Invasive micropapillary type male breast cancer: a case report

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ABSTRACT
Male breast cancer is rarely seen and peaks at the age of 71. Hyperestrogenism, gonadal dysfunction, obesity, and alcohol are among the risk factors for male breast cancer. In hereditary cases, BRCA2 mutation is often observed. The most common symptom is a painless mass that is palpable behind the nipple. Most male breast cancers are ductal carcinomas (81%), papillary carcinomas (13%), and mucinous carcinomas (6%). The invasive micropapillary carcinoma of the breast is important due to its high rate of lymphnode metastasis, recurrence, and distant metastasis. Mortality is 50% higher in men with lymphnode involvement compared to non-involved cases. Furthermore, as the number of affected lymphnodes increases, the prognosis worsens. In this study, we examined a case of invasive micropapillary type male breast cancer with clinical presentation as a palpable mass, lymphnode involvement, and aimed to highlight the radiological considerations that need attention.

Keywords: Breast cancer, male breast cancer, micropapillary type cancer

Male breast cancer is a rare condition, accounting for less than 1% of all male malignancies and only 1% of all breast cancer cases [1]. The average age at diagnosis for men with breast cancer is 67, which is approximately 5-10 years later than the average diagnosis age for women [2]. While most men with breast cancer do not have an identifiable risk factor, factors such as Klinefelter Syndrome, obesity, testicular anomalies, cirrhosis, exogenous estrogen therapy, radiation exposure, occupational exposures, and BRCA mutations are among the risk factors. Gynecomastia, however, is not among the risk factors [1, 3]. The most common symptom is a painless mass palpable behind the nipple. The left breast is more commonly affected than the right, and about 1% of cases are bilateral [1]. In the evaluation of a breast mass in men, ultrasound (USG) is generally the first choice, but mammography can also be used. Mammography can often distinguish between malignancy and gynecomastia. Mammographic features suggestive of malignancy includes plicated margins and eccentric extension. Microcalcifications are less frequently observed in male breast cancer compared to female breast cancer [4]. Most male breast cancers are ductal carcinomas (81%), followed by papillary carcinomas (13%) and mucinous carcinomas (6%) [5]. The term invasive micropapillary breast carcinoma (IMPC) was first introduced to...
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the literature by Siriaunkgul and Tavassoli in 1993 [6]. The World Health Organization's 2012 histological classification of breast tumors requires an invasive micropapillary component of at least 50% to diagnose IMPC. Microscopic papillary growth patterns accompany IMPC types at a rate of 3-6% [7]. The frequency of pure IMPC is reported to be 0.9% in one study [8]. Invasive micropapillary carcinoma of the breast is significant due to its high rate of lymphnode metastasis, recurrence, and distant metastasis [9, 10]. Standard early-stage breast cancer treatment in men involves hormone therapy, chemotherapy, or radiotherapy following surgery. Treatment varies based on the patient's prognostic factors, similar to women [11]. The most important prognostic factors for male breast cancer are tumor size and lymphnode involvement. Lymphnode involvement is 40% higher in patients with tumors measuring between 2-5 cm compared to those with tumor size < 2 cm. Similarly, mortality is 50% higher in men with lymphnode involvement compared to those without. Moreover, prognosis worsens as the number of involved lymphnodes increases [12, 13].

CASE PRESENTATION

A 64-year-old male patient presented to the general surgery outpatient clinic with complaints of swelling and a palpable mass in the right breast. Apart from type 2 diabetes mellitus, the patient had no other significant disease history. Upon physical examination, gynecomastia was noted, along with a palpable mass in the retroareolar area of the right breast and in the right axillary tail. Subsequently, a breast ultrasound was performed. The breast ultrasound revealed a solid lesion in the retroareolar area of the right breast, measuring 15 × 16 mm, with irregular borders and spiculated extensions. The lesion exhibited a hypoechoic appearance, and it raised suspicion for a hypoechoic skin-directed breast cancer, classified as a BIRADS-5 solid lesion (Fig. 1). Additionally, pathological lymphadenopathies (LAP) with a conglomerate appearance were observed in the right axilla, with the largest measuring up to 25 × 43 mm (Fig. 2). Histopathological diagnosis of the mass lesion under local anesthesia, a tru-cut biopsy was performed on the mass in the retroareolar area of the right breast and on the pathological lymphadenopathies (LAP) in the right axillary tail. The biopsy evaluation of the tissue from the retroareolar region revealed invasive ductal carcinoma. Similarly, the biopsy evaluation of the tissue from the LAP in the right axilla indicated metastasis of invasive ductal carcinoma (micropapillary type) (Fig. 3).
After the tissue diagnosis of the patient, a whole-body positron emission tomography-computed tomography (PET-CT) scan revealed a mass lesion approximately 15 × 16 mm in size showing pathological fluorodeoxyglucose (FDG) uptake in the retroareolar area of the right breast (Fig. 4). In addition, multiple lymphnodes with the largest approximately 23 × 45 mm size were observed in the right axillary fossa (Fig. 5).

