Folliculotropic Cutaneous Metastases and Lymphangitis Carcinomatosa: When Cutaneous Metastases of Breast Carcinoma Are Mistaken for Cutaneous Infections

Dear Editor,

Cutaneous metastases (CM) are detected in about 0.6-10.4% of patients with an internal malignancy (1-3). Excluding melanoma, breast and lung carcinomas are the main source of CM in women and men, respectively (1,4,5). CM can have different clinical features, and a diagnosis of CM is usually suspected before performing a biopsy. However, this can be a pitfall for clinicians when the clinical presentation is not the typical inflammatory nodule or mass. Herein we report 2 cases of cutaneous metastases of breast carcinoma, initially treated as a common skin infection.

Case 1

A 51-year-old Caucasian woman presented to our Institute with a four-month history of diffuse and erythematous pustular, lesions on the right arm that were painless and non pruritic (Figure 1). The patient had undergone excision for a breast adenocarcinoma (stage IIIA) 5 years earlier. An initial diagnosis of folliculitis was established, and the patient started systemic and topical antibiotics without any improvement. Based on the clinical features and the patient medical history, we performed a skin biopsy.

Pathologically dermal nests of tumor cells, arranged in a glandular-like pattern and involving the perifollicular and follicular areas (Figure 2, Figure 3), were highlighted. The tumor cells were positive to cytokeratin (CK) 7, CK19, and carcinoembryonic antigen (CEA) and negative for CK20, CK5/6, CD10, and thyroid transcription factor-1 (TTF-1) (Figure 4). According to the clinical history and pathology, a final diagnosis of folliculotropic metastatic breast carcinoma was established. Unfortunately, the patient died after 10 months.

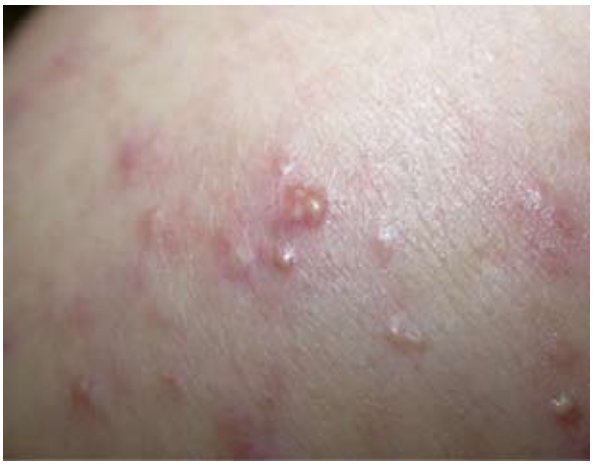

Figure 1. Pustular-like eruption with an erythematous base at the level of the right arm in the deltoid region, without resolution after local and systemic therapy with antibiotics.

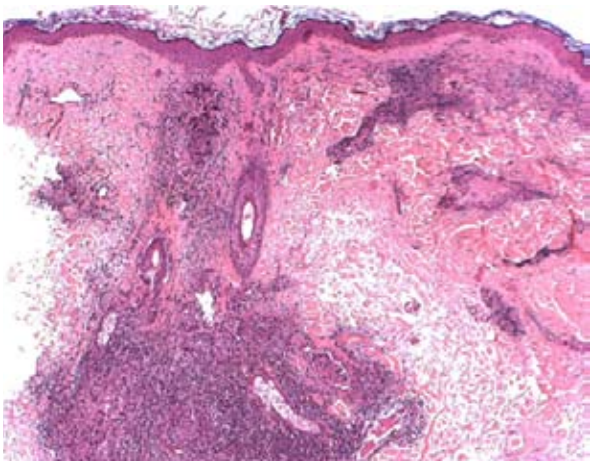

Figure 2. Tumor cells interspersed between collagen bundles and around hair follicles. The malignant cells altered the structure of the hair follicle (hematoxylin and eosin, ×10).

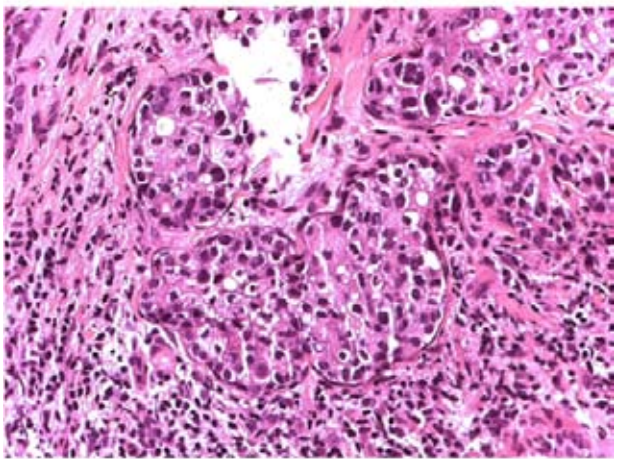

Figure 3. Malignant cells organized in a glandular-like pattern, with hyperchromatic nucleoli and abundant cytoplasm (hematoxylin and eosin, ×40).

