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LATE-ONSET PROXIMAL HUMERUS LESION PRESENTING WITH SOLITARY BONE METASTASIS: A DIAGNOSTIC CHALLENGE AFTER 12 YEARS OF REMISSION
GEÇ BAŞLAYAN, SOLİTER KEMİK METASTAZI İLE PREZENTE OLAN PROKSİMAL HUMERUS LEZYONU: 12 YILLIK REMİSYONDAN SONRA TANISAL BİR ZORLUK

Omer ESMEZ[1], Merve YILDIZ ESMEZ[2], Gulnihal DENIZ[3]

[1] Fethi Sekin City Hospital, Department of Orthopedics, Elazig, Türkiye
[2]Firat University, Faculty of Medicine, Department of İnternal Medicine, Elazig, Türkiye
[3]Erzurum Technical University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Erzurum, Türkiye

ABSTRACT

Breast cancer is one of the most common tumors in women. One in eight women may encounter this disease at some point in their lives, and metastasis may develop even after many years of remission. This case report describes a rare humerus metastasis presenting with pain and swelling in the right shoulder in a woman in her 60s who was diagnosed with mixed-type (invasive ductal and lobular) carcinoma of the left breast in early 2012 and who underwent modified radical mastectomy and adjuvant treatments for 12 years of remission. Positron emission tomography imaging revealed a hyper metabolic lesion in the proximal right humerus. Magnetic resonance imaging and biopsy revealed a malignant epithelial tumor indicating metastatic breast cancer. The patient underwent palliative radiotherapy and was started on ribociclib (Valamor) as systemic treatment. However, widespread itching and vitiligo-like skin changes developed on the hands and face due to the treatment. This case emphasizes the importance of long-term clinical and radiological follow-up and the need to be careful about skeletal metastases that may occur in the late period in breast cancer patients.

Keywords: Bone neoplasms, breast neoplasms, humerus, lobular carcinoma, neoplasm recurrence.

ÖZ

Meme kanseri kadınlarda en sık görülen tümörlerden biridir. Her sekiz kadından biri hayatının bir noktasında bu hastalıkla karşılaşabilir ve metastaz, uzun yıllar süren remisyondan sonra bile gelişebilir. Bu olgu sunumunda, 2012'nin başlarında sol memede karma tip (invaziv duktal ve lobüler) karsinomu teşhisi konulan ve 12 yıl remisyon boyunca modifiye radikal mastektomi ve adjuvan tedaviler uygulanan 60'lı yaşlarındaki bir kadında sağ omuzda ağrı ve şişlikle ortaya çıkan nadir bir humerus metastazı anlatılmaktadır. Pozitron emisyon tomografisi görüntüleme, proksimal sağ humerusta hipermetabolik bir lezyon ortaya koydu. Manyetik rezonans görüntüleme ve biyopsi, metastatik meme kanserini gösteren kötü huylu bir epitel tümör ortaya koydu. Hastaya palyatif radyoterapi uygulandı ve sistemik tedavi olarak ribociclib (Valamor) başlandı. Ancak, tedavi nedeniyle ellerde ve yüzde yaygın kaşıntı ve vitiligo benzeri cilt değişiklikleri gelişti. Bu vaka, meme kanseri hastalarında uzun dönem klinik ve radyolojik takibin önemini ve geç dönemde ortaya çıkabilecek iskelet metastazlarına karşı dikkatli olunması gerektiğini vurgulamaktadır.

Anahtar kelimeler: Kemik metastazı, meme neoplazileri, humerus, lobüler karsinom, geç nüks.

Corresponding Author: Assoc. Prof. Dr. Gulnihal DENIZ, gulnihal.deniz@erzurum.edu.tr; 0000-0002-5944-8841, Erzurum Technical University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Erzurum/Türkiye

Authors: MD, Dr Omer ESMEZ, dresmezomer@gmail.com,0000-0002-4475-3501
MD, Dr Merve YILDIZ ESMEZ**,** dr.merrve@hotmail. com, 0009-0008-1239-8948

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INTRODUCTION

Breast cancer is one of the leading causes of cancer-related morbidity in women worldwide. Despite advances in adjuvant therapy, approximately 20–30% of patients develop metastatic disease years after treatment completion. Bones are the most common site of metastasis for breast cancer; however, isolated skeletal recurrences occurring 10 years or more after treatment are rare.[1,2] Invasive lobular carcinoma, in particular, is known for its unusual metastatic spread pattern and potential for late recurrence. In this case report, a patient diagnosed with mixed-type breast carcinoma who went into complete remission and developed isolated right humerus metastasis 12 years later is presented. This situation underscores the need for long-term follow-up and diagnostic vigilance.[2] Late-onset, solitary bone metastases can pose a significant diagnostic challenge when they occur years later. Effective management requires long-term, careful follow-up and a multidisciplinary approach.[2,3]

