



Case report

When the endometrioid adenocarcinoma and the endometrial stromal sarcoma meet: A report of an extremely rare case

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ABSTRACT

Introduction: Collision tumors are characterized by the coexistence of two adjacent, but histologically distinct tumors. This entity can occur between tumors originating from the same organ or between metastases from other sites.

Case presentation: A 49-year-old postmenopausal female with abnormal vaginal bleeding and abdominal pain was diagnosed with two coexistent tumors, a grade 1 endometrioid carcinoma and a pT2 undifferentiated stromal sarcoma (USS). On the first time, the patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy and one month later, she was diagnosed with recurrence. Then, a second surgical excision of the recurrent tumor was performed including exploratory laparotomy and anterior pelvic exenteration. She had an uneventful postoperative period, but unfortunately a month following the second operation she passed away.

Conclusion: We aim to raise awareness of these rare synchronous malignancies and highlight the importance of having a broad differential diagnosis in a patient presenting with abnormal vaginal bleeding. Further studies with larger patient populations are needed to shed light in etiology and pathogenesis of the concurrence of two malignancies with different embryological origin in the same organ, in order to optimize management of these patients.

1. Introduction

Collision tumors are characterized by the coexistence of two adjacent, but histologically distinct tumors. This entity can occur between tumors originating from the same organ or between metastases from other sites (Murthaiah et al., 2009). The two components are separated from each other by stroma without admixture. In the literature, the presence of collision tumors has been reported in several organs, such as stomach, thyroid gland, esophagus, lung, colon, skin, breast, ovary and uterus (Murthaiah et al., 2009; Diamantis et al., 2021; Diamantis et al.,

2020).

The synchronous presence of endometrioid adenocarcinoma and endometrial stroma sarcoma (ESS), must be distinguished from carcinosarcoma. Uterine carcinosarcomas (previously called malignant mixed Mullerian tumors) are differentiated carcinomas consisted of carcinomatous and sarcomatous elements which arise from a single malignant clone (Kanthan and Senger, 2011). However, it is estimated that approximately 10–20% of carcinosarcoma are biclonal with a distinct carcinoma and sarcoma cellular origin (Kanthan and Senger, 2011; Kim et al., 2015).

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Herein, we report a rare and interesting case of a synchronous endometrial adenocarcinoma and endometrial stromal sarcoma in a postmenopausal patient.

2. Case presentation

A 49-year-old postmenopausal Caucasian female patient, presented to the emergency department due to abdominal pain and irregular vaginal bleeding. The patient's gynecological history included two uncomplicated vaginal full-term births. Menopause was reached at the age of 47 years old, with formerly regular menstrual cycles. She reported no significant past medical or surgical history and she didn't receive any medication. Her family history was unremarkable.

Gynecological examination revealed an endometrial hemorrhagic protruding mass. Biopsies were sent for histological examination, was indicating an endometrioid adenocarcinoma of the uterus. From the radiological examination there were no signs of local or distant metastases. Based on these findings, a decision for a total abdominal hysterectomy with bilateral salpingo-oophorectomy was made (Figs. 1 and 2). Intraoperatively, no lymph node or distal metastasis were identified.

Histopathology report revealed a tumor consisting of an endometrioid adenocarcinoma of the uterus (FIGO GRADE 1) and a stage pT2 Undifferentiated Stromal Tumor (USS). Spindle-shaped cells with mainly subcircular nuclei and a great number of mitotic figures (>10 mitotic figures per 10 high power fields), without cluster or group arrangement were described. Clots, fibrin and necrosis were also presented and at some sections through the neoplasm, some small, glandular formations, without atypia, were entrapped as well as parts of an adenocarcinoma. The development of a malignant neoplasm, invading the superficial part of the myometrium was ascertained. Next to it an endometrioid adenocarcinoma was found (Fig. 3), forming villoglandular formations, invading more than half of the myometrium and a superficial part of the cervix, near the isthmus. The deduction was, that two separate and distinguishable neoplasms, namely were simultaneously present. The immunohistochemical stains were positive for CD10 and negative for keratins AE1/AE3, whereas the adenocarcinoma cells were positive for keratins and for estrogen and progesterone

