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RARE SARCOMA OF BREAST- PRIMARY OSTEOSARCOMA

Oncology

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ABSTRACT

Extraskeletal osteosarcomas are malignant and arise from soft tissue that produce osteoid, without any continuity to skeletal bone. Primary osteosarcoma of breast is a rare clinical entity. Although reported previously, there are no available guidelines for their management. A 52- year old lady who presented with rapidly growing tumor in breast was managed surgically. We discuss the diagnostic challenges and role of adjuvant therapy in our report.

KEYWORDS

Osteosarcoma, Breast, Extraskeletal, sarcoma

INTRODUCTION

Extraskeletal osteosarcomas are malignant and arise from soft tissue that produce osteoid, without any continuity to skeletal bone (Tao et al., 2011). They occur mostly in soft tissue of the thigh, upper limb, and retroperitoneum. Their occurrence in unusual sites, such as larynx, small intestine, parotid and breast has been reported. However, there isn't much clarity on their behaviour and management. Herein, we report a primary osteosarcoma of breast that was managed surgically.

Case Report

A 58 year old lady presented to us with complaint of a rapidly growing painful lump in the right breast since one month. She suffered from interstitial lung disease and her performance status was poor. On clinical examination there was a hard, irregular, mobile lump in the central and lower inner quadrant, measuring 5 x 6 cms. Overlying skin was thinned out, erythematous and fixed to mass; there were no enlarged axillary lymph nodes. Aspiration cytology showed multinucleate giant cells. Sonomammography showed a well defined hetero-echoic lesion, with solid and cystic areas within. X-Ray mammogram showed partial dense calcification on a well-defined mass (figure 1). Tentative diagnosis of malignant phyllodes tumor was made and patient underwent simple mastectomy after counseling.

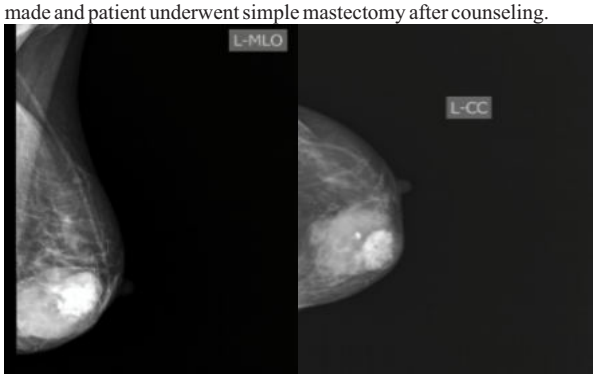

Figure 1- Mammographic Findings Of Left Breast Osteosarcoma

On macroscopic gross examination of the mastectomy specimen, a hard mass measuring 3.7 x 3.7 x 3 cms was identified with adjacent brown areas of cystic change. Microscopic analysis showed a malignant mesenchymal neoplasm composed of spindle cells with bizarre forms which were highly pleomorphic and had hyperchromatic nuclei with abundant eosinophilic cytoplasm. Many multinucleated giant cells were also noted. Characteristically, these neoplastic cells were seen laying down malignant osteoid. High mitotic rate was observed, and the tumour had infiltrative margins. However, the deep margin was uninvolved. On immunohistochemistry, the malignant spindle cells were diffusely positive for vimentin. The epithelial membrane antigen (EMA) showed negative to weak cytoplasmic staining focally (figure 2). The tumour was negative for ER, PgR, HER2/neu, CK, CD34, and SMA. The proliferative index was 70%. Whole body PET CT scan showed no other site of tumor. A diagnosis of primary osteosarcoma of breast was made. Case was discussed in multi-disciplinary tumor board and no adjuvant treatment was given. She was on close follow up when 6 months later she succumbed to interstitial lung disease.

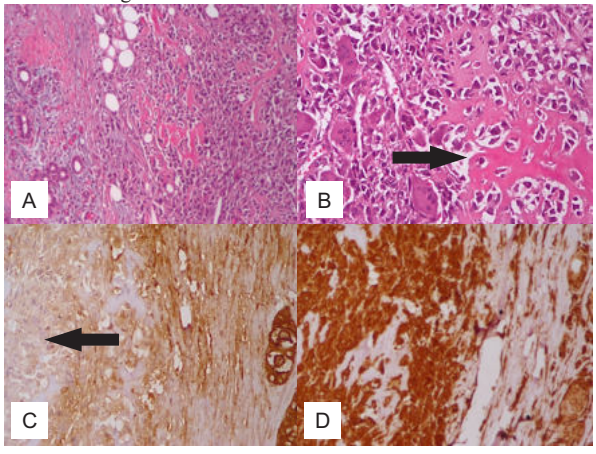

Figure 2: Photomicrograph showing A: Breast tissue with an infiltrating malignant mesenchymal neoplasm(H &E, original magnification X100), B: malignant osteoid (arrow), intimately associated with the neoplastic spindle cells and admixed giant cells(H &E, original magnification X200), C: Immunohistochemistry showing negative staining for EMA in the neoplastic spindle cells(arrow) while adjacent breast tissue showing strong membranous staining, D: Immunohistochemistry showing strong vimentin positivity in the neoplastic spindle cell(both at original magnification X200).

