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Clear cell carcinoma in endometrial pathology: A rare case study

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Abstract

Introduction: Clear cell carcinoma of the endometrium is a rare, aggressive tumor that spreads rapidly and frequently outside the uterus. Multimodal management is the weapon of choice in the treatment of clear cell carcinomas of the endometrium, but treatment must be based on the molecular classification of the tumor.

Report of the case: We report the clinical observation of a 45-year-old female patient followed for clear cell carcinoma of the endometrium. She received palliative chemotherapy with paclitaxel and carboplatin. Clear cell carcinoma of the endometrium belongs to histological type II endometrial cancer. Clear cell carcinoma expresses very little POLEmut and MMRd, but mainly expresses p53abn and p53wt/NSMP. P53abn and p53wt/NSMP tumors have poor outcomes after treatment. It has a poor prognosis despite treatment. Conclusion: Clear cell carcinoma of the endometrium is a rare and aggressive tumor, hence the importance of early diagnosis for rapid and optimal treatment.

Keywords: Clear; Cell; Carcinoma; Endometrial

1. Introduction

Clear cell carcinoma is a rare subtype of endometrial carcinoma described almost a century ago by De Bonnelle (1). It accounts for 1% to 5.5% of all endometrial carcinomas (2). It is a particularly aggressive form of uterine tumor, characterized by rapid and frequent ectopic spread. It occurs mainly in post-menopausal women and responds poorly to platinum-based chemotherapy and radiotherapy (3). Clear-cell carcinoma has a higher probability of recurrence and poorer overall survival than endometrioid carcinoma (4). Today, its management is based on molecular classification. We report the clinical observation of a 45- year-old patient with clear cell carcinoma of the endometrium.

2. Report of the case

A 45-year-old patient with no known pathological history was presenting with menometrorrhagia without pelvic pain for 3 months. She was consulted in August 2022, when an ultrasound scan revealed uterine myomas. Surgical removal of the myomas was performed. Histological examination and immunohistochemistry showed a clear-cell carcinoma of the endometrium. On physical examination, the rectal examination revealed a hard, centro-pelvic mass measuring approximately 7 cm (the vaginal examination was not performed as the patient was a virgin). Local radiological assessment and extension by magnetic resonance imaging revealed a voluminous, locally advanced uterine process, infiltrating almost the entire uterine myometrium, the cervical region, and the vagina; associated with pelvic and parietal masses in favor of a secondary peritoneal and cutaneous location. A bony lesion of the right iliac wing was also

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noted. Thoraco-abdominal CT revealed multiple anterior abdominal masses, sub-umbilical with invasion of sub-eritoneal fat and intimate contact with the anterior bladder wall. A hepatic lesion was straddling segments V and VIII and osteocondensing lesions of the eighth dorsal vertebra and right iliac wing. The patient underwent six courses of palliative chemotherapy (paclitaxel-carboplatin), with a stable tumoral process on assessment.

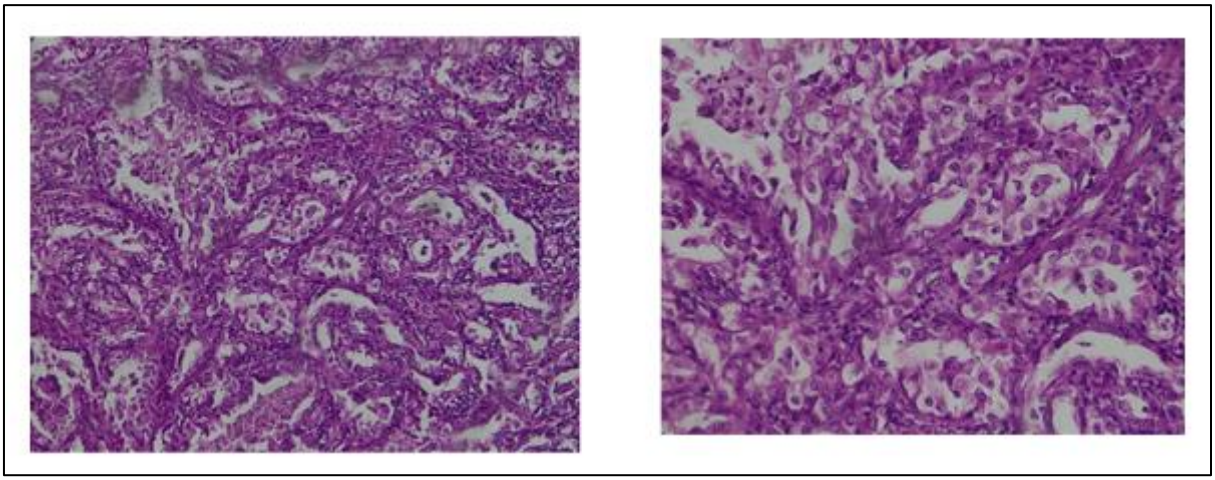

Figure 1 Invasive adenocarcinoma proliferation with an immunohistocheminal profile consistent with clear cell carcinoma

