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Endometrial cancer – Is standardized treatment sufficient? Recurrence of endometrial cancer in the vulva – case report

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ABSTRACT

A 63-year-old woman, previously treated for endometrial cancer using chemoradiotherapy, came in for additional diagnosis. Imaging studies showed uterine tumors that had extended to the parametrium. The patient had a radical hysterectomy along with bilateral salpingo-oophorectomy. The histopathological examination verified G2 endometrioid adenocarcinoma (FIGO stage II) and a borderline ovarian tumor. Because of a p53 mutation, the patient received adjuvant chemotherapy and brachytherapy. Follow-up MRI revealed suspicious lesions in the vaginal and vulvar areas, including a mass in the left labium majus. The doctor initiated hormonal therapy. Given the tumor size, surgical excision of the vulvar lesion and vaginal nodules was performed, with histopathology confirming recurrence of endometrioid carcinoma. Due to further disease progression, the medical team introduced immunotherapy. This case is an example of a rare location of endometrial cancer recurrence on the vulva and in the vagina. It highlights the need for an individualized approach to each patient, analysis of possible treatment strategies, and selection of the appropriate therapy, particularly in patients with high-risk molecular profiles.

Keywords: endometrial cancer, vulvar metastasis, treatment

1. INTRODUCTION

Endometrial cancer (EC) is the most common cancer affecting the female reproductive system in developed countries (Bassette and Ducie, 2024). Early detection of the disease usually leads to a satisfactory outcome in most cases. However, about 15% of patients have cancer at an advanced stage, which significantly reduces treatment effectiveness and limits the response to chemotherapy (PDQ Adult Treatment Editorial Board, 2020). In patients with metastatic disease there are lower survival rates and a higher risk of recurrence (Xu et al., 2016). Typical location of metastasis in EC are: pelvic and para-aortic lymph nodes, vagina and peritoneum (Aalders et al., 1984). Vulvar metastases are very uncommon. It is the result of different lymphatic drainage of this region (Mandato et al., 2021).

When recurrent disease extends beyond the pelvic area, prognosis depends on the location of the lesions, the tumor's molecular type, the patient's age, overall health, and previous treatments. The typical approach involves surgery with cytoreduction. Based on the stage of the illness, suitable additional treatment is provided, usually chemotherapy (six cycles of carboplatin and paclitaxel) and/or radiation therapy. Hormonal therapy is a recommended treatment for patients with advanced or recurrent EC (Concin et al., 2025). This case presents recurrent EC with vulvar metastasis. Despite the use of standard treatment, it was necessary to initiate therapy beyond the established therapeutic protocol.

2. CASE DESCRIPTION

A 63-year-old woman came to the hospital complaining of bleeding from the genital tract and lower abdominal pain that had lasted for a week. The patient had her last menstrual period at the age of 53. On Computed Tomography (CT) of the abdomen and pelvis, it was a multicystic, heterogeneous mass measuring 18 × 10 × 15 cm in the left iliac fossa and at the left lower abdomen, showing evidence of intralesional hemorrhage. The radiologist also described an enlarged uterus with a dilated endometrium and numerous calcifications within the cervix. Imaging showed enlargement of the omental, left external iliac, and inguinal lymph nodes. Histopathological examination of vaginal wall biopsies revealed G2 endometrioid carcinoma (CK7+, PAX8+, vimentin+, ER+, p53+/–, p16+). Clinicians qualified the patient for palliative radiotherapy covering the lower abdomen, reproductive organs, and regional lymph nodes. After improvement in her general condition, she received the paclitaxel 175 mg/m² with carboplatin (AUC 6) regimen every 21 days. The patient had strong allergic reaction after first course of chemotherapy. It was characterized by shortness of breath and facial skin redness. Due to this doctors decided, to continued treatment with carboplatin monotherapy (AUC). A follow-up CT scan after six cycles demonstrated a large predominantly cystic-solid mass in the lower and mid abdomen, somewhat right sided, measuring up to 212 × 143 mm, suspicious for ovarian metastasis; the right ovary was visible adjacent to the lesion, and the left ovary was not clearly delineated. The imaging suggested a possible metastatic lesion in the ovary. Pelvic Magnetic Resonance Imaging (MRI) revealed a lesion in the uterine corpus and cervix (8 × 3.5 × 4 cm) invading both parametria, without definitive involvement of the bladder, rectum, vagina, or ureters. There was also a small amount of fluid in the peritoneal cavity (Figure 1).

