PLACENTAL SITE TROPHOBLASTIC TUMOUR : A CASE REPORT

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ÖZET

Plasental Yerleşimli Trofoblastik Tümör: Vaka Sunumu

Uterusun plasental kaynaklı trofoblastik tümörleri (PSTT) gestasyonel trofoblastik hastalıkların nadir bir formudur. Literatürde 20'si malign olmak üzere 90 tane plasental kaynaklı trofoblastik tümör bildirilmiştir. Plasental kaynaklı trofoblastik tümörlerin tanımlanmasından bu yana 19 yıl geçmesine rağmen teşhis, tedavi ve biyolojik davranışı hakkındaki zorluklar devam etmektedir. Gebeliği takiben persiste düşük hCG titresi, açıklanamayan vajinal kanama veya amenore akla PSTT' yi getirmelidir. Tablonun ortalama görülme yaşı 28 iken, postmenopozal dönem dahil tüm yaş grubunda rastlanılabileceği unutulmamalıdır. Term gebelik, spontan/ terapötik abortus veya molar gebelik terminasyonundan hafta veya aylar sonrasında gelişebilir.

Prognozu belirlemede henüz güvenilir histolojik, immünohistokimyasal ve kromozomal tanı yöntemi yoktur. Tümör nispeten yoğun ve agresif kemoterapiye duyarsız olduğundan, metastaz düşük prognoz göstergesidir.

Biyolojik davranışın önceden tahmin edilemediği PSTT olgularında, multiajan kemoterapisi ve radyoterapiye zayıf yanıt alındığından, küratif oluşu ve uzun dönem surviye imkan tanıyan cerrahi tedavi (TAH+BSO) halen en iyi seçenek olmaya devam etmektedir.

Anahtar Kelimeler: *Plasenta, Trofoblastik Tümör, Gestasyonel Trofoblastik Hastalık, hCG.*

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SUMMARY

The placental site trophoblastic tumours of uterus is a rare form of gestational trophoblastic disease. In literature 90 placental site trophoblastic tumours of which %20 are malign were documented. Although 19 years have passed from the description of trophoblastic tumours, the diffuculties about the diagnosis, treatment and the biological behaviour have been going on. Unexplained vaginal bleeding, amenorrhea and persistant low hCG levels should remind us the PSTT. It may occur weeks or months after term pregnancy, spontaneous or terapotic abortion or termination of the molar pregnancy. Although the average age of the disease is 28, it should not be forgotten that it can be seen in all age groups also including postmenoposal period.

To determine the prognosis there is still no histological, immunohistochemical and chromosomal diagnose method. Since tumour is insensitive to condensed and aggressive chemoteraphy, metastasis is the indicator of low prognosis.

PSTT cases in which the biological behaviour cannot be predicted before, since a poor response is obtained by chemoteraphy and radioteraphy, surgical treatment (TAH+BSO) is still the best choice of treatment which is both curative and gives a chance to the long time survival.

Key Words: *Placenta, Trophoblastic Tumour, Gestational Trophoblastic Disease, hCG.*

INTRODUCTION

The Placental Site Trophoblastic Tumour (PSTT) of the uterus is the rarest form of Gestational Trophoblastic Disease. Approximately 90 cases of PSTT have been reported in the literature, with 20 malignant tumours. Although 19 years have elapsed since the original description of PSTT; difficulties remain in making the diagnosis, predicting the biologic behavior and outlining treatment plans. One should consider this diagnosis in a patient with a persistent low hCG titer or unexplained amenorrhea following a recent pregnancy. In this paper, we present a clinically suspected and histologically confirmed diagnosis of a PSTT case.

CASE REPORT

A 37 year-old turned presented to our institution in May 1995 with the complaint of vaginal bleeding for the preceeding 4 months. She was married for 3 years. She had had a first trimester spontaneus abortion in May 1993 and a full-term delivery by elective cesarean section in September 1994. The female infant was breast fed until December 1994. There was no history of vaginal bleeding until January 1995, when the persistent vaginal bleeding was begun. The vaginal bleeding varied in episodes, duration and amount. On admission, the uterus was found to be top normal in size. Transvaginal ultrasound examination demonstrated a focal heterogeneous lesion of 21x28x30 mm in the fundal uterine wall. A dilatation and curettage were performed and histological examination showed placenta! site trophoblastic tumour. The concurrent serum hCG level was 74 mlU/ml (reference range, <5 mlU/ml). Serum CA 15-3, CA 19-9, CA 125, aFP, TSH, HPL and CEA levels and routine laboratory tests were within normal limits. Metastatic work-up, including chest roentgenogram; CT scan of head, abdomen and pelvis; liver isotope scan and abdominopelvic ultrasonography showed no significant finding. The patient underwent exploratory laparotomy the following week. The uterus was no greatly enlarged. The ovaries were morphologically normal. No other significant pathology was noted on the exploration of the abdominal cavity. A total abdominal hysterectomy and bilateral salpingo-oopherectomy were performed.

