Case report

Benign osseous metaplasia of the breast infiltrated by invasive pleomorphic lobular carcinoma: A case report

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ARTICLE INFO

Keywords:
- Osseous metaplasia
- Pleomorphic lobular carcinoma
- Breast cancer

ABSTRACT

Introduction and importance: Benign osseous metaplasia (BOM) is a rare entity, with only few cases reported in the breast. Here we present an unusual case of pleomorphic lobular carcinoma of the breast infiltrating BOM, discuss potential mimics and review the literature.

Case presentation: An 86 year-old female presented with right breast lump for two weeks. Clinical examination revealed a palpable mass, associated with skin tethering and nipple inversion. Mammography and ultrasound showed a densely calcified lesion associated with parenchymal distortion. Core biopsy confirmed malignancy and the patient underwent mastectomy and sentinel lymph node biopsy. Histological assessment showed a 45 mm mass of benign bone trabecula infiltrated by invasive grade 2 lobular carcinoma of classic and pleomorphic types with nodal positivity (2/2). The patient received adjuvant radiotherapy to chest wall and axilla for 3 months. She remains well on aromatase inhibitors after 9 months of follow up.

Clinical discussion: Few cases of breast BOM have been reported in the literature commonly in association with benign lesions such as fibroadenomas. So far, only two cases associated with invasive classic lobular carcinoma have been reported in the literature. The main differential is metaplastic (mesenchymal/ matrix producing) carcinoma, in which the osseous component is malignant and the cancer if often of a high grade, basal phenotype.

Conclusion: We present the first case of BOM of the breast associated with invasive pleomorphic lobular carcinoma. Awareness of the entity and distinction from metaplastic carcinoma and malignant phyllodes with heterologous element are important to ensure appropriate patient management.

1. Introduction

Benign Osseous metaplasia (BOM) is defined as extra-skeletal bone formation within soft tissue \cite{1}. Its existence within the breast tissue is rare with few cases reported in association with breast neoplasms, most commonly fibroadenomas \cite{2–4}.

We present an unusual case of pleomorphic lobular carcinoma infiltrating BOM of the breast which was managed at a tertiary hospital. Review of literature has shown only two cases of BOM associated with classic lobular carcinoma \cite{5,6} with no reported cases co-existing with pleomorphic lobular carcinoma. In this report, we aim to present the first case of pleomorphic lobular carcinoma in association with BOM, discuss the potential histopathological mimics and review the literature. This report has been written in accordance with SCARE 2020 guidelines \cite{7}.

Abbreviations: BOM, Benign Osseous metaplasia is a heterotopic bone tissue..

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https://doi.org/10.1016/j.ijscr.2022.107716
Received 7 September 2022; Received in revised form 26 September 2022; Accepted 27 September 2022
Available online 30 September 2022

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2. Case presentation

2.1. Patient information

An 86-year-old female presented to the breast clinic with a right breast lump, noticed 2 weeks ago. The patient has a past medical history of hypertension, hypercholesterolemia, arthritis and hay fever. She was on anti-hypertensives and anti-statins. Her mother and sister were diagnosed with breast carcinoma at the age of 61 and 80 respectively. There was no history of cancer, any previous relevant interventions, genetic information, psychosocial history or family history of ovarian cancer.

2.2. Clinical findings

 Revealed a hard lump at 9 o'clock position, measuring 4 cm in diameter. The lump was noticed 3 to 4 cm away from the nipple and was associated with skin tethering and nipple inversion. The overall clinical appearances suggested a malignant lesion.

2.3. Diagnostic assessment

Bilateral mammography and ultrasound of the right breast and axilla were done. The mammogram showed a large dense lobulated calcification in the outer quadrant and central region of the breast, measuring 39 mm in size. It also showed parenchymal distortion around it, with a total dimension up to 49 mm. There was some benign micro-calcifications seen in the anterior aspect of the breast (Fig. 1A&B). The breast ultrasound confirmed the mammogram findings (Fig. 1C&D). The right axillary ultrasound showed lymph nodes within normal size and morphology.

There were no recent mammograms for comparison. However, two previous mammogram reports were retrieved from the hospital electronic records. They were reported twenty-five and fifteen years ago, respectively. First report indicates the presence of mixed density in both breasts with benign calcifications in the right side. The second report pointed out the lack of any no significant changes from previous images. The precise size/location of the calcification was not stated.

In the view of these findings, an ultrasound guided core biopsy was

![Fig. 1. Radiological findings of the right breast lesion. A, B: Mammogram, cranio-caudal and mediolateral oblique views, showing large dense and lobulated calcifications in the outer and central part of the breast. C, D: Ultrasound images showing lobulated calcifications with hyperechoic outline and dense posterior acoustic shadowing. D shows a subtle hypoechoic change (red arrows) adjacent to the dense calcification (yellow arrow). E, F: Computerized tomography (CT) scans showing a calcified lobulated lesion. F is a magnified image showing the heterogeneous osseous nature of the calcifications. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)](image-url)
taken. The histopathological examination revealed a grade 2 invasive classic lobular carcinoma with no calcification or osseous elements seen. The carcinoma was diffusely and strongly positive for oestrogen and progesterone receptors but negative for Her2 immunohistochemistry (score 0).

