

Clear cell carcinoma of cervix in a postmenopausal woman: A case report

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ABSTRACT

Clear cell carcinoma of cervix is a very rare neoplasm accounting only 4% of all cervical adenocarcinomas. Intrauterine exposure to diethylstilbestrol (DES) is supposed to be causative factor for clear cell adenocarcinoma in childhood and young-age patients. We are reporting a case of clear cell carcinoma of cervix in a 49-years-old multiparous post-menopausal woman, who had no exposure to DES (in-utero) or synthetic non-steroidal estrogen.

Key Words: Cervix, clear cell carcinoma, DES, postmenopausal

INTRODUCTION

Cervical carcinoma is the most common malignancy in Indian women and fifth most common cause of cancer related death.^[1] Squamous cell carcinomas are the largest subset, whereas adenocarcinomas constitute only 15% of cervical carcinomas.^[2] Clear cell carcinoma of cervix is a very rare malignancy accounting only 4% of all adenocarcinoma of cervix.^[3] Previous case reports and case series have shown the occurrence of clear cell carcinoma associated with in-utero exposure of synthetic non-steroidal estrogens and diethyl stilbestrol (DES).^[3,4] Here we are reporting a rare case of clear cell carcinoma in a postmenopausal woman who had no previous history of exposure to synthetic non-steroidal estrogens and DES.

CASE REPORT

A-49-year old multiparous lady visited our Gynaecology Outpatient Department (OPD) with complaints of repeated spotting for last 2 months. She had an average

built and had past history of two child birth 20 and 23 years back. She had no history of oral contraceptives (OCP) intake and irregular menstruation. She had menopause 3 years back and had no other major illness. Pervaginal examination showed irregular growth at lower lip of cervix. On per-rectal examination, no adhesion or thickening palpated on both left and right parametrium. Routine hematological examination only revealed hemoglobin 9 gm%. Blood biochemistry was within normal limit. Contrast computed tomography (CT) scan of pelvis was done revealing irregular dense mass $5 \times 3.5 \times 2$ cm occupying inferior lip of cervix and posterior fornix. No pelvic extension and regional lymphadenopathy were noted in CT scan. Punch biopsy was taken with colposcopy guidance and sent for histopathological examination. Histopathology revealed partly solid and tubulo-cystic growth pattern of neoplastic cells [Figure 1]. The tumor cells had abundant clear cytoplasm, round nuclei and hobnailing appearance in many cells [Figure 2]. The nuclei showed hyperchromatia, moderate pleomorphism and prominent nucleoli. Mitoses were frequent in the tumor tissue [Figures 2 and 3]. Histomorphology was diagnosed as clear cell adenocarcinoma of cervix. No other organ

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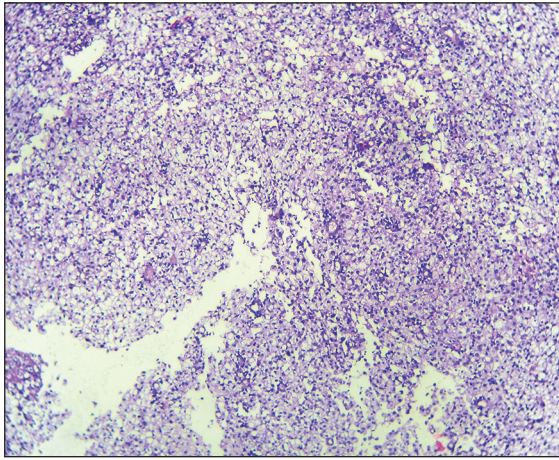


Figure 1: Photomicrograph shows histomorphology of clear cell carcinoma of cervix- solid and tubulo-cystic growth pattern (H and E stain, 10x view)

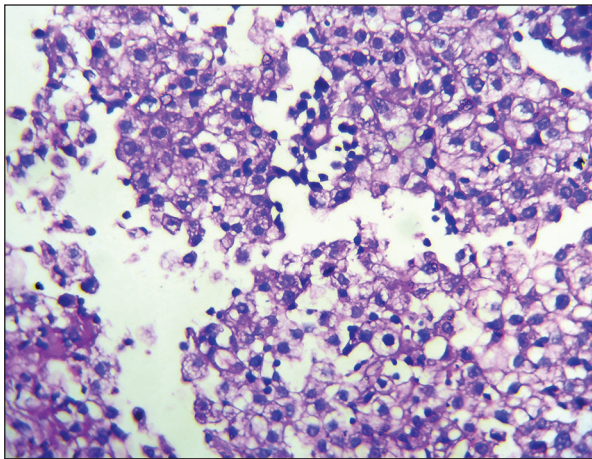


Figure 2: Photomicrograph shows histomorphology of clear cell carcinoma of cervix- abundant clear cytoplasm, round nuclei with hobnailing appearance having moderate pleomorphism and prominent nucleoli (H and E stain, 40x)