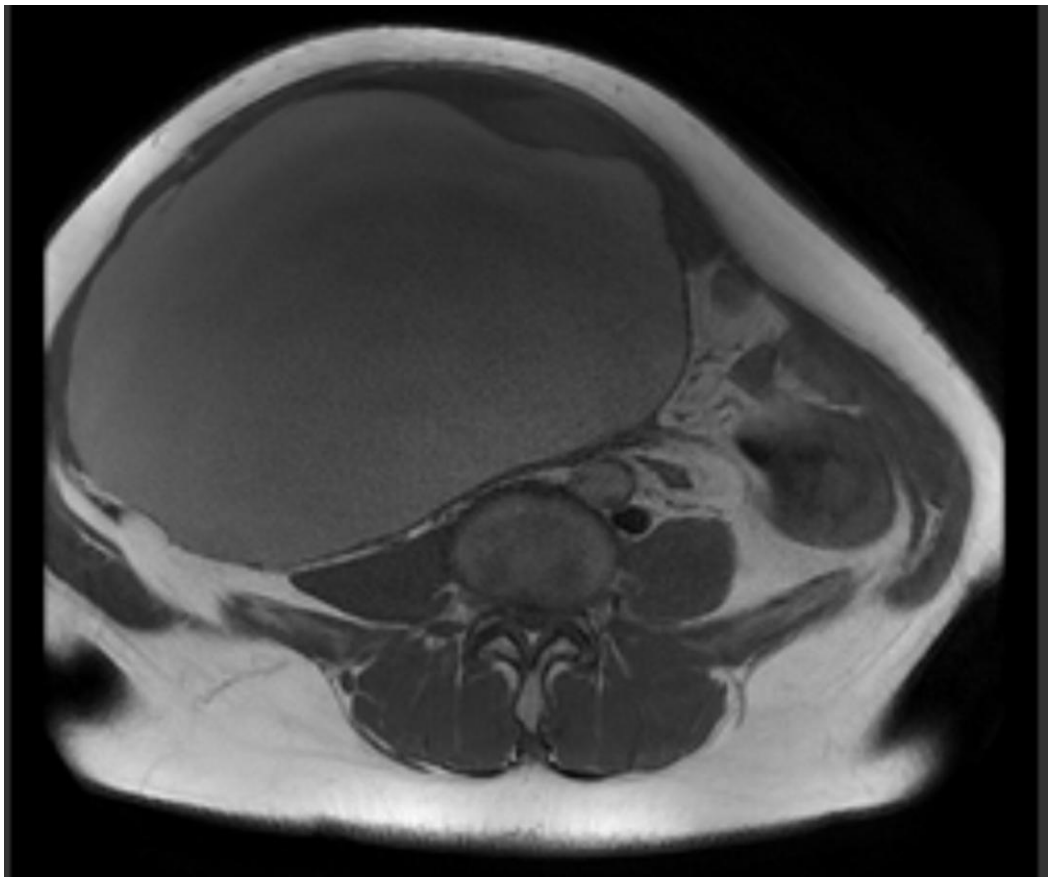

Figure 1. Pelvic MRI

A medical consultation resulted in a decision to proceed with surgical treatment. Surgeons performed a radical laparotomy consisting of total hysterectomy with bilateral salpingo-oophorectomy and partial vaginal cuff resection. Intraoperative histopathological examination confirmed endometrioid cancer of the uterine body infiltrating the mucosa and uterine muscle (pT2, pNx, FIGO II, L0, V0, PNIO; no angioinvasion, no nerve infiltration). Pathological analysis showed a borderline tumor in the left ovary. Molecular testing revealed an unusual protein expression profile, including p53, POLE, PMMR, MSS, and focal mucicarmine positivity. According to these findings, patient received adjuvant carboplatin chemotherapy and brachytherapy. Due to previous external radiotherapy, the patient was not eligible for further teleradiotherapy. Doctors applied supplementary irradiation to the vaginal stump and local lymph nodes at a dose of 45 Gy/df 1.8Gy in 25 fractions using the VMAT technique. The treatment was well tolerated.

