Indian Journal of Medical Case Reports ISSN: 2319–3832(Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jcr.htm
2016 Vol.5 (2) April-June, pp. 1-4/Babeeta et al.
Case Report

PLACENTAL SITE TROPHOBLASTIC TUMOR: A CASE REPORT

***Babeeta[1], Choudhary Deepak[2] and Kulhari Sandeep[2]**
[1]Obstetrics & Gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2]Pediatrics, Sardar Patel Medical College, Bikaner, India
**Author for Correspondence*

ABSTRACT
Placental site trophoblastic tumor is rare. They represent a rare form of gestational trophoblastic disease. They occur mainly in women who have a history of miscarriage, termination of pregnancy, or even a normal or pathological ongoing pregnancy. The clinical course is unpredictable. This malignancy has different characteristics from other gestational trophoblastic tumors. We present a case of PSTT which was managed with surgery and adjuvant chemotherapy. We conducted a literary research and review, focusing primarily on prognostic factors and treatment.

Keywords: *Immunochemistry, Trophoblastic Tumor, Placental Site, Chemotherapy, Pregnancy*

INTRODUCTION
Placental Site Trophoblastic Tumor (PSTT) is a rare form of gestational trophoblastic disease (GTD) and was described by Kurman *et al*., (1976). In 1976, it was thought to be an exaggerated expression of the invasive nature of normal trophoblastic tissue which did not assume the characteristics of a malignant tumor. Twigg's *et al.*, (1981) described a patient with trophoblastic pseudotumor which was progressive and fatal. Scully and Young (1981) described additional 14 cases of which two died from metastatic disease.

Pathologically, the tumor is characterized by mononuclear intermediate trophoblastic cells with occasional multinuclear intermediate trophoblastic cells and occasional multinuclear giant cell which infiltrate both myometrium and blood vessels (Cunningham *et al.*, 2001). Immunohistochemical staining reveals many prolactin cells and few gonadotropin producing ones. Thus, gonadotropin levels may be normal to elevated (Miller and Seifer, 1990). The etiology, epidemiology and risk-factors of PSTT are poorly understood. Presenting symptoms generally include irregular bleeding or amenorrhea and rarely nephrotic syndrome, sepsis, and erythrocytosis (Brewer *et al.*, 1992), or the metastatic sites may be the presenting symptoms.

PSTT presents with metastases in about 10% of the cases (Larsen *et al.*, 1991) and metastases develop in an additional 10% during follow-up (Disaia and Creasman, 2002). Although the majority of patients with non-metastatic PSTT are cured by hysterectomy, a number of cases require aggressive treatment with chemotherapy and/or radiation. This paper presents a case of PSTT treated by combined treatment modalities of hysterectomy and chemotherapy.

CASES
A 37yrs/F, P3013, referred i/v/o rising β-hCG levels, post suction evacuation for H. mole in January 2015, at PGIMER, Chandigarh in obstetrics and gynaecology department for further management from a private hospital Jalandhar, Punjab. She presented with a recent history of amenorrhea followed by heavy bleeding per vaginum, her urine pregnancy test was negative in October 2014, for which she took some local treatment, and records of that treatment were not available. In December she had history of nausea, anorexia, headache and backache for which she advised sonography of whole abdomen and pelvis which showed H. mole and in MRI findings were suggestive of non-invasive H. MOLE, her beta hCG value was 1944 and suction evacuation was done. On HPE:?PSTT?? Exaggerated placental Site reaction. In IHC p63 was negative, Ki67 index positivity was 20-25%and she kept on weekly beta hCG follow up. Due to her plateau beta hCG level (post suction evacuation beta hCG value-2023, 2109, 1798, 2148) she referred to PGIMER, Chandigarh.

