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Case Report

Gestational Choriocarcinoma of the Cervix

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Abstract

Choriocarcinoma is the most aggressive, malignant form of gestational trophoblastic disease and has varying incidence, increasing in patients older than 40 years. It usually develops after a malignant alteration in a molar pregnancy, but rarely after an abortion or normal or ectopic pregnancies. The most common localization is the uterus, but it can also be found rarely in the ovaries, fallopian tubes, vagina, vulva, cervix or pelvic region.

A 38-year-old multiparous woman, with no complications in three previous labors and four miscarriages, presented to her gynecologist one year after the last miscarriage complaining of abnormal vaginal bleeding. Clinical examinations showed normal ultrasound and histopathology findings. Blood analysis demonstrated moderate anemia and low elevated serum b-human chorionic gonadotropin. Due to profuse hemorrhage and anemia after the curettage, the medical council decided that a total hysterectomy should be performed. Macroscopic examination of the post-operative material showed regular morphology of the uterus, fallopian tubes and ovaries. However, a whitish brown lesion with a maximum diameter of 22 mm was noted in a longitudinal section of the cervix. Using standard histopathology and immunohistochemical analysis, a cervical gestational choriocarcinoma was diagnosed.

Knowledge of the characteristics of the choriocarcinoma is very important for accurate diagnosis and treatment, especially when the tumor is localized on the rare locations and where a high level of serum b-human chorionic gonadotropin is absent.

Keywords: Choriocarcinoma, Chorionic gonadotropin beta subunit human, Immunohistochemistry, uterine cervical neoplasms

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Introduction

Choriocarcinoma (CC) is a rare, malignant form of gestational trophoblastic disease. It usually develops after a malignant alteration in a molar pregnancy and rarely after an abortion, or normal or ectopic pregnancies.^{1,2} The most common localization of gestational CC is the uterus; it can be found only rarely in the fallopian tubes, vagina, vulva, cervix or pelvic region.^{3,4} Some cases of an intraplacental CC coexisting with a uterine pregnancy have also been reported.⁵

The diagnostic criteria for extrauterine CC described by Saito, et al. are absence of disease in uterine cavity, pathologic confirmation of disease, exclusion of molar pregnancy and exclusion of a coexisting normal intrauterine pregnancy.⁶ Here we present a patient with gestational cervical CC occurring 13 months after an induced abortion.

Case Report

The patient, 38 years of age, multiparous, with no complications during three previous labors and four previous abortions, contacted her gynecologist because of an irregular vaginal hemorrhage. The bleeding was occasional and sparse and lasted for 13 months

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after the last induced abortion. During that period, the patient underwent ultrasonography of the pelvis, followed by explorative curettage of the endometrium. Endovaginal ultrasonography was not available at that time and transabdominal ultrasound findings were normal, with no signs of pregnancy; both adnexa had regular morphology and the uterine cavity was empty. Microscopy of the material obtained by curettage showed the occasional decidual transformation of endometrial tissue.

The patient underwent blood tests and repeated exploratory curettage. On the fourth day after the intervention, a total hysterectomy was performed because of the profuse hemorrhage and anemia. Blood analysis demonstrated moderate anemia (hematocrit 26%) and low elevated serum b-human chorionic gonadotropin (b-hCG) level (13 mIU/mL; normal value > 5 mIU/mL).

Apart from occasional irregular desquamated cells and decidual transformation of the endometrium, histopathology of the material obtained from explorative curettage showed the presence of clusters and individual polymorphic cells resembling cytotrophoblasts with markedly atypical nuclei. These indicated the possible presence of a trophoblast-derived tumor. Macroscopic examination of the operative material showed regular morphology of the uterus, Fallopian tubes and ovaries, while a longitudinal section of the cervix showed a whitish brown lesion with a maximum diameter of 22 mm covering the isthmus and infiltrating most part of the cervical wall (Figure 1a, 1b). Standard histopathology and immunohistochemistry confirmed the diagnosis of a gestational CC in the cervix. Tumorous tissue was confirmed on routine hematoxylin and eosin (H&E) stained sections of the cervix, consisting of all three trophoblastic cell types, with areas of necrosis and hemorrhage as well as irregular infiltrating edges (Figure 2a).



