

# A case of placental site trophoblastic tumor and a retrospective analysis

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## Summary

Placental site trophoblastic tumor (PSTT) refers to intermediates derived from intermediate trophoblasts, a particular type of trophoblastic tumor from the placenta site (gestational trophoblastic disease, GTD), whose pathological morphology and biological behaviors and other trophoblastic tumors are very different. Here, the authors report one case of PSTT, which is from the Anhui Provincial Hospital Affiliated to Anhui Medical University. A 39-year-old woman presented with abnormal uterine bleeding for four months after she had an abortion. She underwent curettage surgery in a local hospital, revealing a pathology of choriocarcinoma. Methotrexate (MTX) chemotherapy was ineffective, and blood hCG continued to rise, while in this hospital ultrasonographic examination the bottom of the uterus exhibited a uneven echo, with ill-defined and unclear intrauterine boundaries and a “honeycomb” structure in the serosa. After hysterectomy, pathology revealed a bottom PSTT with invasion of the muscle which was greater than 50%. Microscopically, the tumor consists of sheets of intermediate trophoblastic cells invading the myometrium. Immunohistochemistry showed positive results for PCK, inhibin, hPL, and  $\beta$ -HCG (spotty +). A course of combined EMA-CO chemotherapy was performed ten days after the surgery, and the patient was then discharged after reviewing the normal indicators. The patient was followed for 36 months without recurrence.

*Key words:* Placental site trophoblastic tumor; Hysterectomy; Pathology; Immunohistochemistry; Chemotherapy.

## Introduction

Placental site trophoblastic tumor (PSTT) is rarely seen in clinical symptoms. Patients are treated due to amenorrhea, abortion, hydatidiform mole, or full term pregnancy after irregular bleeding of the vagina. Kurman *et al.* [1], firstly identified a “placental site pseudotumor” in 1976 and described the disease, which was then thought to nourish the cells overexpressing erosion characteristics, although its potential for malignancy was not yet recognized. In 1981, Scully *et al.* [2] firstly proposed that this anomaly be named PSTT, therefore suggesting its malignant potential. In the vast majority of cases, the prognosis is favorable, while metastasis will occur in roughly 15-35 percent of these cases, resulting in a poor prognosis. The etiology, epidemiology, and risk factors for this cancer are not very clear. Schmid *et al.* [3] reported that PSTT accounted for only 0.2% of the trophoblastic tumor and 25% of the mortality rate. So far, the global literature has reported about 300 cases of PSTT [4]. A total of less than 60 cases have been reported in China.

## Case Report

AA 39-year-old woman, gravida 4 para 2, was admitted to the hospital in November, 2014, who complained of an abnormal uterine bleeding that had lasted for four months after she got an abortion through ethacridine amniotic injection at the local hos-

pital in April, 2014. Surgical intervention went well, and her menstruation returned to normal within 40 days, while the last menstrual period occurred on August 12<sup>th</sup>, 2014, with irregular uterine bleeding; then, the symptoms of excessive bleeding and blood clots occurred on June 24<sup>th</sup>, 2014, resulting in a visit to a local hospital where the patient had her urine hCG (+) examined. The ultrasonographic examination of uterus showed intrauterine heterogeneous echo, indicating that an incomplete abortion might be considered. Therefore, curettage was performed at a local hospital without any significant pathology findings, which was followed by the dynamic monitoring of blood hCG. However, with a rise in the hCG, the patient was again admitted to another local hospital for treatment on October 23<sup>th</sup>, 2014, in which the curettage surgery was performed again, revealing a pathology of choriocarcinoma, methotrexate (MTX) chemotherapy was ineffective and blood hCG continued to rise. On November 17<sup>th</sup>, 2014, the patient sought treatment at the present hospital, whose local curettage biopsy showed as follows: intrauterine bleeding, tissue necrosis, a small amount of endometrial hyperplasia tissue, the presence of mono-nuclear trophoblast cells with cellular atypia and mitotic activities, no clear villi structures, muscular invasion, and a gestational trophoblastic tumor that had not been completely removed. Laboratory results showed a slight elevation in  $\beta$ -hCG (388 mIU/ml, normal < 1 mIU/ml), while the ultrasonographic examination of the uterus revealed a uterine section 75×68×59 mm in size with shape disorder and an uneven muscle wall distribution. The bottom of the uterus exhibited a 67×37 mm uneven echo, with ill-defined, unclear intrauterine boundaries and a “honeycomb” structure in the serosa. Color Doppler flow imaging (CDFI) showed a very rich blood signal (Figure 1). The clinical diagnosis was a gestational trophoblastic tumor to be ranked. Upon admission, the patient exhibited stable vital signs, which

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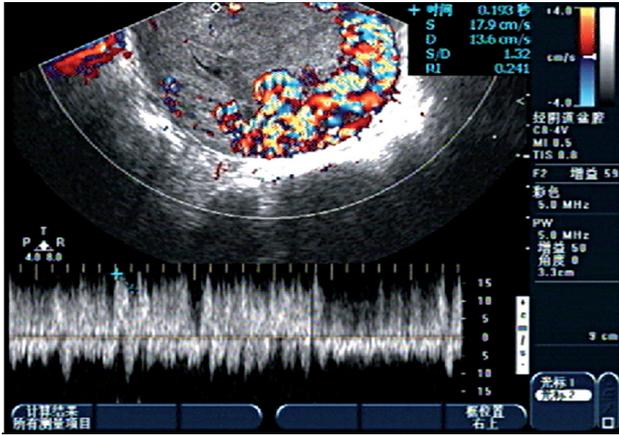


Figure 1. — CDFI showing a very rich blood signal, and a resistance index (RI) of 0.21, with a lower section film thickness of 2 mm.

