



Case report

A rare case of gestational trophoblastic neoplasia following an ectopic molar pregnancy

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1. Introduction

The incidence of hydatidiform mole is approximately 1:1000 pregnancies. Most molar pregnancies are confined to the uterine cavity. Approximately 15% of patients with a complete hydatidiform mole will develop local invasion, and 5% will develop metastatic disease (Goldstein and Berkowitz, 2012). An ectopic molar pregnancy is a rare entity, estimated to occur in 1.5:1,000,000 births (Gillespie et al., 2004). The extraordinary combination of these two gynecological diagnoses – an ectopic pregnancy and a molar pregnancy – has been described in medical journals less than 300 times (López et al., 2018).

This case report describes a rare case of gestational trophoblastic neoplasia (GTN) following an ectopic molar pregnancy. The patient presented with a ruptured ectopic pregnancy and underwent laparoscopic surgery. Following surgery, a histological diagnosis of complete hydatidiform mole was made. When human chorionic gonadotropin (hCG) levels did not decline as expected, a diagnosis of GTN was made, and the patient received chemotherapy until reaching complete remission.

Similar reports of GTN following ectopic molar pregnancies are scant, and to the best of our knowledge this is the only report of GTN following an ectopic complete molar pregnancy.

2. Case description

A 40-year-old generally healthy woman presented at the emergency department (ED) with abdominal pain. She has an obstetric history of five vaginal deliveries and one cesarean section. She has no known gynecological problems; she menstruates regularly and does not use any contraception. She complained of abnormal uterine bleeding beginning two and a half months before presenting in the ED.

Upon arrival to the ED the patient's physical examination revealed her to be hemodynamically stable; however, when an abdominal ultrasound was performed, substantial hemoperitoneum was seen. Her

blood test showed a hemoglobin level of 6.2 g/dL, and a positive hCG result. A working diagnosis of a ruptured ectopic pregnancy was made, and the patient was transferred to the operating room for urgent surgery. Quantitative serum hCG was taken prior to surgery, but was not yet known at this point.

The patient underwent laparoscopic surgery; upon entering the abdominal cavity, 2500 mL of blood and blood clots were evacuated, and pelvic peritoneal adhesions were identified. A ruptured ectopic pregnancy was identified in the right fallopian tube, and a unilateral salpingectomy was performed. During the operation blood products were transfused (three units of packed blood cells, one unit of fresh frozen plasma). Following surgery, the patient was stable, her hemoglobin rose to 9.8 g/dL, and hCG decreased from 68 K IU/L preoperatively to 28 K IU/L. She was discharged on post-operative day 2 and was instructed to perform serum hCG tests as follow-up.

hCG monitoring demonstrated a plateau with three consecutive tests around 23 K IU/L. The patient underwent an abdominal CT scan which ruled out the presence of an abdominal pregnancy or any signs of residual trophoblastic tissue, and demonstrated right ovarian vein thrombosis (OVT). Chest x-ray revealed no evidence of metastatic disease. As the pathologic diagnosis was not yet known, a diagnosis of a persistent ectopic pregnancy was made, and the patient began methotrexate (MTX) treatment as per department protocol. She received three 68 mg intramuscular MTX injections (1 mg/kg) with no adverse effects on days 1, 3 and 5, and hCG levels decreased to 8 K IU/L. She also began daily injections of low molecular weight heparin due to OVT.

Two weeks later the pathology report was finalized, making a histological diagnosis of a tubal complete hydatidiform mole, with a negative staining for p57 (Fig. 1). The patient was then referred for gynecologic oncology consult. She was determined to be at stage 2 GTN due to the combination of histological findings and hCG plateau. She received a low World Health Organization (WHO) risk score of four (one point for age ≥ 40 ; two points for pretreatment hCG 10^4 - 10^5 ; one point for tumor size estimated 3–5 cm), and thus continued single agent

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treatment with MTX. The treatment protocol consisted of intramuscular injections of MTX (1 mg/kg) on days 1, 3, 5 and 7 of a two-week cycle, supplemented by leucovorin treatment on days 2, 4, 6 and 8. Overall she received a total of 11 cycles of MTX until reaching disease remission (hCG < 5 IU/L on three consecutive tests), after which she consented to only two additional cycles for consolidation treatment (Fig. 2).

3. Discussion

We present a rare case of GTN following an ectopic molar pregnancy. Less than 300 cases of ectopic molar pregnancies have been described in Western medical journals (López et al., 2018), and only a few of these patients were later diagnosed with GTN. To the best of our knowledge this is the only report of GTN following an ectopic complete molar pregnancy.

Ectopic molar pregnancies usually present in the same manner as any ruptured ectopic pregnancy. Most patients present with abdominal pain and/or vaginal bleeding, and require emergent surgical intervention for the removal of the ectopic pregnancy (Hassadia et al., 2012). Ruptured ectopic molar pregnancies have been described regarding an ovarian pregnancy (Joneborg et al., 2011) and tubal pregnancies (López et al., 2018; Siozos and Sriemevan, 2010).

