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Rare foot metastasis from breast cancer: A case report and diagnostic challenges

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Abstract
Bone metastases are a common manifestation in advanced solid malignancies, but metastases to the foot are exceedingly rare, accounting for only 0.007% to 0.3% of cases. This case report describes a 65-year-old woman with a history of breast cancer treated in 1994, who presented with progressive left ankle pain 30 years after initial treatment. Imaging studies revealed increased uptake in the left tibiotalar region, with MRI confirming extensive metastatic involvement of the distal tibia, fibula, talus, anterior calcaneal process, and tarsal bones. Diagnosing foot metastases is challenging due to their rarity, non-specific symptoms, and potential to mimic other conditions. This report highlights the importance of maintaining a high index of suspicion for metastatic disease in patients with persistent bone pain and a history of cancer. Multidisciplinary management is essential for optimizing patient outcomes and addressing the complex needs of patients with rare metastatic presentations.

Keywords: Bone metastases, foot metastases, breast cancer, MRI

Introduction
Bone metastases are a common manifestation of distant recurrence in various solid malignancies, particularly those originating in the lung, breast, and prostate. However, metastases to the foot are exceedingly rare, accounting for only 0.007% to 0.3% of cases [1]. This rarity can be attributed to several factors, including vascular patterns and the limited presence of red marrow in the feet. Typically, bone metastases preferentially affect areas with abundant red marrow, such as the skull, axial skeleton, and the medullary portion of long bones. Consequently, the most frequent sites of metastatic involvement are the vertebral column, sacrum, pelvis, and proximal femurs. In rarer instances, metastases may manifest as cortically-based surface lesions. The pattern of bone metastasis distribution may also vary according to the primary tumor type [2-4].
Many metastatic bone lesions are asymptomatic or minimally symptomatic and are often discovered incidentally during staging evaluations for the primary malignancy [3, 5, 7]. In the absence of symptoms, routine imaging for bone metastases is generally unwarranted unless laboratory results indicate elevated levels of alkaline phosphatase or calcium. Despite this, bone metastases are a substantial source of morbidity. In symptomatic patients, pain is the predominant complaint, and most patients with bone metastases will experience significant pain at some point during the course of their disease [3, 8].
Diagnosing foot metastases is particularly challenging due to their rarity, non-specific symptoms, and frequently delayed onset. Additional symptoms may include swelling, erythema, warmth, and neurologic deficits, especially when vertebral metastases result in spinal cord compression or instability. The interval between the diagnosis of the primary malignancy and the development of foot metastases can extend up to 172 months, with the incidence peaking in older populations. Despite their rarity, foot metastases may serve as the initial presentation of occult cancer, mimicking other skeletal disorders and leading to misdiagnosis and treatment delays [5, 6].
With this case, we aim to present a 65-year-old woman with a history of breast cancer who developed rare metastatic involvement of the foot, manifesting as progressive left ankle pain 30 years after her initial cancer treatment, highlighting the diagnostic challenges of rare foot metastases

Case Report
A 65-year-old woman with a medical history of osteopenia, chronic kidney disease, and breast cancer treated in 1994, underwent a radical mastectomy, chemotherapy, and radiotherapy. She developed lymphedema in her left upper limb as a sequela.

In 2017, she was diagnosed with metachronous bone, lung, and lymph node metastases, for which she started treatment with letrozole, ribociclib, and zoledronic acid, and received palliative radiotherapy to her left lower limb in February 2018. In July 2018, she suffered a pathological fracture of the left tibia due to a fall and underwent intramedullary nailing.

During a routine follow-up in Physical and Rehabilitation Medicine in February 2024, she reported progressive left ankle pain with a mechanical pattern. Physical examination revealed diffuse tenderness over the lateral, anterior, and medial aspects of the left ankle, with preserved active range of motion, muscle strength, and sensation. Initial management included tramadol/paracetamol for pain relief.

Reviewing her past bone scintigraphy and CT scans, the most recent bone scintigraphy on December 12, 2023, revealed heterogeneous uptake in the left tibia, consistent with a treated pathologic fracture, and intense uptake at the left tibiotalar joint, likely indicating inflammatory or degenerative changes. However, a repeat bone scintigraphy on May 17, 2024, showed increased uptake in the proximal tibia and more markedly in the tibiotalar region, extending to the proximal tarsal bones. These findings suggested secondary involvement or a possible infectious complication. Fig 1.

An MRI performed on June 11, 2024, revealed altered bone signal in the distal tibia, fibula, talus, anterior calcaneal process, and tarsal bones, suggesting extensive metastatic disease involvement. Fig 2.

Initial management of her pain included tramadol/paracetamol, which provided partial relief. In light of the extensive disease burden identified on imaging, the patient was referred to an oncology team for further evaluation and consideration of additional therapeutic options, including targeted radiotherapy to the affected foot and possible adjustments to her systemic treatment regimen. Given the chronicity and complexity of her condition, multidisciplinary input from orthopedic surgery and palliative care specialists was sought.

