

Zosteriform Cutaneous Metastasis from Breast Cancer: A Case Report

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| Received: 10.07.2024 | Accepted: 16.08.2024 | Published: 19.08.2024

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Abstract**Case Report**

Introduction: Cutaneous metastases are observed in approximately 10% of oncology patients, often indicating either a persistent solid tumor or the recurrence of neoplastic disease. The most prevalent cause of cutaneous metastases in females is breast cancer. Patients with breast cancer may exhibit cutaneous manifestations at the initial diagnosis; however, these metastases more frequently emerge well after the initial diagnosis and treatment. The cutaneous lesions resulting from metastatic breast carcinoma display considerable variability in appearance. Typically, they manifest as firm, flesh-colored to red, smooth or ulcerated, or crusted nodules, papules, and plaques on the ipsilateral chest wall and breast. Additionally, unusual sites for breast cancer cutaneous metastases include the eyelids, inframammary folds, ipsilateral lymphedematous arm, scalp, subungual nail bed, and umbilicus. Skin metastases can also occur in mastectomy scars and radiation therapy ports. Several distinct patterns of skin metastases are recognized in breast cancer patients: carcinoma erysipelatoides, carcinoma telangiectoides, and carcinoma encuirasse. Recently, carcinoma hemorrhagiectoides has also been documented. The pleomorphic nature of breast cancer metastases can mimic various benign and malignant conditions, such as collision tumors, cysts, dermatofibromas, milia-en-plaque, melanoma, non-melanoma skin cancers, cellulitis, folliculitis, herpes zoster, paronychia, erythema annulare centrifugum, urticaria, alopecia areata, dermatitis, hidradenitis suppurativa, scleroderma, angiokeratoma, angiosarcoma, lymphangioma circumscriptum, purpura, and pyogenic granuloma. Consequently, it is crucial to consider the possibility of cutaneous metastasis from breast cancer in any patient, whether previously diagnosed with breast cancer or not, who presents with new or treatment-resistant cutaneous lesions. Confirmation of the diagnosis necessitates a biopsy of the skin lesion.

Case Report: A 45-year-old female patient presented with cutaneous metastatic erythematous-violaceous papular lesions exhibiting a multi-metameric distribution on the left chest wall and left upper limb for the past ten months. These findings were confirmed by a skin biopsy. Three years prior, the patient underwent a radical mastectomy for invasive ductal carcinoma, followed by adjuvant chemotherapy consisting of four cycles of Adriamycin and cyclophosphamide (AC) and twelve cycles of weekly paclitaxel and trastuzumab. Post-chemotherapy, she received radiation therapy to the left chest wall and continued trastuzumab (Herceptin) as part of her ongoing treatment regimen.

Conclusion: Recognition of the wide spectrum of clinical presentations that skin metastases can exhibit is essential to avoid overlooking this diagnosis, ideally at an early stage. Prompt identification is crucial to expedite appropriate management and optimize patient outcomes. A high index of suspicion, particularly in patients with a known history of cancer, should prompt a thorough clinical evaluation and consideration of performing a diagnostic skin biopsy, even in the absence of a prior cancer diagnosis. Multidisciplinary collaboration between the dermatologist, oncologist, and pathologist is critical to ensure timely diagnosis and implementation of the most suitable therapeutic approach for these challenging cases.

Keywords: Breast Cancer, Cutaneous Metastasis, Invasive Ductal Carcinoma, Zosteriform, Metastatic Breast Cancer, Pleomorphic, Skin, Metastasis.

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INTRODUCTION

Breast cancer is the most frequently diagnosed malignant neoplasm among women worldwide, projected to account for approximately 25% of all new cancer cases in the female population [1].

Among women, metastatic cutaneous lesions occur more frequently in breast cancer than any other malignancy, comprising over 20% of all cutaneous metastases [2].

Citation: Souraya Bricha, Sara Amimi, Samir Barkiche, Nezha Oumghar, Mouna Darfaoui, Abdelhamid Elomrani, Mouna Khouchani. Zosteriform Cutaneous Metastasis from Breast Cancer: A Case Report. Sch J Med Case Rep, 2024 Aug 12(8): 1428-1436.

