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Case Report

Primary clear cell adenocarcinoma of the vagina not associated with diethylstilbestrol metastasizing to the lung: a case report

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Abstract

Primary clear cell carcinoma of the vagina (PCCAV) is a rare form of vaginal cancer that typically affects young women with a history of prenatal exposure to DES. However, data on non-DES PCCAV cases are limited. This report describes a case of PCCAV in a 47-year-old patient who presented with post-coital bleeding and was diagnosed with clear cell adenocarcinoma via biopsy and MRI. The patient had no history of DES exposure and further testing showed no signs of metastasis, leading to surgery and chemotherapy. Four years later, the patient presented with dyspnea, and a chest CT scan revealed a lung nodule, later confirmed to be a metastasis of clear cell adenocarcinoma from the vaginal cancer. The patient passed away a month later due to complications from COVID-19.

INTRODUCTION

Primary clear cell carcinoma of the vagina (PCCAV) is a very uncommon kind of vaginal cancer that accounts for 5–10% of all cases. Typically, PCCAV is thought to affect young patients who have a history of prenatal exposure to diethylstilbestrol (DES), although data on the clinical manifestations, course and prognosis of non-DES PCCAV are limited. The lungs, supraclavicular lymph nodes and pelvis are the most common sites of metastasis, while liver, brain and peritoneal metastases are rare.

CASE REPORT

Case presentation

A 47-year-old female patient, in her second pregnancy and second childbirth, has been diabetic for 9 years and is currently on insulin. She has no history of prenatal exposure to DES. Her symptoms began in June 2016 with post-coital metrorrhagia, which gradually worsened and eventually became spontaneous and excessively heavy.

Clinical findings

During the speculum examination, a 1.5 cm vaginal nodule was observed in the left lateral vaginal pouch, which bled upon contact. The uterus appeared normal in volume with no mass detected on the sides, and the rectal examination was also normal.

Diagnostic approach

Following the discovery of a vaginal nodule, a biopsy was performed, which revealed a diagnosis of clear cell adenocarcinoma. To further investigate the extent of the cancer, a pelvic magnetic resonance imaging (MRI) was conducted. The MRI detected an oval formation measuring 19/9 mm on the left posterolateral vaginal wall. The formation exhibited a suspicious-looking T2 hyperintensity. Fortunately, there was no sign of pelvic lymphadenopathy or involvement of nearby organs, including the uterine body, cervix, fallopian tubes and ovaries. This was confirmed by the normal findings in the MRI images (refer to Figs 1 and 2). Subsequently, abdominal and thoracic computed tomography (CT) scans were performed, both of which yielded normal results, providing additional reassurance. Finally, the patient's cervical smear levels were assessed.

Therapeutic intervention, outcome and follow-up

The patient underwent an enlarged colpo-hysterectomy, as illustrated in Fig. 3, and a pelvic lymphadenectomy to treat her condition.

The histopathological examination of the vaginal lesion revealed a carcinomatous tumor proliferation with an essentially papillary architecture. The papillae varied in size and were lined with cells that had an abundant, clarified cytoplasm, rarely eosinophilic. The cells also had hyperchromatic, anisokaryotic

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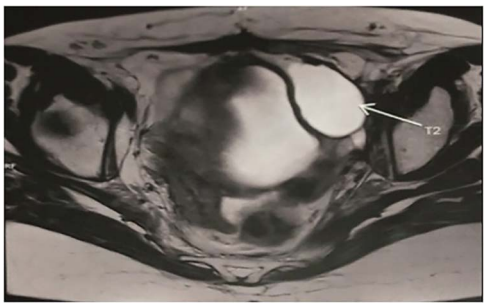

Figure 1. Pelvic MRI objectified presence of oval formation at the left posterolateral vaginal wall measuring 19/9 mm (axial T2-weighted image).

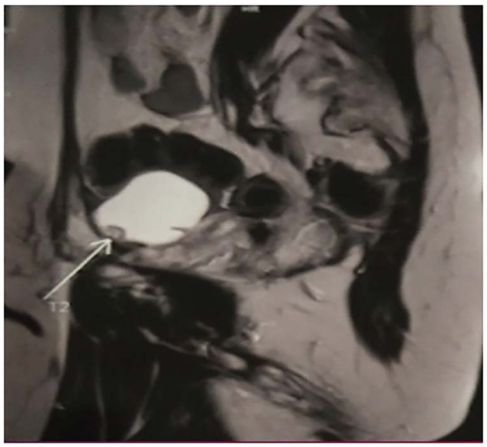

Figure 2. MRI image of the patient's pelvis sagittal T2-weighted image.

