Cutaneous Metastasis of Invasive Ductal Carcinoma of the Breast to an Infusaport Site

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Cutaneous metastasis of a primary internal malignancy is a relatively common phenomenon, occurring in up to 10% of patients with noncutaneous cancer. Cutaneous metastasis can occur via direct extension, hematologic or lymphatic dissemination, or surgical implantation. The most common internal malignancy associated with the development of cutaneous metastases in females is breast cancer.

We present a patient with widely metastatic invasive ductal carcinoma of the breast, status postpalliative mastectomy and chest wall coverage with a vertical rectus abdominus myocutaneous flap, who acquired cellulitis and, subsequently, noncontiguous cutaneous metastasis of her breast cancer to the site of her central venous access device (ie, infusaport). We hypothesize that the local inflammation associated with her recent bout of cellulitis and operations, in conjunction with the presence of a foreign body, may have predisposed the infusaport site to seeding by metastatic tumor cells. This case highlights the importance of considering cutaneous metastasis in the differential diagnosis of new skin eruptions in patients with cancer.

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Breast cancer is the most common malignancy to metastasize to the skin in females.[1] Cutaneous manifestations of breast cancer occur most frequently on the anterior chest[1-3] and can develop from direct extension, hematologic or lymphatic dissemination, or surgical implantation. We present a patient with widely metastatic invasive ductal carcinoma of the breast who acquired a noncontiguous cutaneous metastatic lesion at the site of her central venous access device (ie, infusaport).

Case Report

A 51-year-old woman presented for evaluation of changes to her right breast. Five months prior, she noticed a mass on her right breast that gradually enlarged, developed overlying sores, and became painful. Clinical examination revealed overlying erythema and ulcerations draining clear serous fluid at the superolateral aspect of the right breast. While no discrete lumps were palpated, the right breast was firm and fixed to the chest wall. The left breast had no changes in its appearance, and no masses were palpated. The patient had bilateral axillary lymphadenopathy but no supraclavicular adenopathy. Core and punch biopsies of the right breast and overlying skin revealed the presence of infiltrative grade 3 ductal carcinoma involving the dermis, epidermis, and dermal lymphatics (Figure 1), with erythroblastic leukemia viral oncogene homolog 2, *ERBB2* (formerly *HER2* or *HER2/neu*), and estrogen receptor/progesterone receptor positivity. Imaging studies revealed pulmonary metastases. She was diagnosed with stage IV invasive ductal carcinoma of the breast.

At that time, an infusaport was placed in the right subclavian vein, and the patient underwent systemic chemotherapy, as well as local radiation to the right breast, subclavicular nodes, and axilla. She experienced a partial response to a regimen of vinorelbine, trastuzumab, and anastrozole, and maintained an

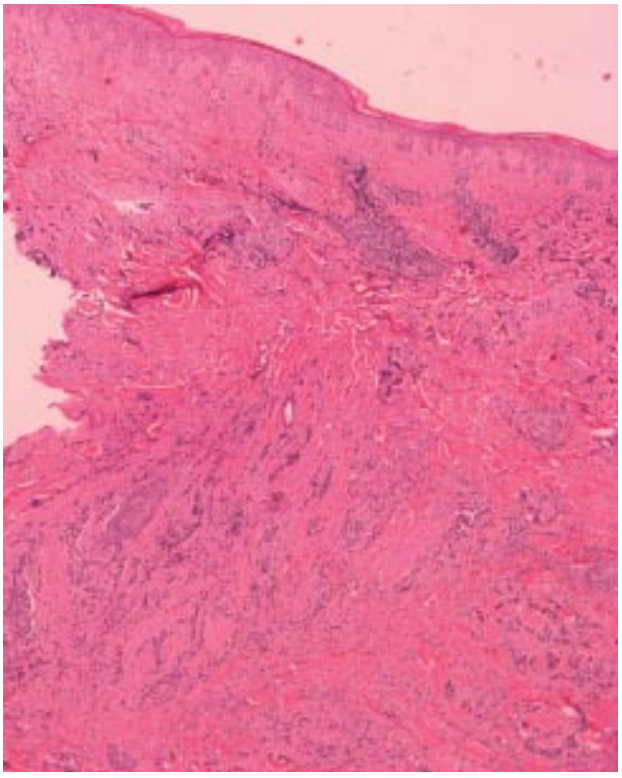

Figure 1. Punch biopsy specimen from the right breast mass at initial presentation in 2002, clinically seen to involve the overlying skin. Histopathology revealed the presence of infiltrative grade 3 ductal carcinoma involving the dermis, epidermis, and dermal lymphatics (H&E, original magnification ×4).