In 2018, López et al described a similar case of a patient with GTN following an ectopic molar pregnancy (López et al., 2018). This patient presented with a ruptured ectopic pregnancy and underwent unilateral salpingectomy. Following surgery, the patient had persistently elevated hCG levels, and a diagnosis of GTN was made. The histological diagnosis was a partial hydatidiform mole, with positive p57 staining. The patient

received MTX as single agent chemotherapy and achieved complete disease remission.

Joneborg et al published a case of a patient who presented with metastatic GTN three years after an ectopic pregnancy (Joneborg et al., 2011). Reevaluation of the histological specimen from the ectopic pregnancy confirmed an ovarian hydatidiform mole, and the later development of choriocarcinoma probably originated from this mole.

Histopathology of the extracted tissue is key to a final diagnosis, and is considered to be the gold standard for diagnosis of molar pregnancies (Tulon et al., 2010). Ectopic molar pregnancies may be more common than previously perceived. In one published study, 79 patients underwent surgery for treatment of ectopic pregnancies, and in 18 cases a histological diagnosis of molar pregnancy was made (Tasha et al., 2010). In this study, hCG levels were significantly higher for patients with molar pregnancies compared with non-molar pregnancies.

It may not be a coincidence that many cases reported in the literature of molar ectopic pregnancies presented with rupture and massive bleeding and required surgical intervention. This may be explained by the histological traits of the molar tissue – these pregnancies are more vascular, tend to grow rapidly, are larger than genetically normal ectopic pregnancies, and have malignant potential – all traits that could contribute to this clinical presentation. There is also potential bias in publications regarding the prevalence of this diagnosis; only patients who underwent surgery had a histological diagnosis and so were described and published. Patients treated conservatively may not have a final histological diagnosis.

This case is one of very few reports of GTN following an ectopic molar pregnancy. This case description demonstrates the role of a