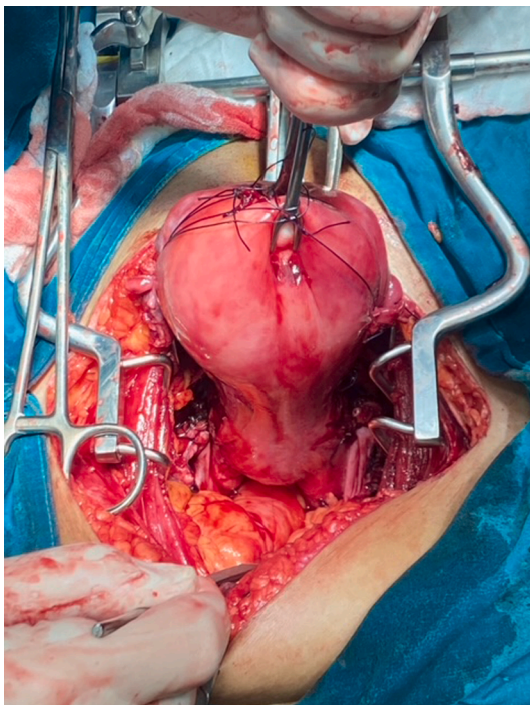


Fig. 1. Intraoperative image of the uterus during the first operation.

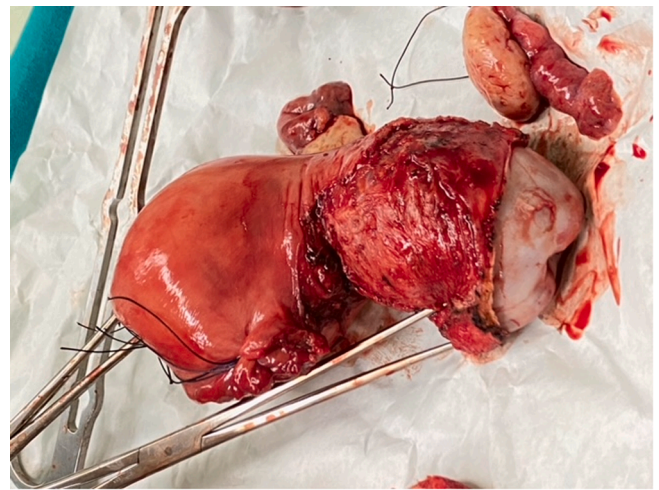


Fig. 2. Macroscopical image of the specimen of the first operation.

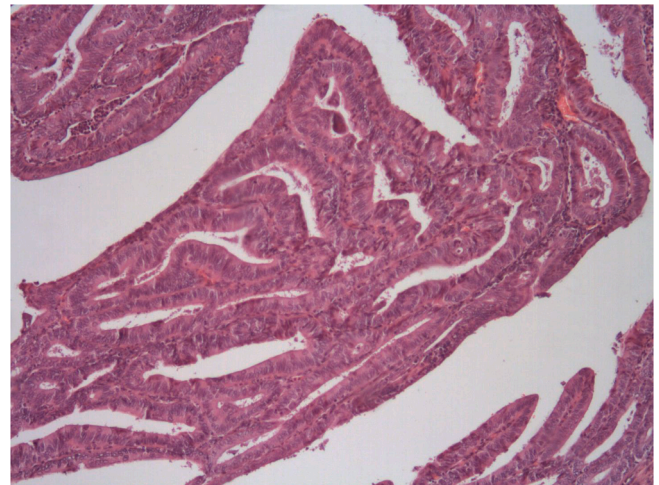


Fig. 3. Histopathology imaging indicating an endometrial adenocarcinoma of the uterus.

receptors, and negative for CD10. All tumor cells were found negative both for smooth muscle actin (SMA) and for Desmin stain.

One month later, before her scheduled appointment with the oncologist, the patient presented at the emergency department of another hospital reporting abnormal vaginal bleeding and hematuria. Radiology imaging revealed tumor recurrence to the vaginal vault with the tumor invading bladder and rectum. Pelvic exenterosis including tumor local excision, Hartmann procedure, partial vaginectomy and bladder excision with removal of distal ureters was performed. Post-operative hospital stay was uneventful, and the patient was discharged the 9th postoperative day.

