

## Case Report

# Clear cell adenocarcinoma of the uterine cervix with malignant pleural effusion in a 29-year old female- A case report

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## ABSTRACT

Primary adenocarcinoma of cervix constitute about 7-15% of all cervical cancer. Clear cell carcinoma, a form of cervical adenocarcinoma is a very rare tumor constituting only 4% of cervical carcinoma. Risk factor and pathogenesis of this disease are not exactly revealed. Intrauterine exposure to diethylstilbestrol and associated non-steroidal estrogen during pregnancy before 18 weeks is the only risk factor. Here we report an unusual case of clear cell carcinoma of cervix presented with bilateral pleural effusion, cytology of which shows adenocarcinoma. This is a rare case since patient had no history of diethylstilbestrol exposure and presented with bilateral pleural effusion. This is the first described case report of clear cell carcinoma of cervix with upfront malignant pleural effusion.

**Keywords:** Cervix, Clear cell carcinoma, Pleural effusion

## INTRODUCTION

Cervical carcinoma is the most common cancer among Indian women. Squamous cell carcinoma constitute 80 to 90% whereas adenocarcinoma constitute 7-15% only. Clear cell carcinoma, a variant of adenocarcinoma constitutes for only 4% of all adenocarcinoma of uterine cervix.<sup>1</sup> Though the etiology and pathogenesis are not revealed, several studies have correlated the occurrence of vaginal clear cell adenocarcinoma in young women with intrauterine exposure to the synthetic non-steroidal estrogenic hormone diethylstilbestrol. Age of the patients with clear cell carcinoma induced by diethylstilbestrol ranges from 15 to 25 year, whereas patient with spontaneous tumor the disease typically occurs at an older age i.e. 50-80 year.<sup>2,3</sup>

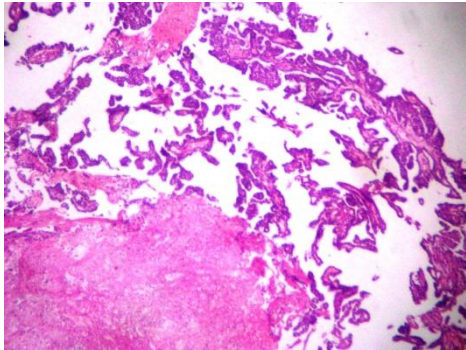
Here is a case report of clear cell adenocarcinoma of cervix who presented with upfront bilateral malignant pleural effusion, in a 29 year old unmarried woman who had no history of diethylstilbestrol exposure in utero. To the best of our knowledge Clear cell carcinoma of cervix with upfront pleural effusion is not yet reported in

literature. We here by reporting a case of clear cell adenocarcinoma of cervix with upfront malignant pleural effusion due to its rarity and for documentation.

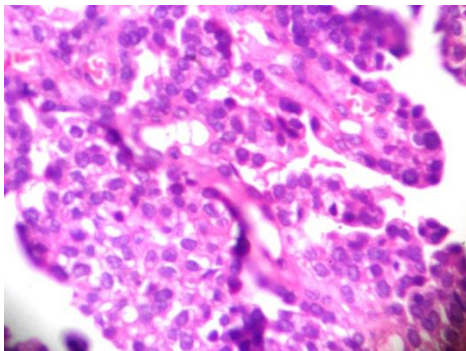
## CASE REPORT

A 29 year unmarried female was presented to department of radiotherapy, of our institute in March 2014 with 6 month history of irregular vaginal bleeding and mild breathing difficulties for one month. On examination breathe sound in left lower lobe was diminished. On Gynecologic examination there was an exophytic mass of size 5×5 cm arising from the cervix involving up to lower 3<sup>rd</sup> of vagina as well as both the parametrium. The histopathological evaluation of the cervical growth showed a highly papillary configuration with focal areas of necrosis (Figure 1). The papillae were mostly lined by single layer of tumor cells having abundant clear cytoplasm with centrally located round to oval nuclei (Figure 2). Mitotic figure were scanty, few hobnail cells were seen. Computed tomography of abdomen and pelvis showed large well defined solid cystic mass of size 59×53 mm in cervix with urinary bladder and rectal wall infiltration (Figure 3). Computed tomography of thorax revealed bilateral pleural effusion (Figure 4). Pleural fluid

cytology analysis revealed presence of adenocarcinomatous cells. Due to advanced stage she was planned for paclitaxel at 175mg/m<sup>2</sup> followed by intravenous infusion of carboplatin dosed to an area under curve of six(maximum dose 600mg) in day 2. Sixth cycle of chemotherapy was completed in September 2014. Evaluation after 6 cycles of chemotherapy revealed complete disappearance of pleural effusion and partial response to primary lesion. She was referred to gynecology oncology for feasibility of surgery, but evaluated inoperable. She was planned for radiotherapy. After completion of external beam radiotherapy she was lost for follow up.



