

Keratoacanthoma-like Cutaneous Metastasis from Invasive Ductal Carcinoma of the Breast: A Case Report

Abbreviation and Acronym List

CK7 – Cytokeratin 7; CK20 – Cytokeratin 20; ER – Estrogen receptor; GATA3 – GATA-binding protein 3; HER2 – Human epidermal growth factor receptor 2; KA – Keratoacanthoma; KA-like – Keratoacanthoma-like; PR – Progesterone receptor.

Introduction

Cutaneous metastases occur in approximately 0.5%–10.4% of patients with internal malignancies, and generally signify advanced disease with an unfavorable prognosis.[1] Breast carcinoma is the most common internal malignancy associated with cutaneous metastases in women, whereas lung carcinoma is the most common primary source in men.[2] Cutaneous metastases from breast carcinoma exhibit diverse clinical morphologies, including papules, nodules, erysipeloid, telangiectatic, ulcerative, zosteriform, and sclerodermoid lesions.[3] Among the rarest clinical presentations is keratoacanthoma-like (KA-like) cutaneous metastasis, which may closely mimic primary cutaneous squamous neoplasms and delay recognition of metastatic disease.

KA-like cutaneous metastases are exceedingly rare and have been reported in association with lung, esophageal, laryngeal, renal, prostatic, and breast carcinomas, with lung carcinoma representing the most frequently reported primary source. [4,5] Because these lesions closely resemble primary cutaneous tumors on clinical examination, accurate diagnosis requires careful clinicopathologic correlation supported by immunohistochemical evaluation.

Herein, we report a rare case of KA-like cutaneous metastasis arising from invasive ductal carcinoma of the breast in a 40-year-old Filipino woman. This case highlights the diagnostic challenge posed by this uncommon morphologic variant and underscores the importance of integrating clinical history with histopathologic and immunohistochemical findings to establish the correct diagnosis and guide appropriate oncologic management.

Case Report

A 40-year-old Filipino woman presented with a rapidly enlarging crateriform lesion on the anterior chest, arising against a background of two metachronous, contralateral primary invasive ductal carcinomas of the breast diagnosed three years apart. Three years earlier, she had undergone modified radical mastectomy with axillary lymph node dissection and breast reconstruction for stage



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IIIC right-sided invasive ductal carcinoma. Immunohistochemistry demonstrated estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and human epidermal growth factor receptor 2 (HER2)-negative disease. She subsequently received adjuvant chemotherapy with doxorubicin and cyclophosphamide, followed by 33 sessions of radiotherapy to the right breast.

During follow-up, a new mass in the contralateral (left) breast was identified and confirmed by fine-needle aspiration biopsy. This second tumor was ER-negative, PR-negative, and HER2-positive — a receptor profile discordant from the first, HER2-negative carcinoma — and was therefore classified as a second, biologically independent primary rather than a local recurrence or contralateral metastasis of the original right-sided tumor, in which the receptor profile would be expected to be preserved. In view of the HER2-positive status, trastuzumab was subsequently added to her treatment regimen.

Two months before consultation, she noted a solitary erythematous papule over the upper anterior chest that rapidly enlarged into a dome-shaped nodule with a central keratin-filled crater. The lesion was mildly pruritic but otherwise asymptomatic.

Physical examination revealed a solitary 2 × 2-cm erythematous crateriform nodule arising on an erythematous plaque over the upper anterior chest (Figure 1). Dermoscopy demonstrated thick yellow-white scales, white-to-red structureless areas, and irregular polymorphous vessels. The clinical differential diagnosis included keratoacanthoma (KA), squamous cell carcinoma, cutaneous metastasis, and a primary adnexal carcinoma.

Excision biopsy demonstrated an ulcerated nodule with a thinned overlying epidermis. Within the dermis were islands of atypical, acantholytic-appearing epithelial cells showing marked nuclear pleomorphism and hyperchromasia, with a markedly increased mitotic rate, extending to the lateral and deep margins

