

# Fertility preservation for a patient with placental site trophoblastic tumor: a case report with literature review

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## Summary

Placental site trophoblastic tumor (PSTT) is a rare trophoblastic tumor with complete hysterectomy as the primary treatment. Here the authors report one case received lesionectomy with fertility preserved under the patient's desire of reproduction. A 24-year-old woman was admitted because of four-month irregular vaginal bleeding following a natural delivery of a full-term baby nine months ago. As the tumor was confined to the uterus, a cross-wall wedge cut was made to remove the lesion together with 1 cm of surrounding healthy tissues. Immunohistochemistry of biopsy accorded with PSTT. No recurrence was evident during 15-month postoperative follow-up. Referring to literature, the authors recommend that patients with reproduction requirement with PSTT restricted to uterus could undergo a lesionectomy to retain fertility. Chemotherapy could be supplemental when high-risk factors exist.

**Key words:** Placental site trophoblastic tumor; Fertility preservation.

## Introduction

Placental site trophoblastic tumor (PSTT) is a rare trophoblastic tumor originating from extravillous intermediate trophoblast cells with a morbidity around 1/100,000. Based on recent literature, the incidence of PSTT is on the rise. The primary treatment is complete hysterectomy. However, most of the women with the illness strongly desire fertility preservation since the onset age is relatively young, 30 years on average. Here the authors report one PSTT case who received a fertility-sparing lesionectomy in the present hospital with no evident recurrence during 15-month postoperative follow-up along with a comprehensive literature review and discussion.

## Case Report

A 24-year-old woman was referred because of irregular vaginal bleeding for four months following a natural delivery of a full-term baby nine months ago. Serum  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) was 88.6 IU/L. Ultrasonography showed an abnormal echo in her uterus. Enhanced pelvic CT scan revealed an unusually rich vascular mass near the right corner of the uterus with a diameter of approximately 4.7 cm spanning all uterine layers (Figure 1A). Hysteroscopy revealed a 1.0×0.5×1.0 cm ulcerative lesion at the fundus of the uterus with many abnormally dilated surrounding blood vessels. Histology of biopsy illustrated secretory endometrium with trophoblastic cells at the edge. Chest CT was normal. A trophoblastic tumor was thus considered, and the first course of a five-day combination chemotherapy consist of actinomycin D (ACTD) and methotrexate (MTX) was initiated, followed by a second course of five-day bleomycin, etoposide,

and cisplatin (BEP). However, the result was unideal with elevated serum  $\beta$ -hCG and increased tumor size post chemotherapy. Operation was suggested consequently.

The patients expressed a strong will to have her fertility preserved. A comprehensive preoperative assessment was conducted. The second hysteroscopy was concordant with the first one showing a 1-cm ulcerative lesion in the uterine fundus with abnormal vasculatures in the uterus walls and a clear boundary with no ev-

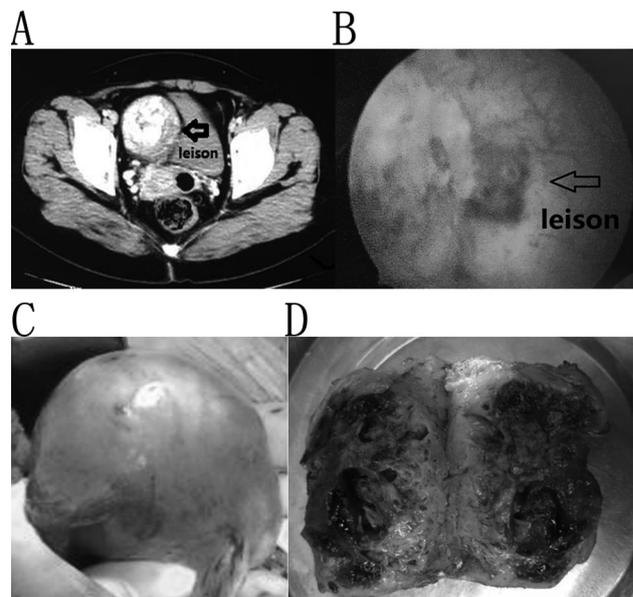


Figure 1. — Morphological presentations of the PSTT.

A: enhanced pelvic CT scan; B: 2<sup>nd</sup> hysteroscopy, front view of uterus; C: front view of uterus during surgery; D: the excised lesion.

