Case Report

Primary clear cell adenocarcinoma of the uterine cervix in a young woman not associated with diethylstilbestrol: A case report and review of literature

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ABSTRACT

We report an extremely rare case of primary clear cell adenocarcinoma (CCA) of the uterine cervix in a 21-year-old Asian female, with no maternal history of diethylstilbestrol ingestion during pregnancy. A review of the relevant literature regarding the possible etiology and treatment of primary CCA of cervix is done.

Keywords: Clear cell adenocarcinoma, diethylstilbestrol, human papillomavirus

INTRODUCTION

Carcinoma of the uterine cervix is the most common gynecological malignancy worldwide. The most common histological type of malignant cervical neoplasms is squamous cell carcinoma. Adenocarcinomas account only for approximately 15% of malignant cervical tumors, and histologically they are categorized into mucinous, endometrioid, clear cell, serous, and mesonephric subtypes. Clear cell adenocarcinoma (CCA) most commonly occurs in the ovary, followed by endometrium, vagina, and cervix. Primary CCA of the vagina and uterine cervix is a rare neoplastic entity, which occurs in young women exposed to diethylstilbestrol (DES) *in utero*. Primary CCA of the uterine cervix inyoungwomen without *in utero* DES exposure is extremely rare. Here, we report a 21-year-old Asian female with primary CCA of the uterine cervix, with no maternal history of DES ingestion during pregnancy. The results of high-risk type of human papillomavirus (HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) were negative in this particular case. The patient's unremarkable medical and sexual history prompted us to report this case.

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.106278

CASE REPORT

A 21-year-old Asian woman, with negative familial cancer history, was presented with complaint of abnormal vaginal bleedingfor last 3 months. Gynecological examination revealed bulky cervix with a 2 × 1.5 cm ulceroproliferative lesion at the anterior lip. A punch biopsy from the lesion was taken. Histopathological examination of the biopsy showed papillary and tubular proliferations of malignant cells with glycogen-rich clear cytoplasm and malignant hobnail cells [Figure 1]. Contrast-enhanced computed tomographic scan of the abdomen and pelvis showed moderately enhanced bulky cervix with paracervical fat stranding and nodularity, without any locoregional lymphadenopathy [Figure 2]. All other hematological, biochemical, and radiological tests were within normal limits. The patient was therefore diagnosed as a case of CCA of cervix, FIGO stage IB1. She had undergone Wertheim's hysterectomy with bilateral pelvic lymph node dissection. Histologically, the initial diagnosis of primary cervical CCA, FIGO stage IB1, was confirmed. After 4 weeks of surgery, she received whole pelvis external beam irradiation upto a total dose of 50.4 Gy in 28 fractions

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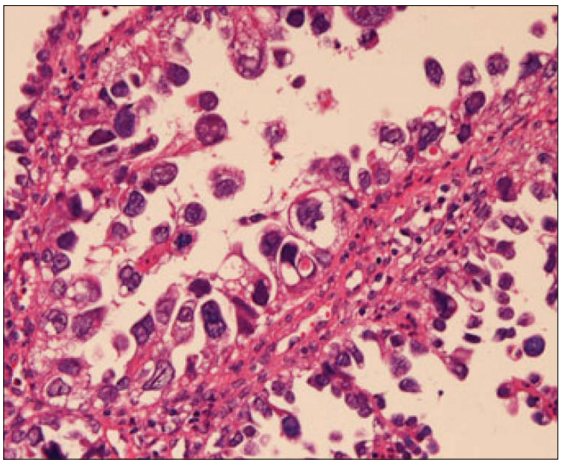

Figure 1: Photomicrograph of the histopathology of cervical punch biopsy showing papillary and tubular proliferations of malignant cells with glycogen-rich clear cytoplasm and malignant hobnail cells (H and E, ×200)

