

**CLEAR CELL ADENOCARCINOMA OF THE CERVIX WITHOUT EXPOSURE TO
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ABSTRACT

Clear cell adenocarcinoma is a histological type rarely found among cervical cancers. It can be seen in women at all ages and very often mentioned in connection with Diethylstilbestrol (DES) taken by the mother during pregnancy. Its prognosis is severe, requiring early and appropriate management. In front of this rare histological form where the literature still lacks enough examples, we find the interest to report the case of our young patient, where the notion of exposure to DES is absent, and which has been treated with an evolution favorable with no sign of recurrence after 5 years of follow-up. Thus, the objective through our article is to study the characteristics of this type of cancer, in particular its etiopathogenesis, its management and its prognosis.

KEYWORDS: Adenocarcinoma with clear cells, cervix, etiopathogeny, radio-chemotherapy, brachytherapy, prognosis.

BACKGROUND

Cervical adenocarcinoma is uncommon and the clear cell subtype is rare. It has often been reported in young women, but is no longer the case.^[6] In utero exposure to Diethylstilbestrol (DES) was largely responsible for its appearance.^[1] Also, its prognosis is generally described as pejorative.^[3] However, the case of our patient does not join the notions often reported in this type of cancer, which makes it special.

CASE

This is a 30-year-old patient, with no particular history (notably no DES taken by her mother during pregnancy) who presented with medium abundant bleeding with pelvic pain 7 months before the consultation at his gynecologist. The biopsy study performed revealed adenocarcinoma. The pelvic MRI objectified a tumor process of the anterior lip of the cervix of 7×18 mm, invading the thickness of the cervix without any sign of loco-regional extension. The remote extension assessment was normal. The tumor was therefore classified stage IB1. The treatment consisted of an enlarged adeno-colpo-hysterectomy, the anatomo-pathological study of which was in favor of clear cell adenocarcinoma, with a size of 14×10 mm, infiltrating the internal half of the cervical wall, without affecting the isthmus, parameters or appendices and without lymph node involvement. But the limit of the vaginal flange was insufficient at 10mm, which indicated an

adjuvant vaginal brachytherapy. The patient therefore benefited from 4 sessions at 7 Gy per fraction. Surveillance over 5 years was without sign of recurrence.

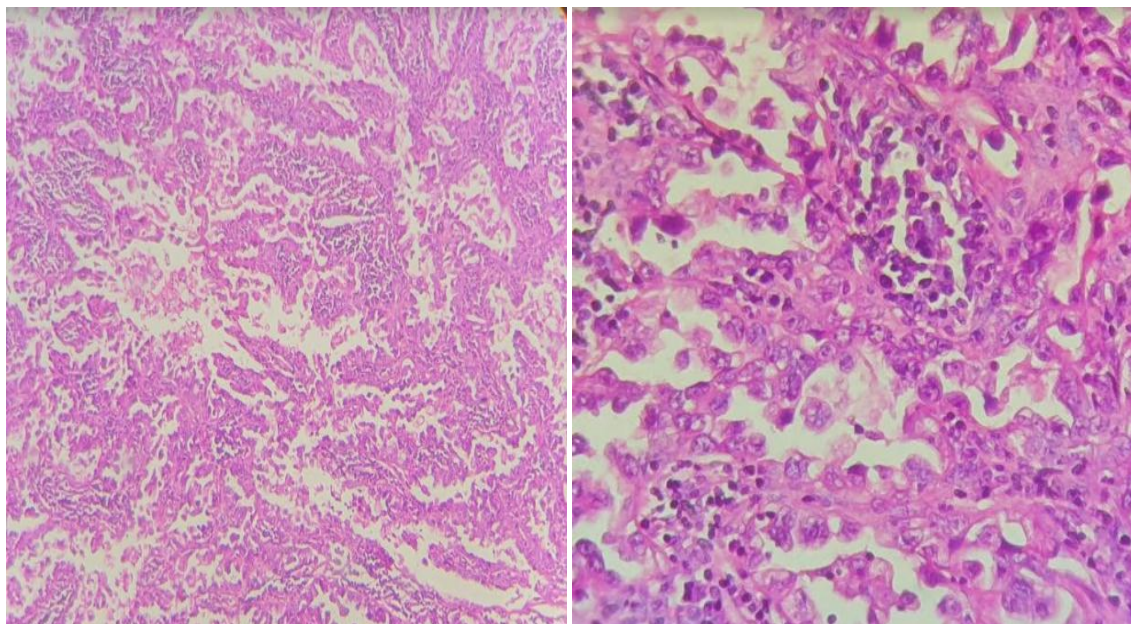


Figure: Microscopic appearance of clear cell adenocarcinoma of the cervix.