Surgical pathology examination from the described tumor reported a high cellular malignant neoplasm with spindle-shaped and subround cells, with eosinophilic cytoplasm with high nuclear atypia 60/10 HPF and frequent nuclear activity. Extensive necrosis was prominent and focal areas of myxoid degradation of the stroma were identified. The immunohistochemical stain of the neoplastic cells was positive for Vimentin, CD10 and weakly positive for S-100, but negative for SMA, Desmin, CD117, CD34, estrogen receptor, and Cytokeratin (Figs. 4A, 4B). The neoplastic cells were invading both the vaginal and bladder wall from the exterior. However, invasion of the colon was not identified. Based on the pathological and the immunohistochemical findings, the lesion was regarded as USS.

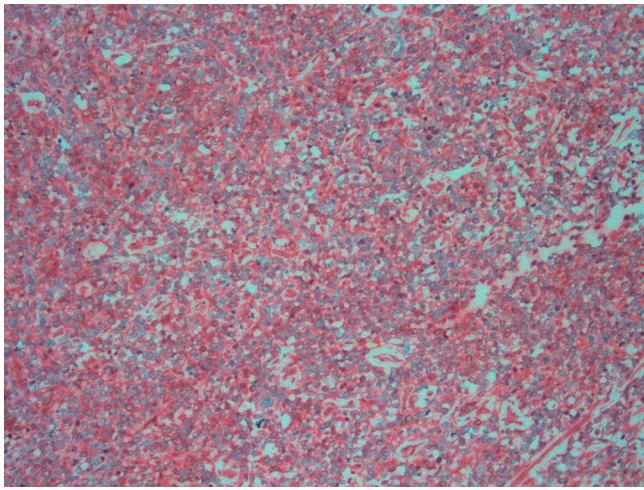


Fig. 4A. Positive immunostaining for Vimentin (x10).

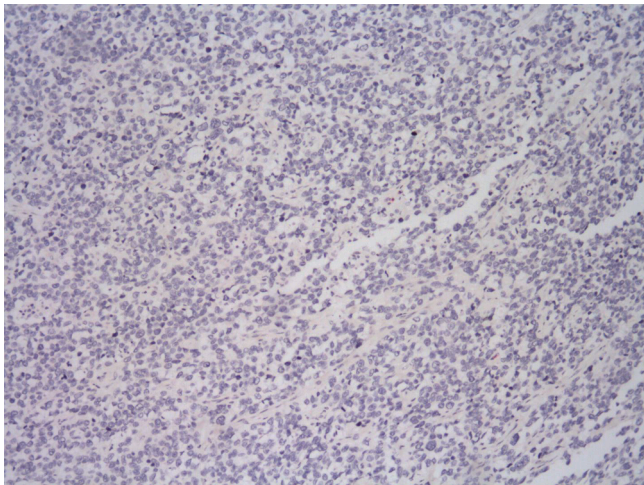


Fig. 4B. Positive immunostaining for CD10 (x10).

A multidisciplinary team suggested for adjuvant chemotherapy, scheduled a month postoperative. Unfortunately, the patient passed away a month after the second operation and three months after the initial diagnosis diagnosed with acute respiratory distress syndrome (ARDS), before receiving any systematic therapy.

3. Discussion

Endometrial cancer is the most common gynecological cancer in developed countries, with an age standardized incidence of 13.6 per 100,000 women and a cumulative risk for a diagnosis of endometrial cancer is 1.71% (Colombo et al., 2016). Endometrial adenocarcinoma is the fourth leading cancer diagnosis in women, classified in two types; the estrogen driven tumor Type I (endometrioid), representing 80% of the newly diagnosed endometrial carcinomas in developed countries and Type II (non-endometrioid) that is estrogen independent and includes serous and clear cell carcinoma (Hacker et al., 2015).

