Pruritic Nodules on the Breast

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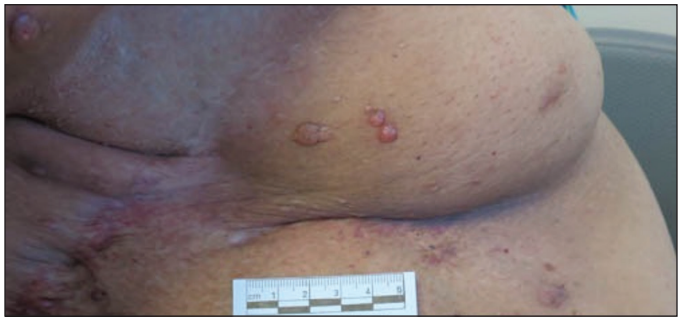

A 51-year-old woman with a history of bilateral breast cancer presented for evaluation of lesions on the underside of the right breast. She was first diagnosed with stage II cancer of the right breast that was subsequently treated with a mastectomy and adjuvant chemotherapy 7 years prior to presentation. One year later, she developed stage IIIC adenocarcinoma of the left breast and was treated with a modified radical mastectomy, adjuvant chemotherapy, and radiation. She had been followed closely by her oncologist with regular surveillance imaging (last at 7 months prior to presentation) that had all been negative for recurrent breast cancer. She presented to our dermatology clinic for evaluation of lesions on the underside of the right breast that were pruritic and occasionally painful with a burning quality. These lesions had recently begun to bleed when scratched but were not otherwise growing or spreading. On physical examination she was afebrile with stable vital signs. Skin examination was notable for numerous violaceous and translucent papules and nodules underneath the right breast and axilla overlying a well-healed mastectomy scar. No lymphadenopathy was present. Shave biopsies were performed and showed well-circumscribed nodular lesions with ectatic vascular channels separated by thin fibrous walls and filled with eosinophilic proteinaceous material and scattered red blood cells. Immunohistochemical staining also showed positivity for D2-40.

WHAT'S THE **DIAGNOSIS?**

a. metastatic breast carcinoma
b. microcystic lymphatic malformation
c. molluscum contagiosum
d. squamous cell carcinoma
e. verruca vulgaris

PLEASE TURN TO PAGE E4 FOR THE DIAGNOSIS

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THE **DIAGNOSIS:** Microcystic Lymphatic Malformation

Microcystic lymphatic malformations, also known as lymphangioma circumscriptum, are rare hamartomatous lesions comprised of dilated lymphatic channels that can be both congenital and acquired.[1] They often present as translucent or hemorrhagic vesicles of varying sizes that may contain lymphatic fluid and often can cluster together and appear verrucous (Figure 1). The differential diagnosis for microcystic lymphatic malformations commonly includes molluscum contagiosum, squamous cell carcinoma, verruca vulgaris, or condylomas, as well as atypical vascular lesions. They most often are found in children as congenital lesions but also may be acquired. Most acquired cases are due to chronic inflammatory and scarring processes that damage lymphatic structures, including surgery, radiation, infections, and even Crohn disease.[2,3] Because the differential diagnosis is so broad and the disease can clinically mimic other common disease processes, biopsies often are performed to determine the diagnosis. On biopsy, pathologic examination revealed well-circumscribed nodular lesions with large lymphatic channels often in a background of connective tissue stroma. Increased eosinophilic material, including mast cells, also was seen (Figure 2A). On immunohistochemistry, staining showed D2-40 positivity (Figure 2B).

Damage to lymphatics from radiation and postsurgical excision of tumors are well-described causes of microcystic lymphatic malformations, as in our patient, with most instances in the literature occurring secondary to treatment of breast or cervical cancer.[4-6] In these acquired cases, the pathogenesis is thought to be due to destruction and fibrosis at the layer of the reticular dermis, which causes lymphatic obstruction and subsequent dilation of superficial lymphatic channels.[6]

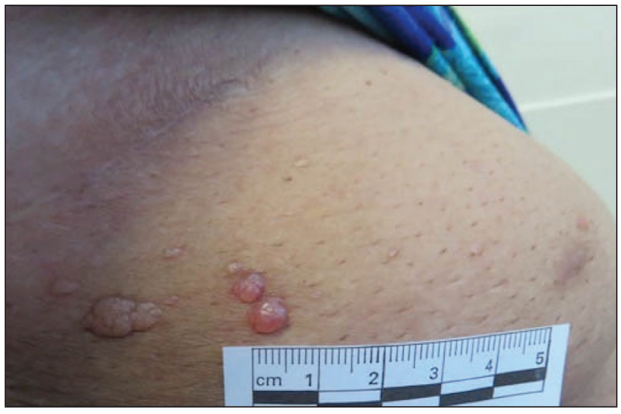
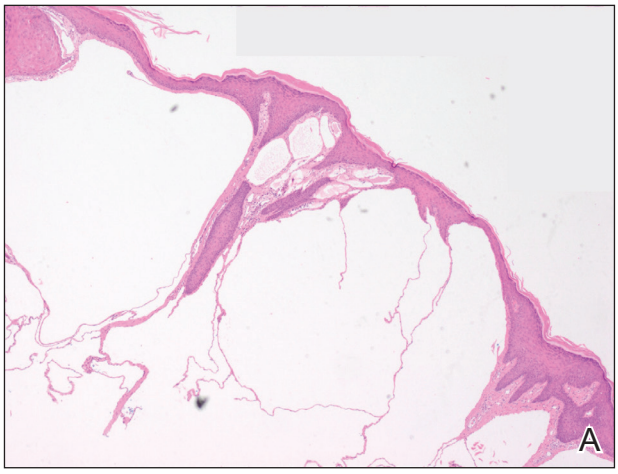


