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Male breast cancer exhibiting features of basal-like subtype female breast cancer

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ABSTRACT

The molecular subtypes of male breast cancer are not well-known, but luminal A is generally regarded as the predominant subtype. We present the clinical and histopathological features in a man with triple-negative breast carcinoma.

1. Introduction

Male breast cancer (MBC) is uncommon, accounting for approximately 1% of all breast cancers and male cancers.[1] The clinical and pathological understanding of male breast cancer is therefore limited, and its management has been extrapolated based on information from female breast cancer. MBC is generally thought to behave like estrogen receptor (ER)-positive breast cancer in post-menopausal women.[2] Recent immunohistochemical studies have identified luminal subtype as the most common subtype of MBC,[3,4] with basal-like subtype occurring in only 4%–5% of cases,[4,5] while HER2-overexpressing MBC has not been observed.[6] We report an extremely rare case of a man with basal-like invasive ductal carcinoma of the breast.

2. Case report

A 57-year-old man presented to the outpatient surgical clinic with a mass in his right breast. The patient was a smoker, and there was no medical history of trauma, gynecomastia, liver disease, or drug use, and no family history of breast cancer. Physical examination revealed a 2 cm tumor located in the left breast, with no retraction or ulceration of the overlying skin. The armpits showed no signs of lymphadenopathy. Fine needle aspiration cytology indicated malignancy. He underwent modified radical mastectomy and was referred to the oncology department. Pathological examination confirmed a 2 cm invasive ductal carcinoma, histologic grade 3 and nuclear grade 3 (Fig. 1). The breast surgical margins were clear, with no infiltration of the pectoralis muscle fascia and nipple. The axillary lymph nodes showed no signs of cancer (0/15), and there was no vascular or perineural invasion. Immunohistochemical staining of the tumor was negative for ER and progesterone receptor (PR), and c-erbB2 (Fig. 2), but positive for cytokeratin (CK) 5/6, P53, and epidermal growth factor receptor (EGFR) (Figs. 3–5). Chest computed tomography revealed a 4-cm lung mass in the right upper lobe. Fiberoptic bronchoscopy revealed no tumors within the visible field, and transbronchial biopsy was performed to rule out the possibility of second primary lung cancer in light of the patient's smoking history. The results of histological examination were consistent with lung metastasis of invasive ductal cancer of the breast. The patient was finally diagnosed with stage IV (T1N0M1) breast cancer and treated with six cycles of chemotherapy with docetaxel, doxorubicin, and cyclophoshamide. The size of the metastatic lesion in the lung decreased remarkably during chemotherapy and had almost disappeared by the end of treatment. However, follow-up revealed multiple brain metastases 7 months after the initial chemotherapy. The patient died of neurological seizures and associated aspiration pneumonia during palliative radiotherapy for brain metastases.

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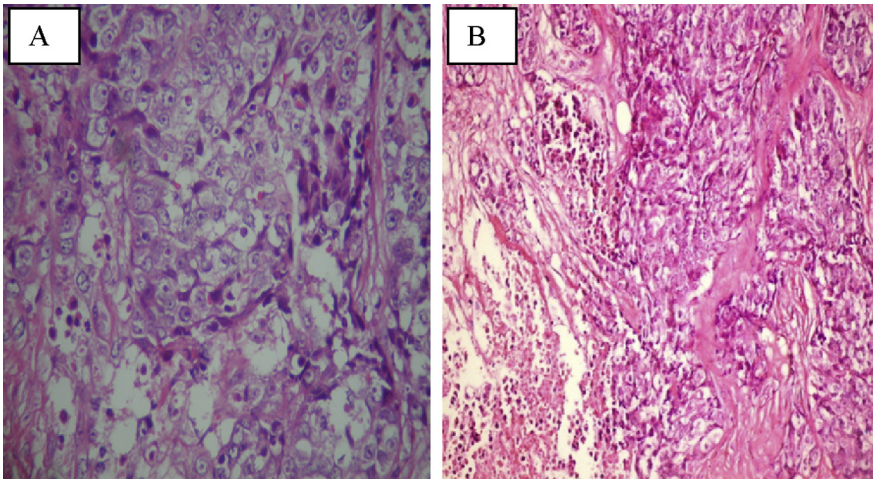

Fig. 1. A: Tumor tissue showing the medullary tumor features (HE X200). B: Tumor consists of oval, poligonal cells with vesicular nucleus and nucleolus with eosinophilic cytoplasm and shows tumor necrosis and solid groups (HEX200)

