

Case Report



Osseous Metaplasia in Hemangiomas of the Breast: Case Reports and Literature Review

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Conflict of Interest

The authors declare that they have no
competing interests.

ABSTRACT

Unusual or prominent calcifications found on screening mammography may prompt additional radiologic and clinical work-up given the possible association with pre-malignant lesions, other high-risk lesions, or malignancies. Osseous metaplasia (OM) of the breast, also referred to as metaplastic ossification or heterotopic bone formation, is an uncommon finding that may present as radiographic calcification. There are isolated case reports of OM associated with benign or malignant tumors of the breast, as well as with a variety of non-neoplastic conditions. We report 2 cases of OM in the breast associated with a hemangioma and review the relevant literature. To the best of our knowledge, these are the first reported cases of this association in the breast.

Keywords: Breast; Calcinosiis; Hemangioma; Metaplasia

INTRODUCTION

Osseous metaplasia (OM), also referred to as metaplastic ossification or heterotopic bone formation, can occur in a variety of neoplastic and non-neoplastic conditions at multiple body sites. However, OM in the breast is uncommon. There have been isolated case reports of OM in the breast associated with benign or malignant tumors, as well as with some non-neoplastic conditions. We report 2 cases of OM associated with hemangioma of the breast. To the best of our knowledge, this association has not been previously reported. The Institutional Review Board (IRB) approval and the requirement for formal written consent was waived by IRB of Houston Methodist Hospital.

CASE REPORT

Case 1

A 60-year-old woman presented for a routine annual examination to her primary care physician. She had no significant past medical or surgical history. There was no family history of breast or ovarian cancer. Physical examination of the breast was unremarkable. She had never undergone routine screening mammography, so as part of her annual examination,

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Conceptualization: Schwartz MR; Data curation: Anton CR, Venta LA; Resources: Anton CR, Venta LA; Writing - original draft: Duhon DJ; Writing - review & editing: Ro JY, Anton RC, Schwartz MR.

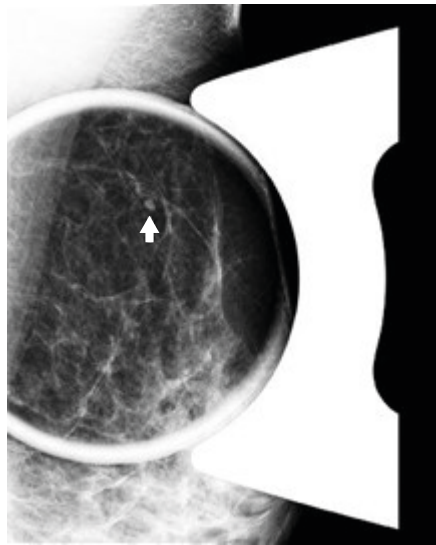


Figure 1. Mammogram with spot compression magnification. There is a single group of lacy calcifications (arrow) in the upper breast.

a screening mammogram was ordered. The bilateral digital screening mammogram with tomosynthesis showed heterogeneously dense breast parenchyma, with calcifications in the upper central left breast, Breast Imaging-Reporting and Data System (BI-RADS) 0, for which diagnostic mammogram and breast ultrasound were recommended. A digital diagnostic mammogram showed heterogeneously dense breast parenchyma, with a single 5-mm area of calcifications in the upper outer quadrant of the left breast having very unusual morphology, with a lacy appearance (**Figure 1**). The indeterminate calcifications were not typical for macrocalcifications and were not associated with ducts. The findings were assessed as BI-RADS Category 4, suspicious, and stereotactic biopsies were recommended. Ultrasound revealed no cystic or solid mass in either breast. Multiple left breast core needle biopsies were obtained under stereotactic guidance with vacuum-assisted needle biopsy. A specimen radiograph confirmed the targeted calcifications in the cores.

Pathologic findings: The core needle biopsies consisted predominantly of adipose tissue with only a few benign breast ducts and lobules. One of the core biopsies had 2 foci of OM with calcifications, each 0.5 mm, characterized by small anastomosing bony trabeculae without associated bone marrow elements (**Figure 2A**). These foci were located in benign adipose tissue, devoid of epithelial breast parenchymal components. Benign breast ducts and lobules were located in the same core, 4 mm from the hemangioma. Hemangioma with capillaries, postcapillary venules, and small veins lined by bland endothelial cells were present in the foci of OM (**Figure 2B**). Faxitron digital radiographic imaging of the paraffin blocks demonstrated calcifications corresponding mainly to the foci of OM. No atypia or malignancy was identified in the numerous levels that were examined.

