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A Case Report of Alveolar Lobular Breast Cancer Metastasized to the Whole Female Reproductive **System**

Kadın Üreme Sisteminin Tamamına Metastaz Yapan Alveolar Lobüler Meme Kanseri Vaka Sunumu

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Lobüler meme kanserinin üreme organlarına metastazı oldukça nadir görülen bir durumdur. Meme kanseri cerrahisi sonrası tamoksifen ve kemoterapi alan hastaların iç genital organ metastazlarının takibi klinik öneme sahiptir. Lobüler meme kanseri nedeniyle 9 yıl önce radikal mastektomi cerrahisi geçiren hasta, adjuvant kemoterapi tedavisi görmüş. Rutin takiplerinde vajinal kanama şikâyeti olan hastaya endometrial biyopsi sonucu endometriuma meme kanseri metastazı olarak raporlandı. Yapılan BT görüntülemede iç genital organlarda yaygın metastaz izlenmesi üzerine hastaya cerrahi prosedür uygulandı. Bu vaka sunumunda hastanemize başvuran ve tedavi gören hastayı sunuyoruz.

Anahtar Kelimeler: Meme kanseri, endometrium, adneks, metastaz

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Metastasis of lobular breast cancer to reproductive organs is a very rare condition. Breast cancer Followup of internal genital organ metastases in patients receiving tamoxifen and chemotherapy after surgery is important. The patient underwent radical mastectomy 9 years ago for lobular breast cancer and received adjuvant chemotherapy. She complained of vaginal bleeding during routine follow-up and endometrial biopsy was reported as breast cancer metastasis to the endometrium. The patient underwent a surgical procedure after CT imaging showed extensive metastasis in the internal genital organs. In this case report, we present the patient who was admitted to our hospital and treated.

Keywords: Breast cancer, endometrium, adnexa, metastasis

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INTRODUCTION

Breast cancer is the most common cancer and the leading cause of cancer deaths in women worldwide. In the United States, breast cancer is the second leading cause of female cancer death after lung cancer (1). As we all know, breast cancer can metastasize to many organs. However, metastasis to the uterus is not common and usually occurs in the case of widespread metastatic disease (2). Lobular carcinoma is the most common form of breast cancer that metastasizes to the uterus (3). We introduced a case of breast lobular carcinoma, which was diagnosed with endometrial metastasis after abnormal uterine bleeding and infiltrated the entire internal reproductive system, peritoneum, and omentum of a patient being treated. The patient was diagnosed with breast lobular carcinoma 9 years ago. For lobular breast cancer, when abnormal uterine bleeding occurs, endometrial infiltration and uterine metastasis should be considered, and probe curettage should be used to examine the endometrium. We believe that our article will contribute to the literature in introducing lobular carcinoma metastasis involving all uterine segments, and have extensive histomorphological and immunohistochemical details.

CASE

Our patient is a 56-year-old G3 woman after menopause. She had undergone a radical mastectomy 9 years ago and was diagnosed with lobular breast cancer (figure 1).

Postoperative pathology, was reported as invasive lobular carcinoma, T2N0, ER 80% positive, PR 98% positive, CerbB2 negative. The adjuvant treatment received 4 cycles of Adriamycin (60 mg/m²) plus cyclophosphamide (600 mg/m2) every 21 days, radiotherapy and 7 years of endocrine therapy. In May 2019, the patient was found shortness of breath and pleural effusion during examination. The cytology report of pleural effusion is malignant. Patient who progressed began to receive weekly paclitaxel (80 mg/m²) plus carboplatin (AUC: 2) chemotherapy. In August 2019, partial remission after 12 weeks of chemotherapy, letrozole maintenance treatment was started. Capecitabine was started in patients with peritonitis carcinomatosis in November 2019, and progress was detected after 17 cycles. Ribociclib 1x600 mg plus fulvestrant was started, and 9 months later, vaginal bleeding occured in patient in September 2021. It was determined that liver metastases detected in MRI examinations performed to evaluate intra-

