Entity with Review of the Literature.

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**Key Clinical Message**

Ovarian molar pregnancy, though a very rare entity, behaves like any other molar pregnancy. After surgical management, close follow-up with β-hCG surveillance is invariable to detect progression to persistent Gestational Trophoblastic Disease.

**ABSTRACT**

Ovarian molar pregnancy, though a very rare entity, behaves like any other molar pregnancy. After surgical management, close follow-up with Beta Human Chorionic Gonadotrophin surveillance is invariable to detect progression to persistent Gestational Trophoblastic Disease, which if develops can be treated successfully with chemotherapy.

**Keywords:** Beta Human Chorionic Gonadotrophin; Chemotherapy; Ovarian Molar Pregnancy; Persistent Gestational Trophoblastic Disease; Salphingo-oophorectomy;

**INTRODUCTION**

An ovarian molar pregnancy is a rare entity where ectopic gestation resulting due to abnormal implantation after abnormal fertilization leads to the growth of abnormal cells or clusters of water filled sacs within the ovarian tissue. Primary ovarian pregnancy is the rarest of the ectopic pregnancies having an incidence of 1/7000-1/40,000 in live births and 0.5-3% of all the ectopic gestations1, the incidence of molar tissue in ovarian pregnancy is even rarer. Patients usually present with symptoms of conventional ectopic pregnancy 1, 2 and it's difficult to differentiate based on presentation and ultrasonography alone. Diagnosis and treatment is usually done laparoscopically or on laparotomy while the diagnosis is confirmed only by histopathology.3

Careful Beta Human Chorionic Gonadotrophin (β-hCG) surveillance is necessary to detect progression to persistent gestational trophoblastic disease (GTD). The persistent GTD is when women retain some molar tissue despite being treated to remove it and occurs in about 8% women with molar pregnancy. It can spread like cancer but has a cure rate of nearly 100% with chemotherapy. 4

**CASE REPORT**

A 21-year-old primigravida with no significant medical, surgical and contraception history presented with amenorrhea for 3 months and right iliac fossa pain for 7 days. Urine pregnancy test (UPT) was positive. She was 13+6 weeks of gestation (WOG) by date. She had self- medicated with medical abortion pills twice at 7+2 WOG and 12+2 WOG after a positive UPT following which she developed scanty vaginal bleeding and pain abdomen.

The patient was stable but abdominal examination revealed tender right iliac fossa. Pelvic examination revealed a cystic mass in the right fornix and cervical motion tenderness. Ultrasonography (USG) confirmed a gestational sac corresponding to 4+5 WOG in the right adnexa with collection of fluid inside peritoneum. Emergency laparotomy was performed with a provisional diagnosis of a ruptured tubal pregnancy. Intraoperative findings revealed hemoperitoneum (100 ml) and a ruptured right ovary containing blood clots and vesicles (Figure 1) whilst the uterus, left ovary and both tube were normal. Ovarian ectopic pregnancy was confirmed as all Speigelberg’s criteria were met. Presence of vesicles gave rise suspicion of molar gestation. Right-sided salphingo-oophorectomy was performed as the gestational tissue was deep seated. Her post-operative period was uneventful, serum β-hCG was 31425 mIU/ml done after 48 hour of operation. And she was discharged on fifth post-operative day.

The patient was reviewed on 11th POD with a histopathology report confirming partial hydatidiform mole of the right ovary (Figure 2) (Figure3). A single-dose Methotrexate 50 mg intramuscular (IM) was administrated after ensuring normal complete blood count (CBC), renal function test (RFT), liver function test (LFT). The same regime was repeated on 17th POD as β-hCG was 69262 mIU/ml.

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| Figure 1: Gross specimen of right ovary consisting of multiple gray-brown tissue measuring approx. 8 cm in diameter. Vesicles like structures were seen. (denoted by white arrows) |

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| **Figure 2.** Edematous villi shows focal trophoblastic proliferation comprising of syncytiotrophoblasts and cytotrophoblasts. | **Figure 3.** Chorionic villi of different sizes with a mixture of small villi and large hydropic villi with the irregular scalloped outline and central acellular cistern. Also seen is the ovarian stroma. |

On 24th POD, BHCG report was 47083mIU/ml hence the diagnosis of persistent GTD was established. The patient was started on Inj Methotrexate 50mg IM and Inj Folinic acid 5 mg IM on an alternate day for 4 doses each *(First cycle)*. CBC, RFT, LFT was ensured to be normal before the administration of each chemotherapy.

