Indonesian Journal of Medicine (2026),11(02): 93-104
Masters Program in Public Health, Universitas Sebelas Maret

Case report
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The Diagnostic and Therapeutic Challenges of A Progressive Male Breast Cancer with Brain Metastases: A Case Report

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Received: 29 January, 2026; Accepted: 07 February, 2026; Available online: 10 April, 2026

ABSTRACT

Background: Male breast cancer (MBC) is a rare malignancy that is often associated with advanced stages and poor prognosis due to lack of public awareness and early screening, along with stigmatization of the disease. Aims: This case report aims to highlight the diagnostic and therapeutic challenges of rapidly-progressive MBC in resource-limited healthcare, particularly those compounded by systemic and patient-attributable delays, and emphasize the importance of prevention and early detection of breast cancer in the male population.

Subject report: We report the case of a 71-year-old man with a three-month history of a progressively enlarging lump on right breast, weight loss, and right-sided hemiparesis. Medical history included chronic heart failure, dyslipidemia, heavy smoking, and labour work background. The diagnosis of invasive ductal breast carcinoma was established through clinical assessment, imaging, and biopsy.

Results: The patient underwent primary tumor resection (PTR) in the form of radical mastectomy, where the main purpose was tumor debulking, revealing tumor invasion into the pectoralis major muscle (pT4 disease). The clinical course was severely impacted by Treatment Delay, encompassing Provider Delay and Patient Delay, which was caused by logistical, operational, and policy barriers. This delay critically postponed the scheduled non-contrast computed tomography (CT) of the head. The delayed CT subsequently revealed multiple metastases. The patient was then referred for immunohistochemistry (IHC) evaluation and systemic therapies but passed away before the scheduled workup due to a declining neurological state from confirmed brain metastases.

Conclusion: This case underscores how the challenges of rapidly progressive MBC with brain metastases, combined with a variety of delays and constrained treatment options, resulted in a poor outcome. It highlights the critical need for increased awareness, stigma reduction, and streamlined resource pathways to improve early detection and timely intervention in resource-limited settings.

Keywords: Breast cancer, Male, Treatment Delays, Metastases

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Cite this as:
Hamdani FM, Putra B, Afnan A (2026). The Diagnostic and Therapeutic Challenges of A Progressive Male Breast Cancer with Brain Metastases: A Case Report. Indones J Med. 11(02): 93-104. https://-doi.org/10.26911/theijmed.2026.927

BACKGROUND

Breast carcinoma is one of the most prevalent malignancies worldwide and a leading cause of cancer-related mortality in women, with an estimated 2.3 million new cases and over 670,000 deaths in 2022 (Katsura et al., 2022). In Indonesia, breast cancer is the most common malignancy among women (42.1 cases per 100,000), while male breast cancer (MBC) accounts for only about 1% of cases (Khare et al., 2024). National data indicates that Central Java has

a particularly high burden of disease, with over 11,000 recorded sufferers. The estimated incidence of new cases in developing countries continues to rise, yet mortality rates remain disproportionately high compared to developed nations. This disparity is largely attributed to the prevalence of misinformation within the community, which leads to significant delays in patients seeking care at health facilities (Agustina & Barokah, 2019).

The development of breast cancer is stimulated by interactions of genetic, environmental, and hormonal factors. Key risk factors include advanced age, family history, smoking, and a lack of regular physical activity (Ketaren et al., 2021). Smoking has also been correlated with increased recurrence rate of breast cancer (Alkhaifi et al., 2022).

Specifically, increased body weight or a high Body Mass Index (BMI) has been shown to raise the risk of various cancers by up to 30% (Agustina & Barokah, 2019). The exact etiology of male breast cancer remains elusive, although it is strongly associated with high-risk factors such as hormonal imbalances, Klinefelter syndrome, chronic liver disease, and prior chest radiation. Furthermore, significant predispositions include a strong family history of breast or ovarian cancer and specific genetic mutations (Khan and Tirona, 2021). Beyond lifestyle risk factors, an elevated incidence of male breast cancer has been observed among workers in the plastics industry, potentially linked to chronic exposure to endocrine-disrupting chemicals (Landrigan et al., 2023).

