© Curr Gynecol Oncol 2016, 14 (3), p. 174–177
DOI: 10.15557/CGO.2016.0021

Received: 13.10.2016
Accepted: 21.11.2016
Published: 30.11.2016

Hyun Young Kwon, Jung-Woo Park

Incidentally diagnosed epithelioid trophoblastic tumor immediately after delivery: a case report

Przypadkowe rozpoznanie nowotworu nabłonkowatokomórkowego trofoblastu bezpośrednio po porodzie – opis przypadku

Department of Obstetrics and Gynecology, Dong-A University, College of Medicine, 26, Daesingongwon-ro, Seo-gu, Busan, 49201, Republic of Korea
Correspondence: Jung-Woo Park, MD, Department of Obstetrics and Gynecology, Dong-A University College of Medicine, 26 Daeshingongwon-ro, Seo-gu, Busan, 602-715, Korea, tel.: +82-51-240-5090, e-mail: mdpjw1216@gmail.com

Abstract

Epithelioid trophoblastic tumor is a rare malignant lesion of gestational trophoblastic disease, and constitutes an abnormal proliferation of placental trophoblasts. Patients with epithelioid trophoblastic tumor are usually of reproductive age, and have had previous gestations including full-term deliveries, molar pregnancies and abortions. The interval between antecedent gestational events and the diagnosis of epithelioid trophoblastic tumor usually ranges from 0 to 264 months (mean, 84 months). Herein, we report a 42-year-old Korean woman (gravida 2, para 2). At 38 weeks of gestation, she underwent a repeat cesarean section and then hysterectomy due to uterine atony. She was incidentally diagnosed with epithelioid trophoblastic tumor, and postoperatively no metastatic disease was observed. The patient presented no clinical evidence of tumor recurrence for 5 years after surgery. This case is remarkable because epithelioid trophoblastic tumor is a rare disease, and the diagnosis of epithelioid trophoblastic tumor followed immediately after delivery.

Key words: epithelioid trophoblastic tumor, gestational trophoblastic disease, rare tumor, uterine neoplasm

Streszczenie

Nowotwór nabłonkowatokomórkowy trofoblastu (*epithelioid trophoblastic tumor*) to rzadka złośliwa postać ciążowej choroby trofoblastycznej. Charakteryzuje się nieprawidłowym rozrostem komórek trofoblastu. Zmiany tego typu rozpoznaje się u kobiet w wieku rozrodczym z ciążą w wywiadzie, zarówno donoszoną, jak i przedwcześnie zakończoną, również z zaśniadem groniastym. Czas między ciążą a rozpoznaniem nowotworu nabłonkowatokomórkowego trofoblastu wynosi od 0 do 264 miesięcy (średnio 84 miesiące). Przedstawiamy przypadek 42-letniej pacjentki z Korei (*gravida* 2, *para* 2), u której w 38. tygodniu ciąży wykonano cięcie cesarskie, a następnie histerektomię ze względu na atonię macicy. Przypadkowo rozpoznano nowotwór nabłonkowatokomórkowy trofoblastu, a po zabiegu nie zaobserwowano przerzutów. Pacjentka nie wykazywała cech nawrotu przez 5 lat po zabiegu. Prezentowany przypadek jest szczególny, ponieważ nowotwór nabłonkowatokomórkowy trofoblastu to rzadkość, a rozpoznano go bezpośrednio po porodzie.

Słowa kluczowe: nowotwór nabłonkowatokomórkowy trofoblastu, ciążowa choroba trofoblastyczna, rzadki nowotwór, nowotwór macicy

INTRODUCTION

Gestational trophoblastic disease (GTD) constitutes an abnormal proliferation of placental trophoblasts, and exhibits specific pathogenesis and clinical features[1]. The modified classification of GTD by the World Health Organization defines complete and partial hydatidiform moles as benign lesions of GTD, and invasive moles, choriocarcinoma (CC), and epithelioid trophoblastic tumors (ETT) as malignant lesions of GTD.
ETT is difficult to recognize as a trophoblastic disease because of its very low incidence, and its growth pattern that simulates a poorly differentiated carcinoma and other GTDs[1,2]. Most cases of ETT occur in women who are of reproductive age and have a prior gestational history. The reported interval between the previous gestation and the diagnosis of the tumor ranges from 0 to 264 months (mean, 84 months)[3–5]. ETT found in the immediate postpartum period is extremely rare; it has been reported only once previously[5]. Here we report a case of ETT found immediately after delivery.

