

## CASE REPORT

# Persistent gestational trophoblastic disease following ovarian molar pregnancy: A case report of a rare entity with review of the literature

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**Abstract**

Ovarian molar pregnancy, though a very rare entity, behaves like any other molar pregnancy. After surgical management, close follow-up with  $\beta$ -hCG surveillance is invariable to detect progression to persistent gestational trophoblastic disease.

**KEYWORDS**

beta human chorionic gonadotrophin, chemotherapy, ovarian molar pregnancy, persistent gestational trophoblastic disease, salphingo-oophorectomy

## 1 | INTRODUCTION

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.

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 gestations,<sup>1</sup> the incidence of molar tissue in ovarian pregnancy is even rarer. Patients usually present with symptoms of conventional ectopic pregnancy,<sup>1,2</sup> and it is 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.<sup>3</sup>

Careful Beta Human Chorionic Gonadotrophin ( $\beta$ -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% of women with molar pregnancy. It can spread like cancer but has a cure rate of nearly 100% with chemotherapy.<sup>4</sup>

## 2 | 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<sup>+6</sup> weeks of gestation (WOG) by date. She had self-medicated with medical abortion pills twice at 7<sup>+2</sup> WOG and 12<sup>+2</sup> 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

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motion tenderness. Ultrasonography (USG) confirmed a gestational sac corresponding to 4 + 5 WOG in the right adnexa with the collection of fluid inside the 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) while the uterus, left ovary and both tubes were normal. Ovarian ectopic pregnancy was confirmed as all Spiegelberg's criteria were met. The presence of vesicles gave rise to suspicion of molar gestation. Right-sided salphingo-oophorectomy was performed as the gestational tissue was deep-seated. Her postoperative period was uneventful, serum  $\beta$ -hCG was 31,425 mIU/ml done after 48 h of operation, and she was discharged on the fifth postoperative day (POD).

The patient was reviewed on 11<sup>th</sup> POD with a histopathology report confirming partial hydatidiform mole of the right ovary (Figures 2 and 3). A single-dose Methotrexate 50 mg intramuscular (IM) was administered after ensuring a normal complete blood count (CBC), renal function test (RFT), and liver function test (LFT). The same regime was repeated on 17<sup>th</sup> POD as  $\beta$ -hCG was 69,262 mIU/ml.



**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)

On 24<sup>th</sup> POD, the BHCG report was 47,083 mIU/ml hence the diagnosis of persistent GTD was established. The patient was started on Injection Methotrexate 50mg IM and Injection 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.

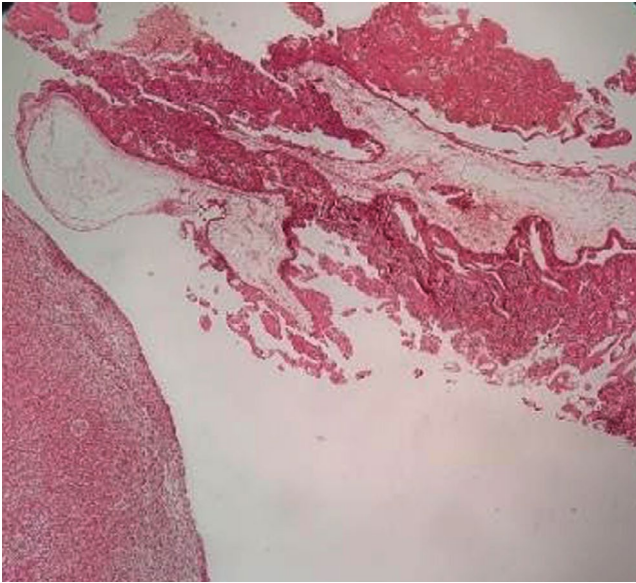
Furthermore, seven cycles of chemotherapy were instituted (Figure 4). Injection Filgrastim was given once for a decrease in total leucocyte count (TLC) before the third cycle of chemotherapy. Chest X-ray and USG abdomen pelvis were normal. The patient tolerated the chemotherapy well except for having oral mucosal ulcers on few occasions which healed well with topical ointments. Serum BhCG level declined rapidly after the third cycle of chemotherapy (Figure 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 thereafter.

### 3 | DISCUSSION

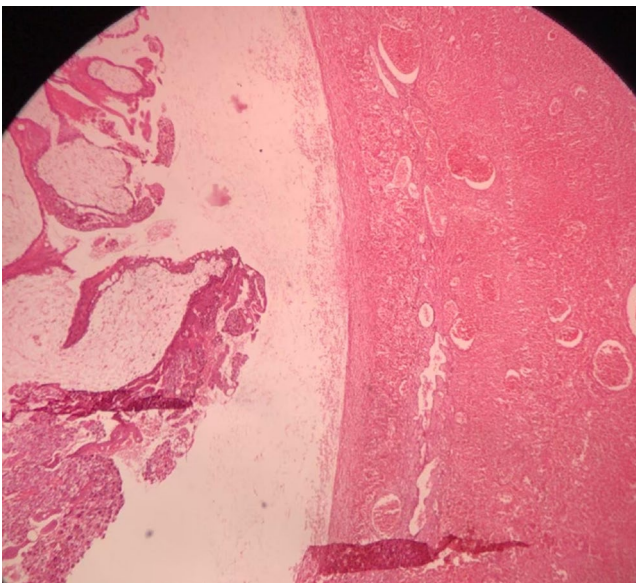
An ovarian molar pregnancy presents with a clinical picture similar to tubal pregnancy but seldom presents with symptoms of molar pregnancy.<sup>2,3,5</sup> Our patient also presented with a feature suggestive of tubal ectopic pregnancy. Among ectopic molar pregnancies, only 16% occurred in the ovary.<sup>6</sup> In a suspected ectopic molar pregnancy, the diagnosis of hydatidiform mole (HM) is made by histology<sup>7</sup> same applies to 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 the higher invasive ability of trophoblasts in GTD in comparison with normal pregnancy.<sup>6</sup> In our case, intraoperative findings revealed ruptured ovary with hemoperitoneum.

