Clinical characteristics and outcomes of placental site trophoblastic tumor: experience of single institution in Korea

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Objective

Placental site trophoblastic tumor (PSTT) is the rarest form of gestational trophoblastic disease (GTD) and the optimum management is still controversial. In this study, we analyzed the clinical features, treatment, and outcomes of 6 consecutive patients with PSTT treated in our institution.

Methods

The electronic medical record database of Samsung Medical Center was screened to identify patients with PSTT from 1994 to 2017. Medical records for the details of each patient's clinical features and treatment were extracted and reviewed. This study was approved Institutional Review Board of our hospital.

Results

A total of 418 cases of GTD, 6 (1.4%) patients with PSTT were identified. The median age of the patients was 31 years. The antecedent pregnancy was term in all 5 cases with available antecedent pregnancy information and the median interval from pregnancy to diagnosis of PSTT was 8 months. The median titer of serum beta human chorionic gonadotropin (β-hCG) at diagnosis was 190.9 mIU/mL. Five (83.3%) patients presented with irregular vaginal bleeding and one (16.7%) had amenorrhea. All patients had disease confined to the uterus without metastasis at diagnosis and were successfully treated by hysterectomy alone. All of them were alive without disease during the follow-up period.

Conclusion

In this study, we observed low level serum β-hCG titer and irregular vaginal bleeding with varying interval after antecedent term pregnancy were most common presenting features of PSTT. In addition, we demonstrated hysterectomy alone was successful for the treatment of stage I disease of PSTT.

Keywords: Placental site trophoblastic tumor; Gestational trophoblastic disease; Prognosis

Introduction

Gestational trophoblastic disease (GTD) defines a heterogeneous group of lesions arising from abnormal cellular proliferation of placental villous trophoblast. Subtypes of GTD include partial and complete hydatidiform mole and gestational trophoblastic neoplasia (GTN). GTNs can be pathologically classified into invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT) with the potential for local invasion and metastasis, leading to fatal condition if left untreated.

PSTT is extremely rare tumor type in this group, originates

from intermediate trophoblastic cells in implantation site. It consists 0.25–5% of all gestational trophoblastic tumors with an estimated incidence of 1 in 100,000 pregnancies [1]. This disease was first recognized in 1976, Kurman et al. [2] used the term 'trophoblastic pseudotumor,' established the trophoblastic origin of the lesion and it was thought at first to be a benign variant of gestational trophoblastic tumors. After reports of several fatal cases, PSTT was named to describe the malignant potential of this tumor in 1981 [3]. Since this initial description, approximately 300 cases have been reported in the literature [4]. Most PSTTs behave in a benign feature, but approximately 10–15% of patients are clinically malignant and the mortality rate is 25% in reported literature [5].

PSTT is distinct from other type of GTN, characterized by slow growth, low concentration of serum beta human chorionic gonadotropin (β-hCG), the late onset metastatic potential, resistance to chemotherapy. The treatment of PSTT is controversial but hysterectomy is an important and valuable primary treatment, in particular for the disease localized to the uterus [6]. In this study, we showed clinical characteristics and outcomes of 6 patients of PSTT treated successfully by hysterectomy alone in our hospital in addition to one case presentation.

Materials and methods

In this retrospective study, data were analyzed from all cases of PSTT managed at the Samsung Medical Center, from 1994 to 2017. Patients were identified from an electronic medical record database of Samsung Medical Center. Institutional Review Board (2017-12-054) approval was obtained for the present study. Data were extracted and analyzed including age at diagnosis, antecedent pregnancy, interval from antecedent pregnancy, presenting features, presenting serum β-hCG level, number and sites of metastases, treatment re-

Table 1. Clinical features, treatment, outcome in 6 patients with placental site trophoblastic tumor

Characteristic	Patient number					
	1	2	3	4	5	6
Age (yr)	29	32	32	29	31	33
AP	N/A	Term	Term	Term	Term	Term
Interval from AP (mon)	N/A	6	N/A	3	10	12
Presenting features	IVB	IVB	IVB	IVB	IVB	Amenorrhea
β-hCG at diagnosis (mIU/mL)	171.0	32.0	0.4	35.9	2.6	903.5
FIGO stage	I	I	I	I	I	I
Mets (No./site)	-	-	-	-	-	-
Myometrial invasion	Superficial	Deep	Superficial	Superficial	N/A	Deep
Mitotic index, (mitoses/0 HPF)	N/A	N/A	N/A	8	N/A	4
IHC	N/A	N/A	Ki-67 (5–10%), CK 8 & 18, CD 10	Ki-67 (>10%)	Ki-67 (>10%), hCG	Ki-67 (20%), hPL, hCG, CK 7
Dx procedure	D/E	D/C/B	D/C/B	D/C/B	D/C/B	Image
Surgery	TAH	TAH, RSO, LS, PLND	SPA-H, BS	TAH, ROC	LAVH	TAH, BS
Chemotherapy	-	-	-	-	-	-
Outcome	NED	NED	NED	NED	NED	NED
Follow-up (mon)	2	84	46	73	48	1

