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Uterine rupture secondary to undiagnosed placental site trophoblastic tumor: case report

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ABSTRACT

Placental site trophoblastic tumor is a rare and malignant form of gestational trophoblastic disease. Its incidence rate is 1/50.000-100.000 pregnancies and accounts for less than 3% of all cases of gestational trophoblastic disease. In addition to its infrequency, the tumor lacks pathognomonic sonographic features, delaying diagnosis until immunohistochemical staining of uterine samples. Early diagnosis is key to avoid metastatic disease. We report a case of an undiagnosed placental site trophoblastic tumor, which caused uterine rupture and hemorrhagic shock.

Keywords: immunohistochemistry, placental site trophoblastic tumor, transvaginal sonography.

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INTRODUCTION

Placental site trophoblastic tumor (PSTT) is a malignant and rare form of gestational trophoblastic disease (GTD).[1-4] PSTT represents 0,2-3% of all cases of GTD and is estimated to affect 1/50.000-100.000 pregnancies.[5]

Only 725 cases of PSTT have been described in the literature.[4] Typical PSTT presentation consists of amenorrhea or abnormal vaginal bleeding, low serum human chorionic gonadotropin (hCG) and unspecific features on transvaginal sonography (TVS).[5,6] PSTT has a lethality of 16-21% and 10-year overall survival of 73%. [2] This study is a case report of PSTT.

METHODS

This case reports the rare case of PSTT. The patient in the study (case report) signed a consent term. This case report was approved by the ethics and research committee (number: 45476321.4.0000.5404).

CASE REPORT

A 20-year-old woman with positive pregnancy test and 17 weeks of amenorrhea. She had a history of two previous abortions She performed a TVS which identified an enlarged uterus (169.88 cm³) with a nodule infiltrating the posterior wall. Color doppler assessment demonstrated the structure to be highly vascularized with low resistance to flow. No fetal heartbeat was present and hCG serum was 234 IU/l. She was diagnosed with a miscarriage and underwent a surgical hysteroscopy that showed an irregular, well-vascularized polypoid formation with areas of necrosis of approximately 3 cm in the posterior wall of the uterus suggestive of ovular debris that were removed in this procedure.

Fifty days later, the woman was brought to the emergency room in hemorrhagic shock, with a blood pressure of 51X40mmHg and heart rate of 115ppm. Upon admission, she was in poor general condition, agitated, cyanotic and with persistent lower abdominal pain. Abdominal examination findings included tenderness and diffuse guarding to palpation. Speculum exam evinced yellow discharge originating from the cervix. Laboratory results were hemoglobin 7g/dl and hCG 390.6 IU/l. Bedside ultrasonography was positive for free fluid in Morison's pouch. Exploratory laparotomy located the source of the bleed: posterior uterine wall rupture extending from the left horn to the isthmus. Total hysterectomy and bilateral salpingectomy were performed. She received a transfusion of two bags of blood cells during the procedure and left the operating room with a hemoglobin of 9.6 mg/dl. During hospitalization, the anatomopathological report of the material removed in the hysteroscopy was ready and confirmed that it was PSTT.

Macroscopic analysis of surgical samples showed a yellow fleshy tumor which had protruded the endometrial cavity and infiltrated the myometrium, leading to uterine rupture and detaching the left fallopian tube from the uterine corpus. Microscopic studies showed polygonal monomorphic cells with eosinophilic cytoplasm and irregular nuclei and absence of chorionic villi. Diagnosis was confirmed by immunohistochemical studies, which demonstrated hCG reactivity confined to a small proportion of multinucleated cells and a Ki-67 labelling index of 20% (Figure 1).