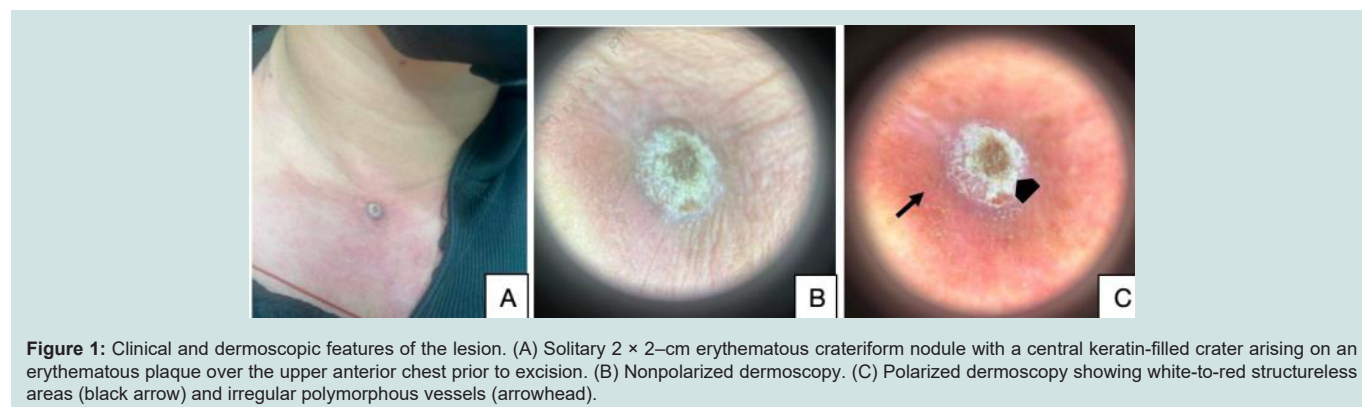


Figure 1: Clinical and dermoscopic features of the lesion. (A) Solitary 2 × 2-cm erythematous crateriform nodule with a central keratin-filled crater arising on an erythematous plaque over the upper anterior chest prior to excision. (B) Nonpolarized dermoscopy. (C) Polarized dermoscopy showing white-to-red structureless areas (black arrow) and irregular polymorphous vessels (arrowhead).

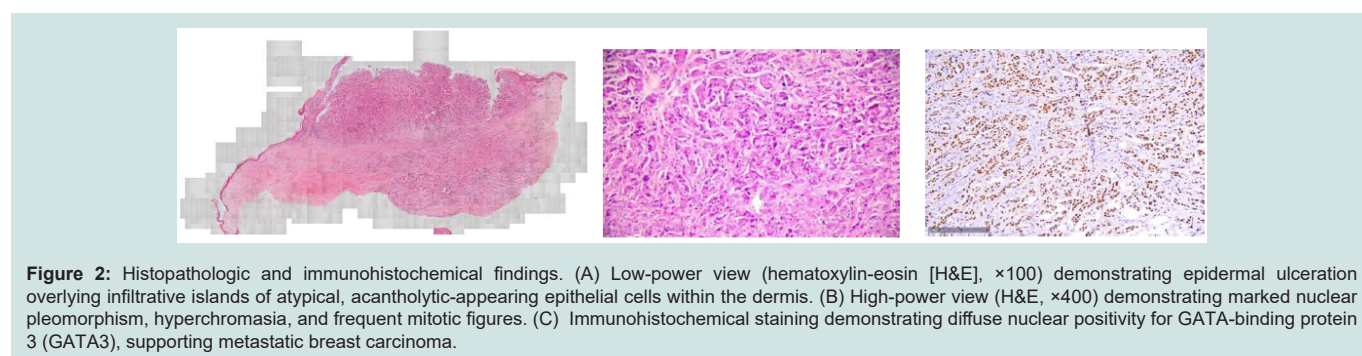


Figure 2: Histopathologic and immunohistochemical findings. (A) Low-power view (hematoxylin-eosin [H&E], ×100) demonstrating epidermal ulceration overlying infiltrative islands of atypical, acantholytic-appearing epithelial cells within the dermis. (B) High-power view (H&E, ×400) demonstrating marked nuclear pleomorphism, hyperchromasia, and frequent mitotic figures. (C) Immunohistochemical staining demonstrating diffuse nuclear positivity for GATA-binding protein 3 (GATA3), supporting metastatic breast carcinoma.

of the submitted sections. Lymphovascular invasion was identified. A dense inflammatory infiltrate composed of lymphohistiocytes and plasma cells surrounded the tumor. (Figure 2). Pancytokeratin staining confirmed epithelial differentiation. Immunohistochemistry demonstrated diffuse positivity for CK7 and GATA3, strong HER2/neu overexpression scored as 3+ by ASCO/CAP criteria, and negativity for CK20, p63, ER, and PR; fluorescence in situ hybridization was not performed for confirmation. Taken together, the morphologic and immunohistochemical findings supported a diagnosis of metastatic breast carcinoma with lymphovascular invasion, and argued against a primary cutaneous squamous neoplasm, including keratoacanthoma (KA) and squamous cell carcinoma.