Further, seven cycles of chemotherapy were instituted (Figure 4). Inj Filgrastim was given once for a decrease in total leucocyte count (TLC) before third cycle of chemotherapy .Chest X-ray and USG abdomen pelvis were normal. The patient tolerated the chemotherapy well except for having oral mucosal ulcers on few occasions which healed well with topical ointments. Serum BhCG level declined rapidly after third cycle of chemotherapy (Fig 4).Patient was kept in close follow-up for six months during which she clinically normal and had normal chest X-ray, USG, BhCG, CBC, RFT and LFT. The patient was lost to follow up there after

Figure 4. β-hCG level (mIU/ml) and chemotherapy

MTX: Methotrexate; MTXFA: Methotrexate therapy with Folinic Acid rescue

**DISCUSSION**

An ovarian molar pregnancy presents with a clinical picture similar to tubal pregnancy but seldom present with symptoms of molar pregnancy. 2, 3, 5 Our patient also presented with feature suggestive of tubal ectopic pregnancy. Among ectopic molar pregnancies, only 16% occurred in the ovary. 6 In suspected ectopic molar pregnancy, the diagnosis of hydatidiform mole (HM) is made by histology 7 same applies for an ovarian molar pregnancy. The rate of rupture and hemoperitoneum in the case of molar ectopic pregnancy was 67% .The high rupture rate may be due to higher invasive ability of trophoblasts in GTD in comparison to normal pregnancy.6 In our case intraoperative findings revealed ruptured ovary with hemoperitoneum.

An ovarian pregnancy is a rare and accounts for 3% of all the ectopics.3 Its pre-surgical diagnosis is difficult, even ultrasonography or transvaginal sonography can misdiagnose it for tubal pregnancy, hemorrhagic corpus luteum, or an ovarian cyst.5 Our case was operated with provisionaldiagnosis of ruptured tubal ectopic based on clinical and USG findings.

In 15% complete and 1% partial molar pregnancies, some remaining abnormal cells are present in the deeper tissues where it was found initially. This is known as a persistent gestational tumor, it can spread to distant site and might cause symptoms there. Thus chemotherapy is indicated to completely eradicate the abnormal cells. 4 In our case persistent GTD may have occurred as some molar tissues may have spread inside peritoneal cavity during rupture of ovary containing of molar tissue.

Persistence of GTD is defined as a persistent elevation of β-hCG, the condition is also known as gestational trophoblastic neoplasia (GTN).4 GTN generally is symptom less, and hence the diagnosis is made by regular β-hCG surveillance. FIGO Gynecology Oncology Committee suggests the diagnosis of post molar GTN to be based on changes in hCG‐levels, histopathology, and other specific investigations.8 Tools for investigation of GTN are chest X‐ray or lung computerized tomography (CT) to diagnose lung metastases and count the number of lung metastases to evaluate the risk score. Liver metastases may be diagnosed by ultrasound or CT scan and brain metastases may be diagnosed by magnetic resonance imaging (MRI) or CT scan.4, 8 In our case β-hCG level was constantly high but there was no evidence of lung or liver metastasis, however brain imaging was never done as our patient was neurologically normal.

Self-administration of abortion pills in undiagnosed ectopic pregnancy is not uncommon. Among medical abortion (MA) related problems taken from over the counter, 8.33% of women were diagnosed with an ectopic pregnancy. Also about 23.5% of women with ectopic pregnancy had a history of consuming MA pills 9 but self-medication with abortive medications complicating ovarian molar pregnancy is rare. Among women who had self-induced abortion by self-medication, 13.5% had an ectopic pregnancy and among them one was case of ovarian molar pregnancy.10

Standard treatment options for GTD differs depending on the implantation location and stage of the disease. Treatment includes chemotherapy, suction evacuation, hysterectomy, or a combination of all.7 Nowadays conservative surgeries like cystectomy or wedge resection are being performed whenever possible for ovarian pregnancy either by laparotomy or laparoscopy in contrast to oophorectomy in past.7 Right sidedSalphingo-oophorectomy was done on our patient as molar tissues were deep seatedand conservative approach could not be done. Some GTD responds well to chemotherapy, either single or combined therapy. The chemotherapeutic agents which are commonly used include methotrexate, cyclophosphamide, actinomycin D, cisplatin and vincristine. Careful regular β-hCG or human placental lactogen monitoring are required to ensure the efficacy of treatment.11 Our case progressed to persistent GTD in spite of oophorectomy and methotrexate therapy thus chemotherapy with β-hCG surveillance was instituted.

With the improvement in management approach, regular follow-up protocols and the use of human chorionic gonadotropin as a biomarker, overall cure rates can exceed 98% with fertility retention.12 Frequent monitoring of β-hCG for at least 12 months with reliable contraception is essential for the surveillance of relapse.13 Patient was followed up closely for six months and β-hCG level was reached to zero at two consecutive instances but after that patient was lost to follow up.

**CONCLUSION**

Ovarian molar pregnancy, though a very rare entity, behaves like any other molar pregnancy. Though its clinical presentations are similar to conventional tubal pregnancy, it is difficult to differentiate clinically or radiologically. Careful follow-up with β-hCG surveillance is required to identify progression to persistent GTD. Despite the need of long course of treatment, persistent GTD can be successfully by chemotherapy.

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