Bilateral Breast Carcinoma in Patients with Klinefeleter Syndrome: Report of Case

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Purpose: Men with Klinefelter syndrome have one or more extra X chromosomes and have endocrine abnormalities. Klinefelter syndrome has been consistently associated with breast cancer in men (MBC).

Case report: We report a 54-year old man was diagnosed as synchronous bilateral breast cancer with Klinefelter syndrome. On clinical examination there was mass in the lateral upper quadrant right breast. The overlying skin was slightly retracted. In the left breast, there was also a subareolar mass. Mammography, ultrasonography imaging showed bilateral suspicious breast masses with microcalcifications. There were no radiological findings of muscle invasion or axillary lymphadenopathy. We performed bilateral fine-needle aspiration biopsy (FNAB), and the aspiration smears were positive for carcinoma. The pathologic diagnosis of infiltrating ductal carcinoma in the biopsy specimen on the bilateral breast. The patient was successfully treated by bilateral radical modified mastectomy according to Madden’s technique followed by external irradiation and adjuvant endocrine therapy.

Conclusion: Breast cancer commonly occurs in women, but now the incidence is also seen in men. Risk factors include age, family history, genes, liver diseases (cirrhosis), alcohol, diet, and obesity. Klinefelter syndrome, in which patients carry XXY chromosome, may be present in men with breast cancer for this reason they often develop gynecomastia. Key word: Klinefelter syndrome, breast cancer, men

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1. INTRODUCTION
Incidence of male breast cancer is still quite uncommon, and accounts for less than 1% of all breast cancers in the United States. In the recent years, its incidence is showing an increasing trend in various parts of the globe. Risk factors that regulate the development of male breast cancer include age, family history, Klinefelter’s syndrome, lifestyle and various susceptible genes (1).

Klinefelter Syndrome, is a congenital condition in which men have more than one X chromosome, affects about 1 of 1000 men. People suffering from Klinefelter Syndrome have been shown to be more susceptible towards breast cancer. As compared with other men, they have lower levels of androgens and more estrogens. For this reason, they often develop gynecomastia which is a benign enlargement of the male breast resulting from a proliferation of the glandular component of the breast. Gynecomastia has been reported to occur in association with breast cancer in men (2).

According to the National Cancer Institute, the types of breast cancer most commonly diagnosed in men are similar to those found in women. The most common type of male breast cancer is invasive ductal carcinoma (IDC). IDC is a cancer that has spread past the ducts of the breast (3).

2. CASE REPORT
We present a report of a 54-year-old man with a bilateral breast masses which appeared 4 months before clinical examination (May 2009). L.P. is a 54-year-old male who noted the onset of painless mass in both breasts. His past medical history was unremarkable except for hypertension controlled with medications and a history of diabetes mellitus type II. Clinical history revealed gynecomastia and adiposity for the previous 10 years. On clinical examination there was a 3x4x3 cm mass in the lateral upper quadrant right breast. The overlying skin was slightly retracted. In the left breast, there was also a subareolar mass which measured 3x3x4 cm. The patient was unmarried and to go without children. There was no history of estrogen administration, but the patient had small firm testiculs, low testosterone, infertility, incomplete masculinization, female body hair distribution (Sparse facial, armpit, and pubic hair), decreased libido and hypoplastic penis. Body shape patterns: pear shaped, tall, abnormal proportions (short trunk, long legs, long arms, lower body larger than upper) there was no familiar history of breast cancer (Figure 1.)

Only the first semen sample was evaluated for this study. Azoospermia was defined as no sperm found after centrifugation and analysis of the pellet. Serum levels of luteinizing hormone LH was 9,8 m/U/ml, normal range in our laboratory for LH is 1,7-8,6 m/U/ml. Level testosterone was 0,72 ng/ml and normal range in our laboratory for testosterone was 2,8-8,0 ng/ml. Follicle-stimulating hormone (FSH) was 20,8 m/U/ml, and normal range in our
laboratory for FSH was 1.5-12.4 m/U/ml. Serum level of estrogen was 16.3 pg/ml and normal range in our laboratory for estrogen is 7.63-42.6 pg/ml. Prolactin level in our patients was 182.3µ/U/ml, an normal range in our laboratory for prolactin is 86-324 µ/U/ml. The levels of thyroid-stimulating hormone (TSH), free-T3 (FT3), free-T4 (FT4) were normal.

