



Case report

Primary clear cell adenocarcinoma of the vagina not associated with diethylstilbestrol: A case report

S. Haddout^{*,1}, Y. Imami¹, M. Benhessou², M. Ennachit², M. El Karroumi³

Mohamed VI Cancer Treatment Center, Ibn Rochd University Hospital of Casablanca, Faculty of Medicine and Pharmacy of Casablanca, Hassan II University, Casablanca, Morocco

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ABSTRACT

Primary vaginal cancers are rare and clear cell adenocarcinoma is a malignant tumor that is all the more rare when the woman has not been exposed in utero to synthetic diethylstilboestrol (DES). We report the case of a 60-year-old woman with a history of balanced essential hypertension and partial mastectomy for neoplasia, who presented with a recurrent left inguinal adenopathy. Clinical examination revealed a 3 cm bulging lesion of the anterior vaginal wall in the lower third with indurated left inguinal adenopathy. Biopsy of the nodule showed an invasive clear cell adenocarcinoma. The extension bial is negative and the multidisciplinary decision is to perform a partial colpectomy with bilateral inguinal curage. The patient is currently undergoing radio-chemotherapy. This is a rare case with a poor prognosis. A poor response to adjuvant therapy with a high frequency of distant metastases is reported in the literature. Due to the rarity of this pathology, individual experience based on case reports is the main source of information. The most effective mode of treatment therefore remains unknown and depends on patient-specific factors such as tumor size, surgeon and oncologist team experiences.

1. Introduction and importance

Primary vaginal cancers are rare and account for less than 1.4 % of all gynecologic malignancies [1]. Clear cell adenocarcinoma is a rare malignancy in the gynecologic tract, rarer in the vagina, usually occurring in young women who have been exposed in utero to synthetic diethylstilboestrol (DES), used to prevent abortion during pregnancy [2]. On histopathological examination, this tumor shows cells with clear cytoplasm and coattails, and it should be distinguished from other differential diagnoses. Immunohistochemical staining is required in doubtful cases [3]. Primary clear cell vaginal adenocarcinoma not associated with DES is extremely rare with a poor prognosis, poor response to adjuvant therapy [4], and a high frequency of distant metastases, especially lung [5]. We report a case of clear cell vaginal adenocarcinoma in an elderly woman who had never been exposed to DES.

Our work is reported according to the criteria SCARE 2020 [6].

2. Case presentation

Our patient is 60 years old, postmenopausal for 5 years followed for essential hypertension balanced on treatment with a history of partial mastectomy of the left breast in 2014 in a neoplastic context. Our patient had received adjuvant chemotherapy and radiotherapy without hormone therapy. She is currently free of recurrence and continues to be followed in the oncology department. She presented in consultation for the appearance of a left inguinal adenopathy that progressively increased in volume evolving for 10 months without any other associated sign.

The initial clinical examination revealed a patient in good general condition. The gynecological examination revealed a 3 cm budding mass

* Corresponding author at: villa 338, lot Laimoune, Casablanca, Morocco.

E-mail address: sana.haddout@gmail.com (S. Haddout).

¹ Intern.

² Professor.

³ Head of department.

