

An Unusual Presentation of Cutaneous Metastatic Lobular Breast Carcinoma

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PRACTICE POINTS

- Clinical providers should be aware of the varying presentations of metastatic cutaneous breast carcinomas.
- Clinicians should remain alert to the possibility of breast cancer as a cause of cutaneous metastases, even in patients with recent negative breast cancer screening.

Breast cancer is the most common malignancy to metastasize to the skin in women. Cutaneous breast carcinoma may arise as cutaneous metastasis or secondary to direct tumor extension to the skin. This report describes an unusual presentation of cutaneous metastatic lobular breast carcinoma that involved diffuse cutaneous lesions and rapid progression from onset of breast mass to development of clinically apparent metastatic skin lesions.

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In women, breast cancer is the leading cancer diagnosis and the second leading cause of cancer-related death,¹ as well as the most common malignancy to metastasize to the skin.² Cutaneous breast carcinoma may present as cutaneous metastasis or can occur secondary to direct tumor extension. Five percent to 10% of women with breast cancer will present clinically with metastatic cutaneous disease, most commonly as a recurrence of early-stage breast carcinoma.²

In a published meta-analysis that investigated the incidence of tumors most commonly found to metastasize to the skin, Krathen et al³ found that cutaneous metastases occurred in 24% of patients with breast cancer (N=1903). In 2 large retrospective studies from tumor registry data, breast cancer was found to be the most common tumor involving metastasis to the skin, and 3.5% of the breast cancer cases identified in the registry had cutaneous metastasis as the presenting sign (n=35) at time of diagnosis.⁴

We report an unusual presentation of cutaneous metastatic lobular breast carcinoma that involved diffuse cutaneous lesions and rapid progression from onset of the breast mass to development of clinically apparent metastatic skin lesions.

Case Report

A 59-year-old woman with an unremarkable medical history presented to our dermatology clinic for evaluation of new widespread lesions that developed over a period of months. The eruption was asymptomatic and consisted of numerous bumpy lesions that reportedly started on the patient's neck and progressively spread to involve the trunk. Physical examination revealed multiple flesh-colored, firm nodules scattered across the upper back, neck, and chest (Figure 1). Bilateral cervical and axillary lymphadenopathy also was noted. Upon questioning regarding family history of malignancy, the patient reported that her brother had been diagnosed with colon cancer. Although she was not up to date on age-appropriate malignancy screenings, she did report having

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a diagnostic mammogram 1 year prior that revealed a suspicious lesion on the left breast. A repeat mammogram of the left breast 6 months later was read as unremarkable.

Two 3-mm representative punch biopsies were performed. Hematoxylin and eosin staining revealed a basket-weave stratum corneum with underlying epidermal atrophy. A relatively monomorphic epithelioid cell infiltrate extending from the superficial reticular dermis into the deep dermis and displaying an open chromatin pattern and pink cytoplasm was observed, as well as dermal collagen thickening. Linear, single-filing cells along with focal irregular nests and scattered cells were observed (Figure 2). Immunohistochemical staining was positive for cytokeratin 7 (Figure 3A), epithelial membrane antigen, and estrogen receptor (Figure 3B) along with