DISCUSSION

Clear cell adenocarcinoma is a rare histological form constituting 3 to 10% of adenocarcinomas of the cervix.^[2] It is no longer limited to young women; This was reported by Tomas *et al.*^[7] where the median age of the patients was 53 years, and only 3 patients were younger than 30 years and also in the study by Dongying Wang *et al* where the age group varied from 31 to 64 years, including Only 2 patients were aged less than 35 years.^[6] This cancer is often linked to prenatal exposure to diethylstilbestrol (DES), a drug that has been prescribed on a large scale since the 1938s during pregnancies at high risk of abortion. Moreover, the first studies having made this drug responsible for the occurrence of this cancer were carried out in 1971, by Herbst *et al*^[4] then banning its prescription in pregnant women, but the deleterious effects of the drug on the offspring were irreversible for the generation of children exposed to DES in utero born between 1940 and 1980. Thus, exposed women must benefit from very regular cytological and colposcopic monitoring. Although other studies came after in 1983 revealing that there are also cases with no history of exposure to DES like that of Kaminski and Maier.^[5] In the study by Dongying Wang *et al*, carried out on 18 patients whose mothers had not received DES, it was found that the human papillomavirus (HPV) test was negative in 88.9%. Also in the study by Pirog *et al.*^[9] who reported the incidence of HPV infection in 760 cases of cervical adenocarcinoma, where the clear cell type had a prevalence of HPV less than 20%. These results came in contrast to what is usually known for other histological types where HPV infection is common.^[6] Which leads us to think of other risk factors responsible for the appearance of this cancer in the same way as other cancers, namely genetic predisposition. Indeed, we find in the literature cases of adenocarcinoma of the family

cervix or even young girls who presented this type of cancer without any known detectable risk factor.^[8]

Regarding the progression of this cancer, most studies judge the aggressive nature and the poor prognosis, with a high risk of pelvic, para-aortic and distant lymphatic extension compared to squamous cell carcinoma.^[3,7] Furthermore, Reich *et al.*^[1] reported that 76% were in stage \leq IIA^[7], as well as Dongying Wang *et al* who found 72.2% of patients in the localized stages IB1-IIA2.^[6] Our case joins these last results because our patient was classified at stage IB1.

The treatment is essentially based on that of adenocarcinomas and squamous cell carcinomas of the cervix. Tumors smaller than 4 cm, without lymph node involvement are mainly treated by surgery and radiotherapy, while more advanced tumors are managed mainly by concomitant radio-chemotherapy (CCR). Surgery is proposed for certain patients (initially treated with RCC), in the event of persistence of a central pelvic tumor residue or in the event of local relapse, in the absence of lymph node or distant metastatic evolution.^[10] Although it is reported that clear cell adenocarcinoma is less sensitive to radiation therapy than squamous cell carcinoma.

In the study by Shimada *et al*, the recurrence rate in patients with clear cell adenocarcinoma (24.6%) was higher than in patients with squamous cell carcinoma (10.5%).^[11] Dongying Wang *et al* in turn reported a 9-59 month progression-free survival rate.^[6] For Reich *et al.*^[1], the results concluded that the 5-year survival rate of patients with early-stage clear cell adenocarcinoma was 67%, which was lower than that of non-clear cell carcinomas (77%), and before an 80% rate for squamous cell carcinomas.^[3] The progress of our patient was

without sign of recurrence after 5 years of follow-up and was therefore deemed satisfactory.

CONCLUSION

Although clear cell adenocarcinoma of the cervix is rare, it has been the subject of studies since the 1971s, relating it to in utero exposure to diethylstilbestrol; Which is not always the case. Management is no different from other histological types, but the course and prognosis are more severe.

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