Staging computerized tomography (CT) scan was done and it confirmed the osseous nature of the breast lesion with no evidence of definite metastasis (Fig. 1E,F). Small lung nodules of uncertain significance were found.

Following multidisciplinary team (MDT) discussion, the patient underwent right mastectomy and sentinel lymph node biopsy after one month of neoadjuvant endocrine therapy. The mastectomy specimen weighed 650 g and measured 190 × 150 × 50 mm. Macroscopically, there was a well circumscribed large bony hard and calcified mass in the central quadrant of the breast, measuring 45 mm in the maximum dimension. Sections from the hard bony mass underwent decalcification before processing. Microscopic assessment of the 45 mm mass showed a bony matrix with fairly circumscribed edges, consisting of benign mature bone trabeculae surrounded by a hyalinised stroma. There was an associated grade 2, invasive lobular carcinoma of both classic and pleomorphic types infiltrating the bone trabeculae (Fig. 2A–E). There was no evidence of malignant osseous or sarcomatous component. A focus of lobular carcinoma in situ was noted.

In addition, there was evidence of tumour response to neoadjuvant endocrine therapy particularly in areas away from the osseous metaplasia. The invasive carcinoma was 1 mm from the closest deep margin. There was a total of two positive sentinel lymph nodes (Fig. 2F).

A panel of confirmatory immunohistochemistry was done. The carcinoma was diffusely positive for GATA-3, oestrogen and progesterone receptors and negative for Her2 (score 0). E-cadherin and Beta catenin were negative in tumour cells, confirming the lobular phenotype (Fig. 2G–J). The carcinoma was negative for basal markers; including p63 and cytokeratin 14. The diagnosis of a grade 2 invasive pleomorphic and classic lobular carcinoma infiltrating benign osseous metaplasia of the breast was therefore confirmed.

2.4. Differential diagnosis

In view of the presence of heterologous element (bone), the differential diagnosis should include metaplastic carcinoma (mesenchymal type/matrix producing), malignant phylloides tumour with heterologous component, primary osteosarcoma and metastases. Metaplastic mesenchymal type carcinomas are often of high grade, basal, triple negative profile. The associated heterologous element is malignant, unlike the current case. Malignant phylloides tumours can show osseous metaplasia and/or malignant bone or osteoid. A biphasic/leaf like pattern may be seen. The tumour is purely stromal and lacks the lobular morphology, cytokeratin expression and luminal phenotype. Primary osteosarcomas of the breast are extremely rare, should include malignant bone/osteoid and should only be considered after excluding primary breast carcinomas including metaplastic carcinoma. Metastases to the breast are diagnosed by careful attention to history of previous malignancy and immunohistochemistry diagnostic of the site of origin.

2.5. Therapeutic intervention

The patient underwent right mastectomy with sentinel lymph node biopsy after one month of neoadjuvant endocrine therapy. In view of the nodal involvement, the patient received post-operative breast and axillary radiotherapy. She is on adjuvant letrozole to continue for at least 5 years. (Table 1).

2.6. Follow-up and outcome

The patient tolerated the procedure and she was followed up regularly. The follow up CT revealed stable lung nodules. She remains well with no evidence of local recurrence or metastasis; nine months post operatively (Table 1).

3. Discussion

Benign osseous metaplasia is usually associated with a neoplastic condition that acts as predisposing factor. However, few isolated cases of BOM without associated lesions have been described [1]. Moreover, occasional cases of BOM in association with non-neoplastic conditions such as breast abscess have also been published [8].

Regarding cases of BOM that occurred in association with neoplasms, the data in the literature is limited with a total of 21 cases reported. These include thirteen reports of BOM with benign neoplasms and eight cases in association with malignancy. Of the malignant cases, only two of the BOM cases were associated with invasive classic lobular carcinoma [5,6] (Table 2).

Interestingly, the ossifications in those two cases were not directly infiltrated by the invasive carcinoma. For instance, Spangolo et al. described the ossification in an area of dystrophic calcification with no direct relation to the neoplastic epithelium [5], while Sahli et al. reported it within a fibroadenoma occurring synchronously with the lobular carcinoma [6]. Moreover, there are no previous reports on its association with pleomorphic lobular carcinoma.

The pathogenesis behind the ossification is still unclear. It has been postulated that osteoblasts develop from modified fibroblasts that transform under certain conditions. These ossifications may develop either directly from the fibrous tissue or can be secondary to cartilage formation [20].

The clinical diagnosis of BOM might be challenging and requires histopathological confirmation as it may simulate carcinoma clinically and radiologically [13]. The mammographic and ultrasound findings of osseous metaplasia can vary according to the associated neoplasm, where present. For instance, osseous metaplasia associated with malignant neoplasms, as in the current case, can appear either as a circumscribed or speculated mass with calcifications [16].