The presence of skin metastases generally signifies extensive systemic disease and is indicative of a poor prognosis [3].

Common anatomical sites for these metastases include the chest wall, abdomen, back, and upper extremities [4]. Clinically, cutaneous metastases from breast cancer present in various forms, including nodular, en cuirasse, erysipeloid, telangiectatic, alopecic, and zosteriform patterns [5].

Associated symptoms can include ulceration, bleeding, pain, foul odor, secretion, and secondary infection [6, 7]. The interval between the initial breast cancer diagnosis and the appearance of cutaneous metastases is variable [8, 9], with nearly 50% of cases occurring within 6 months to 4 years of the primary tumor diagnosis [10].

This medical case report highlights the clinical presentation, diagnosis process, and therapeutic approach for a patient with cutaneous metastasis from breast cancer.

Case Presentation: A Case of ER-/PR- HER2+ Zosteriform Cutaneous Metastatic Breast Cancer

Our patient, a 45-year-old premenopausal woman with a regular menstrual cycle, gravida 2, para 1, and 1 living child. She had menarche at the age of 13, with no history of oral contraception use and a medical history significant only for a penicillin allergy, presented for evaluation of multiple skin lesions located on her trunk, back, and left upper limb.

Three years prior, she had been diagnosed with invasive ductal carcinoma of the left breast. At that time, breast examination revealed a retro areolar mass in the left breast, with a small palpable left axillary lymph node. The skin overlying the tumor appeared normal, and there was no nipple discharge. The contralateral breast was normal. Mammography revealed a hypodense lesion in the upper outer quadrant and retro areolar regions of the left breast, along with a few enlarged suspicious lymph nodes of hypodense texture, the largest measuring approximately 2 x 1.5 cm.

Following her diagnosis, she declined immunohistochemical analysis and the recommended neoadjuvant chemotherapy. She later underwent a radical mastectomy of the left breast. Histopathological examination of the mastectomy specimen confirmed a grade III invasive ductal carcinoma. The pathological staging was determined to be pT3N3Mx, indicating a primary tumor greater than 5 cm (9*8*3cm) with extensive regional lymph node involvement (15N+/23N) and unknown distant metastasis status. Immunohistochemistry revealed that the tumor was negative for both estrogen receptor (ER) and progesterone receptor (PR), but positive for human epidermal growth factor receptor 2 (HER2), suggesting a HER2-positive, hormone receptor-negative breast cancer subtype. The work-up for extension was normal.

Subsequently, the patient received four cycles of AC (Adriamycin and cyclophosphamide) followed by 12 cycles of weekly paclitaxel and Trastuzumab. She received radiation therapy to the left chest wall following completion of chemotherapy. Additionally, she continued taking Herceptin as part of her ongoing treatment regimen.

She self-referred to an outpatient clinic after a ten-month disease-free interval, with symptoms of erythema and painful papular lesions with multi-metameric distribution on the left chest wall and left upper limb associated with lymphedema of the same limb, and which had progressively worsened over the last month. Symptoms, including significant pruritus and discomfort, had progressively worsened over the precedent month. It should be noted that the patient had been treated for these lesions as herpes zoster virus infection with antiviral therapy prior to consulting. Physical examination of the patient revealed extensive erythema and erythematoviolaceous papular lesions, hyperkeratotic areas, topped by erosion, bleeding spontaneously, over the entire left chest wall. No apparent ulcers in the affected area. The lesion was confined to the left chest wall alone, (**figure 1,2,3**). Excisional biopsy revealed the dermal localization of a moderately differentiated infiltrative carcinomatous proliferation, consistent with her previous ER-/PR-HER2+ breast cancer.



Figure 1, 2, 3: Zosteriform cutaneous metastases mimicking varicella-zoster virus infection on the chest, abdomen and left limb of a woman previously treated for an invasive ductal carcinoma of the left breast)

Positron emission tomography-computed tomography (PET-CT) demonstrated nodular cutaneous infiltration involving the left upper limb and hemithorax, with hypermetabolic foci consistent with histologically confirmed secondary metastases. Additionally, there was pronounced hypermetabolism noted in the deltoid, subscapular, and left trapezius muscles, raising suspicion of metastatic involvement in these muscle groups within the clinical context.

