EJGO European Journal of Gynaecological Oncology

Fertility-preserving treatment in three cases of placental site trophoblastic tumor

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Summary

Placental site trophoblastic tumor (PSTT) is a rare variant of gestational trophoblastic disease. Fertility-sparing therapy for affected women, especially for those whose lesions are hypervascular of childbearing age is a challenge. The authors therefore decided to investigate the methods of fertility-sparing therapy for patients with PSTT. The cases of three patients with PSTT are presently described. All presented with disease confined to the uterus, and the lesions were hypervascular. Two patients underwent dilatation and curettage, and combined etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine/oncovin (EMA/CO) chemotherapy. One patient underwent hysteroscopic resection and EMA/CO chemotherapy. All patients underwent ultrasonography postoperatively to re-evaluate the size of the lesion. The patients retained their reproductive function with no serious hemorrhage noted. The authors believe that patients with PSTT may be candidates for conservative therapy, even if the lesion is hypervascular. The sonographic presentation is important in deciding the treatment for affected patients.

Key words: Placental site trophoblastic tumor; Fertility-sparing treatment; EMA/CO; Indications; Hypervascular.

Introduction

A placental site trophoblastic tumor (PSTT) is an extremely rare type of gestational trophoblastic disease (GTD) and occurs when intermediate trophoblastic cells invade the myometrium at the site of implantation [1, 2]. PSTT occurs most frequently in women of reproductive age (median age 28–35 years) and may arise after any type of pregnancy including miscarriages, ectopic pregnancies, complete or partial molar pregnancies, terminations, and term pregnancies.[3] Schmid *et al.* [3] showed that since antecedent pregnancy, mitotic index, disease stage, FIGO score, presence of distant metastases and number of metastases, serum β-hCG concentration, and age could predict overall survival; moreover, the key factor appears to be a time span of 48 months since antecedent pregnancy. PSTT responds well to surgery if the disease is localized; therefore, surgery is the cornerstone of treatment [4]. However,

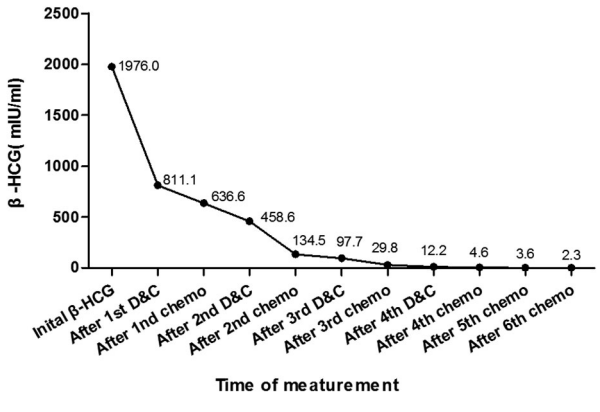

Figure 1. — The variation of serum β-hCG from diagnosis and during treatment of case 1. chemo: chemotherapy

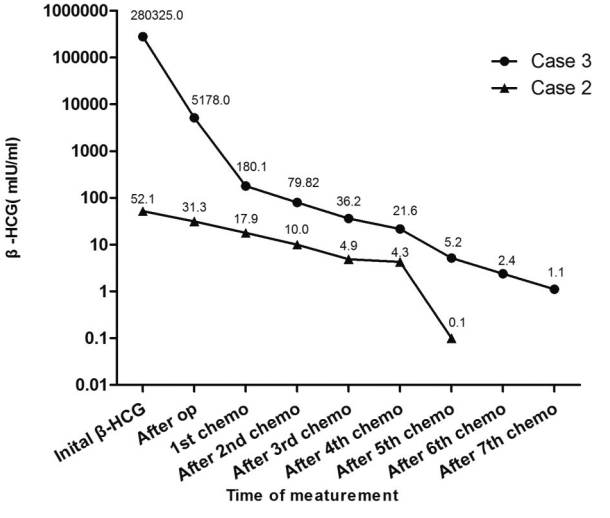

Figure 2. — The variation of serum β-hCG from diagnosis and during treatment of casea 2 and 3. chemo: chemotherapy; op: operation

