Case Report
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Clear Cell Adenocarcinoma of the Cervix in a Young Woman without Exposure to Diethylstilbestrol: A Case Report

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Abstract

Clear cell carcinoma is believed to be one of the rare neoplasms of cervix uteri and vagina. The etiology and pathogenesis of clear cell carcinoma of the cervix are unclear, with scarce information about the clinical behavior, optimal management, and prognosis of the tumor. The current treatment options are based on the experiences accumulated on squamous cell carcinoma and other types of adenocarcinoma. Prior intrauterine exposure to diethylstilbestrol (DES) is presumed to be a predisposing factor for clear cell adenocarcinoma in young patients. Metastasis is uncommon, but local recurrence may occur. The cure rate of this disease is 85%-90% in early stages with a small volume of tumors. In this study, we report a rare case of clear cell carcinoma of the cervix in a 21-year-old woman, who had no exposure to DES (in-utero) or synthetic non-steroidal estrogen; therefore, the present research supports the hypothesis that the risk factors, other than DES exposure, play an important role in carcinogenesis.

Keywords: Adenocarcinoma, Clear cell, Diethylstilbestrol, Cervix uteri

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Introduction

Adenocarcinoma of gynecologic organs is an extremely rare malignant tumor (with much fewer cases than 15% of cervical tumor and very rare in vaginal malignancies).[1] Clear cell carcinoma (CCC) of the uterine cervix is a rare pathological type of cervical cancer, accounting for 4 to 9% of all adenocarcinomas of the uterine cervix. The diagnosis of clear carcinoma of the uterine cervix is mainly done based on histopathological examination. Histologically,

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CCC is predominantly composed of clear or spindle cells with solid, tubulocystic, and/or papillary architectural patterns.[1, 2] This cancer is mostly reported in women with a history of exposure to diethylstilbestrol (DES), but probably a number of unknown etiologies are attributed to CCC of the uterine cervix.[3]

Case Presentation

A 21-year-old P2L1D1 (ND-CS) woman was referred to Mashhad University of Medical Sciences, Iran, Gynecology-Oncology Department in January 2020. The Ethics Committee of Mashhad University of Medical Sciences approved this study (ethics code: IR.MUMS.REC. 1400.149). She complained about abnormal vaginal bleeding since 2018. She did not have any prior medical and familial cancer history or report any history of hormonal contraception usage. She was in an appropriate socioeconomic condition; however, she was a passive smoker by her husband. Her history of the first sexual intercourse experience was at the age of 17. There was no genitalia structural abnormality on her physical examination. Speculum examination showed a 4-cm polypoid shape mass arising from the cervix at the left side of the upper vagina, affecting the parametrium at the left side. Through rectal examination, no additional finding was detected. Pelvic magnetic resonance imaging (MRI) was recommended for better estimation of the tumor local extension and respectability, while abdominal computed tomography (CT) and chest X-ray (CXR) were suggested for an accurate assessment of distant metastasis. MRI of the pelvis showed a vaginal mass of 5 cm in size expanded inside the vagina with parametrial extension. No distant metastasis was revealed via the abdominal CT scan and CXR (Figure 1). The results of a high-risk type of human papillomavirus were negative in this case. Histological study of the sampled tissue revealed large cells with clear cytoplasm, enlarged nucleoli, and tubular structures lined by hobnail cells. Histomorphology was diagnosed as CCC of the cervix (Figure 2). Immunohistochemistry staining study showed that the tumor cells were positive for CK7 and NapsinA. She was classified as FIGO stage 2A2 of the cervix and received chemoradiotherapy. The chemotherapy regimen was carboplatin plus paclitaxel. The patient is still under observation after 8 months of treatment and is free from the disease.

