Case series

Gestational trophoblastic neoplasia presenting as an interstitial ectopic pregnancy

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ABSTRACT

Gestational trophoblastic disease (GTD) is a group of benign and malignant tumors that develop from placental tissue and includes hydatidiform moles and gestational trophoblastic neoplasia (GTN). Invasive molar disease and choriocarcinoma are rare forms of GTN and can arise from any pregnancy event. An interstitial ectopic pregnancy occurs with implantation within the intramural portion of the fallopian tube covered by myometrium. We present two cases of an invasive mole with pathology consistent with choriocarcinoma in situ arising from an interstitial ectopic pregnancies. We review management strategies including a minimally invasive surgical approach. Additionally we present a review of the literature of gestational trophoblastic disease associated with interstitial ectopic pregnancies.

1. Introduction

Gestational trophoblastic disease (GTD) is a group of benign and malignant tumors that develop from placental tissue and includes hydatidiform moles and gestational trophoblastic neoplasia (GTN). Invasive molar disease and choriocarcinoma are rare forms of GTN and can arise from any pregnancy event, including term or and preterm pregnancies, spontaneous abortions, ectopic pregnancies or molar pregnancies Lurain, 2010.

Ectopic pregnancy describes all pregnancies that occur outside the uterine cavity, and are a frequently encountered diagnosis in the field of obstetrics and gynecology. An interstitial ectopic pregnancy occurs with implantation within the intramural portion of the fallopian tube covered by myometrium and is a rare event (Malinowski and Bates, 2006).

We present two cases of an invasive mole with pathology consistent with choriocarcinoma in situ arising from an interstitial ectopic pregnancies. We also present a review of the literature of gestational trophoblastic disease associated with interstitial ectopic pregnancies.

2. Case presentation

2.1. Case 1

The patient is a 31-year-old Asian G4P2012 female with an uncertain last menstrual period who presented to the Emergency Department with vaginal bleeding. She was otherwise healthy with no medical problems. Her obstetrical history was notable for two prior cesarean sections and a spontaneous abortion. On presentation, she was hemodynamically stable. Pelvic exam was notable for an 8-week-sized uterus with mild right adnexal fullness and associated mild tenderness as well as a small amount of vaginal bleeding. Laboratory evaluation revealed anemia with hemoglobin of 9.1 gm/dL, and a beta human chorionic gonadotropin (b-hCG) of 103,724 mIU/mL. Transvaginal ultrasound demonstrated a 31 × 43 × 31 mm mass arising from the right cornua containing echogenic internal debris and significant peripheral vascular flow, concerning for an ectopic pregnancy (Fig. 1).

The patient underwent laparoscopic right cornual wedge resection and right salpingectomy. Intraoperative findings were notable for a mildly enlarged uterus with a right cornual mass consistent with a right interstitial ectopic pregnancy (Fig. 2). Intraabdominal survey was otherwise unremarkable. Histologic examination demonstrated exuberant triphasic atypical trophoblast proliferation consistent with
gestational trophoblastic neoplasia as well as occasional molar villi seen deep within the myometrium, concerning for an invasive mole (Fig. 3).

The patient was referred to Gynecologic Oncology for further management. Chest x-ray was negative for evidence of metastatic disease. Initially, the patient’s b-hCG decreased to 2,489 mIU/mL, and the decision was made to continue observation. She was initiated on combined oral contraceptive pills for contraception. The patient’s b-hCG nadired at 886 mIU/mL and subsequently exhibited a > 20% increase in three values over two weeks to 2,274 mIU/mL. Thus, the patient met criteria for stage I low risk GTN with a WHO score of 5. Methotrexate 0.4 mg/kg IM for five days every 14 days was initiated. The first cycle was complicated by severe mucositis for which day five was held and subsequent cycles were reduced to three days. B-hCG values normalized during cycle two, and she received three additional cycles of methotrexate without complication. At the time of most recent follow-up three months following therapy completion, the patient had no evidence of disease and a negative b-hCG.