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Revised manuscript accepted for publication June 6, 2017

Table 1. — *Clinical data of patients with PSTT.*

Case	Case 1	Case 2	Case 3
Age (years)	23	24	27
Gravida/para	1/0	1/1	1/0
Presenting symptoms	Vaginal bleeding	Vaginal bleeding	Vaginal bleeding
Antecedent pregnancy	Abortion	Term	Term
Time since pregnancy	17 months	11 months	48 months
Uterine mass by ultrasonography			
Blood flow within the mass	Hypovascular	Hypovascular	Hypovascular
Tumor site	Intrauterine mass	Anterior uterine mass	Intrauterine mass
Tumor volume	42 × 52 × 42 mm^3	18 × 17 × 13 mm^3	71 × 52 × 42 mm^3
Operation	D&C	Hysteroscopic resection	D&C
Hemorrhage of the first operation	150 ml	2 ml	100 ml
Uterine mass after the first operation			
Blood flow within the mass	Hypovascular	Hypovascular	Hypovascular
Tumor site	Endometrial mass	Anterior uterine mass	Intrauterine mass
Tumor volume	40 × 43 × 35 mm^3	11 × 7 × 11 mm^3	21 × 20 ×13 mm^3
Times of operation	4	1	1
Chemotherapy	EMA/CO	EMA/CO	EMA/CO
β-HCG normalized	After 4th cycle of chemotherapy	After 3rd cycle of chemotherapy	After 6th cycle of chemotherapy
Cycles of chemotherapy	6	5	7
Resuming normal menstruation	Yes	Yes	Yes
Follow-up	105 months, NED	57 months, NED	12 months, NED

D&C: Dilatation and curettage, EMA/CO: Combined etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine/oncovin, NED: no evidence of disease.

most affected patients are of reproductive age and hysterectomy will render them infertile. Therefore, the potential for a fertility-sparing treatment has been investigated.

In recent studies, the overall response rate of patients to etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine/oncovin (EMA/CO) chemotherapy has been reported at 71% and a complete response was observed in 38% of patients, making EMA/CO a foundation of fertility-sparing treatment [4]. Unfortunately, there are few studies investigating fertility-sparing therapy in patients with PSTT [4, 5]. Combined surgical and chemotherapy have been proven effective in patients with small and hypovascular lesions, but it has not been recommended for hypervascular lesions, which often show severe hemorrhage after curettage [6, 7].

In the present report, the authors describe their experience with three PSTT cases that had hypervascular lesions on the ultrasonography, focusing on the treatment approaches and indications of fertility-sparing treatment for this condition.

Case Report

All individuals enrolled in this study signed the informed consent and the study was approved by the Ethics Committee of Tianjin Central Hospital of Obstetrics and Gynecology.

Case 1: In April 2007, a 23-year-old woman, was admitted to this hospital with a chief complaint of prolonged vaginal hemorrhage for two months. The serum β-hCG concentration and ultrasonography are shown in Figure 1. The first dilatation and curettage (D&C) procedure was performed with ultrasonography guidance and histopathology confirming PSTT. Computed tomography (CT) and chest radiographs were normal with no signs of metastasis. After the D&C procedure, the ultrasonography was taken and the β-HCG concentration was measured (Table 1, Figure 1). The patient wished to preserve her fertility; therefore, a combination of EMA/CO chemotherapy and D&C was performed. The D&C under ultrasonography guidance was repeated a second time to decrease the tumor size and was followed by chemotherapy. This treatment was repeated three times until the diameter of the lesion in the uterine cavity measured less than 3 cm on ultrasonography. Simultaneously, a repeat pathology examination showed severely degenerated tissue with no intermediate trophoblast cells present, suggesting that the lesion was successfully removed. After four cycles of chemotherapy, the β-hCG concentration normalized. Two additional courses of chemotherapy were administered.

