Invasive Lobular Carcinoma of the Male Breast: a Case Report

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A case of lobular carcinoma in a male breast is described. Because the structure of the male breast does not have lobules and acini, lobular carcinoma cases are seen infrequently. The pathological diagnosis was invasive lobular carcinoma of the breast. The karyotype of the patient revealed a 46 XY/46 XY, dmin (double minutes) chromosomal structure. Although 28% of the examined metaphases showed 46 XY, 1–5 dmin, the others were normal. We reviewed the English literature and found 20 reported cases of lobular carcinoma of the male breast. Our case represents lobular carcinoma in a proven genotypic male patient showing no exogenous or endogenous estrogens.

Key words: breast cancer – male – lobular carcinoma

INTRODUCTION
Breast cancer is rare in males (1% of all breast cancers). They are important since they have a more aggressive course. Approximately 85% of female breast cancers are infiltrating ductal carcinoma (1,2). Since the male breast does not have lobules and acini, lobular carcinoma is seen infrequently (3,4). The best recognized lobular carcinoma case in the literature was described in conjunction with Klinefelter’s syndrome (5,6). About 80–90% of male breast carcinomas are estrogen receptor positive and 30–70% are positive for progesterone receptor. Lobular carcinoma cases are infrequent with hormonal receptors, and cytogenetic investigations have not been adequately performed (6,7). A review of the literature revealed only a few cases of lobular carcinoma of the male breast (8–10). We reviewed the English literature and found 20 reported cases of lobular carcinoma of the male breast. Here, we report a case of lobular carcinoma of the male breast in a karyotype-proven male.

CASE REPORT
A 52-year-old male patient who had three children was admitted to Atatürk University School of Medicine in June 1996 with a lump in his right breast. There was no history of predisposing factors to breast lesions such as drug use or gynecomasia. Physical examination revealed a 3×2 cm mass localized in the subareolar area. Fine needle aspiration biopsy was performed on the mass and malignancy was found on histopathological examination. The patient underwent radical mastectomy and axillary lymph node dissection in July 1996. No tumor invasion was seen in the dissected seven lymph nodes. It was determined as stage IIA (T2N0M0) postoperatively. Histopathological examination revealed invasive lobular carcinoma of the breast. The cells in Indian file sequences showed narrow cytoplasm and ovoid nucleus under a light microscope (Fig. 1). Before radiotherapy, 2 ml heparinized peripheralblood samples for chromosome analysis were taken and immediately sent to the cytogenetic laboratory. Chromosome analysis was carried out using standard procedures. Briefly, the sample was cultured with RPMI 1640, including 20% fetal calf serum, phytohemagglutinin, L-glutamine and antibiotics for 72 h at 37°C and treated with 0.05 µg/ml colcemide (10 µg/ml stock solution) during the last 2 h. It was exposed to fresh hypotonic potassium chloride (0.075 M) for 10 min and finally fixed with cold methanol–acetic acid (11). The slides were dried at room temperature and stained with the trypsin–Giemsa banding technique. Fifty-four suitable metaphases were evaluated. The karyotype of the patient revealed a 46 XY, 1–5 dmin (double minutes) chromosomal structure (Fig. 2).

Radiation therapy was applied with γ-rays delivered by a Co-60 machine in August 1996. The affected side of the chest wall was treated with opposed tangential fields. A total dose of 50 Gy was applied to the chest wall with 2 Gy/day/5 fractions per
Nodal irradiation with 50 Gy in 25 fractions in 5 weeks was also applied to the axillary and supraclavicular regions.

In the case, the estrogen and progesterone receptor study resulted in estrogen receptor positive and progesterone receptor negative. In September 1996, 20 mg/day oral tamoxifen was started after completion of radiation therapy.