Her last delivery was 6 year ago. She had not undergone tubectomy. All her deliveries were normal without any antenatal or postnatal complications, her periods were always regular. She had no significant past and family history. On examination uterus was found to be bulky with no other abnormalities. A transvaginal sonography was suspicious for vesicular mole remnants which could not be confirmed however NCCT Head- was normal, CECT Chest and abdomen- was normal and CECT Pelvis – showed finding suggestive of invasive H. mole and Slides of histopathology reviewed in our hospital showed ?PSTT and Ki 67 index positivity in 25- 30%. So, diagnosis of PSTT was made and total abdominal hysterectomy was done in February, 2015. Intra operative findings; uterus enlarged up to 12 weeks size and in anterior wall of uterus - 3cm bulge was seen and overlying myometrium was thinned out however, B/L tubes and ovaries were normal. Postoperative recovery was normal. Repeat b-hCG following the surgery showed a fall to 602mIU/ml. The histopathology examination of the specimen confirmed the diagnosis of Placental Site Trophoblastic Tumor. Stains for b-hCG and human placental lactogen (HPL) could not be done and she was kept on weekly beta hCG follow up but beta hCG level were plateaued (625,693, 806). After three weeks of surgery, patient was started on combination chemotherapy. She was started on EMA-EP regime. Five cycles of chemotherapy was given following which the b-HCG value has fallen to 3 mIU/ml and she was given three more cycles of chemotherapy and is presently on follow up and doing well.

DISCUSSION

PSTT is a tumor of intermediate trophoblast. It is one of four trophoblastic lesions that arise from the intermediate trophoblasts, the others being the exaggerated placental site reaction, placental site nodule and epithelioid trophoblastic tumor. PSTT can occur after any type of gestation. The duration from the preceding conception event is also highly variable. Most patients present with abnormal bleeding per vaginum with varying periods of amenorrhea and/or effects of metastasis to various organs. A wide range of other presenting symptoms have been reported including galactorrhea, virilization, nephritic syndrome, polycythemia and cutaneousmetastases. It is difficult to distinguish between PSTT, ETT, and choriocarcinoma on the basis of clinical history and imaging alone. These patients often have persistent low levels of serum HCG (100-1000 mIU/mL). Initial curettage is often equivocal and the diagnosis can be missed if fragments showing muscle invasion by intermediate trophoblasts are not seen. Failure to respond or persistence of raised hCG levels in a GTN case treated with methotrexate can raise the suspicion of a PSTT. Grossly it is a poorly circumscribed mass with a diffuse infiltration of intermediate trophoblasts between muscle fibers and around blood vessels. Invasion of the vessel wall with fibrinoid change and preservation of lumen can also be seen. Mitosis is variable and is an important prognostic differentiator. On immunohistochemistry, PSTT characteristically show a high proportion of cells positive for human placental lactogen (hPL) than positivity for human chorionicgonadotropin (hCG). The Ki-67 index, which is a surrogate marker for mitotic activity, shows 10-20% positivity in PSTT and is useful for differentiating this lesion from exaggerated placental site reaction where the Ki-67 index is less than 1% and choriocarcinoma, which shows >50% positivity. However, estimations of serum hCG is still the most useful marker for investigation and follow up. A more recent marker for differentiating between choriocarcinoma and PSTT is the association of free non-hyper glycosylated b-hCG with PSTT, while in choriocarcinoma hyper glycosylated hCG is present and there is no free b-hCG (Cole *et al.,* 2006). Imaging studies are useful especially when metastasis is present but are not specific as a diagnostic differentiator.

The clinical and biological behavior of PSTT is difficult to predict and no definitive prognostic index or scheme exits. The FIGO staging and WHO prognostic system for GTN are currently being used but do not correlate very well in PSTT. Poor prognostic factors are an interval of more than 2 years from known antecedent pregnancy, mitotic count >5/10 HPF, extensive necrosis and extension outside the uterus (Baergen *et al.,* 2006). Risk of death is reported 14 times greater if mitotic figures were greater than 5/10 HPF. High mitotic index is associated with not only metastatic disease but appears to be an indicator of recurrence too. Currently GTN are classified into non-metastatic low-risk metastatic and high-risk

metastatic categories. However, as the biological behavior of PSTT is highly variable it does not fit into well-defined prognostic groups, hence, the first diagnostic and therapeutic intervention is usually surgical in the form of hysterectomy. Most patients with localized disease are effectively treated by total abdominal hysterectomy. With locally advanced or metastatic disease, tumor reductive surgery should be performed if disease is considered resectable.

