Placental site trophoblastic tumor on endometrial polyp: a case report

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Summary

Placental site trophoblastic tumor (PSTT) is the least common form of gestational trophoblastic disease (GTD), and is biologically different from other forms of GTD. There is a wide clinical spectrum of presentation and behavior ranging from a benign condition to an aggressive disease with a fatal outcome. The authors document a case of PSTT on an endometrial polyp. A 51-year-old woman had abnormal vaginal bleeding for the duration of two months. Her past history included a vaginal delivery in 1998. Her physical examination was normal. Tumor markers were at normal levels. Serum β- human chorionic gonadotropin (hCG) level was 19 mIU/ml and human placental lactogen (hPL) level was in the normal range. The patient underwent an operative hysteroscopy. On examination the uterine cavity appeared to be occupied by a pedunculated polypoid neoformation measuring about 2.5 cm in diameter which was removed and later determined to be a PSTT. There were occasional mitotic figures (0-1/10 high power field). The patient underwent hysterectomy and bilateral salpingo-oophorectomy. The patient has no evidence of disease six months after surgery. The authors conclude that a high mitotic count and atypical undifferentiated pathological features are significant poor prognostic factors for survival in PSTT. Hysterectomy represents the gold standard of treatment in all cases of disease confined to the uterus.

Key words: Placental site trophoblastic tumor; Gestational trophoblastic disease; Mitosis; Hysterectomy.

Introduction

Placental site trophoblastic tumor (PSTT) is a rare form of gestational trophoblastic disease that accounts for one to two percent of gestational trophoblastic disease (GTD) and is biologically different from others forms of GTD with approximately 200 cases reported in the literature [1-6]. There is a wide clinical spectrum of presentation and behaviour ranging from benign conditions to an aggressive disease with fatal outcome. While most cases confined to the uterus have a benign clinical course, some cases with metastasis are clearly associated with poor prognosis.

Case Report

In November 2011, a 51-year-old woman (gravida 1, para 1) was referred for recurrent uterine bleeding of two months' duration. Her past history included a vaginal delivery in 1998 and after a full-term pregnancy of 40 weeks, she delivered a male infant.

Ultrasound examination showed an overhanging 2.5 cm heterogeneous mass in the uterine cavity with moderate to minimal blood flow with colour Doppler flow imaging (CDFI). The uterine adnexa were normal and the Douglas pouch was empty of fluids.

A diagnostic hysteroscopy was performed showed the presence of an endometrial pedunculated neoformation that was blackish in colour and taut in consistency. The biopsy sample histological examination of the neoformation proved to be an endometrial polyp.

The patient was readmitted one month later for metrorrhagia. On ultrasound examination, the uterus measured 82 x 53 x 69 mm. The endometrium was 18.8 mm at its thickest point and colour Doppler examination showed a poorly vascularised non-homogenous ecostructure. The left ovary was normal and there was a simple cyst in the right ovary. There were no abdominal fluids.

Her physical examination was normal. Tumour markers (squamous cell carcinoma (SCC), carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, alpha-fetoprotein (AFP) and CA125 were at normal levels. Serum β- human chorionic gonadotropin (hCG) level was 19 mIU/ml (normal range (NR), under one mIU/ml) and human placental lactogen (hPL) level was in the normal range.

The patient underwent an operative hysteroscopy under analgesia. On examination the uterine cavity appeared to be occupied by a pedunculated polypoid neoformation measuring about 2.5 cm in diameter which was removed and later determined to be a PSTT.

Microscopic examination showed multiple fragments of endometrial polyp, as well as some fragments with invading tumor cells in nests and cords, separating myometrial muscle fibres, both individually and in groups. These tumour cells were large and polygonal with irregular vesicular nuclei and prominent nucleoli while showing abundant dense eosinophilic to amphophilic cytoplasm with occasional vacuoles (Figure 1). Abundant extracellular fibrinoid material was seen around the tumour nests; multinucleated cells with marked nuclear pleomorphism mimicking syncytiotrophoblast were noted and the villi were absent. There were occasional mitotic figures (0-1/10 high power field) (HPF) (Figure 2). On immunohistochemical analysis, the tumour cells resulted positive for keratin (Figure 3A), hCG (Figure 3B), and epithelial membrane antigen (EMA) (Figure 3C).