Following a multidisciplinary discussion, the patient was initiated to targeted therapy with trastuzumab and pertuzumab in combination with chemotherapy (docetaxel). She responded well to six cycles of this regimen, with significant reduction of her symptoms (**figure 4,5,6**). She is currently continuing with targeted therapy and undergoing regular follow-up.



Figure 4, 5, 6: Evolution of zosteriform cutaneous metastasis after treatment

DISCUSSION

Cutaneous metastatic carcinoma is an unusual clinical finding. Review of the literature indicates that the incidence of cutaneous metastases for all types of carcinomas ranges from 0.7% to 10.0% [11-13]. Similarly, another meta-analysis [14], demonstrated the overall incidence to be closer to 5.3%.

Skin metastases may occur synchronously or metachronously with the diagnosis of the primary tumor. Occasionally, skin metastases may represent an initial manifestation of an occult internal carcinoma.

The appearance of these lesions indicates generalized metastatic disease, implying in poor prognosis. Patients often survive for a short period of time, depending on the type of carcinoma. Breast cancer and lung cancer are the most common primary organ which spread to the skin [15].

Metastatic cutaneous lesions are more often found in women with breast cancer, than in those with other visceral malignancies, with an incidence exceeding 20% [13-17].

The prevalence of cutaneous metastasis from breast cancer in a meta-analysis by Krathen *et al.*, [18], was 24%. In a study of 992 patients with breast cancer by Looking bill *et al.*, [19], 212 patients (21.3%) developed cutaneous metastasis, Abrams *et al.*, [20], in turn, reported a prevalence rate of 18.6% in a series of 167 patients with follow-up data spanning at least 4 years.

The age range with the highest incidence of cutaneous metastases is that between 50 and 70 years old.

The interval between the initial breast cancer diagnosis and the appearance of cutaneous metastases is variable [8, 9], with nearly 50% of cases occurring within 6 months to 4 years of the primary tumor diagnosis [10].

Cutaneous metastasis in solid tumors is generally present in the later stage, but in breast cancer, it depends on the molecular subtype [21]. Patients with triple-negative subtype and HER2-enrich variety can even present in an early stage of the disease [21]. There is an association between estrogen receptors and time to metastasis. Primary tumors with positive estrogen receptors (ER) have significantly longer disease-free periods than ER negative neoplasms [22].

Cutaneous involvement from breast carcinoma preferentially occurs in the skin overlying or proximal to the area of the primary tumor metastases resulting from lymphatic embolization, hematogenous or contiguous dissemination or also direct implantation during surgical procedures [9-23]. Although locoregional involvement is more common, distant cutaneous metastases can also occur. In the study by Bastard *et al.*, 26% of patients

exhibited cutaneous metastases away from the primary tumor site [24].

Cutaneous metastases from breast cancer can manifest in various forms. The most common presentation is nodules, often found on the thoracic wall and abdomen, but they can also appear on the limbs and head-and-neck region. Additional clinical presentations include erysipeloid infiltration, sclerodermiform lesions, en cuirasse, telangiectatic and zosteriform lesions, neoplastic alopecia, and palpebral nodules.

Carcinoma erysipelatoides, also known as inflammatory metastatic carcinoma, resembles erysipelas, an acute streptococcal skin infection. Carcinoma erysipelatoides can present as the sole skin manifestation of cutaneous metastatic breast cancer or in conjunction with other skin patterns of metastatic disease, such as carcinoma en cuirasse. This type of metastasis typically appears at the site of the primary tumor as an erythematous patch or plaque with well-defined borders, mimicking cellulitis. Pathological examination reveals tumor aggregates predominantly infiltrating the superficial dermal lymphatic vessels, leading to their obstruction. Additionally, cancer cells may be found in dermal blood vessels and sparsely infiltrating the dermis. This infiltration can cause a peau d'orange (orange peel) appearance of the skin, which can be mistaken for an infectious process due to localized lymphedema resulting from lymphatic blockage by cancer cell thrombi [25, 26].

