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Case Report

Primary Breast Osteosarcoma: A Case Report and Literature Review

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Abstract

Primary breast osteosarcomas are rare. We report an unusual case of a 58-year-old female presenting with a right breast lump for 1 month. Mammography showed an ill-defined, heterogeneous, and coarse calcification measuring 4 cm over the upper inner quadrant of the right breast. She received an upfront partial mastectomy after core needle biopsy showed osteoid-like tissue with the presence of atypical cells and some multinucleated giant cells. The final pathology revealed Grade 3 extraosseous osteosarcoma, osteoblastic type. Four cycles of adjuvant doxorubicin and cisplatin followed by radiotherapy were given due to the close surgical margin. She has since been free of recurrence for 3 years.

Keywords: Case report, extraosseous osteosarcoma, primary breast osteosarcoma

Introduction

Nonepithelial breast malignancies constitute <1% of all breast cancers.[1] Excluding the more common phyllodes tumor, primary breast sarcomas (PBSs) arising from mesenchymal tissue account for only 0.006% of breast malignancies.[2] Within this category, primary breast osteosarcoma (PBOS) is particularly rare, representing 4.5% of all PBSs.[3] PBOS is an aggressive tumor characterized by a high local recurrence rate and poor overall survival.[3] Given the rarity of this tumor and the lack of evidence regarding its tumorigenesis and genomic background, there is no widely agreed-upon approach to manage this specific malignancy. Here, we present a case of PBOS in the right breast, which has remained disease free for 3 years following treatment.

Case Report

A 58-year-old woman presented with a lump in her right breast for 1 month. She had no history of trauma, chest wall

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irradiation, or previous breast cancer in either breast. On initial management at the local hospital, mammography revealed a 4-cm coarse and heterogeneously dense calcification in the right upper quadrant of the right breast [Figure 1]. A core biopsy showed osteoid-like tissue with the presence of atypical cells and some multinucleated giant cells, leading to the decision for upfront right partial mastectomy without axillary lymph node dissection. The final pathological examination identified Grade 3 extraosseous osteosarcoma, osteoblastic type, measuring 4.0 cm × 3.8 cm. Microscopic analysis revealed an infiltrative bone-forming tumor consisting of neoplastic pleomorphic cells generating sheet-like or lace-like osteoid with mineralization. There were no findings indicative of carcinomatous nests, *in situ* components, or leaf-like projections, suggestive of phyllodes neoplasms. Immunohistochemically, staining of AE1/AE3, low molecular weight (LMW), and epithelial membrane antigen (EMA) was negative, while a strong and diffuse SATB2 expression supported the osteoblastic lineage differentiation in the epithelioid to pleomorphic tumor cells. Following surgery at the local hospital, she underwent imaging evaluations at our institution, which revealed negative findings on chest computed tomography (CT) and bone scan. Due to the close surgical margin (some tumor cells with focal superficial and focal basal margin <1 mm), she received four cycles of adjuvant doxorubicin and cisplatin followed by radiotherapy (66 Gy). The trimodal treatment was completed without complications, and she has since remained disease free during regular clinical follow-ups for 3 years.

Discussion

PBOS has been documented across a broad age spectrum in the literature, with reported onset ranging from 16 to 96 years, and predominantly affecting middle-aged and older women.[4] The typical clinical presentation involves a painless, firm breast mass characterized by progressive enlargement, with an average size of 4.6 cm.[5] Unlike typical breast adenocarcinoma, symptoms such as bloody nipple discharge, nipple retraction, and axillary lymphadenopathy are less frequently observed.[5] To the best of our knowledge, the precise tumorigenesis underlying PBOS remains inconclusive. Several risk factors have been associated with PBOS, including prior trauma, burns, ipsilateral/contralateral epithelial breast cancer, irradiation, and systemic chemotherapy.[5,6] Paired tissue analysis of primary invasive ductal carcinoma and subsequent ipsilateral PBOS in a previous case report showed repeated somatic genetic alterations (*PIK3CA* p.H1047R, *PTEN* p.V275G, and *TP53* p.T81Nfs*64).[7] This suggests the possibility of a shared predominant clone (or identified as multipotent cancer stem cells) during tumor evolution, which is supported by an animal study showcasing canine mammary osteosarcomas originating from pluripotent mammary stem cells.[8] The previous case report[7] also discussed the molecular landscape of PBOS, with more mutations in *PIK3CA* and PI3K/mTOR pathways in extraosseous osteosarcomas compared with conventional osteosarcomas.[9] Mammographic findings in patients with PBOS vary and often present as large hyperdense masses with lobulated contours and ill-defined margins, accompanied by numerous coarse, speckled, and dense calcifications, resembling fibroadenoma.[10] Progressive changes in the patterns of coarse calcifications have also been reported to be a characteristic feature of PBOS.[10] The diagnosis of PBOS should adhere to the criteria proposed by Allan and Soule for extraosseous osteosarcomas, which include ruling out a bony origin, the presence of neoplastic