AP, antecedent pregnancy; IVB, irregular vaginal bleeding; hCG, human chorionic gonadotropin; β-hCG, beta human chorionic gonadotropin; FIGO, International Federation of Gynecology and Obstetrics; Mets, metastasis; HPF, high-power field; IHC, immunohistochemistry; CK, cytokeratin; hPL, human placental lactogen; Dx, diagnostic; D/E, dilatation and evacuation; D/C/B, dilatation and curettage and biopsy; TAH, total abdominal hysterectomy; RSO, right salpingo-oophorectomy; LS, left salpingectomy; PLND, pelvic lymph node dissection; SPA-H, single port assisted laparoscopic hysterectomy; BS, bilateral salpingectomy; ROC, right ovarian cystectomy; LAVH, laparoscopic assisted vaginal hysterectomy; NED, no evidence of disease; N/A, not available in reported pathologic data.

Obstetrics & Gynecology Science

Hye-joo Lee, et al. Placental site trophoblastic tumor

ceived, pathologic reports, outcome during follow-up. Pathologic slides of all patients were reviewed by one gynecologic pathologist . Tumors were staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging system [7].

Results

We identified 418 registrations for GTD and 6 patients had histologically confirmed PSTT for an overall frequency of 1.4%, reflecting the rarity of this condition relative to other forms of GTD. The results of features, treatment, and outcome for all patients are summarized in Table 1.

The median age of the patients was 31 years (range 29–33 years). Among 5 patients who had documented antecedent pregnancy prior to the diagnosis, a full-term pregnancy was identified in all 5 cases: In one case (patient 1), there was no documented information about pregnancies prior to the diagnosis of PSTT. In 4 patients who had documented interval between termination of previous pregnancy and diagnosis, the median interval from pregnancy to diagnosis of PSTT was 8 months (range 3–12 months); Information about period between antecedent pregnancy and diagnosis was not available in one patient (patient 3). The serum β-hCG titers exhibited broad range of relatively low concentration at the diagnosis: The median β-hCG was 34.0 mIU/mL (range 0.4–903.5 mIU/mL).