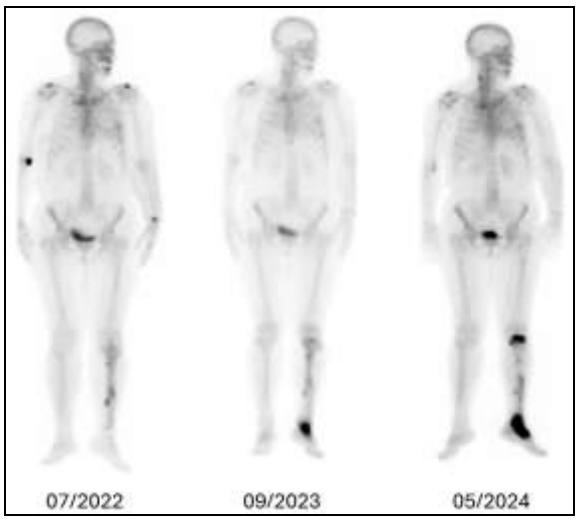

Fig 1: Intense radiopharmaceutical uptake is noted in the left tibiotarsal region, with apparent extension to the proximal planes of the tarsus. These findings show increased extent and intensity of uptake compared to the previous study from 12/12/2023, suggestive of distal metastasis. Additionally, there is heterogeneous fixation of diphosphonates along the diaphysis of the left tibia, related to a history of pathological fracture treated with nailing in 2018.

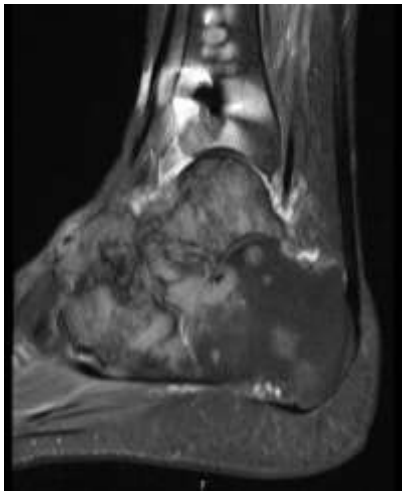

Fig 2: Magnetic resonance imaging shows evidence of bone signal alteration at the distal level of the distal tibia and fibula, involving the entire talus, the anterior process of the calcaneus, and the tarsal bones.

Discussion

Bone metastases to the foot, while rare, pose a significant diagnostic challenge due to their non-specific symptoms, delayed presentation, and potential for mimicking other conditions.

This case highlights the importance of considering metastatic disease in cancer patients with persistent bone pain, even in atypical locations [5]. The differential diagnosis in this case included infectious processes, emphasizing the need for comprehensive evaluation and a high index of suspicion for metastatic disease in patients with a history of cancer presenting with new osseous symptoms. Early detection and awareness of unusual metastatic sites are crucial for proper management and palliative care [7-9].

The characteristics and intensity of the pain may vary depending on the presence or absence of neuromas as part of tumor-induced bone remodeling, endosteal nerve compression by tumor, nerve injury from extension of the bone metastasis out of the bone, and location of the metastasis within the bone. The pain may be somatic (achy, sharp, well-localized), neuropathic (burning, shooting, radiating), or both. It may be constant or exacerbated by movement of the joint or involved bone (incident pain) [5, 8-10]. Incident pain is particularly hard to treat because it comes on and remits suddenly and may be very severe. Neuropathic pain is often worse at night. A complication, such as invasion of adjacent structures, usually results in constant, progressively worsening pain. If the structure is the epidural space, producing compression of the spinal cord, the pain is likely to be worse at night and very intense. Sudden severe pain may be caused by a pathologic fracture, and prompt evaluation, especially in patients with a history of cancer, is necessary. Pathologic fractures are more likely to occur in osteolytic as compared with osteoblastic metastases [11-15].

A basic screening must be performed when one of the signs and symptoms described above are present: a complete blood-cell count to evaluate for anemia and myelosuppression; serum calcium, phosphorus, 25-hydroxyvitamin D, alkaline phosphatase, creatinine, thyroid-stimulating hormone, protein electrophoresis and parathyroid hormone level to identify bone turnover and evaluate hypercalcemia. Management of bone metastases in

cancer: a review. This study must be complemented with imaging data [16-18].

Treatment options may include surgery, radiation therapy, chemotherapy, and targeted therapies, depending on the patient's individual circumstances. A high index of suspicion, thorough history and physical examination, imaging studies, and biopsy are crucial steps in navigating this diagnostic dilemma. Treatment is usually palliative and aims for pain relief and maintaining function.

Early detection and prompt management of bone metastases are crucial for improving patient outcomes and quality of life, usually involving a multidisciplinary approach that includes oncologists, orthopedic surgeons, radiation oncologists, and palliative care specialists.

Conflict of Interest
Not available

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