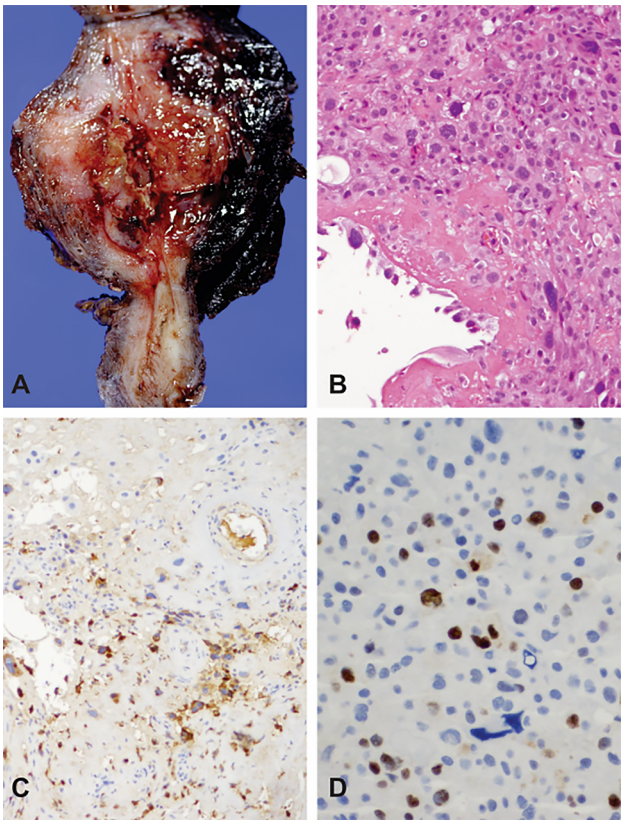

Figure 1. Macroscopy shows the serous presenting a dissecting hematoma in the fundic region on the left, extending to the isthmus. A soft white area measuring 4.5 x 3.5 cm is observed, filling the endometrial cavity, which is predominantly located in the fundic region on the left, infiltrating more than half the thickness of the myometrium (A). Immunohistological profile: hematoxylin and eosin stained uterine samples showing malignant trophoblastic cells infiltrating the decidua (B), positive immunostaining for Ki-67 in 20% of the nuclei (C) and weak staining for hCG (D)

The patient was discharged 5 days later and serum hCG dropped below detectable levels within 3 months. She had no metastases on computed tomography of the cranium, abdomen and chest and was staged as a stage I. She is currently asymptomatic and has presented negative serum hCG for 12 consecutive months.

DISCUSSION

In this case, due to the delay in the anatomopathological result of the material removed during hysteroscopy, the few symptoms and the low levels of hCG, the patient progresses to maternal near miss. The woman at the case was only duly diagnosed upon uterine rupture. The clinical course of PSTT differs from that of other GTDs. Most cases of traphoblastic neoplasia occur after a hydatiform mole, a small percentage after a term pregnancy, and a smaller percentage after an abortion or an ectopic pregnancy. In our case, the PSTT appeared after an abortion. The tumor has low hCG levels and growth rates.[1,3]

As a result, women are often oligosymptomatic, whereas women with hydatiform mole (HM) present elevated serum hCG and symptoms proportional to the increased hormonal dosage.[5]

Symptomatology is usually poor. Abnormal vaginal bleeding and amenorrhea are the most common complaints.[1] Women may present increased uterine volume, theca-lutein cysts and hemoptysis; however, these findings have a higher sensitivity in identifying HM than PSTT.[3] Cough and headache may point to metastases, as tumor cells target lungs, the nervous central system, lymph nodes and genital structures.[4] Amenorrhea and an enlarged uterus were the only clinical features noted in this case.

In this case, the hCG serum levels were at 390.6 IU/l, whereas values >100.000 IU/l can occur in HM.[1,3-5] Since PSTT lacks syncytiotrophoblast, it secretes modest amounts of gonadotropin regardless of the stage of the disease. Thus, hCG titers have no prognostic value in women with PSTT.[3,6,7]

The patient underwent a single TVS that showed a nodule on the posterior wall without infiltrating the myometrium and as she had low levels of hCG, the suspicion was of ovular debris. Thus, we emphasize that the ultrasound did not show the invasion of the tumor to the myometrium and its condition went unnoticed. TVS has limited sensitivity in detecting PSTT.[8,9] Zhout et al propose a sonographic classification of PSTT as Type I, II or III.[10] Type I is defined by a solid heterogeneous mass with minimal to moderate blood supply protruding the uterine cavity. Type II refers to a solid heterogeneous mass with minimal to moderate blood supply infiltrating the myometrium. Lacunar and cystic lesions and prominent vasculature point to Type III.[10] This case fits types I and II since her tumor simultaneously protruded the endometrial cavity and infiltrated the myometrium.