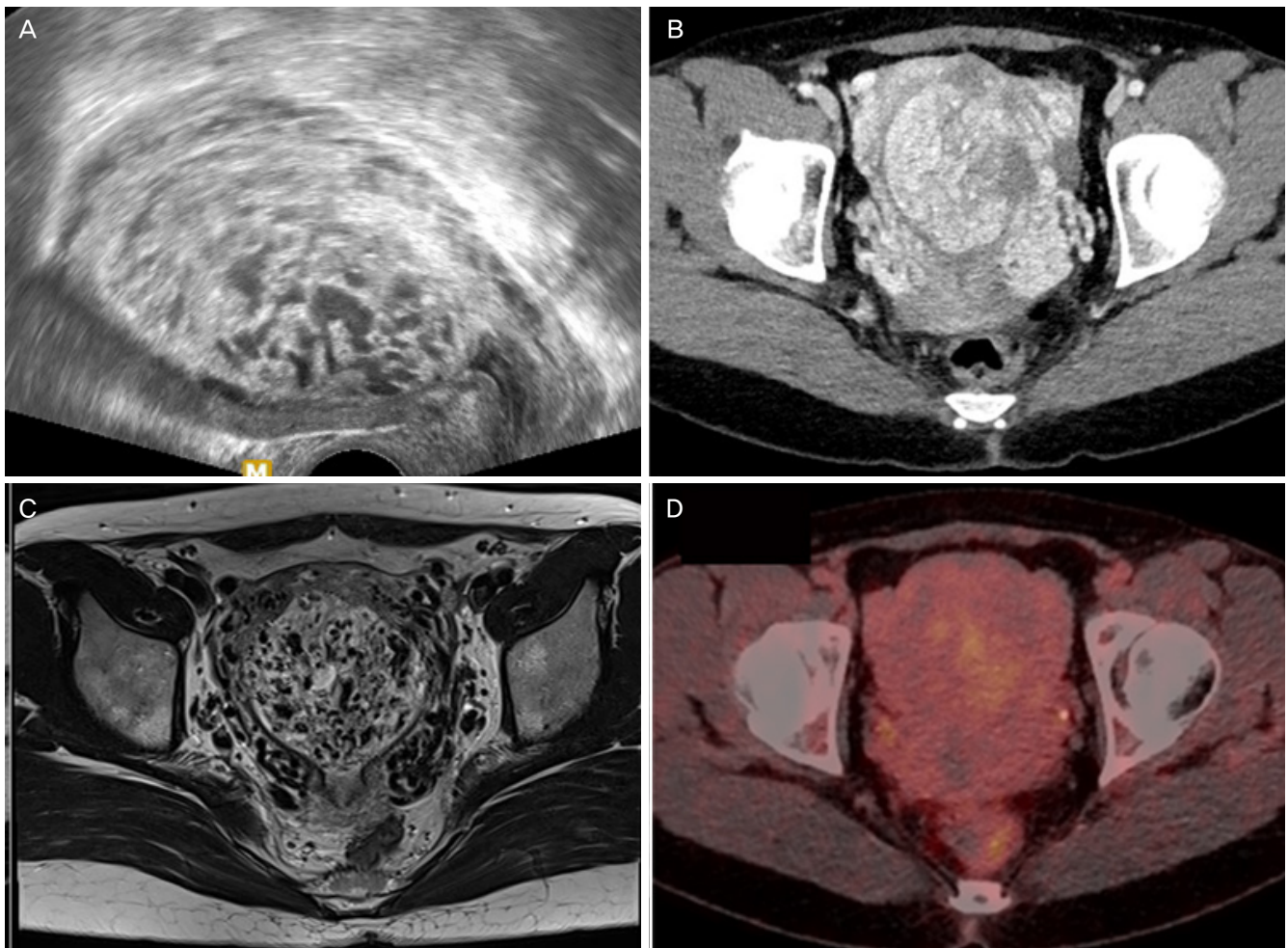Five of the 6 patients had irregular vaginal bleeding at pre-

Fig. 1. Image findings of case 6. (A) Transvaginal ultrasonography showed a multicystic mass measuring 7.8×5.1 cm in the posterior uterine wall with abundant blood flow, suspected gestational trophoblastic neoplasia. (B) Abdomen-pelvis computed tomography. (C) Pelvis magnetic resonance imaging showed about 7.2 cm sized mass with internal vascular structure in uterus. (D) Positron emission tomography-computed tomography.
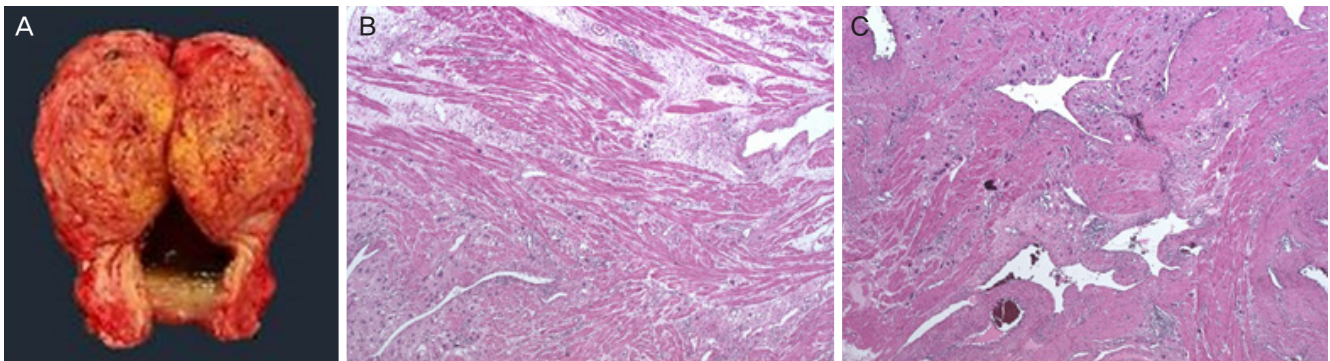
Fig. 2. (A) Macroscopic features of placental site trophoblastic tumor: about 6.5×4.2 cm sized irregular mass with infiltration of full depth of myometrium. (B) The placental site trophoblastic tumor had monomorphic intermediate trophoblastic cells extensively infiltrating the myometrium. (C) The tumor cells are large, mononucleate placental site intermediate trophoblast with scattered multinucleated cells. The cells have abundant eosinophilic cytoplasm and marked nuclear pleomorphism with large convoluted nuclei (hematoxylin and eosin staining, original magnification ×50, ×50).