The patient was treated symptomatically with topical corticosteroid ointment and an oral antihistamine for pruritus. Subsequent contrast-enhanced computed tomography revealed right frontal lobe lesions and multiple bilateral pulmonary nodules consistent with cerebral and pulmonary metastases, respectively. She was referred for systemic oncologic management, and trastuzumab therapy was continued. She underwent 10 sessions of radiotherapy for the cerebral metastases. At 6-month imaging follow-up, computed tomography demonstrated resolution of one right frontal lobe lesion and regression of the remaining lesion with decreased perilesional edema, consistent with a favorable radiologic response. The bilateral pulmonary nodules persisted; therefore, capecitabine was added to the ongoing trastuzumab therapy. At the time of this report, the patient remains on trastuzumab and capecitabine.

Discussion

Cutaneous metastasis from breast carcinoma usually reflects advanced systemic disease and is associated with a poor prognosis; for breast primaries, reported median survival after diagnosis of cutaneous metastasis is approximately 14 months [1,6,10]. Its clinical presentation is nonetheless highly variable and may mimic numerous benign and malignant dermatologic conditions. Cutaneous involvement most commonly occurs on the chest wall through direct extension or lymphatic spread, although hematogenous dissemination may also occur.

Our patient's rapidly enlarging crateriform nodule closely resembled keratoacanthoma, illustrating the diagnostic challenge posed by this rare morphologic variant. KA-like cutaneous metastasis is exceptionally uncommon. To our knowledge, only one previously reported case arising from breast carcinoma has been described in the literature, published in 1985, involving a woman with metastatic carcinoma of the breast who presented with a 2 × 2-cm flesh-colored nodule with a central keratin plug on the lower lip. [4,7] Similar to the present case, the diagnosis was established by histopathologic examination with supportive immunohistochemical findings. Together, these reports broaden the limited clinical spectrum of KA-like cutaneous metastasis from breast carcinoma and emphasize that rapidly enlarging crateriform lesions in patients with a history of malignancy should not be presumed to represent primary cutaneous tumors. A low threshold for biopsy is therefore warranted to facilitate early diagnosis and appropriate management.

Histopathologically, metastatic breast carcinoma typically demonstrates infiltrative nests and cords of malignant epithelial cells within the dermis, often accompanied by stromal fibrosis, although an acantholytic growth pattern, as observed in the present case, has also been described and can closely mimic acantholytic squamous cell carcinoma on hematoxylin-eosin staining alone. Because these findings may overlap with those of primary cutaneous neoplasms, immunohistochemistry is essential for establishing the diagnosis. In our patient, diffuse CK7 and GATA3 positivity supported breast differentiation, whereas CK20 negativity was consistent with the characteristic CK7-positive/CK20-negative immunophenotype of breast carcinoma. Although GATA3 is highly sensitive for breast carcinoma, it is not entirely specific because it may also be expressed in other neoplasms, including urothelial and parathyroid carcinomas.[8] Accordingly, immunohistochemical findings should always be interpreted in conjunction with the clinical history and morphologic features. The absence of p63 expression, a nuclear marker consistently expressed in primary cutaneous squamous cell carcinoma and adnexal carcinomas, further argued against these primary cutaneous entities despite the acantholytic appearance of the tumor cells. The dense lymphohistiocytic and plasma cell infiltrate surrounding the tumor represented a secondary reactive response to the underlying malignancy rather than a primary inflammatory process, which was further excluded by the presence of an atypical, mitotically active epithelial population rather than a granulomatous infiltrate. Importantly, the cutaneous lesion's immunophenotype — HER2 positivity with concurrent ER and PR negativity, scored as 3+ by immunohistochemistry according to current American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) criteria, [9] without confirmatory fluorescence in situ hybridization — was concordant with the patient's second, HER2-positive primary and discordant with the first, triple-negative primary, providing a direct immunohistochemical link between the metastasis and its most probable source tumor rather than the earlier triple-negative carcinoma. Lymphovascular invasion identified in the specimen represents an additional adverse histologic feature associated with a higher propensity for systemic dissemination, consistent with the cerebral and pulmonary metastases subsequently identified in our patient and in keeping with the generally poor prognosis of cutaneous metastasis from breast carcinoma [10]. Nonetheless, HER2-positive metastatic disease treated with HER2-directed therapy carries a comparatively more favorable prognosis than HER2-negative or triple-negative disease, which informed the decision to continue trastuzumab-based systemic therapy despite the visceral spread. This clinicopathologic correlation illustrates the value of immunohistochemistry not only in confirming metastatic breast carcinoma but also in correlating cutaneous metastases with the most likely primary tumor in patients with multiple breast malignancies.

