

Primary osteosarcoma of the breast: pathological and imaging findings

OSTEOSSARCOMA PRIMÁRIO DA MAMA: ACHADOS PATOLÓGICOS E DE IMAGEM

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SUMMARY

Primary osteosarcoma of the breast (POB) is an extremely rare and aggressive tumor. Differential diagnosis of POB includes osteosarcoma of the chest wall and metaplastic breast carcinoma. Imaging tests that exclude the existence of a direct connection between the tumor and chest wall, as well as histopathological and immunohistochemical studies that rule out the presence of an epithelial component are required for the diagnosis of POB. We report a case of a 69-year old woman with POB. Imaging and pathological findings are presented. Therapeutic approach is discussed in the light of current knowledge, including potential complications.

Keywords: breast, breast neoplasms, sarcoma, immunochemistry.

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A 69-year-old woman presented with a 6-month history of a palpable, painless mass in her left breast. Clinical examination revealed a hard, mobile, well-circumscribed, 10 cm mass, occupying practically the entire left breast. Contralateral breast, axilla or nipples showed no abnormalities. She denied having any history of breast trauma, radiotherapy, or breast cancer.

Mammography revealed a relatively well-defined, hyperdense irregular mass without calcifications, unconnected to the underlying sternum and ribs (Figure 1A). Ultrasound revealed a hypochoic irregular mass with hyperechoic areas, indistinct margins, and posterior acoustic shadowing (Figure 1B). Core needle biopsy was performed and microscopy showed a malignant poorly differentiated mesenchymal tumor.

Thoracic and abdominal computed tomography showed no distant metastasis. The patient underwent simple mastectomy and sentinel lymph node biopsy. Grossly, the cut surface of the tumor was white, hard, with

a stony consistency in the center and well-defined margins. The tumor measured 10x9x7 cm (Figure 2).

Microscopy showed a malignant immature mesenchymal bone-forming tumor. There were *foci* of necrosis and cartilage, containing osteoid matrix, some of which were irregularly calcified, surrounded by atypical spindle cells and osteoclast-like multinucleated giant cells. Tumor mitotic count was 16 mitoses/10 high-power field. There was no skin and lymphovascular invasion. Sentinel lymph node was tumor-free. On immunohistochemistry, tumor cells were positive for vimentin. CD68 (KP1) and alpha-1-antitrypsin were positive in osteoclast-like giant cells. Cytokeratin (AE1/AE3), S-100, epithelial membrane antigen (EMA), p63, epidermal growth factor receptor (EGFR), CD99, estrogen and progesterone receptors, and HER2 were negative. The Ki-67 index was 5%. Extensive tumor sampling failed to identify any tumor that was biphasic or had epithelial component. A high-grade primary osteosarcoma of the breast (POB) was di-

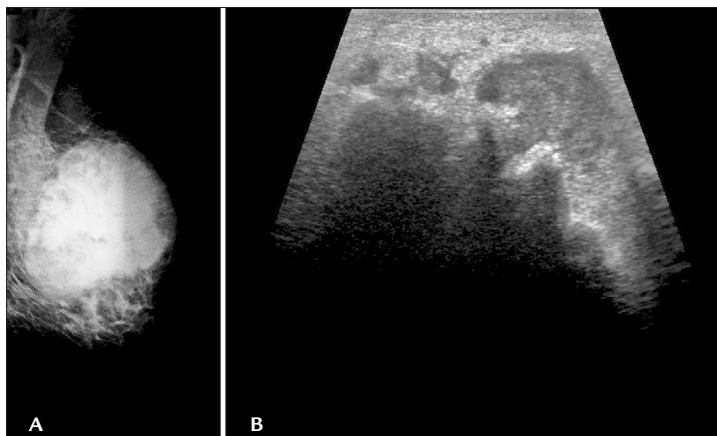


FIGURE 1 Imaging findings. (A) Mammogram showing a relatively well-defined, irregular, hyperdense mass. The tumor was unconnected with the underlying sternum and ribs; (B) Ultrasound demonstrating an irregular, hypoechoic mass with hyperechoic areas and diffuse posterior acoustic shadowing.

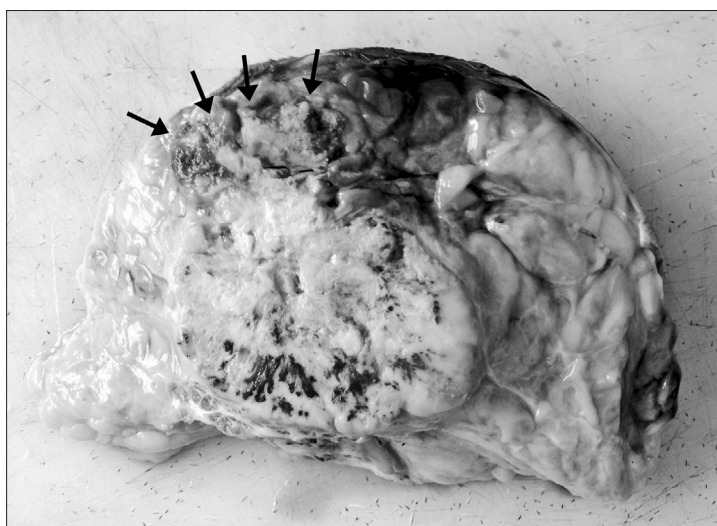


FIGURE 2 Cut surface of the tumor revealed a solid, white mass with well-defined margins. Tumor margin (arrows).

agnosed and the tumor was classified as osteoblastic subtype (Figure 3).