Non-metastatic tumors (FIGO Stage I) can be treated with a variety of single-agent methotrexate or actinomycin Dprotocols, resulting in cure of essentially all patients. In addition metastatic low-risk tumors (FIGO Stages II and III, WHO score <8) should be treated with 5-day dosage schedules of methotrexate and actinomycin D, with cure rates approaching 100%. Metastatic high-risk tumors (FIGO Stage IV, WHO score >7) require combination chemotherapy with etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMA-CO) with or without adjuvant radiation therapy and surgery to achieve cure rates of 80-90%. The most recent data from different centers, suggest that EMA/EP is the most effective treatment for metastatic or recurrent PSTT (Kim, 2003).

Conclusion

Placental site trophoblastic tumors are exceptional tumors, encountering difficult clinical and histological diagnosis. Immunohistochemistry plays an important role. Clinically speaking, their emergence is seldom or not at all predictable because they generally appear after a normal pregnancy. The usual symptoms are non-specific, such as metrorrhagia or amenorrhea, sometimes years after the last pregnancy. From a biological point of view, the dosage and follow up of beta-HCG levels are interesting for the diagnosis, but one must keep in mind that the levels are not as high as in other GTH. The only FIGO classification criticism for GTHs is that the lymphatic spread is not taken into account. In the case of PSTT, the most commonly recognized risk factors are: stage, mitosis rate, and elapsed time since last pregnancy at the time of diagnosis, age of the patient, and the degree of myometrium invasion. With regard to treatment, the leading role of surgery must be underlined, generally through hysterectomy. The possibility of a treatment conservative of fertility can be discussed with patients who wish to become pregnant again, have high motivation, good prognosis factors, and a thorough discussion. A lymph node sampling is generally recommended. Chemotherapy is usually not recommended at stage I, but can play a role in cases of poor prognosis. Currently, there is no consensus on the best chemotherapeutic treatment.

REFERENCE

Baergen RN, Rutgers JL, Young RH *et al.*, (2006). Placental sitetrophoblastic tumor: a study of 55 cases and review of the literature emphasizing factors of prognostic significance. *Gynecologic Oncology* **100**(3) 511-e520.

Brewer CA, Adelson MD and Elder RC (1992). Erythrocytosis associated with a PSTT. *Obstetrics & Gynecology* **79** 846–849.

Cole LA, Dai D, Butler SA, Leslie KK and Kohorn EI (2006). Gestational trophoblastic diseases: pathophysiology of hyperglycosylated hCG. *Gynecologic Oncology* **102** 145- e150.

Cunningham FG, Gant NF and Leveno KJ edition (2001). *Williams Obstetrics*, 21 edition, (McGraw Hill, New York, USA) 835–849.

Disaia PJ and Creasman WT (2002). Gestational trophoblastic disease. In: Disaia PJ, Creasman WT, editor. *Clinical Gynecology Oncology*, 6th edition, (USA, St. Louis, Mosby-Year book) 185–206.

Kim SJ (2003). Placental site trophoblastic tumor best practice and research. *Clinical Obstetrics and Gynecology* **17** 969–984.

Kurman RJ, Scully RE and Norris HJ (1976). Trophoblastic pseudo tumor of the uterus. An exaggerated form of "Syncytial endometritis" simulating a malignant tumor. *Cancer* **7** 1214–1226.

Twiggs LB, Okagaki T, Phillips GL, Stromer JR and Adcock LL (1981). Trophoblastic pseudotumor, evidence of malignant disease potential. *Gynecologic Oncology* **12** 238–248. DOI: 10.1016/0090-8258(81)90153-0.

Larsen LG, Theilade K, Skibsted L and Grete KJ (1991). Malignant placental site trophoblastic tumor. *Acta Pathologica, Microbiologica et Immunologica Scandinavica APMIS* **23** 138–145.

Miller DS and Seifer DB (1990). Endocrinologic aspects of gestational trophoblastic diseases. *International Journal of Fertility* **35** 137–153.
Scully RE and Young RG (1981). Trophoblastic pseudotumor: A reappraisal. *The American Journal of Surgical Pathology* **7** 75–76.