Immunohistochemical dyes for p53 and HER-2 were used and evaluated according to the percentage of the cells which took the dye and to the degree of dyeing. p53 took the dye in 80% of the area (++) and HER-2 (c-erb B2) in 40% of the area (++)

Ca15–3 and CEA were measured in the follow-up. In January 1999, elevation of tumor markers was found [Ca15–3, 42.9 U/ml (reference value: 0–32 U/ml); CEA, 9.6 ng/ml (reference value: 0–3.7 ng/ml)]. Physical examination of the patient did not show any findings and follow-up continued. In July 1999, the patient visited the hospital because of back pain. Tumor markers were measured as high (Ca15–3, 72.9 U/ml; CEA, 42.6 ng/ml). Whole-body bone scintigraphy showed multiple bone metastases. Tamoxifen treatment was stopped and second-line hormone therapy [formestan 4-hydroxysterenedione (Lentaron), 250 mg/2 weeks] was started. Th5,6,8, L1,3 and sacroiliac joints were irradiated with a dose of 400 cGy/5 fractions. Pamidronate (Aredia, 90 mg) was administered once in a four week period.

Eleven months later we detected multiple lung metastases. A biopsy taken from the lung lesion showed lobular carcinoma metastasis. Cyclophosphamide (500 mg/m²) – adriamycin (50 mg/m²) – 5-fluorouracil (500 mg/m²) chemotherapy was administered three times each within a period of 21 days. He died from progression of lung metastases.

DISCUSSION

Michaels et al. (8) reported the first case of lobular carcinoma in a proven genotypic male patient receiving no exogenous estrogens in 1994. In 1997, San Miguel et al. (12) reported the first lobular carcinoma of the male breast due to cimetidine intake and mentioned that it was the 18th case in the English literature.

Sano et al. (13), in a retrospective study evaluating their male breast cancer cases, reported one infiltrating lobular carcinoma out of five male breast cancers in the same year. Scheidbach et al. (10) also reported one very advanced stage lobular breast cancer in an 85-year-old man in 2000. They found BRCA1

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**Fig. 1.** (a) Hyperchromatic, irregular nuclei and indian file cells (H&E, ×100). (b) Lobular carcinoma cells indicated with arrow (Indian file) (H&E, ×400).

**Fig. 2.** Karyotype of the same metaphase (the other pair of the 22nd chromosome is located outside the photograph).
(breast cancer gene 1) new gene mutation in their patient, in whom Klinefelter’s syndrome was excluded.

The male breast does not have lobular and acinar structures (3,4). It has been reported that exposure to estrogens, the use of some drugs such as cimetidine, irradiation and long-term working in electromagnetic fields are etiological factors in male breast cancer (6,12). Eldar et al. (14) reported 10 cases with breast cancer that developed after chest irradiation. However, this was not observed in our patient. Long-term estrogen has been reported to be associated with true lobular and acinar structures. In addition, Pritchard et al. (15) reported breast carcinoma in three transsexual males after estrogen treatment. There was no such estrogen use in our case. Feminization significantly increases the risk of male breast carcinomas. In cases with Klinefelter’s syndrome, the risk is increased about 66.5-fold compared with normal males. Of the few previously reported cases of male lobular cancer, one patient had Klinefelter’s syndrome and one had 46 XY normal karyotype (6). The karyotype of our case demonstrated a 46 XY, 1–5 dmin chromosomal structure in 28% of examined metaphases. Double minutes are very small, ring-shaped chromosomal structures that occur in pairs. Recent molecular studies suggest that double minutes contain circular DNA molecules that lack centromers and telomerase. The most common solid tumors and leukemias have double minute structures or homogeneously stained regions which consist of one or more oncogenes amplified hundreds of times. These changes have been considered to play a role in the progression of tumors (16). We feel that the double minute structure in the karyotype of our case may have resulted from one or more oncogene amplifications.

This case represents lobular carcinoma in a proven genotypic male patient showing no exogenous (i.e. hormonal therapy, cimetidine) or endogenous estrogens (i.e. liver disease, cirrhosis).

References