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Case Report

Male Breast Cancer: Case Study at RSUD dr. Iskak Tulungagung in 2024

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Abstract—*This case study explores the clinical and molecular profile of male breast cancer (MBC) and underscores the diagnostic utility of immunohistochemistry. A 79-year-old man was diagnosed with grade III invasive carcinoma of no special type (NST) via histopathology and immunohistochemistry, showing ER+, PR+, HER2 3+, and Ki67 (30%) expression. The tumor was classified as Luminal B-like (HER2-positive). The findings highlight the relevance of molecular profiling in guiding treatment and prognosis in rare male breast cancer cases.*

Keywords: *breast cancer, male, case study*

Abstrak— This case study explores the clinical and molecular profile of male breast cancer (MBC) and underscores the diagnostic utility of immunohistochemistry. A 79-year-old man was diagnosed with grade III invasive carcinoma of no special type (NST) via histopathology and immunohistochemistry, showing ER+, PR+, HER2 3+, and Ki67 (30%) expression. The tumor was classified as Luminal B-like (HER2-positive). The findings highlight the relevance of molecular profiling in guiding treatment and prognosis in rare male breast cancer cases.

Kata kunci: *kanker payudara, pria, studi kasus*

INTRODUCTION

Breast cancer is a malignant disease that primarily affects women, yet it can also occur in men. Male breast cancer (MBC) accounts for less than 1% of all breast cancer cases and male malignancies, with an incidence of approximately one case per 100,000 population per year [1]. Despite its rarity, recent epidemiological data indicate a steady increase in MBC incidence by approximately 1.1% per year [1], underscoring the importance of deeper investigation into its clinical and molecular characteristics.

MBC often presents at a more advanced stage than female breast cancer, partly due to low awareness, absence of routine screening, and social stigma, contributing to delayed diagnosis and worse prognosis. Clinically and biologically, MBC can display features distinct from its female counterpart, although it shares similar molecular classification systems.

One of the most important tools in breast cancer characterization is immunohistochemistry (IHC). This technique is essential for subclassifying breast tumors into molecular subtypes based on the expression of key biomarkers—estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and proliferation index (Ki67) [2]. The presence of ER and PR is predictive of response to hormonal therapies, such as tamoxifen and aromatase inhibitors [2,3]. Overexpression of HER2, either via protein overexpression or gene amplification, is associated with more aggressive disease behavior and poorer outcomes [4]. The Ki67 index serves as a marker of tumor cell proliferation, providing additional information on tumor aggressiveness [5].

Molecular subtyping—such as Luminal A, Luminal B, HER2-enriched, and triple-negative—has become the foundation of modern breast cancer treatment planning. In particular, Luminal B subtype is characterized by ER/PR positivity, variable HER2 expression, and high Ki67, and it is often associated with poorer prognosis compared to Luminal A [2,7].

This case report describes a male patient diagnosed with invasive carcinoma of no special type (NST) grade III and classified as Luminal B-like (HER2-positive), based on histopathological and immunohistochemical analyses. The case aims to highlight the clinical, pathological, and molecular characteristics of MBC and to emphasize the crucial role of IHC in diagnostic accuracy and therapeutic decision-making. Additionally, this report contributes to the limited literature on MBC, especially in the Indonesian clinical setting.

METHODS

The research method was conducted through a single case study approach involving a male with a diagnosis of breast cancer. Clinical and pathological data from the patient were retrospectively collected from hospital medical records. Histopathologic examination was performed to confirm the diagnosis of breast cancer and to evaluate the expression of relevant immunohistochemical markers. Immunohistochemical examinations were performed using a predefined antibody panel for markers associated with breast cancer. Results from histopathological and immunohistochemical examinations were analyzed descriptively to understand the biological profile of breast cancer in this man. In addition, the discussion also includes a review of relevant literature to compare the findings with previous studies and to support the interpretation of the results.

RESULT

The patient, Mr. W, is a 79-year-old male from Tulungagung Regency who presented with the main complaint of a lump in the left breast, which had been felt for five years before visiting RSUD dr. Iskak Tulungagung. The patient first presented on October 16, 2023. An extended mastectomy was performed, and the surgical specimen was sent to the Anatomical Pathology Laboratory for further examination.