sentation and underwent endometrial biopsy (dilatation/curettage or dilatation/evacuation) for diagnosis, which provided positive diagnosis of PSTT; patient 6 was tentatively diagnosed as choriocarcinoma or PSTT before surgery by clinical features and MRI findings (Fig. 1) and biopsy was not performed before surgery due to risk of severe bleeding during the biopsy. There was no definite evidence of metastasis in the radiologic studies in all 6 patients, so they underwent hysterectomy.

The pathologic reports of 6 patients were reviewed and confirmed as PSTT. All tumors were characterized microscopically by nuclear and cytoplasmic pleomorphism of intermediate trophoblast cells. Interestingly, all 6 cases presented with disease confined to the uterus (Fig. 2). Deep myometrial invasion (tumor infiltration of more than one half of the myometrium) was observed in 3 (50%) patients and superficial invasion (tumor infiltration less than one half of myometrium) in 3 (50%) patients.

In 4 of 6 cases, results of immunohistochemistry were available. The tumor cells were labeled with Ki-67 staining ranged from 5–20%. The tumor cells stained positive for hPL in 2 cases (patient 5, 6) tested for hPL (Fig. 3). Immunoreactivity for hCG was seen in 2 cases (patient 5, 6) tested for hCG but was focally positive in both cases.

After surgical treatment, chemotherapy was not given since all 6 patients were stage I. The median follow-up was 47 months (range 2–84) and none of them have evidence of disease recurrence in the follow-up period.

Discussion

PSTT usually presents with irregular vaginal bleeding months or even years after the last pregnancy. Other presentations are amenorrhea, palpable abdominal mass and postmenopausal bleeding in decreasing order of frequency. Rare symptoms are contingent on site of metastasis such as cough, dizziness, headache, or back pain. In this study, we also observed irregular vaginal bleeding was the most common symptom (83.3%, Table 1).

In the normal implantation site, the invasion of intermediate trophoblast is tightly regulated and is confined to the inner third of the myometrium. In contrast, the tumor cells of PSTT are highly invasive and infiltrate deeply into the myometrium, occasionally penetrating through the uterine wall. One half (50%) of our patients exhibited deep myometrial invasion (Table 1). In pathologic finding, PSTT shows deep infiltration into the myometrium and the tumor cells are large, mononucleate placental site intermediate trophoblasts with scattered multinucleated cells. The cells have abundant eosinophilic cytoplasm and marked nuclear pleomorphism with large convoluted nuclei. These findings were consistent with our cases (Fig. 2B and C).

