

Placental Site Trophoblastic Tumour

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Abstract

Placental Site Trophoblastic Tumour is a rare neoplastic condition developing from intermediate trophoblastic part of cytotrophoblast. Although grouped under Gestational Trophoblastic Neoplasias (GTNs), PSTT varies in its origin, presentation, diagnosis and response to treatment from other GTNs. Delay in treatment due to late presentation or diagnosis is common. Surgery in the form of hysterectomy is the main treatment option but uterus preserving surgical options have been suggested in case of future fertility desire.

Keywords: Placental Site Trophoblastic Tumour, Gestational Trophoblastic Neoplasia, Cytotrophoblast

Introduction

Gestational Trophoblastic Tumour is an umbrella term including both benign and malignant conditions. The malignant variety includes the well known choriocarcinoma, the rare Placental Site Trophoblastic Tumor (PSTT) and a newly described Epithelioid Trophoblastic Tumor. PSTT represents a neoplastic transformation of intermediate trophoblastic cells that normally play a critical role in implantation. PSTT was first described in 1976¹ and since then, only 150 cases have been reported in the literature.²

There is a wide spectrum of clinical presentation and behavior, ranging from a benign condition to an aggressive disease with fatal outcome. When metastatic, it can be difficult to control even with surgery and

chemotherapy. In cases with distant metastasis or delayed treatment, the outcome is dismal. Distinctions in underlying biology, behavior & management justify specific diagnostic and treatment strategies. We are presenting a case, the first one diagnosed at our centre, with this rare disease.

Case Report

A 32 years old P₂⁺⁰ was referred from Department of General Medicine, PIMS with complaints of abdominal distention and low grade fever for past 6 months. She was a self referral from periphery and was already taking antituberculous treatment for 1 month, prescribed by a GP due to exudative ascitic fluid cytology. She presented with marked weight loss and anorexia for 3 months. Her last child was

born 14 months ago and was breast fed. Since then, she was practicing abstinence as contraception. Menstrual cycle was regular and her periods were not overdue. There was no family history of gynaecological or bowel cancer.



Figure 1. Intra operatively grossly normal uterus

Apart from left abducent nerve palsy and left papilledema, general physical examination was unremarkable. Abdominal examination revealed markedly distended abdomen and fluid thrill. Bimanual examination revealed a bulky uterus and fullness in vaginal fornices.

The baseline investigations including serum electrolytes, renal and liver function tests were within normal limits. Ascitic fluid cytology showed lymphocytosis, culture was negative for any growth including AFB. Pelvic ultrasound was negative for RPOCs but suspected molar pregnancy. Urine pregnancy test was advised by gynaecology department which was positive for beta hCG the level of which was 1322 mIU/ml. Her ESR was normal and she had negative hepatitis B and C, ANA, Anti ds DNA, ADA, MTB-DNA tested by PCR & RA factor. Echocardiography

and CT scan of brain were normal. MRI brain revealed kinking of orbital part of left optic nerve but no metastasis. CEA was within normal limits with mildly raised CA 125 (110u/ml). Her beta hCG levels were repeated which remained at a plateau.

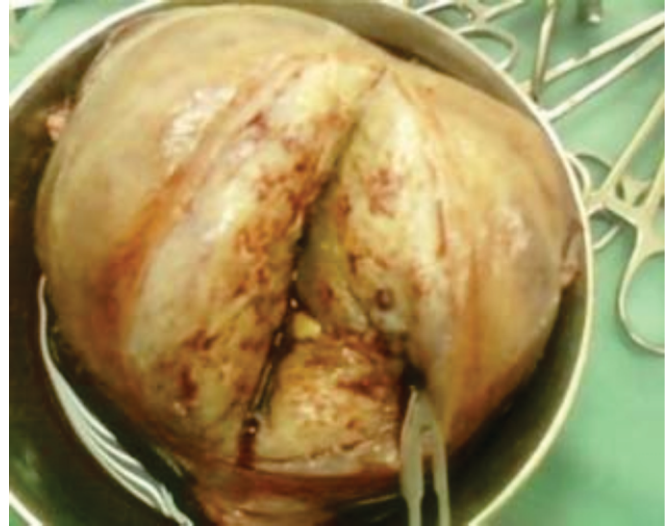


Figure 2. Cut Section of the uterus

The provisional diagnosis was persistent gestational trophoblastic disease and diagnostic D & C was done. Histopathology showed PSTT. It was confirmed on immunohistochemistry. Total abdominal hysterectomy with conservation of both ovaries was carried out at laparotomy and almost 5 litres of ascitic straw colored fluid was drained. There was no involvement of bowel, omentum, liver or undersurface of diaphragm. On cut section of uterus, no gross abnormality was found. Histopathology and immunohistochemistry of uterine specimen confirmed PSTT and ascitic fluid cytology was negative for any malignant cells. Post operatively she developed paralytic ileus and per vaginal leaking of ascitic fluid. She was managed conservatively and later postoperative period remained uneventful. Oncology consultation was sought and chemotherapy was not offered to her.