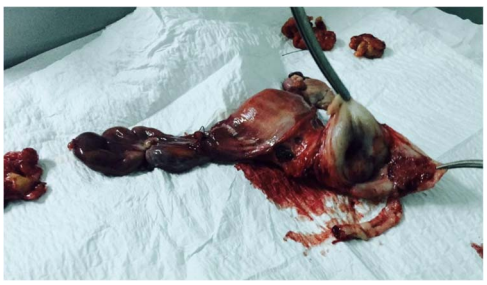

Figure 3. Piece of large colpo-hysterectomy with pelvic lymphadenectomy.

nuclei, often exhibiting an appearance similar to an upholsterer's nail.

The tumor had infiltrated the entire wall and was only 5 mm from the surgical margin. No signs of vaginal adenosis were detected, and the vaginal flanges were undamaged. Furthermore, the cervix, endometrium, parametrium and adnexa were unaffected. The right pelvic dissection was negative (6 N–/6 N), while the left pelvic dissection was positive (1 N+/10 N). The patient was classified as stage III (pT1, pN1, pM0).

The multidisciplinary oncology team evaluated the patient's condition and recommended six cycles of carboplatin and paclitaxel chemotherapy, followed by adjuvant whole pelvic radiotherapy.

The treatment proved to be successful, and the patient had an excellent outcome, with no signs of recurrence or metastasis during the follow-up period. Regular monitoring of the patient's progress was conducted through check-ups and imaging scans, all of which indicated that the treatment had effectively achieved complete remission.

During 4 years of clinical-radiological monitoring, no distant metastases were detected. However, in March 2020, the patient presented with dyspnea and chest pain. A chest CT scan revealed a suspicious lung nodule, which was later confirmed to be a metastasis of clear cell adenocarcinoma from the vaginal cancer. Unfortunately, a month later, the patient passed away due to complications from COVID-19.

DISCUSSION

Primary clear cell adenocarcinoma of the vagina (PCCAV) is a rare form of vaginal cancer, accounting for only 5–10% of cases. It predominantly affects young women, with the median age of diagnosis ranging from 17 to 22 years [1]. The incidence of PCCAV is low, particularly in unexposed women, with a cumulative incidence of only 0.02% [2]. DES use was most prevalent between 1951 and 1953, explaining why the majority of patients were diagnosed during that period. In recent years, the age at which clear cell adenocarcinoma presents has been observed to increase, as was the case with our patient. This highlights the need for further studies on the risk factors associated with this type of cancer. However, some studies suggest that menopause may increase the incidence of PCCAV, which still remains relatively low and predominantly affects patients with no exposure to DES [3].

It is widely recognized that clear cell adenocarcinoma is linked to DES exposure during pregnancy. However, the literature only reports a few cases of PCCAV that are unrelated to DES. PCCAV has occasionally been associated with genitourinary tract congenital malformations or vaginal endometriosis. There have also been a few isolated cases without any other abnormalities or diseases [3]. Our case involves a solitary PCCAV with no additional anomalies.

The most common presenting symptoms of PCCAV include painless metrorrhagia (uterine bleeding), pelvic pain, dyspareunia (painful sexual intercourse), leucorrhea (vaginal discharge), the perception of a vaginal mass, and, in more severe cases, rectal or urinary symptoms may occur. However, 16–25% of patients may be asymptomatic [4]. Asymptomatic forms of PCCAV can be detected during cervical cancer screening.

PCCAV tumors can vary in size, ranging from small masses to large, polypoid, flat, nodular or ulcerated lesions. They typically develop in the upper tier of the anterolateral wall (Table 1) [4].

Histological studies show mainly a tubule-cystic aspect, followed by a solid and papillary aspect. The immunohistochemical profile reveals positivity for CK7, CEA, CA125, Leu-M1 and overexpression of p53 and bcl-2. Hormone receptors may exhibit variable positivity, while CK20, β-hCG and alpha-1-fetoprotein are negative [5].