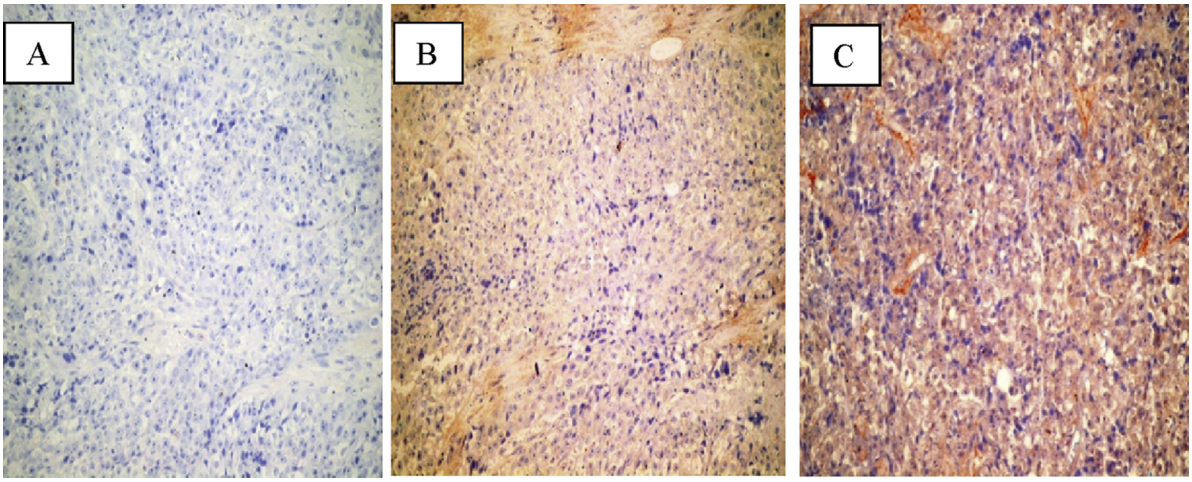

Fig. 2. A: ER negativity (HEX20), B: PR negativity (HEX20), C: cerb-B2 negativity (HEX20)

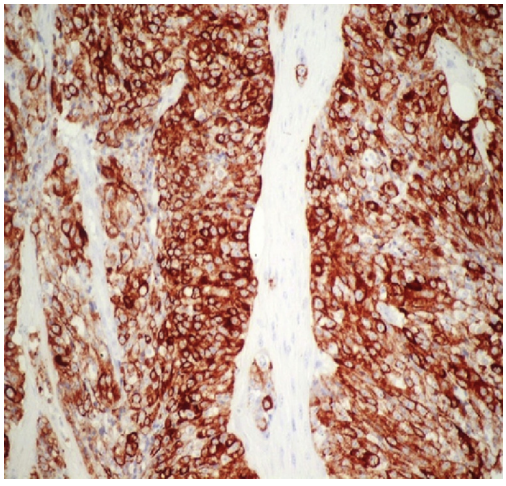

Fig. 3. Immunostaining for CK5/6 shows a positive reaction in all tumor cells (HEX200)

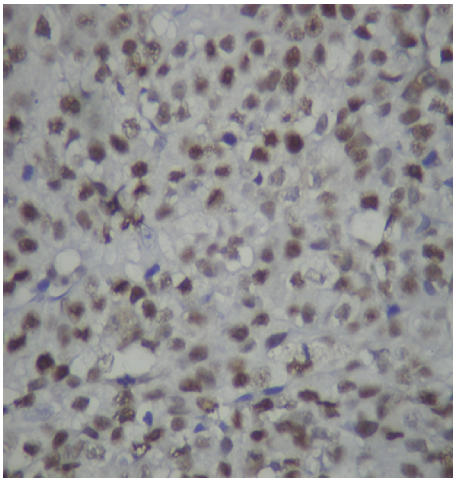

Fig. 4. Immunostaining for P53 shows a positive reaction in tumor cells (HEX200)

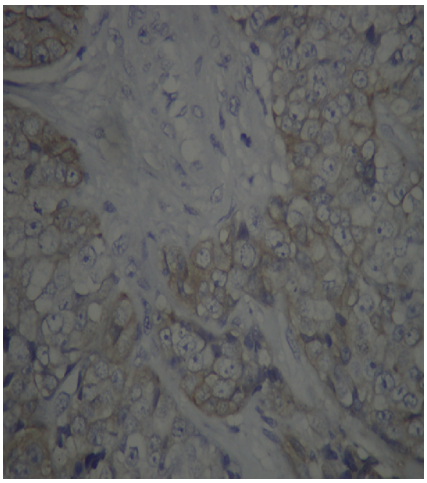

Fig. 5. Immunostaining for EGFR shows a positive reaction in tumor cells (HEX200)

