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Bone Metastasis Disease from Mucinous Carcinoma of the Breast: A Rare Case Report with Immunohistochemical Confirmation

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Abstract

Background: Mucinous carcinoma of the breast (MCB) is a rare histological subtype of invasive breast cancer, comprising 1-7% of all breast carcinomas. It is generally associated with a favorable prognosis due to its indolent course and low metastatic potential. However, distant metastases, including to the bone, are exceptionally rare and pose diagnostic and therapeutic challenges. **Case Presentation**: We present a case of a 64-year-old woman with a history of MCB who developed progressive back pain and lower limb weakness. MRI showed multiple osteolytic lesions with spinal cord compression. A CT-guided biopsy confirmed metastatic mucinous carcinoma, and immunohistochemical (IHC) staining demonstrated GATA3 positivity, confirming breast origin. The patient received denosumab, aromatase inhibitors, and palliative radiotherapy. **Conclusion**: This case highlights the importance of considering bone metastases in patients with a history of MCB presenting with skeletal-related events. IHC, particularly GATA3, is crucial in confirming the metastatic origin and guiding targeted treatment strategies.

Keywords— Mucinous breast carcinoma, bone metastasis, immunohistochemistry, GATA3, skeletal metastases

Abstrak

Latar Belakang: Karsinoma musinosa payudara (MCB) adalah subtipe histologis langka dari kanker payudara invasif, meliputi 1-7% dari semua karsinoma payudara. Umumnya dikaitkan dengan prognosis yang baik karena perjalanannya yang lamban dan potensi metastasis yang rendah. Namun, metastasis jauh, termasuk ke tulang, sangat jarang dan menimbulkan tantangan diagnostik dan terapeutik. **Presentasi Kasus:** Kami menyajikan kasus seorang wanita berusia 64 tahun dengan riwayat MCB yang mengalami nyeri punggung progresif dan kelemahan tungkai bawah. MRI menunjukkan beberapa lesi osteolitik dengan kompresi sumsum tulang belakang. Biopsi yang dipandu CT mengonfirmasi karsinoma musinosa metastatik, dan pewarnaan imunohistokimia (IHC) menunjukkan positifnya GATA3, yang mengonfirmasi asal payudara. Pasien menerima denosumab, inhibitor aromatase, dan radioterapi paliatif. **Kesimpulan:** Kasus ini menyoroti pentingnya mempertimbangkan metastasis tulang pada pasien dengan riwayat MCB yang datang dengan kejadian terkait rangka. IHC, khususnya GATA3, sangat penting dalam mengonfirmasi asal metastasis dan memandu strategi pengobatan yang ditargetkan.

Kata kunci— Karsinoma payudara musinosa, metastasis tulang, imunohistokimia, GATA3, metastasis tulang

I. INTRODUCTION

Breast cancer remains the most prevalent malignancy among women, accounting for nearly 2.3 million cases worldwide in 2020, with an estimated 685,000 deaths (WHO, 2021). While bone metastases are frequently observed in breast cancer, primarily from invasive ductal carcinoma, mucinous carcinoma of the breast (MCB) is an uncommon histological subtype, comprising approximately 2% of all breast cancers [1]. Unlike other subtypes, MCB has a relatively better prognosis, attributed to its distinct histopathological characteristics and typically low metastatic potential.[2-3]

Despite its indolent nature, distant metastasis from MCB, particularly to the bone, has been documented in rare instances. The low propensity for metastasis in MCB is hypothesized to be due to its abundant extracellular mucin production, which may act as a physical barrier against vascular and lymphatic invasion,[4] However, in cases where metastasis does occur, diagnostic and therapeutic challenges arise, given that mucinous tumors can resemble other primary mucin-producing malignancies, such as those from the gastrointestinal tract or lungs.[5] This necessitates the use of immunohistochemical markers, such as GATA3, which plays a crucial role in confirming breast origin and differentiating MCB from other mucinous carcinomas[6]

Clinically, bone metastases from MCB can lead to significant skeletal complications, including pathologic fractures, spinal cord compression, and severe pain, impacting both prognosis and quality of life. Given the rarity of such cases, this report aims to highlight the diagnostic complexities and therapeutic considerations in managing bone metastases from MCB, emphasizing the role of histopathology, immunohistochemistry, and multidisciplinary treatment approaches. Understanding such rare presentations is essential to improving early recognition and personalized management strategies in clinical practice.[2]

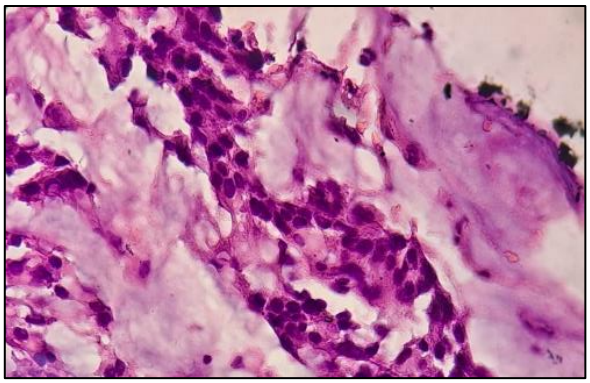
This report presents a rare case of bone metastasis from mucinous carcinoma of the breast in a 64-year-old woman, discussing its clinical implications, histopathological features, and the utility of immunohistochemical markers such as GATA3 in confirming the tumor's origin.

