

## CASE COMMENTARY

# Primary Non-Gestational Uterine Cervical Choriocarcinoma with Metaplastic Transformation from Squamous Cells

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### Abstract

**Background:** Primary non-gestational uterine cervical choriocarcinoma is very unusual and although it has been hypothesized that it can arise by metaplastic transformation of cervical epithelium, solid evidence has been lacking. **Case:** Primary non-gestational uterine cervical choriocarcinoma was diagnosed in a 47-year-old, woman undergoing tubal resection 17 years previously. A histologically- and immunohistochemically-confirmed, non-gestational cervical choriocarcinoma could be diagnosed in which there was metaplastic transformation from squamous cells. The patient underwent 5 courses of an actinomycin-D chemotherapeutic regimen and radical hysterectomy with bilateral pelvic lymphadenectomy. **Conclusion:** Primary non-gestational uterine cervical choriocarcinoma may indeed arise from metaplastic transformation of epithelial tissue.

**Key Words:** Choriocarcinoma - cervical cancer - metaplastic origin

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### Background

Choriocarcinoma of the female genital tract can be either gestational or non-gestational. Gestational choriocarcinoma is the result of a pregnancy and is usually located in the uterine corpus. Primary extra-uterine choriocarcinoma is very rare, found mostly in the ovaries. Non-gestational choriocarcinomas can arise from germ cells but also possibly from metaplastic transformation of epithelium.

A non-gestational origin of primary choriocarcinoma of the uterine cervix can be definitely determined by genetic study, which is generally lacking in case reports (Newlands, 2003). The prognosis of this tumor is extremely poor, despite chemotherapy and surgery. Although it has been hypothesized that primary non-gestational choriocarcinoma of the uterine cervix might be metaplastically transformed from cervical epithelium, no case report with solid evidence of this transformation has ever been published. There were only 2 cases of primary non-gestational choriocarcinoma of the uterine cervix which could be either metaplastically transformed from, or mixed with, cervical adenocarcinoma reported in the literature (Morimura et al., 1996; Shintaku et al., 2000). Herein, we describe a first case of primary, non-gestational, uterine cervical choriocarcinoma in which metaplastic transformation from squamous cells could be shown, thereby supporting the previously described hypothesis.

### Clinical Presentation

Primary non-gestational uterine cervical

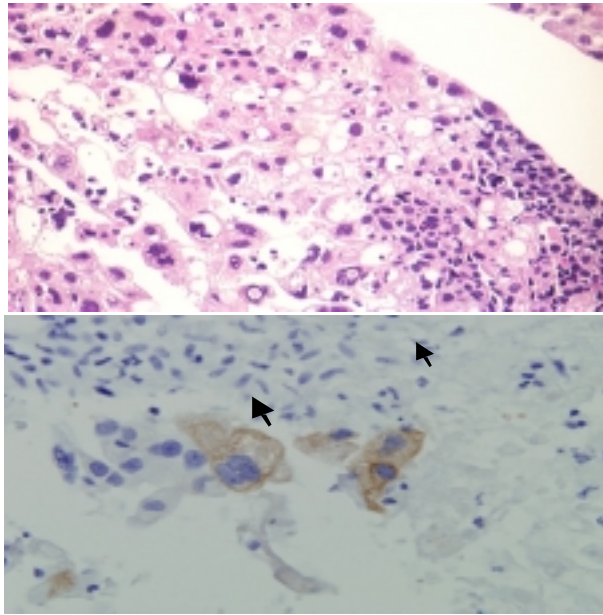
choriocarcinoma was diagnosed in a 47-year-old, 5-year-non-sexually-active patient, who had had a postpartum tubal resection some 17 years prior. Her last Pap smear and pelvic examination were done two years previously and they were all normal. She had had two husbands and her sexual debut was at 18 years of age. She and her husbands had no history of sexually-transmitted disease but her second husband had multiple sexual partners.