Breast cancer results from disruption in the balance between oncogenes and tumor suppressor genes, where the expression of estrogen (ER) and progesterone receptors (PR) in the cell nucleus is vital for normal epithelial growth and response to hormonal therapy (Alharbi et al., 2022). The overexpression of the HER2 (ERBB2), an oncogene which significantly affects cell proliferations alongside mutations in the BRCA1 and BRCA2 suppressor genes, leads to uncontrolled cell proliferations (Gradishar et al., 2022; V. Kumar et al., 2022). These complex interactions broadly classify pathophysiological pathways based on their ER status. The common ER-positive pathway is categorized by HER2 presence, while the aggressive ER-negative pathway often lacks all three primary receptors, resulting in triple-negative breast cancer (Abeloff et al., 2020).

Most male cases follow the ER-positive pathway, progressing from initial changes like flat epithelial atypia to ductal carcinoma in situ (DCIS). Because of the near-universal expression of ER in roughly 80% of male cases, the vast majority of patients are eligible for targeted hormone therapy (Al-Fehaid, 2023). Consequently, the accurate and timely confirmation of full receptor status via immunohistochemistry (IHC) is an absolute necessity for guiding these therapeutic options (Kim et al., 2022; Rivera et al., 2017).

Systematic efforts in early diagnosis and screening remain essential to improve the overall "life sustainability" of breast cancer survivors (Ketaren et al., 2021). However, a primary driver of late-stage presentation in the Indonesian context is the pervasive spread of misinformation within the community (Wati et al., 2019). Worse prognosis in males is frequently associated with advanced stages and poor prognosis due to limited public awareness and lack of early screening, and persistent stigmatization of the disease (Alfaini et al., 2024). Clinical course is impacted by a multifaceted Treatment Delay, encompassing both Provider Delay and Patient Delay driven by a complex interplay of logistical, operational,

and policy barriers (Gondhowiardjo et al., 2021). Such failures within the diagnostic pathway are directly associated with the initiation of suboptimal treatment regimens and significantly worse survival outcomes (Stephens et al., 2023). Crucially, these cumulative delays can transform a typically slow-growing, receptor-positive malignancy into a rapidly-progressive disease that outpaces standard therapeutic interventions (Hutajulu et al., 2022).

This case report aims to highlight the diagnostic and therapeutic challenges of rapidly-progressive MBC in resource-limited healthcare settings and to emphasize the importance of prevention and early detection of breast cancer in men.

CASE PRESENTATION

A 71-year-old male laborer presented with a progressively enlarging right breast mass over three months, accompanied by intermittent pain, unintentional weight loss of 10 kg, and progressive right-sided weakness. His medical history included chronic heart failure and dyslipidemia. He had no family history of malignancy but reported a 30-year history of smoking.

Examination revealed a firm, mobile, ill-defined 10 × 10 × 8 cm was identified in the right breast, with ipsilateral axillary lymphadenopathy. Neurological examination showed right-sided hemiparesis with upper motor neuron (UMN) signs. Labs indicated mild anemia and leukocytosis. Chest X-ray demonstrated cardiomegaly and a right chest wall lesion. Non-contrast computed tomography (CT) of the head was delayed due to unavailability and logistical constraints. An initial incisional biopsy confirmed high-grade invasive ductal carcinoma.

The patient subsequently underwent a primary tumor resection (PTR) in the form of right radical mastectomy for debulking and symptom relief. Intraoperatively, the tumor was found to be adherent to the chest wall with costal invasion, consistent with pathological T4 (pT4) disease. Histopathology from the mastectomy confirmed the definitive diagnosis of invasive ductal carcinoma, with the additional and critical feature of neuroendocrine differentiation. Although resection margins were clear, the deep base margin remained tumor-involved, correlating with intraoperative findings. IHC was subsequently ordered, necessitating external referral due to lack of in-house capacity. Postoperatively, the patient's recovery was initially stable under supportive therapy, after which he was discharged home and referred for adjuvant chemotherapy, radiotherapy, and neurological follow-up.

Figure 1. Macroscopic view of the tumor debulking specimen following radical mastectomy

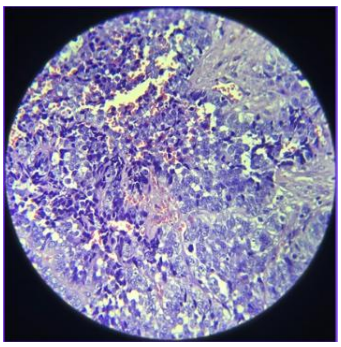

Figure 2. Histopathological section of the tumor at 100x magnification confirming invasive ductal carcinoma

In the following days, the patient's condition worsened with neurological decline, cranial mass development, and poor oral intake. CT confirmed multiple intracranial metastases with perilesional edema and midline shift. Planned systemic therapy was not initiated, and the patient died approximately five weeks postoperatively. Family education emphasized reducing stigma through gender-neutral communication.