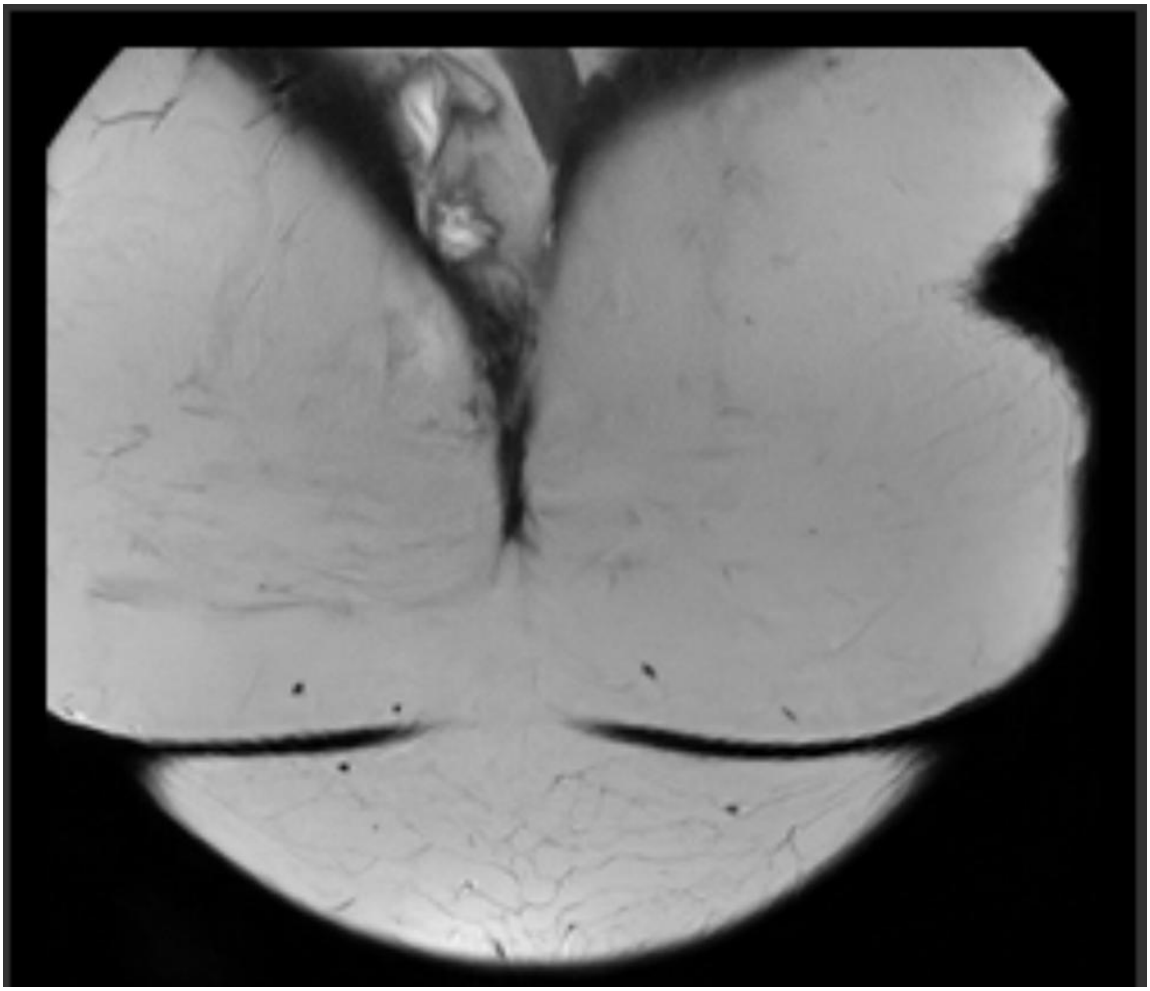

Figure 2. Pelvic MRI; lesions on the vulva

Histopathological examination of a vaginal biopsy revealed G2 adenocarcinoma with vimentin+, ER+, PR focally +, p53-. Features indicate endometrioid carcinoma. Based on the immunohistochemical profile, a multidisciplinary meeting decided to include megestrol acetate (MEGACE) as part of the hormone therapy. The MRI showed a recurrence of the disease. On control MRI there was recurrence of the disease. Radiologists observed diffusion restriction focus on the vaginal vestibular junction (~16 mm) and visualized a mass measuring 32 × 21 × 28 mm in the left labium majus (Figure 2). In imaging, there were enlarged bilateral obturator lymph nodes with necrotic changes (12 mm on the right, 8 mm on the left). A small volume of fluid was present in the pelvis. Imaging revealed no metastatic changes in the bones.

