Case Report

A Rare Case Report of Uterine Carcinosarcoma in Patient with History of Breast Carcinoma

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Abstract

Uterine carcinosarcoma (UCS), or malignant mixed Müllerian tumor, is a rare and aggressive uterine malignancy comprising malignant epithelial and mesenchymal components. We present the case of a 67-year-old postmenopausal woman with abdominal pain and anemia, and a history of breast carcinoma. Initial imaging suggested an endometrial polyp; biopsy was inconclusive. Persistent symptoms led to hysterectomy with bilateral salpingo-oophorectomy. Grossly, the uterus contained a bulky grey-white tumor (7 × 5 × 3 cm). Histopathology revealed serous adenocarcinoma (CK, p53 positive; ER negative) admixed with vimentin-positive homologous sarcoma, with ¿50% myometrial invasion; adnexa were uninvolved (FIGO stage IA). UCS has a poor prognosis and is occasionally linked to prior tamoxifen use, though hormonal therapy history was unavailable in this patient. This case highlights the need for suspicion of UCS in postmenopausal women with uterine masses and prior breast carcinoma, even without confirmed tamoxifen exposure. Early recognition and histopathologic confirmation are vital to guide management in this aggressive malignancy.

Keywords: Uterine carcinosarcoma; Malignant mixed Müllerian tumor; Breast carcinoma; Immunohistochemistry; Postmenopausal; Gynecologic oncology

Introduction

One of the most aggressive uterine malignancies is carcinosarcomas (CS), formerly classified as malignant mixed mesodermal tumors(MMT) [1, 2, 3]. Malignant mesenchymal and carcinomatous components make up the majority of them. There are several classification ideas for uterine carcinosarcomas due to their complex histogenesis and the question of whether CS is monoclonal or biclonal is still up for debate. The ”combination hypothesis,” which holds that CS develops from high-grade cancer with sarcomatous differentiation is supported by the majority of authors. According to the ”conversion hypothesis,” CS originates from a single population of multipotent stem cells that have the capacity to undergo metaplastic transformation. Conversely, the ”collision hypothesis” postulates that two distinct populations of stem cells combine to form a neoplastic tumor. [21, 22].

It is a rare and aggressive gynecological cancer with a dismal prognosis. Monoclonal carcinoma cells that originate from embryonal mesoderm and display sarcomatous metaplasia are the source of tumors. CS/MMT makes up 2% to 5% of all uterine cancers and typically affects postmenopausal women [1, 2]. The five-year survival rates are especially low, ranging from 21% to 39%. CS/MMT following tamoxifen therapy for breast cancer is described in a number of case reports and case series [3, 4, 5, 6, 7, 8, 9]. Although the number of participants with CS/MMT in any of these investigations is limited, retrospective studies indicate that the incidence of these high-risk malignancies is higher than the documented

increase in incidence of endometrial cancers generally following tamoxifen medication(TAM) [10, 11, 12, 13]. It is believed that the alpha estrogen receptor (ERα) has a good trophic impact on the uterine corpus, which is responsible for the rise in uterine malignancies that typically occurs after tamoxifen medication. Despite tamoxifen's identical affinity for ERβ, this receptor has not been shown to be activated [14, 15]. Although it is unclear how tamoxifen can affect the behavior of these cancers, other research indicates that it may increase the expression of the HER2/neu oncogene in UC/MMT cells [16, 17]. Given that metabolites of tamoxifen have the ability to covalently bind DNA, primarily producing (E)- and (Z)-α-(deoxyguanosin-N2-yl)-4-hydroxytamoxifen adducts [18], it has also been suggested that tamoxifen therapy may be carcinogenic by nature. Nevertheless, after oral administration, tamoxifen-DNA adduct formation in uterine tissues happens at levels too low to be compatible with this being the mechanism causing such endometrial malignancies [19].

Given that its etiological characteristics and symptoms are believed to be comparable to those of endometrial adenocarcinoma, uterine carcinosarcoma is currently regarded as one of the aggressive subtypes of the disease. The prognosis of patients with UCS associated with TAM is being studied [20]. The prognosis of patients with UCS associated with TAM is still up for debate, though. Furthermore, there is currently little information on the prognosis of people with UCS after BC who have never had hormone therapy.

