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Fertility preservation of PSTT by interventional therapy: a case report

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Summary

Introduction: Placental site trophoblastic tumor (PSTT) is a rare form of gestational trophoblastic disease (GTD) and this disorder is usually seen in young women with a 20% mortality rate. Although hysterectomy is useful for treating PSTT, it is not the best choice for patients who wish to preserve their fertility. Due to the fact that PSTT is resistant to chemotherapy frequently, it is very important to find new therapeutic schedules used for PSTT. *Case Report:* The patient is a 24-year-old female, gravida 2, para 1, with intermittent vaginal bleeding episodes for ten days following her latest pregnancy of 50 days ago. Pelvic utrasonographic results showed a 4×5×5-cm mass in hypo-hyperechogenic areas of the uterine wall and the initial serum β-hCG level was 6,359 mIU/ml. Immunohistochemical analysis revealed that the Ki-67 proliferative index was about 10%; the tumor cells showed strong diffuse staining with Pan cytokeratin, human placental lactogen (hPL), placental alkaline phosphatase, and epidermal growth factor receptor (EGFR). Meanwhile, the tumor cells also showed focal positive with hCG. The histological and immunohistochemical findings led to the diagnosis of PSTT. At first, the patient took three courses of chemotherapy and three times of curettages, but the condition was not in remission. In order to preserve the patient's fertility, the patient underwent twice uterine artery drug pouring and embolism treatment. The drugs included adriamycin, cisplatin, and methotrexate. This therapy had gained a satisfactory effect. *Conclusion:* When the tumor is localized to uterus without diffuse infiltrative, for younger PSTT patients who wish to conserve fertility, the authors suggest that uterine artery drug pouring and embolism treatment could be considered.

Key words: Placental site trophoblastic tumor (PSTT); Uterine artery drug pouring and embolism treatment; Fertility preservation.

Introduction

As a rare form of the gestational trophoblastic disease (GTD), placental site trophoblastic tumor (PSTT) is derived from the implantation of an intermediate trophoblast and it is biologically different from other forms of GTD [1]. PSTT is usually seen in young women with a 20% mortality rate [2], and it can appear following any type of pregnancy, such as after normal pregnancy, spontaneous abortion, termination of pregnancy, ectopic pregnancy or molar pregnancy [3]. There is a wide clinical spectrum of presentation and behavior ranging from a benign condition to an aggressive disease with a fatal outcome [4]. However no standard therapy for PSTT has been established up to now.

According to some reports, PSTT is resistant to methotrexate and actinomycin D, which were usually used as chemotherapic agents for chorionic tumor [5]. Hence combination chemotherapies and hysterectomy are the main therapies against PSTT. Although some papers reported that the combination chemotherapies were highly effective, cases were also reported that such therapy can not prevent PSTT recurrence completely [6]. Meanwhile, for patients who desire to remain fertile, hysterectomy is not a good choice.

In this paper, the authors present a case of PSTT, in which the 24-year-old patient strongly requested to conserve fertility. Thus, they attempted to satisfy her by using uterine artery drugs pouring and embolism treatment and the drugs in this case included adriamycin, cisplatin, and methotrexate.

Case Report

A 24-year-old female (gravida 2, para 1) was referred to the present hospital with initial diagnosis of hydatidiform mole. One year ago, the patient gave birth to a female baby by normal spontaneous full term delivery. Her complaint was intermittent vaginal bleeding episodes for ten days following her most recent pregnancy of 50 days ago. The gynecological exam result showed an enlargement of eight weeks gestation in uterus. The pelvic ultrasonography results showed a 4×5×5 cm mass in hypo-hyperechogenic areas of uterine wall. Endometrial suction curettage was performed in the present hospital for three times. The general morphological observation of the firstly performed curettage specimen showed a mass of gray red tissue with a total volume of 3×2×1.5 cm. When observations were taken under microscope, the authors found single tumor cell or pieces of tumor cells separated myometrium (Figure1). These tumor cells were composed of single polygon intermediate trophoblasts cells with abundant cytoplasm. The cells were eosinophilic or transparent. Moreover, the neoplastic cells showed various obvious shapes with conspicuous nucleolus. Most of the cells were mononuclear, but some were binuclear as shown in Figure 2. Deposition of fibroid mate-

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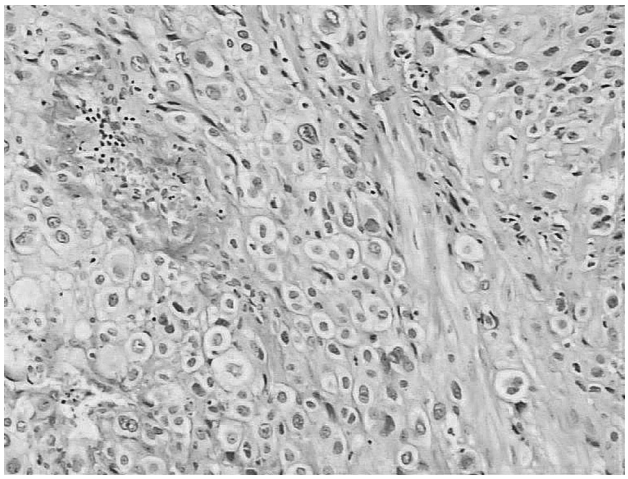

Figure 1. — Single tumor cell or nests of tumor cells separating the myometrium (H&E staining ×100).