PATHOLOGICAL FINDINGS

GROSS FINDINGS

A well circumscribed nodular, myometrial mass lesions about 2 cm in diameter has been detected in the fundus of myometrium. The lesion was yellow- brown in colour and showing focal areas of haemorrhage and necrosis

MICROSCOPIC FINDINGS

Sections of the described mass in the myometrium composed of medium sized (trophoplastic) cells infiltrating between muscle bundles (fig.1) and vascular structures in some areas. Most of the cellular population is monomorphic except only a few scattered syncytiotrophoplastic giant cells. The tumour cells have abundant eosinophilic and amphophilic cytoplasm with occasional vacuoles and hyperchromatic nuclei with moderate degreee pleomorphism (fig 2).

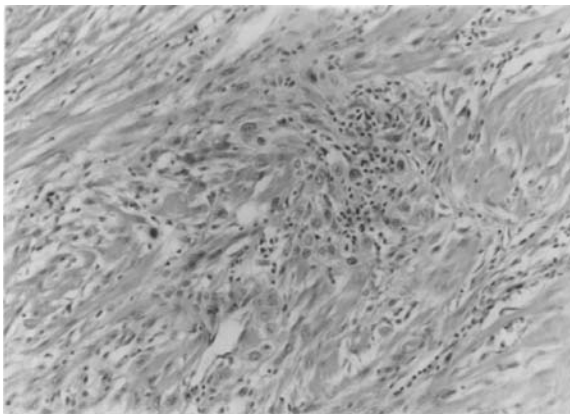

Figure 1 : The intermediate trophoplastic cells characteristically infiltrating between muscle bundles in myometrium (H.E. X 200)

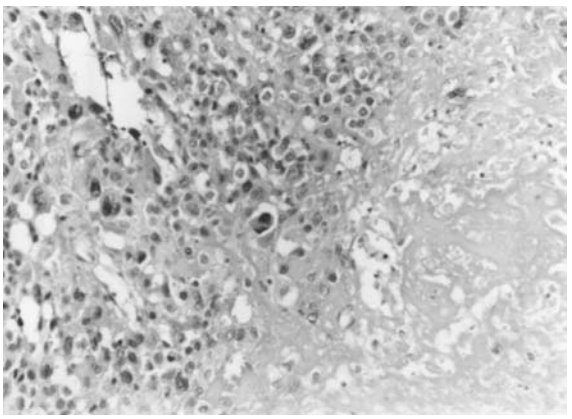

Figure 2 : The medium sized trophoplastic cells with abundant eosinophilic cytoplasm, moderate degree nuclear pleomorphism and necrosis.(H.E.X 200)

DISCUSSION

Immunocytochemical and ultrastructural studies of PSTT demonstrated features similar to (intermediate) trophoblasts of the basal plate of the placenta (1,2,3). These facts suggest that PSTT may originate from or differentiate as the intermediate trophoblast of the placental site, as described by Kurman et al (4).

Diagnosing this rare form of trophoblastic disease and predicting its biologic behavior remain difficult despite knowledge of the histology of these lesions and continued reporting of series of patients.

PSTT affects women in all age groups including postmenauposal years (5,6). The average age at onset of PSTT is 28 years old (1). Although most patients having abnormal vaginal bleeding or amennorhea often accompanied by uterine enlargement, some have an unusual presentation

such as nephrotic syndrome or virilization(6,7,8) At the time of the clinical presentation, hCG levels are certainly below the levels usually encountered with other forms of gestational trophoblastic neoplasms although range from unmeasurable levels to several thousand international units per liter (5).

PSTT may follow any type of gestation including term pregnancy, spontaneous and theraupetic abortion and hydatidiform mole and symptoms may develop from weeks to months after termination of pregnancy. Several cases have occurred years after the last documented pregnancy and even after tubal ligation (9). This supports the observation that PSTT may remain quiescent for long periods of time.

Diagnosis of the tumour based on curetting alone can be difficult (10). Sometimes hysterectomy may be necessary to confirm the diagnosis. Patients found to have PSTT on D&C should undergo a complete work-up, including history and physical examination; hepatic, renal and thyroid function tests; serum hCG levels; chestroentgenogram; CT scan of head, abdomen and pelvis; liver isotope scan and abdominopelvic ultrasonography (11). The hCG levels should not be used to determine the nature of the metastatic work-up; because, some patients with low levels of hCG, may have metastasis at presentation (12).

The clinical behavior of PSTT is difficult to predict. The majority of the patients are found to have nonmetastatic disease and some of them are cured with curettage alone. But at least 15-20% of the patients with PSTT die from widespread metastases despite intensive multimodal therapy. The lung is the main metastatic organ, although metastases to brain, vagina, lymph nodes, liver, kidney, stomach and spleen have been reported (8).