2.2. Case 2

This is a 27 year old Caucasian G2P2012 female who presented to the Emergency Department with acute onset lower abdominal pain, emesis and weakness. She was otherwise healthy with no medical problems, and past surgical history notable for laparoscopic right salpingo-oophorectomy for a tubovarian abscess. The patient was hemodynamically stable, and physical exam was notable for a tender and slightly distended abdomen. Laboratory evaluation revealed hemoglobin on 14.2 gm/dL,
Table 1
Literature review of gestational trophoblastic disease associated with interstitial ectopic pregnancy.

| Author                     | Patient Characteristics | b-hCG at presentation | Imaging                                                                 | Histology                                      | Treatment                          | Outcomes                      |
|----------------------------|--------------------------|------------------------|--------------------------------------------------------------------------|------------------------------------------------|-----------------------------------|--------------------------------|
| Venturini et al. (2001)    | 31 yo with vaginal bleeding, abdominal pain | 13,380 | US: no IUP, subserous 2 cm echogenic mass on left fundus                  | Choriocarcinoma                               | Dx lsc and D&C                    | NED at 2 years                |
|                            | History of abdominal myomectomy |           | HSG: intramural echogenic mass separate from uterine cavity              |                                                 | Two days later laparotomy and cornual wedge resection |                                 |
| Han and Kaye (2018)        | 38 yo G5P2212 with vaginal bleeding, abdominal pain | 79,465 | US: no IUP, 5.6 cm left cornual mass with peripheral hypervascularity and subserosal hemorrhage extending to left lateral fundus | Cornual ectopic pregnancy                      | MTX × 1                           | n/a                           |
|                            | History of ectopic s/p D&C, MTX × 1 |           | Subsequent vaginal wall biopsy with metastatic choriocarcinoma            |                                                | Dx lsc, TAH/BS                    |                               |
| Rotas et al. (2007)        | 35 yo G4P2052 with ectopic pregnancy s/p failed treatment | 1,900 | US: no IUP, thin endometrium                                             | Choriocarcinoma                                | MTX × 3                           | NED at 4 months               |
|                            | History of prior ectopic x 2 s/p RS |           | MRI diffusely heterogeneous mildly enlarged uterus with fibroids          |                                                | D&C                              |                               |
| Meddeb et al. (2014)       | 46 yo G4P3 with vaginal bleeding, abdominal pain | 6,320  | US: no IUP, 3 cm intramural echogenic mass at left fundus                | Choriocarcinoma                                | Dx lsc, left cornual wedge resection | NED at 2 years                |
|                            |                          |           |                                                                          |                                                | Represented with acute hemorrhage: underwent emergent hysterectomy |                                 |
| Khifi et al. (2016)        | 40 yo G1 with abdominal pain | 27,624 | US: no IUP, 4 × 4 cm heterogenous vascular left uterine mass             | Invasive mole                                  | MTX × 3 cycles                    | NED at 48 weeks               |
|                            |                          |           |                                                                          |                                                | Dx lsc, mini-laparotomy, LS, left cornual wedge resection |                                 |
| Siegal, et al³             | 27 yo G6P2 with abdominal pain, nausea, vomiting | n/a   | n/a                                                                     | Hydatidiform mole                               | MTX × 8 cycles                    | Post-op course complicated by rapidly enlarging pelvic mass, sepsis and internal hemorrhage; DOD | NED at 2 years                |
| Chau et al. (2019)         | 25 yo                    | 2,989  | US: 3.4x3.4x3.8 cm echogenic hypervascular mass in right fundus          | Choriocarcinoma, recurrent                      | Mini-laparotomy with right cornual wedge resection, salpingectomy |                                 |
| Oskovi Kaplan et al. (2018)| 24 yo with abdominal pain, vaginal bleeding | 75,144 | US: possible 3 mm gestational sac, 4.1x3.7 cm left adnexal mass          | Invasive mole                                  | EMACO × 4 cycles                   | NED                           |
| Chen et al. (2017)         | 32 yo G2P0 with abdominal pain | 58,789 | US, MRI: solitary left cornual heterogenous mass                         | Gestational trophoblastic neoplasia            | Laparoscopic resection of rudimentary horn |                               |
|                            | History of molar pregnancy s/p D&C 3 months prior |           |                                                                          | Left cornuostomy                               | MTX × 2                           | NED at 16 months               |
| Hwang et al. (2010)        | 41 G9 with vaginal bleeding | 57,738 | US: Hematometra, muticystic echogenic lateral uterine mass with Doppler flow | Partial mole                                   | Left cornuostomy                   | n/a                           |
|                            | History of TAB s/p D&C 2 months prior |           |                                                                          |                                                | Adjuvant MTX                      |                               |
| Chauhan et al. (2006)      | 41 yo P3 with AUB, abdominal pain | 2,905  | US: Hyperechoic mass in posterolateral uterine wall                      | Molar pregnancy                                | TAH for suspected fibroid and AUB | NED at 3 weeks                |
|                            |                          | 97,000 |                                                                          |                                                | n/a                              |                               |