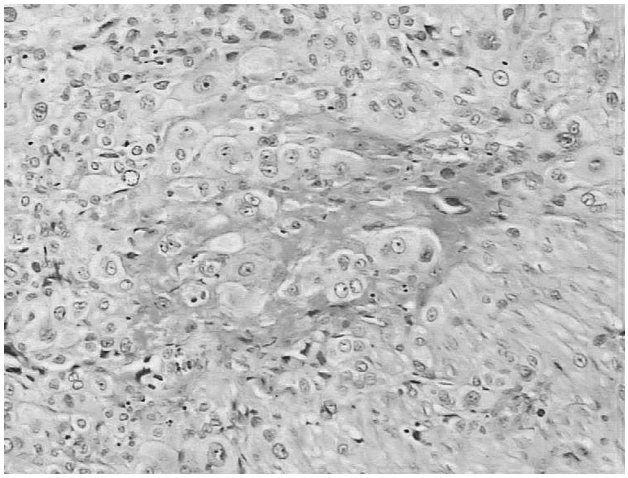

Figure 3. — Deposition of fibrinoid material is noticed between trophoblastic cells. (H&E staining ×100).

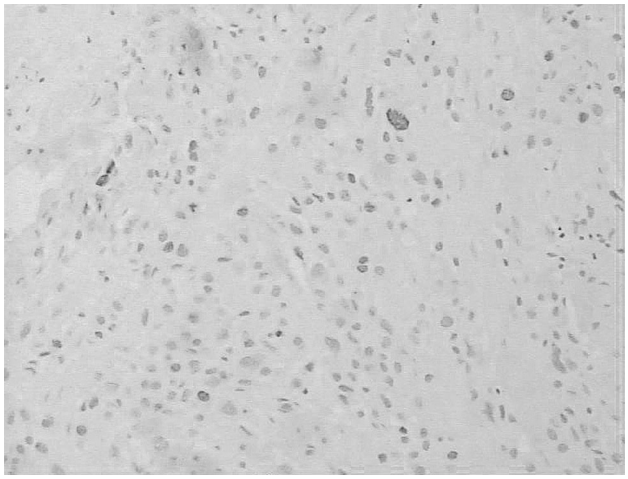

Figure 5. — The Ki-67 proliferative index is about 10% (H&E staining ×100).

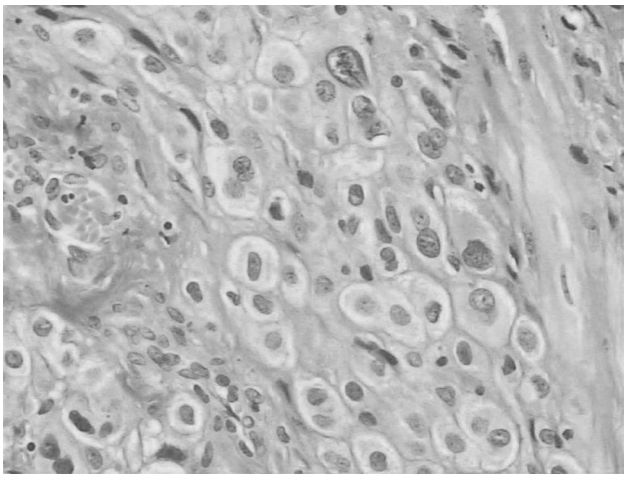

Figure 2. — The tumor cells are composed almost exclusively of intermediate trophoblasts. Cytoplasm is abundant and eosinophilic or clear. The neoplastic cells show pleomorphism and nuclei are conspicuous. Most of the cells are mononuclear, while some are binuclear (H&E staining ×200).

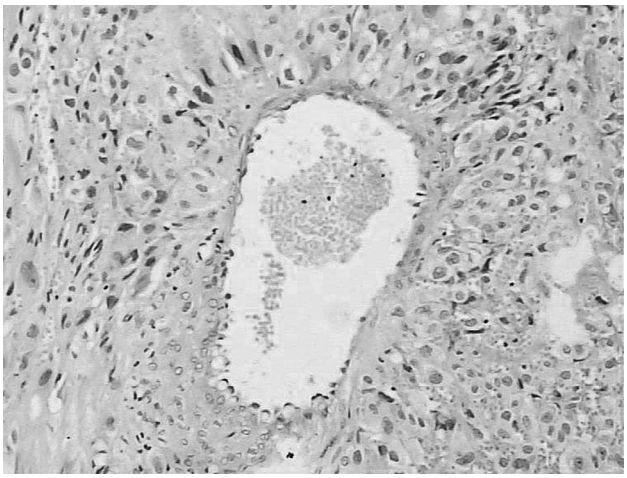

Figure 4. — Intermediate trophoblastic cells with infiltration of the cells in vessel walls (H&E staining ×100).

rial was noticed between trophoblastic cells (Figure 3). Intermediate trophoblastic cells infiltrated the cells in vessel walls (Figure 4). With immunostaining, the Ki-67 proliferative index was about 10% (Figure 5); the cells showed strong diffuse staining with Pan cytokeratin, human placental lactogen (hPL), and focally positive with hCG.