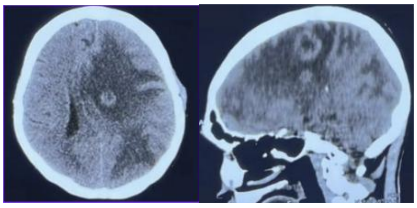

Figure 3. Axial and Sagittal slices of non-contrast head CT scan showing multiple metastatic lesions with significant perifocal edema causing midline shift to the right

DISCUSSION

This case report describes the clinical course of a rare occurrence of MBC, highlighting the diagnostic and therapeutic challenges encountered in a resource-limited setting. Breast cancer is often perceived as a "female disease" contributing to delayed medical consultation and advanced-stage diagnosis in men (Midding et al., 2018). In Indonesia, treatment delay is a significant and complex problem. To effectively analyze this issue, delays are typically categorized into Patient Delay (time from symptom to initial consultation or diagnosis to definitive treatment) and Provider Delay (which includes System Delay and Physician Delay). Our patient experienced both types of delay (Gondhowiardjo et al., 2021).

The patient's symptoms duration was three months, and while time-to-presentation can vary widely between 1 to 120

months, (Co et al., 2020) a major factor contributing to such delays in our context is the lack of public knowledge, and specifically in MBC, the stigma associated with discussing a "female disease", is visible in our case, and classified as patient delay (Midding et al., 2018).

Advanced age remains a significant risk factor, with the mean age of onset being approximately 70 years (AlFehaid, 2023; Fentiman, 2022). MBC is rarely observed in younger individuals; however, older findings have documented its relatively small crowd occurrence in this age group (Li et al., 2018; Madeira et al., 2011). The patient also presented with other significant risk factors, including a history of smoking for over 30 years, which has been associated with an increased risk of breast cancer and disease recurrence (Alkhaifi et al., 2022).

Occupational exposure, while not clearly implicated in construction work, has been suggested in other industries such as plastics, pointing to a possible role of environmental factors in the pathogenesis of male breast cancer. Further researches are needed to investigate the impact of significant chemical or radiation exposure in construction and agricultural settings on the development of MBC (Chen et al., 2023).

Physical examination revealed a firm, mobile breast mass 10 × 10 × 8 cm was palpated, accompanied by ipsilateral axillary lymphadenopathy. While mobility might suggest a less advanced local stage, the lymph node involvement raised concern for systemic spread. The patient's right-sided hemiparesis with UMN signs was a critical finding, primarily raising high suspicion for brain metastasis from the breast cancer (Emos & Rosner, 2023). Stroke was also considered, given the malignancy-associated prothrombotic state and history of heart failure, the possibility of systemic dissemination remained high (Doehner et al., 2023).

A routine chest X-ray was performed in our case, and while it can assist in assessing pulmonary invasion, bone destruction, or a possible osseous origin of the tumor, a thoracic CT scan offers greater sensitivity in confirming these findings (Mattei & Chang, 2022). Several cases have demonstrated normal chest X-ray findings in patients with breast carcinoma (Kim et al., 2022; Sari et al., 2023).

Preoperative imaging workup was ultimately incomplete due to limitations in diagnostic facilities; specifically, mammography was unavailable at our hospital and therefore could not be conducted. While breast ultrasonography was available, it was intentionally omitted. Based on clinical findings a firm, mobile mass with palpable axillary nodes the lesion's mobility suggested a lower stage (T2 or T3) that could be adequately managed with primary surgery, allowing clinical judgment to deem these findings sufficient to proceed directly to incisional biopsy to expedite the definitive tissue diagnosis.

This approach is supported by the National Comprehensive Cancer Network (NCCN) Basic Resources Framework, which encourages moving directly to biopsy when clinical suspicion is high and essential imaging, such as mammography, is lacking in a low-resource environment (R. Kumar et al., 2024). This operational decision prioritizes minimizing the time-to-diagnosis, a factor validated by a retrospective study which found that this occurrence was not uncommon, with 76% of evaluated patients diagnosed without prior imaging, reflecting historical clinical practices in non-screening and low-resource settings (Mathew et al., 2008).

The definitive diagnosis of invasive ductal carcinoma was established through histopathological examination of a sample obtained via incisional biopsy. Several reports of MBC describe the use of incisional biopsy in settings with limited resources, where fine needle aspiration or core needle biopsy was not available as in our case (Sari et al., 2023). The use of incisional biopsy was in accordance with the older NCCN basic resources guidelines (Silva et al., 2023).

