

# A Solitary Neck Nodule as Late Evidence of Recurrent Lobular Breast Carcinoma

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## Key Words

Breast cancer · Lobular breast carcinoma · Cutaneous metastasis · Immunohistochemical techniques for diagnosis of breast carcinoma

## Abstract

Recurrent lobular breast carcinoma manifesting as a cutaneous neck nodule in a woman, 14 years after successful chemotherapy, illustrates the importance of following at-risk patients with a high level of clinical suspicion. This case emphasizes the value of combining clinical findings with appropriate histopathologic and immunohistochemical analysis when evaluating a cutaneous lesion in such a patient.

## Introduction

Breast carcinoma is the most common malignancy in women, and accounts for the most common primary source of cutaneous metastases [1–3, 6–9]. Cutaneous metastatic lesions may present as solitary nodules or nondescript localized rashes. For this reason, it is important for clinicians to consider a differential diagnosis of malignancy when evaluating a cancer survivor who demonstrates a benign-appearing skin finding, even if the lesion is distant in either location or time to the primary lesion [4]. Once an interdermal skin lesion is removed, immunohistochemical stains can prove invaluable in expediting accurate diagnosis by identifying expression profiles for primary tumors. Expression profiles helpful in differentiating breast cancer from other primary carcinomas include cytokeratin 7 (CK7), cytokeratin 20 (CK20), estrogen receptor (ER), progesterone receptor (PR), gross cystic disease fluid protein 15 (GCDFP-15), thyroid transcription factor 1 (TTF-1) and CDX2 (an intestinal epithelia-specific nuclear transcription factor) [5]. We present a case in which a patient presented with cutaneous metastases as the primary sign of disease recurrence over 15 years after her initial

diagnosis and treatment. A low threshold for biopsy and detailed immunohistochemical staining was essential to making the correct diagnosis and rapidly initiating treatment.

### Case Report

The patient was a 71-year-old Caucasian female with a remote history of breast carcinoma, successfully treated with simple mastectomy in 1993 followed by chemotherapy (tamoxifen) for 5 years. She presented to the dermatology clinic for evaluation of a small, non-pruritic, non-tender nodule on her posterior right neck that had been slowly enlarging over the past year. The patient denied a history of ulceration, bleeding, discharge, or pain.

On physical exam, the patient had a 0.5 × 0.3 cm flesh-colored, soft, freely mobile nodule on her right neck. There was no ulceration, tenderness to palpation, erythema or edema. There was no palpable cervical or axillary lymphadenopathy. A punch biopsy was performed and submitted for histologic examination. The clinical diagnosis was sebaceous cyst.

On microscopic examination, within the dermis there were infiltrative tumor cells with enlarged, hyperchromatic nuclei (fig. 1). The tumor cells infiltrated between collagen bundles in a single file pattern (fig. 2). Perineural infiltration was also identified, along with occasional tumor cells in mitoses. A partial immunohistochemical profile was performed and interpreted with appropriately staining control slides. The tumor cells were shown to be positive for cytokeratin-AE1/AE3, CK7, ER, PR, and GCDFP-15. The tumor cells showed absence of staining for CK20, TTF-1, and CD45 (fig. 3). The histomorphology combined with the immunohistochemical profile were consistent with metastatic lobular carcinoma involving the skin.

The patient was referred to medical oncology where she underwent chest, abdomen, and pelvic computed tomography, magnetic resonance imaging of the head, and a positron emission tomography scan which showed no evidence of metastatic disease. She did have elevated tumor markers, however, which included a carcinoembryonic antigen (CEA) of 64 ng/dl and a CA15.3 of 314. The patient was treated with an aromatase inhibitor (anastrozole), which resulted in complete clearance of the skin lesion. She has had no signs of recurrence by physical examination after 3 months of follow-up.

### Discussion

Cutaneous metastases are present in 23.9% of breast carcinomas over the course of the disease [1, 2]. In one study, skin metastases were seen at the time of diagnosis in 6.3% of patients, and 3.5% had cutaneous involvement as the presenting sign of disease [1].

Grossly, most cutaneous metastases present as dermal or subcutaneous nodules that are firm, painless, and often immobile [9]. Their growth pattern is not predictable, and they may grow rapidly, appear in clusters, or grow slowly and appear as a solitary lesion. In our female patient, the lesion was located on the right posterior neck, which is consistent with the propensity of lobular breast carcinoma to distantly metastasize. Our patient had a remote history of breast cancer in 1993, status-post simple mastectomy and chemotherapy.

Immunohistochemical evaluation is an increasingly important diagnostic tool for characterizing the primary malignancy in cutaneous metastases. Park et al. [5] evaluated the organ-specific immunostaining profiles that provided high sensitivity, specificity, and positive predictive value in detecting primary adenocarcinomas. The expression profile GCDFP-15(+)/TTF-1(-)/CDX2(-)/CK7(+)/CK20(-) was determined to have a sensitivity of 74.4%, a specificity of 99.6%, and a positive predictive value of 96.9% in identifying the breast as the primary site of metastatic adenocarcinoma [5]. Although no available marker has shown complete site specificity, GCDFP-15 is considered a relatively specific and sensitive marker of breast cancers [10, 11].