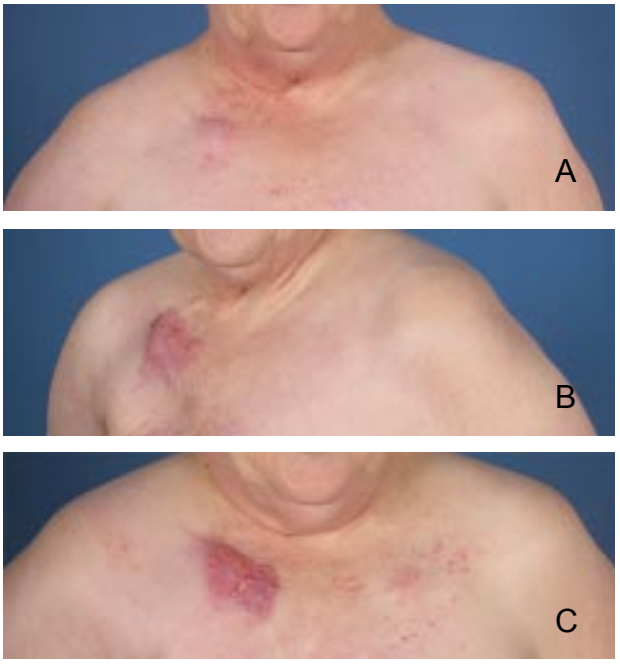

Figure 2. Central venous access device (ie, infusaport) site one month prior to palliative mastectomy and chest wall coverage with a vertical rectus abdominus myocutaneous flap (A). There was no evidence of surrounding induration or nodularity. Three months postoperatively, a nontender, erythematous, indurated plaque developed over the infusaport site (B). Seven months postoperatively, following treatment with systemic chemotherapy, the lesion demonstrated increased nodularity but slight regression in overall size (C).

Eastern Cooperative Oncology Group performance status score of 1.

Three and a half years after the initial diagnosis, the patient underwent a salvage mastectomy of the right breast for palliation of her breast symptoms. Preoperative appearance of the infusaport site is shown in Figure 2A. The posterior margin was multifocally positive for metastatic disease, with foci of involvement measuring up to 4 mm. All other margins, including the cranial margin, were uninvolved. A vertical rectus abdominus myocutaneous flap was then placed for chest wall coverage. One month later, she presented to the local emergency department with warm erythema overlying her right subclavian infusaport site. Cellulitis was diagnosed and the infection responded to intravenous ceftriaxone sodium and a full course of oral doxycycline hyclate. Three months after her procedure and 1 month after the patient developed cellulitis, the region surrounding her infusaport became increasingly erythematous, firm, indurated, and nodular (Figure 2B). The skin lesion was noncontiguous with the right breast mass and located within an area that had previously received radiation. A punch biopsy specimen of the involved skin revealed cutaneous metastasis of her original breast carcinoma (Figure 3). A new infusaport was placed in the left subclavian vein, and she continued with vinorelbine, trastuzumab, and anastrozole therapy. In the following 7 months, the cutaneous metastases became slightly more nodular but slightly regressed in overall size with systemic chemotherapy (Figure 2C).