Case 2

A 64-year-old woman with no family history of breast or ovarian cancer and no history of oral contraceptive use or hormone replacement presented for her annual routine examination. On screening mammography, focal asymmetry with suspicious calcifications was found in the upper outer quadrant of the right breast. She was called back for a diagnostic mammogram with computer-assisted detection. On the diagnostic mammogram, there was persistent

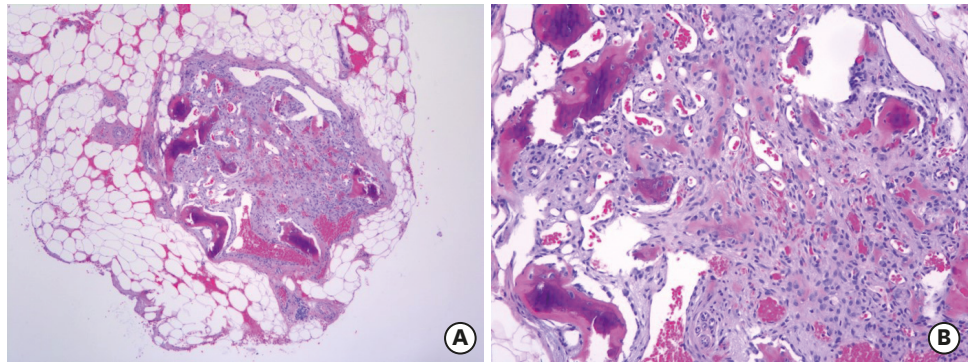


Figure 2. OM with associated hemangioma. (A) A circumscribed lesion is composed of vessels and bony spicules (H&E stain, $\times 40$). (B) The vessels are lined by flattened endothelial cells and are intimately associated with foci of OM (H&E stain, $\times 100$).

OM = osseous metaplasia; H&E = hematoxylin and eosin.

focal asymmetry with grouped punctate and round calcifications in the right breast at the 10 o'clock position at middle depth (**Figure 3**). Right breast ultrasound demonstrated a $1.6 \times 1.4 \times 0.9$ -cm irregular hypoechoic mass parallel to the skin with internal flow on color Doppler imaging at the 10 o'clock position, 10 cm from the nipple, which likely correlated with the mammographic abnormalities (**Figure 4**). No axillary adenopathy was noted. The findings were assessed as BI-RADS category 4C, suspicious, and ultrasound-guided biopsies were recommended. The patient underwent biopsies of the mass under ultrasound guidance.

Pathologic findings: The core needle biopsies revealed a venous hemangioma composed mainly of muscular vessels with surrounding fibrous stroma, with focal post-capillary venules and focal dilated endothelial-lined vascular spaces without associated muscle (**Figure 5A**). The hemangioma was associated with OM, focal benign lymphoid aggregates, and microfocal hemosiderin deposition (**Figure 5B**). No breast ducts or lobules were seen in the surrounding adipose tissue.

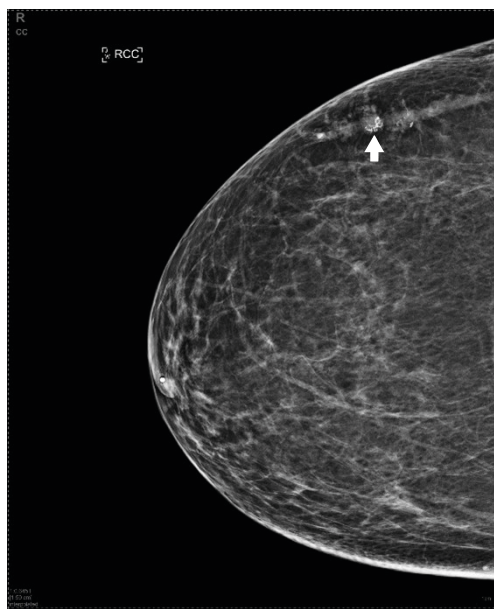


Figure 3. Mammogram in craniocaudal projection. There is a cluster of 3 partially calcified masses (arrow) lateral to the nipple.

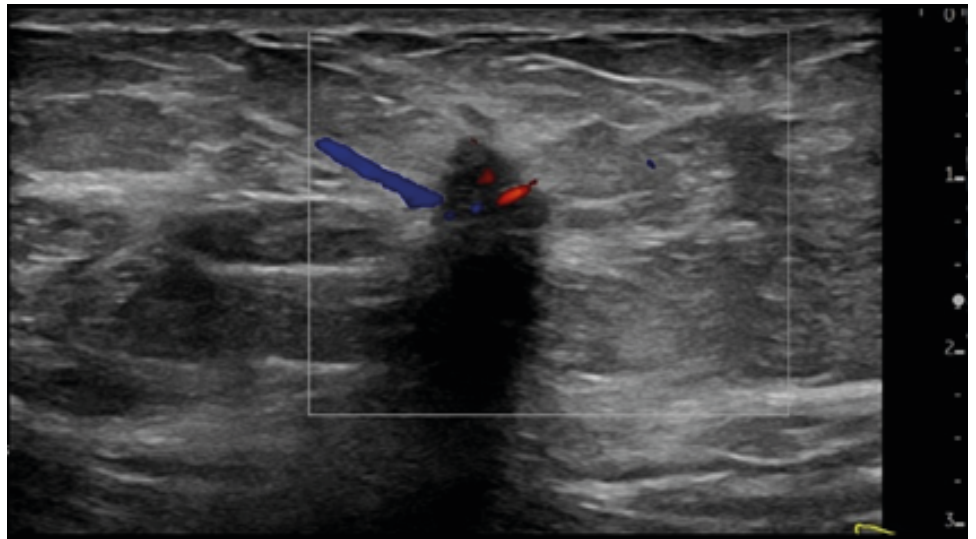


Figure 4. Color flow ultrasound image. There is an irregular vascular mass with acoustic shadowing.