All findings described above were consistent with PSTT without evidence of disease outside the uterus. Ten days after the first complete curettage of uterine cavity, weekly intravenous methotrexate at 100 mg/m^2 with folinic acid were used as primary treatment. Three days later the serum β-hCG level was 982.2 mIU/ml; eight days later the serum β-hCG level decreased to 563 mIU/ml and pelvic utrasonography results revealed a 4×5×5-cm mass in hypo-hyperechogenic areas of uterine. In uterine, the au-

thors found a 4.3×3.7×2.4-cm heterogeneous area in which a strong echo was predominant. Meanwhile, liquid dark areas were also detected. In duplex Doppler ultrasound, tumors display more abundant blood flow within and higher resistance index of 0.44. A month later, endometrial suction curettage was performed for the second time. Through the examination of the curettage specimen, the authors found some necrotic materials, and few couples of atypical intermediate type trophoblasts. Nine days later, the serum β-hCG level decreased to 185.3 mIU/ml. After the second course of chemotherapy, the serum β-hCG level increased to 424.3 mIU/ml. The third performed curettage specimen demonstrated a few couple of atypical intermediate type trophoblasts. Before the third chemotherapy with methotrexate; serum β-hCG level decreased to 188 mIU/ml. However after the third chemotherapy, the serum β-hCG level increased to 240.4 mIU/ml and pelvic utrasonography results revealed a 2.1×1.5-cm mass with hyperechoic area in uterine. In duplex Doppler ultrasound, the mass displayed more abundant blood flow within and higher resistance index of 0.5.

After the patient underwent three courses of chemotherapy and three curettages, and the condition was not in remission. Some doctors suggest that hysterectomy maybe the best choice. However as a 24-year-old woman, the patient strongly requested to preserve fertility. Fortunately the tumor was localized to uterus without diffuse infiltrative and its histopathological results showed no poor prognostic factors. So the authors attempted to retain her fertility by using uterine artery drugs pouring and embolism treatment in which the drugs include adriamycin, cisplatin, and methotrexate. A week later her serum β-hCG level decreased to 3 mIU/ml. The second uterine artery drug pouring and embolism was performed a month latter. The patient's pelvic utrasonography results were satisfying and the serum β-hCG level back to normal. She is still alive with no evidence of local recurrence or distant metastasis 77 months after therapy.

Discussion

Due to the heterogeneity of the clinical manifestations, the diagnosis for PSTT is usually difficult [7] and requires a combination of clinical manifestation, including blood β-hCG test, imaging and histological examinations, and immunohistochemical staining. Clinically, vaginal bleeding is a common symptom and it rarely combines with amenorrhea [8]. Moreover, unlike choriocarcinoma, reports have recently shown that serum β-hCG is a reliable marker for diagnosis of PSTT and it would be reasonable to measure serum β-hCG whenever the diagnosis of PSTT is considered [9]. However, an elevated proportion of serum β-hCG is a helpful but not a definitive test to distinguish PSTT from other forms of GTD [10].

Immunohistochemically, PSTT is positive for human placental lactogen (hPL), CD146, cytokeratin AE1/AE3, E-cadherin, epidermal growth factor receptor (EGFR), cytokeratin, hCG, and PLAP [11]. In the present case, the Ki-67 proliferative index was about 10%, the cells showed strong diffuse staining with Pan cytokeratin, hPL, PLAP, and EGFR, and focal positive with hCG. E-Cadherin staining was negative in tumor cells, which was obviously consistent with PSTT.

The treatment of choice for patients with disease localized to the uterus is hysterectomy. Local uterine resection may be considered if a patient is resistant to chemotherapy and desires to preserve future fertility [12]. In the absence of reliable prognostic indicators, conservative therapy in the form of curettage alone should be performed with caution [3]. The patient must be properly assessed before conservative therapy is determined, otherwise, the treatment will be ineffective [13].

After the present patient underwent three courses of chemotherapy and three curettages, the condition was not in remission. In order to preserve the patient's fertility, the authors performed twice uterine artery drug pouring and embolism treatment. In this case, the drugs included adriamycin, cisplatin, and methotrexate. Finally, the patient's pelvic utrasonographic results and serum β-hCG level returned to normal, indicating that this treatment had gained a satisfactory effect.

Although the etiology, epidemiology, and risk factors for the development of PSTT are not well understood [11], the authors hope that this case can provide some experience in attaining full knowledge of PSTT.

Conclusion

When the tumor is localized to uterus without diffuse infiltration, for younger PSTT patients who strongly request to conserve fertility, the authors suggest that uterine artery drug pouring and embolism treatment, in which the drugs include adriamycin, cisplatin, and methotrexate, perhaps could be better choice, but this conclusion needs further verification.

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