Cutaneous Metastasis from Breast Carcinoma: A brief report of a rare variant and proposed morphological classification

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Abstract

Background

Breast carcinoma is the second commonest cancer in women after non-melanoma skin cancers and, excluding melanoma, the most common tumor to metastasize to the skin in women. Cutaneous metastasis from breast cancer has varied presentations but there is no well-established classification which includes them all.

Objective and Conclusion

We report a 69 year-old lady with advanced primary ductal carcinoma of right breast (cT₄cN₁cM₀) who presented five months after radical mastectomy with very extensive cutaneous metastases in absence of distant spread. Skin involvement was in the form of nodules and purpuric papulo-vesicles on a background of erythema which clinically mimicked lymphatic malformation. We also propose a morphological classification of the cutaneous metastasis from breast cancer.

Keywords

Breast Carcinoma, Cutaneous metastasis, lymphatic malformation.

Introduction

Cutaneous metastasis occurs in 0.7% to 10.4% of all patients with visceral cancer(¹). It usually occurs late in the progression of malignancy. However it can rarely be an initial presentation of an internal malignancy(²,³). Breast carcinoma is the second commonest cancer in women after non-melanoma skin cancers(⁴) and, excluding melanoma, the most common tumor to metastasize to the skin in women⁵. Cutaneous involvement is seen in 23.9% of patients with breast cancer(⁴). The metastasis from breast cancer to the skin has varied presentations and many clinical variants are reported in the literature. In a series of 164 cases of skin metastasis from breast carcinoma papules and/or nodules were seen in 131 patients (80%), telangiectatic carcinoma in 19 (11.2%), erysepeloid carcinoma in 5 (3%), “en cuirasse” carcinoma in 5 (3%), alopecia neoplastica in 3 (2%) and a zosteriform pattern in 1 patient (0.8%). Sites of cutaneous metastases were the trunk (145), head and neck(14) and extremities (5)⁵. However there is no well established classification of this fairly common form of cutaneous metastatic disease with varied clinical presentation and much confusion exists in the terminology of various clinical variants. For example, telangiectatic metastatic breast carcinoma (TMBC) is a term that has been used in literature to describe a wide variety of presentations ranging from a variant of carcinoma erysepeloides on one hand(⁶) to violaceous papulo-vesicles resembling lymphangioma circumscripptom(²) on the other. In addition to breast carcinoma, telangiectatic metastatic carcinoma has been described in the pubic area in a woman who had a hysterectomy for adenocarcinoma of the uterus(⁷) and from ductal carcinoma of parotid gland(⁸) (Table 1a). We suggest the term “cutaneous metastasis from breast carcinoma (CMBC)” to be used as a primary diagnosis and its further division be based on morphological subtypes (Table 1b).

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A 69-year-old lady was diagnosed three years back with primary ductal carcinoma of the right breast (cT4cN1cM0). She had received neo-adjuvant FEC (fluorouracil, epirubicin and cytoxan) chemotherapy which was followed by right mastectomy with axillary lymph node dissection. (pT1cpN1cM0). Pathology review showed residual invasive ductal carcinoma, with perineural extension, presenting as two pathologic nodules one measuring 2 cms and another one 1.5 cms. The margins were clear. Fourteen out of eighteen axillary nodes were positive for metastasis with peri-nodal infiltrate and vascular infiltration. The tumor was negative for estrogen (ER) and progesterone (PR) receptors but positive for human epidermal growth factor receptor 2 (HER-2/neu). Post-operatively the patient was planned for chemotherapy using Paclitaxel. However after one cycle it was discontinued after the patient expressed poor tolerance in the form of generalized weakness, body aches and severe mucositis. She then received regional chest wall radiotherapy using 6 MV x-ray technique. A dose of 4500 cGy in 22 fractions over 32 days was used also encompassing the regional lymph nodes. Five months later she presented with local recurrence in the form of dermal nodules overlying the antero-lateral chest wall and the right shoulder. Metastatic work-up which included a bone scan and CT scan of chest, abdomen and pelvis showed no distant metastases. On developing local recurrence she received two cycles of 5 FU /leucovorin which was later on replaced by Vinorelbine every three weeks in addition to weekly herceptin (transtuzumab) and palliative electron beam therapy to the chest wall consisting of 3,000 cGy (in 20 fractions). The second course of radiation therapy was started about 14 months after the initial radiation therapy as her disease progressed in spite of receiving many chemotherapeutic agents. Subsequently, she received treatment with capecitabine and docetaxel with no clinical response. Her skin lesions continued to progress and in addition to firm papules and papulonodules she developed painful hemorrhagic papulovesicles and soft cystic nodules.