IHC was recommended by the pathology report, but the unavailability of in-house IHC testing for these essential biomarkers mandated external referral, initiating a Provider Delay. This logistical barrier directly triggered a System-Diagnosis-Delay and consequently impacted the System-Treatment-Delay. A retrospective observational study of breast cancers showed 64.7% patients had diagnosis delay, and subsequently increased the likelihood of presentation with a more advanced stage of disease (Hutajulu et al., 2022).

Given the patient's advanced symptoms and potential diagnostic delays in confirming systemic metastasis, the decision was made to perform PTR to reduce tumor burden. This prioritization of urgent local control over administrative sequencing is categorized as Physician Delay. Accordingly, a radical mastectomy was performed with the primary goal of tumor debulking.

The concept of debulking, or cytoreductive surgery, refers to the removal of as much tumor mass as possible and involves an intentional incomplete resection in cases of unresectable malignant tumors (Wu et al., 2024). In our case, the approach was considered with symptomatic intent, aiming to reduce local disease progression while maintaining cost-effectiveness. Evidence regarding PTR in MBC remains very limited and controversial across studies. A randomized controlled trial with a 10-year follow-up demonstrated a survival benefit in patients with stage IV breast cancer and bone-only metastases who received systemic therapy combined with PTR, compared to systemic therapy alone (Soran et al., 2018).

Consistent findings were reported in the Eastern Cooperative Oncology Group and the American College of Radiology Imaging Network (ECOG-ACRIN) E2108 trial, where quality of life did not significantly improve, but local disease progression was reduced. However, no overall survival benefit from PTR was observed, suggesting that the procedure may primarily serve as local or palliative control (Khan et al., 2022).

Several indications for PTR were recommended by meta-analysis for selected patients such as those with oligometastatic disease or a low metastatic burden. In this case, the metastatic status was retrospectively determined using a head CT scan, while comprehensive imaging to assess metastases in other sites was not performed (Wu et al., 2024). Tumor debulking itself carries potential benefits in terms of cost-effectiveness. Systematic review on palliative care in cancer patients concluded that palliative care is significantly less expensive. However, further research on cost-effectiveness should be conducted in larger populations (Arabshahi et al., 2022).

A non-contrast head CT scan was performed postoperatively to investigate the neurological signs observed during the physical examination. This initial workup was critical for differentiating between alternative diagnoses, such as a chronic infarction (given the hemiparesis onset exceeding two weeks), and providing a

baseline for subsequent, more definitive contrast-enhanced imaging required for metastatic assessment (Nowinski, 2024). While the NCCN guidelines favor contrast-enhanced brain MRI, contrast-enhanced brain CT remains an acceptable alternative for diagnosing brain metastases, particularly in resource-limited settings (Gradishar et al., 2022).

In this case, a non-contrast head CT scan was initially scheduled in the outpatient setting following the standard hospital referral pathway. However, the diagnostic process was immediately compromised, initiating a System Diagnosis Delay. This delay occurred when operational limitations of the CT scanner in our facility necessitated redirection to an affiliated private hospital.

This change further complicated the administrative process, requiring a different reimbursement system, (Santoso, 2024) instead of the standard Indonesia Case Based Groups (INA CBG) service billing system under the Indonesian National Health Insurance system (BPJS Kesehatan) (Tamburaka et al., 2024).

These combined technical and complex policy barriers, all of which exemplify the System Diagnosis Delay, ultimately postponed the CT scan. The examination was then scheduled 16 days post-hospitalization, but was further delayed by an additional 11 days because the patient's family had a limited understanding of the complex referral system, compounded by logistical constraints. This failure in compliance is classified as Patient Delay. A qualitative study highlighted that a lack of patient and family knowledge is a critical factor contributing to diagnostic delays in cancer care (Gondhowiardjo et al., 2021). Despite this prolonged workup, the overall duration remained within the timeframes suggested by the Breast Health Global Initiative (less than 60 days from initial breast cancer diagnosis) and the recommendation from the Union for International Cancer Control (UICC) alongside the American Joint Committee on Cancer (AJCC), where definitive metastasis diagnosis is recommended within 4 months (Brierley et al., 2025; El Saghir et al., 2011).