FIGURE 1. Skin lesions demonstrating the translucent nature of the papules of microcystic lymphatic malformations.

Microcystic lymphatic malformations can be difficult to distinguish from atypical vascular lesions, another common postradiation lesion. Both are benign well-circumscribed lesions that histologically do not extend into surrounding subcutaneous tissues and do not have multilayering of cells, mitosis, or hemorrhage.[7] Although lymphatic lesions tend to form vesicles, atypical vascular lesions arising after radiation treatment present as erythematous or flesh-colored patches or papules. They also tend to be fairly superficial and often only



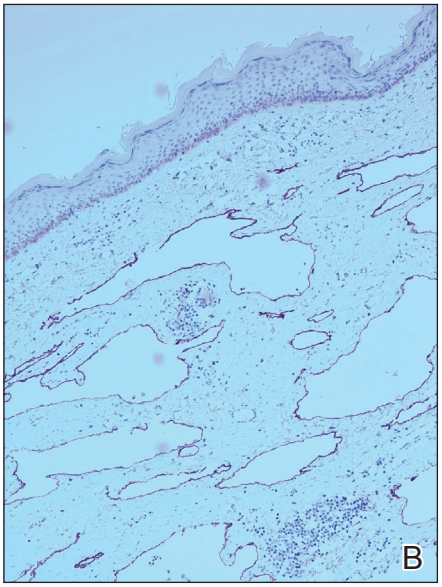


FIGURE 2. A, Biopsy showed a well-circumscribed nodular lesion consisting of ectatic vascular channels separated by thin fibrous walls (H&E, original magnification ×10). B, Immunohistochemical staining showed the lining endothelial cells to be positive for D2-40 (original magnification ×10).

involve the superficial to mid dermis. On histology they show thin-walled channels without erythrocytes that are lined by typical endothelial cells.[7] Despite these differences, both clinically and histopathologically these lesions can appear similar to acquired microcystic lymphatic malformations. It is important to differentiate between these two entities, as atypical vascular lesions have a slightly higher rate of transformation into malignant tumors such as angiosarcomas.

Although angiosarcomas clinically may present as erythematous patches, plaques, or nodules similar to benign postradiation lesions, they tend to be more edematous than their benign counterparts.[7,8] Two other clinical factors that can help determine if a postradiation lesion is benign or malignant are the size and time of onset of the lesion. Angiosarcomas tend to be much larger than benign postradiation lesions (median size, 7.5 cm) and tend to be more multifocal in nature.[8,9] They also tend to arise on average 5 to 7 years after the initial radiation treatment, while benign lesions arise sooner.[9]

Small, asymptomatic, acquired microcystic lymphatic malformations can be followed clinically without treatment, but these lesions do not commonly regress spontaneously. Even when asymptomatic, many clinicians will opt for treatment to prevent secondary complications such as infections, drainage, and pain. Moreover, these lesions can have notable psychosocial impacts on patients due to poor cosmetic appearance. Unfortunately, there is no gold standard of treatment, and recurrence is common, even after treatment. Historically, surgical excision was the treatment of choice, but this option carries a high risk for scarring, invasiveness, and recurrence. Recurrence rates of up to 23.1% have been reported with decreased effectiveness of resection, particularly in areas of deeper involvement.[10] For these deeper lesions, CO_2 laser therapy is a promising evolving therapy. It can penetrate up to the mid dermis and seems to destroy the lymphatic channels between deep and surface lymphatics, preventing the cutaneous manifestations of the disease. It has the added benefit of minimal invasiveness and fewer side effects than complete excision, with most studies reporting hyperpigmentation and scarring as the most common side effects.[11] Additional emerging therapies including sclerotherapy and isotretinoin have shown benefits in case studies. Sclerotherapy causes local tissue destruction and thrombosis leading to destruction of vessel lumens and fibrosis that halts disease progression and clears existing lesions.[12] Oral therapy with isotretinoin appears to work by inhibiting certain cytokines and acting as an antiangiogenic factor.[13] Given the rarity of microcystic lymphatic malformations, further research must be done to determine definitive treatment.

Acquired microcystic lymphatic malformation is an important sequela of radiation therapy and surgical excision of malignancy. Despite its striking clinical appearance, it is sometimes difficult to diagnose given its rarity. It is important that clinicians are able to recognize it clinically and understand common treatment options to prevent both the mental stigma and complications, including secondary infections, drainage, and pain.

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