Case Report

A 67-year-old postmenopausal woman (G3P3) presented to our institution with a three-month history of progressively worsening lower abdominal pain, generalized weakness, and decreased appetite. She was found to be severely anemic (Hb 7.0 g/dL) on follow-up evaluation. Her medical history was significant for long-standing hypertension on regular medication. She had no history of diabetes, thyroid disorder, or thromboembolic disease.

She reported a history of breast carcinoma diagnosed approximately 6–7 years earlier, for which she had undergone left-sided modified radical mastectomy. According to the patient, the tumor was "infiltrating," but exact histological subtype, hormone receptor status, and stage were not available, as previous records could not be retrieved. She recalled receiving adjuvant chemotherapy, but she was uncertain about any endocrine therapy, and specifically could not confirm tamoxifen exposure. Family members also denied knowledge of long-term hormonal medication use.

On transvaginal ultrasonography, a heteroechoic intrauterine lesion measuring 4.3 × 4.0 cm was noted, appearing to arise from the endometrium with a vascular pedicle suggestive of a polyp. Bilateral adnexa were unremarkable. Based on these findings, an endometrial polyp was suspected, and a polypectomy with biopsy was performed, measuring 2 × 1.5 × 1.2 cm. Histopathology was reported as a benign endometrial polyp.

Despite removal of the lesion, the patient's abdominal pain persisted, and her anemia did not improve. A repeat endometrial aspiration biopsy was undertaken after two weeks, which showed only blood clots, necrotic debris, and inflammatory exudate, without diagnostic tumor tissue. Because of continued symptoms and discordance between imaging and pathology, a repeat biopsy was advised. Given the clinical uncertainty and persistent symptoms, the patient subsequently underwent a transabdominal hysterectomy with bilateral salpingo-oophorectomy under general anesthesia. Intraoperative examination revealed no macroscopic evidence of intra-abdominal dissemination and no palpable pelvic or para-aortic lymphadenopathy.

We received a hysterectomy specimen measuring 9 X 8 X 4 cm. (Fig. 1A) Endomyometrium measured 2.0 cm (0.2 + 1.8 cm). Cervical canal measured 2.0 cm in length. A polyp measuring 1.5 X 1 cm was identified obliterating the endometrial cavity. On serial sectioning, uterus appeared bulky and homogenous grey white areas were identified involving whole uterine cavity and measuring 7 X 5 X 3 cm (Fig. 1B). The histological examination revealed that the tumor consisted of two components (Fig. 2A–B): One was an adenocarcinoma, exhibiting papillary growth and tubular architecture, while the other was a sarcoma containing atypical mesenchymal cells. The tumor was mainly an adenocarcinoma, but part of the tumor comprised both adenocarcinomatous and sarcomatous components. Since the adenocarcinoma exhibited a mainly papillary architecture and was positive for CK(Fig. 3A) and p53 and negative for ER (Fig.3C), it was diagnosed as a moderately differentiated serous adenocarcinoma. The sarcoma was positive for vimentin (Fig. 3B). The tumor was therefore diagnosed as a carcinosarcoma (serous adenocarcinoma with a homologous sarcomatous component). The myometrial thickness measured 18 mm, of which the tumor invaded 11 mm, corresponding to approximately 61% myometrial invasion. According to the FIGO 2009 staging system, uterine carcinosarcoma is staged identically to endometrial carcinoma. In this case, the tumor was confined to the uterus with ¿50% myometrial invasion and no adnexal, nodal, or extra-uterine spread, corresponding to pT1b (FIGO Stage IB).

Although the patient had a history of breast carcinoma, metastatic disease was considered unlikely due to the characteristic biphasic morphology and the aberrant p53-positive, ER-negative serous carcinoma profile. Therefore, additional breast markers such as GATA3, mammaglobin, or GCDFP-15 were not required to exclude metastatic breast carcinoma.