CASE REPORT

A 42-year-old Korean woman (gravida 2, para 2) was transferred to our hospital for antenatal care because she was pregnant at an advanced maternal age and had gestational diabetes mellitus. Her obstetric history was uncomplicated: she had delivered by cesarean sections earlier, 4 and 5 years before, and we had no prior knowledge of her other medical history. Preoperatively, her serum HbA1C level (5.7%) and other laboratory findings were unremarkable. At 38 weeks of gestation, she underwent a repeat cesarean section, and a healthy infant weighting 5010 g was delivered. Unexpectedly, during surgery, we saw the lower uterine segment bloated with active bleeding and uterine atony. Therefore, we made a decision to perform hysterectomy to control bleeding; there were no postoperative complications.
Grossly, the uterus appeared to have nonspecific findings (Fig. 1). Pathological examination revealed that a minute portion of the endometrium exhibited aberrant proliferation of trophoblasts, and these tumor cells were epithelioid with occasional mitotic figures (Fig. 2A). On immunohistochemical staining, these cells were strongly positive for p63 (Fig. 2B) and CD10 (Fig. 2C). In addition, the proliferation index, as assessed by the Ki-67 labeling index, was higher than 10%, and lymphocytic infiltration was not conspicuous (Fig. 2D). These histological and immunohistochemical findings were consistent with features of ETT.
Postoperatively, computed tomography of the abdomen, pelvis and chest was performed for ruling out metastases. It revealed no significant findings. Although the preoperative serum-*B*-human chorionic gonadotropin levels of the patient were not checked, the postoperative levels were normal. She was followed-up regularly every 3 months by blood tests for complete blood cell count, liver and kidney function tests and chest radiography. There was no clinical evidence of tumor recurrence for 5 years after surgery.

DISCUSSION

ETT is a rare tumor composed of chorionic-type intermediate trophoblasts, and was initially described as an atypical choriocarcinoma in patients with lung metastases in 1998 by Whin and Kurman[1,2,6,7]. Patients with ETT are usually of reproductive age, ranging from 15 to 50 years of age (mean, 34.9 years), and have had previous gestations, including, full-term deliveries (67%), molar pregnancies (16%) and abortions (16%)[6,8]. The interval between the antecedent gestational events and the diagnosis of ETT ranges from 0 to 264 months (mean, 84 months)[5]. It is extremely rare to find ETT immediately after delivery, as was the case with our patient[5,9]. Tab. 1 compares the intervals from antecedent pregnancies in several case reports of ETT before 2016[1,3–5,9,10]. Tab. 2 compares the previous history, documented in the literature published in English, which summarizes the factors of mixed GTD. It documents the shortest intervals from antecedent pregnancy for mixed GTD cases before 2015, the shortest of which was 7 months after term delivery[8].
The most common symptom of ETT is abnormal vaginal bleeding. Other symptoms are amenorrhea and irregular menstruation[2,5]. Fifty percent of ETTs are located in the lower uterine segment of the cervix; 30%, in the uterine corpus; and 20%, in extrauterine sites including the lungs and the small bowel[4]. It is reported that 25% of patients with ETT develop metastases, most frequently in the lungs. Ten percent of patients die of the disease. Therefore, exact diagnosis is very important[2].

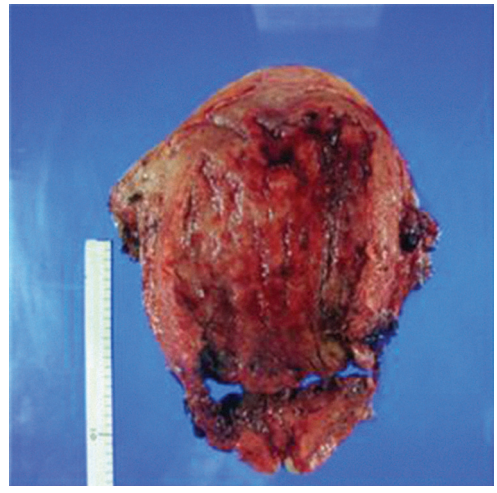

Fig. 1. Grossly, this uterus appeared to have nonspecific findings after hysterectomy for treatment of bleeding due to uterine atony

