

# Metrorrhagia Revealing Clear Cell Adenocarcinoma of the Uterine Cervix: A Case Report

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## Abstract

Cervical adenocarcinoma is uncommon, and the clear-cell subtype is rare.

The particularity of this observation lies in the absence of known factors predisposing to this type of cancer, as well as its rarity.

This is a young woman who reported metrorrhagia associated with leucorrhoea for three years, and whose examination revealed a five centimetres mass of the uterine cervix, Anatomopathological study of the biopsy revealed clear-cell tumour proliferation, A pelvic MRI showed a cervical mass can be classified IIIB according to FIGO classification.

The patient received courses of chemotherapy, radiotherapy and brachytherapy.

A follow-up pelvic MRI showed an almost complete response after treatment.

Through this observation, we emphasize the rarity of this type of adenocarcinoma and the need for research to improve its management.

**Keywords:** The Clear Cell Adenocarcinoma of the Cervix, Diethylstilbestrol, Rare Pathology

**Abbreviations:** DES: Diethylstilbestrol, HPV: Human Papillomavirus

## Introduction

Cervical adenocarcinoma is uncommon, and the clear-cell subtype is rare [1].

The latter has a very poor prognosis [2].

In addition to in utero exposure to diethylstilbestrol (DES), genetic factors such as microsatellite repeat sequence instability, human papillomavirus (HPV) infection, bcl-2 protein overexpression, p53 gene mutation and exogenous risk factors other than DES exposure may play an important

role [3].

The particularity of this observation lies in the absence of known factors predisposing to this type of cancer, as well as its rarity.

## Clinical Observation

Thirty-five years old woman, married, menarche at 14 years, with antecedent fetal death in 2003, operated in 2017 for tubal impermeability (under laparoscopy), chronic smoker since

2015, with no history of Di-Ethyl-Stilboestrol treatment taken by her mother during pregnancy and no family history of gynecological cancer, who presented for three years with metrorrhagia of moderate abundance with fetid leucorrhoea associated with weight loss and asthenia.

General examination revealed an asthenic patient, with slightly discoloured conjunctivae. Gynaecological examination revealed a five centimetres mass of the uterine cervix reaching the proximal third of the vagina, with infiltration of the parametrium (**figure 1**).

Anatomopathological study of the biopsy revealed clear-cell tumour proliferation, with immunohistochemical studies showing positive anti-CK7 antibodies, diffusely positive anti-PAX8 antibodies and focally positive anti-CD10 antibodies, all in favour of a clear-cell carcinoma of the cervix

A pelvic MRI showed a cervical mass with discrete T2 hypersignal, diffusion hypersignal, T1 hyposignal, moderate and heterogeneous enhancement after injection of gadolinium, measuring 57 x 40 mm and 55 mm in height, prolapsed into the vagina and responsible for infiltration of the proximal parametrium and the upper 1/3 of the vagina without pelvic lymphadenopathies; the ovaries were normal (**figure 2**).

The patient received twenty three sessions of radiotherapy (46 Gy) spread over one month, five courses of paclitaxel-

carboplatin-based chemotherapy one week apart, and two sessions of brachytherapy.

A follow-up pelvic MRI showed an almost complete response after treatment (**figures 3-4**).

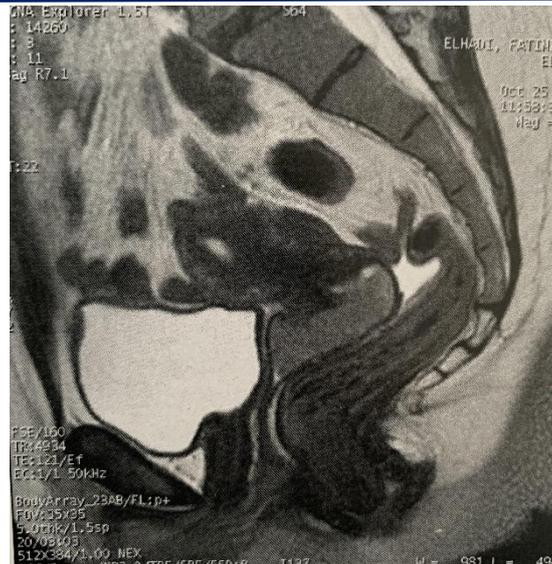
The patient is currently under clinical and radiological surveillance with pelvic MRI every six months.

