




# Cutaneous metastases of invasive lobular breast cancer as the first clinical manifestation: a case report

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## Abstract

Cutaneous metastasis (CM) is a rare phenomenon, occurring in only 0.6% to 10.4% of oncology patients. Breast carcinoma represents nearly one-third of all CM cases, although it manifests in a minority of patients with breast cancer (BC). Notably, CMs are detected at the time of primary tumor diagnosis in 6.3% of patients with BC and serve as the initial clinical presentation in only 3.5% of patients. We present a case involving a 53-year-old woman with a 5-month history of asymptomatic infiltrating nodules in the axillae and trunk. Skin biopsy and immunohistochemical analysis confirmed metastatic breast carcinoma with positive estrogen receptor staining. This case underscores the importance of early detection and precise diagnostic techniques in managing metastatic adenocarcinoma with cutaneous manifestations. Despite the promising outcome of the initial treatment, the disease progression in this case highlights the aggressive nature of CMs and the ongoing need for research and advanced therapeutic strategies.

## Keywords

Breast cancer, hormone receptor-positive breast cancer, lobular breast carcinoma, cutaneous metastasis, skin lesion, case report

Date received: 6 October 2024; accepted: 6 January 2025

## Introduction

Cutaneous metastasis (CM) is an uncommon clinical manifestation resulting from the spread of cancer cells from an internal tumor to the skin, either by direct extension or through vascular or lymphatic

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pathways.<sup>1</sup> This phenomenon occurs in a small but significant proportion of oncology patients, with an estimated incidence ranging from 0.6% to 10.4%.<sup>2</sup> It accounts for approximately 2% of all skin tumors and, in some cases, serves as the first indication of an internal malignancy.<sup>2</sup> Patients with CM often experience concurrent metastases to other organs, including the bones, liver, and brain.<sup>3</sup> While various cancers can lead to CMs, lung cancer is the most common source in men, whereas breast cancer (BC) is the leading cause in women, particularly affecting the thoracic area.<sup>2,3</sup> In BC, CMs are detected at the time of primary tumor diagnosis in 6.3% of cases and represent the initial clinical presentation in only 3.5% of patients.<sup>1</sup> The prognosis for patients with CM remains poor, regardless of whether the skin lesions are solitary or multiple, with a mortality rate exceeding 70% within the first year following BC diagnosis.<sup>3</sup> This report details the case of a patient with BC initially identified through asymptomatic infiltrating nodules

in the axilla and trunk. Further investigations confirmed these lesions as CMs of BC.

### **Case presentation**

A 53-year-old woman presented to the dermatology department with a 5-month history of bilateral nodules in the armpits, which had spread to the trunk. Clinical examination revealed asymptomatic, erythematous, infiltrating skin-colored nodules measuring 2 × 3 cm in the axillae and trunk (Figure 1). The patient reported associated symptoms of asthenia, anorexia, and weight loss of approximately 10 kg. A clinical breast examination showed no palpable masses, and the patient had no history of smoking, alcohol use, medical conditions, or relevant family history. Differential diagnoses included cutaneous lymphoma, sarcoidosis, CM, Merkel cell carcinoma, cutaneous plasmacytoma, and progressive nodular histiocytosis. Diagnostic tests and imaging were employed to rule out these conditions, and a detailed clinical discussion was