 DOI: 10.15557/CGO.2016.0021

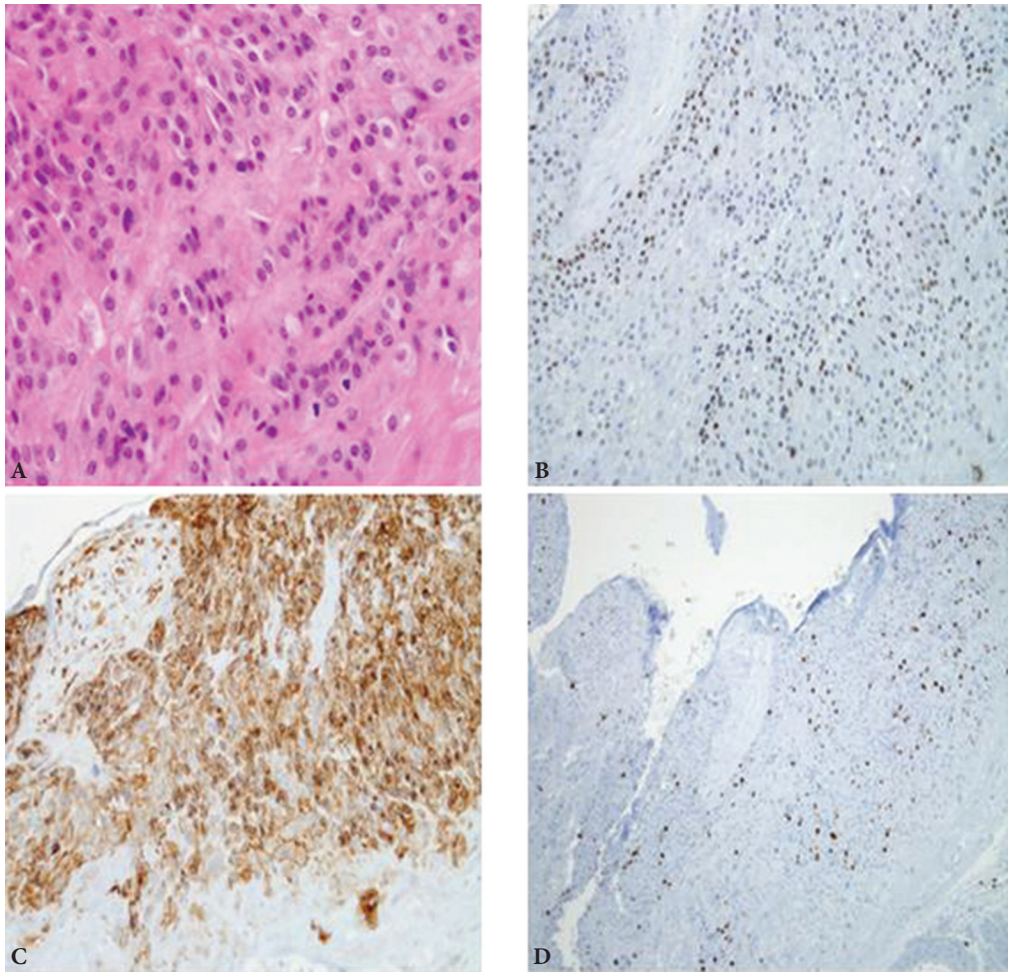

Fig. 2. Pathological examination, these tumor cells were epithelioid with occasional mitotic figures (A, hematoxylin and eosin staining, ×400). On immunohistochemical staining, these cells were strongly positive for p63 (B, ×400) and CD10 (C, ×400). In addition, the proliferation index, as assessed by the Ki-67 labeling index, was higher than 10%, and lymphocytic infiltration was not conspicuous (D, ×400)

Reference Number	Age (years)	Antecedent pregnancy	Interval from antecedent pregnancy (months)
5	36	Term	0
9	45	Nulliparous	0
4	36	Hydatidiform mole	12
2	32	Artificial abortion	12
5	24	Term	20
5	28	Term	26
5	33	Abortion	26
5	38	Abortion	36
1	44	Term	48
9	41	Term	48
5	37	Term	72
5	39	Abortion	144
10	43	Term	156
5	40	Term	168
5	44	Term	264

Tab. 1. Cases of ETT in women of reproductive age with prior gestation

DOI: 10.15557/CGO.2016.0021

Reference Number	Age (years)	Antecedent pregnancy	Interval from antecedent pregnancy (months)	Mixed GTD (proportion of component)
8	20	Term	7	ETT + Focal areas CC
8	32	Artificial abortion	12	ETT + Focal CC
8	41	Cesarean delivery	12	ETT + PSTT (not mentioned)
8	15	Complete mole	12	ETT + Focal areas PSTT
8	50	Complete mole	36	1/3 CC + 2/3 ETT
8	39	Term	84	ETT + Focal areas CC + Focal areas PSTT
GTD – gestational trophoblastic disease; **ETT** – epithelioid trophoblastic tumor; **CC** – choriocarcinoma; **PSTT** – placental site trophoblastic tumor.				