CASE REPORT

Case Presentation and Investigation: A female patient in her 60s was diagnosed with mixed-type breast carcinoma (invasive ductal and lobular carcinoma) in the left breast in early 2012. The initial pathology report from 2012 confirmed a diagnosis of mixed-type breast carcinoma and demonstrated a hormone receptor-positive profile. Immunohistochemical analysis showed high expression of estrogen receptors (ER: 90% +++), progesterone receptors (PR: 60% ++), and CerbB2 (HER2: ++), indicating a triple-positive tumor. The patient underwent modified radical mastectomy, followed by neoadjuvant chemotherapy (4 cycles of AC, one cycle of docetaxel), adjuvant radiotherapy, hormonal therapy with Arimidex for 5 years, and targeted therapy with trastuzumab (Herceptin). After completion of hormonal treatment, she was followed in clinical remission without medication for approximately 12 years. In April 2024, the patient applied to the orthopedic clinic, complaining of pain and swelling in the right shoulder. In the right upper extremity MRI, a 44×28 mm lesion was detected in the right humeral head, hypointense on T1A (Figure 1), with heterogeneous contrast enhancement and mild cortical destruction. PET imaging showed a hypermetabolic lesion in the proximal right humerus (Figure 2). The findings were interpreted in favor of bone metastasis due to breast cancer. Also, in the 2024 recurrence, a bone biopsy of the proximal right humerus revealed a malignant epithelial tumor. Immunohistochemistry confirmed tumor positivity for Pan-Cytokeratin (PanCK), CK7, GATA3, GCDFP15, and Mammaglobin, all of which strongly support a breast origin. The tumor also showed Ki-67 positivity (~35%), indicating a moderate proliferation index. S100 and CK20 were negative, ruling out differential possibilities such as melanoma and gastrointestinal tumors. These findings collectively supported the diagnosis of metastatic breast carcinoma and were consistent with the patient's known oncological history. Based on imaging and biopsy findings, the case was considered to have metastatic breast cancer. Palliative radiotherapy was initiated for the lesion in April 2024, and systemic treatment with Valamor was initiated in June 2024. However, widespread pruritus and vitiligo-like depigmentation in the hand-face region accompanied the treatment in a short time. A dermatological evaluation revealed bilateral vitiligo.

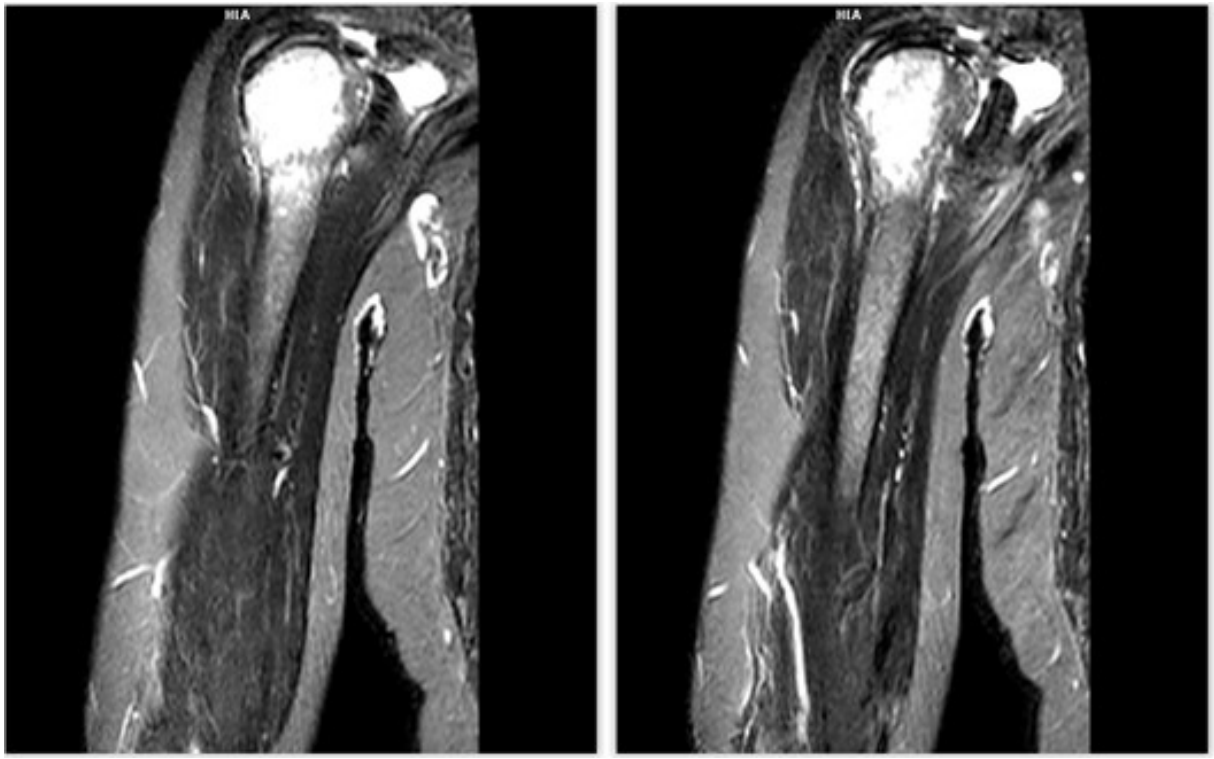

Figure 1. Coronal MRI image showing a lytic, expansile lesion in the proximal right humerus with cortical destruction, consistent with bone metastasis.