A pelvic examination revealed an 8x8x6 cm diameter tumor mass (measurement by transvaginal sonography) occupying the uterine cervix. Cervical biopsy was repeated because the authors wanted more diagnostic accuracy and a second opinion. The serum beta-hCG was positive with only a low titer (8 mIU/mL). Metastatic investigations (CXR, IVP and ultrasonography of the upper abdomen) were done and the patient was confirmed with cervical cancer, FIGO stage IB2. After all previous biopsy slides and repeated biopsy slides were reviewed, the diagnosis of primary cervical choriocarcinoma showing metaplastic transformation from squamous cell was established. Then the patient underwent 5 courses of actinomycin-D chemotherapeutic regimen beginning on September 28, 2006. Radical hysterectomy with bilateral pelvic lymphadenectomy was performed on December 6, 2006 (13 days after the 5th course's first day). All lymph nodes, parametrial and margins were negative without any LVSI. Six months after surgery (June 4, 2007), the patient was still in remission with both the Pap smear and beta-hCG still negative (<5 mIU/mL).

### Histological Presentation

The first histological biopsy revealed malignant cells

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**Figure 1. A) Note Multinucleated Giant Cells with Hyperchromatic Nuclei. B) These are Positive For hCG (arrows)**

with some multinucleation and hyperchromatic nuclei (Figure 1A), immunohistochemically positive for hCG (Figure 1B). The first diagnosis was choriocarcinoma of the cervix suggestive of a non-gestational origin. The histology of the hysterectomy specimen demonstrated non-keratinizing squamous cell carcinoma and abnormal cells similar to the previous biopsy. The other areas also displayed squamous cell carcinoma in situ. The immunohistochemical studies of hCG were positive in the latter cells. The markers of squamous cells were positive in the former groups; therefore, the final diagnosis was non-keratinizing squamous cell carcinoma with choriocarcinoma differentiation.

## Discussion

Primary, non-gestational uterine cervical choriocarcinoma is extremely rare and may arise from metaplastic transformation of epithelial tissue. This hypothesis has been proposed by many authors (Morimura et al., 1996; Shintaku et al., 2000; Baykal et al., 2003; Maesta et al., 2005). This case's pathological examination is the first case showing evidence supporting the hypothesis in a squamous cell carcinoma of the uterine cervix. Previously, it was supported by one case of clear cell (Morimura et al., 1996) and one of adenocarcinoma (Shintaku et al., 2000). Authors did not agree with Maesta et al. (2005) in staging such a case as a choriocarcinoma, therefore, we staged our case as a cervical cancer as per Baykal et al (2003). We did, however, agree with Maesta et al (2005) in using a chemotherapeutic regimen for choriocarcinoma, directing us to use actinomycin-D as a neoadjuvant chemotherapeutic agent. In addition, because we stage this case as a cervical cancer, we performed a type III radical hysterectomy with bilateral pelvic lymphadenectomy as the definitive treatment for her, again, as per Baykal et al (2003).

Poorly differentiated squamous cell carcinoma of the uterine cervix can mimic a primary non-gestational cervical choriocarcinoma in 2 different ways: (1) a similar histologic appearance misleading diagnosis (Horn et al., 1997), and (2) the occasional production of hCG (Nishimura et al., 1998; Hameed et al., 1999 ). Notwithstanding, our diagnosis in this case was based on a careful review of histological evidence, immunohistochemical staining, serum beta-hCG and finally confirmed by an inter-institutional pathologic panel consensus.

Primary gestational choriocarcinoma of the uterine cervix is rare with only 60 cases reported in the English-language literature (al Hassani and Ejeckam, 1995; Lema et al., 1997; Yahata et al., 1997; Roopnarinesingh et al., 2004 ). In some cases, surgery is needed because of the size of the tumor and its poor responsiveness to chemotherapy, as in our case. Serum beta-hCG might not be detected in some of those cases using usual protocols (Mehra et al., 2005). This also can vice versa mimic the poorly differentiated squamous cell carcinoma of the cervix. We were, however, confident of our diagnosis, based on the criteria mentioned above until we examined the specimens from the radical hysterectomy which revealed squamous cell carcinoma differentiation to choriocarcinoma. Our final diagnosis was changed because our first diagnosis was based upon a small piece of tissue, which does not have the diagnostic weight of a large and complete sample. Therefore, our last examination completed the evidence supporting the origin of this cancer type.

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