

Cutaneous Lesions As A Presenting Sign Of Metastases In Male Breast Cancer: A Rare Clinical Entity

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SUMMARY

Male breast cancer accounts for only 1% of cancers in men and 1% of breast cancers. Cutaneous metastases occur less than 10% of all patients with visceral malignancies and are considered a rare and late event in progression of metastatic disease. A 45-year-old man presented with a lump in the left breast which was confirmed to be infiltrating ductal carcinoma. He underwent a left mastectomy and axillary clearance followed by chemotherapy and radiotherapy to the left chest wall. However, he was non-compliant to adjuvant tamoxifen due to hot flushes. One year later, he presented with biopsy proven cutaneous metastases. Initially he had complete excision of the lesions, however, two months later more skin lesions appeared predominantly over the chest wall and back. Hormonal therapy failed to control the metastases as such he was treated with systemic chemotherapy. He is currently on third line chemotherapy.

KEY WORDS:

Male breast cancer, cutaneous metastases

INTRODUCTION

Male breast cancer (MBC) is a relatively rare disease accounting for only 1% of cancers in men¹. It typically presents in older men, with a peak age of 71 years¹. As in women, male breast cancers usually occur sporadically. However, possible risk factors include genetic disorders such as Klinefelter's syndrome, BRCA2 mutation, gonadal dysfunction and obesity¹.

Prognostic factors, survival by stages and patterns of metastases are similar to women with breast cancer, however, MBC tends to present at a later stage and there is a higher chance of chest wall infiltration due to minimal breast tissue¹.

Cutaneous metastasis from MBC is extremely rare. A MEDLINE search from 1960 to the present revealed only 4 reported cases of male breast carcinoma metastasizing to the skin².

CASE REPORT

A 45 year-old man presented with a six month history of a lump in the left breast which was gradually increasing in size. His only past medical history of note was asthma well controlled on inhalers. He did not have a family history of cancer.

On examination, a hard non-tender mobile mass was palpable below the nipple, measuring 2 x 2 cm in size. There were no overlying skin changes or palpable lymphadenopathy in the axilla or supraclavicular fossa. The rest of the clinical examination was within normal limits.

Fine needle aspiration cytology was done, and malignant cells were noted. He then underwent a left mastectomy and axillary lymph node dissection and histopathology revealed a grade 3 invasive ductal carcinoma, measuring 3.0 x 2.7 x 2.5 cm in size. The margins were clear of tumour. One out of the 10 dissected axillary lymph nodes contained a metastatic deposit. There was no vascular or lymphatic invasion seen. Estrogen and progesterone receptor status was positive.

He then underwent six cycles of chemotherapy (5-Fluorouracil 600mg/m², Epirubicin 75mg/m², and Cyclophosphamide 600mg/m²) followed by adjuvant radiotherapy (45Gy in 25 fractions) to the left chest wall and supraclavicular fossa.

Staging investigations which included a bone scan, chest radiograph and abdominal ultrasound revealed no evidence of distant metastasis. He was then started on tamoxifen as part of his adjuvant therapy for a planned duration of five years.

However, the patient was not compliant to tamoxifen as he was having unbearable hot flushes. He stopped taking his tamoxifen within a few months, and defaulted follow up. One year later, he presented with three small hard skin nodules over the posterior chest wall. He had noticed the nodules gradually increasing in size and they were causing him discomfort.

Biopsy of the skin nodule was performed, and this confirmed the diagnosis of cutaneous metastasis from breast carcinoma, which was positive for estrogen receptor (ER), identical to his primary tumour.(Fig. 1a and 1b)

He had the lesions completely excised; however, new lesions appeared predominantly over the anterior and posterior chest wall and lower back. He was started on tamoxifen and re-staging investigations were ordered.

Staging computerized tomography (CT) scan of the thorax and abdomen revealed a few heterogeneous nodules in the left upper and lower lobes, with the largest measuring 1.2 x 1.0 cm, and a lytic lesion of the posterior left 9th rib.

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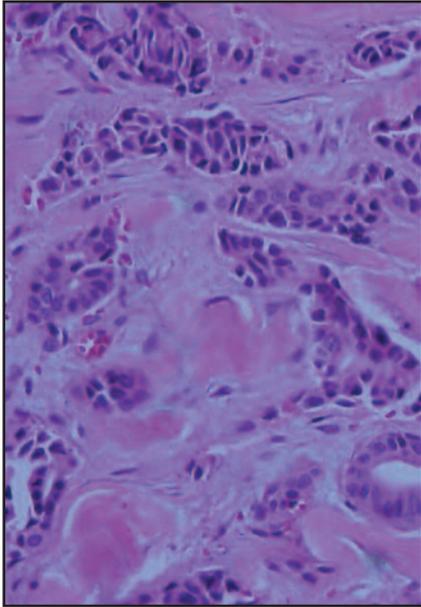


Fig. 1a : Image1a-H&E Section shows malignant ductal cells arranged in clusters on higher magnification.

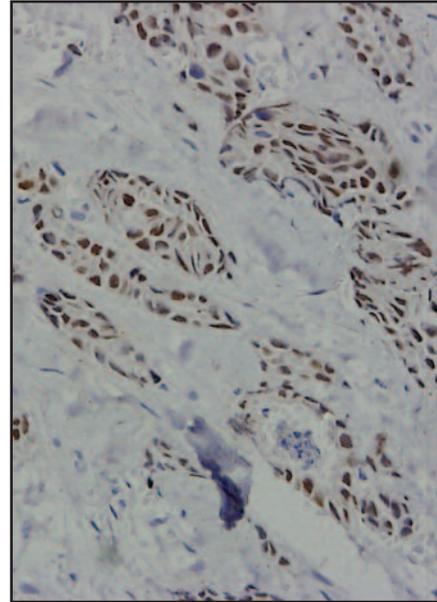


Fig. 1b: Immunohistochemistry shows the malignant cells express nuclear staining for estrogen receptor (ER).



