Zosteriform Metastatic Adenocarcinoma of Breast Cancer: A Case Report

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ABSTRACT:

Zosteriform cutaneous metastasis is a rare form of cutaneous metastasis. It accounts for only 3.6% of all cutaneous metastases and is predominantly associated with breast cancer, malignant melanoma, and lung cancer. The clinical presentation of zosteriform cutaneous metastases is characterized by a dermatomal distribution and includes morphologies such as papules, vesicles, or bullae, which resemble herpes zoster. Consequently, zosteriform cutaneous metastases are often subject to delayed diagnosis and treatment. We report a case of a 55-year-old woman with underlying breast cancer and bony metastases, who had been receiving capecitabine for 1 year. She presented with multiple vesicles on her right chest that did not improve with oral valacyclovir treatment over 2 weeks.

Key words: Breast cancer, Cutaneous metastasis, Metastatic adenocarcinoma, Resistant herpes zoster, Zosteriform

Introduction

Cutaneous metastasis from internal malignancy occurs in 0.7%–10%[1] or approximately 2% of all skin tumors[2]. Breast cancer is the most common source of cutaneous metastasis in women. The median survival rate for breast cancer patients who developed only cutaneous metastasis was 57.43 months, and the prognosis decreased to 25.22 months for patients with combined cutaneous and visceral metastatic involvement[3]. Clinically, most of these metastases are firm, painless, atypical papules and nodules located on the anterior thoracic wall, while zosteriform-type cutaneous metastases remain rare[4].

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Case report

In this case, a 55-year-old Thai woman presented with breast pain in 2019. A mammogram reported BIRADS 4. Surgical wide excision was performed twice due to a positive margin after the first surgery. Pathology revealed intraductal carcinoma without residual tumor, negative ER, PR, positive HER2, negative DISH, and KI67 at 53%. She was diagnosed with breast cancer stage T2N1M0 and treated with complete adjuvant chemoradiation of 50 Gy/25 fractions in June 2020, resulting in cancer remission. During her annual check-up in July 2021, the recurrent disease was identified. She complained of nocturnal bone pain. A bone scan and computed tomography of the chest revealed bony metastases in her fourth right anterior rib and sacrum. Palliative chemotherapy with capecitabine was initiated, and the disease remained stable.

In January 2022, a computed tomography examination of her chest and abdomen showed a similar size of the target mass in the right breast, axillary lymph node, and osteolytic lesion at the rib. The patient visited the dermatology clinic in July 2022 with vesicles on her right chest and axilla persisting for 2 weeks. She reported pain with a visual analog score of 5/10 and itching along the rash. Physical examination revealed multiple groups of vesicles on the right T1 and T4 dermatomes without lymphadenopathy. Other organ systems were unremarkable. Wright's staining of a lesion scrape showed multinucleated giant cells. She was treated with valacyclovir 1 gram orally twice daily for 2 weeks, but there was no clinical improvement. The lesions gradually extended to her right arm and T5-T6 dermatomes (Figure 1). A diagnosis of refractory herpes zoster disease was made. She was admitted for intravenous acyclovir 1,500 mg per day, but her condition did not improve. A skin biopsy from her right chest was subsequently obtained.