Clinically, distinguishing PSTT from other types of GTN or other neoplastic disease is important as far as treatment plans are concerned. Immunohistochemistry examination has distinct value in diagnosing PSTT and is currently considered to be the golden standard for diagnosis of PSTT [8]. The tumor cells usually have a high level of Ki-67 expression which is a
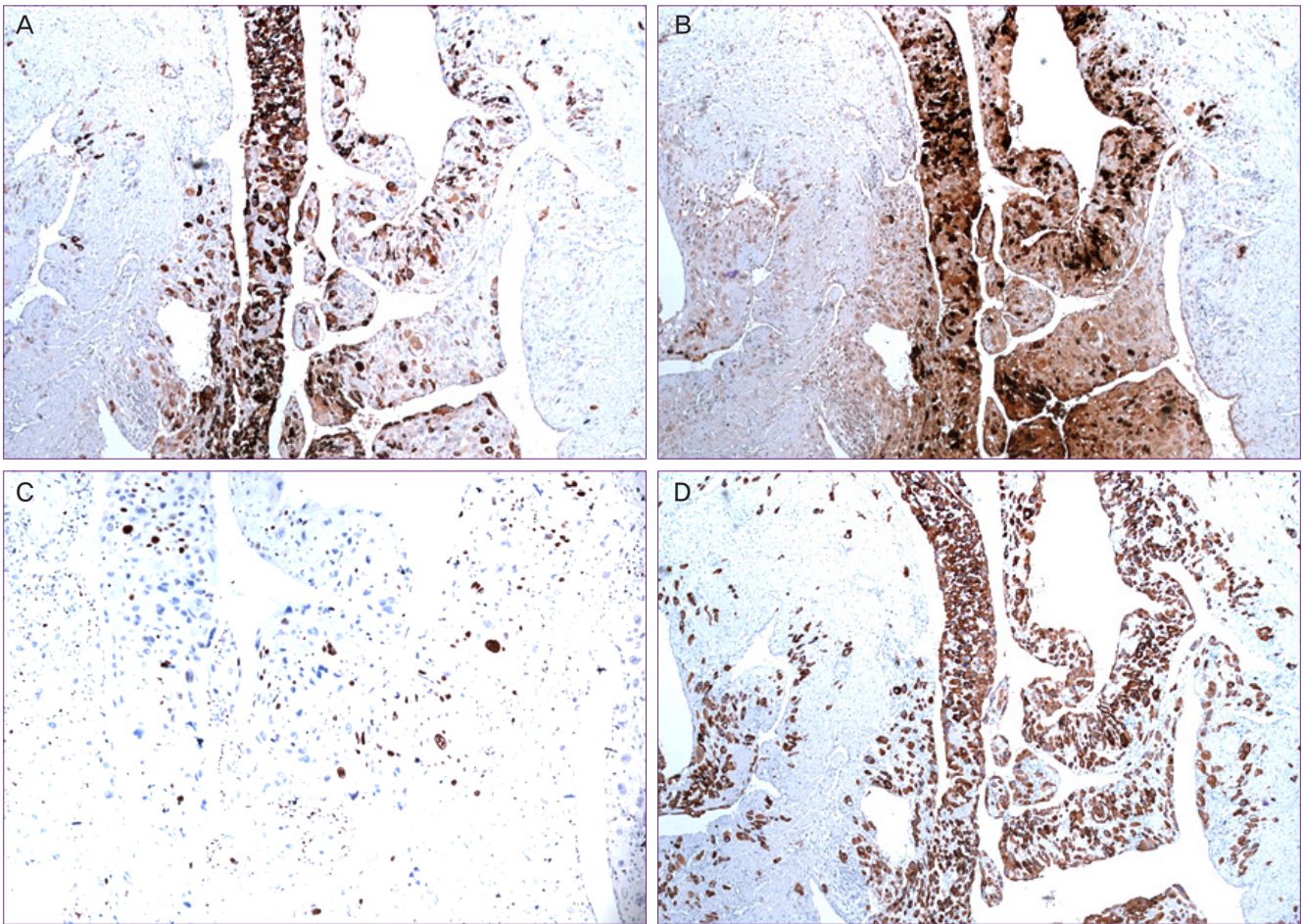
Fig. 3. Immunohistochemical findings of case 6. (A) Tumor cells were positive for human placental lactogen. (B) Tumor cells were focally positive for human chorionic gonadotropin. (C) About 20% of the tumor cells were positive for Ki-67. (D) Tumor cells were strongly positive for cytokeratin 7.

marker of cell proliferation activity in tissues [9]. Determining the Ki-67 labeling index can be useful for the differential diagnosis of trophoblastic tumors. Choriocarcinomas are diffusely labeled with Ki-67 (>50%), whereas most of PSTT contain approximately 8–20% of Ki-67 positive cells [9]. In our cases, we found Ki-67 expression in 5–20% consistent with literature (Table 1, Fig. 3). hPL, normally secreted by syncytiotrophoblast, is highly expressed in the trophoblasts of PSTT and is expressed in most of the trophoblastic cells of PSTT. hCG and placental alkaline phosphatase are secreted by syncytiotrophoblast cells, these markers are rarely evident or even absent in a PSTT [9]. In this study, we also observed diffuse hPL expression and relatively focal expression of hCG in patient 5, 6 specimens (Fig. 3).

Histological findings from a PSTT are specific, but it is difficult to distinguish the benign or malignant characteristics of a

PSTT. A high mitotic rate of more than 5/10 high-power field and substantial hemorrhaging and necrosis within the tumor has been suggested malignancy and the essential pathologic predictor for disease recurrence [10].