Figure 1. Macroscopic examination of the surgically removed specimen showed normal morphology of the uterus, Fallopian tube and ovaries, but a pale brown lesion was noted in a longitudinal section of the cervix with a largest diameter of 22 mm (a and b).

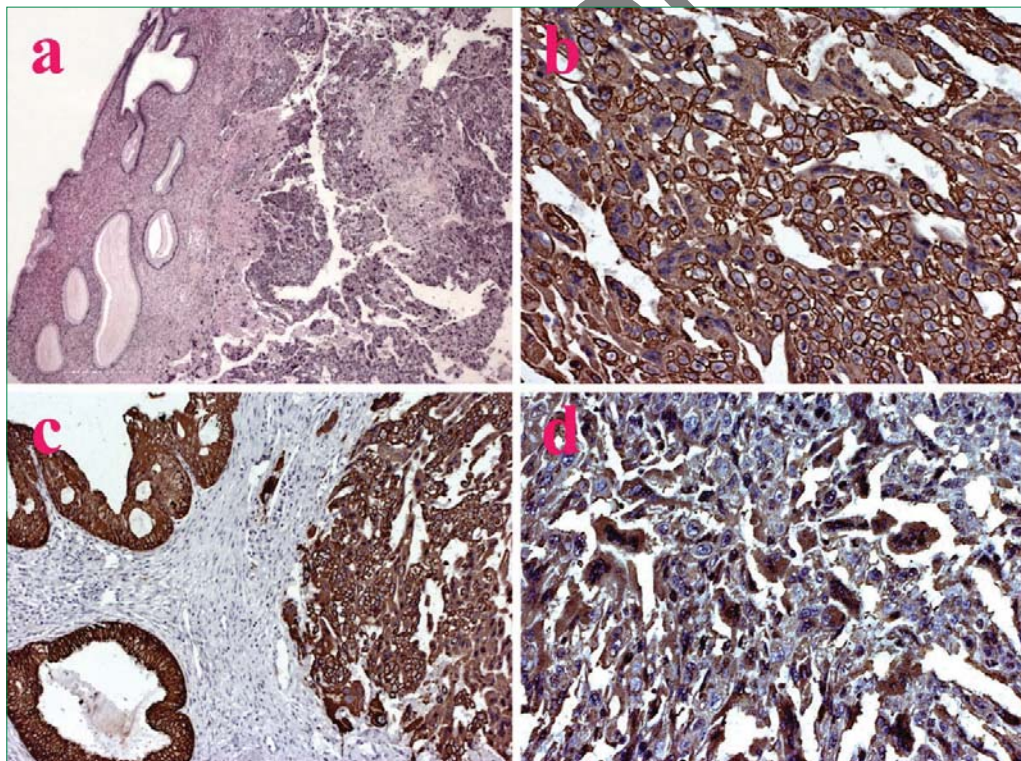


Figure 2. Tumorous tissue was confirmed on routine H&E stained sections of the cervix, consisting of all three trophoblastic cell types with areas of necrosis and hemorrhage and with **a)** irregular infiltrating edges, x100; **b)** Immunohistochemistry showed diffuse positivity in most cells for CK18, x400 **c)** A1/3, x200; **d)** hCG, x400.

The tumor consisted of alternately and randomly scattered zones of cytotrophoblasts, with marginally distributed syncytiotrophoblasts and inserted areas of intermediary trophoblasts. Numerous foci of vascular invasion were identified. Immunohistochemically, the tumor cells were CK18, CK A1/3 and hCG positive (Figure 2b – 2d), while the proliferation index was very high with about

70% of the nuclei expressing Ki-67.