Chest X-ray, electrocardiography, and echographic study of the abdomen showed no abnormalities.

Fine needle aspiration biopsy was performed on the mass and malignancy was found on histopathological examination.

There patient underwent bilateral radical mastectomy with axillary lymph node dissection in August 2009.

Histopathological examination of the tumor revealed infiltrating ductal carcinoma, moderately differentiated (Grade 2 according to Modified Scarff-Bloom-Richardson grading system). In addition, there were foci of intraductal comedo carcinoma featuring dilated ducts lined by malignant epithelial cells with central necrosis (Figure 2).

Immunohistochemical staining of tumor cells showed strongly positive nuclear staining for estrogen and progesterone receptors (Figure 3and 4.) and negative staining for HER-2 neu protein over-expression.

Histological examination of the right axillary nodes showed that three of the eleven lymph nodes dissected from the axilla were harboring deposits of metastatic ductal carcinoma.

For chromosome analysis were taken 5 ml heparinized peripheral blood samples and immediately sent to the cytogenetic laboratory. Chromosome analysis was carried out using standard procedures. The karyotype of the patients revealed a 47 XXY, chromosomal structure.

3. DISCUSSION

Male breast cancer (MBC) is rare in contrast to female breast cancers, which are the most common cancer and second leading cause of cancer deaths in women (4).

In an ours report, we found male patients with breast cancer were examples of the chromatin-positive Klinefelter syndrome (KS).

It was estimated that the incidence of breast cancer in association with KS is 66.5 times higher than in non-KS and it is clear that the 2 conditions are causally related. The development of breast cancer in patients with sex chromosome abnormalities has been reported before. Although the etiological factors are still unclear, hormonal abnormality is thought to contribute to its development (5).

In 1997, Kasami et al. reported a single case of bilateral breast tumors in a 46, XX/46, XY mosaic woman with a family history of breast cancer. They assumed that the Y-chromosome played a role in promoting cell growth (6).

The increased incidence of breast cancer in persons with sex chromosome abnormalities suggests that altered sex chromosomal constitution may be a strong predisposing factor; however, the precise incidence of such cancers in intersex persons is difficult to determine because many alleged cases were reported many years ago, before the advent of karyotyping.
A low testosterone level, with an elevated LH and normal to high estrogen level indicates primary hypogonadism. If the history suggests Klinefelter Syndrome, then a karyotype should be performed for definitive diagnosis. Formal cytogenetic analysis is necessary to make a definite diagnosis (7).

Possible reasons for the large relative risk are that men with Klinefelter syndrome have an estradiol-to-testosterone ratio that is several fold higher than that of karyotypically normal men or that there is increased peripheral conversion of testosterone to estradiol in men with Klinefelter syndrome compared with karyotypically normal men. Another possibility is that the presence of two X chromosomes per se might increase the genetic risk of breast cancer in men with Klinefelter syndrome (8).

Pathologically, the disease developed bilaterally in this patient, and histopathological studies of multiple sections of the resected specimen found almost no normal ductal tissue and almost entirely breast cancer cells. We cannot exclude the possibility that the breast cancer in this patient developed only due to these hormonal abnormalities.

Measurements were carried out three times at set intervals, but each time the PRL level was slightly elevated. As noted earlier, prolactin (PRL) has been ruled out as a cause of breast cancer. However, there have been reports of bilateral MBC accompanied by hyperprolactinemia, and in this light we cannot exclude the possibility that PRL may indeed be somehow involved. In addition, there have been reports that MBC clearly differs from postmenopausal female breast cancer, including recommendation of use of a gonadotropin-releasing hormone analog to interrupt the feedback from the pituitary that occurs at the time of administration of an aromatase inhibitor as therapy for breast cancer in males. In the future, we hope to further elucidate the causes of MBC (9).

REFERENCES
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