After undergoing whole-body PEC-CT scanning,
the patient was started on neo-adjuvant cyclophosphamide + adriamycin therapy to be administered every three weeks. In the follow-up ultrasound (USG) after completing chemotherapy, it was observed that the lesion size in the retroareolar area of the right breast had decreased to $9 \times 13$ mm, and the largest

**Fig. 4.** The mass lesion showing pathological fluorodeoxyglucose uptake in the retroareolar area of the right breast.

**Fig. 5.** Multiple lymph nodes showing pathological fluorodeoxyglucose uptake in the right axillary fossa.
pathological lymphnode size in the right axillary fossa had decreased to 10 × 20 mm. Following neo-adjuvant chemotherapy, the patient underwent modified radical mastectomy and right axillary lymph node dissection. Adjuvant radiotherapy was applied to the right breast localization and right axillary fossa following surgery in a patient with negative surgical margins. follow-up USG was recommended three months later for further monitoring.

**DISCUSSION**

As the incidence of male breast cancer cases, which is increasing everyday, most cases are referred to radiology clinics for further evaluation of the mass after being detected through manual examination. Among the initial imaging methods, mammography and ultrasound are preferred. Following imaging, tru-cut biopsy under ultrasound guidance is performed for cases suspected of malignancy [14].

Risk factors typically revolve around hormonal imbalances such as androgen deficiency or estrogen excess. While some patients have organic causes contributing to hormonal imbalances, such as testicular or liver damage, in most cases, no clear cause can be identified. Mutations in the BRCA tumor suppressor gene are also a risk factor for male breast cancer. BRCA-2 gene mutation is more common than BRCA-1 mutation in this context [15].

Male breast cancer is often detected at later ages and stages, which adversely affects treatment and survival outcomes. The average age of diagnosis for IMPC is 69.8 years, slightly older than in women. In a retrospective study, the incidence of IMPC among included cases of invasive ductal carcinoma was found to be 0.4% [14].

Micro papillary type breast cancer tends to be more aggressive compared to other types of breast cancer, which further emphasizes the importance of early diagnosis and treatment. In a study, it was found that IMPC exhibits lymphotropic behavior, with lymphnode metastasis detected in 73.7% of cases, as in our case. In a study conducted by Luna-More et al. [9], the positivity rates for estrogenreceptor (ER), progesteronereceptor (PR), and HER2/neureceptor were reported as 71.3%, 48.3%, and 51%, respectively [9]. However, in a study by Gokce et al. [16], it was stated that in IMPC cases showing ER and PR negativity along with c-erb-B2 overexpression, the rate of local recurrence was higher [16]. In our case, ER and PR were found to be negative, and c-erb-B2 overexpression was detected. Furthermore, in the same study, a positive correlation was found between overall survival rate and ER positivity, while no correlation was found between PR positivity and c-erb-B2 overexpression with survival.

Diagnosis and treatment of male breast cancer are fundamentally similar to those of female breast cancer, although there are some differences. Numerous studies have demonstrated the benefits of adjuvant, neo-adjuvant hormone therapy, chemotherapy, and andradiotherapy. Tamoxifen remains the gold Standard for adjuvant hormone therapy. Selective aromatase inhibitors such as anastrozole, letrozole, and exemestane can also be used in hormone therapy. There are many studies supporting the effectiveness of the combination of adjuvant hormone therapy and chemotherapy. In surgical treatment, radical mastectomy and lymphnode dissection, which are associated with lower rates of local recurrence, are performed [17, 18].

**CONCLUSION**

In our case, modified radical mastectomy with lymphnode dissection was performed following neo-adjuvant chemotherapy. Subsequently, the treatment process was completed with radiotherapy, and the patient was placed under USG monitoring at regular intervals.

**Patient’ Consent**

Patient was informed about the purpose of the case report, and informed consent was obtained from the patient for this publication.

**Authors’ Contribution**

Study Conception: MSA, ŞŞ, FEU, MK; Study Design: MSA, ŞŞ, FEU, MK; Supervision: MK; Funding: ACP, KK; Materials: ŞŞ; Data Collection and/or Processing: N/A; Statistical Analysis and/or Data Interpretation: N/A; Literature Review: MSA, FEU; Manuscript Preparation: FEU and Critical Review: FEU.
Conflict of interest
The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing
The authors disclosed that they did not receive any grant during conduction or writing of this study.

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