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## Case report

# Persistent free-floating pelvic trophoblastic cysts following an interstitial ectopic pregnancy

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## SUMMARY

Persistent trophoblast after ectopic pregnancy has been demonstrated at the surgical site or as peritoneal implants. A 37-year-old woman (G5P2) experienced persistently low levels of beta-human chorionic gonadotropin (hCG) after surgical treatment for an interstitial pregnancy. Evaluation for persistent trophoblast, gestational trophoblastic neoplasm and heterophilic antibodies was negative. After 15 months without resolution, she elected for hysterectomy. We found four smooth, freely floating avascular cysts intraoperatively; pathological evaluation identified the cysts as trophoblastic tissue. Serum beta-hCG resolved postoperatively and remained negative at 1 year. Our case demonstrates the novel finding of trophoblastic tissue existing as free-floating cysts in the peritoneal cavity. With appropriate suspicion, these cysts can be identified on radiologic investigation and removed laparoscopically.

## BACKGROUND

In cases of persistently low levels of human chorionic gonadotropin (hCG) after ectopic pregnancy, the differential diagnosis includes persistent trophoblastic tissue, heterophilic antibodies and gestational trophoblastic neoplasm. Most commonly, persistent trophoblast can exist at the surgical site or as peritoneal implants.<sup>1</sup> Our case demonstrates the possibility of extratubal trophoblastic tissue existing as free-floating cysts in peritoneal fluid.

## CASE PRESENTATION

A 37-year-old previously healthy Caucasian woman (G5P2) was referred to our institution with persistently low serum hCG levels after surgical treatment of a right interstitial ectopic pregnancy. Initial diagnosis was made by ultrasound examination with hCG of 8309 mIU/mL. Her gynaecologist performed a laparoscopic cornuostomy. Ten days later, she presented to her local emergency department (ED) with non-persistent chest pain and her hCG was 1453 mIU/mL.

At a 6-week postsurgical visit, she had a positive urine pregnancy test. While en route the next day for follow-up serum beta-hCG testing, she developed acute severe right lower quadrant pain and presented to the ED. Her hCG levels had increased to 2017 mIU/mL for which her gynaecologist performed a right uterine wedge resection and salpingectomy. Operative findings included hemoperitoneum, a ruptured right uterine cornua

and endometriosis-like lesions on the posterior cornua, anterior pelvic peritoneum and cul-de-sac peritoneum. Pathological evaluation from both surgical specimens demonstrated grossly normal trophoblasts.

Serum hCG levels decreased rapidly over 2 months but then plateaued between 10 and 25 mIU/mL. She received a single injection of methotrexate 50 mg/m<sup>2</sup> intramuscularly 4.5 months after the initial surgery for presumed persistent trophoblast. Over 2 months, her levels fluctuated between 9 and 18 mIU/mL. Her gynaecologist referred her to our family planning service for evaluation of persistent hCG. At that time, she was 7.5 months from her original surgery and she was using a combined oral contraceptive, and desired future fertility.

## DIFFERENTIAL DIAGNOSIS AND INVESTIGATIONS

In our office, transvaginal ultrasound examination demonstrated a normal uterus except for a small hyperechoic focus in the right cornua. Her beta-hCG was 22.5 mIU/mL. Evaluation for hyperglycosylated hCG and heterophilic antibodies using the USA hCG Reference Service Laboratory (Albuquerque, New Mexico, USA) returned as negative.

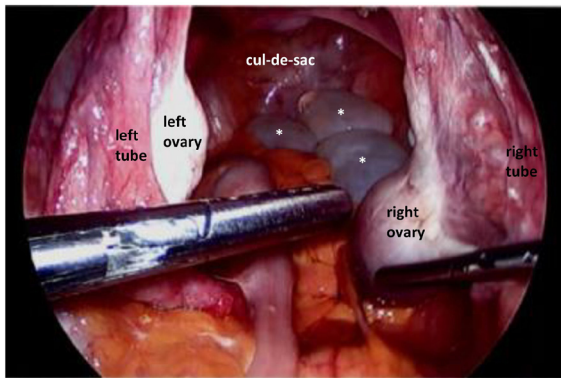
We continued to monitor monthly hCG levels, which remained approximately 20–30 mIU/mL. At 11 months from the initial surgery, her hCG increased to 40 mIU/mL, which prompted a hysteroscopy with dilation and curettage to evaluate for intrauterine persistent trophoblastic or molar tissue. Operative and pathological findings were unremarkable. Serum hCG increased to 75 mIU/mL 2 weeks after hysteroscopy, then declined to 21 mIU/mL 6 weeks later (13 months from initial surgery). The hCG increased again to 86 mIU/mL at 14 months from initial surgery, at which time we still presumed the cause to be persistent trophoblast within the interstitial pregnancy surgical site. Because the patient then expressed that she no longer desired fertility and preferred no further follow-up, we planned a hysterectomy.