**Figure 1: Photomicrograph of tumor tissue showing papillary pattern (upper right) with areas of necrosis (lower left) {H&E, 100X}.**



**Figure 2: Photomicrograph showing papillae lined by large cells with abundant clear cytoplasm {H&E, 400X}.**



**Figure 3: CT evaluation of pelvis showing a mixed attenuated lesion present at the cervix involving the posterior wall of bladder and anterior wall of rectum.**



**Figure 4: Computed tomography scan of thorax showing bilateral pleural effusion.**

## DISCUSSION

Clear cell carcinoma of cervix was rare until 1970s where a significant increase in the incidence in young patients around 8 to 29 years of age has been noticed as diethylstilbestrol was used therapeutically in early pregnancy to decrease complications such as abortion, toxemia of pregnancy, premature birth. It has been considered as a teratogen which crosses placental barrier.<sup>4</sup>If administered before 18 weeks of pregnancy diethylstilbestrol stimulates the persistence of the Mullerian epithelium or inhibits its replacement by squamous epithelium in the vagina.<sup>5</sup> Diethylstilbestrol exposed woman have a 40 fold increased risk of developing clear cell carcinoma. The risk of development of clear cell carcinoma is 0.14 to 1.4 in 1000women exposed in utero to diethylstilbestrol. However, 25% of cases of clear cell carcinoma had no history of maternal hormone exposure. In our case patient was not exposed to diethylstilbestrol. Several factors, such as non-steroidal estrogen exposure during pregnancy, maternal history of spontaneous abortion and premature births are considered to contribute to clear cell adenocarcinoma.

It has bimodal age distribution with two distinct peaks. One is the young age group between 17 to 37 year with mean age of 26 year and another at older age between 44 to 88 years, mean age 71 years. The young age group is largely composed of woman exposed to diethylstilbestrol, whereas the latter is constituted mostly by those without history of exposure.<sup>6</sup>Several studies showed better prognosis in diethylstilbestrol induced carcinoma than those with spontaneous clear cell carcinoma.<sup>7,8</sup>

The treatment of clear cell carcinoma is similar to that of cervical cancer. Radical hysterectomy and pelvic lymphadenectomy are standard surgical treatment for patient with FIGO stage IB or IIA. External beam radiotherapy is standard of care for stage IIB and IIIB. In our case as the patient presented with malignant pleural effusion, she was planned for chemotherapy. A recent phase III trial assessed four cisplatin doublet regimens (cisplatin-paclitaxel, cisplatin-gemcitabine, cisplatin-topotecan, cisplatin-vinorelbine). No significant difference in overall survival were seen, however trends

for response rate, PFS, and overall survival suggests that cisplatin-paclitaxel is the preferred regimen. This regimen have comparable response rate for the treatment of advanced adenocarcinoma of cervix without toxicity.<sup>7</sup>In the present case malignant pleural effusion respond well to paclitaxel+carboplatin regimen.

Important parameters for the determination of prognosis of clear cell carcinoma are FIGO stage, tumor size, growth pattern, nuclear atypia, mitotic activity, depth of stromal invasion. In the current study an unfavorable prognosis corresponds with high stage. Several authors have reported similar survival rates for equivalent stages of adenocarcinoma or squamous cell carcinoma. However distant metastasis was more frequent in patients with adenocarcinoma.

## CONCLUSION

Clear cell carcinoma of cervix in a young female of 29 year with malignant pleural effusion without maternal exposure of diethylstilbestrol is a rare entity. As this patient was inoperable she was treated with paclitaxel and carboplatin which has responded well to the treatment. We are reporting this case due to its rare presentation and response to taxane based chemotherapy for documentation.

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