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Taiwanese Journal of Obstetrics & Gynecology 50 (2011) 372–374
www.tjog-online.com

Research Letter

Two cases of placental site trophoblastic tumor☆

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Accepted 9 April 2010

Placental site trophoblastic tumors (PSTTs) are an extremely rare form of gestational trophoblastic disease (GTD). Marchand and Ewing made the first observations in 1895 and 1910, respectively, and Kurman and Scully described the clinical and pathological characteristics of PSTTs in 1976, when the term trophoblastic pseudotumor was adopted to characterize the apparently benign nature of the disease [1,2]. Subsequent case reports have presented evidence of a sometimes aggressive, malignant, and fatal course of the disease, and the name was changed to PSTT in 1981 [3]. Histopathologically, PSTTs are characterized by a neoplastic monomorphic population of implantation-like intermediate trophoblastic cells, often as sheets of polyhedral, rounded, or occasionally spindle-shaped cells that infiltrate the myometrium extensively. Because of the rarity of this type of tumor, there is little information about its epidemiology and etiology, and few large series on diagnosis and treatment have been published [4]. PSTTs are most often seen in patients of reproductive age and can follow a normal pregnancy, miscarriage, or GTD. Irregular vaginal bleeding is the most common presenting feature, although a wide range of other symptoms has also been reported, including galactorrhea, virilization, nephrotic syndrome, and polycythemia [5]. We report two cases of PSTT treated successfully in our clinic.

A 38-year-old woman had not menstruated for 12 months after a term vaginal delivery during lactation and consulted a gynecologist. Because of suspicious uterine signs and persistent high beta-human chorionic gonadotropin (β-hCG) levels, she was referred to our medical center. On ultrasound examination, we detected a 100 mm × 90 mm × 75 mm pelvic mass in the uterine wall. Color Doppler ultrasound suggested a tumor (Fig. 1). The β-hCG level measured previously and in our clinic was persistently high. After curettage, the sample was revealed to be a PSTT histopathologically. A laparotomy was planned. At surgery, the uterus was large, soft, and extremely vascular, and the tumor involved both ovaries (Fig. 2). The uterus was ligated at the isthmus using a Foley catheter to limit bleeding. After sampling the pelvic fluid, we performed a radical total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node sampling, and omental sampling for staging, and both hypogastric arteries were ligated for hemostasis. The histopathology showed PSTT (Fig. 3). The tumor had invaded the serosal surface. No metastasis was seen on cranial, chest, or abdominal computed tomography. Combined chemotherapy [etoposide, methotrexate, actinomycin D alternating with cyclophosphamide and vincristine/oncovine (EMA/CO)] was initiated postoperatively and followed with a weekly β-hCG. The patient received six courses of EMA/CO.

A 34-year-old woman had a spontaneous abortion in the 2nd month of pregnancy. She complained of vaginal bleeding for 2 months afterward. She visited another health care center, where she was examined and diagnosed with a uterine leiomyoma, and a laparotomy was performed. At surgery, the surgeons suspected that the tumor was a degenerative leiomyoma and partially removed it. Histopathological examination revealed that it was a PSTT, and she was referred to our clinic. Her physical examination was normal. On ultrasound examination, the uterus measured 86 mm × 50 mm and an 18 mm × 16 mm hyperechogenic area was seen on the posterior uterine wall. The left ovary was normal and there was a simple 60 mm × 50 mm cyst in the right ovary. The first β-hCG level was 763 mIU/mL and the other tumor markers were normal. The histopathology is shown in Fig. 4. Immunohistochemical and morphologic features of the cells correspond to those of intermediate trophoblast. Immunohistochemically, the tumor cells were positive for epithelial membrane antigen, hCG, and placental alkaline phosphatase. After informing the patient, a laparotomy and a total abdominal hysterectomy and right ovarian cystectomy were performed. The postoperative specimens were confirmed as PSTT. Postoperatively, the patient

☆ Conflict of interest: The authors declare no conflict of interest.