Clinical oncologists treated the patient with chemotherapy, administering doxorubicin plus cisplatin. After the second course of chemotherapy, she developed neutropenia, severe sepsis and died, despite therapy.

POB is an extremely rare and aggressive tumor, accounting for less than 1% of all breast malignancies.¹ It is classified as fibroblastic, osteoblastic and osteoclastic, according to cell composition. In the largest series of POB published up to now, including 50 cases, 56% of POB cases were of the fibroblastic subtype, followed by osteoclastic (28%) and osteoblastic (16%) subtypes. Prognosis in patients with POB is poor, and a 5-year overall survival rate of 38% has been reported.²

From 2010 to 2014, 345 women with breast cancer were treated in our institution. One case of POB was detected during this period, accounting for 0.3% of all breast cancers. Skeletal osteosarcoma and metaplastic carcinoma

are differential diagnoses of POB. In this case, the tumor was not connected directly to the underlying sternum and ribs, excluding a diagnosis of osteosarcoma arising from the chest wall. Immunohistochemistry showed no epithelial component, ruling out the diagnosis of metaplastic carcinoma.

Carcinogenesis of POB is unknown. It has been suggested that POB may arise from totipotent mesenchymal cells of the breast stroma or from transformation of pre-existing phyllodes tumor or fibroadenoma.^{2,3} Furthermore, there may be an association between a history of trauma or irradiation and POB.² Our patient had none of these conditions.

POB is managed similarly to other sarcomas. Surgery is aimed at achieving tumorfree margins, since margin status is the major risk factor for recurrence.⁴ Routine axillary dissection is not indicated, since lymphatic spread is unusual.^{2,4,5} The use of radiotherapy and chemotherapy is controversial. Radiotherapy improves local control.⁵

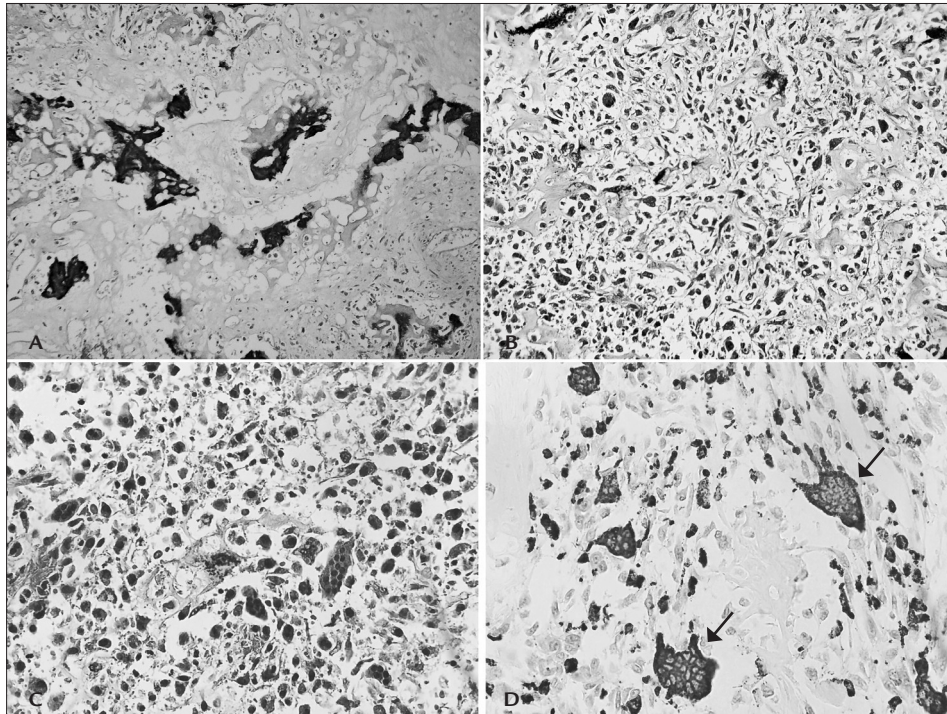


FIGURE 3 Pathology findings. (A) Immature mesenchymal bone-forming neoplasm (HE, 40x); (B) atypical spindle-cell neoplasm and immature osteoid matrix (HE, 200x); (C) mesenchymal neoplasm producing osteoid matrix surrounded by osteoclast-like giant cells and atypical mesenchymal cells (HE, 400x); (D) osteoclast-like giant cells were CD68-positive (200x) (arrows).

Patients with large (> 5cm) and/or high-grade tumors may benefit from chemotherapy, using drugs such as doxorubicin, cisplatin, methotrexate, and ifosfamide that show anti-tumor activity in osteosarcoma.⁶ It is worth mentioning that chemotherapy has toxicity that may result in death.⁷ This aspect needs to be taken into consideration in therapeutic planning.

RESUMO

Osteossarcoma primário da mama: achados patológicos e de imagem.

O osteossarcoma primário da mama (OPM) é um tumor extremamente raro e agressivo. O diagnóstico diferencial do OPM inclui o osteossarcoma da parede torácica e o carcinoma metaplásico da mama. Exames de imagem que excluam a existência de uma conexão direta entre o tumor e a parede torácica, e estudos histopatológico e imuno-histoquímico que descartem a presença de um componente epitelial são necessários para o diagnóstico de OPM. Relatamos um caso de OPM em uma mulher de 69 anos de idade. Os achados de imagem e patológicos

são apresentados. A abordagem terapêutica é discutida à luz do conhecimento atual, incluindo potenciais complicações.

Palavras-chave: mama, neoplasias da mama, sarcoma, imuno-histoquímica.

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