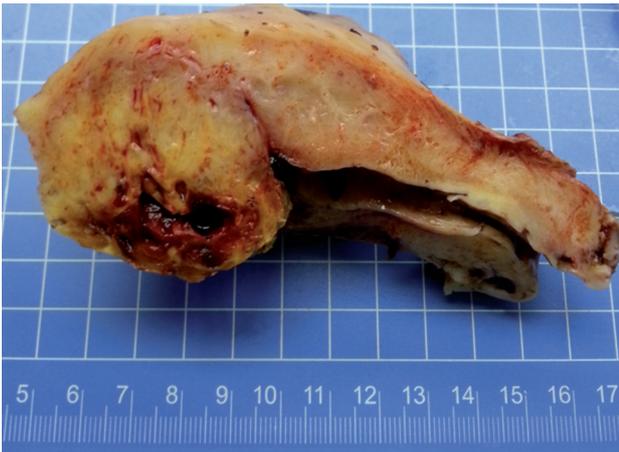


Figure 2. — A cross-sectional view of the uterus showing 40×30 mm vegetation and unclear uterine boundaries.

showed no skin jaundice and had less swollen lymph nodes. Gynecological examination revealed vaginal patency, no abnormal secretions, a smooth cervix without lifting pain, and a posterior uterus of increasing size consistent with pregnancy after 50 days, tenderness, dual attachment area, and no obvious anomalies. The admission diagnosis was a gestational trophoblastic tumor. Auxiliary examination after admission showed that tumor markers were normal. Chest CT scan found no abnormal symptoms. Urinary tract and digestive B ultrasonic examination showed no abnormal symptoms. MRI showed an increased uterine volume with a greater intrauterine signal, uneven nodules, and flaky abnormal signal, but there was no significant swelling of the pelvic lymph nodes. According to the patient's condition, upon the first consideration for gestational trophoblastic tumor, the patient and their family requested a hysterectomy. Then, laparoscopic exploratory surgery was performed, which revealed enlarged uterus, consistent with 50 days of pregnancy with soft, substantial and uniform increases. Left attachment did not have an abnormal appearance, while the right ovary had a 20×10-mm cyst and the right fallopian tube had 30×20-mm cysts. Laparoscopic hysterectomy with right

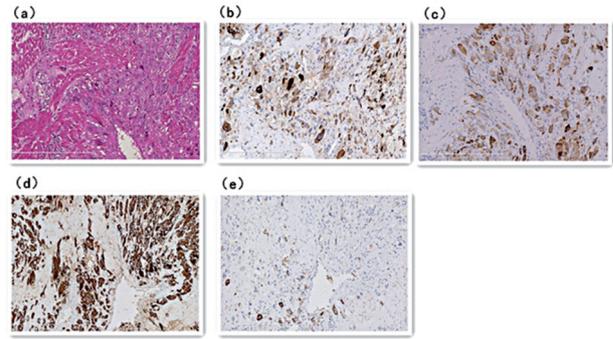


Figure 3. — Immunohistochemical stains show differences using positive HE (a), HPL (b), inhibin (c), PCK (d), and (e)  $\beta$ -hCG indices ( $\times 100$ ).

fallopian tube surgery and right ovary cyst removal was performed. A cross-sectional view of the uterus showed 40×30-mm vegetation and the unclear uterine boundaries (Figure 2). Pathology revealed a bottom PSTT with tumor invasion of the muscle which was greater than 50%. Microscopically, the tumor consists of sheets of intermediate trophoblastic cells invading the myometrium. Immunohistochemistry showed positive results for PCK, inhibin, hPL, and  $\beta$ -hCG (spotty +) (Figure 3). Blood  $\beta$ -hCG was 39.3 mIU/ml for seven days after the surgery. A course of combined EMA-CO chemotherapy was performed for ten days after surgery, and the patient was then discharged after reviewing the normal indicators.

### Discussion

PSTT is more common in women at the reproductive age, but it occurs occasionally in women after menopause. At the median age of 32-years-old, the incubation period of 3~15 months, can be secondary to the full-term production, abortion, and hydatidiform mole. However, the latter is relatively rare, which is occasionally combined live birth pregnancy [5].

