Clear cell carcinoma of cervix in post-menopausal female

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ABSTRACT

Clear cell carcinoma of cervix is a rare neoplasm accounting for round 4% of all adenocarcinomas. It is usually seen in patients with a history of intrauterine exposure to diethylstilbestrol. We are reporting a case of clear cell carcinoma of cervix in a 50 years old P_1L_1 postmenopausal woman, with no history of exposure to diethylstilbestrol in-utero or synthetic non-steroidal estrogen, and who was managed with neoadjuvant chemotherapy followed by modified radical hysterectomy with pelvic lymphadenectomy and adjuvant chemotherapy.

Keywords: cervix, clear cell carcinoma, diethylstilbestrol, postmenopausal

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INTRODUCTION

Carcinoma of cervix is the second leading cause of cancer mortality in women worldwide. Its incidence worldwide is approximately 510,000 new cases annually with approximately 288,000 deaths.[1] The World Health Organization estimates that the incidence rate of cervical carcinoma in Nepal is 24.2 per 100,000 women per year, with 3,504 new cases diagnosed every year with 1,872 deaths.[2]It is the most common cancer in females in Nepal.[3] While squamous cell carcinoma is the predominating subset, adenocarcinoma accounts for only 15% of cervical carcinomas. Among adenocarcinomas of cervix, clear cell carcinoma accounts for only 4% of the cases.[4] The etiology and pathogenesis of the tumor is unclear. However, it is usually seen in young women, associated with diethylstilbestrol exposure in-utero or older women.[4-6] Here, we are reporting a rare case of clear cell carcinoma in a postmenopausal woman who had had no previous history of exposure to diethylstilbestrol or synthetic non-steroidal estrogens.

CASE

A 50 years old lady visited at gynecology outpatient department (OPD) of Kathmandu Model Hospital with complaints of per vaginal discharge for last 6 months followed by per vaginal spotting for last 3 months. She attained menarche at the age of 12 years and menopause at 40 years of age. She used to have regular menstrual cycles with normal flow. She is para one with one living issue. She had delivered vaginally 35 years back. She had no history of use of contraceptive measures and had no known medical or surgical comorbidities. On per-speculum examination, around 2x3 cm irregular growth was seen in the anterior lip of cervix which bled on touch. On per-vaginal examination, there was no abnormality except the cervical mass, and per-rectal examination was also normal. Blood biochemistry was within normal range. Ultrasonography revealed a 2x2 cm heterogenous mass and MRI revealed 18x24x11 mm sized lesion in the anterior lip of cervix. No pelvic extension or regional lymphadenopathy was noted. Cervical punch biopsy revealed clear cell carcinoma of cervix. Patient received 4 cycles of neoadjuvant chemotherapy followed by modified radical hysterectomy with pelvic lymphadenectomy. Endometrium, parametrium and pelvic lymph nodes were free from tumour invasion and metastasis (TNM stage 1B1). She then underwent adjuvant chemotherapy.

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COMMENT

Squamous cell carcinoma is the most common variety of cervical malignancy, whereas adenocarcinoma accounts for 15% of cases. Clear cell carcinoma of cervix is a rare malignancy accounting for about 4% of all adenocarcinomas.[4] Till date, no proven etiology and pathogenesis have been established. However, several articles have been published which shows a causal relationship between the incidence of clear cell carcinoma of cervix and diethylstilbestrol exposure in-utero.[4-5] The median age of diethylstilbestrol related clear cell carcinoma in 18.9 years.[5] Diethylstilbestrol is considered as a teratogen which can cross placental barrier during 4-18 weeks of gestation and stimulate the persistence of Mullerian epithelium.[5] Meanwhile, clear cell carcinoma without previous history of diethylstilbestrol exposure is an extremely rare neoplasm. It is usually seen at a median age of 53 years. Suspected etiological factors include cervical endometriosis, use of oral contraceptive pills and HIV infection.[6] Unlike squamous cell carcinoma of cervix, HPV infection has no clear association with clear cell carcinoma.[7]

Clear cell carcinoma of cervix commonly presents with abnormal per vaginal bleeding. In our case, patient presented with postmenopausal bleeding. Usually, clear cell carcinoma is superficial with ulcerative lesions.[8] However, in our case, it was an exophytic mass. Microscopically, it may be arranged as solid, tubulocystic, papillary patterns or a combination of features. Sheets of cells containing abundant glycogen-rich clear cytoplasm, atypical nuclei with hobnailling and mitoses may be seen.[8] The prognosis depends upon the stage, size of tumor, stromal invasion, nuclear atypia, mitotic activity and lymph node involvement.[8,9] Primarily, early stage tumors are treated with radical surgery with pelvic and para-aortic lymphadenectomy.[8] Larger size (>4 cm), higher stage, high mitotic rate, a solid or mixed growth pattern, positive surgical margins, parametrial involvement and lymphovascular spread are associated with unfavourable prognosis.[8,9] Neoadjuvant chemoradiation are indicated in such cases.[9] Cure rate is 85- 90% in early stage disease (stage I/II).[9,10] As compared to squamous cell carcinoma, clear cell carcinoma has a higher risk of extension to the uterine corpus, parametrium and lymph node metastasis.[10] The clear cell histology itself doesn't appear to embark poor prognosis.[11]

CONCLUSION

Clear cell carcinoma of cervix is a rare entity, especially when there is no history of exposure to diethylstilbestrol in-utero. It is unrelated to HPV infection. There may be other unidentified risk factors responsible for its etiopathogenesis. Surgery accompanied by chemotherapy or radiotherapy is found to be the preferred mode of treatment. However, further studies are required to know about its etiopathogenesis, best treatment modality and further prognosis.

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