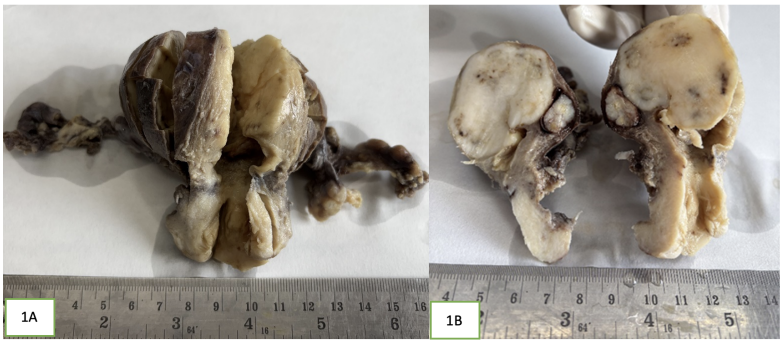

Figure 1: Macroscopic appearance of the resected uterus, fallopian tubes and ovaries. (A) External appearance of the resected surgical specimen and (B) macroscopic appearance of the uterine cavity.

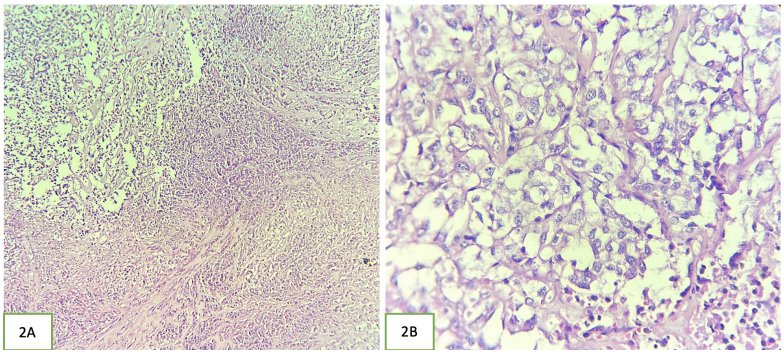

Figure 2: Histological examination of the uterine carcinosarcoma. H&E staining at a magnification of (A) × 4 and (B) ×40.

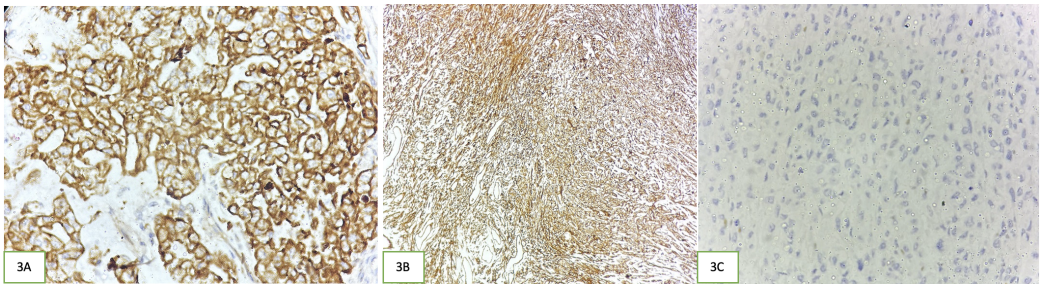

Figure 3: Immunohistochemical analysis of the uterine carcinosarcoma. (A) The adenocarcinomatous component was positive for CK. The sarcomatous component was (B) positive for vimentin and negative for ER (C). Magnification, ×4 in (B) and ×40 in (A, C).

Discussion

The most common symptoms of carcinosarcomas are uterine enlargement and vaginal bleeding, and they often appear in women approximately 15–17 years after menopause [23, 27, 28]. A percentage of cases also cause abdominal pain [30].

A very bad prognosis and an aggressive clinical history are characteristics of carcinosarcomas. 70–90% of tumor-related fatalities have been documented to occur within 18 months of diagnosis [31]. However, with an overall median survival of 39 months, a recent study found that the prognosis for uterine carcinosacomas had improved [32].