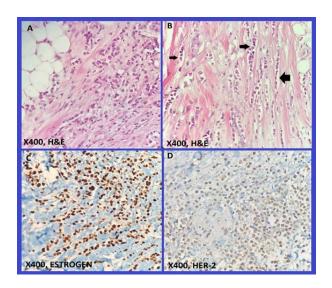


Figure 1. The histomorphological appearance of breast cancer at the time of first diagnosis A)X400,H&E; Infiltration of malignant lobular carcinoma cells with small hyperchromatic nuclei in breast stroma and fibrous stroma B)X400,H&E; 'Indian file' infiltration of malignant lobular carcinoma cells with small hyperchromatic nuclei in the breast stroma (arrow) C)X400,Estrogen; Strong nuclear estrogen expression in malignant lobular carcinoma cells in breast stroma D)X400,Her-2; Weak membranous Her-2 expression in malignant lobular carcinoma cells in breast stroma (score1, negative)

abdominal organs regressed after chemotherapy. During the radiological examination, the progress of bilateral adnexal masses and peritoneal implants was observed.

The thickness of the endometrium was measured at 8 mm during the pelvic ultrasound examination of the patient. In addition, bilateral pelvic masses and ascites were also observed. Several tumor biomarkers were examined, (CA)-15.3 was elevated [545 ng/ml (0-27)], while carcinoembryonic antigen and CA-125 levels were normal. The patient underwent an endometrial biopsy. The result is reported as metastatic breast cancer. Atypical epithelial islets are composed of small cells with a Ki-67 index of about 60%, which were independent cell groups that fall into fibrin and stain positive for pancytokeratin. GATA-3 and estrogen are positive, and CD10 is rarely positive. Pancytokeratin, CD45, S100, synaptophysin, p53, progesterone, p16, p63, chromogranin, mammaglobin, E-cadherin and Her-2 were all negative (score 0). (Figure 2).

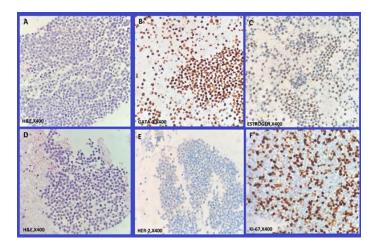


Figure 2. Analysis of lobular carcinoma cell groups in probe curettage material taken for abnormal uterine bleeding A)X400,H&E; Malignant cell groups with small hyperchromatic nuclei are seen B)X400,GATA-3; Malignant groups show positive nuclear reaction in GATA-3 immunohistochemistry staining supporting the breast primer X400, Estrogen; Malignant groups of show moderate nuclear positivity with Estrogen immunohistochemical staining consistent with Breast Lobular Carcinoma D)X400,H&E; Malignant cell groups with small hyperchromatic nuclei are seen in the middle of the pink colored fibrin material observed at the edges E)X400,Her-2; Her-2 expression is not seen in malignant groups (score 0, negative) F)X400,Ki-67; In malignant groups, approximately 60% of Ki-67 proliferation index nuclear positivity is present.

The patient was discussed in the oncology committee of our hospital. The patient underwent transabdominal hysterectomy and bilateral salpingo-oophorectomy, peritonectomy, and omentectomy. The pathological examination results of the specimens taken out during the operation were reported as metastasis of alveolar lobular breast cancer. The pathology report also included that the uterus, cervix and bilateral adnexa were completely infiltrated by cancer (Figure 3).

The peritonectomy and omentectomy materials are also infiltrated by cancer. The presence of tumor cells were also observed in abdominal washing fluid, and malignant cytology was reported to be compatible with lobular carcinoma.

