Low-Grade Endometrial Stromal Sarcoma Following Tamoxifen Treatment

Tamoksifen Tedavisini Takiben Gelişen Düşük Gradeli Endometriyal Stromal Sarkom

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ABSTRACT

Tamoxifen (TMX) is supposed to be related with development of uterine sarcomas. Due to the low incidence of uterine sarcomas, establishment of a causal relationship with TMX is difficult. These sarcomas mostly appear 5 or 8 years after TMX administration and tend to display an aggressive behaviour. In this report, we present a rare case of endometrial stromal sarcoma detected in a breast cancer patient who had been treated with TMX for only two years. Up to now, nearly 65 endometrial stromal sarcoma cases have been reported after TMX treatment in the literature, and a meticulous follow-up is important in patients that will receive TMX therapy.

Keywords: Endometrial stromal sarcoma, tamoxifen, breast.

ÖZ

Tamoksifen (TMX) kullanımının, uterin sarkom gelişimi ile ilişkili olduğu düşünülmektedir. Uterin sarkomların görülme insidansının düşük olması nedeniyle TMX kullanımına bağlı nedensel bir ilişki kurmak zordur. Bu sarkomlar çoğunlukla TMX tedavisi başladıktan 5 ile 8 yıl sonrasında ortaya çıkarlar ve daha agresif bir davranış sergileme eğilimindedirler. Bu yazıda, sadece iki yıl TMX tedavisi almış meme kanseri olan hastada tespit edilen endometriyal stromal sarkom olgusunu sunduk. Literatürde şimdiye kadar yaklaşık 65 TMX kullanımı sonrası gelişen uterin sarkom vakası rapor edilmiştir. TMX tedavisi alan meme kanseri hastalarında jinekolojik titiz takip esastır.

Anahtar Kelimeler: Endometriyal stromal sarkom, tamoksifen, meme.

Introduction

Endometrial stromal tumors are mesenchymal tumors of uterus that constitute less than 10% of all uterine sarcomas and about 1% of all uterine malignancies (1). Endometrial stromal tumors have historically been classified as either low-grade or high-grade neoplasms. High-grade endometrial stromal tumors are mostly referred to as undifferentiated endometrial sarcomas or high-grade undifferentiated uterine sarcomas, because they may consist of anaplastic cells with little or no evidence of endometrial stromal differentiation. The term endometrial stromal sarcoma (ESS) is usually used to descibe the former “low grade” neoplasms (1).

Tamoxifen is an anticancer agent that is frequently used in breast cancer treatment. However, tamoxifen treatment has been associated with increased risk of uterine sarcomas, including endometrial stromal sarcoma. In the literature, a daily dose of 20 mg of TMX can be sufficient for development of uterine sarcomas (2). In this report, we present a woman who developed a low-grade ESS after receiving tamoxifen therapy subsequent to mastectomy.

Case Report

A 45-year-old multiparous woman with a history of breast cancer admitted to obstetrics and gynecology department due to complaints of severe menorrhagia and anemia. The patient had undergone both radical mastectomy and axillary lymphadenectomy and had been treated with 8 cycles of chemotherapy and tamoxifen (at a dose of 20 mg/day) for only 2 years as an adjuvant therapy. Her endometrial biopsy was reported as endometrial hyperplasia and there was no increase in tumor markers.. The patient underwent hysterectomy and bilateral salpingo-oophorectomy. The pathological diagnosis was consistent with low-grade ESS. Because of the co-existence of breast and uterine cancer, gene mutations were investigated but genetic study did not reveal a mutation of p53 tumor supressor gene.

As seen in Figure 1, tumor cells displayed bland oval cells arranged concentrically around spiral arterioles and exhibited low mitotic activity. As shown in Figure 2 the tumoral invasion was obvious in the endocervix. Lung metastasis was detected and she died 1 year after hysterectomy.

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Figure 1: Tumor cells displayed bland oval cells arranged concentrically around spiral arterioles and exhibited low mitotic activity (HE)