Microscopically, the PSTT, there is a diffuse monomorphic infiltrate of mononuclear trophoblastic cells arranged as cords and sheets infiltrating between myometrial bundles. The tumour cells have irregular hyperchromatic nuclei and dense eosinophilic to amphophilic cytoplasm. Chorionic villi are generally absent. In contrast to PSTT, the cells of epithelioid trophoblastic tumor (ETT) are smaller and display less nuclear pleomorphism. ETT arises from the chorionic-type intermediate trophoblast, islands of relatively uniform intermediate trophoblastic cells with moderate amount of eosinophilic to clear cytoplasm and round nuclei are surrounded by extensive necrosis and associated with a hyaline-like matrix.The choriocarcinoma shows absence of chorionic villi and presence of abnormal intermediate trophoblast and cytotrophoblast, rimmed with syncyotrophoblasts with areas of necrosis, and hemorrhage.[11]

In trophoblastic neoplasia, hCG correlates well with tumour bulk and persistence of disease e hCG evaluation is therefore integral to treatment protocols and management strategies. Unfortunately, hCG although it may be helpful in diagnosis, is not an accurate marker of PSTT disease burden. As with immunohistochemical staining, this is a reflection of the intermediate trophoblast cell population from which they originate e this cell type produces little hCG but large quantities of hPL. This ability of the intermediate trophoblast cell population to produce hPL does not, however, mean that hPL is a useful tumour marker for PSTT. [12]

Diagnosis is confirmed by immunohistochemical profiling. The main findings endorsing PSTT are strong positivity for human placental lactogen (hPL) and focal expression of hCG, suggest that PSTT is a tumor of the intermediate trophoblast. Ki-67 labelling index ranges from 8 to 20%.[2,13-15] Immunohistochemical staining has detected positive hCG in a small proportion of cells, which reflects the lack of syncytiotrophoblasts in the PSTT. Positivity for hPL could not be verified due to laboratory restrictions. KI-67 is an inumohistochemical marker used to differentiate trophoblastic tumors according to their mitotic activity, that is, it is more expressed in tumors with greater mitotic activity. It is negative in the exaggerated placental site, infrequent in PSTT and very frequent in choriocarcinoma.[16] In our case, Ki-67 staining was positive in 20% of the cells.

PSTT is ranked according to the Federation International of Gynecology and Obstetrics staging system. Stage I refers to disease confined to the uterus and Stage II, to the involvement of genital structures. Stage III denotes pulmonary metastases and Stage IV, other distant metastases.[3] In the time of diagnosis, 30% of women have metastatic PSTT.[3,5]

Treatment is guided by the interval from the last pregnancy. In stage I and an antecedent pregnancy <48 months, hysterectomy and surveillance are advised. In case of an interval higher than 48 months, adjuvant platinum containing chemotherapy can be initiated after hysterectomy according to the negative effect of this long interval on recurrence free survival. In stage II and III with an interval from the antecedent pregnancy <48 months, hysterectomy followed by platinum-based combination chemotherapy (e.g. EP/EMA) is suggested. Resection of any visible residual disease post chemotherapy is advised. In case of an interval higher than 48 months or in stage IV regardless of interval, besides this treatment, also high dose chemotherapy or pembrolizumab can be considered.[12]

PSTT in stage I has a favorable prognosis, with an 85% cure rate and a 10-year survival rate of 90%. The prognosis of stage II-IV is less favorable because the response of PSST to chemotherapy is incomplete.[3]

PSTT is a rare and difficult to diagnose condition. This is relevant since early diagnosis is key to positive treatment outcomes. Therefore, PSTT must be considered a diagnostic hypothesis whenever a woman presents intrauterine lesions and low hCG serum levels.

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