II. CASE PRESENTATION

A 64-year-old woman presented with progressive back pain and lower limb weakness for six months. She had a history of mucinous carcinoma of the left breast, diagnosed three years prior, for which she underwent a modified radical mastectomy followed by adjuvant chemotherapy. At the time of initial treatment, there was no evidence of metastasis.

Magnetic resonance imaging (MRI) of the spine revealed multiple osteolytic lesions involving the thoracic vertebrae with evidence of spinal cord compression. A bone scan demonstrated widespread skeletal involvement. A CT-guided biopsy of the affected vertebra was performed.

Microscopic examination of the bone biopsy revealed clusters of malignant epithelial cells floating in abundant extracellular mucin, consistent with metastatic mucinous carcinoma (Fig 1). Immunohistochemical staining demonstrated positivity for estrogen receptor (ER), progesterone receptor (PR), CK7, and GATA3, confirming the breast origin. The tumor was negative for HER2 and CK20, ruling out gastrointestinal and pulmonary mucinous tumors. (Fig 2)



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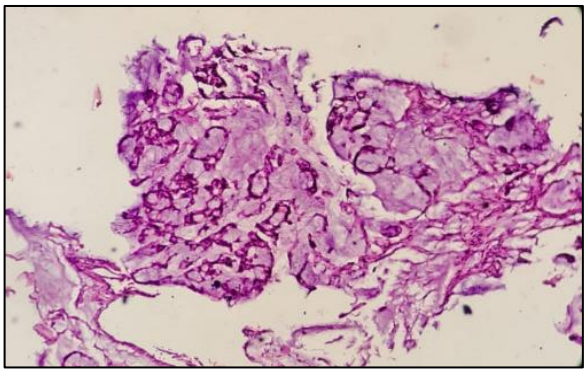

b

FIG 1. A,B MICROSCOPIC IMAGE HE WITH 400X MAGNIFICATION, SHOWS THE PRESENCE OF GROUPS OF MUCINOUS CARCINOMA CELLS BETWEEN THE BONE SQUESTERS

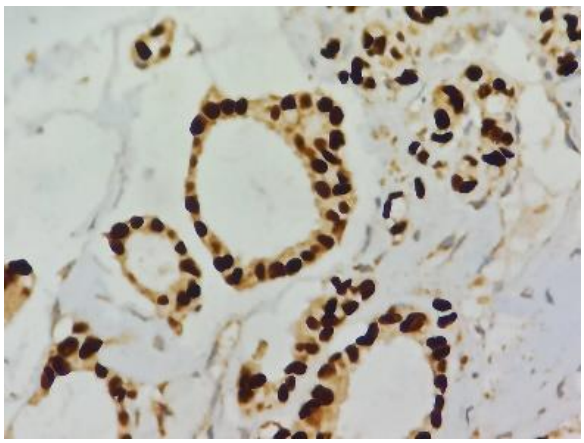

FIG 2. MICROSCOPIC PICTURE WITH POSITIVE IHK GATA 3 STAINING, VISIBLE BROWN STAINING ON THE TUMOR CELL MEMBRANE

III. DISCUSSION

Mucinous carcinoma of the breast (MCB) is a rare histological subtype known for its low metastatic potential and indolent course. Despite its favorable prognosis, distant metastasis, including bone involvement, has been reported, although infrequently [5]. Metastatic MCB represents a diagnostic and therapeutic challenge, particularly in distinguishing it from mucinous tumors of gastrointestinal or pulmonary origin. This case underscores the complexity of metastatic MCB, its clinical management, and long-term outcomes.[2]

Despite its generally indolent nature and favorable prognosis, MCB can, in rare cases, present with distant metastases, posing a diagnostic challenge. Bone is a frequent site of metastasis, even in MCB, as illustrated in the cases presented. The expression of hormone receptors (ER and PR) and the absence of HER2 overexpression align with typical MCB profiles, reinforcing the role of IHC in distinguishing metastatic breast lesions from other mucinous carcinomas, such as those of gastrointestinal or pulmonary origin[7]

The present case highlights the complexity of managing metastatic MCB. While chemotherapy and radiation remain options for more aggressive disease, palliative care with bone-modifying agents like denosumab plays a crucial role in alleviating symptoms and preventing skeletal-related events. The presence of bone metastasis, despite the tumor's mucinous component — often thought to act as a physical barrier to invasion — suggests that certain biological mechanisms in MCB might facilitate distant spread, warranting further molecular investigation[8]

These findings emphasize the need for personalized treatment strategies, combining histopathological evaluation with molecular profiling, to optimize patient outcomes in rare cases of metastatic MCB.