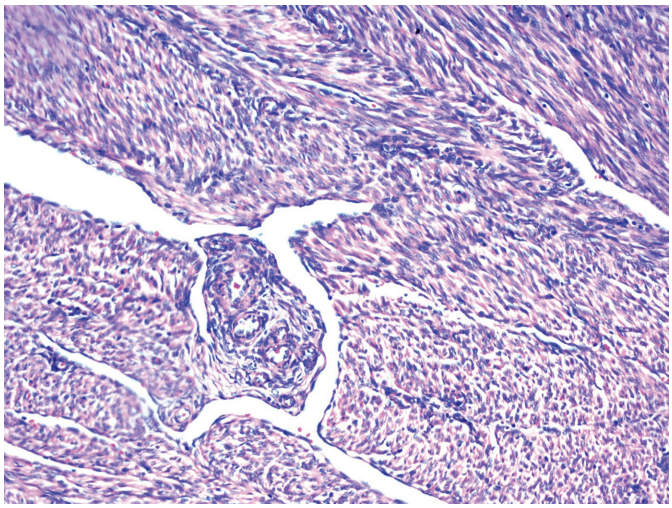
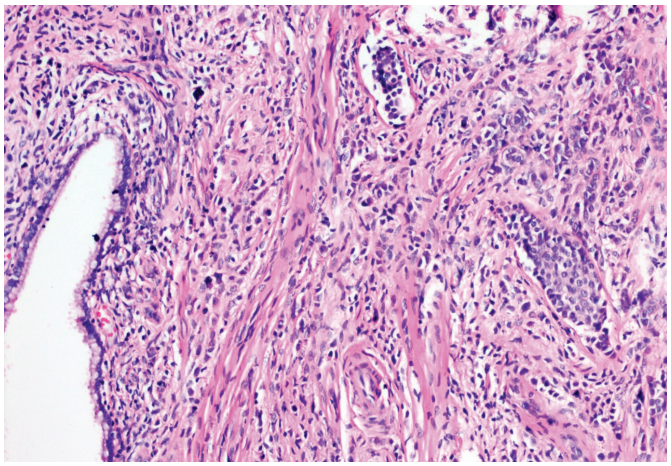


Figure 2: Tumoral invasion in the endocervix



Discussion

Uterine sarcomas are rare forms of uterine cancer accounting for approximately 5–7% of all uterine cancers and 1–3% of all gynecological cancers (3) . They occur in women from 4th to 6th decades and usually have poor prognosis, high rate of local recurrences and distant metastases. The most important pathological types of uterine sarcomas are carcinosarcomas (50%), leiomyosarcomas (30%), endometrial stromal sarcomas (10–15%), and adenosarcomas (3). Owing to their rarity and existence of various pathological subtypes, there is a lack of knowledge about their behavior and therefore there is still debate on the best treatment option.

History of radiation exposure, tamoxifen treatment, race and hereditary conditions may be risk factors for endometrial stromal sarcoma. In our patient, we thought of a genetic basis due to the co-existence of breast cancer and uterine sarcomas. However, genetic study did not reveal a mutation of p53 tumor supressor gene.

Tamoxifen is a nonsteroidal antiestrogen used as an adjuvant treatment for all the stages of breast cancer possessing receptors. Long-term treatment with TMX may cause endometrial proliferative changes, such as uterine polyps, endometrial hyperplasia, and stromal alterations. Its prolonged use has been linked to malignant pathologic changes, a higher incidence of endometrial adenocarcinoma (3). To our knowledge, we have found 65 cases in the literature (from Medline search since 1966) that describe an association between TMX treatment and uterine sarcomas. Usually, sarcomas present 5 or 8 years subsequent to the start of TMX therapy and are often at an advanced stage (4). In our case this period was 2 years.

Endometrial stromal sarcoma can display myometrial and/or vascular invasion and distinctive finger-like projections indicating the invasion into the myometrium, veins, and lymphatics are obvious (2). Scarce mitotic figures uniform stromal cells, mild nuclear atypia minimal cellular pleomorphism are typical histological features. In our case, tumoral involvment has extended to ovary, endocervix and myometrium.

Chief complaints of patients with uterine sarcomas are vaginal bleeding, pelvic pressure symptoms, abdominal distension or enlarged uterus. Various amount of vaginal bleeding may be accompanied by a foul smelling discharge. On pelvic examination, the uterus is often enlarged and it is not always feasible to distinguish between a leiomyoma and a leiomyosarcoma by history or physical examination. Endometrial stromal sarcoma occurs as a heterogeneous hypoechoic endometrial mass on ultrasound and extensive myometrial involvement can be observed.

In uterine sarcomas, overall survival at 10 years ranges from 65% to 76%. Late recurrences can be detected in 14-60% of cases (4). Randomized trials performed for the optimal treatment options are limited due to the rarity of disease. Hence, a standard treatment could not be yet established. Treatment options include surgery, radiotherapy, chemotherapy and endocrine treatment. The American College of Obstetricians and Gynecologists advises that women taking tamoxifen be advised of the risk of uterine sarcoma, along with other risks (5).

In conclusion, both long and short-term use of TMX can constitute a risk factor for development of uterine sarcomas for woman with breast cancer. Tamoxifen treatment must be carefully planned and risk/benefit ratio must be taken into account for each patient on an individualized basis. In women receiving TMX therapy, regular and careful control is mandatory.

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