There has been many histological and clinical criteria proposed to predict which tumours have the greatest risk of developing metastases. Levels of hCG and HPL have been poor predictors of clinically aggressive behavior. Some authors have recommended the use of mitotic counts. This feature, however, vary substantially from endometrial curettings and hysterectomy specimens to metastatic lesions. Among the reported deaths from PSTT, some patients developed disseminated tumours although they had a mitotic count of two to three mitoses per 10 high-power fields (11,13). A preceding term pregnancy ending in delivery of a female infant has been reported to be a risk factor for death and recurrence of PSTT (11). This has not been subjected to statistical review. On the other hand; term pregnancies ending in female offspring have been reported for many of the surviving cases, therefore, it does not appear to be a reliable predictor of aggressive biologic behavior. Flow cytometric DNA analysis of six cases of PSTT revealed a diploid DNA stemline with S-phase fractions ranging from 6% to 19% and one case that was tetraploid (1). In summary, there are no reliable histological, immunohistochemical or DNA ploidy features that predict prognosis. Metastasis is a sign of poor prognosis, since the tumour is relatively insensitive to aggressive cytotoxic chemotherapy.

Although some cases may benefit from combination chemotherapy (14,15), various combinations of chemotherapeutic agents have not been curative in the treatment of PSTT. Resistance to chemotherapy is thought to correlate with the predominant cell type which resembles intermediate trophoblast with little differentiation toward syncytiotrophoblast. Radiation therapy has been reported to provide local control and palliation of symptoms of recurrent disease (13,16).

Because of the tumour's poor response to multiagent chemotherapy and radiotherapy and the inability to predict its biologic behavior, surgery continues to be the best chance of long-term survival and maximizes the opportunity for a cure (11). Total abdominal hysterectomy and bilateral salpingo-oopherectomy have been recommended for the non-metastatic tumours although there have been some patients having metastatic disease 4 to 5 years after hysterectomy (14,17). Hysterectomy makes possible the pathological assesment of the extent of the lesion and evaluation of the histologic features that may have prognostic importance.

REFERENCES

1. *Fukunaga, M., Ushigome, S. Metastasizing Placental Site Trophoblastic Tumour. Am.J. Surg.Pathol. 17(10): 1003-10,1993.*
2. *Duncan, D., Mazur, M. Trophoblastic Tumours: Ultrastructural Comparison of Choriocarcinoma and Placental Site Trophoblastic Tumour. Hum.Pathol.20:370-81,1989.*
3. *Gloor, E., Dialdas, J., Hartimann, J. et al. Placental site trophoblastic tumour (trophoblastic pseudotumour) of the uterus with metastases and fatal outcome. Clinical and autopsy observations of a case. Am.J.Surg. Pathol. 7:483,1983.*
4. *Kurman, R.J., Main, C., Chen, H. Intermediate Trophoblast: A Distinctive Form of Trophoblast with specific morphologic, biochemical and functional features. Placenta. 5:349-70:1984.*
5. *Mclellan, R., Buscema, J., Currie, J. et al. Placental site tumour in a postmenopausal woman. Am.J.Clin.Pathol 95:670-5,1991*

6. *Ecktein, R.P., Paradinas, F., Bagshawe, K. Placental Site Trophoblastic Tumour (Trophoblastic Pseudotumour): A Study of Four Cases Requiring Hysterectomy Including One Fatal Case. Histopathology.6:211-6,1982.*
7. *Young, R., Scully, R. Placental Site Trophoblastic Tumour: Current Status. Clin. Obstet. Gynecol.27:248-58,1984.*
8. *Young, R., Scully, R., Mccluskey, R.A. Distinctive Glomerular Lesion Complicating Placental Site Trophoblastic Tumour: Report of Two Cases. Hum.Pathol.16:35-42,1985.*
9. *Driscoll, S.G. Placental site chorioma: The neoplasm of the implantation site. J. Reprod. Med. 29:821 -25,1984.*
10. *Young, R.H., Kurman, R.J., Scully, R.E. Proliferations and tumours of intermediate trophoblast of the placental site. Semin. Diagn. Pathol. 5:223-37, 1988*
11. *Finkler, N.J. Placental site tumour: Diagnosis, clinical behavior and treatment. J.Rep.Med. 36:27-30,1991.*
12. *Lathrop, J.C., Lauchlan, S., Nayak, R. et al. Clinical characteristics of placental site tumour (PSTT). Gynecol.0ncol.31:32,1988*
13. *Finkler, N.J., Berkowitz, R.S., Driscoll, S.G. et al. Clinical experience with placental site trophoblastic tumours at the New England Trophoblastic disease center. Obstet. Gynecol. 71:854-7,1988.*
14. *Dessau , R., G.J.S. Rustin, D., Dent. J et al. Surgery and chemotherapy in the management of placental site tumour. Gynecol.Oncol. 39:56-9,1990.*
15. *Newlands, E.S., Bagshave, K.D., Begent, R.H.J. et al. Developments in chemotherapy for medium and high risk patients with gestational trophoblastic tumours (1979-1984). Brit.J. Obstet. Gynaecol. 93:63-9,1986.*
16. *Hopkins, M., Nunez, C., Murphy, J.R. et al. Malignant placental site trophoblastic tumour. Obstet. Gynecol. 66:95S-100S,1985*
17. *Gloor, E., Hurlimann, J. Trophoblastic Pseudotumour of the Uterus: Clinicopathologic Report with Immunohistochemical and Ultrastructural Studies. Am.J.Surg.Pathol.5:5-13,1981.*