Macroscopic findings revealed a single left mammary tissue weighing 480 grams, measuring 14.3 × 10.5 × 5 cm and covered by skin (16 × 9 cm). An ulcer was found on the areola mammae, with no distinct papillae or peau d'orange. The tumor mass almost filled all quadrants, with dimensions of 9.7 × 9 × 4.3 cm. It was located 0.2 cm from the base, 0.5 cm from the skin, 0.3 cm from the inferior, 0.1 cm from the superior, 3 cm from the lateral, and 1.6 cm from the medial margin. Nineteen nodules with diameters ranging from 0.6 to 5.5 cm were found, gray-white, with a solid and spongy consistency.



Figure 1. Macroscopic tissue examination.
Source: author's documentation

Microscopic examination with hematoxylin-eosin smears showed that the mammary tissue sections contained tumor growth, arranged in a glandular and solid pattern with tubular formation of 30%. The tumor consisted of a proliferation of round to oval, moderately pleomorphic, hyperchromatic, epithelial cells growing invasively into the fibrous connective

tissue stroma with minimal fibrosis and minimal lymphocyte inflammatory cell infiltrates. Mitosis 21/10 HPF. The cut showed lymphangionvation and metastasis in 19 lymph nodes found. It was concluded that the diagnosis of mammary sinistra resulting from extended masectomy surgery was invasive breast carcinoma of NST grade III dd High Grade Adenocarcinoma.

Mitotic count is now calculated per specific area in mm^2 instead of per 10 High-Power Fields (HPFs), for better standardization and accuracy. HPF stands for "High-Power Field" in English. In the context of histopathological examination, the term refers to a magnified microscopic field of view, which is used to count the number of specific cells or structures in a specimen. In mitotic examinations, HPF is used to count the number of cell divisions occurring within a given area of tumor tissue. In other words, mitotic 21/10 HPF means that there are 21 cell divisions counted in 10 magnified microscopic fields of view. Based on the calculation of mitotic 21 per 10 high power field of view (HPF), Mr. W's tumor falls into the mitotic category. Mr. W's tumor falls into the high mitotic count category. In breast tumor classification, a high mitotic count such as this is often associated with a higher grade, signifying a higher degree of cell proliferation and greater potential for aggressiveness.

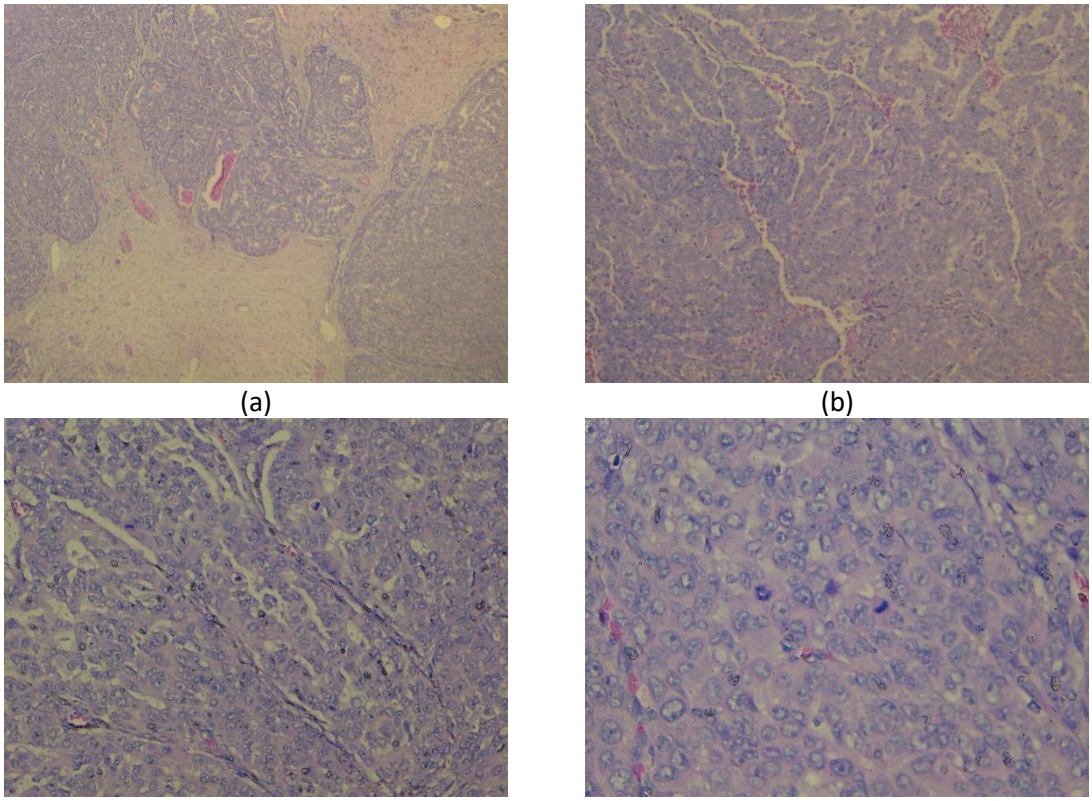


Figure 2. Histopathology of male breast cancer with hematoxylin eosin (HE) staining (a) 40x magnification (b) 100x magnification (c) 200x magnification (d) 400x magnification. Source: author's documentation

