MALE BREAST CANCER TREATMENT: CLINICAL CASE

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ABSTRACT

Relevance: Male breast cancer (BC) is one of the rarest diseases and accounts for 1/100 of detected BC cases in both sexes. About 30-70% of breast cancer cases in men develop against the background of gynecomastia, particularly its nodular form. The biology of this disease differs in men, but the approaches to diagnostics and treatment are usually extrapolated from those used in women.

This study aimed to demonstrate the results of each stage of a male patient with BC diagnostics and treatment.

Methods: The article presents a clinical case of a male patient diagnosed with «Cancer in the right breast St III (T4NxM0), Edematous-infiltrative form with an intraductal component, upper outer localization. Immunohistochemically luminal subtype B without Her2neu expression». The data from literary sources and clinical protocols on the male BC diagnosis and treatment were also reviewed.

Results: The patient received four courses of preoperative chemotherapy according to the “AC” scheme Doxorubicin 60 mg/m² (CD 120 mg) + Cyclophosphamide 600 mg/m² (CD 1200 mg). Intermediate instrumental and laboratory control and assessing the response to treatment according to the RECIST criteria are planned.

Conclusion: The presented rare clinical case of male BC demonstrates that diagnostics and treatment at the initial stage remain the same as recommended for women. Identical preoperative and adjuvant chemotherapy regimens are applicable. Since most male BC express estrogen receptors, endocrine therapy such as tamoxifen is the kind of routine for adjuvant male BC treatment. This article describes the performed laboratory and instrumental diagnostics and preoperative chemotherapy treatment of the patient. The second part of the publication will present the results of the performed chemotherapy and surgical treatment and recommendations issued to the patient.

Keywords: Clinical case, male breast cancer (BC), Luminal subtype B without Her2neu expression, Klinefelter syndrome (gynecomastia).

Introduction: Malignant neoplasia of the breast in men is one of the rarest diseases; its frequency is 1 per 100 detected breast cancer cases (BC) in both sexes [1]. Given the rare occurrence of breast cancer in men, this pathology is of increasing interest to clinicians yearly. It is believed that 30-70% of male breast cancers develop against a background of gynecomastia, particularly its nodular form [2]. However, there are significant biological differences between male and female breast cancer. Thus, male BC is exclusively positive for estrogen and progesterone hormone receptors (+) and is associated with an increased prevalence of germline BRCA2 mutations [3]. Endocrine abnormalities are factors that influence the development of BC in men. For example, Klinefelter’s syndrome, a rare genetic disorder associated with testicular dysgenesis, androgen and estrogen imbalance, and increased gonadotropin levels, increase the risk of male BC by up to 50 times compared to men without such disorders [4, 5]. Other factors that influence the development of male BC include decreased testosterone levels in the body, hereditary predisposition, kidney and liver pathologies, hormone therapy in prostate diseases, hormone-producing neoplasms of testes, adrenal glands, pituitary gland, radiation, psycho-emotional trauma [6].

At the same time, the same approaches to diagnostics and treatment in men with BC are applied as in women.

This study aimed to demonstrate the results of each stage of a male patient with BC diagnostics and treatment.

Materials and methods: The article presents a clinical case of a male patient with the diagnosis “Right breast cancer St III (T4NxM0), edematous-infiltrative form with the intraductal component, upper-external localization. Immunohistochemical luminal subtype B without Her2neu expression.” Also, the data from the literature and clinical protocols on diagnosing and treating BC in men were reviewed.

Patient information: male, born in 1958 (64), ethnicity – Kazakh, occupation – vehicle driver.

Past medical history: The patient has been noticing breast enlargement for four years (since 2018). There-
before he applied to the local polyclinic. After examination by a mammologist, Klinefelter’s syndrome (gynecomastia) was diagnosed, and the patient refused treatment. It is known that in April 2021, the man suffered a psycho-emotional trauma. Against the background of psychological stress, the patient noticed the appearance of a neoplasm in the right mammary gland. He did not address medical help. The mass increased in size, redness, and a retracted nipple appeared. The patient denied taking hormonal drugs. No hormone-producing neoplasms of testicles, adrenal glands, or pituitary glands were noted. He explains his disease development to psychological trauma.