DISCUSSION

Breast cancer rarely spreads to female reproductive

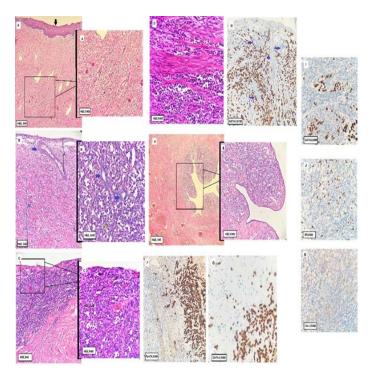


Figure 3. As a result of detailed analysis of all uterine segments in the surgical material, Cervix (A; stratified squamous epithelium that covers the cervix is indicated by arrow), Endometrium (B; Endometrial layer E, myometrium layer M is marked. Endometrial glands are indicated by blue arrow. Stroma outside the glands completely infiltrated with malignant lobular carcinoma (yellow arrows), Myometrium (B, D), Ovary (C; Tumor cells appear to infiltrate the ovarian capsule seen above (black arrow)) Tuba Uterina (E; Tuba uterina lumen visible, mucosa at high magnification) malignant infiltration is observed) malignant infiltration compatible with the morphology of cells belonging to malignant small hyperchromatic breast lobular carcinoma with nuclei is observed. Malignant infiltration observed in the ovary reacts positively with the general epithelial marker Pan cytokeratin (PanCK) (F), and also with GATA-3, which supports the breast primer (G). Tumor infiltrating the endometrium and myometrium also has a positive reaction with GATA-3, which supports the breast primary (H; Endometrial glands are indicated by blue arrow). GATA-3 (I), Estrogen (ER) positivity (J) Her2 negativity (K) are seen in malignant cells in myometrium.

organs. It usually affects the ovaries. Mazur et al. analyzed 325 female genital tract metastases in a study. They found that 75.8% of metastases involved the ovaries. The number of patients with endometrial

metastases was seven. In this study, 52 cases of breast cancer metastasized to the female reproductive tract. 46 of them had ovarian metastases, while two of them had endometrial metastases (4). Akhtar et al. conducted a review of the literature. In 2017, 25 cases of breast cancer that had spread to the uterus were observed (5). In these 25 cases, only one infiltrating ductal carcinoma case metastasized to the entire inner genital system and bone. We presented that the endometrium, myometrium, cervix, fallopian tubes, and ovaries were all involved in a case of invasive lobular cancer that spread throughout the female internal genital system. The tumor had also invaded the peritoneum of the pelvic side walls and the omentum.

Breast cancers with invasive lobular carcinoma account for 9.7% of all cases. Invasive lobular carcinoma is more likely than infiltrating ductal breast carcinoma to spread to the gynecologic organs. According to Borst et al, around 4.5 percent of invasive lobular breast carcinomas spread to gynecological organs, while 0.8% of infiltrating ductal breast carcinomas moved to gynecological organs (6). The probability of metastasis to the endometrium of infiltrating ductal carcinoma was found to be lower than that of invasive lobular carcinoma in a study conducted between 1984 and 2015, in which 13 cases of endometrial metastases from breast cancer were evaluated (7).

Abnormal uterine bleeding is the most prevalent indicator that breast cancer has spread to the uterus (8). Chemotherapy caused postmenopausal uterine hemorrhage in our instance. The endometrium, myometrium, fallopian tubes, and ovaries were all involved in this patient's hysterectomy and bilateral salpingo-oophorectomy. Cancer had invaded the peritoneum, which covered both the pelvic side walls and the omentum. In November 2021, the patient was given paclitaxel (80 mg/m²) and carboplatin (AUC:2) as a postoperative treatment.

In our case, during chemotherapy, a 56-yearold female patient with metastatic breast cancer experienced postmenopausal bleeding and pelvic pain. The patient was diagnosed and treated appropriately as a consequence of the patient's consultation with the gynecological oncology clinic and the prompt evaluation of the endometrium.

CONCLUSION

It should be kept in mind that breast cancer may metastasize to the endometrium in patients

receiving chemo-hormonotherapy for breast cancer. Regular pelvic examination should be performed and transvaginal ultrasound scans should be performed. The endometrium should be evaluated. In case of suspected vaginal bleeding, endometrial sampling should be performed.

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