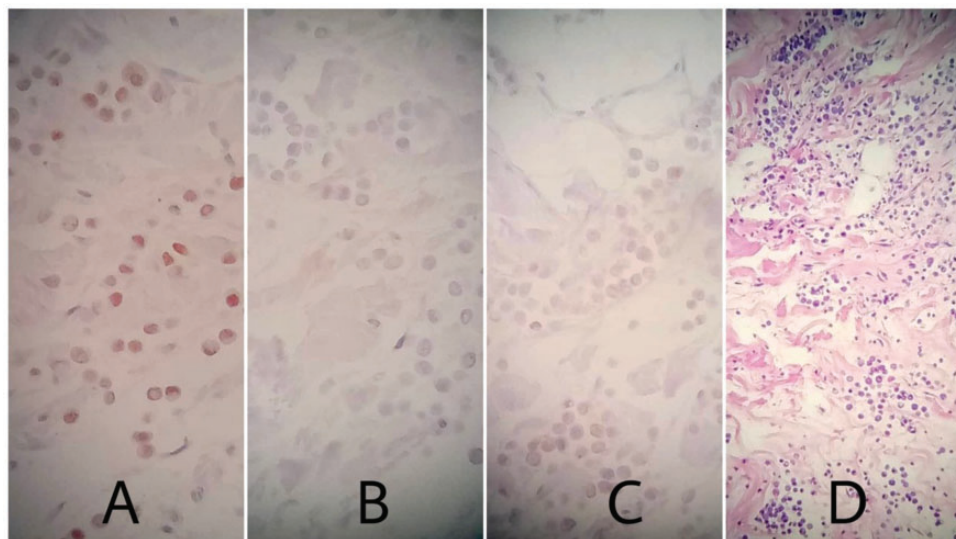


**Figure 1.** Asymptomatic, skin-colored, erythematous infiltrating nodules on the armpits and trunk.

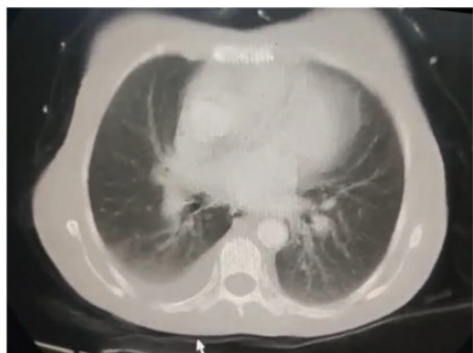
conducted. Routine laboratory tests were normal except for an elevated erythrocyte sedimentation rate (98 mm/hour). A punch biopsy was performed in collaboration with the surgical department, and histopathological analysis revealed diffuse infiltration of atypical cells with large nuclei, prominent nucleoli, and atypical mitoses, consistent with metastatic undifferentiated carcinoma. Immunohistochemical staining showed positive nuclear staining for estrogen receptor (ER) in 50% of tumor cells with ++/+++ intensity, negative progesterone receptor (PR) staining, and faint cytoplasmic and negative membranous staining for HER2-neu (c-erbB-2) (Figure 2). Controls confirmed the mammary origin of the metastases, consistent with lobular-type metastatic adenocarcinoma involving the skin. Additional tests revealed an elevated cancer antigen (CA 15-3) level of >500 U/mL and carcinoembryonic antigen (CEA) level of

6.37 ng/mL. A structured timeline was created, highlighting the patient's symptom progression, treatment adjustments, and biomarker trends, offering a comprehensive overview of her clinical course.

The patient was referred to the oncology hospital and began treatment with palbociclib at a dose of 125 mg, selected for its demonstrated efficacy in similar clinical scenarios and in accordance with current treatment guidelines. Palbociclib was administered alongside hormone therapy with aromatase inhibitors to maximize therapeutic outcomes, while alternative treatments were considered but ultimately not pursued. Although the skin lesions resolved, the CA 15-3 and CEA levels continued to rise, indicating ongoing disease progression. Four months after initiating treatment, the patient developed symptoms of cough, ascites, and lower extremity edema. A computed tomography scan revealed a significant



**Figure 2.** Subcutaneous soft tissue nodule. Resection revealed metastatic adenocarcinoma with single-cell infiltrate involving the skin, consistent with mammary origin, lobular type. (a) Immunohistochemical staining showed positive nuclear staining for estrogen receptors in 50% of the tumor cells, with staining intensity of ++/+++. (b) Negative nuclear staining for progesterone receptors in the tumor cells. (c) Faintly cytoplasmic positive and negative membranous staining for HER2-neu (c-erbB-2) and (d) Hematoxylin and eosin staining.



**Figure 3.** Computed tomography scan showing a large amount of ascites and pleural effusion, with no evidence of lung metastases.

accumulation of ascites and pleural effusion, though no lung metastases were identified (Figure 3). Despite the initial improvement in the cutaneous lesions, the patient's condition progressively worsened, and she died of her illness 7 months after the diagnosis of CM originating from primary breast carcinoma.