## Discussion

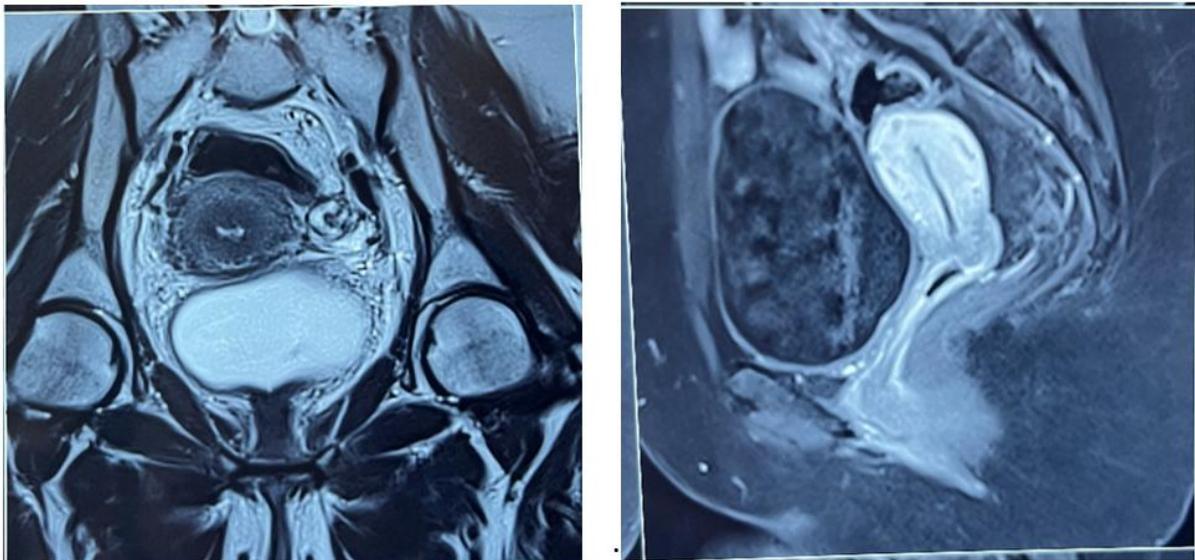
In recent decades, there has been a significant increase in the incidence of adenocarcinoma of the cervix, particularly in young women under thirty-five years [4]. Currently, adenocarcinomas account for 5-25% of cervical carcinomas [4,5]. They are classified by the OMS into five types, including clear-cell adenocarcinoma, which remains very rare [1,4]. In terms of etiopathogenesis, like squamous cell carcinoma, there is a significant association with HPV (Human Papilloma Virus), particularly with the HPV-18 subtype [6-8]. Nevertheless, and particularly in the case of clear-cell adenocarcinoma, since the 1970s, the work of Herbst and Noller has demonstrated the responsibility of diethylstilbestrol taken during pregnancy in the development of clear-cell adenocarcinoma of the cervix or vagina in girls from these pregnancies [9].



**Figure 1:** Speculum examination showing a five-centimetre cervical mass



**Figure 2:** Prolapsed cervical mass in the vagina, responsible for infiltration of proximal parametria and the upper third of the vagina



**Figure 3-4:** Control MRI (post concomitant radio chemotherapy + brachytherapy) showing almost complete response

This risk is higher for women whose mothers started DES before the 12th week of pregnancy, and persists from birth until the age of 34. Women exposed to DES in utero should therefore undergo regular cytological and colposcopic surveillance. However, in our case, the notion of in utero exposure to DES had not been found. This leads us to think of other risk factors not incriminated in this type of cancer, even though they play a crucial role in its carcinogenesis in the same way as other cancers, namely genetic predisposition. In fact, in the literature, cases of cervical adenocarcinoma have been reported in the same family, or young girls have presented with this type of cancer without any known detectable risk factor [10]. Consequently, it is necessary to

suggest the presence of one or more genes responsible for this predisposition. It is necessary to develop the oncogenetics of cervical cancer, particularly clear-cell adenocarcinoma, in order to better elucidate its etiopathogenesis [10]. In our case, the patient refused the genetic study, which limits our observation.

As for its evolution, the majority of reported cases illustrate the very poor prognosis of this pathology, whereas in our case, the patient responded well to concomitant radio-chemotherapy plus brachytherapy and rigorous surveillance was established.



## Conclusion

Cervical adenocarcinoma is uncommon, and the clear-cell subtype is rare, with a very poor prognosis.

In addition to in utero exposure to diethylstilbestrol (DES), there are other risk factors.

In contrast to squamous cell carcinoma, the etiopathogenesis is still poorly understood, which makes its management difficult, so we need more research in gynaecology, anatomopathology and oncology in order to establish a good codified management and thus improve the prognosis.

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