Comment

Tumor metastasis to the skin occurs in up to 10% of patients with noncutaneous cancer and frequently is the first sign of extranodal metastasis.[2] Breast cancer is the most common cause of cutaneous metastasis in females, while lung cancer is the most common cause in males.[1] Although most cutaneous metastases of breast cancer resemble nonspecific dermal or subcutaneous nodules,[1,2] other morphologies have been described.[1,2,4-8] Biopsy with comparison to histopathology of the original tumor can confirm diagnosis. In cases of skin metastases with no known primary

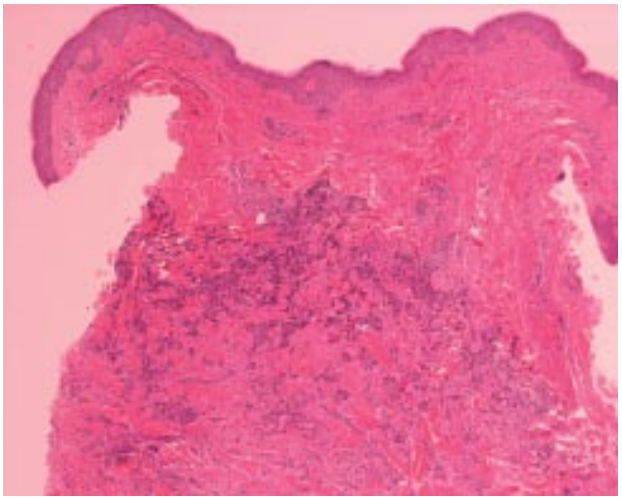

Figure 3. Punch biopsy specimen from the right subclavian infusaport site in 2006 after palliative mastectomy and chest wall coverage with a vertical rectus abdominus myocutaneous flap. Histopathology revealed infiltrating ductal carcinoma of the breast involving the cutaneous dermis. Comparison with histopathology of original breast carcinoma demonstrated recurrence (H&E, original magnification ×4).

site and estrogen receptor/progesterone receptor negativity, immunostaining for androgen receptor has been found to be a relatively sensitive marker for breast cancer.[9]

The natural history of cutaneous metastases involves a rapid proliferative stage, followed by a prolonged stationary stage.[1] In one study, the mean patient survival was 31 months after recognition of skin metastases.[2] Treatment may include systemic chemotherapy; skin lesions can be monitored as a reasonable indicator of systemic therapeutic response.[1] Other modalities, including surgical resection,[1] topical chemotherapy,[10] pulsed brachytherapy,[11] and photodynamic therapy,[12] may offer some benefit.

Pathogenic mechanisms of cutaneous metastasis include direct extension, hematologic or lymphatic dissemination, or surgical implantation.[1,8] Both laboratory and clinical findings suggest that skin metastases may be more likely to develop in areas of inflammation or previous trauma.[1,13,14] Indeed, surgical placement of medical devices can cause localized inflammation,[15] and metastatic seeding of device sites has been previously reported with Hickman,[16] Broviac,[17] percutaneous transhepatic biliary,[18] and ventriculoperitoneal shunt catheters.[19] We found only one prior report of cutaneous metastasis to an infusaport site, which involved squamous cell carcinoma of the cervix.[13]

Retrospectively, we hypothesize that a combination of factors may have predisposed our patient to develop cutaneous metastasis at her infusaport site, an area that was not contiguous with the primary tumor. First, the patient's infusaport site had been subjected to substantial inflammation during her recent bout of cellulitis, which may have permitted the hematologic or lymphatic spread of microscopic metastases to the area. Second, the presence of a foreign body (ie, the infusaport) can be associated with acute and chronic inflammation as part of the foreign body reaction,[15] which also may have predisposed the infusaport site to an increased risk of seeding by micrometastases of the primary tumor. Finally, the patient had undergone a salvage mastectomy and chest wall coverage with a vertical rectus abdominus myocutaneous flap 1 month prior to the development of cellulitis and 3 months prior to the diagnosis of cutaneous metastasis. Generalized tissue trauma and inflammation associated with these operative interventions also may have contributed but are less likely, as the infusaport site was not directly contiguous with the operative region.

Conclusion

This patient's clinical course illustrates how multiple sources of localized tissue inflammation may have culminated to increase the risk for cutaneous breast cancer metastasis to our patient's infusaport site. Moreover, this case emphasizes the importance of having a high index of suspicion for cutaneous metastasis in the differential diagnosis of refractory skin eruptions in patients with cancer, particularly when they arise at sites of local inflammation or trauma.

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