## Discussion

Cutaneous malignancies are characterized by neoplastic lesions originating from primary tumors in the dermis or subcutaneous tissue.<sup>4</sup> These malignancies can spread through vascular or lymphatic pathways, contiguous tissue growth, or iatrogenic implantation.<sup>4,5</sup> Although often associated with advanced metastatic disease, cutaneous malignancies can also serve as the initial indication of an internal malignancy.<sup>4</sup> CMs, a relatively infrequent clinical occurrence, are more commonly observed in elderly individuals.<sup>4</sup> They typically appear alongside visceral metastases and may develop months to years after the initial tumor diagnosis.<sup>6</sup> The incidence of CMs in all metastatic cases is low, ranging from 0.7% to 9%, and is associated with poor prognostic outcomes.<sup>5,6</sup> Approximately 60% of metastatic cancers presenting as cutaneous

malignancies are adenocarcinomas, with the breast, lungs, and large intestine being the most common primary sites.<sup>4</sup> Adenocarcinomas account for approximately 60% of cancers that metastasize to the skin, with the breast, lungs, and large intestine being the predominant primary sites.<sup>4</sup> Breast carcinoma is responsible for nearly one-third of all CM cases; however, only a minority of individuals with BC develop this type of metastasis.<sup>4</sup> Carcinoma erysipelloides is the most common form of skin metastasis from BC, predominantly affecting patients with inflammatory BC and spreading to the subcutaneous and dermal layers via lymphatic channels.<sup>7</sup> The clinical presentation of CMs varies widely, often characterized by the sudden appearance of multiple discrete, non-tender, and movable nodules typically less than 2 cm in diameter upon initial observation.<sup>4,8</sup> CMs may also manifest as plaques, areas of alopecia, or lesions resembling dermatological conditions such as erythema annulare, lupus erythematosus, herpes zoster, or condyloma, frequently mimicking other clinical entities.<sup>4</sup> Consequently, CMs frequently simulate other clinical entities.<sup>4</sup> The lesions may initially grow rapidly before stabilizing.<sup>8</sup> Cutaneous breast metastases commonly develop on the chest wall, although other frequently affected sites include the abdomen, back, head and neck, scalp, upper extremities, and post-surgical scars.<sup>5,8</sup> They usually appear on the side of the chest opposite the primary tumor.<sup>6</sup> In the case under discussion, the patient presented with bilateral asymptomatic infiltrative nodules in the axillary and trunk regions, including a clinically discernible 2- × 3-cm skin-colored, erythematous, infiltrative nodule. Clinical breast examination revealed no palpable masses, while systemic symptoms included asthenia, anorexia, and significant weight loss of approximately 10 kg. Differentiating between primary adenocarcinomas of the skin and CMs from other malignancies requires

histological evaluation.<sup>9</sup> A definitive diagnosis depends on histopathological assessment and immunohistochemical analysis.<sup>9</sup> Therefore, patients with suspected CMs of BC should undergo biopsy of the identified skin nodule, erythematous lesion, or papule to confirm the diagnosis.<sup>2,10,11</sup> The histological characteristics and immunohistochemical profile of the biopsy specimen are critical in identifying the cellular patterns and determining the origin of the primary neoplasm.<sup>10,11</sup> Certain diagnostic imaging techniques show reduced sensitivity when used individually, with sensitivity rates of 57% to 81% for mammography and 68% to 98% for ultrasound.<sup>10</sup> Combining these methods with magnetic resonance imaging, which has a high sensitivity of 93%, improves diagnostic accuracy.<sup>10</sup> In this case, pathological examination of an incisional biopsy specimen revealed metastatic adenocarcinoma with solitary cell infiltration involving the skin, consistent with mammary origin and the lobular subtype. The National Comprehensive Cancer Network and the American Society of Clinical Oncology guidelines recommend periodic assessment of biomarkers such as CEA, CA 15-3, and/or CA 27-29 in patients with metastatic disease.<sup>12</sup> In our patient, CA 15-3 exceeded 500 U/mL and CEA was 6.37 ng/mL. Careful evaluation of the microscopic and molecular characteristics of the primary tumor is crucial for developing a tailored management plan for skin metastases, which may include external beam radiotherapy, systemic chemotherapy, or hormone therapy.<sup>8,11</sup> CMs of BC significantly impact the patient's quality of life and present substantial therapeutic challenges.<sup>13</sup> Currently, no universally accepted standard guideline exists for managing CMs of BC.<sup>8,10</sup> In most cases, CMs signify widespread disease and tumor progression, making local interventions, such as surgery or radiation, often unsuitable.<sup>8,11</sup> Symptomatic management, including local radiation therapy, can be