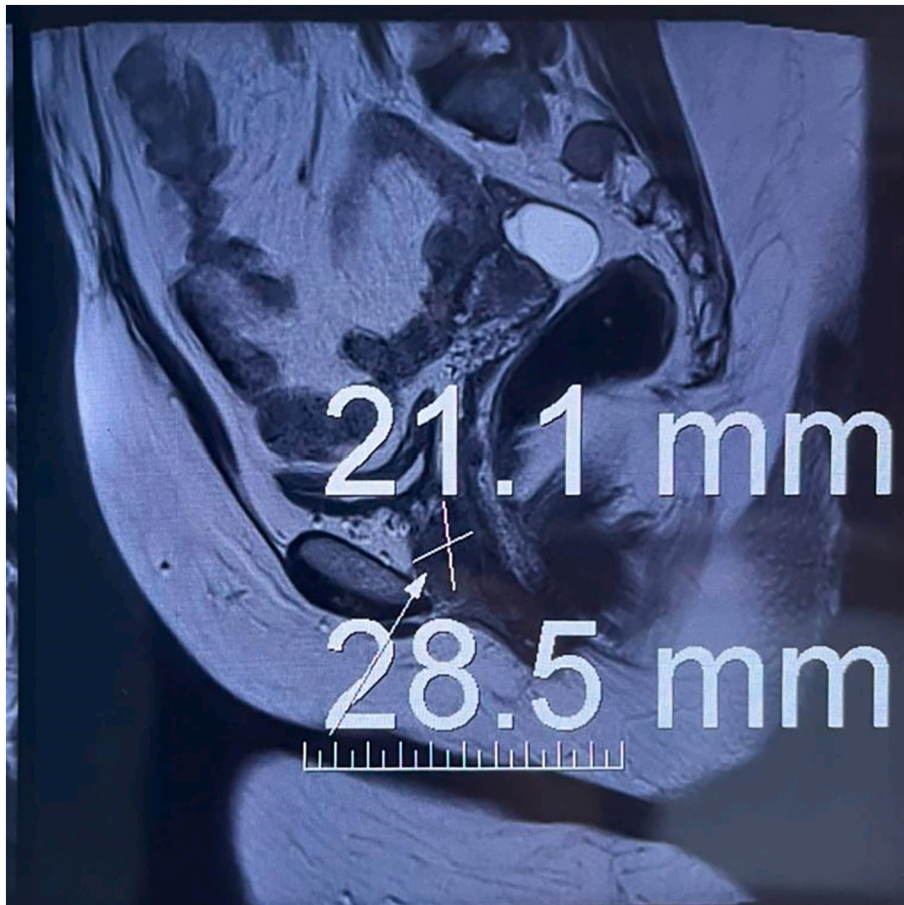


Fig. 1. Sagittal section on MRI showing tissue damage to the anterior wall of the vagina (→).

in the lower third of the vagina, opposite the anterior wall, parurethral, with a 2 * 2 cm left inguinal adenopathy indurated and attached to the skin and the deep plane. Biopsy of the nodule showed an invasive clear cell adenocarcinoma with immunohistochemistry: CKAE1/AE3 and CK7: (+) and CK20/CD31/Napsin A/CD34: (-). An adenectomy was performed confirming the secondary lymph node location of a clear cell adenocarcinoma of gynecologic origin.

Pelvic MRI with perineal slices showed a 2 cm tissue process of the right anterolateral wall of the vaginal cavity with invasion of the perivaginal fat without any other locoregional extension with suspicious looking left inguinal adenopathies, the largest of which was 4 cm, FIGO stage 3 (Figs. 1 & 2).

The PET-SCAN found a focus of pathological hypermetabolism on the lower half of the right anterior and anterolateral vaginal wall associated with two left inguinal adenopathies. Cystoscopy showed a normal looking urethra with a free urethral meatus and the urethral biopsy did not reveal any signs of malignancy. MRI of the breast is free of abnormalities. The decision of the multidisciplinary consultation meeting was to perform a conservative surgery.

A partial colectomy removing the vaginal lesion was performed with bilateral inguinal curage and recutting of the urethral surface (Figs. 3, 4, 5, 6). The surgical procedure was performed by the head of the department, professor of surgery. The postoperative follow-up is simple. The anatomopathological examination revealed a vaginal location of a clear cell adenocarcinoma with marked cytonuclear atypia and irregular nuclei. The resection borders are flush with the anterior and

posterior borders and within 1 mm of the right inferior and superior borders (Figs. 7, 8). There is infiltration by the same proliferation at the urethral cut. Right inguinal curage: 0 N+/4 N and left inguinal curage: 1 N+/2 N of 4 cm without capsular effraction (Fig. 9).

The patient was referred to the oncology department and a simultaneous chemo-radiotherapy treatment was planned. The patient is still under observation after 6 months of treatment and remains disease free.