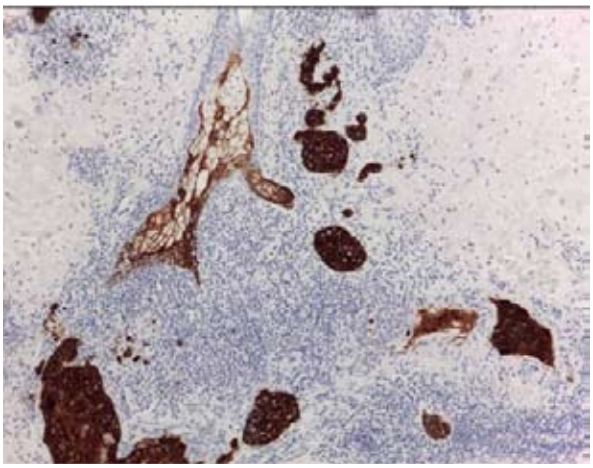

Figure 4. Malignant cells positive for cytokeratin 7 (CK-7).

Case 2

A 61-year old Caucasian woman presented to our Department with a two-month history of pink/violet macular lesions with diffuse telangiectasia on the left breast and arm (Figure 5, Figure 6). Five years earlier she had undergone excision for a breast adenocarcinoma (stage II A). A previous diagnosis of cellulitis had been made, and systemic antibiotic therapy had been started without any improvement. Based on the clinical features and the patient medical history, a punch biopsy was performed. Examination of skin biopsy showed a diffuse, sclerotic, and mixoid stroma with several dense ectatic lymphatic vessels (Figure 7, Figure 8). The dermal and hypodermal lymphatic lumens were filled with neoplastic cells. Thus, a diagnosis of cutaneous lymphangitis carcinomatosa (CLC) was established. Unfortunately, the patient died after 8 months.

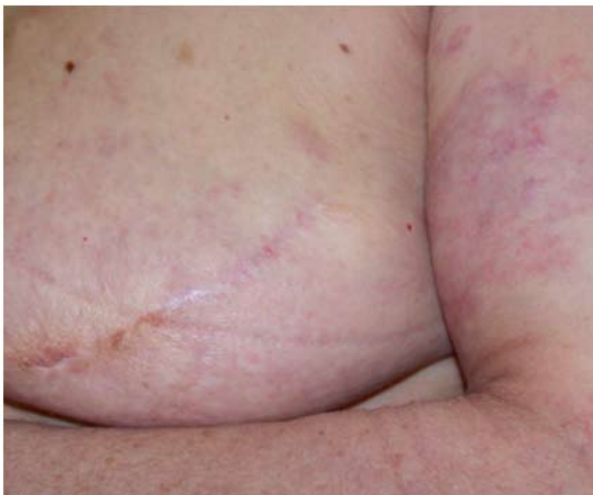

Figure 5. Pink/violet macular lesions with diffuse telangiectasia at the level of the left breast, also involving the sub-mammary region and the arm.

Discussion

CM are present after breast carcinoma in about 23.9% of patients, often involving the chest and abdomen and manifesting on average 5 years after surgical removal of the first malignancy (1,6).

CM of breast cancer are usually solitary or multiple nodular pinkish lesions (ranging between 1 and 3 cm) (1). However, several clinical features have been reported in the literature, including telangiectatic carcinoma, erythema-like, erythema annulare centrifugum-like, morphea-like, erysipelas-like, dermatofibroma-like, herpes-zoster-like, and alopecia-like lesions (1,7-10).

Clinical and pathological images of folliculitis-like metastases are rarely reported in the literature, especially after breast cancer (11,13)

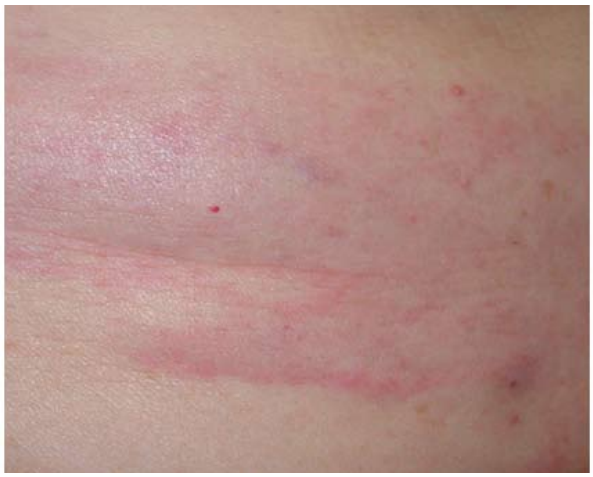

Figure 6. Detail of the cutaneous lesions.