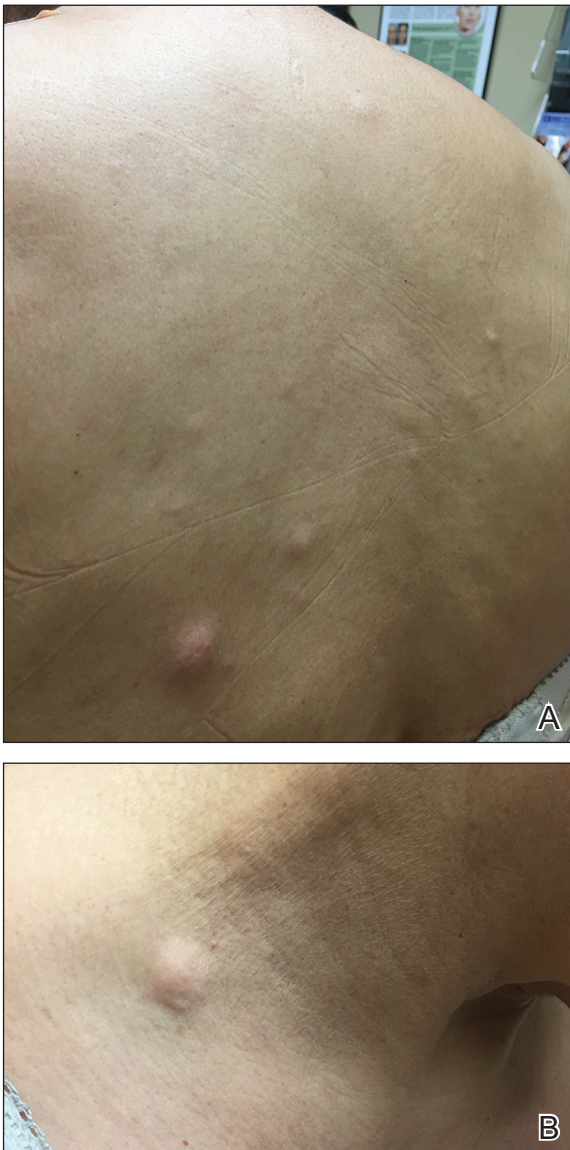


FIGURE 1. A and B, Firm, flesh-colored nodules scattered across the upper back and neck.

gross cystic disease fluid protein 15; focal progesterone receptor positivity also was present. Cytokeratin 20, cytokeratin 5/6, carcinoembryonic antigen, p63, CDX2, paired box gene 8, thyroid transcription factor 1, and human epidermal growth factor receptor 2/neu stains were negative. Findings identified in both biopsies were consistent with metastatic cutaneous lobular breast carcinoma.

A complete blood cell count and complete metabolic panels were within normal limits, aside from a mildly elevated alkaline phosphatase level. Breast ultrasonography was unremarkable. Stereotactic breast magnetic resonance imaging (MRI) revealed a 9.4-cm mass in the upper outer quadrant of the right breast as well as enlarged lymph nodes 2.2 cm from the left axilla. A subsequent bone scan demonstrated focal activity in the left lateral fourth rib, left costochondral junction, and right anterolateral fifth rib—it was unclear whether these lesions were metastatic or secondary to trauma from a fall the patient reportedly had sustained 2 weeks prior. Lumbar MRI without gadolinium contrast revealed extensive abnormal heterogeneous signal intensity of osseous structures consistent with osseous metastasis.

Subsequent diagnostic bilateral breast ultrasonography and percutaneous left lymph node biopsy revealed pathology consistent with metastatic lobular breast carcinoma with near total effacement of the lymph node and extracapsular extension concordant with previous MRI findings. The mass in the upper outer quadrant of the right breast that previously was observed on MRI was not identifiable on this ultrasound. It was recommended that the patient pursue MRI-guided breast biopsy to have the breast lesion further characterized. She was referred to surgical oncology at a tertiary center for management; however, the patient was lost to follow-up, and there are no records available indicating the patient pursued any treatment. Although we were unable to confirm the patient's breast lesion that previously was seen on MRI was the cause of the metastatic disease, the overall clinical picture supported metastatic lobular breast carcinoma.

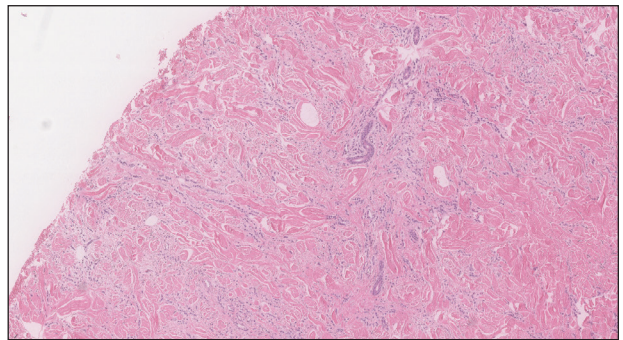


FIGURE 2. A relatively monomorphic epithelioid cell infiltrate extending from the superficial reticular dermis into the deep dermis was observed along with dermal collagen thickening. Linear, single-filing cells along with focal irregular nests and scattered cells were noted (H&E, original magnification $\times 4$).