PATHOPHYSIOLOGY OF BONE METASTASIS

Breast cancer metastasizes to bone via hematogenous dissemination, adhering to the

"seed and soil" hypothesis proposed by Paget (1889). Tumor cells (seeds) preferentially colonize the bone microenvironment (soil), where they interact with osteoclasts and osteoblasts, leading to osteolytic lesions. The RANK/RANKL pathway is pivotal in this process, as RANKL activation promotes osteoclast differentiation, facilitating bone resorption and tumor progression.[9]

Bone metastases occur through hematogenous dissemination, where tumor cells interact with the bone microenvironment via the RANK/RANKL pathway. RANKL, expressed by osteoblasts, binds to RANK receptors on preosteoclasts, stimulating osteoclastogenesis and bone resorption. Mucinous carcinoma cells may exploit this pathway, leading to osteolytic metastases. Targeting RANKL with denosumab inhibits osteoclast activation, reducing bone turnover and metastatic progression.[9-10]

TREATMENT CONSIDERATIONS

Upon diagnosis of metastatic mucinous carcinoma, the following treatment strategies were initiated :

- Bone-Targeted Therapy: Denosumab, a RANKL inhibitor, was administered to prevent further skeletal-related events.
- Systemic Therapy: Aromatase inhibitors were prescribed due to the patient's ER+/PR+ status.
- Radiotherapy: Palliative radiation was delivered to the thoracic spine to relieve pain and mitigate spinal cord compression risk.
- Pain Management: Opioid analgesics and physical therapy were introduced to improve mobility and quality of life.

Denosumab was chosen over bisphosphonates in this case due to its superior efficacy in inhibiting osteoclast-mediated bone destruction and its rapid onset of action compared to bisphosphonates. Denosumab directly targets the RANKL pathway, preventing osteoclast activation and thereby reducing bone turnover and metastatic progression.[11] Clinical studies have shown that denosumab is more effective in preventing skeletal-related events (SREs), such as fractures and spinal cord compression, particularly in patients with bone metastases from breast cancer. Additionally, denosumab is administered subcutaneously, offering a more convenient option and avoiding the renal toxicity risks associated with bisphosphonates. These advantages make denosumab the preferred choice for patients with metastatic mucinous carcinoma involving the bone, particularly in hormone receptor-positive cases where long-term bone preservation is critical for maintaining quality of life.[12]

PROGNOSTIC FACTORS IN METASTATIC MCB

The prognosis of metastatic MCB depends on several key factors. Hormone receptor status, particularly ER+/PR+ tumors, is associated with a more favorable prognosis due to their responsiveness to endocrine therapy. Patients with HER2-negative MCB, like in this case, often experience a less aggressive disease course.[13] The extent of metastasis also plays a crucial role; patients with bone-only metastases generally have better survival rates than those with visceral involvement. Additionally, treatment response significantly influences outcomes, with those receiving denosumab or bisphosphonates demonstrating improved skeletal-related event (SRE) prevention and bone pain relief.[2] The combination of hormonal therapy and targeted bone-directed agents continues to be the cornerstone of effective management, aiming to reduce disease progression and enhance the patient's quality of life.

The findings from this case emphasize the importance of early recognition and accurate diagnosis of metastatic mucinous carcinoma

of the breast, especially in rare cases involving bone metastases. Given the indolent nature of MCB, metastases may present late, often leading to complications such as skeletal-related events and spinal cord compression. The use of immunohistochemical markers like GATA3 is crucial in differentiating metastatic breast carcinoma from other mucinous tumors, ensuring appropriate management strategies are implemented. Additionally, targeting the RANK/RANKL pathway with denosumab provides significant benefits in preventing bone degradation and improving patient quality of life. Long-term survival is achievable with individualized therapy, particularly for hormone receptor-positive patients, reinforcing the need for a multidisciplinary approach in managing metastatic MCB. Continued follow-up and tailored treatment regimens are essential in optimizing patient outcomes and reducing morbidity associated with bone metastases.[3,6]

IV. CONCLUSION

Bone metastasis from mucinous carcinoma of the breast is rare but can cause significant morbidity. This case underscores the importance of correlating clinical, radiological, and pathological findings for accurate diagnosis. Immunohistochemistry, particularly GATA3, plays a crucial role in distinguishing metastatic breast carcinoma from other mucinous neoplasms. Although mucinous carcinoma generally has a favorable prognosis, metastatic cases require comprehensive multidisciplinary management to optimize patient outcomes.

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