Immunohistochemistry showed strong ER (>90%) and PR (80%) positivity, HER2 overexpression (3+), and a Ki67 index of 30%. The tumor was classified as Luminal B-like (HER2-positive). No axillary lymph node metastasis was found.

DISCUSSION

Male breast cancer (MBC) is a rare malignancy, constituting less than 1% of all breast cancer cases and male cancers. Despite its low incidence, MBC demonstrates unique clinical,

pathological, and molecular features compared to female breast cancer. Delayed diagnosis and limited awareness contribute to its late-stage presentation and poor prognosis. Immunohistochemical profiling—including assessment of estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67—is crucial for determining tumor subtype, guiding prognosis, and informing therapeutic strategies. In Mr. W's case, comprehensive pathological and immunohistochemical evaluation offers insights into tumor aggressiveness, molecular classification, and treatment implications.

Histopathological examination revealed grade III invasive carcinoma of no special type (NST), characterized by poor differentiation, low tubular formation, marked nuclear pleomorphism, and high mitotic activity (21 mitoses/10 high-power fields), all indicating rapid proliferation and aggressive behavior [6]. These features justify the grade III classification and signify a tumor with high recurrence and metastatic potential. Therefore, aggressive treatment and close follow-up are essential.

Immunohistochemically, Mr. W's tumor showed high ER expression in 90% of tumor cell nuclei and high PR expression in 85%, indicating hormone receptor positivity. This hormonal sensitivity aligns with the Luminal molecular subtypes—particularly Luminal A and B—implying potential responsiveness to endocrine therapies such as tamoxifen or aromatase inhibitors. The intense nuclear staining for ER and PR (Figure 2) confirms a hormonally driven tumor, reinforcing the relevance of hormone-based treatment.