The distance from the previous pregnancy termination of the length of time, the shortest in the cesarean section, was found in the PSTT. A previous termination of 33 years after pregnancy and menopause was reported [6]. A Rumsfeld trophoblast cell-center study found that the vast majority of PSTT patients with previous pregnancy were pregnant with a female fetus [7]. Menopause and irregular vaginal bleeding are the most common symptoms in a small number of cases are transferred into the first symptom. The transfer site is made to the main lung, which also passes through the blood of other parts of the spread. Signs are mainly as follows: uterus increased or irregular larger, only 15% to 35% of cases of metastasis, in the event of frequent spread, and poor prognosis. Due to improper treatments, the mortality can be as high as 10% to 20% [8]. Involved areas mainly include the lung, vagina, brain, liver, kidney, and pelvic and abdominal aortic lymph nodes [9]. About 10% of patients will complicate with the nephrotic syndrome which are often in the PSTT after the treatment of

nephrotic syndrome also disappeared [10].

$\beta$ -hCG in patients with PSTT was mostly lower than 1,000 U/L. Furthermore, the severity of PSTT lesions, with or without distant metastasis, is not proportional to the level of hCG [6]. hCG is still the best serologic marker for detection and follow-up assessment of the treatment. Lower levels of hCG often result in confusion with early choriocarcinoma, gestational trophoblastic tumor, or quiescent gestational trophoblastic disease (GTD). In addition, hCG levels should be considered in the differential diagnosis of non-trophoblastic disease, such as arteriovenous fistula myometrium, missed abortion, and germ cell tumors. In contrast, other tumors may secrete low levels of hCG. Because these diseases are responsive to different treatments. Differential diagnoses are particularly important. The determination of  $\beta$ -hCG is generally of no value in differentiating when selecting treatment options for PSTT and GTD [11]. However, some studies proposed that the proportion of  $\beta$ -hCG in the overall hCG is a valuable indicator to measure, which can subsequently be used in the differential diagnosis of PSTT. Thus, Cole *et al.* [12] recommended that the cut-off point (the proportion of  $\beta$ -hCG in overall hCG) should be more than 35% and more than 80%, respectively. If 35% is the cut-off point, the PSTT, choriocarcinoma and quiescent trophoblastic tumor can be identified. The PSTT detection rate can reach 100%, without false positive, if 80% is the cut-off point. PSTT and non-trophoblastic malignancies can be identified, the detection rate is 77%, and its false positive rate is 23%.

B ultrasound examination of the PSTT also has some diagnostic value, which is often manifested as uterine enlargement with no embryonic sac. Myometrial multiple cystic structure showed heterogeneous strong echo, color shows the uterine or lesions rich blood flow; peripheral high-speed low-resistance blood flow signal; cystic area showed low blood flow signal or no blood flow signal; PSTT showed the infiltrating growth of muscle fibers [13].

PSTT belongs to middle trophoblastic tumors. Therefore the diagnostic criteria must be based on the pathological diagnosis. Tumor sections are mostly brown, yellow or white. The soft brittle tissue may have focal bleeding and necrosis, but no choriocarcinoma-like extensive necrosis. Excessive intermediate trophoblast activity is an important diagnostic standard for PSTT. As reported in the literature, the positive rates of hPL and hCG immunohistochemical staining were 94.3% and 64.5% for patients with PSTT [6]. PSTT is not sensitive to chemotherapy drugs, while hysterectomy is the preferred treatment program.

For patients with extensive metastases or relapses, the resection of primary metastatic lesions combined with multi-drug chemotherapy is still an important treatment. Young patients without ovarian metastasis can retain fertility [14]. Because the PSTT can pass lymphatic metastasis, Schmid *et al.* [3] recommended hysterectomy at the same time pelvic and retroperitoneal lymph node biopsy, and Hyman

*et al.* [8] that the imaging is limited to the uterine lesions, which cannot be lymph node biopsy and surgery. The need for a biopsy of lymph nodes is still under discussion.

Patients with high risk factors often show poor prognosis. Thus, it is recommended to combine it with chemotherapy after surgeries. The prognostic high risk factors are as follows: 1) tumor cell mitotic index > 5/10 HP, coagulation necrosis, vascular invasion, and deep myometrial invasion [15], 2) from the previous pregnancy time > 2 years [3], 3) extracardiac metastasis lesions [8], and 4) > 40-years-old [3]. Patients with PSTT have different sensitivities to chemotherapy. Adjuvant chemotherapy regimens include MAC (MTX + actinophosphate + cyclophosphamide), PVB (cisplatin + vinblastine / vincristine + bleomycin) or EMA/CO program. It has been reported that there has been a transfer of PSTT surgery, which was combined with chemotherapy after treatment failure. In summary, the external irradiation can effectively control recurrence [16].

In summary, due to its low incidence, the occult disease and non-specific clinical aspects have different features. PSTT usually needs to be diagnosed by curettage, biopsy or even postoperative pathological examination. For the preferred treatment of surgery, the principle is to remove all lesions. According to the patient's age and fertility requirements, it can be chosen to retain fertility with the surgical approach. Most patients can be cured after the removal of lesions. The prognosis is effective. Patients with high risk factors should choose EMA/CO or EMA/EP regimen after chemotherapy in order to improve the prognosis. Furthermore, the postoperative follow-up will be done regularly.

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