While these treatment delays complicated care, the patient's rapidly aggressive clinical course likely reflects a challenging underlying tumor biology. While most ductal tumors are typically ER/PR-positive, highly aggressive ER/PR-negative or triple-negative subtypes are known for poorer outcomes and limited therapeutic options (Kesireddy et al., 2024).

The critical IHC workup was significantly delayed and ultimately unobtainable, a failure in the diagnostic pathway associated with suboptimal treatment and worse survival (Stephens et al., 2023). Consequently, definitive systemic therapy and radiotherapy could not be initiated prior to the patient's decline. This delay in treatment initiation, even by a short duration, has been quantitatively linked to a significant increase in the risk of cancer mortality across surgical, systemic, and radiation treatment indications (Hanna et al., 2020).

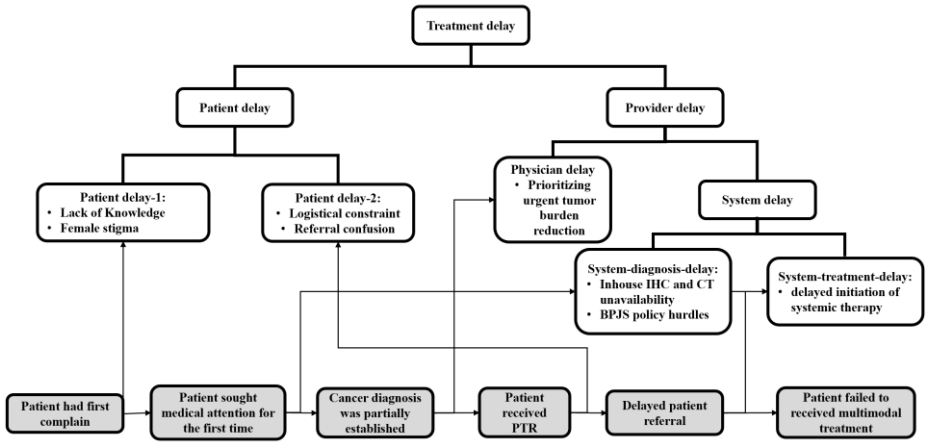

Figure 4. Analysis summary of Treatment Delay's classification in an MBC Patient (Adapted from Gondhowiardjo et al. (2021)) (Co et al., 2020; Gondhowiardjo et al., 2021; Hutajulu et al., 2022)

Despite the patient's grim outcome, a structured preventive education program was delivered to his family to proactively mitigate future risk. Given that MBC remains rare and disease-specific prevention is limited, the intervention was focused on early detection and risk awareness. Genetic counseling and routine screening were strongly recommended for all family members, regardless of prior oncological history, as genetic mutations are a key risk factor for MBC (Pensabene et al., 2022).

A major focus of the counseling was addressing the feminine disease stigma surrounding MBC (Midding et al., 2018). (Awareness campaigns and materials typically exclude men, which inadvertently leads to delayed recognition and care-seeking. To counter this, the family was educated on the importance of gender-neutral health communication (Zhao et al., 2025). There is also the urgent need of advocating for awareness materials such as brochures, websites, etc. to explicitly include men and avoid "pink-only" visuals (Midding et al., 2018). Psychosocial support was emphasized as a means to counter the perception that discussing breast symptoms is a sign of weakness, which often leads men to delay medical consultation. Furthermore, proactive encouragement and emotional support from family members, particularly spouses, are crucial for reducing care-seeking delays, improving treatment adherence, and promoting mental well-being while normalizing these health discussions in men (Co et al., 2020).

This case highlights the challenges of a progressive male breast cancer with brain metastases, demonstrating how systemic diagnostic failures and resource constraints precluded planned multimodal therapy, leading to a poor outcome. To mitigate such fatal delays, greater awareness and stigma reduction are essential for earlier detection and intervention, as is streamlining BPJS-mandated resource pathways to ensure timely specialized care.

AUTHORS CONTRIBUTION

Fakhriel Muhammad Hamdani oversaw clinical management and surgical intervention, while Benaya Putra and Alvin Afnan performed data collection and manuscript drafting. All authors contributed to the literature review, critical revision of the intellectual content, and final approval of the manuscript.

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FINANCIAL SUPPORT AND SPONSORSHIP

There was no external fund.

ACKNOWLEDGEMENT

The authors would like to thank the patient's family for their cooperation and for providing informed consent to share this clinical case for medical education. We also express our gratitude to the nursing and surgery staff at 45 Kuningan General Hospital for their dedicated care during the patient's hospitalization and postoperative recovery

CONFLICT OF INTEREST

There are no conflicts of interest

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