DISCUSSION

Primary osteosarcoma of breast is a rare clinical entity (Kallianpur et al., 2013). The histogenesis of breast osteosarcoma is not clear. Like other sarcomas of breast, it arises from mammary stromal mesenchymal tissue. Prior local irradiation, trauma and foreign body are some risk factors associated with extraskeletal osteosarcoma (Rizzi et al., 2013). Few authors have reported staged progression of breast metaplastic ossification and adenomyoepithelioma to full blown osteosarcoma with distant metastasis (Gafumbegete et al., 2016; Guo et al., 2016). This suggests that breast osteosarcoma may be a result of continuous metaplastic change. Therefore, mere presence of osteoid does not confirm diagnosis of primary breast osteosarcoma. Metaplastic carcinoma and cystosarcoma phyllodes must be excluded from differential diagnosis. Metaplastic carcinoma has a carcinomatous component and its neoplastic spindle cells are cytokeratin positive. Phyllodes is a biphasic tumor with characteristic

leaf-like architecture and epithelial component which can be picked up with extensive sampling (Adem et al., 2004). In the case presented here, IHC workup helped clinch the diagnosis.

Unlike carcinomas of breast which have spiculated margins or microcalcifications, sarcomas are round or oval with well circumscribed margins (Morales-Miranda et al., 2018). It is difficult to distinguish phyllodes tumors and metaplastic carcinomas from primary breast sarcomas and benign fibroepithelial lumps on mammography and ultrasound. One way to differentiate is that metaplastic carcinoma frequently involves the axillary lymph nodes (34%), which is unusual for primary breast sarcomas (Smith et al., 2012). Technetium 99-methylene diphosphonate (Tc-99m) scintigraphy may show intense localized uptake at site of tumor and help rule out bone primary (Krishnamurthy, 2015). Dense mineralization of a well-defined tumor on mammogram and increased vascularity combined with clinical findings of stony hard tumor and gritty feel during biopsy may alert the clinician to diagnosis of osteosarcoma.

Mastectomy or breast conservation surgery can be offered to patients; the emphasis is on R0 resection (Gutman et al., 1994). However, these tumors often grow rapidly to very large sizes, thereby limiting the option of BCS. Axillary dissection is not indicated in osteosarcoma breast (Silver & Tavassoli, 1998). Metaplastic carcinomas require axillary staging.

Multiple small series have found that radiotherapy and chemotherapy do not improve survival in extraskeletal osteosarcomas (Sio et al., 2016). A trend towards better local control with radiotherapy has been reported for phyllodes tumor of the breast (Varghese et al., 2017). Many authors have studied the behavior of breast sarcomas, excluding phyllodes. Osteosarcoma breast forms a very small proportion of these series- 5.2% of sarcomas in SEER database, 1 out of 25 cases in mayo series (Adem et al., 2004; Yin et al., 2016). Tumor behaviour and management of breast osteosarcomas can be extrapolated from this data and few case reports.

Gafumbegete et al reported a case of metaplastic ossification of breast excised completely with margins which recurred one year later as a large ulcerative mass and was diagnosed to be primary osteosarcoma after mastectomy (Gafumbegete et al., 2016). Similarly, Guo et al reported multiple recurrences after wide excision (Guo et al., 2016). Both these patients did not receive adjuvant radiation. In another report, patient rapidly developed lung metastasis despite mastectomy followed by chemotherapy and radiation for close margins (Crèvecoeur et al., 2015). Irrespective of the treatment modality used, patients may develop fatal lung recurrences within 1 to 2 years (N et al., 2006; Saber et al., 2008; Szajewski et al., 2014). There are also reports of patients reaching 5 year survival (Kallianpur et al., 2013). Thus, we see a varied behavior, which is classical to sarcomas.

It is important to follow up closely and understand each individual's tumor biology, though most portend a poor prognosis. Silver et al reported 5-year survival of 38%(Silver & Tavassoli, 1998). Yin et al in their analysis of primary breast sarcomas from SEER database report worst overall survival for osteosarcomas, contrary to the belief that angiosarcoma carries worst prognosis. They found benefit with adjuvant radiation following surgery for sarcomas than 5cms (Yin et al., 2016). Response rates to systemic therapy in breast sarcoma have been poor (Pencavel & Hayes, 2009).

Preoperative core biopsy forewarns the surgeon about malignancy and aides in planning a wide excision which is crucial to prevent local recurrences. Our patient however, refused a core biopsy as she was recovering from an exacerbation of interstitial lung disease. Many factors were taken into consideration before offering a mastectomy without adjuvant treatment to our patient- (i) poor performance status of patient (iii) rapidly growing tumor with impending ulceration (ii) small breast-tumor ratio, (iii) marginal benefit of adjuvant radiation in sarcomas of breast.

CONCLUSION

Whether one views it as a breast sarcoma or an extraskeletal osteosarcoma, breast osteosarcoma should be treated like sarcomas elsewhere in the body. Achieving negative margins in the first surgery is important as they are aggressive tumors with possibly limited benefit of adjuvant radiation and chemotherapy.

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