Endometrial stromal tumors (ESTs) are rare mesenchymal neoplasms of the uterus representing less than 2% of uterus malignancies (Ali and Rouzbahman, 2015). According to World Health Organization (WHO) classification, there are four subtypes of ESTs based on both pathological and clinical features: the endometrial stromal nodule, the low-grade endometrial stromal sarcoma (LG-ESS), the high grade endometrial stromal sarcoma (HG-ESS) and the undifferentiated uterine sarcoma

(USS) (Conklin and Longacre, 2014). ESSs usually affect postmenopausal woman with significant predisposing factors including race, age, pelvic radiation and use of tamoxifen. Diagnosis of an ESS is considered uncommon, accounting approximately for 6–20% of all uterine sarcomas (Conklin and Longacre, 2014).

Undifferentiated uterine sarcoma (USS) is an even rarer aggressive uterine sarcoma subtype that lacks morphologic and immunophenotypic evidence of cell differentiation, representing approximately one quarter of all ESS (Cotzia et al., 2019). USS has been associated with a lower disease-specific survival rate comparing with LG-ESS and HG-ESS, as most of the cases have extrauterine disease at the time of diagnosis and typically relapses within a short-frame leading to high mortality rate (Conklin and Longacre, 2014). An ESS is frequently misdiagnosed due to the presence of multiple histological variants and the presence of many common characteristics with other types of cancer (Masand, 2018).

Synchronous occurrence of two distinct malignant neoplasms represents a rare event. Concurrent gynecological cancers are rarely described accounting for approximately up to 6% of female genital tract malignancies (Dudzic et al., 2017). The most common synchronous gynecologic malignancies include endometrial and ovarian cancer; however, cases of synchronous endometrial adenocarcinoma and USS are considered as extremely rare, with only a few being reported to date (Abbas et al., 2020). Herein, we report a case of a synchronous USS with an endometrial adenocarcinoma. To the best of our knowledge, this is the second case that reports the coexistence of these two malignancies of the uterus (Liu et al., 2015) and the first case that resulted in recurrence after excision.

Diagnosis of a synchronous tumor can be challenging and in most of the cases final diagnosis can be established only postoperatively in the pathology report. In general, it is important to differentiate a USS from a malignant mixed müllerian tumor (carcinosarcoma), adenocarcinoma and leiomyosarcoma. For this purpose, it is necessary to examine a great range of samples before we reach a diagnosis (Liu et al., 2015).

Carcinosarcomas are mostly high-grade cancers and their typical histological findings involve a combination of stromal sarcomatous cells with easily distinguishable carcinomatous features (Liu et al., 2015). The opposite applies to our case, where simultaneously two distinct, different tumors are depicted in microscopic and immunohistochemical examinations and there was no sign of transition. An additional interesting aspect of our case is, that one of the synchronous tumors was a smaller grade 1 endometrioid carcinoma, which separated from USS, something that differs from carcinosarcomas, where usually both elements are high-grade (Kim et al., 2015).

Due to the rarity of the disease, there are no standard guidelines for the management of these cases. Total abdominal hysterectomy with bilateral salpingo-oophorectomy is considered as the best practice in cases without metastatic disease. According to the latest National Comprehensive Cancer Network (NCCN) guidelines for USS, surgical resection is recommended in stages I-III and in advanced stages the use of systemic therapy is recommended (NCCN, 2022). In recurrent disease, where surgical excision is feasible, surgical treatment is recommended with postoperative chemo, radiotherapy (NCCN, 2022).

In the present study, we aim to raise awareness of these rare synchronous malignancies and highlight the importance of having a broad differential diagnosis in a patient presenting with abnormal vaginal bleeding. Further studies with larger patient populations are needed to shed light in etiology and pathogenesis of the concurrence of two malignancies with different embryological origin in the same organ, in order to optimize management of these patients.

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CRedit authorship contribution statement

Antonios Koutras: Conceptualization, Writing – original draft. **Athina A. Samara:** Conceptualization, Writing – original draft. **Thomas Ntounis:** Data curation, Writing – original draft. **Zacharias Fasoulakis:** Data curation, Writing – original draft. **Prokopis-Andreas Zotos:** Investigation, Data curation. **Savia Pittokopitou:** Investigation, Data curation. **Athanasios Pagkalos:** Investigation, Data curation. **Stavros Moraitis:** Investigation, Data curation. **Kallirroï Goula:** Investigation, Data curation. **Sotirios Sotiriou:** Supervision, Writing – review & editing. **Emmanuel N. Kontomanolis:** Conceptualization, Writing – original draft, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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