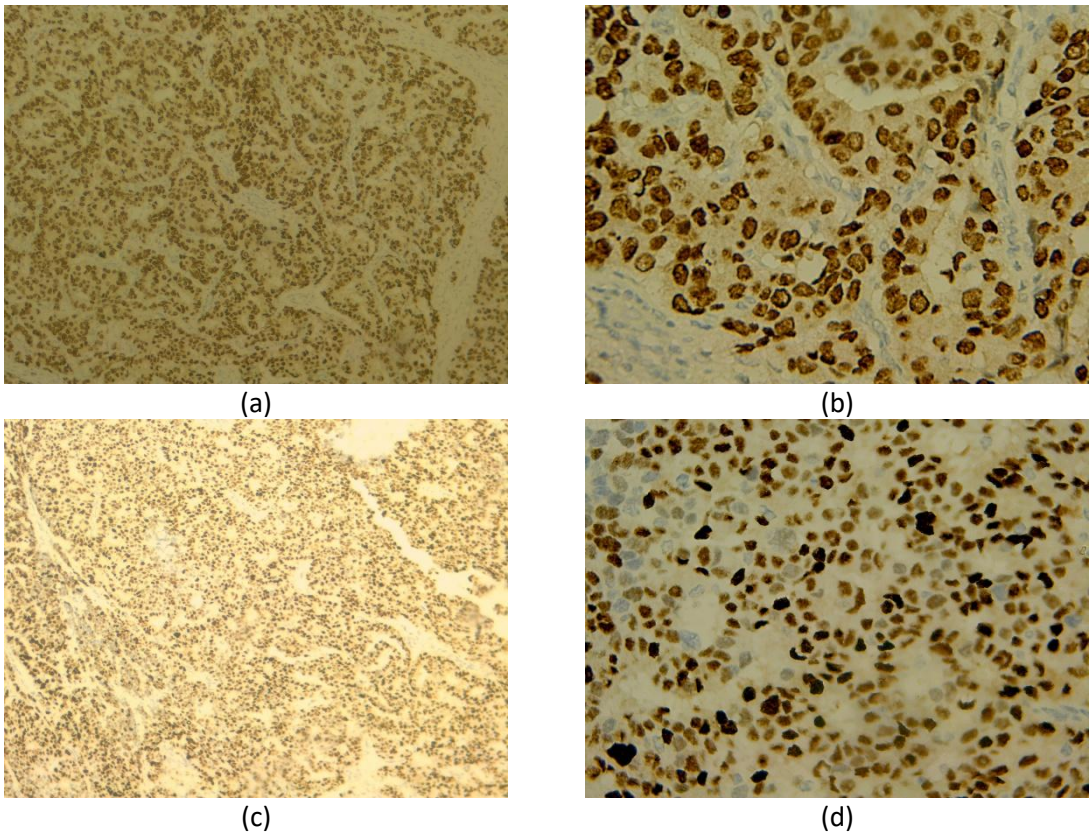
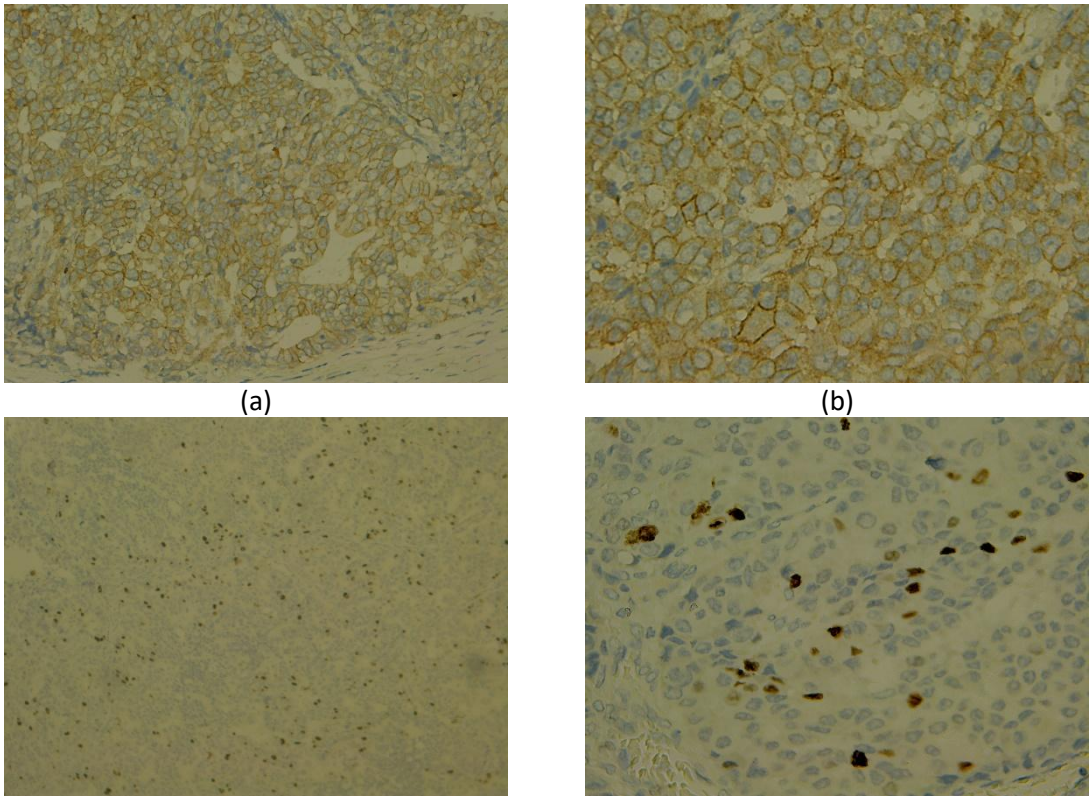


Figure 3. Immunohistochemical smears of male breast cancer
(a) IHC ER smear 100x magnification (b) IHC ER smear 400x magnification (c) IHC PR smear 100x magnification (d) IHC PR smear 400x magnification.
(Source: author's documentation)

HER2 immunostaining scored 3+, reflecting gene amplification and suggesting a more aggressive phenotype with poor prognosis if untreated. HER2 overexpression necessitates anti-HER2 therapies like trastuzumab alongside endocrine or chemotherapeutic agents. Ki-67

staining revealed 30% nuclear positivity, indicating intermediate-to-high proliferative activity, associated with increased recurrence risk and justifying inclusion of chemotherapy. HER2 and Ki-67 staining patterns (Figure 3) support this aggressive profile.



