Case Report

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Uterine Carcinosarcoma Associated with Tamoxifen Use in a Menopausal Patient: A Case Report

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ABSTRACT

BACKGROUND AND OBJECTIVE: Uterine carcinosarcoma, also known as malignant mixed Mullerian tumor, is a rare uterine malignancy. Although the origin and prognosis of this cancer remain undetermined, the Mullerian ducts are believed to be the main origin. This tumor has the ability to change into epithelial and mesenchymal components and is more common among black and postmenopausal women. Prior history of radiation therapy and use of tamoxifen also contribute to this condition. The clinical characteristics of uterine carcinosarcoma, including postmenopausal bleeding, are similar to those of endometrial cancer. This condition with a poor prognosis and aggressive nature may be overcome by a combination of therapies including surgery, chemotherapy, and radiotherapy. Herein, we present a case of uterine carcinosarcoma associated with tamoxifen use in a menopausal patient.

CASE REPORT: The patient was a 67-year-old menopausal woman (G9, P5, L5, Ab4), who underwent lumpectomy and chemoradiotherapy ten years ago due to estrogen receptor-positive breast cancer (ductal carcinoma). The patient received 40 mg of tamoxifen on a daily basis, and after six years of tamoxifen use, she experienced postmenopausal bleeding. Increased endometrial thickness appeared in the ultrasound, and uterine carcinosarcoma was diagnosed, based on pathologic evaluations. The patient received multi-modal therapy, and after a year of follow-up, no specific problems were reported.

CONCLUSION: According to the results, symptoms of uterine cancer should be taken into account in menopausal patients consuming tamoxifen.

KEY WORDS: Uterine Carcinosarcoma, Tamoxifen, Breast Cancer.

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Introduction

Uterine carcinosarcoma or mesenchymal mixed Mullerian tumor is a rare uterine neoplasm. This condition, which is mostly reported in older women, accounts for 1.5% of all uterine cancers. Uterine carcinosarcomas as high-grade neoplasms are mixed epithelial/non-epithelial endometrial tumors, consisting of epithelial (carcinomatous) and mesodermal (sarcomatous) components.Uterine carcinosarcoma has a poor prognosis and an aggressive nature. In the past, this tumor was a sub-group of uterine sarcomas, whereas today it is regarded as an endometrial cancer. The sarcomatous component, which is a secondary transformation, is a result of metaplasia or re-differentiation; also, this tumor may be metastatic at early stages (1).

Increased rate of uterine carcinosarcoma is associated with exposure to radiation, excess amounts of estrogen, obesity, and nulliparity. Consumption of tamoxifen for the treatment of breast cancer is also accompanied by the increased risk of uterine sarcoma. Tamoxifen is an anti-estrogenic, non-steroidal agent, which was developed in England in 1960. This agent was approved by the U.S. Food and Drug Administration (FDA) for the treatment of breast cancer in 1977. Tamoxifen is a selective estrogen receptor modulator (SERM) with anti-estrogenic effects on the breasts and estrogenic effects on the bones, endometrium, and cardiovascular system (1-3). The most common pathological finding associated with the use of tamoxifen is endometrial polyp (3).

According to the majority of conducted studies, use of tamoxifen results in a two- to three-fold increase in the risk of endometrial cancer (4). Endometrial tumors are associated with the use of tamoxifen. Following endometrial cancer, carcinosarcoma is the second tumor associated with tamoxifen use. The mechanism involved in the development of carcinosarcoma due to tamoxifen use is unclear. However, immunohistochemistry and molecular analysis have suggested that uterine carcinosarcoma is similar to adenocarcinoma, which undergoes sarcomatous changes through time (3).

Given the low prevalence of uterine carcinosarcoma, it is difficult to find a relationship between tamoxifen use and this malignancy. According to the literature, use of 20 mg of tamoxifen per day can be sufficient for the development of uterine sarcoma. Sarcomas are basically reported in the first eight years of tamoxifen use.

Postmenopausal patients, who receive tamoxifen, should be carefully examined. Moreover, the possible relationship between tamoxifen use and uterine carcinosarcoma in patients with breast cancer, especially during menopause, should be taken into consideration (4). On the other hand, the role of tamoxifen in the treatment and prevention of breast cancer is far more significant than the associated risk of uterine cancer. Therefore, patients receiving tamoxifen for breast cancer should be closely followed-up for malignant uterine transformations.

