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Case Report

Placental site trophoblastic tumor as a rare cause of irregular bleeding in a female of reproductive age

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Summary

Objective: A case of placental site trophoblastic tumor (PSTT) that presented with abnormal vaginal bleeding is reported because of its rarity. Case report: The patient presented with 8 weeks of amenorrhea, vaginal bleeding and a persistently low titer of β-human chorionic gonadotropin (βhCG). A large circumscribed mass in the uterus was revealed by ultrasound and magnetic resonance imaging. Hysteroscopic biopsy confirmed the presence of PSTT and a hysterectomy was subsequently performed. The patient is well after 6 months of follow up and her βhCG titer normalized. Conclusion: Rare forms of trophoblastic disease should be considered in the differential diagnosis of persistent bleeding and low titers of βhCG.

Key words: Placental site trophoblastic tumor; Gestational trophoblastic disease; Trophoblastic tumor; Intermediate trophoblasts.

Introduction

Placental site trophoblastic tumor (PSTT) is a rare form of gestational trophoblastic disease (GTD), with an incidence of approximately 1-5 per 100,000 pregnancies and representing just 0.2% of all GTD cases [1]. As less than 500 cases have been reported worldwide, the optimal management remains controversial. PSTT can occur during or after a normal pregnancy, a miscarriage, an abortion, or a molar pregnancy. Due to its relative resistance to chemotherapy, PSTT poses considerable therapeutic challenges. The most frequently reported symptoms and signs are abnormal bleeding, amenorrhea and mildly elevated serum β-human chorionic gonadotropin (β-hCG) levels ($<$ 1000 mIU/mL in 79% of cases) [2]. The main treatment for early stage disease is hysterectomy. The ovaries may be preserved in premenopausal patients, however metastatic or recurrent disease often requires chemotherapy and/or surgery. The most common sites of metastases are the lung, vagina and central nervous system [2, 3].

We describe here a patient with localized PSTT who presented with abnormal vaginal bleeding and was managed with hysterectomy. The subject provided informed consent.

Case presentation

A 42 year old Caucasian woman, P2+0 with her last child born 6 years earlier, presented with irregular bleeding after 8 weeks of amenorrhea. She was not under any medication and both her past history and family history was unremarkable. Her general condition was good and systematic examination was normal. Pelvic examination revealed a bulky uterus with normal cervix and adnexae. A urine pregnancy test was weakly positive and her β-hCG levels, measured serially, were between 13 and 20 mIU/ml. Pelvic ultrasound revealed a solid mass sized 46 mm x 43 mm with echogenity similar to the myometrium and arising from the posterior uterine wall and protruding into the endometrial cavity (Figure 1). Power Doppler revealed moderate vascularity in the center of the mass (Figure 2). The ovaries were of normal size and texture. Magnetic resonance imaging of the lower abdomen revealed similar findings with no other lesions visualized in the pelvis (Figure 3). A diagnostic hysteroscopy and biopsy of the lesion was undertaken the following week. The uterine cavity was filled with a yellowish mass with moderate vascularity arising from the fundus of the uterus. The rest of the endometrial cavity and tubal ostiae were normal. Several biopsies were taken from the tumor and subsequent histology showed the tumor was a PSTT. The patient was assessed for malignant trophoblastic disease with computed tomography imaging of the chest, abdomen and cranium. The β-hCG values remained around 20 mIU/ml during the entire course of the disease. Following thorough discussion, the patient stated she did not want to have more children and therefore a hysterectomy was decided and performed soon afterwards. The postoperative course was uneventful. Histopathology of the uterus confirmed the findings. The patient was well at postoperative follow-up and her βhCG titers remain below 5 mIU/ml.

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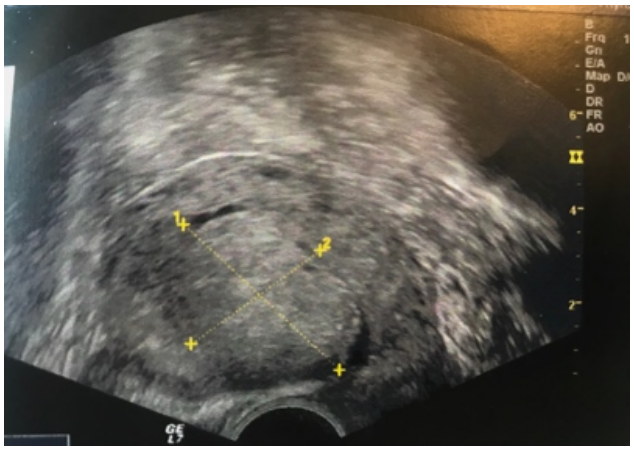

Figure 1. — Transvaginal ultrasound of the uterus.