Case 2: A 24-year-old woman, was admitted due to a five-month history of irregular vaginal hemorrhage. The serum β-hCG concentration and ultrasonography were taken to evaluate the condition (Figure 2, Table 1). The hysteroscopic resection was performed with ultrasonography guidance. A 2 × 2 cm^2 tumor was resected from the anterior uterine wall, and no residual mass was left. The ultrasonography was repeated seven days postoperatively and combined EMA/CO chemotherapy was initiated (Table 1).

Case 3: A 27-year-old woman, was examined in 2012, four years after a normal vaginal delivery, complaining of irregular vaginal hemorrhage of five months. After the vaginal delivery, she used an intrauterine contraceptive device and removed it one year before the onset of irregular vaginal hemorrhage. The serum β-hCG concentration and ultrasonography were taken to evaluate the condition (Figure 2, Table 1). The D&C procedure was performed under ultrasonography guidance. The ultrasonography was repeated seven days postoperatively and combined EMA/CO chemotherapy was initiated (Table 1).

Discussion

In the present study, three patients with PSTT who had hypervascular lesions on the ultrasonography retained their reproductive function and had no significant hemorrhage after multimodal treatment. Studies reported that fertility-preserving treatment is feasible in patients with localized, hypovascular lesions, but in hypervascular PSTT, massive hemorrhage has been reported following D&C [6, 7]. In the present study, D&C and hysteroscopic resection were performed to decrease the tumor size. The operation was performed by experienced doctors and under ultrasonographic guidance to reduce potential injuries. Moreover, the present authors only removed the right amount of lesions per operation, in order to avoid serious hemorrhage caused by removal of excessive tissue. In case 1, the D&C was performed four times and after each surgery, and combined EMA/CO chemotherapy was administered. The size of the lesion was reassessed on ultrasonography. After the fourth D&C, the diameter of lesion was 2 cm, and treatment was discontinued. The lesion in case 2 measured only 2 cm less in diameter than the lesions in the other two cases, but instead, resectoscope of the tumor was performed. After the procedure, EMA/CO, chemotherapy was administered. In case 3, where a much larger lesion was seen than that present in case 1, D&C was performed for the same reason. After the procedure, the lesion was reduced to 21 × 20 × 13 mm^3, and EMA/CO chemotherapy was administered. All the patients responded well to treatment.

The sonographic presentation of PSTT is an important component in determining treatment. Pfeffer *et al.* [8] reported that multifocal microscopic disease within the uterus was not amenable to conservative treatment; however, small tumors confined to the endometrium can be excised hysteroscopically [9, 10]. The present authors recommend that fertility-preserving treatment be based on the sonographic presentation. If the lesion is a small, solid mass in the myometrium, hysteroscopy, and chemotherapy can be considered. For a solid mass in the uterine cavity, EMA/CO chemotherapy alternating with D&C can be considered. Moreover, ultrasonography should be repeated after each D&C to reassess the size of the lesion and plan additional D&C procedures.

All cases preserved their reproductive function. The patient in case 1 is at 12 gestational weeks now and the patient in case 2 had a normal delivery in June 2016. They both conceived spontaneously. The patient in case 3 suffered from irregular vaginal hemorrhage for five months, but her urine or serum β-hCG was not detected until she was admitted. Therefore, the authors are unsure whether her last pregnancy was 48 months prior or five months prior. The PSTT may be secondary to a miscarriage, presenting with irregular vaginal hemorrhage. The present authors regret not being able to obtain her pregnancy status. She was lost to follow up 12 months after ending treatment because she moved to another city.

In conclusion, for lesions confined to the uterus, patients with PSTT may be candidates for conservative therapy, even if the lesion is hypervascular. The sonographic presentation is important when determining the appropriate treatment. Importantly, the patient must be counseled on the potential for chemotherapy toxicity and treatment failure when using this conservative approach [11, 12]. The present report comprises only three cases, and much more data are needed in the future.

Acknowledgements

The authors thank Chunumila Maharjan for her assistance with paper-writing.

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