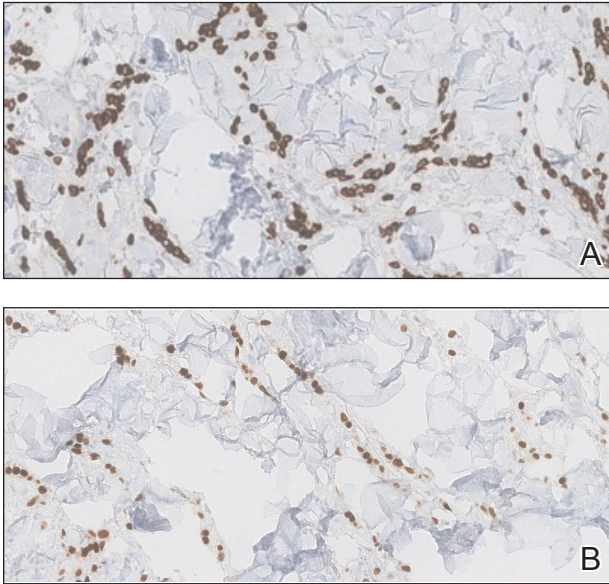


FIGURE 3. A and B, Immunohistochemical staining was positive for cytokeratin 7 and estrogen receptor, respectively (original magnifications $\times 20$).

Comment

Tumor metastasis to the skin accounts for approximately 2% of all skin cancers⁵ and typically is observed in advanced stages of cancer. In women, breast carcinoma is the most common type of cancer to exhibit this behavior.² Invasive ductal carcinoma represents the most common histologic subtype of breast cancer overall,^{6,7} and breast adenocarcinomas, including lobular and ductal breast carcinomas, are the most common histologic subtypes to exhibit metastatic cutaneous lesions.⁸

Invasive lobular breast carcinoma represents approximately 10% of invasive breast cancer cases. Compared to invasive ductal carcinoma, there tends to be a delay in diagnosis often leading to larger tumor sizes relative to the former upon detection and with lymph node invasion. These findings may be explained by the greater difficulty of detecting invasive lobular carcinomas by mammography and clinical breast examination compared to invasive ductal carcinomas.⁹⁻¹¹ Additionally, invasive lobular carcinomas are more likely to be positive for estrogen and progesterone receptors compared to invasive ductal carcinomas,¹² which also was consistent in our case.

Cutaneous metastases of breast cancer most commonly are found on the anterior chest wall and can present as a wide spectrum of lesions, with nodules as the most common primary dermatologic manifestation.¹³ Cutaneous metastatic lesions commonly have been described as firm, mobile, round or oval, solitary or grouped nodules. The color of the nodules varies and may be flesh-colored, brown, blue, black, pink, and/or red-brown. The lesions often are asymptomatic but may ulcerate.²

In our case, the distribution of lesions was a unique aspect that is not typical of most cases of metastatic

cutaneous breast carcinoma. The nodules appeared more scattered and involved multiple body regions, including the back, neck, and chest. Although cutaneous breast cancer metastases have been documented to extend to these body regions, a review of PubMed articles indexed for MEDLINE using the terms *cutaneous metastatic lobular breast carcinoma*, *breast carcinoma*, and *metastatic breast cancer* suggested that it is uncommon for these multiple areas to be simultaneously affected.^{4,14} Rather, the more common clinical presentation of cutaneous metastatic breast carcinoma is as a solitary nodule or group of nodules localized to a single anatomic region.¹⁴

Another notable feature of our case was the rapid development of the cutaneous lesions relative to the primary tumor. This patient developed diffuse lesions over a period of several months, and given that her mammogram performed the previous year was negative for any abnormalities, one could suggest that the metastatic lesions developed less than a year from onset of the primary tumor. A previous study involving 41 patients with a known clinical primary visceral malignancy (ie, breast, lung, colon, esophageal, gastric, pancreatic, kidney, thyroid, prostate, or ovarian origin) found that it takes approximately 3 years on average for cutaneous metastases to develop from the onset of cancer diagnosis (range, 1–177 months).¹⁴ In the aforementioned study, 94% of patients had stage III or IV disease at time of skin metastasis, with the majority of those demonstrating stage IV disease. However, it also is possible that these breast tumors evaded detection or were too small to be identified on prior imaging.¹⁴ A review of our patient’s medical records did not indicate documentation of any visual or palpable breast changes prior to the onset of the clinically detected metastatic nodules.

Conclusion

Biopsy with immunohistochemical staining ultimately yielded the diagnosis of metastatic lobular breast carcinoma in our patient. Providers should be aware of the varying clinical presentations that may arise in the setting of cutaneous metastasis. When faced with lesions suspicious for cutaneous metastasis, biopsy is warranted to determine the correct diagnosis and ensure appropriate management. Upon diagnosis of cutaneous metastasis, prompt coordination with the primary care provider and appropriate referral to multidisciplinary teams is necessary. Clinical providers also should maintain a high index of suspicion when evaluating patients with cutaneous metastasis who have a history of normal malignancy screenings.

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