3. Clinical discussion

Primary vaginal cancer is a rare tumor that occurs in women aged 60 to 70 years. Adenocarcinoma is a rare disease entity and occurs in 14 % of primary vaginal tumors. The clear cell type is more common in young girls previously exposed to DES during pregnancy [7]. Previous articles have reported that age 26 years was the most common age for this type of carcinoma, supporting the hypothesis of early (intrauterine) exposure to DES as the most common etiology for this type of cancer. However, recently, the presenting age has increased, as in our patient's case, suggesting that further studies on the risk factors for clear cell adenocarcinoma is needed [3–8–9].

The entity of clear cell adenocarcinoma (CCA) due to in-utero exposure to diethylstilbestrol (DES) is well documented, but only a few cases of primary clear cell carcinoma of the vagina not associated with DES have been reported in the literature. Among these cases, CCA in association with vaginal endometriosis [10] and congenital anomalies of the genitourinary tract have been reported [11,12]. A few sporadic

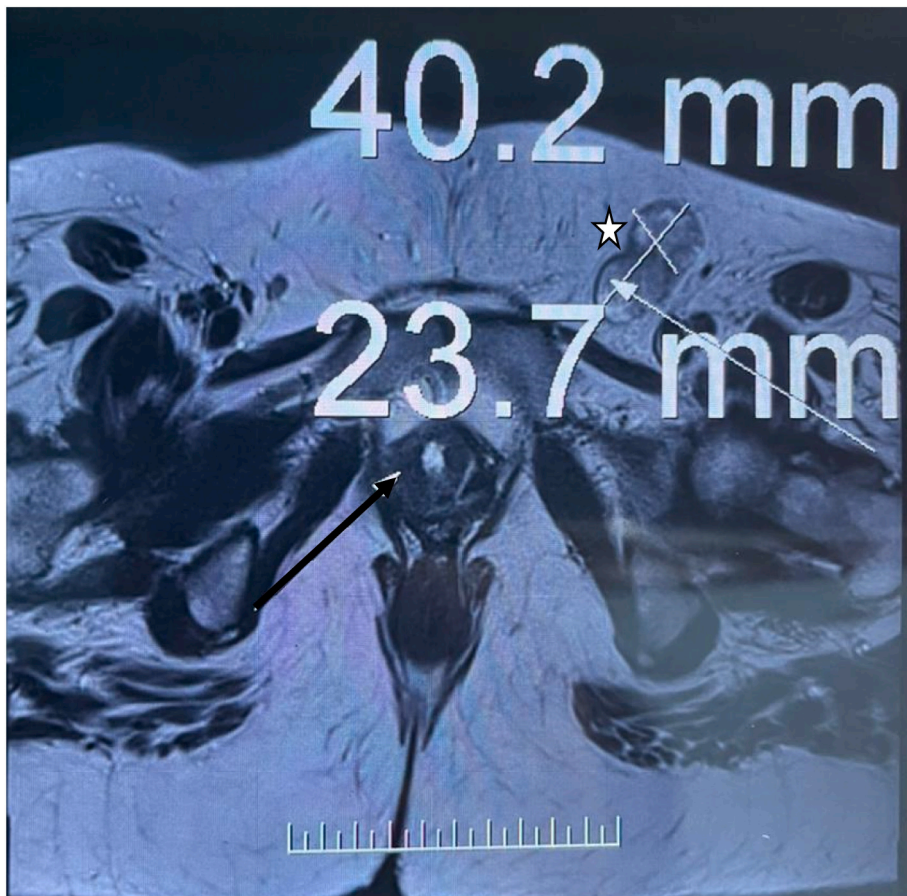


Fig. 2. Cross-section of the MRI showing the magma of left inguinal adenopathies (☆) and the vaginal lesion (→).

