**Case Report** 

# Primary Cervical Placental Site Trophoblastic Tumor: A Rare Entity with an Unusual Presentation

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#### INTRODUCTION

Placental site trophoblastic tumour (PSTT) is a rare form of gestational trophoblastic disease, which may follow normal pregnancy, abortion or an earlier molar pregnancy [1-4]. It accounts for only 1-2% of all trophoblastic tumors. Approximately 200 cases are reported in English literature. They commonly localized in the endomyometrium, hence abnormal uterine bleeding is the most common presenting symptom. However, less frequently, it may involve the cervix [4]. They need to be differentiated from gestational trophoblastic neoplasia and nontrophoblastic tumors as their management and prognosis is different [3]. The recognition of the morphologic features and immunophenotype allows their accurate diagnosis. Herein, we report a rare case of placental site trophoblastic tumor, presenting as a cervical mass, in a 38 year old female, and review the literature.

#### Abstract

Placental site trophoblastic tumour (PSTT) is the least common form of gestational trophoblastic neoplasia accounting for only 1-2% of trophoblastic tumors. Approximately 200 cases are reported in English literature. PSTT presenting as a cervical growth is even less common. Differentiation of PSTT from other types of GTN, non-neoplastic gestational trophoblastic disease and non-trophoblastic tumors is important clinically due to differences in their therapeutic approaches. Appreciation of the morphologic features and immunophenotype allows their accurate diagnosis. Although most of the cases of PSTT behave in a benign fashion, the clinical behavior of PSTT can sometimes be variable and several prognostic factors can help to predict the biological behavior of this condition. We report a rare case of placental site trophoblastic tumor, presenting as a cervical mass, in a 38 year old female, and review the literature.

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# CASE PRESENTATION

A 38 year old woman married for 8 years presented with premenstrual and postmenstrual spotting per vagina since 6 months and one episode of post-coital bleeding. She had 3 children and had her last vaginal delivery of a female child, 5 years back, after which she had resumed normal menstrual cycles by 3-4 months. On clinical examination, there was a firm mass arising from the anterior lip of the cervix with smooth and intact mucosal surface, measuring 2.5 X 2 cm and a clinical diagnosis of cervical fibroid was made. Patient was advised myomectomy, during the postmenstrual period. On follow-up a month later, she complained of smelling vaginal foul discharge along with intermenstrual bleeding, and the mass was found to have increased in size, bled on touch, and was friable, involving the anterior and posterior lip of cervix and extending into the vaginal fornices. A biopsy was taken with a clinical differential diagnosis of degenerated cervical fibroid and to rule out squamous cell carcinoma.

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Histopathological examination of the cervical biopsy showed intact cervical epithelium overlying sheets of intermediate trophoblasts, some of which were multinucleate, exhibiting high mitotic rate. Also seen were occasional syncitiotrophoblasts in a background of abundant hemorrhage. No chorionic villi were seen. A diagnosis of gestational trophoblastic neoplasia was suggested to the gynecologist, and serum beta-hCG levels were requested for correlation. Serum hPL (human Placental Lactogen) could not be done due to financial constraints.

Pelvic ultrasonography showed a heterogeneously enhancing solid and cystic mass measuring 4.5x 6x 3 cm in the region of uterine cervix. Doppler examination revealed low resistance flow within the tumor. MRI revealed the infiltration of the mass upto the serosa, but the parametrium, rectum, ureters and bladder were free. Serum beta hCG value was 1400 mIU/ml.

The patient underwent type 2 radical hysterectomy with bilateral salphingo-oophorectomy and bilateral iliac and obturator lymph node sampling.

Resected uterus showed a partly circumscribed, haemorrhagic & focally necrotic tumor in the cervix measuring 5x4x4 cms, extending deep into the wall of the cervix (Fig 1a) Sections from the tumor showed proliferation of intermediate trophoblasts, exhibiting high mitotic rate > 6-7/ HPF with marked nuclear pleomorphism, scattered tumor giant cells in a background of lakes of fibrin and haemorrhage (Fig 1b). Serosa and parametrium were free of tumor involvement.Iliac lymph nodes were negative for metastases. These histologic features prompted a diagnosis of placental site trophoblastic tumor with high mitotic index suggesting poor prognosis. Immunohistochemical staining with hPL and beta-HCG could not be done due to lack of resources.

Post-operatively the beta HCG level slowly dropped, and it was 4.4 mIU/mL one month after surgery.

In view of poor prognostic factors such as: interval of > 2 years since last child birth, high mitotic index, the patient was started on chemotherapy with EMA/CO (Etoposide, Methotrexate, Actinomycin D, Cisplatin, Vincristine) regime post-operatively for 6 cycles.