3. Discussion

MBC differs from female breast cancer. Compared with women, male patients tend to be older at the time of diagnosis (mean age 60–70 years) and have higher-stage disease and more lymph node involvement.[7] The present patient was a 57-year-old male, and although the tumor was small (T1) and there were no signs of lymph node metastasis (N0), or vascular or lymphatic invasion, lung metastasis was present at diagnosis. Even low-grade MBCs appear to have a higher rate of hormone-receptor positivity than female breast cancer, are less likely to show HER2 overexpression/amplification, and are more likely to be p53 negative.[3–6,8] The tumor in the current patient was high-grade, negative for hormone receptors and c-erbB2, and positive for p53. This case show that MBCs may have a more distinct pathological profile than expected. The clinical course in our patient was similar to that of triple-negative female breast cancer in terms of its initial response to chemotherapy and subsequent development of brain metastasis.

The molecular subtypes of female breast cancer have been identified by gene expression analysis.[9] However, it is not always possible to carry out such analysis, and immunohistochemical markers are currently used as surrogate markers for breast-cancer subtyping. Carey and colleagues reported immunohistochemical subtype definition of female breast cancers as luminal A (ER-positive and/or PR-positive, HER2-negative), luminal B (ER-positive and/or PR-positive, HER2-positive), HER2-overexpressing (ER- and PR-negative, HER2-positive), basal-like (ER-, PR-, and HER2-negative, CK5/6-positive), and unclassified (negative for all markers).[10] The distribution of genetic and molecular subtypes of MBC has been documented in three trials,[11–13] which classified MBC as either luminal M1 or luminal M2. These subgroups do not fully match those of female breast cancer, and the results of genetic analysis of MBC in relation to ER, PR, and HER2 expression are unclear.

The triple-negative phenotype accounts for approximately 7%–20% of all female breast cancers, and can be divided into basal-like and non-basal-like subtypes. The basal-like subtype is characterized by lack of ER, PR, and HER2 expression, and CK5/6- and/or EGFR-positivity. It is associated with an aggressive clinical course and poorer survival than luminal subtypes. The non-basal-like subtype is characterized by lack of ER, PR, HER2, CK5/6, and EGFR expression.[14] Chavez-MacGregor et al reported that men with hormone receptor-negative tumors showed poorer survival than with hormone receptor-positive tumors,[15] suggesting that the triple-negative phenotype may be a potential prognostic factor in MBC, as well as female breast cancer. The biological markers CK5/6 and EGFR were both positive in the current patient with triple-negative MBC, according to immunohistochemistry. EGFR status correlates negatively with survival in patients with triple-negative breast cancer[16]; despite initial chemosensitivity, patients exhibit a deteriorating clinical course and poor survival.[17] The reported rate of EGFR expression in MBC ranges from 8.5% to 76%.[16–18]

Genetic predisposition is an important risk factor for both male and female breast cancers. Mutations in BRCA1 (breast cancer 1, early-onset gene) and BRCA2 (breast cancer 2, early-onset gene) occur in approximately 10% of all MBCs.[19] Silvestri et al analyzed data for 419 MBCs, including 375 with BRCA1 and 44 with BRCA2 mutations, indicating that 89.5% of MBC cases carried BRCA2 mutations. MBC patients with BRCA2 mutations were diagnosed at a younger age (<50 years old) and had more lymph node involvement, their tumors were significantly higher stage and histologic grade, and were more likely to be ER and PR positive compared with women with breast cancer and BRCA2 mutations.[20] BRCA1 MBCs were also more likely to be ER- and PR-positive (non-triple negative), while most breast tumors arising in female BRCA1 mutation carriers are known to be ER- and PR-negative.[21] Unfortunately, we were unable to identify the BRCA1/2 status in our patient. However, our patient presented a heterogeneous tumor status, including features characteristic of male breast cancer BRCA2 mutation carriers, as determined by Silvestri et al, as well as receptor negativity seen in female breast cancer BRCA1 mutation carriers.