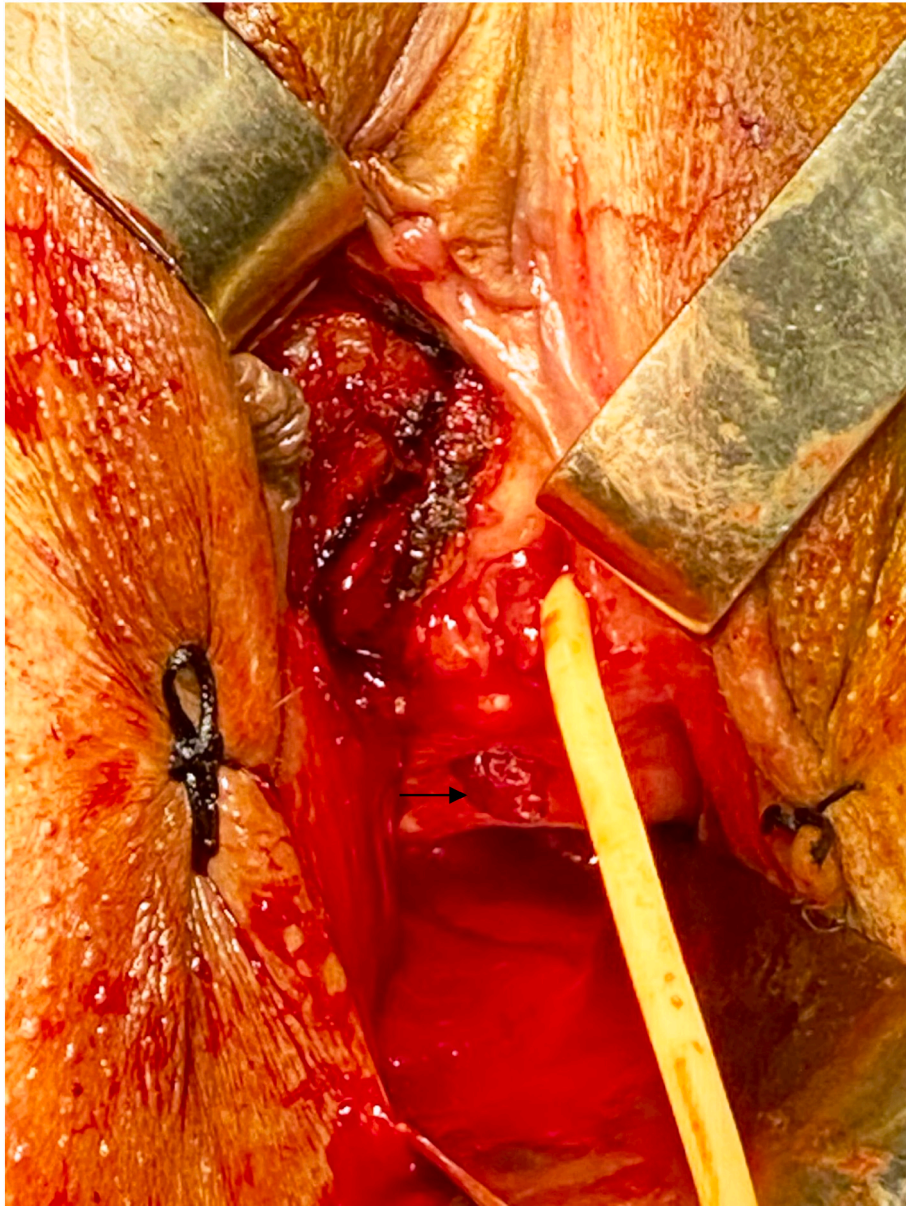


Fig. 3. Anterior wall vaginal lesion on examination under general anesthesia (→).