A computerised tomography (CT) scan of the chest showed micronodules, not calcifications, in the parenchyma of both lungs as well as paracervical lymph node swelling; Abdominal CT detected thickening of the left levator ani muscle (Figure 4) and hypodensity of the endometrium that extended in the right half of the myometrium (Figure 5).

Open laparoscopy was scheduled for March 2013. The authors carried out a total hysterectomy with bilateral salpingo-oophorectomy. The procedure was with four entrance ports, hysterectomy with vaginal delivery of the uterus, and colporraphy vaginal repair. No pelvic fluid was found in the abdominal cavity. The uterus,

Revised manuscript accepted for publication June 24, 2013

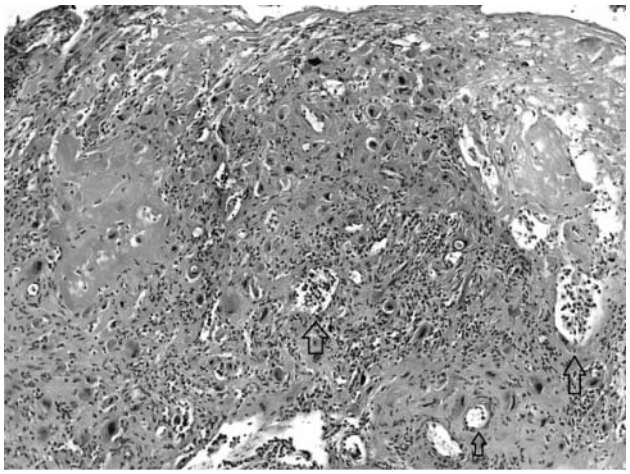

Figure 1. — Large pleomorphic polyhedral cells with abundant amphophilic cytoplasm, invading the miometrium. Typical intraluminal "vascular invasion" (arrows) by trophoblastic cells.

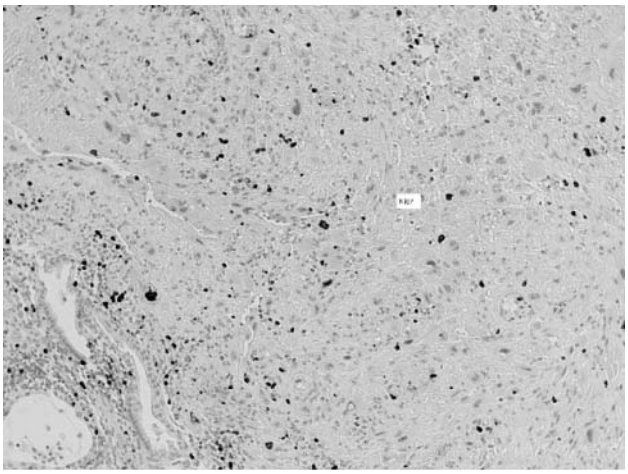

Figure 2. — Low mitotic index.