Preoperatively, she underwent CT scans with intravenous contrast of her head, chest, abdomen and pelvis demonstrating no apparent metastatic disease. The pelvic CT incidentally demonstrated possible loculated free fluid in the dependent posterior pelvis.



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**Figure 1** Laparoscopic evaluation demonstrating three of four free-floating cysts found incidentally during hysterectomy. Asterisk symbol shows free-floating pelvic cysts.

### TREATMENT

We performed a laparoscopic hysterectomy with left salpingectomy 15 months after the initial surgery. During initial laparoscopic survey, we identified four smooth, white, 1–4 cm discoid cystic structures floating freely in the poster cul-de-sac (figure 1). After the hysterectomy, we removed the cysts, which were completely free of vascular attachment or supporting tissue.

### OUTCOME AND FOLLOW-UP

Pathological examination revealed a normal uterus with granulation tissue in the right cornual region and no evidence of gestational tissue. The cystic structures were filled with clear, gelatinous fluid and had smooth internal walls without excrescences. Histology demonstrated avascular cysts containing hydropic, hypocellular villi lined by thin epithelium with cell structure consistent with syncytiotrophoblasts showing variable to moderate nuclear pleomorphism. The tissue demonstrated strongly positive staining for beta-hCG, positive staining to GATA3 and p63, and negative staining for calretinin. Polyclonal Carcinoembryonic Antigen testing showed apical membrane staining. The tissue also demonstrated positive nuclear staining for p57 in a minority of cells, suggesting non-molar tissue. The pathologists at our institution reviewed the specimens from the original cornuostomy and salpingectomy surgeries; both specimens showed normal p57 staining and diploid DNA.

Serum beta-hCG evaluations were 1 mIU/mL at 1 and 2 months after surgery, then <1 mIU/mL at 3 and 4 months post-surgery and 1 mIU/mL at 12 months postsurgery.

### DISCUSSION

Persistent trophoblast is a known complication of ectopic pregnancy that can occur at the pregnancy site or as extratubal implants.<sup>1</sup> Our case demonstrates trophoblastic tissue persisting as free-floating avascular cysts in peritoneal fluid. The diagnosis was unexpected, though, in retrospect, the CT findings initially interpreted as pelvic fluid loculations were consistent with the pelvic cysts identified at surgery.

Peritoneal fluid is an ultrafiltrate of plasma; under normal conditions it has a similar composition of glucose and nutrients as blood and can therefore act as a culture medium for tissue lacking vascular supply. While the oxygen content of peritoneal fluid is lower than that of blood, placental tissue is uniquely equipped to function in hypoxic conditions.<sup>2</sup> The cysts did not respond to methotrexate; it is unlikely that a therapeutic dose reached the cysts given the lack of vasculature and the slow

### Patient's perspective

I had progressive and severe anxiety throughout the course of this process. I had to have repeated testing over time of my pregnancy hormone levels which was stressful, especially because the diagnosis remained unclear for so long. I ultimately chose a hysterectomy because even the specialists could not figure out what was the case of the persistent pregnancy hormone levels. I had previously desired to have another child but with all of the issues related to this last pregnancy (being ectopic and then having persistent pregnancy hormone in my body), I no longer wanted to risk going through anything like that again. After my hysterectomy I was relieved, and I was especially happy 1 year later to learn my hormone level was still negative.

equilibrium of methotrexate between plasma and peritoneal fluid.<sup>3</sup>

We found no similar cases in the literature; however, cases of intraperitoneal free-floating cystic papillary mesothelioma support the notion that this physiology is possible. These cysts have been described as smooth, white and avascular, grossly similar to our case.<sup>4</sup> Papillary mesothelioma can mimic chorionic villi histologically,<sup>5</sup> but negative calretinin and positive hCG staining exclude this possibility in our case.

On pathological evaluation, the cystic tissue resembled complete hydatidiform mole, but demonstrated a p57 staining pattern suggesting non-molar tissue. Since the pathologists confirmed the initial surgical specimens were non-molar, the placental tissue more likely underwent hydropic degeneration leading to a grossly molar appearance.

This case represents a novel site of persistent trophoblast after ectopic pregnancy. These extratubal trophoblastic cysts can be evident with appropriate suspicion on radiologic investigation and confirmed with diagnostic laparoscopy.

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**Contributors** KDC and MDC involved in care of patient, assessment of data in report, preparation of manuscript, editing of manuscript and review of final submission of text and figures. MJC and MYH involved in care of patient, assessment of data in report, editing of manuscript and review of final submission of text and figures.

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### Learning points

- ▶ In unusual cases of persistent serum beta-human chorionic gonadotropin after ectopic pregnancy, consider extratubal trophoblastic cysts in the differential diagnosis.
- ▶ Extratubal trophoblastic cysts can resemble hydatidiform mole on pathological evaluation; immunohistochemistry is necessary to make this distinction.
- ▶ If ultrasound or CT imaging of patients with persistent trophoblast suggests cystic pelvic structures, surgical evaluation for extratubal trophoblastic cysts should be considered before excisional procedures.

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