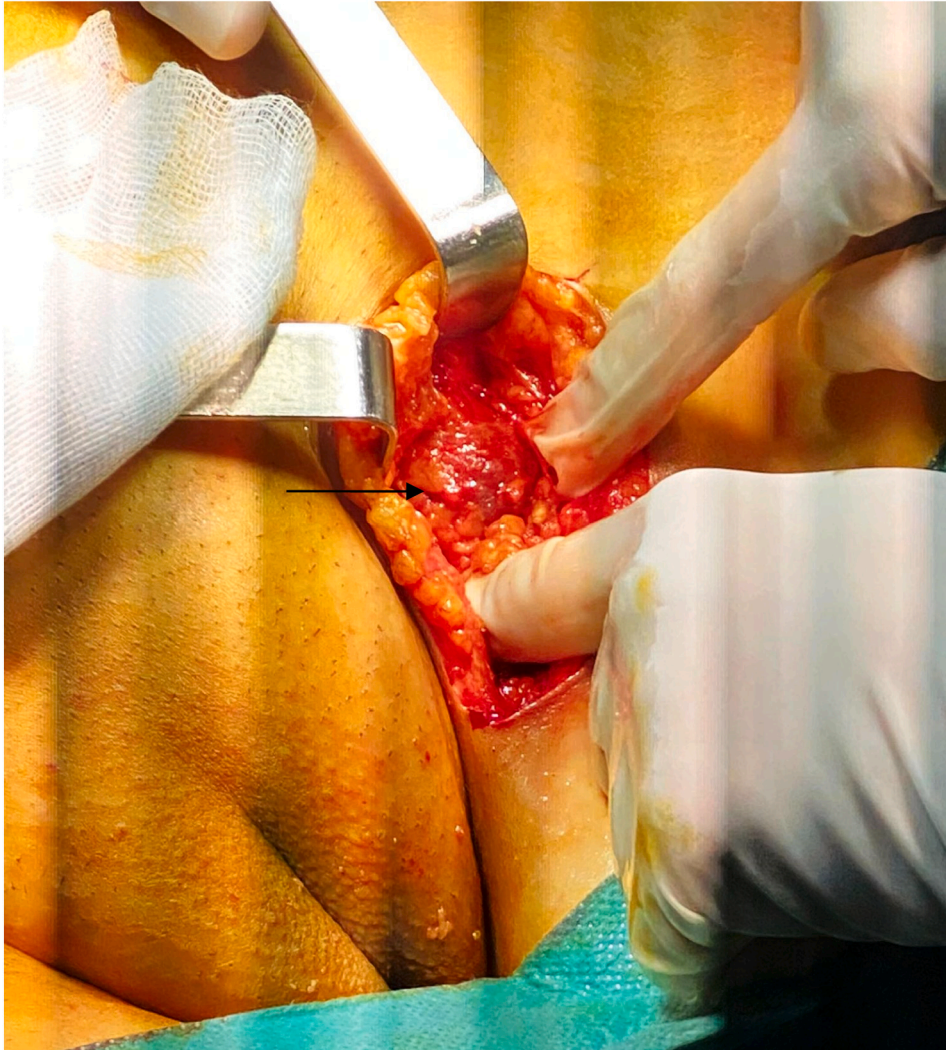


Fig. 4. Left inguinal curage with left adenectomy (→).



Fig. 5. Per operative photo showing the colpectomy in progress.



Fig. 6. Suture of the colpectomy by simple stitches with absorbable thread.