(a) (b)

(c) (d)

Figure 4. Immunohistochemical smears of male breast cancer
(a) IHC HER2 smear 100x magnification (b) IHC HER2 smear 400x magnification (c) IHC Ki67 smear 100x magnification (d) IHC Ki67 smear 400x magnification.
(Source: author's documentation)

The molecular profile—ER/PR positive, HER2 3+, Ki-67 30%—classifies the tumor as Luminal B-like (HER2-positive). This subtype exhibits variable PR and Ki-67 expression, high histological grade, and greater aggressiveness than Luminal A [7]. Patients with Luminal B breast cancer are often older and more likely to present with axillary lymph node involvement, consistent with Mr. W's advanced nodal metastasis (19/19 nodes).

Luminal B breast cancer includes two subtypes: HER2-positive and HER2-negative. The HER2-positive subtype (as in Mr. W) is ER/PR/HER2-positive with variable Ki-67. In contrast, the HER2-negative subtype lacks HER2 expression but has either high Ki-67 (≥14%) or low PR (<20%) [9]. Luminal B tumors typically exhibit higher proliferation and worse prognosis than Luminal A. Low PR expression and elevated Ki-67 in Luminal B are linked to growth factor pathway activation and reduced tamoxifen responsiveness.

Mr. W's tumor characteristics—high ER (90%), PR (85%), HER2 3+, and Ki-67 30%—confirm a Luminal B-like (HER2-positive) classification. High ER/PR indicates hormone sensitivity and good endocrine therapy response [10], while HER2 positivity signifies aggressive growth requiring trastuzumab [4]. A high Ki-67 index reflects elevated proliferation and supports chemotherapy inclusion [5].

The tumor's biological aggression is underscored by its histological grade (III), mitotic activity, and complete lymph node involvement. Poor differentiation and high mitotic rate suggest rapid tumor progression and high metastatic risk. Although ER/PR positivity usually

indicates a favorable prognosis, this is offset by HER2 overexpression and Ki-67 elevation, necessitating combined endocrine, HER2-targeted, and chemotherapeutic strategies.

Comparatively, MBC generally shows higher hormone receptor positivity and lower HER2 amplification than female breast cancer. Mr. W's case is atypical due to its simultaneous ER/PR positivity and HER2 amplification—features more common in female Luminal B tumors [7]. Additionally, Ki-67 levels in MBC are usually lower; thus, Mr. W's 30% index reflects atypical, aggressive tumor biology. Invasive NST remains the dominant histological subtype in both sexes, though men often present with more advanced disease, as seen in Mr. W.

Etiologically, MBC is influenced by hormonal imbalances—elevated estrogen from liver disease, obesity, or estrogen-secreting tumors—genetic mutations (e.g., BRCA2, CHEK2, PALB2), radiation exposure, estrogen therapy, alcohol use, and advanced age. Mr. W's older age is consistent with the epidemiology of Luminal B tumors, which are more frequent in elderly patients [8]. While family history was not documented, it remains a significant risk factor, particularly with BRCA2 involvement.

Overall, Mr. W's tumor is a high-grade Luminal B-like (HER2-positive) invasive NST carcinoma, displaying aggressive features such as high histological grade, HER2 amplification, elevated Ki-67 index, and widespread lymph node metastasis. These factors necessitate a multimodal approach—endocrine therapy, chemotherapy, and HER2-targeted agents—to optimize clinical outcomes.

Endocrine therapy is standard for hormone receptor–positive Luminal B breast cancer. However, HER2 expression and high Ki-67 may reduce its effectiveness, indicating the need for combination strategies. Resistance to endocrine therapy can occur, especially in tumors with aggressive features, leading to poorer prognosis. Thus, understanding the prognostic implications of HER2 and Ki-67 is essential for tailoring treatment in Luminal B breast cancer [111].

CONCLUSION

Breast cancer cases in men are rare, with an incidence of approximately 1 case per 100,000 people per year. However, there is an increasing incidence trend of 1.1% per year. This study highlights the importance of using immunohistochemical techniques in the diagnosis and management of breast cancer in men. In the case studied, a 79-year-old man was diagnosed with NST grade III invasive carcinoma breast cancer after undergoing extended mastectomy surgery. Histopathology and immunohistochemical examination showed positive expression for estrogen receptor (ER), progesterone receptor (PR), and HER2, as well as a high Ki67 index, identifying the tumor as Luminal B-like subtype (HER2 Positive).

These results confirm that breast cancer in men has clinical and biological characteristics that can differ from breast cancer in women, and the need for a tailored treatment strategy based on the molecular profile of the tumor. The use of immunohistochemical techniques may prove important in supporting prognosis prediction and more effective and personalized treatment planning. Further research is needed to understand the characteristics and management of breast cancer in men, which is increasing in incidence.

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