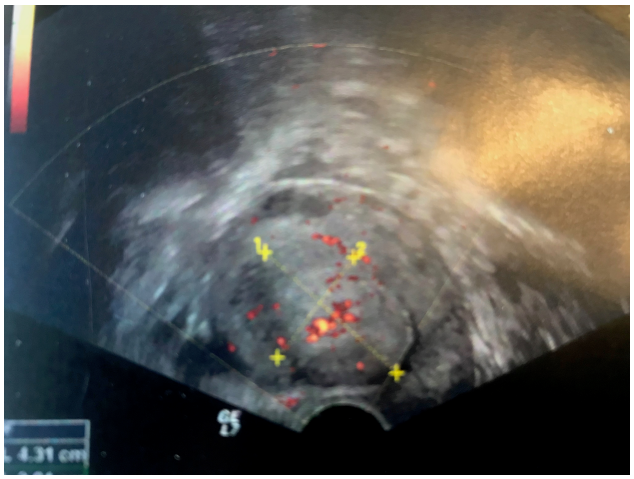

Figure 2. — Power Doppler of the uterus.

Discussion

Kurman and Scully [4] were the first to describe PSTT in 1976 under the term of trophoblastic pseudo-tumor. PSTT originates from intermediate trophoblasts and the neoplastic cells are often arranged as sheets of polyhedral, round, or occasionally spindle-shaped cells which infiltrate both the myometrium and blood vessels. In 1981, Twiggs reported a patient who died from the tumor and in another report that year Scully highlighted its malignant potential [5, 6]. Finally, in 1983 the World Health Organization acknowledged its neoplastic nature and adopted the terminology PSTT. Immunohistochemistry of the tumor reveals many lactotropes and a few gonadotropin-producing cells that are responsible for the elevated levels of βhCG.

The diagnosis of most cases of PSTT is based on symptoms, imaging and mildly elevated serum hCG levels, followed by histological confirmation [7]. The most common sites of metastases are the lung, vagina and central nervous system [2, 3]. Optimal treatment strategies for PSTT and knowledge regarding prognostic factors are limited due to the rarity of this disease. Moreover, there is still much debate on whether the International Federation of Gynecology and Obstetrics prognosis score system for gestational trophoblastic neoplasia (GTN) is suitable for PSTT. About 10% of PSTT cases present with metastases, while a further 10% of patients develop metastases during follow up. According to some authors, a high mitotic index appears to be an adverse prognostic indicator for recurrence [8]. Although there is evidence that PSTT tends to spread to lymph nodes, the role of lymphadenectomy has yet to be established [4]. Additionally, the interval from the antecedent pregnancy to the initiation of treatment has been reported to correlate with recurrence of the disease. An interval of > 2 years seems to be an aggravating prognostic factor [9]. Zhao *et al*. conducted a multi-center study of 108 PSTT cases and concluded that the key prognostic factor is stage [10].

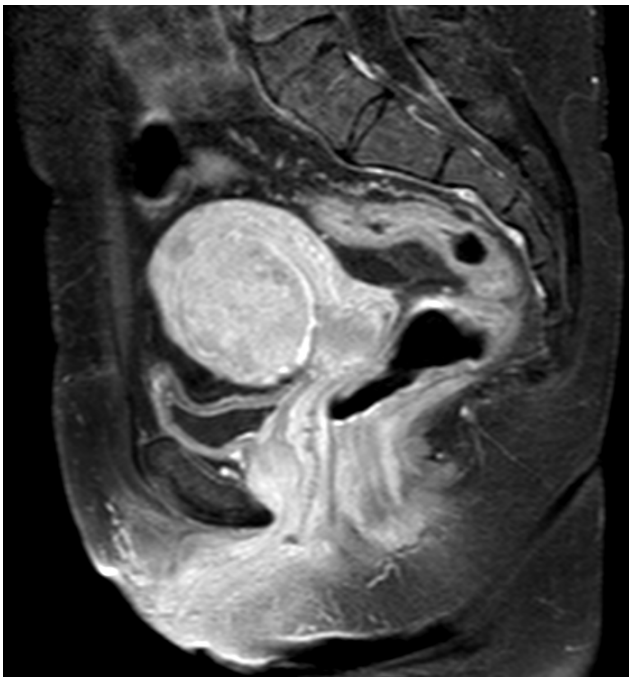

Figure 3. — Abdominal magnetic resonance imaging.

Surgery without chemotherapy is recommended as the first line treatment for patients with stage I disease that are low-risk [4, 10]. Conservative surgery has been attempted in some cases for patients wishing to retain fertility. There have been some reports of cases that resolved spontaneously after curettage or excision of all removable lesions, or after chemotherapy without hysterectomy and very careful follow-up monitoring [11, 12]. Hysterectomy combined with chemotherapy is commonly recommended for patients with stage II–IV disease [13]. There is still much debate over which combination of chemotherapy is optimal. The etoposide, cisplatin/etoposide, methotrexate and actinomycin-D (EP/EMA) regimen and the EMA/cyclophosphamide plus vincristine (CO) regimen are commonly used [13]. Overall, the mortality rate for patients with advanced stages of

PSTT remains high at 25% [10]. The 10-year survival rate for stage I patients who undergo hysterectomy is almost 90%, whereas the corresponding survival rate for stage II-IV patients after hysterectomy and chemotherapy is approximately 50% [5].

In conclusion, rare forms of trophoblastic disease should be considered in the differential diagnosis of persistent bleeding and low, non-falling, titers of βhCG.

Ethics Approval and Consent to Participate

The subject gave her informed consent for inclusion before she participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Medical School of the Aristotle University of Thessaloniki (approval number 5863).

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Conflict of interest

The authors declare no conflict of interest.

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