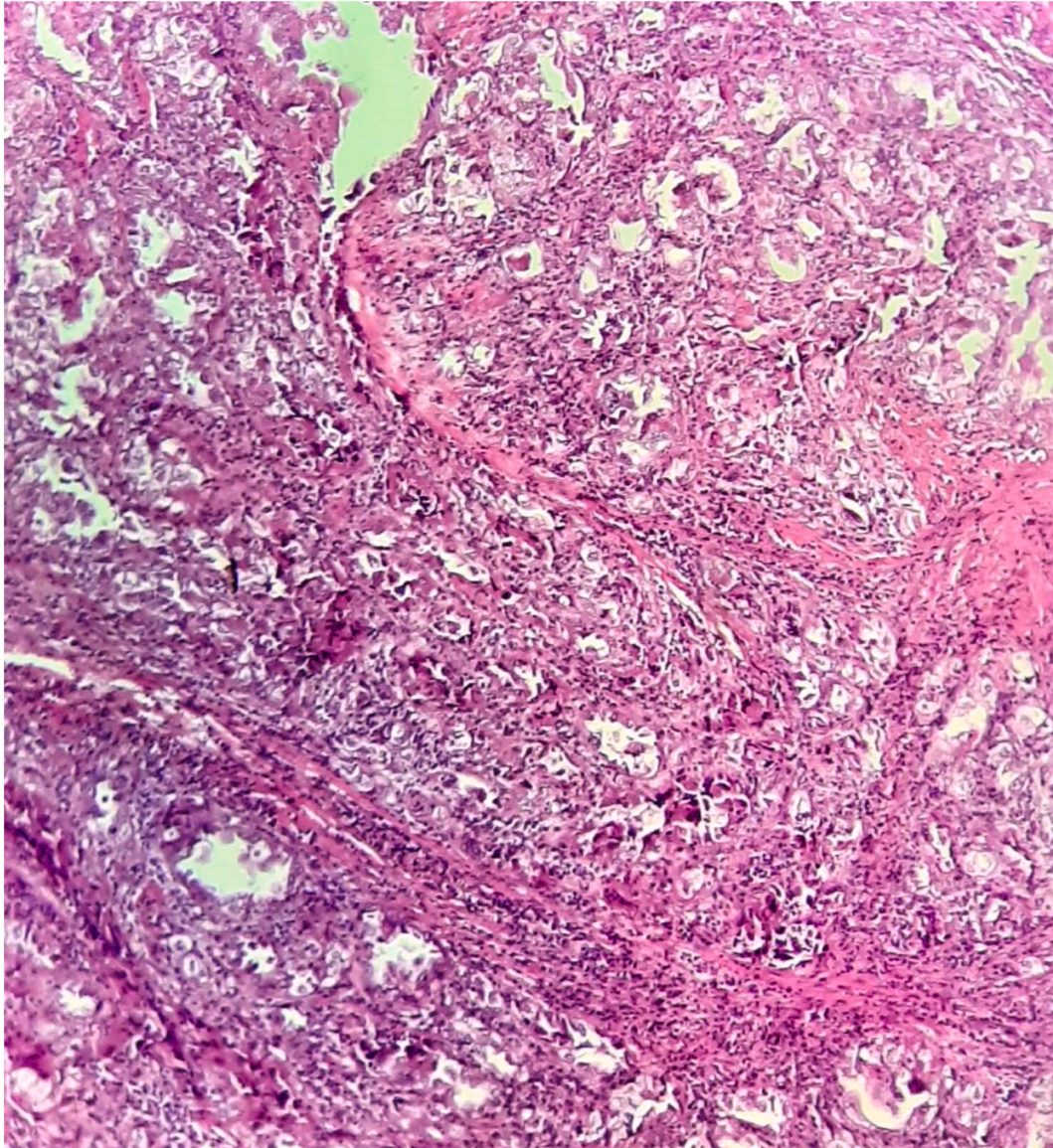


Fig. 7. Photo of histological slides revealing a vaginal location of a clear cell adenocarcinoma with marked cytonuclear atypia and irregular nuclei.

