



Case Report

Metastases after mastectomy for ductal carcinoma in situ of the male breast; A case report

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ABSTRACT

Introduction: and importance: Male breast cancer is a rare entity. Ductal carcinoma in situ (DCIS), constituting 10% of all male breast cancer, is confined within the breast ducts and lobules, rarely metastasizing and even less so after mastectomy.

Case presentation: A 71 years old male with no history of trauma presented with pain, swelling, and deformity of the left arm. He had continuous back pain for 6 months and a history of mastectomy of the right breast. Fracture of shaft of the left humerus was detected on X-ray. Computed tomography (CT) showed multiple vertebral metastases later confirmed to be metastasized from the breast by biopsy. Tumor cells were progesterone receptor (PR) positive, estrogen receptor (ER) negative, and human epidermal growth factor receptor 2 (HER2) negative. The fracture was treated and the patient was kept on Tamoxifen. On follow-up after four months, the patient is doing well with relief of back pain.

Clinical discussion: Despite mastectomy and the histopathological diagnosis of pure DCIS, distant metastases can occur even in absence of locoregional recurrence. Therefore, the aggressive phenotype of DCIS rather than diagnostic or treatment variables can be thought to bring worse outcome in the form of metastases. Early hormonal status identification and hormone therapy could result in a better outcome.

Conclusion: Skeletal metastases should be strongly suspected in patients presenting with bone pain and having a history of DCIS of the breast, even after mastectomy. Even though distant metastasis after mastectomy is rare, regular follow-up and surveillance is necessary.

1. Introduction

Male breast cancer is a rare entity with an incidence of 1% of total malignancies in males and less than 1% of all diagnosed breast cancer [1]. The lifetime risk of breast cancer in men is 1:1000, which is far less than 1:8 in women [2]. Only 10% of male breast cancer is Ductal carcinoma in situ (DCIS) [3]. As DCIS is confined within the breast ducts and lobules, it rarely metastasizes. Distant metastases after mastectomy for DCIS is even rarer reported in females to be far less than 1% [4,5].

We now report a case of male DCIS presenting with multiple skeletal metastases and pathological fracture after years of mastectomy for DCIS. This report has been reported in line with the SCARE 2020 criteria [6].

2. Case presentation

A 71 years old male with no significant personal and family history presented to BPKIHS, a tertiary care centre in Eastern Nepal on 7th April 2017 with the chief complaint of gradually increasing painless swelling in the right breast for one year. On physical examination, well-defined irregular swelling 4 × 4 cm below the nipple-areola complex, freely mobile, not attached to the chest wall with no overlying skin changes, nipple retraction, or discharge was found. On ultrasonography, a well-defined heterogeneous lesion 40 × 35 mm arising from the subareolar region of the right breast with intrinsic vascularity and scattered calcifications was reported. Fine Needle Aspiration Cytology of the right breast showed a papillary lesion with mild epithelial atypia. Based on

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epithelial atypia, a simple mastectomy was performed. Postoperative histopathological examination revealed intermediate-grade DCIS with an apocrine component with no evidence of invasion. Multiple sections examined showed several foci revealing proliferation of ductal epithelial cells filling the duct lumina with central comedo necrosis. These cells were monotonous, had high nucleo-cytoplasmic ratio, hyperchromatic nuclei, irregular nuclear membrane and prominent nucleoli. These epithelial cells lacked myoepithelial cell layer. Areas of micropapillary ductal carcinoma in situ were also observed. The patient was advised for immunohistochemistry for confirmation of diagnosis and absence of invasion but lost to follow-up.

On July 15th, 2021, he presented to the emergency department with presenting complaint of pain, swelling, and deformity of the left arm with restriction of movement at the shoulder and elbow. He also had a history of continuous back pain. He had no history of trauma. On metastasis workup, multiple lytic lesions with enhancing soft tissue components in multiple bilateral ribs, left scapula, pelvic bones, and multiple thoracic, lumbar, and sacral vertebrae with the collapse of T12 vertebra were detected suggestive of metastases (Fig. 1). Prostate-Specific Antigen was in the normal range. The absence of recurrent disease and another primary tumor in the contralateral breast was confirmed by clinical breast examination, mammography, ultrasonography, and computer tomography. Fracture of shaft of the left humerus was detected on x-ray (Fig. 2A). Imprint cytology from the shaft of the left humerus showed definite evidence of malignancy which was later confirmed to be metastasized from the breast by biopsy (Fig. 3). Tumor cells were positive for progesterone receptor (PR), and negative for estrogen receptor (ER) and human epidermal factor receptor 2 (HER2). Fracture of the left humerus was managed with 5 cm segment excision and shortening followed by plate fixation (Fig. 2B). The patient was administered tamoxifen 20mg daily, and on follow-up after four weeks, bone pain was relieved.

