

## Case Report

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## Isolated Bone Marrow Metastasis in Metastatic Carcinoma Breast: A Rare and Unique Case

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### ABSTRACT

#### Background

Bone metastasis (BM) accounts for about 65%–75% of metastatic breast cancer (MBC) cases. Unlike BM, symptomatic bone marrow metastasis (BMM) is uncommon in MBC. The reported incidence of BMM is only 0.17% in MBC and 0.6%–1.7% in other solid tumours such as gastric and lung cancer. The extent of bone marrow infiltration leading to BMM manifestations is varied and complex. Diagnosis of BMM primarily relies on bone marrow aspiration smears and biopsies. The lack of specific clinical signs in BMM makes early diagnosis challenging, underscoring the need for expertise in this field. Due to limited data in this area, the appropriate treatment of breast cancer with BMM is not extensively discussed in significant guidelines. Most patients with BMM have hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2–) tumours. The goal is to improve understanding of this disease and provide effective diagnostic and treatment strategies.

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### Introduction

Breast cancer is the most common cancer in women, posing a significant public health issue, with an estimated 2,261,419 new cases (11.7%). Bone metastases are prevalent in breast cancer, accounting for 65–75% of metastatic breast cancer (MBC). However, bone marrow metastasis in MBC is rare, with an incidence of only 0.17%. Bone marrow metastasis (BMM) refers to the spread of malignant tumours from non-hematopoietic tissues to the bone marrow. The cancer cells infiltrate the bone marrow, destroying its structure and leading to hematopoietic disorders, such as repetitive fever, progressive anaemia, and thrombocytopenia. BMMs have complex and diverse clinical manifestations. The current diagnosis of BMM relies mainly on bone marrow aspiration smears and biopsies, with biopsies being more sensitive. Therefore, the early diagnosis of BMM is limited by the lack of specific clinical manifestations and is easily overlooked by clinicians. In the majority of breast cancer cases, bone marrow infiltration is seen simultaneously with bone metastasis. Isolated bone marrow infiltration in the absence of bone metastasis is rarely seen, while in 86% of cases, it is bone metastasis alone. Common presentations include low-grade fever, unexplained anaemia, and pancytopenia. If there is an unexplained reduction in haemogram and thrombocytopenia and unexplained fever without chills among breast cancer patients with bone marrow metastasis, BMM should be suspected. Most patients with BMM have hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2–) tumours.

The metastasis of breast cancer to the bone marrow is not common, and it can be challenging to diagnose early. Bone marrow

metastasis does not have well-established treatment options and poses a significant threat to the survival of patients.

In this report, we discuss a case of isolated bone marrow metastasis and provide a review of the available literature on the clinical features, prognosis, and factors that can affect the prognosis of breast cancer patients with symptomatic bone marrow infiltration.

The prognosis of patients with BMM could be better due to the lack of definitive treatment guidelines.

### Case report

A 41-year-old, normotensive, nondiabetic, premenopausal female presented with a history of a lump in her left breast, which she first noticed a year ago. Her initial biopsy report was inconclusive. She was initially told it was a benign lump, but eight months later, she observed darkening and thickening of the skin in the same breast. Upon evaluation, she was diagnosed with breast cancer and started on Tamoxifen. The mammogram showed a 2.68 x 1.07 x 2.1 cm (BIRADS V) lesion with left axillary lymphadenopathy. A skin biopsy confirmed Invasive ductal carcinoma and revealed ER 8/8, PR 0/8, and Her2neu negative. In June 2024, she presented to our hospital with general weakness, loss of appetite and weight loss, and a history of menorrhagia and polymenorrhoea. On examination, her left breast showed a hard mass involving the whole breast, with fixity to the underlying muscle, overlying skin, and medial distortion of the nipple. Neck examination revealed a firm nodule of size 1.5 x 2 cm, moving with deglutition. Blood reports revealed anaemia and thrombocytopenia. Her ALP and GGT were 129 and 226, respectively.

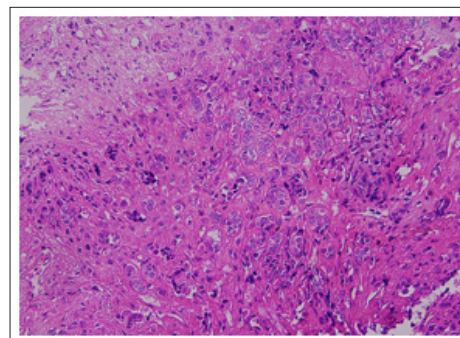
Further evaluation with PET/MRI revealed an FDG-avid left breast mass and diffuse bone marrow lesions involving the entire marrow, suggestive of metastases. Subsequent bone marrow biopsy showed normal haemopoietic cells with metastatic deposits, tumor cells were HR+ and Her-2 neu Negative. She was started on letrozole and abemaciclib, which were chosen based on their efficacy in treating HR+/HER2-tumours and their potential to target bone metastases.