Physical examination revealed two types of cutaneous lesions over background of diffuse erythema: (i) grouped, firm, purpuric, tender, papulovesicles and soft cystic nodules over the right anterolateral chest wall and the right shoulder varying in size from 2 to 20 mm [Fig
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1(a)] and (ii) multiple, firm, non-tender, fixed, erythematous dermal nodules approximately 10 to 15 mm in size over the right posterior shoulder and chest wall [Fig 1(b)]. She had no lymphadenopathy, hepato-splenomegaly or ipsilateral lymphedema.

The histological examination of group (i) purpuric lesion showed widely ectatic blood vessels in superficial dermis mimicking lymphatic malformation. Blood vessels were embolized with red blood cells and tumor cells; however, there were no tumor cells in the dermis (Fig 2). The histological examination of group (ii) nodular lesion showed diffuse infiltrate of tumor cells involving whole of the dermis with areas of fibrosis (Fig 3). The morphology of the tumor cells was similar to that of the primary ductal carcinoma of breast and of the same histological grade. The receptor status was unchanged. The above biopsies did not show any radiation changes to account for the background erythema.

Her skin lesions continued to progress despite several cycles of chemotherapy and radiotherapy. Palliative treatment with topical 6% miltefosine (Miltex; Asta-Medica, Frankfurt, Germany) was tried. It was applied in a dose of 2 drops/10cm² of skin area, applied initially once daily for the first week and thereafter twice daily for a period of 12 weeks. Miltefosine was rubbed into the affected skin and 2.5 cms around it in a circular movement and left uncovered until completely absorbed. She tolerated this medication well and no toxic effects were noted. Miltefosine helped in clearing small superficial flat lesions and also prevented the appearance of new lesions in the treated area, however, patient continued to develop new lesions in the surrounding normal looking skin. Her condition deteriorated and she died 26 months after development of extensive skin metastases.
Discussion

Our patient had CMBC of papulovesicular and nodular type on background of erythema. The background erythema can be explained by congestion of blood vessels. A similar presentation of annular erythema (ER/PR negative and HER 2 positive) has been recently reported as a sign of recurrent breast cancer. Purpuric hue of these lesions is due to presence of aggregates of red blood cells and tumor cells in the ectatic superficial blood vessels as shown on the histology of our patient (Fig 2).

Topical 6% miltefosine was used for twelve weeks, which resulted in clearance of small superficial flat papuric papulovesicles. Miltefosine is a topical cytotoxic drug being considered as effective palliative treatment option for cutaneous metastases of breast carcinoma. It is applied once daily for 1st week and thereafter twice daily. Local skin reactions include scaling, erythema and cigarette paper skin. Miltefosine is effective in clearing only superficial flat lesions with estimated depth of 1cm or less probably because of its poor penetration. Its cytotoxicity is being attributed mainly to protein kinase C inhibition. In our patient small superficial papulovesicles were cleared with miltefosine and she tolerated the medication well, however, she continued to develop new eruptions in surrounding uninvolved skin. The treating oncologist selected miltefosine as palliative treatment for our patient because her skin lesions were progressive and were not manageable with surgery, radiotherapy or chemotherapy.

What is peculiar about our patient is the presence of very extensive local metastases in absence of distant spread. Local recurrence in breast carcinoma is reappearance of cancer in the ipsilateral breast, chest wall, or skin overlying the chest wall after initial therapy and, after mastectomy; it usually appears as one or more asymptomatic nodules in the skin of the chest wall. Other patients may present with diffuse chest wall involvement with multiple nodules; this seems to be common in patients who had locally advanced tumor originally, as was in our patient (cT4cN1cM0). About 25% to 30% of patients with local or regional recurrence have preceding distant metastases. Another 25% of patients are diagnosed as having simultaneous local and distant treatment failure or develop distant metastases within a few months of the discovery of local recurrence. Despite aggressive local treatment, almost all patients with local recurrence after mastectomy eventually develop distant metastases. The interval between mastectomy and local recurrence is probably the most reliable indicator of the subsequent survival time, as is true for patient with distant metastases. In our patient the interval between mastectomy and local recurrence was five months. This short duration can possibly be explained by advanced tumor originally (cT4cN1cM0), the histological grade and receptor status. However, it is hard to explain the lack of distant metastases with this advanced tumor and such an extensive local recurrence. The exact pathogenesis of breast cancer spread remains controversial and the reason as to why breast cancer so frequently
metastasizes to skin is not known. Perhaps the possible reasons are anatomical location of the breast tissue and extensive network of breast lymphatics.

As discussed in this case report, the ambiguity of the terminology of CMBC needs to be addressed and our proposed classification is a step towards that goal. The clinical significance in terms of prognosis of different morphologies of CMBC needs to be evaluated.

**References**