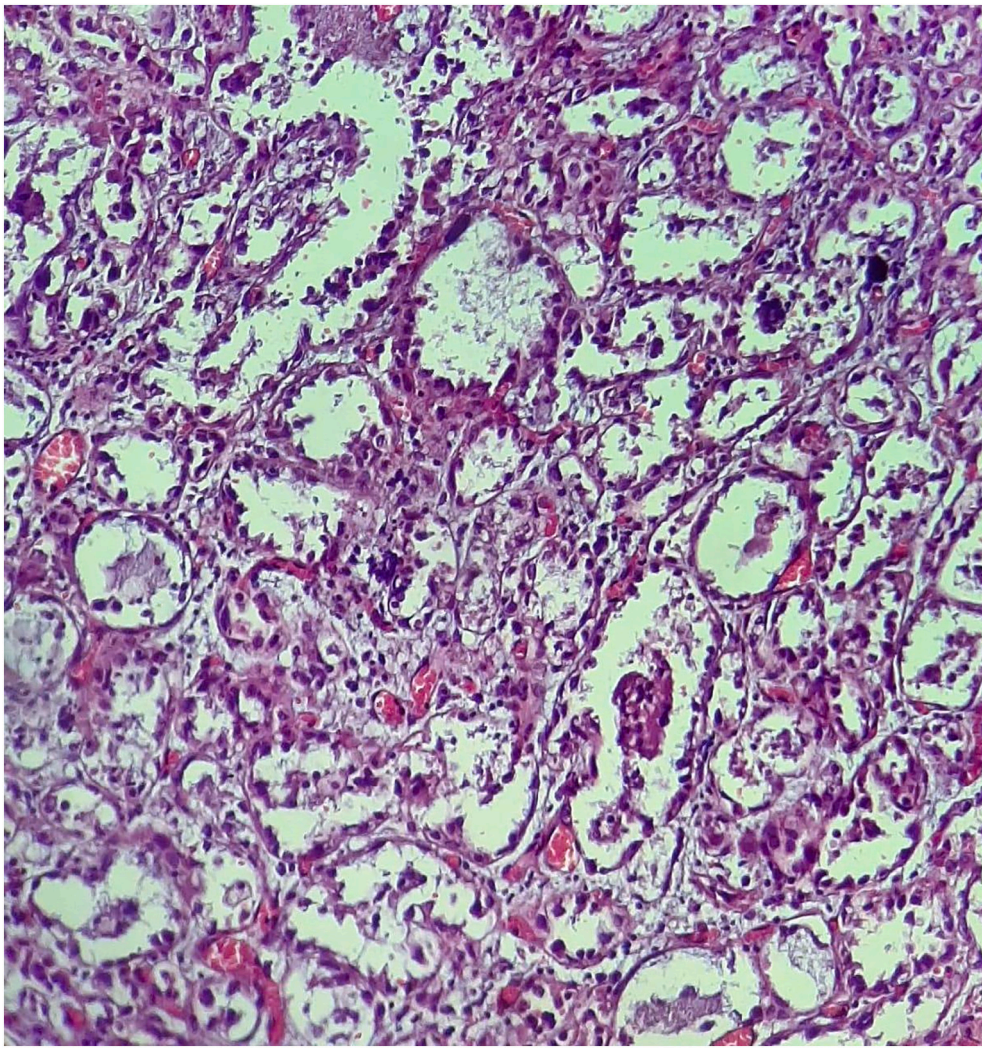


Fig. 8. Photo of histological slides revealing a vaginal location of a clear cell adenocarcinoma with marked cytonuclear atypia and irregular nuclei.