The patient was admitted to the Chemotherapy Center of Kazakh Scientific Research Institute of Oncology and Radiology (KazIOR, Almaty, Kazakhstan) in April 2022. At the pre-hospital stage, the patient was adequately diagnosed. The clinical diagnosis was: “Right breast cancer St III (T4NxM0), edema-infiltrative form with the intraductal component, upper-external localization. Immunohistochemical luminal subtype B without Her2neu expression.”

Clinical findings: On examination, the mammary glands are asymmetrical, with a mass about 10.0 cm in diameter, painless, and bluish skin in the right breast in the upper outer quadrant along the anterior axillary line of the chest. The mass is rounded, dense, and adherent to the surrounding tissues. The nipple was pulled to the nipple from the periphery, retracted, deformed, and its borders were indistinct. A dense lymph node about 2.0 cm in size was palpable in the axillary region on the right. Left mammary gland: skin unchanged, subcutaneous fat layer unchanged. Gynecomastia on the left side is noted.

Diagnostics: The patient underwent comprehensive pre-hospital instrumental and laboratory diagnostics.

Ultrasonic examination of the mammary glands, March 2022: a mass of the right breast, located in the upper outer quadrant, with precise irregular contours, measuring 9.0 cm with infiltrating growth.

Digital mammography of both breasts in 2 projections: evidence for C-r of the right breast is noted. BI-RADS – 6/2. There was a high-intensity, 6.8x6.1 cm mass in the right breast centrally on the border of the quadrants and in the upper outer quadrant with indistinct, jagged contours. Diagnosis – left-sided gynecomastia. Radiological density according to ACR-category criteria. A predominance of fibroglandular tissue was observed (Fig. 2 and 3).

Considering the evidence of right mammary gland neoplasia, the patient underwent a trepan biopsy of the right mammary gland and the right axillary lymph node. Histologically, “infiltrating breast carcinoma G III” was diagnosed.

Immunohistochemical study: estrogen receptors – 8, progesterone receptors – 8, tumor status – Her2 negative, Ki67 proliferation degree – 38%. Immunohistochemical luminal subtype B without Her2neu expression. Scanty cellular composition of the axillary lymph node trepanobiopsy materials, with lymphocytes and unstructured masses. No tumor cells were detected in the preparations.

Computed tomography (CT) of the brain, April 2022: a lacunar cyst in the basal nuclei on the left side.
Chest and abdominal CT scan, April 2022: no evidence for distant metastases. Lymphadenopathy of the axillary lymph nodes on the right.

Pelvic MRI, April 2022: Pattern of prostatic hyperplasia noted.

Hormone test, April 2022: Prolactin – 26.99 ng/mL (normal: 4.60 to 21.40 ng/mL), Estradiol – 24.2 ng/mL (normal: 7.63-42.6 ng/mL), Testosterone – 1.01 ng/mL (normal: 2.80-8.00 ng/mL), LH – 8.87 mU/mL (normal: 1.70 to 8.60 mU/mL), FSH – 37.9 mU/mL (normal: 1.5-12.4 mU/mL), SHBG – 39.67 mU/mL (normal: 20.60-76.70 mU/mL).

Treatment: The treatment tactics were discussed at the chemotherapy council of the KazNIIOIR Chemotherapy Center. Considering the clinical and instrumental examinations, histology, and IHC results, the patient was clinically diagnosed with “Right breast cancer St III (T4NxM0), edema-infiltrative form with the intraductal component, upper-external localization. Immunohistochemical luminal subtype B without Her2neu expression.” Based on these data, it was recommended that the first step was to start preoperative chemotherapy courses according to the AC regimen: Doxorubicin 60 mg/m² (daily dose 120 mg) + Cyclophosphamide 600 mg/m² (daily dose 1,200 mg), 4 courses, with a follow-up after three months.

The clinical case timeline is provided in Fig. 4.