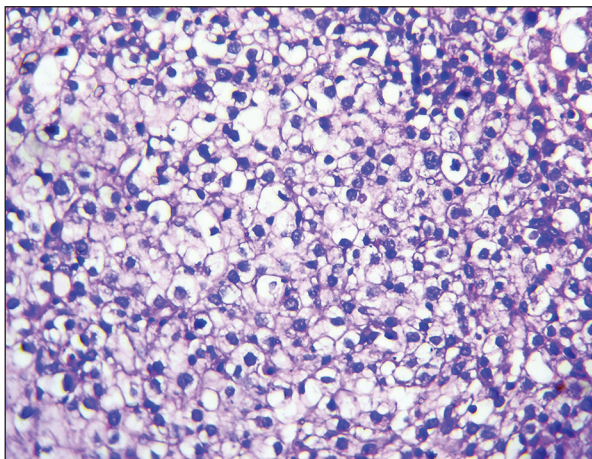


Figure 3: Photomicrograph shows histomorphology of clear cell carcinoma of cervix- abundant clear cytoplasm, round nuclei with hobnailing appearance having moderate pleomorphism and prominent nucleoli (H and E stain, 40x)

involvement was noted and she was staged as stage Ib2. She was treated with total hysterectomy with bilateral salpingo-oophorectomy and para-aortic and pelvic lymph node dissection. On further histopathology examination, endometrium, both sided parametrium, pelvic lymph nodes were free from tumor invasion and metastasis. She was referred to radiotherapy department for further management.

DISCUSSION

Squamous cell carcinomas are the most common malignancies of cervix. Only 15% of cervical carcinomas are adenocarcinoma.^[1,2] Clear cell adenocarcinomas are very rare entity, constitute only about 4% of all adenocarcinomas.^[4] Association of clear cell carcinoma of cervix and vagina with in-utero exposure of DES was first published in 1971.^[2] Several articles were published during 1970-1980 about the increased incidence of clear cell carcinoma among the cohorts of DES exposure and a causal association was established.^[1,3] DES was previously used for therapeutic purpose to reduce the complications of pregnancy like toxemia, bleeding, premature birth and neonatal death.^[3] Estimated risk of developing clear cell carcinoma of vagina and cervix is <1 in 1000.^[2] Median age of DES related clear cell carcinoma is 18.9 years.^[4,5] DES is considered as teratogenic hormone which can cross placental barrier during 4-18 weeks of development and stimulate the persistence of müllerian epithelium.^[4,5]

Primary clear cell carcinoma without any previous history of DES exposure is an extremely rare neoplasm. These subgroups commonly occur at elderly post-menopausal women. Median age of clear cell carcinoma non-associated with DES exposure is 53 years and it commonly presents with irregular vaginal bleeding (80%).^[1,6,7] No established risk factor or etiology has been isolated for non-DES related clear cell carcinoma. Cervical endometriosis, use of oral contraceptive pill and HIV infection are the suspected etiological factors.^[2,4] Liebrich *et al.*,^[8] and Waggoner SE *et al.*,^[9] studied association of cervical clear cell carcinoma with HPV infection, but unlike SCC, no clear association has been proved till now. Few case reports were published about association of clear cell carcinoma with cervical and ovarian endometriosis, but any causal association has not been proved.^[2,6] In our case also, the patient had no history of OCP intake. No evidence of endometriosis was noted and HPV-DNA test was negative.

Clear cell carcinoma of cervix commonly presents with abnormal per-vaginal bleeding (menorrhagia, menometrorrhagia, post-menopausal bleeding) refractory

to hormonal therapy.^[4] Most of the clear cell carcinomas are superficial with invasion to deeper stroma rather than exophytic mass forming lesions. In our case it was invasive superficial ulcerated lesion. Clear cell carcinomas should be differentiated from Aris-stella reaction, micro glandular hyperplasia and mesonephric hyperplasia in adult. In children, it also to be differentiated from yolk sac tumor and embryonal rhabdomyosarcoma.^[3] Most of the cases are stage II and stage III malignancies. In our case it was stage Ib2. Prognosis of clear cell carcinoma depends on the stage, size of the tumor, stromal invasion, growth pattern, nuclear atypia, mitosis and lymph node involvement.^[1,4,5] Primary treatment of early stage disease is radical surgery with para-aortic and pelvic lymphadenectomy.^[4] Unfavorable prognosis is related with larger size, higher stage, high mitotic rate, positive surgical margin, parametrial involvement and lympho-vascular spread.^[1,4] Neo-adjuvant chemoradiation are indicated for these cases.^[1,6] Metastasis is uncommon but local recurrence may occur.^[4] Cure rate is 85-90% in early stage diseases and small volume of tumors.^[2] In adult women (post-menopausal) prognosis is similar to non-clear cell adenocarcinomas.

On conclusion, clear cell carcinoma is a rare entity in present time after cessation of DES therapy. Though it is a subgroup of adenocarcinoma, clinic-pathological features and prognosis are different than conventional adenocarcinoma.

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Conflict of interest

There are no conflicts of interest.

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