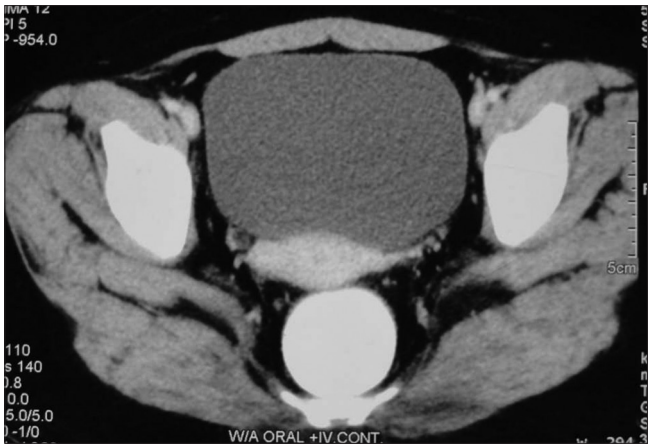

Figure 2: Contrast-enhanced computed tomographic scan of the abdomen and pelvis showing moderately enhanced bulky cervix with paracervical fat stranding and nodularity, without any locoregional lymphadenopathy

along with concurrent chemotherapy (Cisplatin, 40 mg/m^2 weekly × five cycles), followed by vaginal brachytherapy (6 Gy × two fractions). The patient is still under observation in our department, 6 months after completion of treatment. No signs of recurrence have been detected since then.

DISCUSSION

The association between CCA of the vagina and cervix and *in utero* exposure to DES was first described in a case series in 1971,[1] and after that the causal association between *in utero* DES exposure and CCA of the vagina and cervix has been firmly established through the follow-up of several DES-exposed cohorts.[2,3] Primary CCA of the vagina and cervix primarily occurs in young women exposed to DES *in utero*. The median age of diagnosis is 18.9 years, and the estimated risk of developing CCA of the vagina andcervixin an exposedfemaleup to age 24 is between 0.14 and 1.4 in thousand.[4] The national cooperative DES adenosis project estimates the risk to be less than 1 in thousand.[5] Althoughearly analyses described an excess of CCA of the vagina and cervix that peaked during late adolescence and early adulthood,[2-4] but follow-up of established cohorts suggests an elevation in risk persisting as the cohort aged.[6,7]

Primary CCA of cervix is extremely rare in women without *in utero* DES exposure and in such cases it concerns mostly postmenopausal women.[8] There have been very few case reports of CCA of cervix in young women without *in utero* DES exposure.[9,10] Moreover, we have to emphasize the negative family history of cancer and the lack of epidemiological risk factors of cervical cancer, such as HPV infection, multiple sexual partners, smoking, low socioeconomic status, and oral contraceptive use in the presented case.[11,12] In a retrospective analysis, Liebrich *et al*. have reported 18 cases of primary cervical cancer, persistently negative for high-risk HPV-DNA, in virgins and very young women. Most of them had rare subtypes of adenocarcinoma, such as clear cell or endometrioid variety, or with unknown histology. Finally, the authors concluded that rare adenocarcinoma of the uterinecervix in virgins and young adolescents may represent a distinct entity unrelated to HPV.[13] This may be a possible explanation of rapid onset cervical cancer in our patient. It is well known that ovarian CCA is closely associated with ovarian endometriosis.[14] There have been a case report of association between CCA of cervix with cervical endometriosis.[15] But the question of whether cervical CCA is related to endometriosis has never been addressed in any study. There is also a reported case of CCA of cervix associated with hemihypertrophy and bilateral Wilms' tumor in a young girl with no maternal history of DES ingestion during pregnancy.[16]

The data from the literature indicate that in primary CCA of cervix, either radiation or radical hysterectomy and bilateral lymph node dissection results in cure rates of 85-90% for patients with small volume disease.[17] The mode of treatment depends on patient factors and available local experience. In smaller foci of disease, as in our patient, upfront surgery followed by radiation therapy is the preferred mode of treatment.[18]

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Cite this article as: Chaudhuri T, Sharma D. Primary clear cell adenocarcinoma of the uterine cervix in a young woman not associated with diethylstilbestrol: A case report and review of literature. Clin Cancer Investig J 2012;1:239-41.

Source of Support Nil, **Conflict of Interest:** No.