Both the stromal and epithelial components of uterine carcinosarcomas are malignant [25, 30]. Fibrosarcoma, endometrial stromal sarcoma, and/or leiomyosarcoma all have a sarcomatous component, as do homologous carcinosarcomas. The heterologous kind, on the other hand, consists of sarcomatous components composed of tissues that are not native to the uterus. Adenocarcinomas of the endometrioid, serous, or clear-cell types make up the majority of the carcinomatous component. The epithelial tumor in our instance was likely a serous adenocarcinoma because of a dominant epithelial lesion that showed papillary development and was p53-focal positive on immunohistological examination. Nevertheless, the stroma of the serous adenocarcinoma included atypical mesenchymal cells. The vimentin-positive nature of these atypical mesenchymal cells indicated that the sarcoma in this tumor was composed of homologous components. These findings imply that the carcinosarcoma in our instance was a homologous one. The epithelial component of the tumor met established diagnostic criteria for uterine serous carcinoma, characterized morphologically by complex papillary and micropapillary structures, marked nuclear pleomorphism, prominent nucleoli, and brisk mitotic activity. Immunohistochemically, this component displayed a mutant-type p53 pattern with diffuse strong overexpression and was CK positive and ER negative, a profile

supporting serous lineage and helping exclude high-grade endometrioid carcinoma. The sarcomatous component showed sheets of atypical spindle cells with nuclear pleomorphism, hyperchromasia, and high mitotic activity, without evidence of cartilage, skeletal muscle, or other heterologous elements. Its diffuse vimentin positivity and absence of desmin, SMA, myogenin, and S100 expression supported classification as a homologous sarcoma, composed of uterine-type mesenchymal elements. A comprehensive differential IHC panel—including p53, p16, ER/PR, WT-1 for epithelial characterization and desmin, SMA, myogenin, MyoD1, S100, CD10, and cyclin D1 for mesenchymal differentiation—was applied to confirm the biphasic nature of the tumor and exclude mimics such as high-grade endometrioid carcinoma, leiomyosarcoma, rhabdomyosarcoma, and other heterologous sarcomas. Together, the combined morphologic and immunophenotypic features established the diagnosis of uterine carcinosarcoma with serous carcinoma and homologous sarcoma components.

TAM's estrogen agonist action on the endometrium is thought to be the reason for the elevated risk of endometrial carcinoma. This mechanism is comparable to the mechanism for the higher incidence of endometrial cancer in women receiving unopposed estrogen as hormone replacement therapy. Although the exact method by which TAM administration causes uterine sarcoma is still unknown, nonestrogenic actions of TAM may also be the cause. Experimental research has demonstrated that TAM damages DNA in human tissues, including the endometrium. According to Giorda et al., the endometrium contains larger concentrations of TAM's metabolites than serum, and this buildup may contribute to carcinogenesis. Additionally, TAM users have been known to have estrogen-independent primary cancers, usually in the gastrointestinal system. All of these findings suggest that TAM carcinogenesis may possibly be influenced by estrogen-independent processes [33].

In consequence, because of the long latent period and the low frequency of uterine malignancy symptoms, early detection of TAM-related uterine sarcoma requires orderly gynecological examination in patients using TAM. Physicians should be aware of uterine sarcoma apart from endometrial polyp, hyperplasia, and carcinoma in women taking TAM for breast cancer.

Conclusion

This case highlights the importance of maintaining a high index of suspicion for uterine carcinosarcoma in postmenopausal women presenting with uterine masses, particularly those with a prior history of breast carcinoma. Discordance between clinical findings, imaging, and initial pathology must prompt timely re-evaluation. Early diagnosis, comprehensive histopathological assessment, and appropriate surgical management remain essential for improving outcomes in this aggressive malignancy.

Abbreviations: UCS: Uterine Carcinosarcoma; MMT: Malignant Mixed Mesodermal Tumor; CS: Carcinosarcoma; TAM: Tamoxifen; ER: Estrogen Receptor; IHC: Immunohistochemistry; FIGO: International Federation of Gynecology and Obstetrics; CK: Cytokeratin; SMA: Smooth Muscle Actin; MyoD1: Myogenic Differentiation 1; S100: S100 protein; CD10: Cluster of Differentiation 10; PR: Progesterone Receptor; WT-1: Wilms Tumor 1.

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