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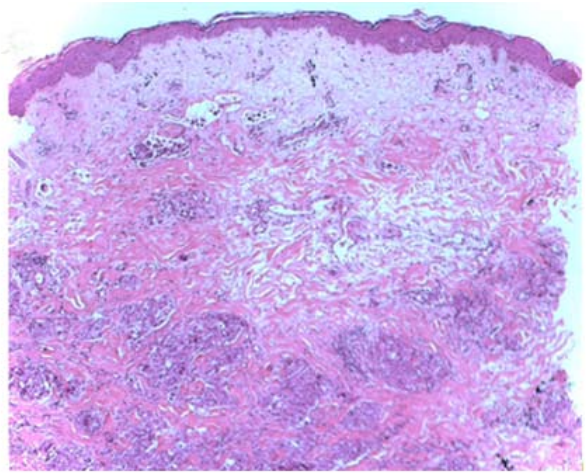

Figure 7. Diffuse sclerotic and mixoid stroma with several dense ectatic lymphatic vessels (hematoxylin and eosin, ×10).

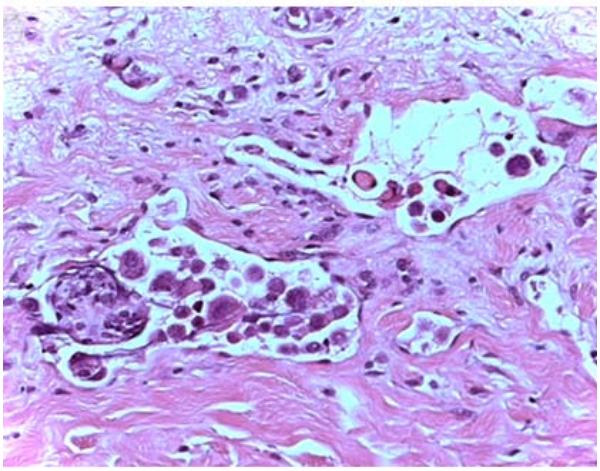

Figure 8. Ectatic lymphatic vessels with neoplastic cells (hematoxylin and eosin, ×40).

Clinically, folliculitis-like metastases could resemble a zosteriform-like metastatic lesion (7,14,15) although they do not follow a dermatome and are pustular lesions rather than violaceous indurate papules and/or nodules (13,14)

Pathologically, our cases showed an infiltration of the dermis and pilosebaceous units growing through the pilosebaceous unit in a "pseudo-eruptive way". In this regard, folliculitis-like CM could be similar to alopecia neoplastica, where the metastatic process involves and destroys the pilosebaceous units completely, leading to scarring alopecia (9,10). However, in our case, the pilosebaceous unit was still slightly recognizable, and clinically there were no scar-like features.

The mechanism of folliculitis-like metastasis formation is currently unknown. As reported in zosteriform-like metastases, the lymphatic and hematogenous spread of malignant cells or the koebnerization at the site of a previous viral and/or bacterial infection could lead to metastasis (7,14-16). However, unlike zosteriform-like metastases, the spread of neoplastic cells from the dorsal root ganglia was not a plausible mechanism of metastasization in our cases because of the absence of dermatome involvement. Furthermore, there were no signs of possible koebnerization in a previous bacterial and/or viral infection site (7,13)

In our opinion, folliculitis-like metastasis may be a result of the skin extruding malignant cells through the pilosebaceous unit to limit the neopalstic proliferation. This could explain the clinical and pathological features of folliculitis-like metastasis. Alternatively, the adnexotropic behavior of malignant cells may be explained by homing mechanisms, involving the up-regulation of the intercellular adhesion molecule 1 (ICAM-1) on the follicular epithelium, such as folliculotropic mycosis fungoides (17). In our patient, the folliculitis-like eruption was the first sign of recurrence after 5 years of disease-free survival. It is evident that the unusual folliculitis-like eruption of CM led to a delay in the diagnosis.

CLC is a rare presentation of skin metastasis, characterized by an occlusion of dermic lymphatic vessels by neoplastic cells (18). CLC has been reported in the literature in association with several malignancies, including lung, breast, and ovarian cancer (19). CLC shows pink/violet macular lesions with diffuse telangiectasias, often associated with itching and burning sensation. The main differential diagnoses are erysipelas and cellulitis. However, CLC is not associated with fever, chills, and leukocytosis. Furthermore, CLC shows no response to antibiotic therapies.

Several clinicopathological types of cutaneous metastasis have been reported in the literature, including telangiectatic metastatic breast carcinoma (TMBC) and carcinoma erysipelatous (CE). TMBC is characterized by yellowish/reddish or violaceous papulo-vesicular lesions. CE usually shows blistering erythematous eruptions resembling erysipelas. However, CLC, TMBC, and CE are different clinical expressions of the same metastatic process, pathologically characterized by edema of the dermis and ectatic lymphatic vessels. Positivity to CD31 and podoplanin in the endothelial cells shows that the tumor metastatises predominantly via lymphatic vessels (20).

In conclusion, we stress that every cutaneous lesion should be studied and examined carefully in patients with a personal history of cancer. Indeed, a

correct diagnosis remains the pivotal point for a better management of these patients.

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