Figure 1. A: A large hemorrhagic mass in the cervix protruding from external orifice of the uterus. B: The striking histopathologic appearance is the presence of the pleomorphic intermediate trophoblastic cells surrounded by hemorrhage underneath normal cervical squamous epithelium (H&E, x200)

# DISCUSSION

Placental site trophoblastic tumor (PSTT) is the rarest type of gestational trophoblastic disease (GTD) forming approximately 0.2–2% of the cases of GTD seen in specialist centers [1]. PSTT can follow a normal term pregnancy, abortion, medical termination of pregnancy (MTP), or a mole/ectopic pregnancy. Most of PSTT were derived from the antecedent female conceptus and were likely to have possessed a functional paternal X chromosome [2]. The interval from previous known pregnancy varies from several months to as long as 18 years [3]. Amenorrhea or irregular vaginal bleeding are common symptoms. Our patient had normal menstrual cycles following her last delivery. Her symptoms were pre and post menstrual spotting and post-coital bleeding, probably because the lesion primarily involved the cervix, and not the endometrium and uterine corpus. Commonly, lesions occur primarily in the endomyometrium, but may occur or involve the cervix [4]. Zwischenberger et al reported a case of PSTT in a parous lady presenting with abnormal uterine bleeding [5]. In their case, the tumor was primarily involving the endometrium, growing to the cervix, and was seen protruding out through the cervical Os. Our case presented primarily with a cervical mass, clinically mimicking other cervical tumors like necrotic fibroid polyp and cervical malignancy, endometrium and uterine corpus being uninvolved. Size may vary from several millimeters to large bulky masses up to 10 cm. Sometimes they may be deeply invasive causing perforation of the uterine wall.

They can be confused with a variety of trophoblastic non-trophoblastic tumors.The histologic and differential diagnosis of PSTT includes gestational choriocarcinoma, epithelioid trophoblastic tumor, placental site nodule, exaggerated placental site reaction, and non-trophoblastic tumors such as epithelioid leiomyosarcoma and poorly differentiated carcinoma, such as squamous cell carcinoma (SCC) of the cervix or endometrial adenocarcinoma. The histopathology of PSTT has been distinctly described as a proliferation of implantation site intermediate trophoblast cells, mostly mononuclear with occasional multinucleated tumor cells. The cells have marked nuclear atypia, and tend to form confluent sheets while extensively invading the uterus in nests that separate the myometrial fibers reminiscent of normal implantation. Unlike choriocarcinoma, which is usually dimorphic, PSTT is monophasic. However, there are overlapping morphologic features and immunoprofiles between subtypes of gestational trophoblastic neoplasia (GTN), which can make a definitive diagnosis difficult. In addition, the small amount of tissue obtained from biopsy or endometrial curettage may limit the accuracy of the initial pathologic examination, as in our case. In equivocal case, intense HPL positively, ultrastructural image and determination of serum hPL with beta-hCG are recommended .The minimally elevated β-HCG level that does not increase with serial determinations can help differentiate placental site trophoblastic tumor from other types of gestational trophoblastic disease. More-over PSTT cells stain with specific monoclonal antibodies for b core segment of hCG and for HPL than for intact HCG. The proliferation rate of PSTT as measured by Ki67 labeling is approximately 14%, which helps to distinguish it from exaggerated placental site reaction that demonstrates no proliferation 131. The clinical behaviour of PSTT varies and prediction of

its biological behaviour remains difficult. Most behave in a benign manner, but 15-20% may develop metastases, and above half of these are fatal. The significant prognostic factors in PSTT are anatomical stage, age at diagnosis, interval from the previous pregnancy, deep myometrial invasion, and high tumor mitotic rates [6].However, tumors with low mitotic index can also metastasize [7].Although the cut-off limits for these factors vary among different reports, high tumor stage, age more than 35 years, and interval from previous pregnancy more than 24 months are factors associated with poor prognosis.

Hysterectomy remains the mainstay of treatment, particularly in patients with disease limited to the uterus. Chemotherapy is indicated for patients with metastases and may be indicated in non- metastatic cases when associated with poor prognostic factors (such as interval from last known pregnancy to diagnosis >2 years, deep myometrial invasion, tumor necrosis, and mitotic count of 6/10 high power fields or more). However, patients with metastases have not experienced the success with chemotherapy as seen with choriocarcinoma [4]. The complete response rate for metastatic PSTT managed with EMA/CO chemotherapy is only 28%. Chemotherapeutic regimen should be EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine) for first line chemotherapy. EMA/EP (etoposide, methotrexate, actinomycin, and cisplatinum) should be used in EMA/CO refractory cases. The survival rate is approximately 100% for non-metastatic disease and 50-60% for metastatic disease. Radiation treatment may play a role in recurrent disease, but must be evaluated on a case-by-case basis. Serial beta-HCG results are recommended for follow-up to monitor response to treatment and detect recurrence of the PSTT [7].In our patient, the presence of poor prognostic factors such as: a long interval from previous pregnancy, high mitotic index on histological examination, and deep invasion of the wall were indications for starting post-operative chemotherapy.

In conclusion, PSTT can be confused with a variety of trophoblastic and non-trophoblastic tumors, but an appreciation of the morphologic features and immunophenotype allows their accurate diagnosis. Clinically, it is prudent for physicians to differentiate PSTT from other forms of GTN because PSTT is less sensitive to chemotherapy, and surgery including hysterectomy plays a major part in optimal treatment. It is important to suspect malignancy/unusual histopathological diagnoses in any cervical lesion which grows in size or exhibits unusual characteristics.

# **CONFLICTS OF INTEREST**

Authors declare that they have no any conflict and disclosure.

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