Postirradiation Morphea: Unique Presentation on the Breast

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PRACTICE **POINTS**

- Radiation therapy is an often overlooked cause of morphea.
- The increasing popularity of lumpectomy plus radiation therapy for treatment of early-stage breast cancer has led to a rise in postirradiation morphea incidence.
- Tissue changes occur as early as weeks or as late as 32 years after radiation treatment.
- Postirradiation morphea may extend beyond the radiation field.

To the Editor:

Postirradiation morphea (PIM) is a rare but well-documented phenomenon that primarily occurs in breast cancer patients who have received radiation therapy; however, it also has been reported in patients who have received radiation therapy for lymphoma as well as endocervical, endometrial, and gastric carcinomas.[1] Importantly, clinicians must be able to recognize and differentiate this condition from other causes of new-onset induration and erythema of the breast, such as cancer recurrence, a new primary malignancy, or inflammatory etiologies (eg, radiation or contact dermatitis). Typically, PIM presents months to years after radiation therapy as an erythematous patch within the irradiated area that progressively becomes indurated. We report an unusual case of PIM with a reticulated appearance occurring 3 weeks after radiotherapy, chemotherapy, and surgery for an infiltrating ductal carcinoma of the left breast.

A 62-year-old woman presented to the dermatology department with a stage IIA, lymph node–negative, estrogen and progesterone receptor–negative, human epidermal growth factor receptor 2–negative infiltrating ductal carcinoma of the left breast. She was treated with a partial mastectomy of the left breast followed by external beam radiotherapy to the entire left breast in combination with chemotherapy (doxorubicin, cyclophosphamide, paclitaxel). The patient received 15 fractions of 270 cGy (4050 cGy total) with a weekly 600-cGy boost over 21 days without any complications.

Three weeks after finishing radiation therapy, the patient developed redness and swelling of the left breast that did not encompass the entire radiation field. There was no associated pain or pruritus. She was treated by her surgical oncologist with topical calendula and 3 courses of cephalexin for suspected mastitis with only modest improvement, then was referred to dermatology 3 months later.

At the initial dermatology evaluation, the patient reported little improvement after antibiotics and topical calendula. On physical examination, there were erythematous, reticulated, dusky, indurated patches on the entire left breast. The area of most pronounced induration surrounded the surgical scar on the left superior breast. Punch biopsy for hematoxylin and eosin staining and tissue cultures was obtained at this appointment. The patient was started on doxycycline 100 mg twice daily and was instructed to apply triamcinolone ointment 0.1% twice daily to the affected area. After 1 month of therapy, she reported slight improvement in the degree of erythema with this regimen, but the involved area continued to extend outside of the radiation field to the central chest wall and medial right breast (Figure 1). Two additional biopsies—one from the central chest and another from the right breast—were then taken over the course of 4 months, given the consistently inconclusive

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The authors report no conflict of interest.

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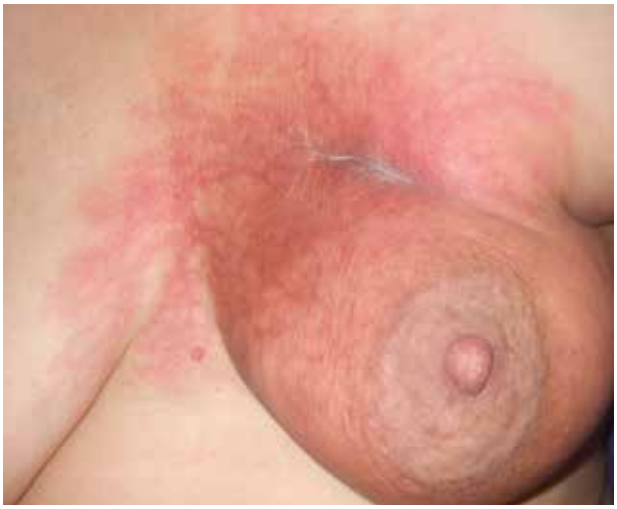

FIGURE 1. Postirradiation morphea presenting as an erythematous, reticulated, indurated patch extending from the left breast to the central chest wall and medial right breast.

clinicopathologic nature and failure of the eruption to respond to antibiotics plus topical corticosteroids.