The KA-like morphology observed in this and other reported cases likely reflects a reactive, pseudoepitheliomatous hyperplasia

of the overlying epidermis in response to an underlying dermal metastatic focus, producing the crateriform, keratin-filled clinical appearance that mimics true KA rather than representing squamous differentiation of the metastatic tumor itself. Pseudoepitheliomatous hyperplasia is a well-recognized reactive epidermal response to a variety of dermal processes, including infection, trauma, and underlying neoplasms, and is thought to arise from chronic irritation and altered local growth-factor signaling at the dermoepidermal junction overlying the tumor focus. As the hyperplastic epidermis proliferates and keratinizes centripetally around the underlying dermal deposit, it produces the dome-shaped, centrally crateriform, keratin-plugged lesion that clinically and dermoscopically mimics a true keratoacanthoma, even though the causative process is entirely dermal, arising from an underlying carcinomatous deposit rather than the epidermis itself. Clinically, several features should raise suspicion for cutaneous metastasis rather than a primary KA in a patient with known malignancy: absence of the spontaneous involution that characterizes true KA within weeks to months, rapid growth outside chronically sun-damaged skin, and lesion multiplicity or an atypical distribution. A new or rapidly evolving lesion arising in a patient with a hormone receptor- or HER2-discordant second malignancy, as in our patient, should further heighten suspicion, since receptor discordance itself signals biologically distinct disease that may behave and metastasize differently from the original primary. Histologically, KA-like cutaneous metastasis can be distinguished from conventional KA and cutaneous squamous cell carcinoma by the absence of continuity with the overlying epidermis or follicular epithelium and, classically, the presence of glandular rather than squamous differentiation. In our case, however, the tumor cells were acantholytic-appearing rather than overtly glandular on hematoxylin-eosin staining, a recognized but less common morphologic pattern of metastatic breast carcinoma that can closely simulate acantholytic squamous cell carcinoma; the distinction therefore rested on the immunophenotype (CK7-positive, GATA3-positive, p63-negative) rather than on morphology alone, contrasting with the p63-positive, CK5/6-positive profile typical of primary cutaneous squamous neoplasms. This immunophenotypic divergence reflects the differing embryologic origin of the two processes — glandular/ductal epithelium in metastatic breast carcinoma versus follicular/squamous epithelium in primary cutaneous KA and SCC — and offers a reliable diagnostic framework even when the clinical and histomorphologic appearances overlap substantially, as in the present case.

This case adds to the limited literature on KA-like cutaneous metastasis from breast carcinoma and highlights the importance of maintaining a high index of suspicion for metastatic disease in rapidly enlarging crateriform lesions, particularly in patients with a history of breast cancer. Early biopsy, judicious use of immunohistochemistry, and careful clinicopathologic correlation are essential for accurate diagnosis, appropriate systemic staging, and timely oncologic management.

Author Contributions

1. **Princess Marie F. Paredes, MD:** Conceptualization, literature review, data collection, manuscript preparation, manuscript revision, and visualization.
2. **Andrea Mendoza, MD, FPDS:** Clinical supervision, histopathologic interpretation, manuscript review, and critical revision.
3. **Lillian Villafuerte, MD, FPDS:** Clinical supervision, manuscript review, critical revision, and final approval of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical photographs.

Institutional Review Board Statement

This case report was reviewed and approved by the Institutional Review Board of Jose R. Reyes Memorial Medical Center (IRB Approval No. 2024-162).

Data Availability Statement

No datasets were generated or analyzed during the current study. Data sharing is therefore not applicable.

Ethical Compliance

The authors affirm that this study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Prior Presentation

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