An ovarian pregnancy is rare and accounts for 3% of all ectopics.<sup>3</sup> Its pre-surgical diagnosis is difficult, and even ultrasonography or transvaginal sonography can misdiagnose it for tubal pregnancy, hemorrhagic corpus luteum, or an ovarian cyst.<sup>5</sup> Our case was operated on with a provisional diagnosis 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 a distant sites and might cause symptoms there. Thus chemotherapy is indicated to completely eradicate the abnormal cells.<sup>4</sup> In our case persistent GTD may have occurred as



**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

some molar tissues may have spread inside the peritoneal cavity during rupture of the ovary containing molar tissue.

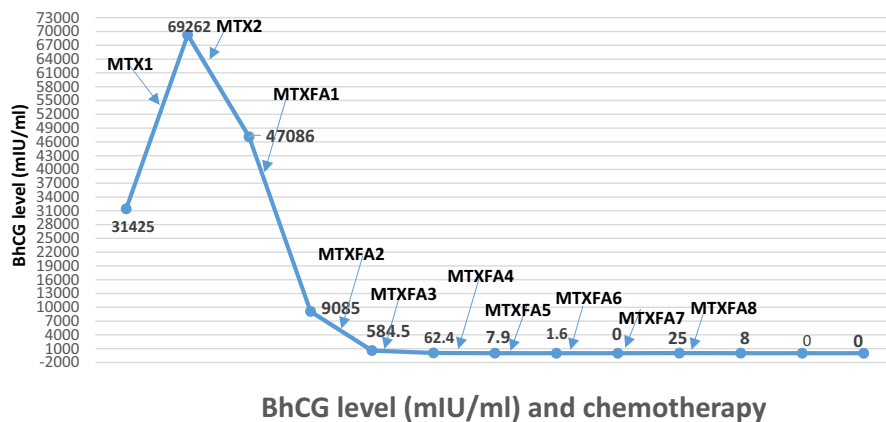
The persistence of GTD is defined as a persistent elevation of  $\beta$ -hCG, and the condition is also known as gestational trophoblastic neoplasia (GTN).<sup>4</sup> GTN generally is symptomless, and hence, the diagnosis is

made by regular  $\beta$ -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.<sup>8</sup> 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.<sup>4,8</sup> In our case,  $\beta$ -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<sup>9</sup> but self-medication with abortive medications complicating ovarian molar pregnancy is rare. Among women who had a self-induced abortion by self-medication, 13.5% had an ectopic pregnancy and among them, one was the case of ovarian molar pregnancy.<sup>10</sup>

Standard treatment options for GTD differ depending on the implantation location and stage of the disease. Treatment includes chemotherapy, suction evacuation, hysterectomy, or a combination of all.<sup>7</sup> 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.<sup>7</sup> Right-sided Salpingo-oophorectomy was done on our patient as molar tissues were deep-seated and a conservative approach could not be done. Some GTD responds well to chemotherapy, either single or combined therapy. The chemotherapeutic agents which are commonly used to treat GTD include methotrexate, cyclophosphamide, actinomycin D, cisplatin, and vincristine. Careful regular  $\beta$ -hCG or human placental lactogen monitoring is required to ensure the efficacy of treatment.<sup>11</sup> Our case progressed to persistent GTD despite oophorectomy and methotrexate therapy thus chemotherapy with  $\beta$ -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.<sup>12</sup> Frequent monitoring of  $\beta$ -hCG for at least 12 months with reliable contraception is essential for the surveillance of relapse.<sup>13</sup> Patient was followed up closely for six months, and the  $\beta$ -hCG level was



**FIGURE 4**  $\beta$ -hCG level (mIU/ml) and chemotherapy. MTX: Methotrexate; MTXFA: Methotrexate therapy with Folic Acid rescue

reached zero at two consecutive instances but after that patient was lost to follow-up.

## 4 | 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  $\beta$ -hCG surveillance is required to identify progression to persistent GTD. Despite the need for a long course of treatment, persistent GTD can be successfully by chemotherapy.

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## CONFLICT OF INTEREST

All authors have no conflicts of interest to disclose.

## AUTHOR CONTRIBUTIONS

Bibechan Thapa performed literature review, information collection, manuscript writing and consent taking. Meenu Maharjan and Heera Tuladhar was involved in case management, case follow up, literature review, manuscript review and manuscript editing.

## ETHICAL STATEMENT

Informed written consent was obtained from the patient. Approval from concerned department and hospital was taken as per guideline of the institution. Patient's anonymity has been maintained in the manuscript. The manuscript was created in compliance with the ethical standards of our institution.

## DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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