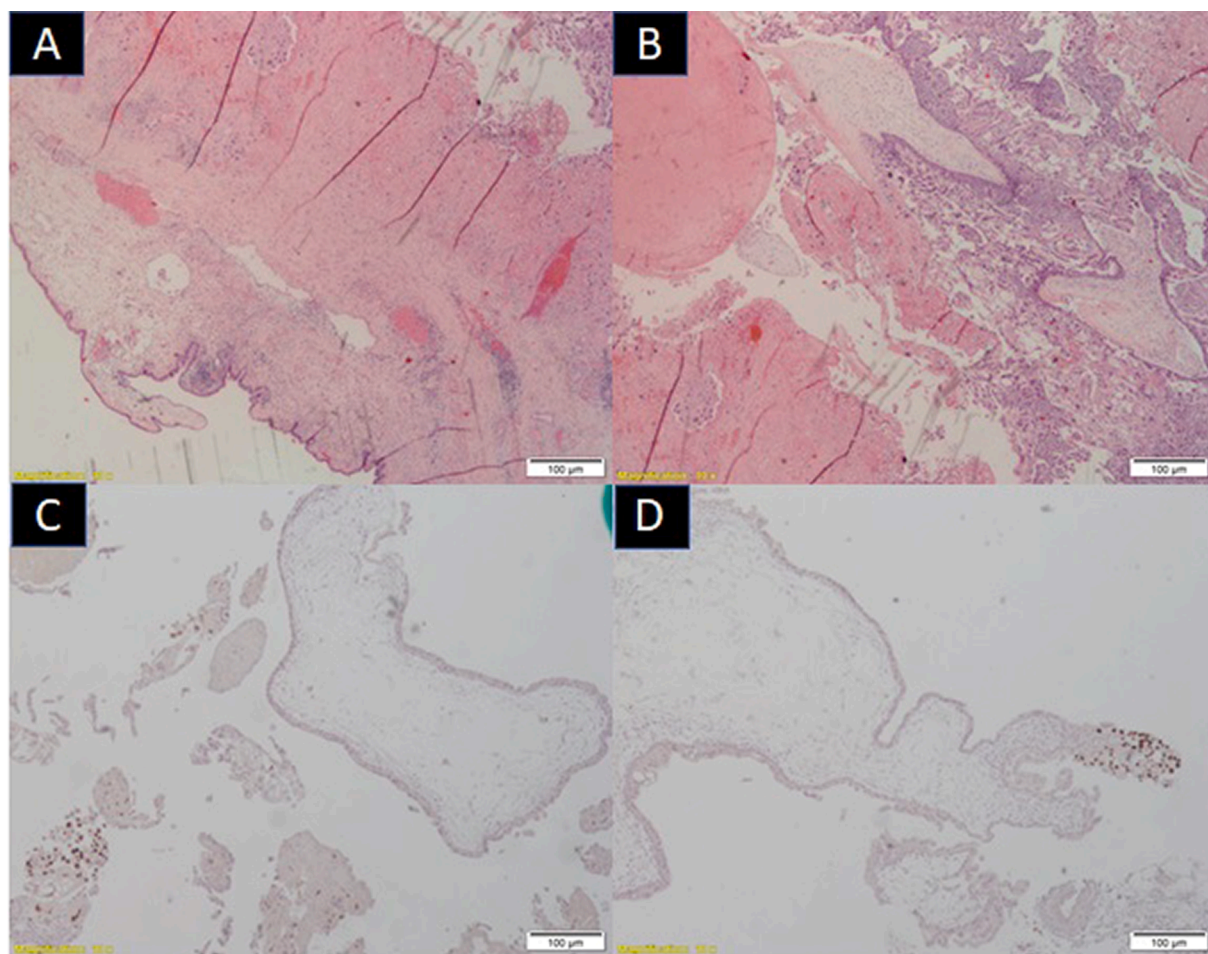


Fig. 1. Histopathology images from laparoscopic salpingectomy: A, fallopian tube tissue on bottom left, trophoblastic tissue invading fallopian tube stroma on top right. B, trophoblastic tissue indicative of molar pregnancy. C + D, hydropic villi with negative p57 staining.

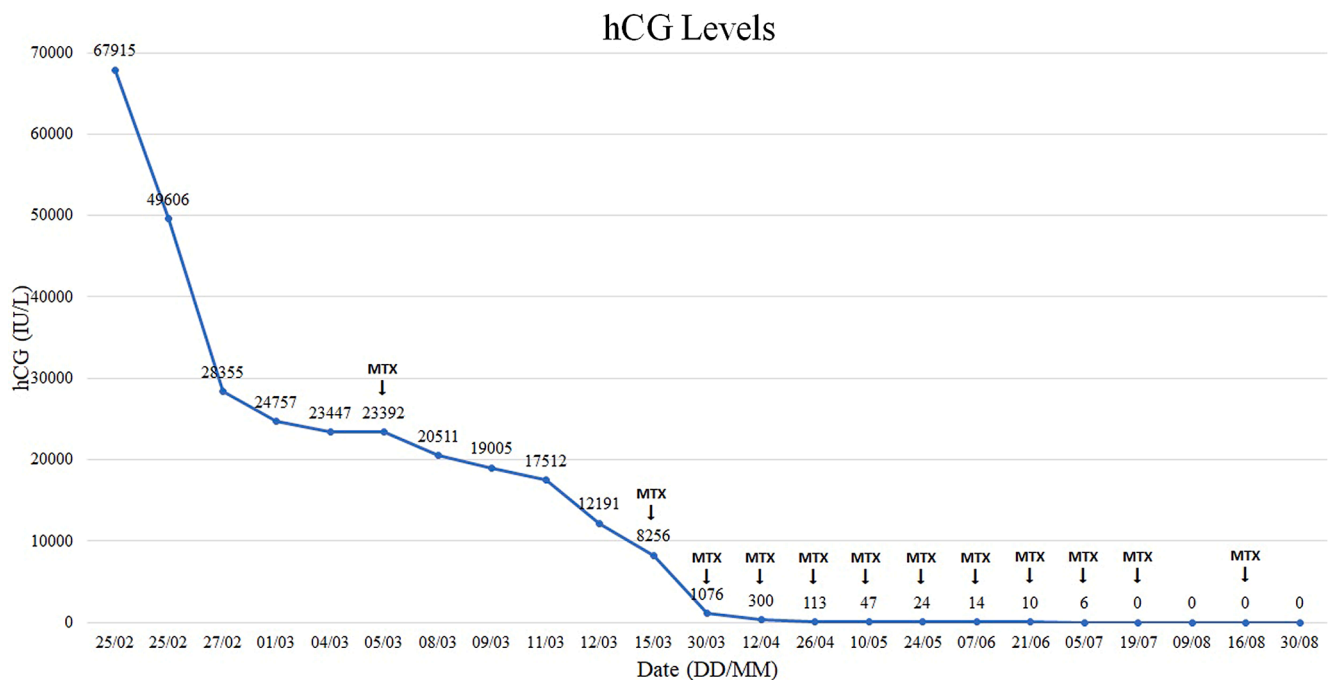


Fig. 2. Graph showing hCG monitoring. Arrow indicates beginning of methotrexate/leucovorin cycle. The patient received a total of 11 treatment cycles, and one consolidation treatment cycle.

histopathologic diagnosis when ectopic molar pregnancy is suspected, and the importance of following up on pathology reports after surgical treatment of an ectopic pregnancy. In addition, treating gynecologists should keep in mind that meticulous monitoring of serum hCG following any molar pregnancy is key for timely diagnosis and treatment of GTN.

CRediT authorship contribution statement

Sarah Dollinger: Writing - original draft, Writing - review & editing.
Effi Yeoshoua: Conceptualization, Writing - review & editing.
Ram Eitan: Conceptualization, Methodology, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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