Placental site trophoblastic tumor (PSTT) with multiple metastases and extremely poor prognosis

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Abstract Placental site trophoblastic tumor (PSTT) is a rare type of gestational trophoblastic disease. There is a wide clinical spectrum of presentation and behavior ranging from a benign condition to an aggressive disease with a fatal outcome. PSTT limited to the uterus is in a good prognosis group, but PSTT with metastasis is a lethal disease. We document a case of PSTT with multiple metastases and extremely poor prognosis. A 36-year-old woman had abnormal irregular vaginal bleeding 14 months after her third pregnancy and delivery. The mitotic count of the tumor cells was quite high (23/10 high-power fields). It would have been difficult to remove the tumor by surgery because of the tumor size and its invasion, so we suggested chemotherapy. We treated her with EMA/CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine) as a first-line regimen. During the sixth cycle of EMA/CO, the disease became drug-resistant and she died 8 months after the first symptom. This was a rare case among documented patients with PSTT with metastasis, with the patient having short-term survival (<1 year). We conclude that a high mitotic count and atypical undifferentiated pathological features are significant poor prognostic factors for survival in PSTT.

Key words Placental site trophoblastic tumor · Prognosis · Mitosis

Introduction

Placental site trophoblastic tumor (PSTT) is rare and accounts for 1%-2% of cases of gestational trophoblastic disease (GTD). There is a wide clinical spectrum of presentation and behavior ranging from a benign condition to an aggressive disease with a 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

A 36-year-old woman (gravida 3, para 3) had abnormal irregular vaginal bleeding 14 months after a pregnancy. This pregnancy had been full-term at 40 weeks, with vaginal delivery, and she had delivered a female infant, her third child. After 14 months she had vaginal bleeding and low-grade fever which continued for 2 months before she visited a nearby clinic (16 months after the pregnancy). Cervical cancer was suspected at the clinic. Then she was referred from the clinic to our center. Upon her first visit to our center, a speculum examination revealed a bloody, fragile tumor of the uterine cervix. Ultrasonography detected the tumor as a low-echoic lesion and the size was 64 × 52 mm. Her blood data were unremarkable, except for inflammation (WBC, 9.97 × 10^9/μl, C-reactive protein [CRP], 3.36 mg/dl). Tumor markers (squamous cell carcinoma [SCC], carcinoembryonic antigen [CEA], carbohydrate antigen [CA] 19-9, and alpha-fetoprotein [AFP]) were at normal levels, except for CA125, at 69.3 IU/l (normal range [NR], under 37 IU/l). Serum β- human chorionic gonadotropin (hCG) level was 80 mIU/ml (NR, under 10 mIU/ml) and human placental lactogen (hPL) level was in the normal range (under 0.05 μIU/ml).

In cervical cytology, tumor cells with centrally located nuclei and abundant cytoplasm stained light green and showed no specific structures such as sheets or ducts (Fig. 1a). Histological examination of a punch biopsy specimen showed that round to polygonal large tumor cells had diffusely infiltrated the cervical tissue in which mucous glands remained (Fig. 1b). The mitotic figures in the tumor cells were numerous, with mitotic counts of up to 23/10 high-power fields (HPFs).
Immunohistochemistry showed that the round to polygonal tumor cells were positive for hPL (Fig. 1c), keratin, and vimentin, and negative for placental alkaline phosphatase [PLAP], Human Melanin Black 45 [HMB45] and leukocyte common antigen [LCA]. A minor component, less than 0.1% of the tumor cells showed an admixture of syncytiotrophoblasts (ST) and cytotrophoblasts (CY). The tumor was diagnosed as a placental site trophoblastic tumor (PSTT) with microscopic foci of choriocarcinoma. A differential diagnosis of PSTT from choriocarcinoma (CC) is necessary for the treatment of GTD. The patient’s serum hCG level was very low for CC. A clinico-pathological diagnosis of PSTT was made, though there were tiny foci of CC in the cervical biopsy specimen.

First, magnetic resonance imaging (MRI) showed the uterine cervix tumor (Fig. 2). Then a chest computerized tomography (CT) scan showed multiple metastatic nodules and swollen lymph nodes in both lungs (Fig. 3) and in the pelvis, as well as paraaortic lymph node swelling, and an abdominal CT detected the uterine cervix tumor (Fig. 4).

Hysterectomy is the primary mode of treatment for localized PSTT. However, in this patient, it was difficult to remove the tumor by surgery because of its size and invasion, so we suggested chemotherapy. We treated the patient with EMA/CO (etoposide, 100 mg/m² on days 1 and 2; methotrexate, 100 mg/m² plus 200 mg/m² as a 12-h infusion on day 1; actinomycin-D, 0.5 mg/m² on days 1 and 2; cyclophosphamide, 600 mg/m² on day 8; and vincristine, 1.0 mg/m² on day 8; with each cycle repeated every 14 days) as a first line regimen. After the patient had been given five cycles of EMA/CO, the cervical tumor was reduced from 64 × 52 mm to 43 × 42 mm on ultrasonography. On the control CT, the pulmonary metastatic lesions were slightly reduced in size. So we thought this regimen was effective and it was continued, in order to prepare for surgery. But during the sixth cycle of EMA/CO, she had irregular vaginal

**Fig. 1.** a Cytology of the cervical smear. Tumor cells with centrally located nuclei and abundant cytoplasm. b Histology of the cervical biopsy. Round to polygonal large tumor cells have diffusely infiltrated the cervical tissue in which scattered mucous glands remain. Mitotic figures (arrows) are evident. c Immunohistochemistry. The round to polygonal tumor cells were positive for human placental lactogen (hPL). d Minor component of the cervical tumor. Less than 0.1% of the tumor cells showed an admixture of syncytiotrophoblasts (ST) and cytotrophoblasts (CY). The tumor was diagnosed as a placental site trophoblastic tumor (PSTT) with microscopic foci of choriocarcinoma. a Papanicolaou, ×600; b H&E, ×400; c ×400; d H&E, ×400