## Discussion

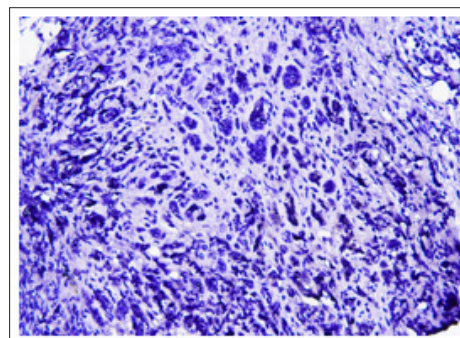
Metastatic breast cancer to the bone marrow (BMM) is a rare condition with a poor prognosis, resulting in haematological disorders and a life expectancy of 6.4–19 months after diagnosis [1]. The specific mechanism of breast cancer BMM is not fully understood, but it has been confirmed that bone marrow adipocytes (BMAs) and adipokines secreted by breast cancer cells play a crucial role in promoting breast cancer metastasis [2]. BMAs release cytokines and adipokines such as leptin, adiponectin, IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and VEGF, which promote breast cancer cell metastasis [3]. Additionally, BMAs can activate dormant mesenchymal stem cells (MSCs) and cancer stem cells (CSCs) to increase their proliferation and promote breast cancer BMM [4].

The literature indicates that the median age of patients with bone marrow metastasis (BMM) is 48 years, ranging from 22 to 75. BMM is primarily observed in invasive lobular carcinomas and is often estrogen receptor-positive, which differs from our case of invasive ductal carcinoma. Most patients with BMM have hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) tumours. Among these patients, 73.1% have HR+/HER2- tumours, 13.4% have HER2+ tumours, and 13.4% have triple-negative tumours, which aligns with our case. Anaemia is a common presentation in cases of BMM, often accompanied by thrombocytopenia or pancytopenia. The diagnosis of BMM can be challenging, and it is often detected after bone marrow involvement in 86.6% of cases.

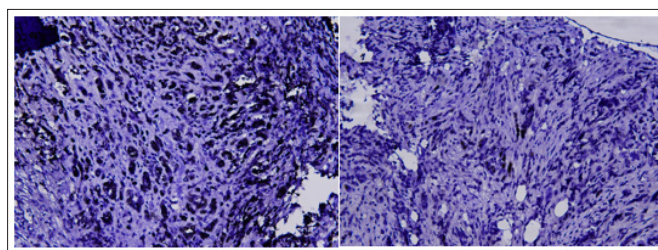
In comparison, the remaining 13.4% are simultaneously diagnosed with bone marrow involvement. In our patient's case, isolated BMM was present. Patients with BMM often experience significant abnormalities in their blood counts, and chemotherapy, which can worsen these abnormalities, poses an increased risk. Tumour invasion causes bone marrow suppression, and the treatment can only briefly improve blood cell levels by destroying tumour cells. Guidelines recommend endocrine therapy as the preferred treatment for patients with advanced HR+ breast cancer unless there are concerns about a life-threatening disease or endocrine resistance. Endocrine therapy and targeted therapy aimed at HR+/HER2- tumours further enhance patient prognoses. Expert consensus suggests that patients with extensive BMM and poor clinical tolerance to chemotherapy could be treated with CDK4/6 inhibitors combined with endocrine drugs. Studies have shown that this combination can significantly improve the survival of hormone receptor-positive breast cancer patients. Patients with HR+/HER2- BMM could also benefit from endocrine therapy. The RIGHT Choice study explores the combination of endocrine therapy and a CDK4/6 inhibitor in comparison with chemotherapy in the setting of significant visceral impairment. Patients diagnosed with late-stage BMM may lose the opportunity to receive the usual dose and course of radiation and chemotherapy, leading to reduced survival. The prognosis of patients with BMM is still not ideal due to the lack of definitive treatments.



**Figure 1:** FDG Avid Diffuse Bone Marrow Uptake Seen Suggestive of Metastases



**Figure 2:** Bone Marrow Biopsy Showing Aggregates of Pleomorphic Cells Showing Cell to Cell Molding, Atypical Nuclei with Coarse Chromatin and Irregular Nuclear Margin Suggestive of Metastatic Deposits within Normal Hematopoietic Cells



**Figure 3:** Bone Marrow Biopsy Showing Metastatic Deposits which Stained Positive for ER and PR

## Conclusion

In cases where breast cancer patients show signs of anaemia and fever despite a negative test to determine the cause, it is essential for bone marrow examination (BMM) to be taken into consideration. For hormone receptor-positive (HR+)/HER2-negative patients with good overall health who can undergo active treatment, combining CDK4/6 inhibitors with endocrine therapy can help manage the progression of the disease, enhance the quality of life, and extend survival.

Bone marrow trephine biopsy is not a standard procedure for breast cancer and can result in a certain percentage of dry taps [5-21].

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