This case exemplifies the diagnosis and management process of a rare late-onset isolated bone metastasis in a breast cancer patient who had been in long-term remission. It also draws attention to rare dermatological side effects that may occur due to systemic treatment.

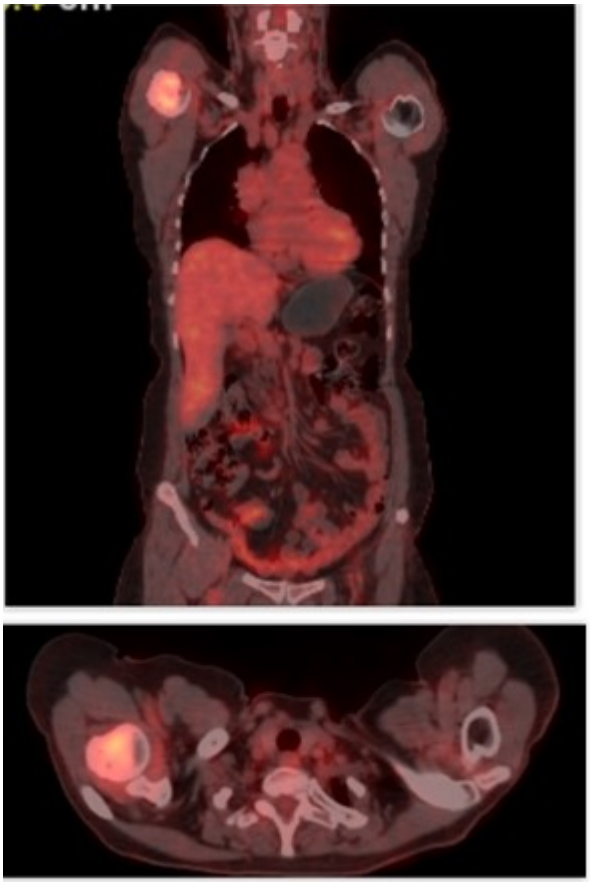

Figure 2. Axial and Coronal PET-CT image showing increased fluorodeoxyglucose uptake in the proximal right humerus, indicative of a metabolically active metastatic lesion.

Differential Diagnosis: The differential diagnosis for the lesion detected in the right proximal humerus in a breast cancer patient with a long-term remission history includes various possibilities. Considering the hypermetabolic activity on PET and computed tomography (CT), cortical irregularity observed on MRI, and destructive bone lesion, metastatic recurrence due to primary breast cancer was considered in the foreground.[4,5] Since the lesion was solitary, primary bone tumors such as chondrosarcoma or osteosarcoma were also considered in the differential diagnosis. However, the patient's oncological history and histopathological findings supported secondary (metastatic) bone neoplasia rather than primary. Also, possibilities that could mimic malignancy, such as infectious osteomyelitis, were considered. However, the absence of systemic signs of infection (e.g., fever, elevated inflammatory markers) and the features on imaging made this diagnosis less likely. Reactive or degenerative changes were also evaluated due to the patient's age, but this possibility was excluded due to the aggressive appearance of the lesion and fluorodeoxyglucose (FDG) uptake. Histopathological detection of malignant epithelial tumor and the patient's known breast cancer history supported the clinical picture as recurrent metastatic breast cancer.

Treatment: Radiation therapy was initiated in April 2024 due to a metastatic lesion detected in the right proximal humerus. After radiotherapy, the patient's pain was partially reduced, and swelling regressed. Based on the diagnosis of a malignant epithelial tumor of breast origin confirmed by biopsy, systemic treatment was re-evaluated by the multidisciplinary oncology board.

In June 2024, Valamor treatment was initiated for systemic disease control. However, widespread pruritus and significant pigmentation changes in the hand-face area developed shortly after treatment. The dermatological evaluation showed that these changes were compatible with vitiligo.

Valamor treatment was temporarily discontinued; symptomatic treatment with topical corticosteroids and moisturizers was initiated. The dermatology department recommended closely monitoring the process; desensitization protocols or alternative systemic treatment options were discussed. The patient was taken under regular clinical and radiological evaluation with the joint follow-up of the oncology, orthopedics, and dermatology departments.