3. Discussion

Male Pure DCIS presents clinically as mass (58%), nipple discharge (35%), and gynecomastia (19%) with a median age of presentation of 65 years. Major risk factors implicated for male DCIS are similar to invasive breast cancer [7]. These include demographic factors; increasing age,

black race and family history of breast cancer, genetic factors; BRCA2 and BRCA1 mutations, environmental factors; radiation exposure and hormonal factors; Klinefelter's syndrome, gynecomastia, liver disease, obesity, and testicular abnormalities. Hormonal factors by increasing estrogen to androgen ratio increase the risk of male breast cancer [8]. None of these factors were present in our patient except older age and BRCA mutation which could not be investigated due to the unavailability of the testing facility in our setting.

So far the randomized controlled trial hasn't been conducted for the optimal surgical management of male breast cancer. Treatment decisions for male breast cancer are based on research done on female breast cancer [9].

There has often been a dilemma in choosing the best surgical option for the treatment of DCIS. Breast-Conserving treatment (BCT) which includes wide local excision (WLE) and WLE with radiotherapy may be under treatment leading to recurrence and metastases. On the other hand, mastectomy may be overtreatment leading to psychological distress. The eight years recurrence rate and distant metastasis rate after BCT is 12% and 4% respectively. However, after mastectomy, both eight years recurrence rate and distant metastasis rate are less than 1% [4].

Out of 297 DCIS patients diagnosed by core needle biopsy who also underwent sentinel lymph node biopsy, only 10 patients were found to be sentinel lymph node positive [10]. In our case, a definite diagnosis of pure DCIS was made after postoperative histopathological examination and no evidence of invasion was found. Therefore, sentinel lymph node biopsy was not done at the initial diagnosis of DCIS to avoid unnecessary morbidity.

Younger age (55 years or less), diagnosis by core needle biopsy, DCIS size of greater than 4 cm, and high-grade DCIS are the independent predictors of invasive breast cancer in patients with the initial diagnosis of DCIS [11]. So far, there is an unavailability of data regarding the pathological and clinical predictors of metastasis after treatment for DCIS in the male breast due to its rarity. In our patient, none of these factors were present.

In an analysis of pure DCIS cases from 1996 to 2009, the rate of distant metastasis after original treatment of DCIS was 0.14%. Major Predictors for distant metastasis were found to be DCIS with necrosis, negative estrogen receptor status, and preceding or simultaneous locoregional recurrence. The patients who developed distant metastases