In conclusion, we describe a case of MBC with characteristics similar to those of female basal-like breast carcinoma. Higher-stage disease with larger tumor size and more extensive lymph node invasion has been associated with poorer prognosis in MBC. However, although the present patient presented with small tumor size and no lymph node metastasis, lung metastasis was present at the time of diagnosis. This case suggests that molecular subtypes may be prognostic factors in MBC, as well as in female breast cancer, though the molecular subtypes may differ between male and female breast cancers.

Consent

Written informed consent was obtained from the patient's wife for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. Ly D, Forman D, Ferlay J, et al. An international comparison of male and female breast cancer incidence rates. *Int J Cancer*. 2013;132(8):1918–1926.
2. Deb Siddhartha, Lakhani Sunil R, Ottini Laura, et al. The cancer genetics and pathology of male breast cancer. *Histopathology*. 2016;68:110–118.
3. Deb S, Jene N, Fox SB. Genotypic and phenotypic analysis of familial male breast cancer shows under representation of the HER2 and basal subtypes in BRCA-associated carcinomas. *BMC Cancer*. 2012;12:510.
4. Yu Xing-Fei, Feng Wei-Liang, et al. The prognostic significance of molecular subtype for male breast cancer: a 10-year retrospective study. *Breast*. 2013;22:824–827.
5. Ge Y, Sneige N, Eltorky MA, et al. Immunohistochemical characterization of subtypes of male breast carcinoma. *Breast Cancer Res*. 2009;11(3):R28.
6. Kornegoor R, Verschuur-Maes AH, Buerger H, et al. Molecular subtyping of male breast cancer by immunohistochemistry. *Mod Pathol*. 2012;25:398–404.
7. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population based comparison with female breast cancer. *J Clin Oncol*. 2010;28:232–239.
8. Wang-Rodriguez J, Cross K, Gallagher S, et al. Male breast carcinoma: correlation of ER, PR, Ki-67, Her2-Neu, and p53 with treatment and survival, a study of 65 cases. *Mod Pathol*. 2002;15:853–861.

9. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. *Nature*. 2000;406:747–752.
10. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the carolina breast cancer study. *JAMA*. 2006;295:2492–2502.
11. Johansson I, Nilsson C, Berglund P, et al. High-resolution genomic profiling of male breast cancer reveals differences hidden behind the similarities with female breast cancer. *Breast Cancer Res Treat*. 2011;129:747–760.
12. Callari M, Cappelletti V, De Cecco L, et al. Gene expression analysis reveals a different transcriptomic landscape in female and male breast cancer. *Breast Cancer Res Treat*. 2011;127:601–610.
13. Johansson I, Ringner M, Hedenfalk I. The landscape of candidate driver genes differs between male and female breast cancer. *PLoS One*. 2013;8:e78299.
14. Minami Christina A, Chung Debra U, Chang Helena R. Management options in triple-negative breast cancer. *Breast Cancer Basic Clin Res*. 2011;5:175–199.
15. Chavez-Macgregor M, Clarke CA, Lichtensztajn D, et al. Male breast cancer according to tumor subtype and race: a population-based study. *Cancer*. 2013 May 1;119(9):1611–1617.
16. Willsher PC, Leach IH, Ellis IO, et al. Male breast cancer: pathological and immunohistochemical features. *Anticancer Res*. 1997;17:2335–2338.
17. Chung HC, Kim DL, Koh EH, et al. Expression of prognostic factors (EGFR, ER) by immunohistochemical staining method in male breast cancer. *Yonsei Med J*. 1991;32:126–130.
18. Fox SB, Rogers S, Day CA, Underwood JC. Oestrogen receptor and epidermal growth factor receptor expression in male breast carcinoma. *J Pathol*. 1992;166:13–18.
19. Rizzolo P, Silvestri V, Tommasi S, et al. Male breast cancer: genetics, epigenetics, and ethical aspects. *Ann Oncol*. 2013;24(8):75–82.
20. Silvestri Valentina, Barrowdale Daniel, Marie Mulligan Anna, et al. Male breast cancer in BRCA1 and BRCA2 mutation carriers: pathology data from the consortium of investigators of modifiers of BRCA1/2. *Breast Cancer Res*. 2016;18:15.
21. Mavaddat N, Barrowdale D, Andrulis IL, et al. Pathology of breast and ovarian cancers among BRCA1 and BRCA2 mutation carriers: results from the consortium of investigators of modifiers of BRCA1/2 (CIMBA). *Cancer Epidemiol Biomarkers Prev*. 2012;21(1):134–147.