Fig. 2 : skin metastases seen on arm, face and chest.

As the disease was not being controlled on tamoxifen, he was commenced on chemotherapy, Taxotere 75mg/m² of which he completed six cycles. He had a good partial response with all skin nodules completely resolving and the lung nodules also decreased in size. The patient was restarted on tamoxifen.

However, six months later, he relapsed with new skin nodules over the left arm, back and face. (Fig. 2) Restaging CT scan also revealed new nodules in both lungs and previous lung nodules had increased in size. He has been commenced on third line chemotherapy, Capecitabine 1000mg/m² twice daily for 14 days out of 21 days.

DISCUSSION

Cutaneous metastases

Patterns of metastases in MBC are similar to that seen in the female counterpart with the common sites of hematogenous spread being bone, lungs, brain and liver². Cutaneous metastases occur in 0.7 to 9% of all patients with visceral malignancies and are considered a rare and late event in the progression of metastatic disease³.

The morphologic characteristic of cutaneous metastasis may be variable. In a review of 164 cases of cutaneous metastases in female breast carcinoma, the most common presentation is nodular metastatic carcinoma which is seen in 80% of the cases⁴. This form can present as cutaneous or subcutaneous, solitary or multiple, pink to reddish, firm and rarely as ulcerated nodules.

Other presentations of cutaneous metastases which are less common include the following; telangiectatic carcinoma characterized by its purpuric papules, nodules or plaques; "en cuirasse" metastatic carcinoma which appears as an infiltrated and extensive plaque in the mammary region; and inflammatory metastatic carcinoma which presents as an erythematous, warm, tender patch or plaque with a raised well-defined margin⁴.

The location of the cutaneous metastases usually occurs in certain regions depending on the site of the primary cancer⁴. Skin metastasis on the chest wall commonly originates from breast and lung cancers, whereas skin metastases on the abdomen are usually from primary cancers originating from the colon, ovary and bladder⁴.

In the review of 164 cases of cutaneous metastasis of female breast carcinoma, the commonest sites were located at the

site of mastectomy and anterior chest in over 75% of the cases. Other locations include the axilla, back and scalp. Our patient is unusual, in that he initially presented with lesion in the posterior chest wall. The median time to presentation of the cutaneous metastases are usually 4.1 years following the diagnosis of breast carcinoma⁴. However, our patient presented with cutaneous metastases just over 18 months from initial diagnosis.

In cases of occult metastases, biopsy of the skin nodule will help in confirming the diagnosis, and the microscopic appearance will suggest the likely tissue of origin. Usually, the histologic features of the metastasis are similar to the primary tumor.

Male breast cancer

Male breast cancer is a rare disease, with an incidence of only 1% of all breast cancers¹. The incidence increases exponentially with age and there is no bi-modal age distribution as seen in women¹. The most common clinical presentation is a painless, sub-areolar mass, usually in the left breast, which is similar to our patient¹. 90% of the male breast carcinoma are invasive ductal carcinomas, and 90% of them are hormone receptor positive¹.

As most of the MBCs are hormone receptor positive, tamoxifen is recommended following local therapy in early breast cancer or as initial therapy in advanced breast cancer⁵. However, the side effects of tamoxifen may be less tolerable in men. A study showed that in less than one year, 21% of men discontinue their treatment because of side effects, compared to just 4% of the women⁵, as seen in our patient.

There is lack of data on the role of aromatase inhibitors in male breast carcinoma. In advanced stage breast cancer, aromatase inhibitors are the preferred agent for postmenopausal women with hormone-responsive breast cancer. Preclinical data suggest that it may be less effective in men, as animal models demonstrate significant increases in follicle-stimulating hormone (FSH) and testosterone, but no change in levels of estradiol¹. However, there are a few reports of responses to aromatase inhibitors⁵. In one retrospective case series of 15 male patients with metastatic breast cancer who received aromatase inhibitors, a response was seen in 6 of them⁵. Its role in advanced stage male breast cancer remains unclear.

Systemic chemotherapy regime can also be used, and is commonly thought to result in higher and more rapid response rates than hormonal therapy, and thus, is often used as initial treatment for patients with hormone-positive metastatic breast cancer with a poorer prognosis. However, the role of taxanes or dose-dense chemotherapy have not been established in MBC and also, there is no data on the use of anti-angiogenic therapy in this setting¹.

Unlike in women, Her-2 proto-oncogene is less likely to be over-expressed in MBC¹. A recent series reported that only 11% of MBCs had both Her2 gene amplification and protein over-expressed. Although no data exists on the use of trastuzumab in MBC, it should be considered in Her2neu positive cancers, based on data in women⁵.

CONCLUSION

Due to the small number of cases, there is lack of prospective studies in the management of male breast cancer especially in the management of cutaneous metastases. In women, cutaneous metastasis of breast cancer is usually managed with surgical excision or radiotherapy to symptomatic lesions. Systemic therapy such as hormonal therapy, systemic chemotherapy and immunotherapy may be considered if there are multiple lesions or involvement of other organs. This treatment strategy is employed in MBC; however, there is limited data on aromatase inhibitors and anti-angiogenic treatment.

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