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doi:10.1016/j.tjog.2011.01.026

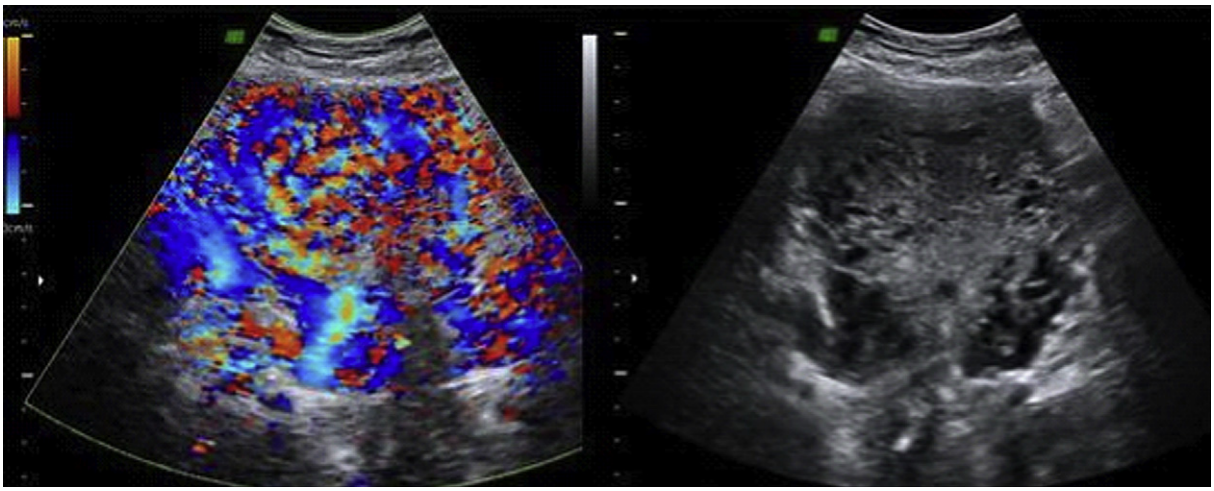

Fig. 1. A 100 mm × 90 mm × 75 mm size pelvic mass was not distinguished from uterine wall. Doppler velocimetry of the mass showed increased blood flow, which was considered to be malign.

underwent six courses of combined chemotherapy with EMA/CO and was followed with a weekly β-hCG.

Neither patient has had a recurrence in the 6–8 months since surgery. Both patients are followed up regularly with laboratory tests and radiological imaging.

PSTTs are extremely rare in GTD and have an unpredictable malignant potential and highly variable clinical course. They can present as fulminant metastatic disease, resistant to conventional treating modalities. PSTTs account for 0.31–2% of all trophoblastic disease. The reported rate of PSTT to choriocarcinoma is 1 of 138. The disease is usually seen in young women, although cases have been reported in postmenopausal women. The mean age at diagnosis is 31–33 years, and it can appear following any type of pregnancy [6]. The adverse factors affecting survival in PSTT were reported as age above 35 years, interval since the last pregnancy of more than 2 years, Stage III or IV deep myometrial invasion, maximum hCG level higher than 1000 mIU/mL, extensive coagulative necrosis, high mitotic rate, and the presence of cells with clear cytoplasm [7]. Our patients were 34 and 38 years old, and the tumor occurred after a term pregnancy in the first patient and a spontaneous abortion in the second.

This tumor produces human placental lactogen (hPL) and lower hCG levels than those seen in choriocarcinoma. Unlike choriocarcinoma, the serum β-hCG level in PSTT is not correlated with tumor burden or malignant behavior. Therefore, β-hCG appears to have no predictive value and the disease may still progress even if β-hCG levels are not elevated. The range of serum β-hCG concentrations at diagnosis is lower than 1000 mIU/mL in 79% of the patients and lower than 500 mIU/mL in 58% of the patients. We cannot measure hPL in our laboratory. The β-hCG level was 337 mIU/mL in the first patient and 763 mIU/mL in the second; these levels are lower than those seen in choriocarcinoma. The most frequent presenting symptom is vaginal bleeding (79%). In the Feltmate

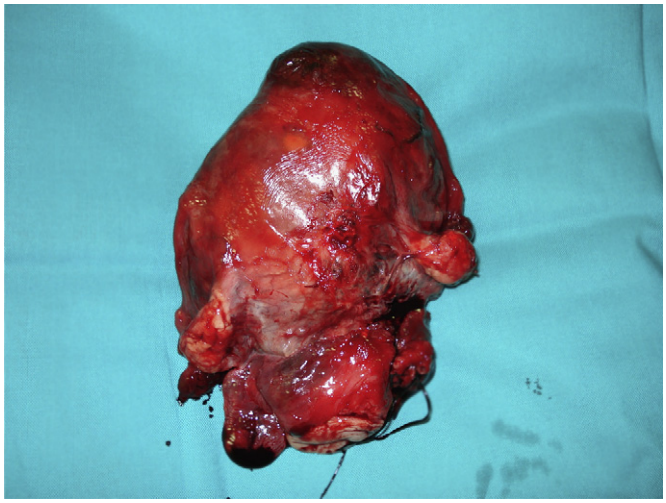

Fig. 2. . The postoperative photograph of the case. Uterus was large, soft, and included extremely vascular; in addition, the tumor penetrated both the ovaries.