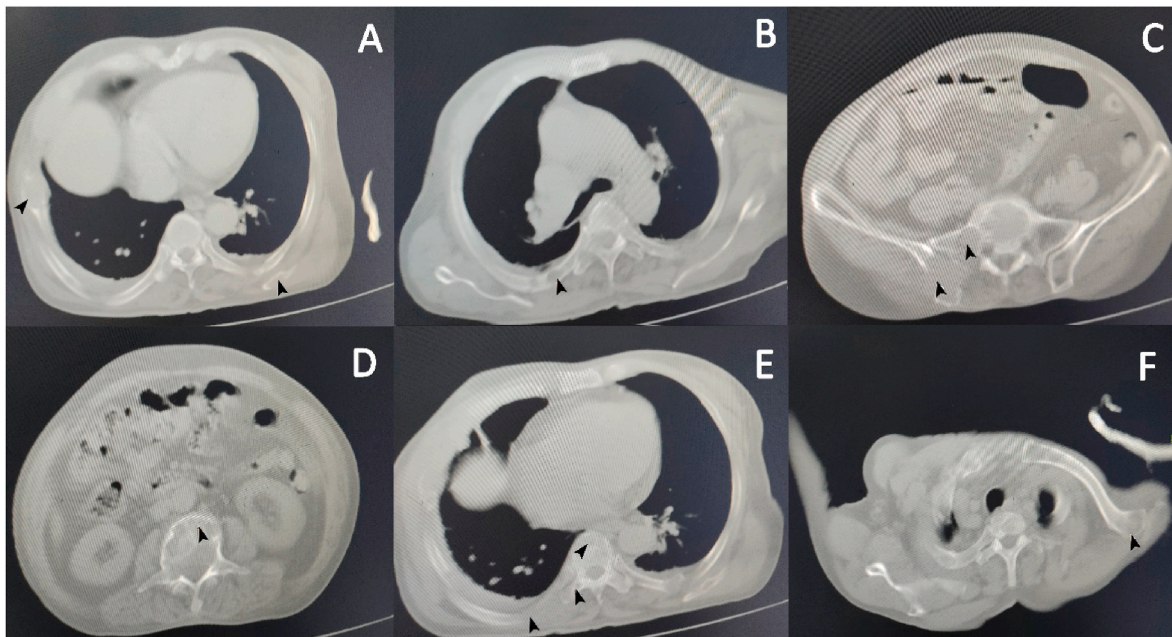


Fig. 1. Lytic lesions suggestive of metastases (black arrow) in A. Rib and left scapula, B. Rib, C. Ilium and sacrum, D. Vertebral body, E. Vertebral body and transverse process, and rib F. Left clavicle.

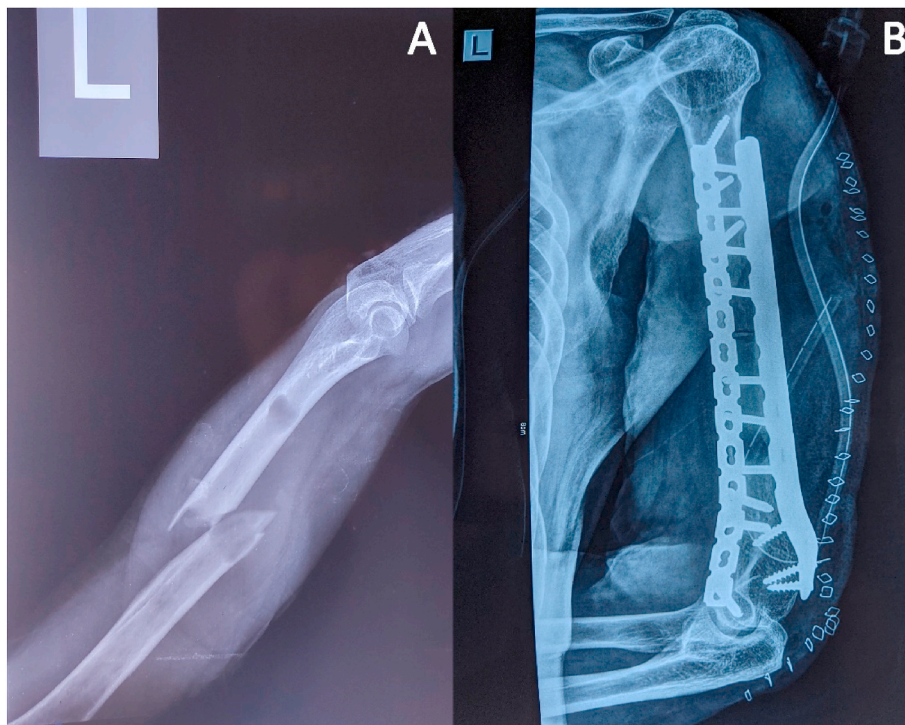


Fig. 2. A. X ray showing two lytic lesions in shaft left humerus and fracture through one of them. Fig2B. X ray showing plating done for fracture of shaft of left humerus.