Surgeons excised a lesion from the left labia majora with clear surgical margins. The tumor was mobile, clearly demarcated with ulceration on the surface. They also excised several millimeter nodules from the vagina and confirmed that the clitoris and urethra were free of infiltration. The procedure and postoperative period were uneventful. However, 10 days after the procedure, dehiscence of the postoperative wound on the vulva occurred.

A pelvic MRI after surgical removal of the vaginal and vulvar lesions showed vaginal recurrence. There was a small hemorrhagic focus at the site of the excised vulvar tumor. The most severe vulvar oedema was in the right labia majora. Between the vagina and the vaginal vestibule, there was a focus of diffusion restriction measuring approximately 28mm, involving the urethral opening. In addition, there was a cystic-solid lesion measuring 19 × 15 mm at the top of the vagina. Radiologists identified a metastatic focus in the left sacrum (S4–S5) with widening of the bone contour. After exhausting standard treatments, they started off-label immunotherapy with pembrolizumab.

3. DISCUSSION

EC is the most common type of gynecological cancer in developed countries, and it's occurrence is increasing worldwide (Crosbie et al., 2022). Although most women suffering uterine cavity cancer are cured through surgery, about 10 to 20% of patients experience a recurrence that spreads to distant parts of the body, and this is usually not curable (Volinsky-Fremond et al., 2024). This case presents an unusual development of endometrial cancer. Despite surgical treatment, chemotherapy, and radiotherapy, the patient had recurrence in the vagina and vulva. Vulvar recurrences are a rare location for secondary tumors. Metastatic lesions in the vulva account for 5-8% of all vulvar cancers, and in nearly 10% of cases, their origin remains undetermined (Mandato et al., 2021). Data available in the literature are limited to case reports and small series. It is most likely related to the distinct regional lymphatic drainage of the uterus and vulva. Lymph from the uterus drains to the pelvic and paraaortic lymph nodes, while that from the vulva drains to the superficial inguinal lymph nodes. This results in a lack of reliable population-based data determining the incidence of these metastases as a percentage of all EC cases. It presents a significant treatment challenge, especially for patients who have already received radiotherapy and have limited options for re-irradiation. Lesions on the vulva can take very nonspecific forms: exophytic, nodular, follicular, or ulcerated. The presence of neoplastic foci in this location often correlates with an advanced stage of the disease and a poor prognosis, and the use of conventional treatment in this case proves insufficient.

Molecular classification of EC is gaining increasing importance in the therapeutic process. It takes into account POLE mutations, DNA repair defects (dMMR/MSI-H), and p53 mutations as factors that predict outcomes and guide treatment, helping to choose the best adjuvant therapy (Galant et al., 2024). Guidelines allow a combination of chemotherapy and immunotherapy in treatment advanced or metastatic EC with dMMR/MSI-H features (Boreham, 2025). A meta-analysis by Bogani et al., (2024) showed that patients who received immunotherapy in addition to chemotherapy had a notably higher progression-free survival (HR: 0.70), especially those with MMRd/MSI-H tumors. The study shows that using chemotherapy along with immunotherapy led to better survival rates overall compared to chemotherapy alone. The U.S. FDA has approved using Pembrolizumab, which is a PD-1 inhibitor, along with Lenvatinib, the inhibitor of tyrosine kinase, for patients with advanced or recurring EC with MSI-H or dMMR profile. It is necessary to note that this treatment is only a therapeutic option after ineffective systemic therapy (Arora et al., 2020). A question that remains is whether immunotherapy works effectively in monotherapy.

Studies have not confirmed that combination therapy is more effective than immunotherapy alone. In this case, due to progression of disease in an unusual location and after exhausting standard treatment options, the doctors decided to use immunotherapy as a salvage strategy. Individualized treatment based on qualifications and patients' health conditions allowed for control the disease. Although there are not enough studies on the use of immunotherapy alone in MSS/pMMR cases, it is essential to highlight the need for future research into immunotherapy as a potential treatment option in recurrent EC.

4. CONCLUSION

To conclude, this case illustrates EC with a very unusual recurrence in the vulva. Immunotherapy is an alternative treatment option when conventional treatment cannot control the disease. These findings highlight the importance of selecting therapy individually, considering the cancer's molecular characteristics and the risk of recurrence.

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Author contributions

First author- Framing of the study, data collection and writing of paper. Second author- writing of paper, data collection. Third and fourth authors- supervisors.

Informed consent

Written & Oral informed consent was obtained from individual participant included in the study.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interests, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data collected during this study are available upon reasonable request from the corresponding author.

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