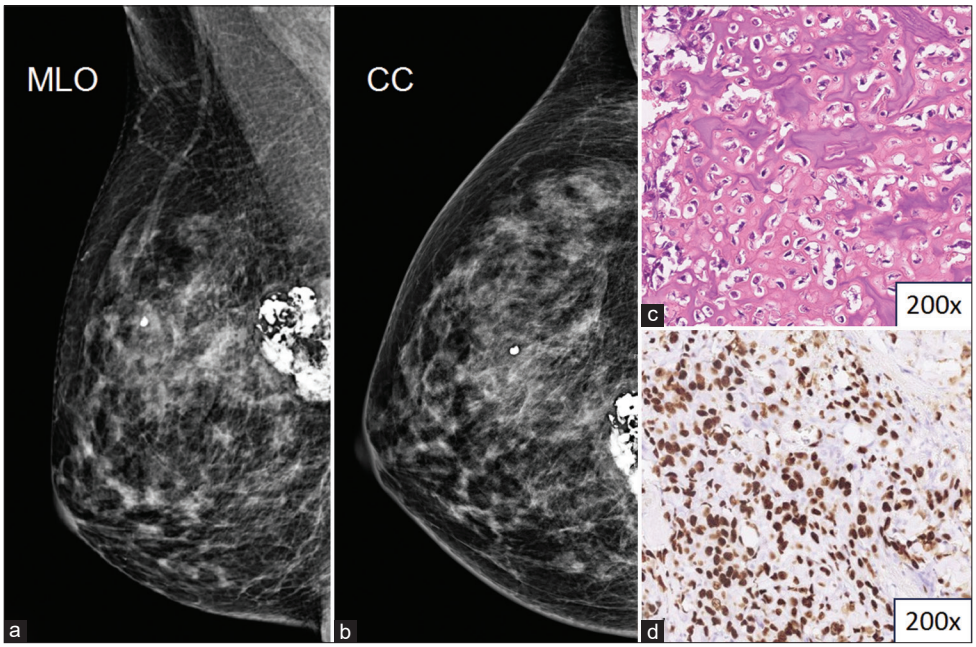

Figure 1: (a and b) Mammography revealed a 4-cm heterogeneously high-density coarse calcification at the upper inner quadrant of the right breast. (c) The neoplastic cells formed an abundant osteoid matrix. (d) Immunohistochemistry staining showed a diffuse and strong SATB2 expression

bone or osteoid, and the absence of an epithelial component.[11] Therefore, imaging modalities such as CT, positron emission tomography/CT, magnetic resonance imaging, and bone scintigraphy may be helpful in identifying neighboring origins such as the underlying rib, sternum, pectoralis muscles, as well as metastatic bone osteosarcomas. It is imperative in the pathological diagnosis to differentiate PBOS from other breast tumors displaying osteoid- and bone-forming traits such as metaplastic carcinoma and malignant phyllodes tumors with osteosarcomatous differentiation.[6] Using immunohistochemistry to confirm the absence of epithelial cells can effectively aid in excluding metaplastic carcinoma. In our case, the nonepithelial characteristic was evidenced by negative AE1/AE3, LMW, and EMA staining, while the strong and diffuse SATB2 expression supported the osteoblastic lineage differentiation in the tumor cells. Core needle biopsy may be advantageous in diagnosing PBOS. However, a previous case study reported false-negative results in a patient with benign metaplastic calcification, and a diagnosis of breast osteosarcoma was established solely through lumpectomy.[12]

Similar to primary bone osteosarcomas, PBOSs are biologically aggressive neoplasms. A case series of 50 patients diagnosed with PBOS reported a combined rate of local recurrence and distant metastasis of 59%.[5] In addition, the prognosis of the patients was poor, with a 5-year overall survival rate of only 38%, and large tumor size (>4.6 cm) and osteoclastic or osteoblastic subtypes were reported to be poor prognostic factors.[5] Furthermore, a crucial finding of the study was the clear association between surgical margin and outcomes. All of the 28 patients who remained free of recurrence had undergone complete surgical excision with unequivocally negative margins. This emphasizes the critical importance of achieving complete tumor excision to improve the chances of long-term disease control and survival in patients with PBOS.

Given the rarity of PBOS, a standardized approach to its management remains elusive. However, the current evidence suggests that surgical intervention, either through wide excision or mastectomy without axillary lymph node dissection to achieve negative margins, is the preferred treatment modality.[6,10] Regarding adjuvant therapy, chemotherapy options comprising doxorubicin, cisplatin, ifosfamide, methotrexate, and bleomycin, commonly used for conventional osteosarcomas, may be considered. A preclinical study of a patient-derived orthotopic xenograft model in nude mice provided valuable insights into the treatment of PBOS. The study revealed that PBOS exhibited sensitivity to cisplatin and doxorubicin, both as stand-alone treatments and in combination.[13] However, the efficacy of adjuvant or neoadjuvant chemotherapy in localized extraosseous osteosarcoma is uncertain, as highlighted by a recent meta-analysis.[14] Similarly, the role of radiotherapy in the management of PBOS is not universally advocated, and it is typically reserved for cases with larger tumor sizes or unclear margins.[15] Therefore, the decision to perform adjuvant chemotherapy and radiotherapy should be carefully deliberated to weigh the potential benefits against the risk of treatment-related adverse events in the context of PBOS treatment.

In our case, the patient was previously in excellent health with no identifiable risk factors. The diagnosis of PBOS was only conclusively established following mastectomy and based on the final pathology report. She then underwent a partial mastectomy and extensive systemic imaging assessments at our institution. Given the high-risk features including close surgical margins and the osteoblastic type, the medical team determined that the inclusion of radiotherapy and adjuvant chemotherapy was imperative. This particular case highlights the necessity for oncologists to maintain a high index of suspicion for this uncommon entity.

In conclusion, PBOS is a rare but aggressive tumor that eludes detection during routine mammographic screening due to its lack of specific imaging characteristics. The cornerstone of treatment is the wide excision of the tumor to secure clear margins. In cases where the patient presents with high-risk features, the use of adjuvant systemic chemotherapy and radiotherapy is an important consideration to optimize outcomes.

Declaration of patient consent

This study was performed in accordance with and conforming to the Declaration of Helsinki. The authors certify that they have obtained all appropriate patient consent form. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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