Hysterectomy is recommended for patients with PSTT if fertility need not be preserved and the disease is localized to the uterus. Additionally, oophorectomy is not considered routinely because ovarian metastases are uncommon and an oophorectomy cannot improve prognosis [11]. In a recent study, PSTT tend to spread through lymphatic pathways, resulting in relative resistance to chemotherapy [12]. But the role of lymphadenectomy in the surgical management of PSTT is still controversial [13]. In the current study, all our 6 patients were treated successfully by hysterectomy alone since they were stage I and alive without evidence of disease until last follow-up indicating surgery is appropriate treatment for localized

Table 2. Summary of reports of placental site trophoblastic tumor in literature

Author	No. of cases	Age (mean, yr)	AP	Interval to AP (median, mon)	β-hCG (median, IU/L)	Prognostic risk factors	Treatment (percent of patients)	Outcome (survival or NED[a])
Chang et al. [20]	88	30.0	Term/preterm (59%) Abortion (26%) H-mole (13%) Choriocarcinoma (2%) Unknown (13%)	12.00	467.3	FIGO stage	Hysterectomy (84%) Adjuvant CTx (25%) Primary CTx (34%)	OS - Stage I/II: 93.5% - Stage III/IV: 33.3%
Feltmate et al. [15]	13	31.2	Term (54%) Abortion (38%) H-mole (8%)	16.50	257.0	Interval from AP (>24 mon) Mitotic index Metastatic disease	Hysterectomy (92%) Adjuvant CTx (55%) Primary CTx (44%) - Immediate CTx (≤1 wk from surgery) in high risk - EMA-EP for adjuvant CTx	Not reported
Hassadia et al. [17]	17	36.1	Term (59%) Abortion (12%) Unknown (29%)	18.00	13,923	FIGO stage (IV) Interval from AP (>48 mon) β-hCG (>10,000) Age (>40 yr)	Hysterectomy (65%) Adjuvant CTx (29%) Primary CTx (35%)	NED - Stage I: 47% - Stage III: 29%
Baergen et al. [6]	55	32.0	Term (57%) Abortion (17%) H-mole (26%)	18.00	691.0	FIGO stage (III/IV) Interval from AP (>24 mon) β-hCG Deep invasion Mitotic index Clear cytoplasm Tumor necrosis Age (>35 yr)	Hysterectomy (89%) Adjuvant CTx (35%)	OS: 80–86% - Stage I: 91–92% - Stage III/IV: 41%
Schmid et al. [18]	62	34.6	Term (60%) Stillbirth (16%) Abortion (10%) H-mole (15%)	18.00	<1,000.0	FIGO stage Interval from AP (>48 mon) Prognostic score Mitotic index β-hCG Age No. of metastasis	Hysterectomy (85%) Adjuvant CTx (13%) Primary CTx (32%)	OS: 70% - Stage I: 93% - Stage II: 52% - Stage III/IV: 49%
Lan et al. [12]	5	36.4	Term (60%) Stillbirth (20%) Abortion (20%)	7.00	50.0	LN metastasis	Hysterectomy (100%) Adjuvant CTx (60%)	NED - Stage I: 40% - Stage II: 20%
Chen et al. [16]	17	31.7	Term (88.2%) Abortion (12.8%)	14.20	556.7	Not reported	Hysterectomy (100%) Adjuvant CTx (47%) - EMA-CO for adjuvant CTx	NED - Stage I: 82.3% - Stage III:12.8%

Obstetrics & Gynecology Science

Hye-joo Lee, et al. Placental site trophoblastic tumor

Table 2. Continued

Author	No. of cases	Age (mean, yr)	AP	Interval to AP (median, mon)	β-hCG (median, IU/L)	Prognostic risk factors	Treatment (percent of patients)	Outcome (survival or NED[a])
Hyman et al. [21]	17	34.1	Term (53%) Abortion (35%) H-mole (12%)	9.00	132.0	FIGO stage Interval from AP (>12 mon) Term AP β-hCG Age (>40 yr)	Hysterectomy (94.1%) Adjuvant CTx (100%) - Beneficial Tx for Stage I: hysterectomy only	NED - Stage I: 85.7% - Stage III/IV: 33%
Zhao et al. [19]	108	31.8	Term/preterm (62%) Abortion (28.7%) H-mole (7.4%) Unknown (1.9%)	25.13	154.3	FIGO stage Interval from AP (>36 mon) Prognostic score Tumor necrosis Deep invasion (>50%)	Hysterectomy (78.7%) Preserve fertility Tx[b] (21.3%) - No significant difference in stage I PSTT Adjuvant CTx (79.6%)	OS: 93.5% - Stage I: 100% - Stage III/IV: 87.9%
Our study	6	31.0	Term (83.3%) Unknown (16.7%)	8.00	34.0	Not determined	Hysterectomy (100%)	NED - Stage I: 100%

AP, antecedent pregnancy; β-hCG, beta human chorionic gonadotropin; NED, no evidence of disease; FIGO, International Federation of Gynecology and Obstetrics; CTx, chemotherapy; OS, overall survival; EMA-EP, etoposide, methotrexate, actinomycin D/etoposide, cisplatin; LN, lymph node; EMA-CO, etoposide, methotrexate, actinomycin D/cyclophosphamide, vincristine; Tx, treatment.
[a]Until last follow-up; [b]Curettage (10.2%), excision of uterine lesion (9.3%), pulmonary lobectomy (1.8%).