4. Conclusion

This is the first case of pleomorphic lobular carcinoma infiltrating BOM of the breast. BOM is rare but the recognition of this entity, and distinction form its mimics, is essential to enable appropriate patient management.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Not required for case reports.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

Not applicable.

Guarantor

Hessa Aljhdali.
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Fig. 2. Macroscopic and microscopic appearances of the lesion with the immunohistochemical profile.
A: Macroscopic image showing the hard bony and calcified breast mass (red arrows).
B, C: Low and high power views for the mature bone trabecula lined by osteoblasts.
D: The invasive pleomorphic and classic lobular carcinoma. Note the dyscohesive lobular cells growing in linear cords and single cells.
E: The decalcified bony trabecula are infiltrated by carcinoma cells.
F: A sentinel lymph node with a large metastatic deposit of invasive carcinoma.
The invasive carcinoma is GATA 3 positive (G), oestrogen receptor positive (H), e-cadherin negative (I) and beta catenin negative (J) confirming the lobular phenotype. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
The patient’s history and presentations in order of events.

| Date | Patient’s visits and follow up | Diagnostic assessment | Plan |
|------|-------------------------------|-----------------------|------|
| Initial presentation | Presented to breast clinic with a hard lump in right breast. | - Bilateral mammogram showed right breast lesion, highly suspicious for malignancy. - Breast ultrasound confirmed mammographic findings. - Right axillary ultrasound showed normal lymph nodes. | Breast core biopsy. |
| After 15 days | Follow up | Breast biopsy showed grade 2, ER/PR positive, HER2 negative invasive lobular carcinoma. | - Start letrozole 2.5 mg once a day - CT staging. - Follow up visit |
| After 22 days | Follow up | Staging CT revealed several small lung nodules of uncertain significance and liver lesions (most likely cysts by ultrasound). | - Right mastectomy and sentinel lymph node biopsy, done after 6 days by breast and oncoplastic surgeons. - Follow up lung CT in 3 months’ time. - Refer to clinical oncologists. |
| After 6 weeks | Follow up | - Patient had no complaints after surgery. - Final histopathology showed 65 mm Grade 2 invasive pleomorphic and classic lobular carcinoma infiltrating benign osseous metaplasia with two positive sentinel lymph nodes. Hormone receptors status was similar to those in the previous biopsy. | |
| After 2 weeks | Follow up with clinical oncologists | Patient is well with no complaints. | - Letrozole for at least 5 years. - Radiotherapy to chest and axilla for 3 months. - Bone density assessment. |
| After 5 months | Follow up | - Patient is well with no complaints and the radiotherapy was tolerated well. | - Continue Letrozole. |
| | | - Follow up lung CT scan shows stable lung nodules with no new features. - Bone density scan shows osteoporosis. | - Follow up mammogram 12 months from surgery - Next visit in 12 months. |

Table 2
Summary of cases of BOM of the breast with associated neoplasms reported in the literature.

| Author | Year | Associated breast lesion (Benign Total = 13 cases) | Malignant (Total = 8 cases) |
|--------|------|---------------------------------------------------|-----------------------------|
| Fleming et al. | 1954 | 2 fibroadenoma | |
| Jernstrom et al. | 1963 | 1 osteogenic sarcoma of mammary gland | |
| Patel et al. | 1966 | 1 metastatic carcinoma of the rectum | |
| Gonzalez-Licea et al. | 1967 | 1 undifferentiated malignant tumour | |
| Spangnolo et al. | 1983 | 1 fibroadenoma, 1 pleomorphic adenoma | |
| | | 1 invasive classic lobular carcinoma | 1 invasive ductal carcinoma |
| Imai et al. | 1984 | 1 papilloma with adenosis | |
| Nishida et al. | 1989 | 1 fibroadenoma | |
| Lynch et al. | 1993 | 1 primary localized amyloid tumour, bilateral | |
| Mayers et al. | 1994 | 1 fibromatosis | |
| Yokoo et al. | 1998 | 1 primary localized amyloid tumour | |
| Evans et al. | 1999 | | |
| Haj et al. | 2004 | 1 neuroma | |
| Murali et al. | 2006 | 1 fibroadenoma | |
| Christensen et al. | 2019 | 1 malignant phyllodes tumour | |
| Dubson et al. | 2021 | 2 haemangiomas | |
| Salh et al. | 2022 | 1 synchronous case of invasive lobular carcinoma and fibroadenoma | |

Provenance and peer review
Not commissioned, externally peer-reviewed.

CRediT authorship contribution statement
SB and VG operated on the patient and obtained consent. SK performed imaging, image guided biopsy and provided radiological photographs. HA wrote first draft and reviewed the literature. AMS diagnosed the case, provided histological photographs, contributed to literature review, writing, editing and overall supervision. All authors approved the final manuscript.

Declaration of competing interest
The authors of this article have no conflict of interests, and the case report was not supported or funded by any company.

Acknowledgements
None.

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