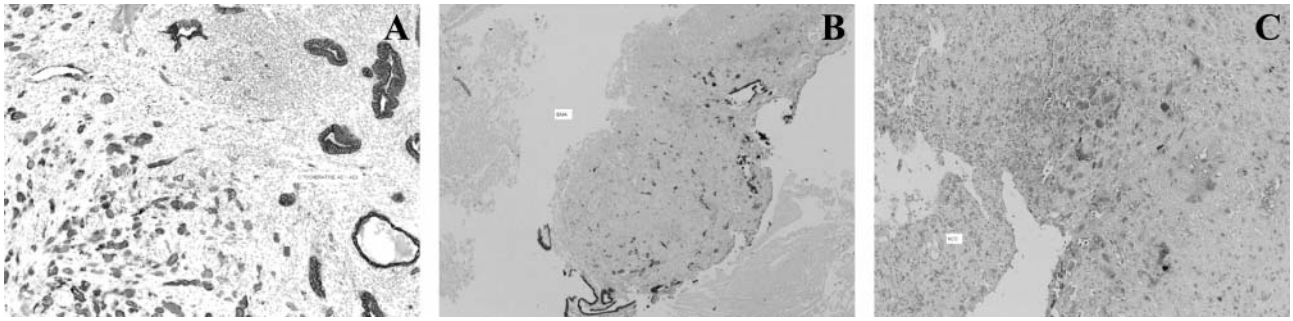

Figure 3. — Immunohistochemistry. A) Diffuse positivity for cytokeratin (CK) AE1-AE2 and B) epithelial membrane antigen (EMA). C) Focal positivity for human chorionic gonadotropin (hCG).

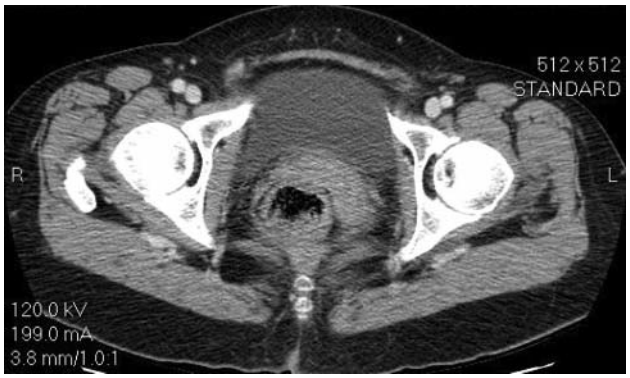

Figure 4. — Abdominal CT scan detecting thickening of the left levator ani muscle.

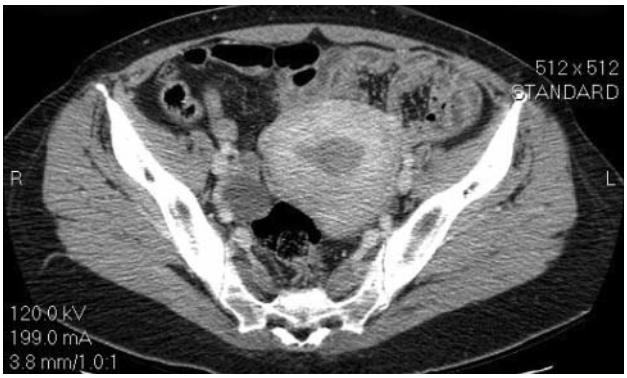

Figure 5. — Abdominal CT scan demonstrating hypodensity of the endometrium that infiltrates the right half of the myometrium.

the left annex and the right tube appeared within morpho-volumetric norms. The right ovary was the site of a three-cm cystic formation with regular walls. A frozen section was negative for neoplasia.

Histology was reviewed by an expert pathologist in the present centre and PSTT was not performed. The histological examination results showed: endometrium with proliferative aspects; chronic cervicitis; bilateral ovarian tissue with no neoplastic localisation; tubular tissue with no neoplastic localisation. A pre-operative β-hCG test showed 33 mU/ml (NR< 5 mU/ml).

The patient is on regular follow-up. Since the procedure, blood samples have been taken for β-hCG tests every 15 days. Only one of these samples resulted positive: β-hCG: 2.54 mUI/ml (NR< 2.4 mIU/ml). Clinical examination, pelvic abdominal sonography and control CT have shown no signs of local or systemic disease in the six months since surgery.