effective for cases involving large breast tumors with ulceration or local metastatic lesions.<sup>8,11</sup> Therapeutic strategies should prioritize systemic disease management over local interventions, even when cutaneous lesions are solitary.<sup>8</sup> BC is classified into three major subtypes based on its cellular structure and microanatomy.<sup>14</sup> The first subtype includes hormone receptor-positive cancers, characterized by the presence of ER and/or PR. These can be treated with hormonal therapies such as letrozole and anastrozole, which reduce estrogen levels, or tamoxifen, which blocks ERs.<sup>14</sup> The second subtype involves HER2-positive BCs, where the tumor cells express HER2; these are treated with a combination of anti-HER2 monoclonal antibody therapy and chemotherapy.<sup>14</sup> The third subtype is triple-negative BC, which lacks ER, PR, and HER2 expression. Hormonal therapies and HER2-targeted agents are ineffective in triple-negative BC because of the absence of targetable receptors, but chemotherapy remains a viable option.<sup>14</sup> Hormone receptor-positive BC often presents in progressive disease stages and is initially treated with hormonal therapy.<sup>11</sup> If hormonal therapy is ineffective for managing CMs, chemotherapy may be considered.<sup>11</sup> CDK4/6 inhibitors such as palbociclib, ribociclib, and abemaciclib have shown promising results when combined with aromatase inhibitors.<sup>14</sup> Additionally, combining fulvestrant with CDK4/6 inhibitors has demonstrated superior survival benefits compared with fulvestrant monotherapy.<sup>14</sup> In the present case, immunohistochemical staining of tumor cells revealed positive nuclear staining for ER in 50% of cells, negative PR, and negative HER2-neu membranous staining. Based on these findings, the patient was started on 125 mg of palbociclib. After 3 months of treatment, the skin lesions resolved, but the CA 15-3 and CEA levels continued to rise with no signs of clinical recovery.



## Conclusion

Effective and early clinical assessment is crucial to reducing the spread of BC. Skin metastases, while uncommon, are significant indicators of BC and can mimic common skin conditions such as cellulitis or lymphedema, requiring clinicians to remain highly vigilant. Persistent skin lesions, particularly those on the chest or in patients with a history of cancer, should be thoroughly evaluated, including biopsy, to confirm the diagnosis. Multidisciplinary collaboration across healthcare fields is essential for the appropriate management of these rare and challenging cases.

## Acknowledgements

Dr. Saja Karaja would like to express her sincere gratitude to Dr. Maher Nassar, Department of Pathology, Al-Bairouni University Hospital, Damascus, Syria, for kindly providing the pathological images utilized in this study.

## Authors' contributions

Saja Karaja: Data collection.

Saja Karaja, Ahmad Almohamed, Ayham Qatza, Ahmed Aldolly, and Sanaa Mansour: Drafted the main manuscript and prepared the figures.

Saja Karaja and Sanaa Mansour: Revised the final manuscript.

Alae Aldin Almasri: Chief supervisor.

Saja Karaja: Submitted the final manuscript.

All authors read and approved the final manuscript.

## Availability of data and materials

The data and materials used in this study are available upon request from the corresponding author.

## Declaration of conflicting interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Ethics

This work has been reported in line with the CARE criteria.<sup>15</sup> Our institution does not require ethical approval for reporting individual cases or case series.

## Funding


The authors received no financial support for the research, authorship, and/or publication of this article.

## Informed consent

Written informed consent was obtained from the patient's husband for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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