Results: Adequate laboratory and instrumental examinations were performed at baseline. The patient underwent preoperative chemotherapy in the AC regimen: Doxorubicin 60 mg/m² (daily dose 120 mg) + Cyclophosphamide 600 mg/m² (1200 mg per day). Interim instrumental and laboratory tests, analysis, and assessment of the response to treatment by RECIST are scheduled.
**Discussion:** Analysis of literature data [1-6] and clinical guidelines for diagnosing and treating male BC [7] showed that male BC is very rare. BC literature, research, clinical trials, and the development of new treatment options have focused primarily on female BC. Although knowledge of female breast cancer may assist in diagnosing and treating male breast cancer, the molecular and clinicopathologic features of male and female breast cancer are different. In addition, biological factors such as sex differences, hormonal regulation, and response to treatment (tolerance and activity) must be considered when identifying this disease in men and choosing treatment options [8]. The initial diagnosis of male BC often occurs at a later stage than in female BC, and male BC often shows more pronounced signs of disease, such as larger tumor size, lymph node involvement, and distant metastases at the time of diagnosis [3-5]. Male BC treatment includes four main approaches: surgery, radiation therapy, chemotherapy, and endocrine therapy [7, 8]. Generally, men with BC are treated with modified radical mastectomy, axillary lymph node dissection, or signal lymph node biopsy [9]. In addition, data on the use of chemotherapy in male BC are limited. Clinicians who choose to use chemotherapy typically evaluate the same clinicopathologic risk factors (including tumor size, node involvement, hormone receptor status, HER2 status, and underlying cancer biology) in male patients with breast cancer as they do in women with breast cancer. Although significant efforts have been made to increase women’s awareness of breast cancer, screening, diagnosis, and treatment options, there has been limited research and outreach regarding male breast cancer. Treatment of male BC has primarily been based on clinical practices developed for women [4, 10]. Based on the data from these literature sources and clinical protocols for treating breast cancer in women, it was decided to perform the first-stage courses of chemotherapy as preoperative therapy.

As hormone therapy, tamoxifen was prescribed long-term (5 to 10 years). Although tamoxifen is effective in male breast cancer, it has drawbacks: recurrence rates and side effects that include hot flashes, vision changes, cognitive changes, and decreased sexual drive [10]. These quality-of-life issues may discourage male patients from continuing treatment, as 20 to 25% of men with breast cancer discontinue tamoxifen because of side effects [11].

Adjuvant hormone therapy with aromatase inhibitors is not recommended because it is associated with poorer long-term results than tamoxifen therapy, presumably due to insufficient estradiol suppression. If tamoxifen is contraindicated, treatment with aromatase inhibitors with concomitant administration of gonadotropin-releasing hormone analogs (or orchietomy) is recommended [12]. The fulvestrant monotherapy is also effective in women. However, her2-neu favorable breast cancer treatment remains the same in women [13].
Conclusion: The presented rare clinical case of male breast cancer demonstrates that the biology of the disease is different in men, but the approaches to diagnosis and treatment are generally the same as in women with breast cancer. Identical regimens are used as preoperative and adjuvant chemotherapy. Because most male BC expresses the estrogen receptor (ER), the use of endocrine therapies such as tamoxifen is routine for adjuvant treatment of male BC.

The clinical case description is divided into two parts because the patient is under treatment. This article describes the patient’s laboratory, instrumental diagnostics, and preoperative chemotherapy treatment. The second part will present the results of the chemotherapeutic and surgical treatment and the recommendations given to the patient.

References:
КЛИНИЧЕСКИЙ СЛУЧАЙ ЛЕЧЕНИЯ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ У ПАЦИЕНТА МУЖСКОГО ПОЛА

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Аннотация

Цель исследования – продемонстрировать результаты диагностики и лечения на каждом этапе ведения пациента мужского пола с РМЖ.

Методы: В статье представлен клинический случай пациента мужского пола с диагнозом «Рак правой молочной железы St III (T4NхM0), отечно-инфильтративная форма с внутрипротоковым компонентом, верхне-наружная локализация. Иммуногистохимическая картина повторяет таковую, как у женщин с РМЖ.

Результаты: Пациент получил лечение в объеме 4 курсов предоперационной химиотерапии по схеме «АС» Доксорубицин 60 мг/м2 (СД 120 мг) + Циклофосфамид 600 мг/м2 (СД 1200 мг). Планируется промежуточный инструментальный и лабораторный контроль, оценка ответа проведённого лечения по критериям RECIST.

Заключение: Представленный редко встречающийся случай РМЖ у мужчины демонстрирует, что диагностика и лечение на начальном этапе остаются аналогичны рекомендациям для женщин. В качестве предоперационной и адъювантной химиотерапии применяются субстанции, которые в рамках общепринятого лечебного протокола включены в химиотерапию РМЖ у женщин.

Ключевые слова: Клинический случай, рак молочной железы (РМЖ) у мужчин, люминальный подтип «В» без экспрессии Her2/neu, синдром Кайнфельтера (синемастия).