PSTT. Although there is no conclusive evidence to support adjuvant chemotherapy in PSTT, it is reasonable to consider adjuvant chemotherapy in patients with risk factors associated with bad prognosis. In the literature [14], adjuvant chemotherapy may be considered for patients with a time interval of (≥4 years) from the antecedent pregnancy and advanced stage (FIGO stage III–IV) disease. While some investigators suggest adjuvant chemotherapy in stage I disease with deep myometrial invasion or serosal involvement, there is currently no data to support this recommendation [13]. Although there are several chemotherapy regimens used to treat PSTT with metastatic disease, optimal regimen is not identified because of the rarity of disease and the lack of controlled trials. Despite the lack of any conclusive differences between regimens, etoposide, methotrexate, actinomycin D/ cyclophosphamide, vincristine [15] or etoposide, methotrexate, actinomycin D/ etoposide, cisplatin [16] are the preferential adjuvant chemotherapy (Table 2).

In 2002, the FIGO defined criteria for the diagnosis of postmolar disease and adopted a combined anatomic staging and modified World Health Organization risk factor scoring system for GTN [7]. The factors are FIGO staging, age, type and interval of antecedent pregnancy, β-hCG at diagnosis, tumor size, site and number of metastasis, previous chemotherapy. But, individual FIGO risk scores were not a reliable predictor and do not correlate well with outcome for most patients of PSTT since the range was narrow and clustered around the low/high risk cut off [17]. So, PSTT is classified separately and it is now recommended that scores should not be used to guide treatment in PSTT since chemotherapy is not routinely given in patients with PSTT [14].

There is still controversy for potential prognostic factors in PSTT. In the literature, several risk factors appear to be associated with clinical outcomes and Table 2 summarized the reported analyses. These are FIGO stage, advanced age, an interval from the preceding pregnancy, deep myometrial invasion, a high mitotic rate and high β-hCG level; further studies are warranted to determine accurate significance of each risk factors.

The survival rate has been known approximately 100% for non-metastatic disease and 50–60% for metastatic disease [14]. According to the retrospective study [18], long term survival for stage I patients with PSTT with low risk disease after hysterectomy is nearly 90% at 10 years. In patients with stage II–IV disease, surgical resection and che-

motherapy have resulted in approximately 50% overall survival at 10 years. In patients with stage I disease who underwent hysterectomy for initial treatment have excellent prognosis (overall survival range 92–100%), except one study [12] with small number of cases (Table 2). If young patients want to preserve fertility, they should be carefully counseled. Zhao et al. [19] demonstrated that fertility preservation is feasible for young patients with localized PSTT lesions with the intention of preserving fertility. They reported that the patients had preserved fertility neither resulted in poor outcome nor an increased risk of relapse. However, the preservation of fertility is not recommended routinely, especially for patients whose lesion is diffuse or who have adverse prognostic factors.

In conclusion, PSTT is the extremely rare type of GTN with unpredictable biological behavior. The diagnosis should be suspected when intrauterine mass is observed in sonographic and/or radiologic examinations and the serum β-hCG titer is elevated in low level in patients presented irregular vaginal bleeding with varying interval after antecedent term pregnancy. Pathologic and immunohistochemistry findings are most important for the accurate diagnosis. Total hysterectomy remains main stay for the primary treatment of patients with PSTT, in particular disease confined to uterus. In this study, we also demonstrated hysterectomy alone was successful for the treatment of stage I disease of PSTT. Although PSTT has been known relatively resistant to chemotherapy, further studies are necessary to determine the role of chemotherapy in this disease as well as appropriate indication of chemotherapy in stage I disease.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