Carcinoma hemorrhagiectoides is a recently observed pattern of cutaneous metastasis in a breast cancer patient. It typically presents as large, violaceous, confluent, hemorrhagic, and erythematous dermal plaques across the chest from the neck to the abdomen; in some patients, their carcinoma hemorrhagiectoides cutaneous metastases have been described as a shield sign since the presentation of the skin metastasis is reminiscent of a medieval knight's shield. In addition, metastatic skin lesions of carcinoma hemorrhagiectoides can also mimic angiokeratomas within the plaques. Pathology shows not only extensive infiltration of the dermis by tumor cells but also endothelial-lined vessels of lymphatic and/or blood origin containing cancer cells. Also, there is hemorrhage of the erythrocytes into the tumor-filled lymph vessels [27].

Carcinoma telangiectoides manifests as red and purple patches and papules, commonly found on the chest wall, often accompanied by prominent telangiectasias. These lesions can resemble those seen in lymphangioma circumscripta. Pathological examination reveals dilated blood vessels filled with tumor cells, which account for the violaceous coloration of the lesions. Additionally, cancer cells may be sparsely distributed within the dermis [25, 26].

Carcinoma en cuirasse is a form of breast cancer cutaneous metastasis that mimics scleroderma. The term "cuirass" refers to the breastplate worn by cuirassiers, cavalry soldiers, originally made of leather, and later of metal. This condition presents as morphea-like lesions that are bound-down, flesh-to-red colored, and indurated dermal plaques, which may become crusted or ulcerated. Pathologically, it is characterized by a linear distribution of single cancer cells between collagen bundles in the fibrotic dermis [25, 26].

Alongside benign-appearing lesions like papules, nodules, and plaques, breast cancer cutaneous metastases can also resemble benign cutaneous neoplasms such as cysts, dermatofibromas, or milium cysts [2-6]. Although cystic skin metastases from breast carcinoma are rare, a case was observed where a cutaneous metastasis mimicking a cyst appeared on the thigh of a woman with breast cancer [25].

Cutaneous metastases from breast cancer can mimic primary cutaneous malignancies. For example, breast carcinoma in the inframammary crease can present as primary basal cell carcinoma or squamous cell carcinoma [28]. Furthermore, skin metastases from breast cancer can exhibit morphological features similar to keratoacanthoma, melanoma, and pigmented basal cell carcinoma [29, 30].

Cutaneous metastases from breast cancer can closely resemble bacterial and viral infections. Carcinoma erysipelatoides and conditions such as folliculitis are among the bacterial infections that breast cancer skin metastases can mimic. Additionally, varicella-zoster virus infection can present as zosteriform metastases when breast carcinoma spreads to the skin [12-32].

Folliculotropic cutaneous breast cancer metastases may manifest as folliculitis. A notable case involved a 51-year-old woman presenting with a painless, non-pruritic, diffuse pustular eruption over four months on an erythematous base of the right deltoid region. This patient had a history of breast adenocarcinoma excised five years earlier. Initially, these lesions were misdiagnosed as folliculitis, and she was treated with topical and systemic antibiotics. The lack of improvement prompted a biopsy, which revealed folliculotropic metastatic breast carcinoma [31].

Zosteriform metastases, as observed in our case presentation, are characterized by breast cancer-related skin lesions that are indurated, flesh-colored to red or violaceous, and may be papular, nodular, or pseudo-vesicular, typically appearing in a dermatomal distribution. These metastases can also be crusted or ulcerated. The chest and abdominal wall are the most commonly affected sites. Although these lesions can be asymptomatic, they are sometimes painful, leading to misdiagnosis and treatment for herpes zoster virus

infection with antiviral therapy before the correct diagnosis is established [12-32].

Unlike lesions associated with varicella-zoster virus, zosteriform skin metastases can extend across more than two to three adjacent dermatomes and may even present bilaterally [12-32].

Papillomatosis cutis lymphostatica, also known as elephantiasis nostras verrucosa, is an uncommon and asymptomatic manifestation of either primary (hereditary) lymphedema or secondary (acquired) lymphedema. The latter is often associated with damaged lymphatics, such as in patients with diabetes. Clinically, hyperkeratotic, verrucous, and papillomatous lesions typically develop on the distal aspect of the lymphedematous extremity [33].