Postoperatively, positive emission tomography (PET) scanning, pathological tumor–node–metastasis (pTNM) staging and normal b-hCG levels defined a FIGO stage I of the disease. Adjuvant chemotherapy was advised, but the patient refused to take it and one year after surgery, there is no sign of recurrence or any other ailments.

Discussion

Choriocarcinoma is the most aggressive malignant form of gestational trophoblastic disease, with varying incidence, increasing in cases of molar pregnancy and in patients older than 40 years.⁷ Data suggest that 0.76% – 4% of all cases of gestational CC arise from an ectopic pregnancy.⁸ The latent period between the last pregnancy and the occurrence of CC can be from a few months up to 15 years.⁹

Cervical CC is very rare. A MEDLINE search with the key words “cervical gestational choriocarcinoma” shows 36 published papers. Among them, there are only two series with four cases each, whereas the others report individual presentations.^{10,11}

Several hypotheses have been postulated to explain the pathogenesis of cervical CC. It might develop via cervical metastases from a primary tumor in the corpus that later spontaneously regresses, from the malignant transformation of a cervical pregnancy, or by transport of chorionic cells from a previous pregnancy that have undergone malignant transformation after a dormant period.¹²⁻¹⁴ The macroscopic presentation of a typical CC is a hemorrhagic mass with areas of necrosis and irregular edges. Microscopically, they show a typical biphasic image. The central area consists of cytotrophoblasts, with marginal syncytiotrophoblasts being distributed alternately. Rarely these two cell types can rotate in an alternating sequence with insertions of intermediate trophoblast. There are nuclear atypia with numerous mitotic figures with clear zones of necrosis and hemorrhage. There are also numerous foci of vascular invasion.

For a differential diagnosis, a CC must be distinguished from an undifferentiated carcinoma and variants of epithelioid smooth muscle tumors. Accurate diagnosis is facilitated by immunohistochemistry, because the CC cells express variable trophoblastic markers such as hCG, inhibin, human leukocyte antigen-G and Mel-CAM (CD146).¹⁵ It is very important to diagnostically exclude intermediate variants such as placental trophoblastic and epithelioid trophoblastic tumors. Intermediate trophoblastic tumors are not sensitive to chemotherapy, and in the clinical treatment of affected patients hysterectomy is the procedure of choice.^{16,17} Finally, in the case of extrauterine localization of the tumor, it is necessary to differentiate whether it has a gestational or non-gestational origin. This is achieved by molecular genotyping and finding unique paternal genetic material in the tumor, as well as demonstrating immunohistochemical positivity for p57KIP2.^{18,19} We did not have the technical means for this analysis, therefore we declared this cervical CC as being of gestational origin based on data from an induced abortion 13 months previously.

Trophoblastic tumors, particularly CCs, produce up to 100 times the amount of b-hCG compared to a normal pregnancy. Therefore, the measurement and monitoring of the b-hCG concentration are of great diagnostic significance, and after therapy this hormone is the most important marker of disease recurrence.²⁰ However, in some cases of ectopic pregnancy, there have been cases of a very small increase or even a normal level of β -hCG.²⁰⁻²² In our case, the serum b-hCG level of 13 mIU/mL created additional diagnostic confusion. In general, the diagnosis of a primary extrauterine CC is challenging because the clinical symptoms can be nonspecific and often mimic other pathological conditions.³

Choriocarcinomas show a great ability for vascular invasion

and can metastasize into the lungs, brain, liver and bone, and very rarely into the fetus.⁷ Because of the high metastatic potential, in cases of an extrauterine localization of a CC some authors recommend surgical resection followed by adjuvant chemotherapy.³ In most cases, a CC is treated effectively with chemotherapy, whereas hysterectomy is the option only in cases of extensive uterine hemorrhage, as with our patient.^{16,23}

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توجه: بررسی مقاله ای متون (مقدماتی)

کارگاه آنلاین
بررسی مقابله ای متون (مقدماتی)

PROPOSAL
پروپوزال

توجه: پروپوزال نویسی و پایان نامه نویسی

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پروپوزال نویسی و پایان نامه نویسی

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