Tab. 2. Cases of mixed gestational trophoblastic disease (GTD) in women of reproductive age with prior gestation

ETT can be misdiagnosed as other forms of GTD or as squamous cell carcinoma of the cervix because of the resemblance in behavior and the epithelioid appearance of tumor cells. Immunohistochemical staining for cytokeratin 18 and inhibin helps to distinguish ETT from these forms of disease, as these markers are positive in ETT but negative in squamous cell carcinoma[2,11]. Additionally, the Ki-67 proliferative index can be useful for differential diagnosis, because it is low in placental site trophoblastic tumor (PSTT) (15–25%) and ETT (10–25%), but relatively high (>50%) in squamous cell carcinoma and CC[12]. Raised serum β-hCG levels in most cases of ETT are associated with a large mass and high mitotic activity[2,9]. In addition, p63 is expressed in chorionic-type intermediate cells of ETT, but not in PSTT[8].

In summary, we have reported an ETT found incidentally in a patient undergoing hysterectomy for treatment of uterine atony. As is seen in Tabs. 1 and 2, ETT is associated with a prior gestational history, but its pathogenesis is yet unclear. Additional cases need to be studied to determine the relationship between the occurrence of ETT and previous gestations. Therefore, our patient deserves attention not only because she had a rare disease, but also because she was diagnosed with ETT immediately after delivery by cesarean section.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

1. Liu Q, Shi QL, Zhang JM *et al.*: Epithelioid trophoblastic tumor of the uterus: a report of. Chin Med J (Engl) 2007; 120: 729–730.
2. Meydanli MM, Kucukali T, Usubutun A *et al.*: Epithelioid trophoblastic tumor of the endocervix: a case report. Gynecol Oncol 2002; 87: 219–224.
3. Madhu B, Gerbi R, Nabila R: Epithelioid trophoblastic tumor and its diagnostic dilemmas: a rare case report. Gynecol Oncol Case Rep 2011; 2: 42–43.
4. Oldt RJ 3rd, Kurman RJ, Shih IeM: Molecular genetic analysis of placental site trophoblastic tumors and epithelioid trophoblastic tumors confirms their trophoblastic origin. Am J Pathol 2002; 161: 1033–1037.
5. Shen X, Xiang Y, Guo L *et al.*: Analysis of clinicopathologic prognostic factors in 9 patients with epithelioid trophoblastic tumor. Int J Gynecol Cancer 2011; 21: 1124–1130.
6. Shih IM, Kurman RJ: The pathology of intermediate trophoblastic tumors and tumor-like lesions. Int J Gynecol Pathol 2001; 20: 31–47.
7. Shih IM, Kurman RJ: Ki-67 labeling index in the differential diagnosis of exaggerated placental site, placental site trophoblastic tumor, and choriocarcinoma: a double immunohistochemical staining technique using Ki-67 and Mel-CAM antibodies. Hum Pathol 1998; 29: 27–33.
8. Shih IM, Kurman RJ: Epithelioid trophoblastic tumor: a neoplasm distinct from choriocarcinoma and placental site trophoblastic tumor simulating carcinoma. Am J Surg Pathol 1998; 22: 1393–1403.
9. Shih IM, Seidman JD, Kurman RJ: Placental site nodule and characterization of distinctive types of intermediate trophoblast. Hum Pathol 1999; 30: 687–694.
10. Sung WJ, Shin HC, Kim MK *et al.*: Epithelioid trophoblastic tumor: clinicopathologic and immunohistochemical analysis of three cases. Korean J Pathol 2013; 47: 67–73.
11. Vencken PM, Ewing PC, Zweemer RP: Epithelioid trophoblastic tumour: a case report and review of the literature. J Clin Pathol 2006; 59: 1307–1308.
12. Zhang X, Zhou C, Yu M *et al.*: Coexisting epithelioid trophoblastic tumor and placental site trophoblastic tumor of the uterus following a term pregnancy: report of a case and review of literature. Int J Clin Exp Pathol 2015; 8: 7254–7259.