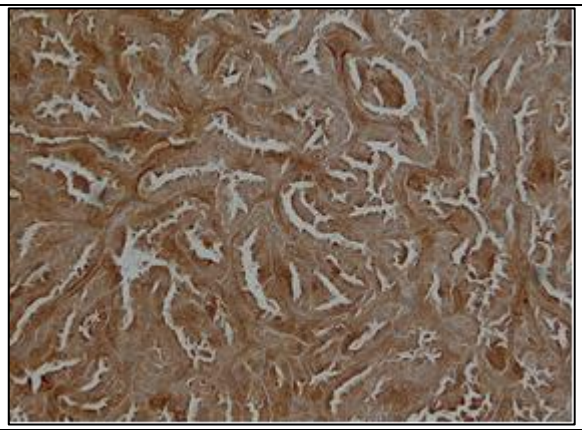

Figure 2 Positive expression of tumor cells by Napsin A

Figure 3 Positive expression of tumor cells by estrogen receptors

3. Discussion

Endometrial cancer remains the most common malignancy of the genital tract in women in the USA. The incidence of endometrial cancer is approximately the same as that of all other malignancies of the female genital tract combined (5). By far the most common histological type is endometrioid endometrial cancer, which accounts for over 50% of all histological types of endometrial cancer (5,6). This is followed by papillary serosa, diagnosed in 17-22% of cases (7). In contrast, clear-cell endometrial cancer is rare, accounting for only 1-6% of all endometrial cancers (8,9). It is classified as a "type II" pathogenetic type, with no identified endocrine or metabolic influence on its development and an aggressive clinical course (10). The etiology of clear-cell endometrial cancer is not well understood but appears to be unique in terms of endometrioid histology. A recent study identified putative precursor lesions in 90% of uterine samples from women with clear-cell endometrial cancer. These lesions were usually isolated glands or surface epithelium in an otherwise normal endometrial region that showed cytoplasmic clarity and/or eosinophilia with varying degrees of nuclear atypia (5).

The majority of women with clear-cell endometrial cancer are diagnosed after presenting with postmenopausal bleeding (11). Pelvic ultrasound and magnetic resonance imaging can aid in diagnosis. The diagnosis of clear-cell endometrial cancer can be made using the same tests used for the diagnosis of other types of endometrial cancer. Endometrial biopsy is a highly reliable diagnostic tool, with a sensitivity of over 99% (12). Histologically, it may have one of the following patterns: papillary, tubulocystic, or solid. These features may exist alone or in combination. Other common features include intraluminal mucin, the focal presence of intracytoplasmic vacuoles containing eosinophilic hyaline mucin droplets, and stromal hyalinization and deposition of basement membrane material (5). Clear cell histology must include more than 50% of its features before the tumor can be designated as clear cell carcinoma (5). Immunohistochemistry shows a high Ki-67 index, low immunoreactivity for p53, and the absence of estrogen receptor (ER) and progesterone receptor (PR). These can also help distinguish clear-cell endometrioid cancer (usually ER/PR positive) from papillary endometrial cancer (high p53 immunoreactivity) (13).

Treatment of clear-cell endometrial cancer includes surgery, chemotherapy, and/or radiotherapy, often in intermodal combination (5). Complete surgery in women diagnosed with clear-cell endometrial cancer should include evaluation of the peritoneal cavity with lavage, smears, and biopsies of suspicious areas of the peritoneum and total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, and omentectomy. Post- operative radiotherapy improves local control in women at increased risk of local recurrence. Given its propensity for early recurrence and aggressive nature, it seems reasonable to discuss the option of adjuvant platinum-based chemotherapy in all women diagnosed with clear-cell endometrial cancer, including those whose disease was confined to the uterus at the time of diagnosis (5).

The clinical management of clear cell carcinoma has followed the recommendations for the most common serous carcinoma, the prototypical "type II" tumor; however, more recently, the mutational diversity within clear cell carcinomas has been appreciated and this strategy questioned (10). A recent analysis of data from the PORTEC3 clinical trial provides another example where, given the very favorable results observed in the 13% of POLEmut tumors (98% RFS), it is unclear whether treatment added any benefit in this cohort; on the other hand, the high recurrence rate in p53abn tumors justified treatment and showed better results with chemotherapy combined with radiotherapy in this molecular subtype, while MMRd EC showed no benefit with the addition of chemotherapy to radiotherapy (14,15). Older women with endometrial clear cell carcinoma express more p53abn and younger women MMRd or POLEmut (10).

4. Conclusion

Clear cell carcinoma of the endometrium is a rare histological subtype of endometrial cancer. It is a more aggressive disease and has a poorer prognosis than endometrioid endometrial cancer. This poorer prognosis has led several studies to support the use of adjuvant treatment consisting of radiotherapy, chemotherapy, or both.

Compliance with ethical standards

Disclosure of conflict of interest

All authors contributed to the writing and development of this article. They also all read and approved the final version of the manuscript.

The authors declare no conflicts of interest.

Statement of informed consent

Consent for publication was obtained from the patient.

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