In a notable case, breast cancer cutaneous metastases mimicked papillomatosis cutis lymphostatica as the initial presentation of recurrent neoplastic disease. A 60-year-old woman developed multiple painless, non-confluent, oval red nodules on the volar aspect of her lymphedematous left arm and forearm, resembling papillomatosis cutis lymphostatica. She had previously undergone a complete mastectomy and axillary lymph node dissection one year earlier as initial treatment for invasive lobular carcinoma of the left breast. This was followed by local radiotherapy, adjuvant chemotherapy, and ongoing letrozole hormonal therapy. A skin biopsy was performed after the cutaneous lesions increased in diffusion and redness over two months of physiotherapy with bandages and plastic devices. The biopsy revealed metastasis of invasive breast carcinoma in the dermis and subcutaneous fat [33].

Paget's disease is primarily an intraductal mammary carcinoma. However, metastatic breast cancer can also present with clinical features that mimic Paget's disease. In some patients, these lesions are pigmented and resemble melanoma [26]. Beyond the areola and nipple, breast cancer cutaneous metastases at other sites on the breast or body can also be pigmented, thereby masquerading as melanoma [29].

Erythematous skin metastases of breast cancer can present as erythema reaginata, characterized by confluent erythematous macules with annular or irregular margins. They may also mimic urticaria or centrifugal erythema annulare [26-35]. In a 75-year-old woman with no prior cancer history, cutaneous metastases of breast cancer initially appeared as urticaria on the upper half of her body. She observed the sudden onset of numerous painless, non-pruritic, firm, red, five-millimeter dermal plaques three months earlier. These lesions, stable in size and location, differed from true urticaria. A biopsy revealed tumor cells infiltrating the dermis, indicating breast cancer. Further workup confirmed invasive lobular carcinoma of the right breast, positive for estrogen, progesterone, and HER2 receptors,

with metastases to bilateral axillary lymph nodes, liver, and bone [35].

Cutaneous metastases of inflammatory breast cancer mimicking erythema annulare centrifugum were the presentation of locally recurrent breast carcinoma in a 38-year-old woman. She presented with several enlarging, annular, erythematous macules with central clearing on the back for which the clinical diagnoses of erythema annulare centrifugum and subacute cutaneous lupus erythematosus were considered. Five years earlier, she had been diagnosed with metastatic invasive ductal right breast carcinoma (that was negative for estrogen receptor, and progesterone receptor, and HER2-positive) involving the dermal lymphatics and lymph nodes. She was treated with chemotherapy, surgery, and radiotherapy. However, 40 months later, she developed inflammatory carcinoma of the left breast with dermal lymphatic and lymph node metastases; surgery was followed by additional chemotherapy and localized radiotherapy. Her new back lesions appeared after completing treatment. Biopsy of the skin lesions showed invasive ductal carcinoma not only in the superficial dermis but also within the lymphatic vessels [34].

Metastatic breast cancer can sometimes mimic other dermatological conditions, such as alopecia areata, dermatitis, and hidradenitis suppurativa [12-37]. The hair loss caused by cancer is referred to as alopecia neoplastica, and it can be either primary (originating from a neoplasm within the scalp, e.g., dermatofibrosarcoma protuberans or mycosis fungoides) or secondary (resulting from a tumor that has metastasized to the scalp from a distant site, such as the breast) [25-36].

In patients with breast cancer cutaneous metastases, the alopecia typically presents as patches of absent hair, though in some cases, nodules may also be present in the affected areas [25-36]. Interestingly, the cancer-associated hair loss can mimic the appearance of alopecia areata in some patients, while in others, the neoplasm-related alopecia may resemble the patterns observed in discoid lupus erythematosus, lichen planopilaris, morpheaform basal cell carcinoma, or pseudopelade [25-36].

Breast cancer cutaneous metastases can sometimes mimic the appearance of dermatitis, making them challenging to diagnose. Specifically, cutaneous metastases located in the skin folds beneath the breasts can masquerade as eczema [12-28].

This diagnostic pitfall is illustrated by the case of a 66-year-old man whose initial presentation of unsuspected breast carcinoma was a skin lesion on his left leg that had been clinically misdiagnosed as dermatitis and vasculitis for the prior year. Despite treatment with traditional Chinese medicine, oral antihistamines, antibiotics, diuretics, and topical

corticosteroids, the skin lesion persisted as a large, erythematous, non-pitting edematous area on the left buttock and posterior thigh. Biopsy of the presumed dermatitis and vasculitis lesion surprisingly revealed metastatic carcinoma within the lymphatic vessels.