1. Behnamfar F, Mousavi A, Rezapourian P, Zamani A. Placental site trophoblastic tumor, report of a case with unusual presentation. Placenta 2013;34:460-2.
2. Kurman RJ, Scully RE, Norris HJ. Trophoblastic pseudotumor of the uterus: an exaggerated form of "syncytial endometritis" simulating a malignant tumor. Cancer 1976;38:1214-26.
3. Scully RE, Young RH. Trophoblastic pseudotumor: a reappraisal. Am J Surg Pathol 1981;5:75-6.
4. Luiza JW, Taylor SE, Gao FF, Edwards RP. Placental site trophoblastic tumor: Immunohistochemistry algorithm key to diagnosis and review of literature. Gynecol Oncol Case Rep 2014;7:13-5.
5. Piura B, Rabinovich A, Meirovitz M, Shaco-Levy R. Placental site trophoblastic tumor: report of four cases and review of literature. Int J Gynecol Cancer 2007;17:258-62.
6. Baergen RN, Rutgers JL, Young RH, Osann K, Scully RE. Placental site trophoblastic tumor: a study of 55 cases and review of the literature emphasizing factors of prognostic significance. Gynecol Oncol 2006;100:511-20.
7. Ngan HY, Bender H, Benedet JL, Jones H, Montruccoli GC, Pecorelli S, et al. Gestational trophoblastic neoplasia, FIGO 2000 staging and classification. Int J Gynaecol Obstet 2003;83 Suppl 1:175-7.
8. Huang F, Zheng W, Liang Q, Yin T. Diagnosis and treatment of placental site trophoblastic tumor. Int J Clin Exp Pathol 2013;6:1448-51.
9. Shih IeM. Trophogram, an immunohistochemistry-based algorithmic approach, in the differential diagnosis of trophoblastic tumors and tumorlike lesions. Ann Diagn Pathol 2007;11:228-34.
10. Zheng Y, Bao L, Ning Y, Lu X, Hua K, Yi X. Retrospective analysis of the clinicopathologic and prognostic characteristics of stage I placental site trophoblastic tumor in China. Int J Gynaecol Obstet 2015;129:67-70.
11. Saso S, Haddad J, Ellis P, Lindsay I, Sebire NJ, McIndoe A, et al. Placental site trophoblastic tumours and the concept of fertility preservation. BJOG 2012;119:369-74.
12. Lan C, Li Y, He J, Liu J. Placental site trophoblastic tumor: lymphatic spread and possible target markers. Gynecol Oncol 2010;116:430-7.
13. Horowitz NS, Goldstein DP, Berkowitz RS. Placental site trophoblastic tumors and epithelioid trophoblastic tumors: biology, natural history, and treatment modalities. Gynecol Oncol 2017;144:208-14.
14. Lurain JR. Gestational trophoblastic disease II: classification and management of gestational trophoblastic neoplasia. Am J Obstet Gynecol 2011;204:11-8.
15. Feltmate CM, Genest DR, Wise L, Bernstein MR, Goldstein DP, Berkowitz RS. Placental site trophoblastic tu-

Obstetrics & Gynecology Science

Hye-joo Lee, et al. Placental site trophoblastic tumor

mor: a 17-year experience at the New England Trophoblastic Disease Center. Gynecol Oncol 2001;82:415-9.

16. Chen Y, Zhang X, Xie X. Clinical features of 17 cases of placental site trophoblastic tumor. Int J Gynaecol Obstet 2011;115:204-5.

17. Hassadia A, Gillespie A, Tidy J, Everard RG, Wells M, Coleman R, et al. Placental site trophoblastic tumour: clinical features and management. Gynecol Oncol 2005;99:603-7.

18. Schmid P, Nagai Y, Agarwal R, Hancock B, Savage PM, Sebire NJ, et al. Prognostic markers and long-term outcome of placental-site trophoblastic tumours: a retrospective observational study. Lancet 2009;374:48-55.

19. Zhao J, Lv WG, Feng FZ, Wan XR, Liu JH, Yi XF, et al. Placental site trophoblastic tumor: a review of 108 cases and their implications for prognosis and treatment. Gynecol Oncol 2016;142:102-8.

20. Chang YL, Chang TC, Hsueh S, Huang KG, Wang PN, Liu HP, et al. Prognostic factors and treatment for placental site trophoblastic tumor-report of 3 cases and analysis of 88 cases. Gynecol Oncol 1999;73:216-22.

21. Hyman DM, Bakios L, Gualtiere G, Carr C, Grisham RN, Makker V, et al. Placental site trophoblastic tumor: analysis of presentation, treatment, and outcome. Gynecol Oncol 2013;129:58-62.