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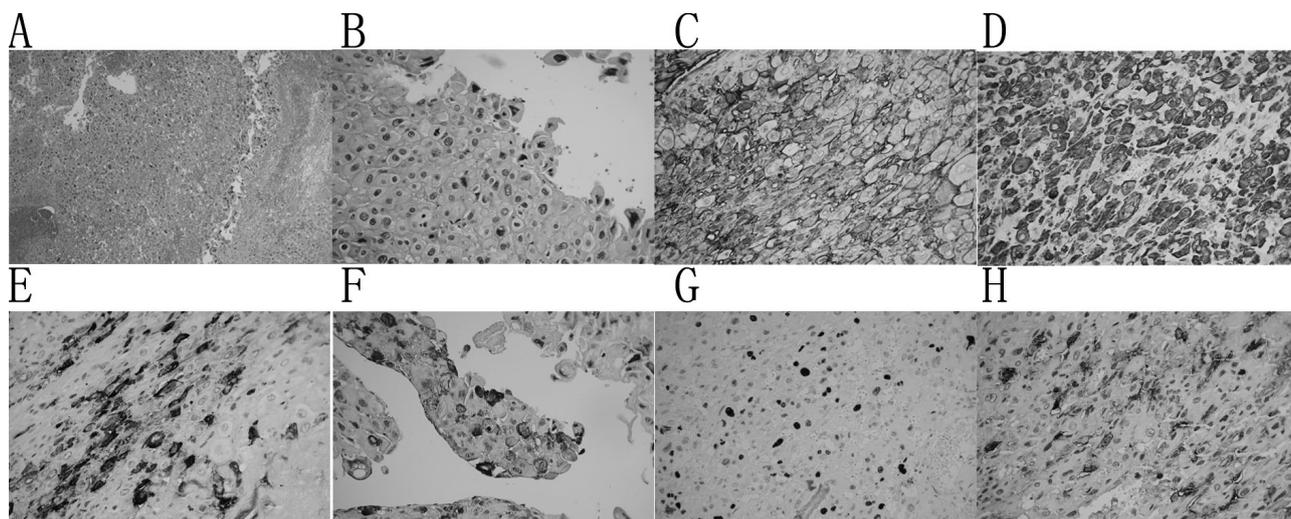


Figure 2. — H&E stain and immunohistochemistry. A: H&E stain of lesion, magnification  $\times 100$ ; B: 2-3 mitotic figures (MF) /10 high-power fields ; C: CD146 +++; D: CK18 ++; E: hCG +++; F: HPL (partial +); G: Ki67 50% +; H: PLAP partial +.

ident peripheral infiltration, which indicated a lesion confined to the uterus (Figure 1B). Transabdominal lesionectomy was thus decided. During surgery, the authors observed that part of the front wall was light yellow in color and  $4 \times 4 \text{ cm}^2$  in size with clear boundary (Figure 1C). A wedge cut across all layers of uterine wall was made to remove the tumor along with 1 cm of peripheral healthy-looking tissues. The excised tissue was  $4 \times 4 \times 3 \text{ cm}^3$  in size, light yellow with a distinct boundary from adjacent normal tissue (Figure 1D), and the reserved uterus had no region with significant color change. Postoperative pathology reported trophoblastic tumor, muscle infiltration, extensive hemorrhage, and necrosis (Figure 2A) with 2-3 mitotic figures (MF) /10 high-power fields (HPF) (Figure 2B). Immunohistochemistry showed CD146 +++ (Figure 2C), CK18 ++ (Figure 2D), hCG +++ (Figure 2E), human placental lactogen (HPL) partial + (Figure 2F), Ki67 50% + (Figure 2G), PLAP partial + (Figure 2H), EMA +, ER -, and PR -. PSTT was thus diagnosed. Serum  $\beta$ -hCG decreased to normal level three weeks post-operation. Chemotherapy was not carried out due to fear of risk factors. Menses occurred two months after surgery with no evident recurrence during 35-month postoperative follow-up.