She had a follow up visit on 12 weeks post operatively and was free of any symptoms. At present, she is maintaining good health and has no active complaints.

Discussion

PSTT is a rare form of gestational trophoblastic disease (GTD) having a variable spectrum of clinical behavior. PSTT accounts for 1–2 % of patients with trophoblastic disease.³

The etiology, epidemiology and risk factors for the development of PSTT are not well understood. In contrast to the mixture of syncytio- and cytotrophoblasts in choriocarcinoma, PSTT is composed of a monomorphic population of intermediate trophoblasts developed from cytotrophoblast. Like other forms of GTD, PSTT can occur after a normal pregnancy, spontaneous miscarriage, termination of pregnancy, ectopic pregnancy or molar pregnancy. Presenting symptoms generally include irregular bleeding or amenorrhea and sometimes with nephrotic syndrome, sepsis and erythrocytosis. Spiderangiomata and splenomegaly may be present but abdominal distention and fever are rare. Our patient presented with fever and ascites and, therefore, the diagnosis was delayed due to the rare presenting complaints. Most cases are confined to the uterus but pelvic involvement, lung and other organ metastasis has been reported.⁴ PSTT presents with metastasis in about 10% of cases and metastases develop in an additional 10% during follow up.⁵ Overall, PSTT has 20 % fatality rate.⁶ The risk factors leading to mortality include lung metastasis and an antecedent pregnancy interval of 4 years or more. The only significant independent predictor of overall survival is the time elapsed since the preceding pregnancy.

There are two systems used for staging PSTT. Staging correlates well in both systems, however, FIGO staging is generally preferred over American Joint Committee on Cancer (AJCC) staging system. Our patient had stage 1 disease as the tumor was limited to the uterus with negative cytology and no evidence of distant metastases.

Unlike other forms of GTD, PSTT is a diagnostic dilemma and thus increased index of suspicion is required to make the diagnosis. Serum beta-hCG levels may not be markedly elevated. Free fraction of beta hCG has been recommended as a seemingly absolute test for GTN, however, it is not a diagnostic test to discriminate PSTT from other forms of GTN.⁷

Probably the most useful new marker for differentiation between choriocarcinoma and PSTT is the association of **free** non-hyperglycosylated beta hCG in PSTT while in histologic choriocarcinoma, hyperglycosylated hCG is present and there is no free β -hCG.⁸

Expression of human placental lactogen (hPL) is increased on histological section as well as in the serum.⁹ Both free fraction of beta hCG and human placental lactogen estimation is however not available in Pakistan.

Diagnosis is confirmed by histopathology of either endometrial curetting or the uterus but meticulous evaluation of metastasis is mandatory. Immunohistochemical stain for human placental lactogen shows that PSTT is diffusely positive (brown staining in cytoplasm) but rarely positive for placental alkaline phosphatase.¹⁰

Hysterectomy is the cornerstone of treatment.⁴ The ovaries may be conserved if they seem normal.¹¹ Management is stage adapted with surgery for stage

I disease, and combined surgery and chemotherapy for stage II, III and IV disease. Interval of 48 months since antecedent pregnancy as a prognostic indicator of survival can help select patients for risk-adapted treatment. Given the rarity of this tumor, few reliable comparisons among surgical approaches or chemotherapeutic regimens can be made.

Chemotherapy has an established role in loco-regionally advanced and metastatic disease. Chemotherapy within one week of hysterectomy results in lower rates of recurrence.¹¹ Adjuvant surgery, such as hysterectomy, excision of lung metastases, or removal of obstructing abdominal lesions, has been associated with favorable disease control.

For patients desiring future fertility, D and C and adjuvant chemotherapy is an option. The combination of operative hysteroscopy and chemotherapy in women with localized disease, who want to preserve their fertility, can be a possible treatment option in highly selected cases. Repeated chemotherapy with EMA/EP, even in patients who relapse after treatment with Etoposide, Methotrexate, Adriamycin / Etoposide, cisplatin for PSTT can induce prolonged remission and even cure.¹²

Open uterine resection of PSTT following appropriate chemotherapy can achieve long term remission.⁶ The overall 5-year survival for metastatic PSTT is 10–27% for all stages.¹³

Conclusion

PSTT is a rare form of gestational trophoblastic disease often diagnosed late and requires surgical excision unlike the other commoner varieties of GTD which are chemosensitive. The addition of immunohistochemistry to the armamentarium of the pathologist has led to increased accuracy in diagnosis.

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