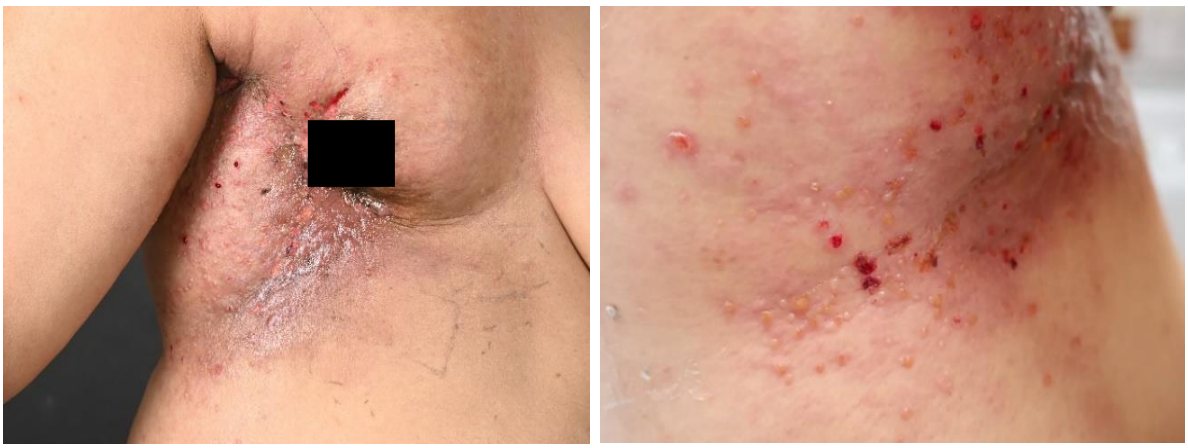

Figure 1 Multiple vesicles and erosions on the right chest, axilla, and volar part of upper arm

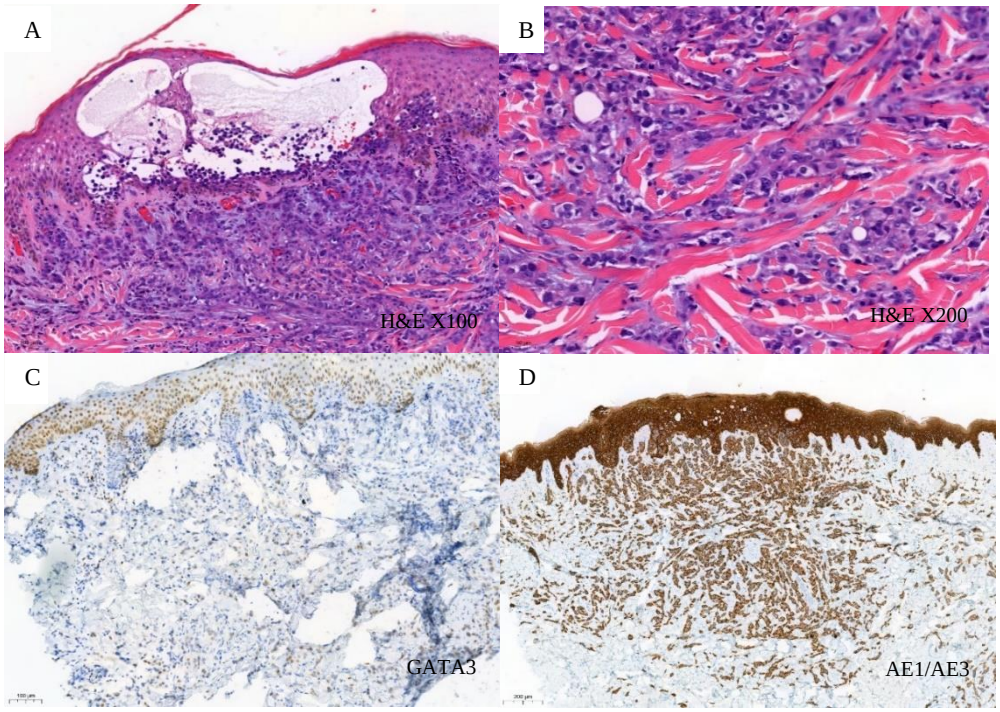

Figure 2
(A) The neoplastic cells exhibited a high nuclear-cytoplasmic ratio, pleomorphism, and increased mitoses. No angiolymphatic invasion, perineural invasion or viral cytopathic changes were identified (B)Immunohistochemistry revealed that the neoplastic cells were positive for GATA3
(C) and AE1/AE3 (D) and negative for ER, PR, and HER2/neu

Laboratory investigations revealed Hb 12.0 g/dL, Hct 37.2%, WBC 4520 cells/µL (neutrophil 74.2%, lymphocyte 17%, eosinophil 1.5%), platelets 333 000 cells/µL, and creatinine 0.47 g/dL. Lesion scrapes for herpes simplex virus- and varicella zoster virus-specific antigen detection by direct immunofluorescence were negative. Histological examinations (Figure 2) demonstrated intraepidermal vesicles with pan-dermal to subcutaneous neoplastic infiltration and focal ductal/glandular formations. The neoplastic cells exhibited a high nuclear-cytoplasmic ratio, pleomorphism, and increased mitoses. No angiolymphatic invasion, perineural invasion nor viral cytopathic changes were identified.