Discussion

PSTT is a rare form of GTD that originates from the implantation site of an intermediate trophoblast. It accounts for about one percent of all GTDs with an estimated incidence of one per 100,000 pregnancies [7]. PSTT was originally termed "atypical chorioepithelioma" by Marchand in 1895 [8]. In 1976, under the title "trophoblastic pseudotumour of the uterus", Kurman *et al.* [9] recognized the entity as a form of trophoblastic disease, distinct from choriocarcinoma. Five years later, Scully and Young [10] introduced the term "placental site trophoblastic tumour" to indicate possible malignant behaviour.

Although the age of most patients at presentation was reproductive age [11,12], a few cases have been reported in post-menopausal women [13].

The mean age at diagnosis is 31 to 33 years, and the disease can appear following any type of pregnancy [14, 15]. The antecedent pregnancy is full term normal in 53% of the cases [12, 15] or molar pregnancy seen in 21% of cases [12, 16]. The mean interval from the last pregnancy and diagnosis of PSTT can vary from several weeks to up to 15 years [11].

Unlike choriocarcinoma, the level of serum β-hCG in PSTT correlates with neither tumor burden nor the malignant behavior. β-hCG thus appears to have no predictive value and the disease may still progress even if levels are not raised [3, 11].

Irregular vaginal bleeding is the most common presenting feature, although a wide range of other symptoms has also been reported, including galactorrhea, virilization, nephritic syndrome, and polycythemia [17].

The outcome of PSTT as reported in literature is highly variable [18]. All cases of metastasis to vital organs, such as the brain, result in mortality despite all forms of treatment.

In the majority of cases, PSTT behaves in a benign fashion, with only about 10-15% being clinically malignant.

Extrauterine spread of the disease appears to be the most useful prognostic factor for progression [19,20]. The interval from the last known antecedent pregnancy appears to be a second major prognostic variable in PSTT. In a multivariate analysis, the risk for unfavorable behavior of the disease increased considerably with the length of this interval [18,21]. Diagnosis less than two years from the antecedent pregnancy, and the disease localized to the uterus, are associated with better outcomes [12,18]. How *et al.* found that the likelihood for fatal outcome was 14 times higher if the mitotic count was well above 5 [20]. Baergen *et al.* [2] reporting on 55 cases, showed that a high mitotic rate was more likely to be associated with metastasis or death. They noted that mitotic count was one of the strong predictors of survival with 88% to 100% of surviving patients having mitotic counts of less than 2.5/10 HPFs versus 48% to 52% survival in those patients with mitotic counts greater than 6/10 HPFs.

Table 1. — *TNM classification and FIGO Staging system of Gestational Trophoblastic Tumors [22].*

TNM Classification	FIGO Staging system	Description
TX		Primary tumor cannot be assessed
T0		No evidence of tumor primary
T1	I	Disease limited to uterus
T2	II	Disease outside of uterus but limited to genital structures (ovary, tube, vagina, and broad ligaments)
M1a	III	Lung metastates
M1b	IV	All other distant metastasis

On first being hospitalized, the present patient presented recurrent uterine bleeding and other significant adverse prognostic factors, such as interval from antecedent pregnancy > two years and age > 40 years.

On a subsequent second hospitalization, histological examination revealed the presence of PSTT on an endometrial polyp.

Generally studies conducted to establish a general staging of PSTT (Table 1) revealed that 65.5% of patients are affected by the disease confined to just the uterus, 11.8% extension to the pelvis (Stage II), 15.1% with lung metastases (Stage III), and 7.6% with metastases in other sites (Stage IV).

In contrast to choriocarcinoma, PSTT is relatively resistant to chemotherapy. Consequently surgery is the mainstay of treatment. In other cases the treatment of metastases can be successful through chemotherapy, although some PSTT cases exhibit fatal course even with treatment.

In conclusion, PSTT is difficult to diagnose by its symptoms and diagnosis is usually delayed.

High mitotic count and atypical undifferentiated pathological features are significant poor prognostic factors for survival in PSTT. The only approach at present remains hysterectomy which represents the gold standard of treatment in all cases of disease confined to the uterus.

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