Further evaluation then detected a previously undiagnosed 2-cm left breast subareolar mass, as well as swollen lymph nodes in the axilla and groin. Ultimately, lumpectomy of the left breast confirmed an underlying intraductal carcinoma.

Hidradenitis suppurativa is a chronic inflammatory condition that typically presents with tender red nodules, abscesses, fistulas and sinus tracts in the intertriginous areas such as the axilla, groin, buttocks, and inframammary creases [37]. In some cases, cutaneous metastases from breast cancer can closely mimic the appearance of hidradenitis suppurativa, making the diagnosis challenging. It is exemplified by the case of a 30-year-old woman who presented with an enlarging red nodule, draining sinus tracts, and skin nodules of seven months' duration affecting her axilla, groin, chest, and breasts. Based on the clinical presentation, a diagnosis of hidradenitis suppurativa was made, and the patient was treated with oral minocycline and topical benzoyl peroxide and clindamycin. However, at the three-month follow-up visit, while the other skin lesions had resolved, the right breast nodule had become larger. Biopsy of this persisting nodule revealed that it was in fact a metastasis from an underlying breast adenocarcinoma, rather than the expected hidradenitis suppurativa.

Targetoid breast cancer cutaneous metastases have also been observed. Metastatic breast cancer presented with targetoid-appearing cutaneous lesions appearing as annular plaques that had depressed hyperpigmented centers in a 40-year-old woman; six months earlier, she had surgery for right breast carcinoma. Examination demonstrated not only a lump on the right breast under the postoperative scar but also papulonodules and targetoid plaques over the right breast and inframammary regions. Fine needle aspiration cytology of a lymph node was suggestive of metastatic breast carcinoma, and biopsy of a skin lesion showed nests of tumor cells [38].

Cutaneous metastases from breast carcinoma can occur in a variety of anatomical locations, the most common being the ipsilateral and contralateral chest wall and breast [12-26]. However, metastatic skin lesions can also develop in other unique locations, such as the areola and nipple (resembling dermatitis or Paget's disease), the eyelids (with periorbital edema), the inframammary folds (mimicking dermatitis or non-melanoma skin cancer), the subungual regions of the fingers (masquerading as acute paronychia) and the umbilicus (like a Sister Marie-Joseph nodule) [12-28].

Cutaneous metastases of breast cancer may also appear on the scalp, either as alopecic lesions or nodules [12-25]. The lymphoedematous arm is another potential site for these metastatic skin lesions [12-25]. In addition, skin metastases can develop in scars, such as those from a previous mastectomy, or in the radiotherapy port used to treat the primary tumour [12-25].

In addition to carcinoma telangiectoides (mimicking lymphangioma circumscripta) and carcinoma hemorragiectoides (mimicking angiokeratomas), breast cancer skin lesions can also masquerade as other vascular lesions. This includes purpura mimicking vasculitis. It also includes skin metastases that appear similar in morphology to benign and malignant vascular neoplasms, such as pyogenic granuloma and angiosarcoma [25-41].

CONCLUSION

Cutaneous metastases of breast cancer can present with a wide spectrum of pleomorphic clinical appearances, which can closely mimic a variety of benign dermatologic conditions, cutaneous malignancies, infectious processes, reactive inflammatory states, vascular anomalies, and other miscellaneous skin disorders. These varied cutaneous manifestations can serve as harbingers of persistent or recurrent neoplastic disease. Given the diverse morphologic manifestations, a high index of suspicion is warranted, especially in patients with a known history of breast cancer. In such cases, a comprehensive clinical assessment coupled with histopathologic confirmation via skin biopsy is essential to establish the accurate diagnosis of breast cancer cutaneous metastasis.

Even in the absence of a prior cancer diagnosis, the development of a new or treatment-refractory cutaneous lesion should prompt consideration of performing a diagnostic skin biopsy. Prompt recognition and precise diagnosis of these potentially deceptive cutaneous metastases is paramount, as it directly informs appropriate management strategies and carries important prognostic implications for the patient.

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