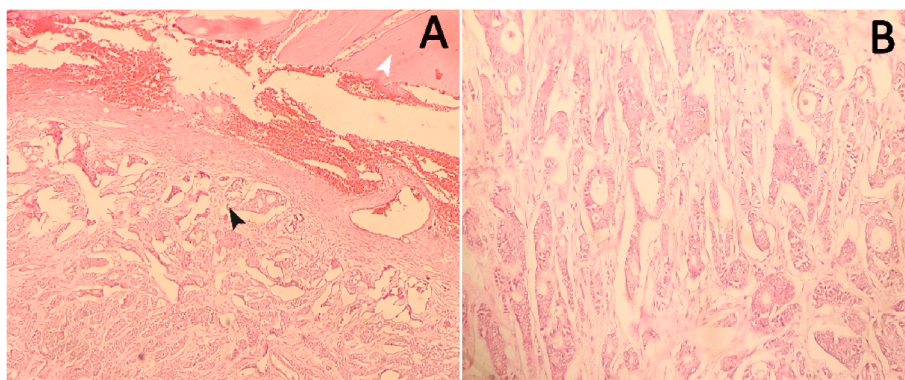


Fig. 3. A. Section reveals proliferation of tumor cells arranged in trabeculae and few forming glands (black arrow). Overlying cortical bone is unremarkable (white arrow). (H & E, x40) B. Section reveal tumor cells arranged predominantly in glands and in cribriform pattern having high nucleocytoplasmic ratio, vesicular chromatin, irregular nuclear membrane, and moderate amount of cytoplasm. (H & E, x100).

had undergone adequate treatment either as total mastectomy or partial mastectomy with adjuvant radiotherapy [5]. As Male DCIS is very rare, such data are not available. Our patient had a simple mastectomy and postoperative diagnosis of pure DCIS. Therefore, the aggressive phenotype of DCIS rather than diagnostic or treatment variables can be thought to bring worse outcome in the form of metastases. Furthermore, our patient developed distant metastases without locoregional recurrence, the incidence of which is reported to be 0.004% [5].

Postoperative tamoxifen after surgical resection of hormone-positive DCIS has been found to decrease the incidence of primary invasive ipsilateral and contralateral carcinomas. However, there is no reduction in the risk of distant metastases [12].

Breast cancer cells hamper the normal bone remodeling pattern activating the osteoclasts and causing an increase in apoptosis of osteoblasts resulting in degradation of bone leading to pathological fracture [13].

ER negative/PR positive is not a reproducible entity, and most of the

breast cancers initially classified as ER negative/PR positive are ER positive/PR positive on retesting [14]. Because of the economic reason of our patient for retesting, and the evidence that male breast cancer is almost exclusively hormone positive with 99% of them expressing ER, our case was considered to be hormone positive [15]. Furthermore, in our case, IHC was sent from bone tissue as there was no evidence of recurrence in breast tissue. This could be the reason why ER might not have been represented. For male patients with hormone positive, HER2 negative metastatic breast cancer with no visceral crisis or rapidly progressive disease, endocrine therapy is the first-line therapy. Tamoxifen, an aromatase inhibitor with a gonadotropin-releasing hormone agent, and fulvestrant are the options [9]. Because of low cost and easy affordability, our patient was prescribed tamoxifen. As chemotherapy is reserved for visceral crisis [16], and our patient had only bone metastasis with no evidence of visceral crisis, it was not prescribed.

IHC helps to distinguish in situ and invasive carcinoma by using myoepithelial markers [17]. In our patient, IHC was not done after the

initial histopathological diagnosis of DCIS five years back as the patient lost to follow-up. Therefore, whether it was in situ or invasive at that time was not confirmed. This is the limitation of our case.

4. Conclusion

The behavior of DCIS is heterogeneous and may account for worse outcomes despite the favorable prognosis. If a patient after mastectomy for DCIS presents with bone pain, it shouldn't be thought of as age-dependent changes rather bone metastases should be strongly suspected. Even though distant metastasis after mastectomy for pure DCIS is rare, regular follow-up and surveillance is necessary. Mechanisms for distant metastasis in the absence of locoregional recurrence need to be investigated.

Patient consent

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

Provenance and peer review

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Ethical approval

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Author contribution

Ved Prakash Pant, Nishanta Dallakoti, Nabin Pokhrel: literature review, follow-up the patient, writing the manuscript, and final approval of the manuscript. Sushant Chaudhary: literature review and writing the manuscript. Soniya Dulal: treating medical oncologist, follow-up the patient, and final approval of the manuscript. Punam Paudyal: pathologist, data collection, writing the manuscript, and final approval of the manuscript.

Registration of research studies

Not applicable.

Guarantor

Ved Prakash Pant.

Declaration of competing interest

There is no conflict to be declared.

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