Abnormal bleeding or uncommon uterine discharge is the most important sign of lesion growth in the uterus. Also, patients may be admitted to hospitals with pelvic tumors, cervical cytologic abnormalities, ascites, or postmenopausal bleeding. Cancer antigen 125 (CA 125) as a tumor marker and magnetic resonance imaging/computed tomography can be helpful in examining ectopic conflicts before surgery (5). Generally, fertility preservation is not recommended in patients with uterine carcinosarcoma, and sentinel lymph node mapping is performed with utmost caution (3). Multi-modal therapy is applied for the treatment of carcinosarcoma, with surgery and maximal tumor removal (in patients with the detectable disease) as the primary options.

Overall, multi-modal therapy varies for each person. For patients in the IA stage without myometrial involvement, follow-up, chemotherapy with or without brachytherapy, and direct radiography to the tumor area are recommended. For all patients in the advanced stages, chemotherapy with or without direct radiotherapy in the tumor area is the preferred mode of treatment; moreover, paclitaxel and ifosfamide can increase survival among these patients (6). Given the rarity of uterine carcinosarcoma and the contributing role of tamoxifen use in the postmenopausal phase, signs such as postmenopausal bleeding in these patients should be taken into account (7). Herein, we present the case of a woman, who was diagnosed with uterine carcinosarcoma due to tamoxifen use.

Case Report

The patient was a 67-year-old menopausal woman (G9, P5, L5, Ab4), who underwent lumpectomy and chemoradiotherapy ten years ago due to estrogen receptor-positive breast cancer (ductal carcinoma). The patient received 40 mg of tamoxifen on a daily basis. After six years of tamoxifen use, she experienced postmenopausal bleeding. On sonography, the uterus showed a normal size, endometrial thickness was 20 mm, and the ovaries had a normal status. Afterwards, the patient underwent diagnostic hysteroscopy and curettage, which indicated a polypoid lesion in the posterior wall of the endometrium and a submucosal lesion in the anterior wall of the uterus. Biopsy was performed and the pathologic evaluations indicated carcinosarcoma.

The patient underwent omentectomy, bilateral oophorectomy, hysterectomy, lymphadenectomy, and staging. The pathologic results indicated a 10 cm carcinosarcomal tumor (grade III), while no omental or lymph node involvement was noted (stage I). The patient underwent chemotherapy, and after one year of follow-up, she did not experience any problems..

Discussion

We presented the case of a 67-year-old woman with breast cancer, who developed uterine carcinosarcoma after 10 years of menopause, following the use of tamoxifen. Two cases of uterine carcinosarcoma have been reported in England. These patients, who were 72 and 90 years old, respectively, had received 20 mg/day of tamoxifen and had no prior history of pelvic radiotherapy or hormonal therapy. One had referred to the hospital with vaginal bleeding and the other with a pelvic tumor. The patients underwent hysterectomy, bilateral oophorectomy, and staging (4). Similarly, this condition was reported in India in a 46-year-old woman with postmenopausal vaginal bleeding, receiving 20 mg/day of tamoxifen for two and a half years. The patient underwent hysterectomy, bilateral oophorectomy, staging, and chemotherapy (1). Tamoxifen is a non-steroidal triphenyl ethyl compound, which is used as an adjuvant therapy for breast cancer. Its anti-estrogenic effect in the treatment of breast cancer is exerted through its competitive binding with estrogen receptors. Due to interaction with estrogenic receptors, poor estrogenic effects are applied in the uterus, leading to the appearance of endometrial proliferative lesions (1).

Uterine carcinosarcoma is a rare cancer with a poor prognosis and an aggressive nature. Radiotherapy and tamoxifen use are introduced as the major causes of this condition. Uterine carcinosarcoma usually manifests with postmenopausal bleeding, which is treated by a combination of surgery, chemotherapy, and radiotherapy (7,8).

Patients with uterine carcinosarcoma due to tamoxifen use are at more advanced stages of endometrial cancer. Overall, carcinosarcomas are high-grade invasive tumors.

The prognosis of patients suffering from uterine carcinosarcoma due to tamoxifen use does not differ from patients with no history of tamoxifen use. Also, postmenopausal patients, who consume tamoxifen and show signs of endometrial involvement, should be carefully monitored in order to diagnose this invasive disease at early stages (1).

Overall, tamoxifen remains as a useful agent in the adjuvant therapy of breast cancer. However, caution should be taken considering the probability of uterine malignancies, associated with tamoxifen use (2, 3).

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