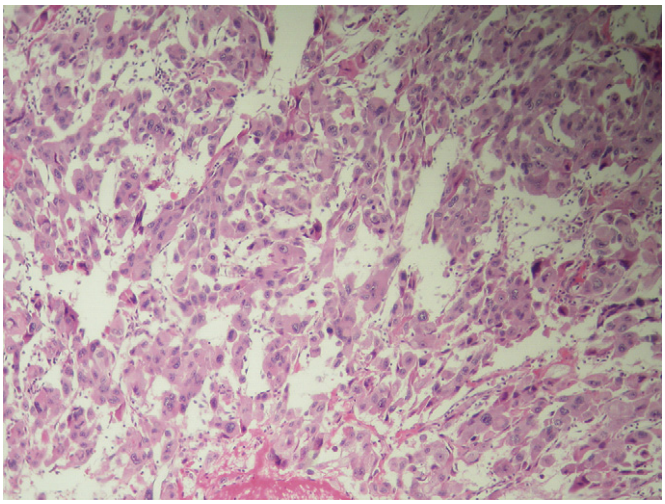

Fig. 3. The tumor cells showing medium-sized intermediate trophoblastic cells (hematoxylin-eosin stain, ×100).

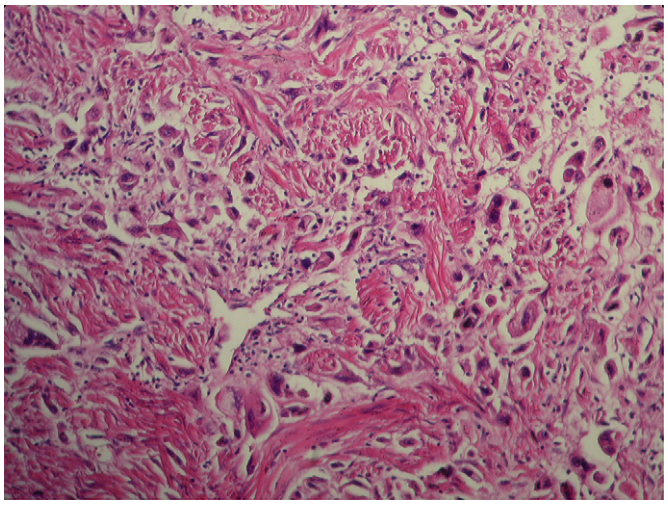

Fig. 4. Medium sized intermediate trophoblastic cells infiltrating the myometrium (hematoxylin-eosin stain, ×200).

series, 92% presented with amenorrhea or abnormal bleeding [8]. One of our patients had amenorrhea and the other had vaginal bleeding.

The reported outcome of PSTT is highly variable. All cases of metastasis to vital organs, such as the brain, result in mortality despite all forms of treatment. In our first case, the tumor extended to the parametrium, whereas the second was limited to the uterine wall. Unlike choriocarcinoma, PSTT is relatively resistant to chemotherapy. Consequently, surgery is the mainstay of treatment. The most recent data from different centers suggest that EMA alternating with etoposide and cisplatin is the most effective treatment for metastatic or recurrent PSTTs [7]. Schmid et al [9] reported that the probability of overall survival for PSTT cases was 70% and recurrence-free survival was 73% and they also told that surgery is the sufficient therapy for Stage I cases, whereas combined surgery and chemotherapy is needed for Stage II, III, and IV. We treated both cases with combined EMA/CO chemotherapy; β-hCG levels subsequently decreased to the normal range and have remained normal. There has been no recurrence during the follow-up period.

In conclusion, PSTTs are extremely rare worldwide. This type of tumor may be seen after term pregnancy or spontaneous abortion and produces hPL and lower β-hCG levels than those seen in choriocarcinoma. We suggest that gynecologists should consider this tumor during the postpartum and postabortion periods. With surgery and subsequent combined chemotherapy, PSTT is curable.

Acknowledgment

The authors thank www.textcheck.com (http://www.textcheck.com/certificate/mD9eDE) for English revision.

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