Case Report

Malignant Mixed Mullerian Tumor Secondary to Tamoxifen for Ca Breast: Shadow of the Past!

Surendra Bisu, Vinu Choudhary[1]

Department of Obstetrics and Gynaecology, S. P. Medical College, Bikaner, [1]Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur, Rajasthan, India

Abstract

Tamoxifen is used in the treatment of hormone-responsive breast cancer because of its antiestrogenic effect. However, it also has an estrogenic effect on the uterus, thereby increasing the risk of endometrial hyperplasia, endometrial polyp, and malignant mixed Mullerian tumor (MMMT). This case describes the pathogenesis and risk of MMMT due to long-term tamoxifen intake in hormone-responsive breast cancer.

Keywords: *Antioestrogenic effect, malignant mixed mullerian tumor, tamoxifen*

Introduction

A malignant mixed Müllerian tumor (MMMT), also known as malignant mixed mesodermal tumor, MMMT[1] is a malignant neoplasm found in the uterus, the ovaries, the fallopian tubes and other parts of the body that contains both carcinomatous and sarcomatous components. MMMT account for between 2% and 5%[1,2] of all tumors derived from the body of the uterus and are found predominantly in postmenopausal women with an average age of 66 years. Risk factors are similar to those of adenocarcinomas and include obesity, exogenous estrogen therapies, nulliparity, and tamoxifen therapy. There is evidence that some tumors are better explained by the composition theory, due to the aggressive nature of the epithelial cells involved which tend to metastasize much more readily than the sarcomal component. Three predominant theories are proposed for its origin:

1. The collision theory
2. The combination theory
3. In conversion theory.

Tamoxifen also has a weak estrogenic effect on the endometrium, thereby increasing the risk of endometrial polyp, endometrial hyperplasia, endometrial adenocarcinoma, and sarcoma of the uterus. We report a case of uterine MMMT occurring with tamoxifen therapy in a patient with a history of breast cancer.[3]

Case Report

A 58-year-old woman presented with bleeding per vaginum, generalized weakness, decreased urine output, and abdominal distension. Imaging revealed a large polypoid mass within the endometrial cavity, and endometrial biopsy was suggestive of MMMT. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and bilateral pelvic and para-aortic lymphadenectomy. Histopathological examination confirmed the diagnosis of MMMT infiltrating less than half of the myometrium. Cervix, bilateral adnexae, omentum, and all lymph nodes were free of tumor. The patient had a history of estrogen receptor (ER)-positive breast cancer, diagnosed 3 years back and was on tamoxifen 20 mg OD daily dose.

At present, the patient is on adjuvant radiation therapy and chemotherapy comprising of paclitaxel at 175 mg/m^2 followed by carboplatin for a total of 6 cycles every 21 days. As shown in Figure 1 Specimen included uterus with bilateral ovaries and Figure 2 Shows HPR depicting malignant stromal component with spindle cell showing marked nuclear pleo morphism and nuclear hyper chromasia.

Discussion

MMMTs, although very rare, with an incidence of <2/100 000 women in a year, are aggressive tumors of the uterus resulting in >15% of deaths. Tamoxifen

Address for correspondence: Dr. Vinu Choudhary, Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur, Rajasthan, India.
E-mail: vinuc16@gmail.com

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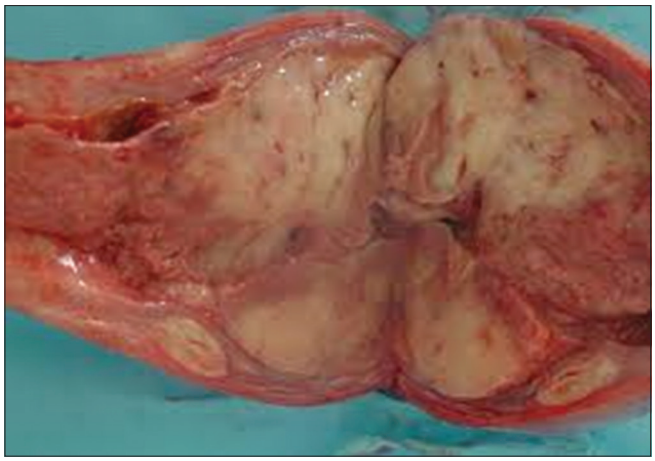

Figure 1: Gross cut section of uterus

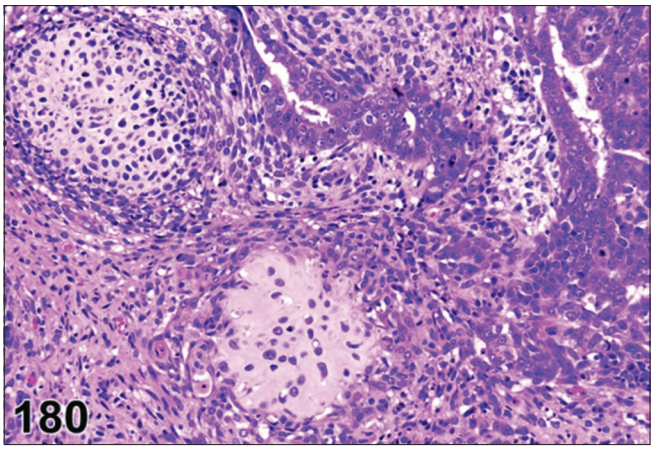

Figure 2: Malignant stromal component with spindle cells displaying marked nuclear pleomorphism and nuclear hyperchromasia, ×40

intake for hormone-responsive breast cancer is one of the factors that has been associated with the development of MMMT. Depending on the target organs, tamoxifen exerts both an estrogenic and an antiestrogenic effect. The variability of response to tamoxifen depends on the differences in tissue distribution of ER subtypes (ERα and ERβ are two subtypes of ERs),[3,4] various transcriptional activating factors and function of co-regulator proteins. Due to its antiestrogenic effect, it is used in the treatment of ER-positive breast cancer in adjuvant and metastatic settings.

The outcome of MMMTs is determined primarily by the depth of invasion and stage. As with endometrial carcinomas, the prognosis is influenced by the grade and type of the adenocarcinoma, being poorest with serous differentiation.

Points to be remembered

- Although tamoxifen is used in the treatment of hormone-responsive breast cancer due to its antiestrogenic effect, it has an estrogenic effect on the uterus, thus it increases the risk of MMMT and other neoplasms
- Variability of response to tamoxifen depends on the differences in tissue distribution of ERs, function of coregulatory proteins.[4,5]

Conclusion

Uterine carcinosarcoma is a rare, highly aggressive, rapidly progressing neoplasm associated with a poor prognosis that has not significantly improved in the past 30 years despite advances in imaging and adjuvant therapies. The optimal management modality remains controversial, with discrepancies regarding patient outcome to lymphadenectomy and radiation therapy. To maximize the probability of cure, prospective multicentric, multi-institutional collaborative randomized trials of treatment protocols have to be performed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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