## Discussion

With the improvement of quality of life and the opening of a two-child policy in China, many young women have strong desires for reproduction. Currently, the fertility-preserving treatment for PSTT patients is still exploratory without a clear guideline due to controversial results from small-scale clinical studies. Fertility-preserving treatment was not supported in some studies, e.g. Saso *et al.* [1] reported five cases of fertility-sparing surgery with only one success, and all the others underwent secondary complete hysterectomy due to unclear tumor incision; secondary operation increases injury and complications, and may also cause iatrogenic cancer metastasis. In agreement with Leisrowitz and Webb [2] that preserving fertility for Stage I

SPTT patients is possible, but a full preoperative assessment is essential and necessary to ensure the operation success, the present authors strongly promote hysteroscopy on top of imaging. Imaging, e.g. ultrasound, MRI, CT, and PET, provides three-dimensional view of the lesion including the location, size, and the layer(s) spanned, but may spare minor lesions as pointed out by Pfeffer *et al.* [3]. Hysteroscopy allows direct vision of the lesion at endometrial level with high resolution, including location, color, size and boundary to adjacent tissues, and biopsy can be performed simultaneously. In this case reported here, surgery observed the same result as the hysteroscopy suggesting the reliability of hysteroscopy for preoperative evaluation.

Adjuvant chemotherapy could be applied pre- or postoperatively, or both ways to reduce tumor size and decrease cancer recurrence, but only help sensitive cases. Tsuji *et al.* [4] applied two-course EMA/CO (etoposide + methotrexate + actinomycin D/cyclophosphamide + vincristine) chemotherapy preoperatively, followed by fertility-preserving surgery to patients with shrunken lesions, and no recurrence was evident, even chemotherapy was not done postoperatively. In this case, chemotherapy was not applied either pre- or postoperatively due to patient's insensitivity to chemotherapy as well as lack of risk factors.

Surgical approaches, including trans-abdominal lesionectomy, laparoscopic excision, trans-hysteroscopic lesionectomy and curettage, demonstrated similar success rate in preserving fertility for PSTT patients. Table 1 summarizes 25 patients receiving fertility-sparing surgery [1-6]. There was no postoperative recurrence in eight of 13 cases (62%) receiving transabdominal lesionectomy, three of three (100%) using laparoscopic excision, two of two (100%) by trans-hysteroscopic lesionectomy, and four of seven (57%) receiving curettage. Six of 25 (24%) patients

Table 1. — Outcome of PSTT patients by different fertility-preservation surgeries.

Author	Number of case	Surgical approach	Outcomes	Fertility
Pfeffer [3]	1	Transabdominal lesionectomy	Relapse during chemotherapy, no recurrence after total hysterectomy	
Tsuji [4]	1	Transabdominal lesionectomy	No recurrence	
Leiserowitz [2]	1	Transabdominal lesionectomy	No recurrence	Childbirth
Machtlinger [6]	1	Transabdominal lesionectomy	Incision margin was not clear and relapse, and operate hysterectomy	
	1	Transhysteroscopic lesionectomy	No recurrence	
Saso [1]	5	Transabdominal lesionectomy	4 cases underwent transabdominal hysterectomy because incision margins were not clear, 1 case succeeded	
Zhao [5]	4	Transabdominal lesionectomy	No recurrence	2 cases of childbirth
	3	Translaparoscopic lesionectomy	No recurrence	2 cases of childbirth
	7	Curettage	4 cases with no recurrence, 1 case died, 2 cases were lost	
	1	Transhysteroscopic lesionectomy	No recurrence	Childbirth

became pregnant followed by delivery after surgery during postoperative follow-up. Zhao *et al.* [5] also presented similar prognosis and recurrence rate between fertility-sparing surgery and complete hysterectomy, and concluded feasibility of PSTT cure by fertility-sparing surgery and necessary chemotherapy.

Based on the present case and previous reports, the authors formulated criteria to guide their clinical practice to treat PSTT patients with reproduction requirement. Fertility-preserving treatment should be chosen cautiously based on individual situation, and only for patients younger than 35 years with strong reproduction requirement. Imaging along with hysteroscopy should be performed to fully evaluate feasibility of fertility-preserving treatment. Lesionectomy can be considered for lesions relatively small and confined to the uterus without diffuse invasion. Complete hysterectomy should be considered for patients with large lesions insensitive to chemotherapy since the remaining uterus will be insufficient for pregnancy. Complete hysterectomy is recommended when incision edge is observed unclear during lesionectomy. Patients with high-risk factors including age > 35 years, more than two years from last pregnancy,  $\beta$ -hCG > 1,000 IU/L, > 5 MF/10 HPF, deep myometrial invasion, bleeding, and necrosis should be treated with adjuvant chemotherapy [2, 6]. Life-long postoperative follow-up is necessary with serum  $\beta$ -hCG as the primary biomarker along with imaging, such as ultrasound and chest X-ray, to monitor recurrence and metastasis. Chemotherapy and/or surgery shall be considered a sign of recurrence. Pregnancy was unrecommended until one year post operation[7].

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