Outcome and Follow-Up: The patient tolerated radiotherapy and systemic treatment with Valamor to a moderate level. However, pruritus and vitiligo-like depigmentation developed on the hands and face shortly after the start of treatment. These side effects were managed conservatively under the supervision of dermatologists.

No new metastatic focus was observed in the control PET-CT imaging performed in August 2024, but minimal progression was observed in the existing humeral lesion. As of October 2024, the patient stated that she tolerated the treatment regimen better, and a plateau phase was reached without progression in cutaneous symptoms. During this period, hematological and hepatic parameters remained within normal limits.

As of February 2025, the disease showed an indolent (slowly progressing) course without clinically significant deterioration. The patient continues systemic treatment and is monitored with regular check-ups under the joint follow-up of oncology, orthopedics, and dermatology units. Multidisciplinary management is maintained to ensure early detection of treatment-related toxicities and disease progression.

DISCUSSION

Breast cancer is the most frequently diagnosed malignancy in women worldwide. Although advances in diagnosis and treatment have significantly increased survival, the risk of distant recurrence continues for many years. Late-onset bone metastasis is a well-documented phenomenon in breast cancer, particularly among patients with hormone receptor-positive and lobular subtypes.[6] Bone is the most common site of distant metastasis in breast cancer, and approximately 70% of breast cancer patients with metastatic disease have skeletal involvement.[7] However, solitary bone metastasis occurring more than ten years after treatment is difficult to diagnose.[8] In a large retrospective analysis, Pan et al.[9] reported that approximately 60% of patients with

breast cancer who experienced a late recurrence (>10 years) developed bone metastasis as the initial site of distant disease. Invasive lobular carcinoma is particularly noted for its atypical metastatic behavior, including late and solitary skeletal involvement, due to its unique histopathologic and molecular characteristics.[10] Furthermore, molecular subtypes such as luminal A and B have been associated with prolonged disease-free intervals before recurrence, reinforcing the need for long-term surveillance. The presence of solitary bone metastasis, even years after remission, should be carefully evaluated as it has therapeutic and prognostic implications.[6]

This case presents a late-onset solitary bone metastasis in the proximal humerus 12 years after treatment in a patient diagnosed with mixed-type (invasive ductal and lobular) breast cancer who received curative treatment. Such a long latency period is remarkable and should not be ignored, especially in lobular histology, which has an atypical spread pattern and a slow clinical course.[11]

Imaging methods played a critical role in the diagnosis process. Findings specific to malignancy, such as cortical destruction and FDG hypermetabolism, were detected in PET-CT and MRI, and then further evaluation was performed with biopsy.[12] Histopathological confirmation of the malignant epithelial tumor detected in the humerus and the patient's history of breast cancer allowed the diagnosis to be made as breast cancer recurrence. The differential diagnosis included primary bone tumors, infectious/inflammatory conditions such as osteomyelitis, and reactive-degenerative lesions. However, clinical presentation, imaging findings, and histopathological examination supported the diagnosis of metastatic breast cancer. Hypermetabolic signals detected in the nasopharynx and vertebral regions on PET -CT were also evaluated. Still, these areas were not prioritized in the clinical decision process, considering isolated humerus involvement confirmed by biopsy was the priority.[13]

The treatment was planned with a multidisciplinary approach. Palliative radiotherapy was effective in controlling the symptoms. Valamor treatment was started within the scope of systemic disease management, but the patient developed remarkable dermatological toxicities such as widespread pruritus and vitiligo-like skin changes. Skin toxicities are increasingly reported in modern targeted therapies, and such side effects necessitate close monitoring and personalized management approaches. This case draws attention to the need for long-term follow-up, even in breast cancer patients whose remission period exceeds five years. Although metastases in the late period are rare, they can create clinical pictures that can be confused with primary bone pathologies, especially when seen as solitary lesions.[14]

CONCLUSION

This case demonstrates how late-onset solitary bone metastases in patients with breast cancer can be diagnostically and therapeutically complex. Regardless of the length of clinical remission, the possibility of metastatic disease should be considered in newly developing bone lesions in patients with a past oncological history. Integration of all clinical components, such as imaging, pathology, and multidisciplinary evaluation, is essential for timely diagnosis and effective treatment.

Ethics Committee Approval: The Helsinki Declaration was adhered to in the study.

Informed Consent: Signed consent form were obtained from the patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Conceptualization–ÖE, MYE; Design–MYE, ÖE, GD; Supervision–MYE; Sources–MYE, ÖE, GD; Materials–MYE, ÖE; Data Collection and/or Processing–MYE, ÖE; Analysis and/or Interpretation–MYE, ÖE, GD; Literature Review–MYE, ÖE, GD; Written by– MYE, ÖE, GD; Critical Review–GD.

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