(continued on next page)
and h-bCG of 23,397 mIU/mL. Transvaginal ultrasound demonstrated a large amount of free fluid in right adnexa and anterior and posterior cul-de-sacs extending to the abdomen without evidence of intrauterine pregnancy.

The patient initially underwent diagnostic laparoscopy which noted hemoperitoneum and a deeply embedded right interstitial pregnancy. The decision was made to proceed with laparotomy and open cornual wedge resection. Histologic examination revealed villous trophoblasts with large, pleomorphic nuclei and consistent with choriocarcinoma.

Initially, the patient’s h-bCG values decreased but subsequently demonstrated a > 20% increase in three values over two weeks. She was referred to Gynecologic Oncology. Computed tomography of the chest, abdomen and pelvis revealed pulmonary nodules consistent with metastases but no evidence of intraabdominal disease. Brain MRI was performed for persistent headaches and did not reveal evidence of metastasis. Patient met criteria for stage III GTN with WHO score of 4. Methotrexate 0.4 mg/kg IM for five days every 14 days was initiated, and h-bCG normalized after cycle two. The patient received a total of five cycles, and she had no evidence of disease with a negative h-bCG at the time of most recent follow-up 18 months after therapy completion.

3. Discussion

GTD is a group of benign and malignant tumors that develop from placental tissue and includes hydatidiform moles and GTN. GTN is a rare diagnosis, carries metastatic potential, and includes invasive moles, placental tissue and includes hydatidiform moles and GTN. GTN is a rare disease that presents with symptoms similar to those of normal pregnancy, such as nausea, vomiting, and amenorrhea. The diagnosis of GTN is often delayed due to the similarity of symptoms to normal pregnancy. The diagnosis is confirmed by elevated hCG levels in the absence of an intrauterine pregnancy. The treatment of GTN is typically surgical, with the option of chemotherapy for those with metastatic disease. The outcomes of patients with GTN are generally favorable with early diagnosis and treatment.

Table 1 (continued)

| Author          | Patient Characteristics | b-hCG at presentation | Imaging                              | Histology          | Treatment                                      | Outcomes        |
|-----------------|-------------------------|-----------------------|--------------------------------------|--------------------|-----------------------------------------------|-----------------|
| Zite et al. (2002) | Female with nausea, vomiting, abdominal pain | US: Intrauterine molar pregnancy near fundus | Dx lsc, laparotomy, cornual wedge resection, D&C | n/a                |                                              |                 |
| Fang et al. (2014) | 28 yo G2P1 with amenorrhea × 3 months | 2,764 | 6 cm right adnexal mass | ETT                | Dx lsc, laparotomy, right cornual wedge resection | n/a             |

Abbreviations: yo, year old; n/a: not available; s/p: status post; US: ultrasound; IUP: intrauterine pregnancy; dx lsc: diagnostic laparoscopy; TAH: total abdominal hysterectomy; RS/LS: right/left salpingectomy; NED: no evidence of disease; MTX: methotrexate; DOD: dead of disease; EMACO: etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine; TAB: therapeutic abortion; AUB: abnormal uterine bleeding; ETT: epithelioid trophoblastic tumor.