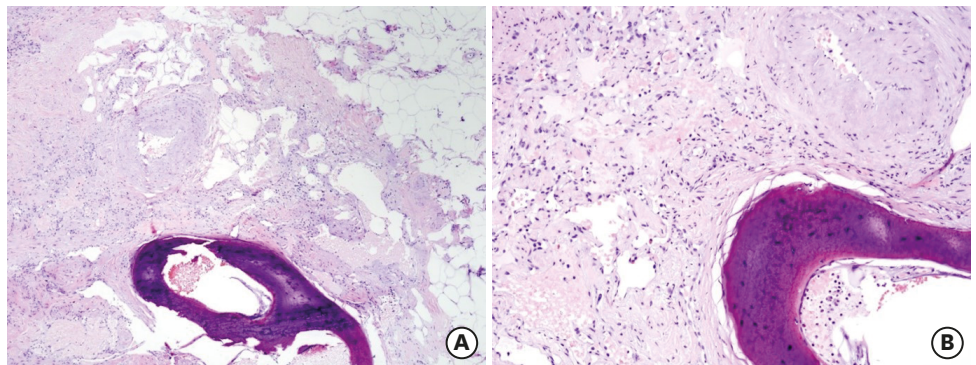


Figure 5. OM with associated hemangioma. (A) There are variably sized vessels adjacent to a calcified bony trabeculum (H&E stain, $\times 40$). (B) OM within a vascular proliferation lined by bland endothelial cells (H&E stain, $\times 100$). OM = osseous metaplasia; H&E = hematoxylin and eosin.

Faxitron digital radiographic imaging of the paraffin blocks demonstrated calcifications corresponding to the foci of OM. No atypia or malignancy was identified in the numerous levels examined.

DISCUSSION

Bonet may have been the first to record a case of OM in the breast when he described a tumor that could not be cut with a knife [1]. Since then, there have been over 200 reports of OM in the breast associated with primary breast cancers, metastatic tumors to the breast, benign breast tumors, a variety of non-neoplastic conditions, and as an isolated finding.

The pathogenesis of OM is unclear. Suggested mechanisms include transformation of stromal fibroblasts into osteoblasts, epithelial-stromal metaplasia, and ossification of calcific debris. The roles of stem cells, cytokines, growth factors, extracellular matrix, and bone morphogenic proteins have been postulated.

For many, especially those involved in the care of patients with breast cancer, matrix-producing metaplastic breast carcinoma with heterotopic bone formation is highest in the differential diagnosis of a breast lesion with OM [2]. Other reported malignancies in the breast with associated OM include primary breast fibrosarcoma, malignant mesenchymoma, and primary osteosarcoma of the breast [3,4], as well as malignant phyllodes tumor [5] and metastatic osteosarcoma to the breast [6]. There are case reports of OM associated with benign and borderline tumors of the breast, including fibroadenoma [1,7], phyllodes tumor [5], pleomorphic adenoma of the breast [7], localized amyloid tumors [8], intraductal papilloma, and hamartoma.

OM has been reported in association with a variety of benign non-neoplastic conditions in the breast, including abscess [9], chronic mastitis [10], hematoma, trauma [11], fat necrosis, myositis ossificans [12], fasciitis ossificans [13], and cholesterol granuloma [14]. OM has also been reported as a lesion without other associated findings [15].

OM in the breast is uncommon. Spagnolo and Shilkin [7] found OM in 1/90 fibroadenomas (1.1%) and 2/158 breast cancers (1.3%).

To the best of our knowledge, these are the first reported cases of an association between OM and hemangioma in the breast. The long-term clinical significance of this finding is unknown. While OM associated with benign lesions is usually considered a curiosity, Gafumbegete et al. [4] reported a case of primary osteosarcoma of the breast occurring one year after complete surgical removal of 2.1 cm area of OM in the ipsilateral breast.

Calcifications seen on screening mammography may prompt additional radiologic work-up. Selected characteristics of the calcifications may lead to recommendations for biopsy due to the increased risk of pre-malignant or malignant lesions associated with certain patterns of calcifications. OM may manifest radiographically as pleomorphic or heterogeneous calcifications, which are considered radiographically suspicious for malignancy (BI-RAD 4 or 5). Recognition of suspicious calcifications associated with OM on biopsy is important to exclude a clinical or radiologic consideration of malignant processes such as matrix-producing metaplastic carcinoma or other high-grade malignancies. We report the first 2 cases of OM associated with a hemangioma of the breast. Recognition of OM and its association with a variety of lesions is important to expand the differential diagnosis and enhance clinical, radiologic, and pathologic correlation, as well as subsequent management and follow-up of the patient.

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