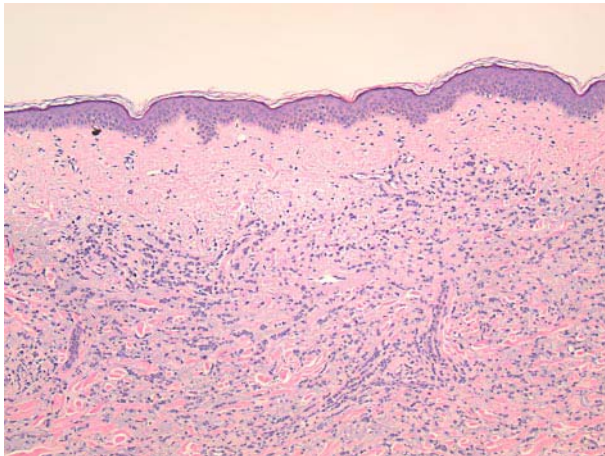
Histologically, the differential diagnosis included metastatic lobular carcinoma, metastatic gastric carcinoma (signet ring cell carcinoma) [5], primary adnexal carcinoma [12], and lymphoma. No histological features for adnexal differentiation were present to suggest a primary skin tumor. The immunohistochemical profile of CK7(+), CK20(–), ER(+), PR(+), GCDFP-15(+) ruled out a primary gastric carcinoma. The absence of CD45 ruled out a lymphoma.

Invasive lobular breast carcinoma accounts for 0.7 to 14% of all primary invasive breast carcinomas [13]. This report emphasizes the importance of a combination of clinical, histologic, and immunohistochemical analyses to accurately identify cutaneous involvement in metastatic breast carcinoma. A high level of suspicion is warranted when evaluating cutaneous lesions in patients with a past history of breast carcinoma, even if the patient was successfully treated in the distant past.

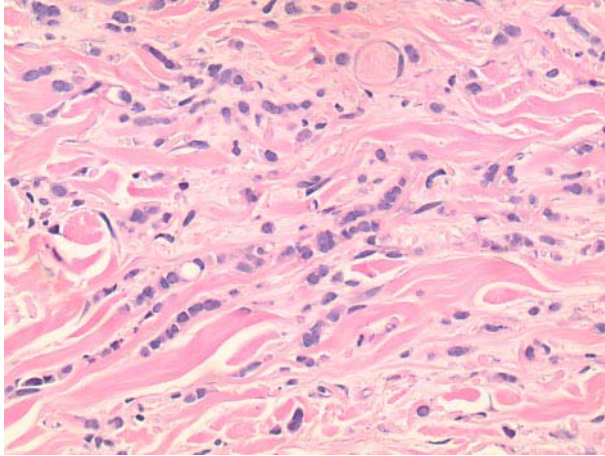
### Acknowledgement

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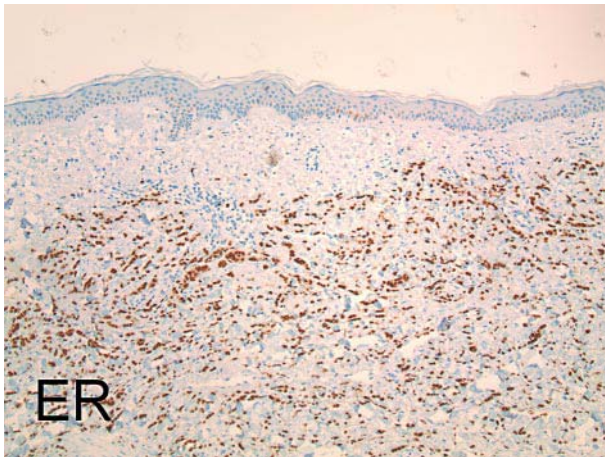
**Fig. 1.** Infiltrative tumor cells within the dermis with large, hyperchromatic nuclei (microscopic magnification  $\times 10$ ).

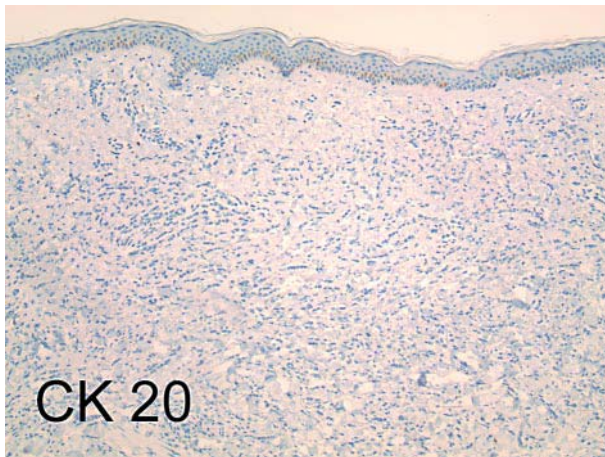
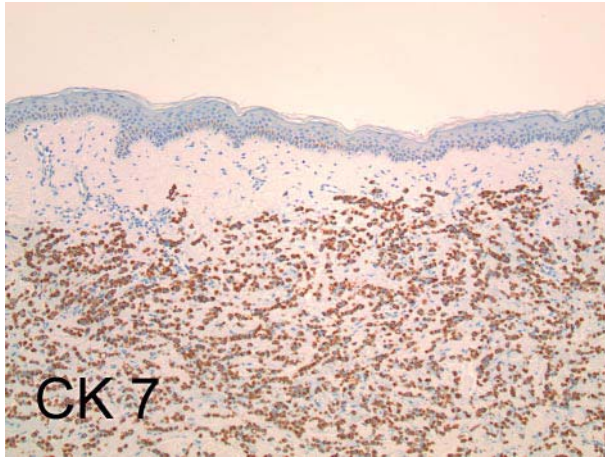


**Fig. 2.** Tumor cells infiltrate between collagen bundles in a single file pattern (microscopic magnification  $\times 40$ ).



**Fig. 3.** The immunohistochemical profile shows tumor cells positive for ER, CK7 and negative for CK20.







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