Immunohistochemistry revealed that the neoplastic cells were positive for GATA3 and AE1/AE3, and negative for ER, PR, and HER2/neu. The diagnosis of zosteriform cutaneous metastatic adenocarcinoma was made. The patient was referred to an oncologist for re-evaluation and received palliative chemotherapy with eribulin. Despite treatment, the disease progressed. The patient developed pleural metastases, and the rashes increased in pain and number. She eventually succumbed to systemic metastasis 7 months after the diagnosis of zosteriform cutaneous metastasis.

Discussion

Breast cancer is the most common primary cancer associated with cutaneous metastasis in women, with cutaneous metastasis rates ranging

from 18.6% to 26.5% in breast cancer patients[3,5]. The most common sites of cutaneous metastasis from breast cancer are the chest wall and abdomen. Cutaneous nodular carcinoma is the most prevalent type of metastasis, representing 46.8% of all cutaneous metastases of breast carcinoma, while zosteriform metastasis is relatively rare, accounting for only approximately 3.6%[4].

In previous studies, zosteriform pattern cutaneous metastasis has primarily been identified in malignancies such as breast cancer, malignant melanoma, lung cancer, lymphoma, and squamous cell carcinoma[6]. The clinical pattern of zosteriform metastases is distributed along dermatomes and may vary in clinical morphology, including nodular, papulovesicular, or vesiculobullous presentations[4].

The mechanism underlying the zosteriform distribution in metastatic skin cancer remains inconclusive. Hypotheses explaining this mechanism include (a) a Koebner-like phenomenon at the location of a prior herpes zoster infection; (b) neural lymphatic dispersion through the fenestrated vessels of the dorsal root ganglion; (c) accidental medical or surgical inoculation; and (d) perineural lymphatic spread[6,7].

Zosteriform cutaneous metastasis is often misdiagnosed for various reasons, which may result in delayed or incorrect treatment[7]. First, its clinical indicators can closely resemble those of a herpes zoster infection, a common type of infection in immunosuppressed patients. Breast cancer is present in approximately 10% of patients who, while undergoing systemic chemotherapy for solid tumors, are also infected with the varicella zoster virus[8]. Additionally, a study reported that herpes zoster occurred in 3.7% of breast cancer patients who received postoperative radiotherapy, mainly within the first 2 years after radiotherapy completion, with an estimated risk 3–5 times higher than that of the general population[9].

In terms of morphology, zosteriform cutaneous metastasis and herpes zoster infection share similar manifestations, such as papules, nodules, vesicles, and bullae with dermatomal distributions.[4] Moreover, both conditions can present with no symptoms, minor pain, burning, or tingling[4,6]. Although Tzanck's test can support the diagnosis of clinically suspected herpes zoster by identifying multinucleated giant cells, it can produce a false positive result in metastatic cancer with atypical cells, as occurred in this patient. More specific laboratory investigations, such as polymerase chain reactions with high sensitivity and specificity, could help exclude herpes zoster infection[10]. Whereas directed fluorescent antigen testing yielded mainly intermediate results[10]. A definitive diagnosis of metastatic cancer can be made through histopathologic examination, with immunohistochemistry proving particularly helpful in diagnosing zosteriform-type cutaneous metastasis.

In conclusion, we presented a case of suspected herpes zoster due to clinical presentation with bedside laboratory investigation of a multinucleated giant cell. Concurrent immunosuppression from breast cancer and a history of postoperative radiotherapy supported the herpes zoster diagnosis. However, prolonged zosteriform rashes in patients with malignancy should raise suspicion of cutaneous metastasis, particularly in cases where antiviral drugs are ineffective. Therefore, diagnoses should be confirmed with more specific investigations, especially histopathologic and immunohistochemistry examination, in patients with a history of breast cancer and early treatment is highly recommended.

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