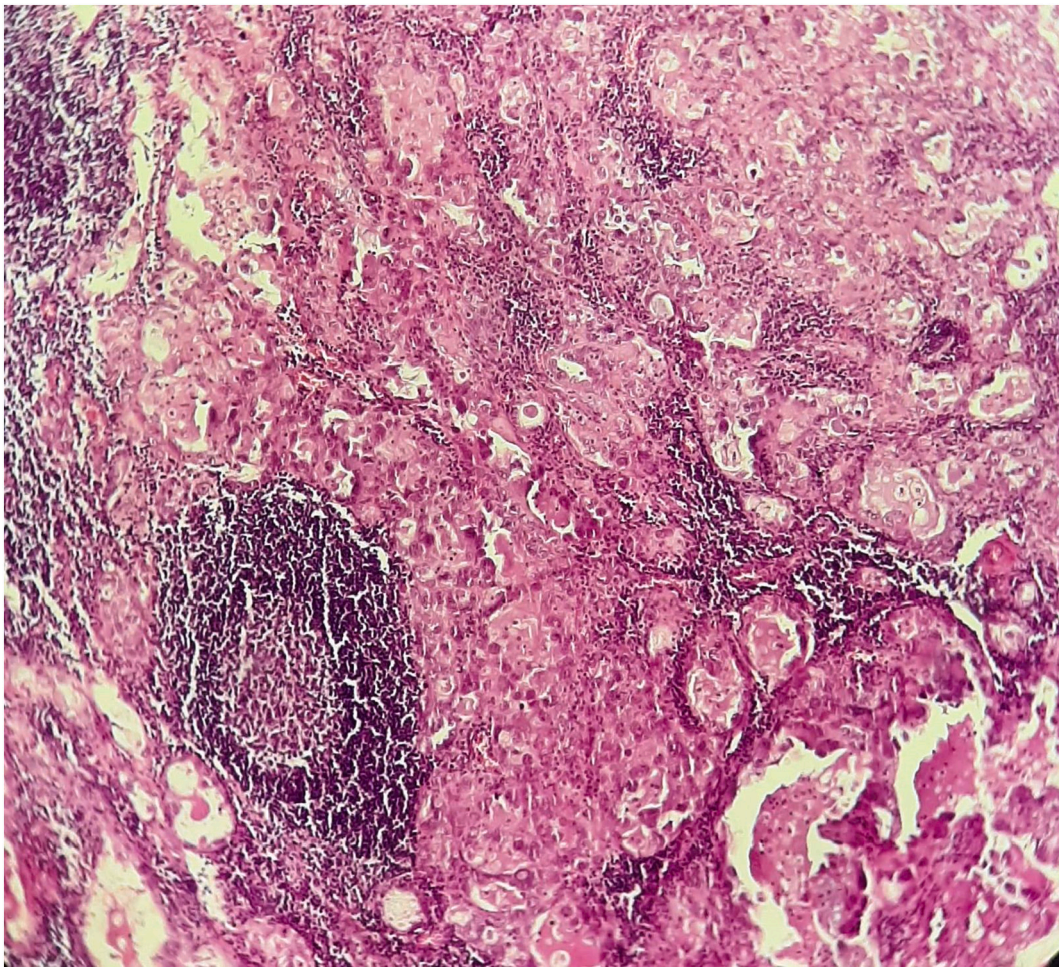


Fig. 9. Anatomopathological examination of metastatic lymph nodes.

cases not associated with any other anomaly or pathology have also been reported. Other anomalies/pathologies have also been reported [7–13]. In patients not exposed to DES, the age distribution is bimodal with young women mostly with congenital genitourinary anomalies [12] and postmenopausal women mostly with coexisting endometriosis [10]. Because of the rarity of CCA, individual experience based on case reports is the main source of information.

The diagnosis is most often made after the onset of non-painful metrorrhagia, sometimes leucorrhoea or pelvic pain, urinary or rectal signs for the more advanced stages. Asymptomatic forms can be diagnosed during cervical cancer screening. Clinical examination is important for diagnosis, treatment and prognosis. CCAs not associated with DES generally have a worse prognosis than CCAs associated with DES, which have a more favorable prognosis. Atypical clinic and difficult examination associated with one or more congenital abnormalities may be partially responsible for the poor prognosis of clear cell carcinomas.

MRI is the most reliable and accurate imaging technique to assess the locoregional extension and stage of the tumor, which will determine not only the therapeutic choice but also the prognosis, thanks to its excellent soft tissue resolution. It should specify the site, which is most often located in the upper third of the vagina, the tumor volume, the extension to the bladder, the rectum, the pelvic wall and the lymph nodes [5].

Depending on the stage and grade of the disease, most patients are treated with a combination of radical surgery and radiotherapy [14]. Chemotherapy is rarely used because of the poor associated outcomes. The 5-year survival in stage I CCA is only 56 % [12]. The overall recurrence rate for clear cell carcinoma is approximately 21 %. Recurrence has been observed up to 20 years after primary therapy,

emphasizing the importance of prolonged follow-up [14]. Surgery is reserved for early clinical stages, with favorable rates of specific survival and local control at five years, considered mutilating for advanced stages [1]. It may be the curative option of choice in a salvage situation for advanced clear cell vaginal adenocarcinoma persisting after irradiation [15].

4. Conclusion

Because of the small number of cases of clear cell adenocarcinoma reported in women who have not been exposed to DES, the likely etiology and most effective mode of treatment remain unknown. It depends on patient-specific factors such as the size of the tumor, the experiences of the surgeon and the oncology team.

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None.

Ethical approval

I declare on my honor that the ethical approval has been exempted by my establishment.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Haddout Sana: Corresponding author writing the paper.

Imami Youssef: study concept.

Benhessou Mustapha: study concept.

Ennachit Si Mohamed: study concept.

El Karroumi Mohamed: correction of the thesis and operating surgeon.

Research registration

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Guarantor

DR HADDOUT SANA.

Declaration of competing interest

The authors declare having no conflicts of interest for this article.

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