In summary, we present two cases of an GTN arising from an interstitial ectopic pregnancy. Our first case represents unique pathology, demonstrating invasive mole with elements of early choriocarcinoma. Both cases support existing evidence that GTN arising from interstitial pregnancies often have favorable prognoses with appropriate therapy.

Author contribution

Dr. Coralee Toal is the corresponding author of the research letter, and the contributing authors are Dr. Alison Garrett, Dr. Kostadinov and Dr. Michelle Boisen. All authors have made a significant contribution to this report, and all authors have read and approved the final version submitted.

Informed consent

Informed consent was obtained from all individual participants for who identifying information is included in this article.

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.

References

Lurain, J.R., 2010. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am. J. Obstet. Gynecol. 203 (6), 531–539.

Malinowski, A., Bates, S.K., 2006. Semantics and pitfalls in the diagnosis of cornual/interstitial pregnancy. Fertil. Steril. 86 (6), 1764.e11–1764.e14.

Siegel, H.A., Rudolph, L., 1949. Interstitial hydatid mole with spontaneous perforation and rupture of the uterine cornu. West J Surg Obstet. Gynecol. 57 (10), 477–480.

Venturini, F.L., Golder, F., Ferraiolo, A., Valenzano, M., Fulcheri, E., 2001. Gestational choriocarcinoma arising in a cornual pregnancy. European J. Obstet. Gynecol. Reprod. Biol. 96 (1), 116–118.

Han, V., Kaye, S., 2018. A Rare Case of Gestational Choriocarcinoma Presenting as Cornual Ectopic Pregnancy. Journal of Obstetrics and Gynaecol. Canada 40 (3), 351–355.

Rotas, M., Khulpatena, N., Binder, D., 2007. Gestational choriocarcinoma arising from a cornual ectopic pregnancy: a case report and review of the literature. Arch. Gynecol. Obstet. 276 (6), 645–647.
Meddeb, S., Rhim, M.S., Zarrouk, W., Bibi, M., Yacoubi, M.T., Khairi, H., 2014. Unusual gestational choriocarcinoma arising in an interstitial pregnancy. Int. J. Surgery Case Rep. 5 (11), 787–788.

Khelifi, A., Mkhinini, I., Yacoubi, M.T., Khairi, H., 2016. A cornual invasive hydatiform mole: A literature review. Medical Journal Armed Forces India 72, S94–S97.

Chau, D.B., Beavis, A.L., Ronnett, B.M., et al., 2019. Genetically related choriocarcinoma developing 5 yr after a complete hydatidiform mole and simulating a cornual ectopic pregnancy. Int. J. Gynecol. Pathol.

Oskovi Kaplan, Z.A., Şirvan, A.L., Topçu, H.O., 2018. Invasive molar pregnancy in rudimentary uterine horn. J. Exp. Ther. Oncol. 12 (2), 207–210.

Chen, P.-L., Jhuang, J.-Y., Lin, H.-H., Hsiao, S.-M., 2017. Successful treatment of gestational trophoblastic neoplasia in the uterine cornus with laparoscopic cornostomy and postoperative methotrexate injection. Taiwanese J. Obst. Gynecol. 56 (2), 261–263.

Hwang, J.H., Lee, J.K., Lee, N.W., Lee, K.W., 2010. Molar Ectopic Pregnancy in the Uterine Cornus. J. Minimally Invasive Gynecol. 17 (2), 239–241.

Chauhan, M.B., Chaudhary, P., Dahiya, P., Sangwan, K., Sen, J., 2006. Molar cornual ectopic pregnancy. Acta Obstet Gynecol Scand 85 (5), 625–626.

Zit, N.B., Lipscomb, G.H., Merrill, K., 2002. Molar Cornual Ectopic Pregnancy. Obstet. Gynecol. 99 (5, Part 2), 891–892.

Fang, F.-Y., Lai, C.-R., Yang, M.-J., Huang, B.-S., Chen, C.-Y., Li, Y.-T., Yen, M.-S., Peter Wang, P.-H., 2014. Diagnostic challenges in cornual epithelioid trophoblastic tumor. Taiwanese J. Obst. Gynecol 53 (2), 235–238.