The majority of patients are treated with a combination of radical surgery and radiotherapy, depending on the stage and grade of the disease. Chemotherapy is rarely utilized due to poor results [6]. For early clinical stages of clear cell vaginal adenocarcinoma, surgery is the preferred treatment option, as it yields favorable rates of specific survival and local control at 5 years. In cases where the cancer persists after irradiation, surgery may be employed as a curative option of last resort [3].

PCCAV carries a high risk of metastasis, with distant metastases sometimes occurring without local extension to the pelvis. Robboy et al. found that 35% of PCCAV recurrences were distant metastases (supraclavicular, lung or lymphatic), without local extension to the pelvis [7].

Table 1. Summary table of clinical and therapeutic data for PCCAV cases

Cases	Age	Past medical history	Meno pause	DES exposure	Functional signs	Physical examination	Histology	Metastasis	Treatment
Yoh Watanabe et al. [2]	63	No past medical history	yes	No	Abnormal vaginal bleeding	Friable, hemorrhagic tumor.	PCCAV Immunohistochemistry: p53 microsatellite stable tumor	Liver Para-aortic lymph node	General supportive care
S. Haddout et al. [3]	60	mastectomy adjuvant chemotherapy and radiotherapy	Yes	No	Left inguinal adenopathy	3 cm budding mass in the lower third of the vagina, opposite the anterior wall.	PCCAV immunohistochemistry: CKAE1/AE3 and CK7: (+) and CK20/CD31/Napsin A/CD34: (−).	No	Partial colpectomy with bilateral inguinal curage Simultaneous chemo-radiotherapy
K Güzin et al. [4]	23	No past medical history	No	No	Pain, dysuria, leukorrhe, abnormal genital bleeding.	Rectal examination (patient was a virgin): semisolid mass 8–9 cm in diameter, originating from the right vaginal wall	PCCAV immunohistochemistry: no data	No	Radiotherapy and then cisplatin-based chemotherapy
MC Renaud et al. [6]	19	No past medical history	No	No	No data	1 cm lesion in the right vaginal fornix.	PCCAV immunohistochemistry: no data	No	Radical local vaginal excision, laparoscop, sentinel node mapping, pelvic node dissection, and omentectomy Chemotheraoy six cycles of paclitaxel/carboplatin. No Radiation therapy
M Hasanzadeh et al. [8]	49	anti-depressant therapy (sertraline)	yes	No	Purulent watery vaginal discharge and abnormal vaginal bleeding.	2 × 2 cm, polypoid mass (post fornix at the left side of upper vagina).	PCCAV immunohistochemistry: no data	No	Radical hysterectomy bilateral salpingo-oophorectomy Pelvic and peri-aortic lymphadenectomy Excision of ∼4 cm of the vaginal wall. Chemo-radiotherapy
Shah C et al. [10]	55	No past medical history	yes	No	Abnormal vaginal bleeding.	2 cm polypoid lesion at the posterior vaginal apex,	PCCAV immunohistochemistry: no data	No	Radical hysterectomy Radical upper vaginectomy, bilateral salpingo-oophorectomy, pelvic and peri-aortic lymphadenectomy—Chemo-radiotherapy—Progestin therapy
Our case	47	Diabetic on insulin	Peri-menopause	No	post-coital vaginal bleeding	1.5 cm vaginal nodule in the left lateral vaginal pouch	PCCAV	No	Colpo-hysterectomy and pelvic lymphadenectomy Chemo-radiotherapy

For stage I of PCCAV, the 5-year and 10-year survival rates are 93% and 87%, respectively. Favorable prognostic factors include higher age at diagnosis, tubule-cystic type and asymptomatic presentation [8].

Large size, deep wall invasion and nuclear atypia are unfavorable prognostic indicators [9]. Recurrences mostly occur within two decades after initial treatment [10].

CONCLUSION

PCCAV is a rare type of clear cell adenocarcinoma that predominantly affects young patients who were exposed to DES in utero. Unfortunately, cases of PCCAV not linked to DES exposure have a poor prognosis, requiring extended and vigilant follow-up. While sporadic cases of PCCAV in patients not exposed to DES exist, the probable cause and optimal treatment approach remain uncertain and may vary based on individual patient factors, such as tumor size and the expertise of the surgical and oncological teams involved.

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Not applicable.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

FUNDING STATEMENT

This study was not funded.

ETHICAL APPROVAL

Not applicable.

CONSENT FOR PUBLICATION

Written consent has been obtained from the patient and the patient's family for the publication of this case report.

GUARANTOR

Benlghazi Abdelhamid.

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