Discussion

The most prevalent demonstration of CCC,

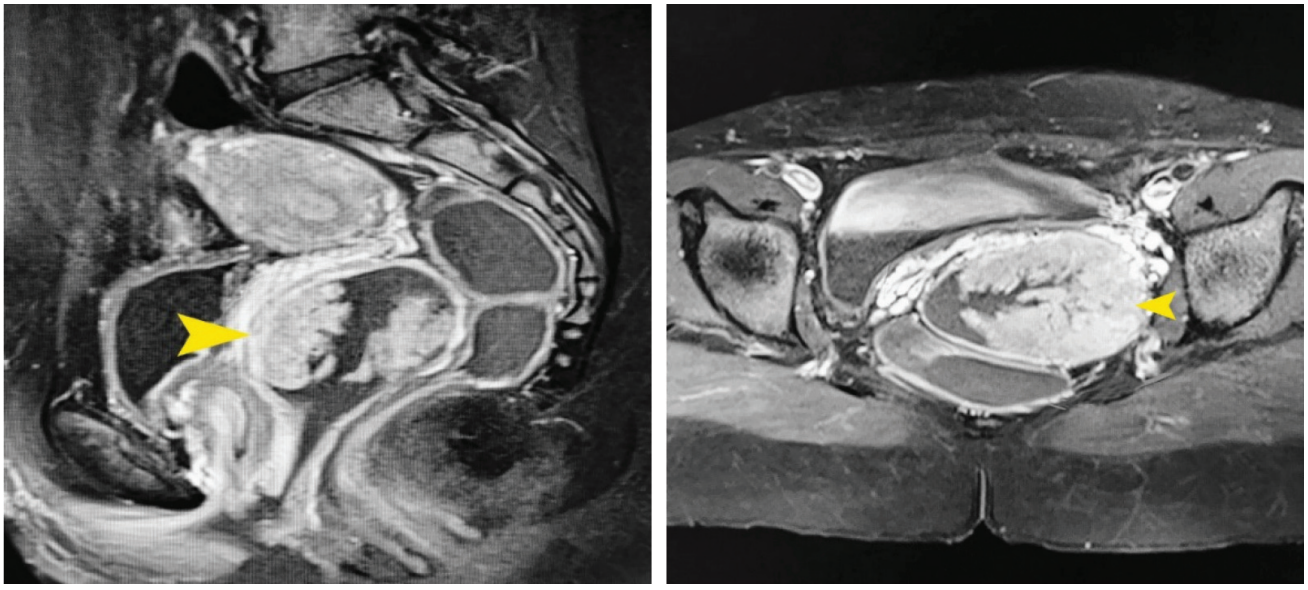

Figure 1. Sagittal (left) and axial (right) view of pelvic MRI revealed a heterogenous lobulated margins enhancing mass located in the proximal vagina. Anterior wall and left lateral wall of upper vagina is infiltrated by the mass. Lower vagina was normal.
MRI: Magnetic resonance imaging

like other neoplasms of this structure, is atypical vaginal discharge and/or bleeding, which has been reported in case series.[4] Prognosis of CCC depends on the stage, size of the tumor, stromal invasion, growth pattern, nuclear atypia, mitosis, and lymph node involvement. Unfavorable prognosis is attributed to the larger size, higher stage, high mitotic rate, positive surgical margin, parametrial involvement, and lymphovascular invasion.[5] Fertility-preserving surgery for early-stage CCC in a young patient was recommended by the National Comprehensive Cancer Network (Fort Washington) in 2013.[6] Metastasis is uncommon, but local recurrence may occur. The cure rate of this disease is 85%-90% in early stages with a small volume of tumors.[7] The etiology and pathogenesis of CCC of the cervix are imprecise. However, many reports have demonstrated an association between this cancer subtype and prior intrauterine exposure to DES, a synthetic non-steroidal estrogen hormone which is teratogen and crosses through the placenta. Herbst, in 1999, surveyed 705 cases of vaginal and cervical CCC. Out of these cases, 60% were clearly exposed to intrauterine DES, 30% did not have DES exposure, and 10% had an unclear exposure history.[8] There have been very few case reports of CCC of cervix in young women without in utero DES exposure. Waggoner and colleagues, in 1994, conducted a study about the association among HPV positivity and CCC and vagina; nonetheless, there was no clear association.[9] It is unclear at this point whether HPV infection is a cofactor in the development of CCC or just a coincidental finding. Further research is required to find the association between CCC and HPV infection. Cervical endometriosis has also been assumed as a risk factor for the development of CCC since endometriosis is a predisposing factor for ovarian CCC. There have been reports of CCC originating in cervical endometriosis; however, no clear association has been found.[7,10] The etiology and risk factors associated with the development of non-DES-related CCC still remain unclear. 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, low socioeconomic status, and oral contraceptive use in the presented case. Further research is needed to accurately determine the CCC-associated risk factors. This study supports the hypothesis that the risk factors other than DES exposure play an important role in carcinogenesis.

Conclusion

In conclusion, this case study exhibited a CCC arising in a young adult who presented with vaginal bleeding. Although CCC is an uncommon tumor, it must be considered in the differential diagnosis in young women with cervicovaginal lesions and abnormal vaginal bleeding even without in utero DES exposure history. CCC without DES exposure continues to be a rare disease. It is an invasive malignant tumor whose pathogenesis may not be associated with HPV

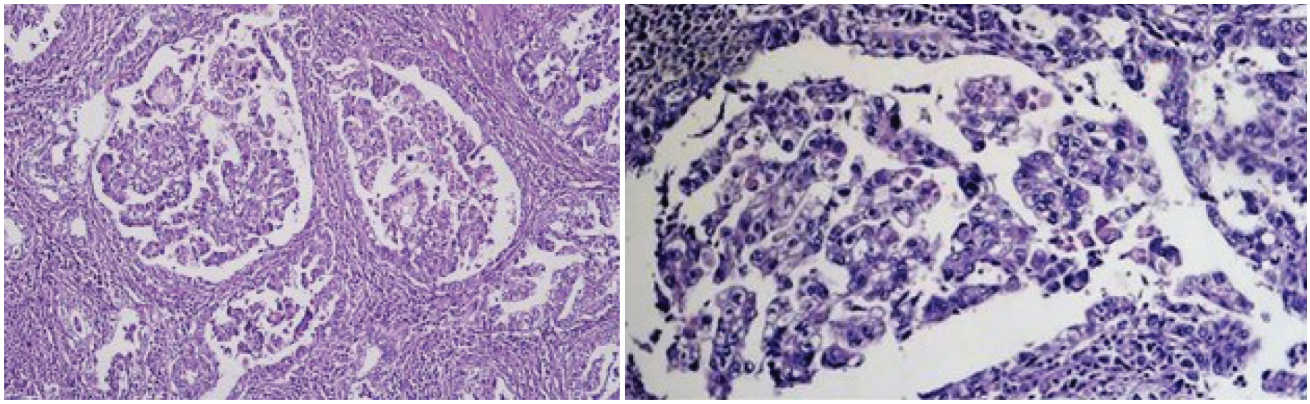

Figure 2. This figure shows the CCC of vagina, representing carcinoma with tubulopapillary architecture, hobnail nuclei cell, and clear cell (H&E, ×100, ×400).

CCC: Clear cell carcinoma

infection, which necessitates more studies about CCC risk factors.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Acknowledgement

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Conflict of Interest

None declared.

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