Punch biopsy from the central chest revealed a sparse perivascular infiltrate comprised predominantly of lymphocytes with occasional eosinophils (Figure 2). There were foci suggestive of early dermal sclerosis, an increased number of small blood vessels in the dermis, and scattered enlarged fibroblasts. Metastatic carcinoma was not identified. Although the histologic findings were not entirely specific, the changes were most suggestive of PIM, for which the patient was started on pentoxifylline (400 mg 3 times daily) and oral vitamin E supplementation (400 IU daily). At subsequent follow-up appointments, she showed markedly decreased skin erythema and induration.

Morphea, also known as localized scleroderma, is an inflammatory skin condition characterized by sclerosis of the dermis and subcutis leading to scarlike tissue formation. Worldwide incidence ranges from 0.4 to 2.7 cases per 100,000 individuals with a predilection for white women.[2] Unlike systemic scleroderma, morphea patients lack Raynaud phenomenon and visceral involvement.[3,4]

There are several clinical subtypes of morphea, including plaque, linear, generalized, and pansclerotic morphea. Lesions may vary in appearance based on configuration, stage of development, and depth of involvement.[4] During the earliest phases, morphea lesions are asymptomatic, asymmetrically distributed, erythematous to violaceous patches or subtly indurated plaques expanding centrifugally with a lilac ring. Central sclerosis with loss of follicles and sweat glands is a later finding associated with advanced disease. Moreover, some reports of early-stage morphea have suggested a reticulated or geographic vascular morphology that may be misdiagnosed for other conditions such as a port-wine stain.[5]

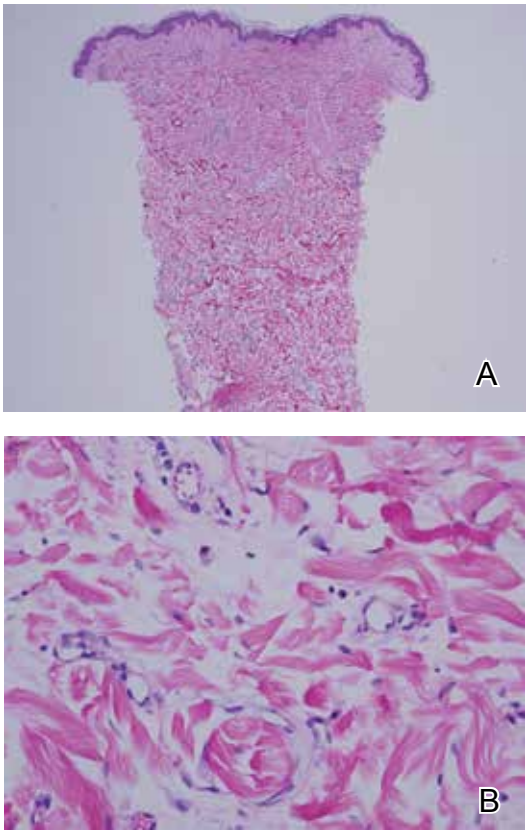

FIGURE 2. A punch biopsy from the central chest revealed a sparse perivascular infiltrate comprised predominantly of lymphocytes with occasional eosinophils, foci suggestive of early dermal sclerosis, and an increased number of small blood vessels in the dermis (A)(H&E, original magnification ×4). Scattered enlarged fibroblasts were present within the dermis (B)(H&E, original magnification ×40).

Local skin exposures have long been hypothesized to contribute to development of morphea, including infection, especially *Borrelia burgdorferi*; trauma; chronic venous insufficiency; cosmetic surgery; medications; and exposure to toxic cooking oils, silicones, silica, pesticides, organic solvents, and vinyl chloride.[2,6,7]

Radiation therapy is an often overlooked cause of morphea. It was first described in 1905 but then rarely discussed until a 1989 case series of 9 patients, 7 of whom had received irradiation for breast cancer.[8,9] Today, the increasing popularity of lumpectomy plus radiation therapy for treatment of early-stage breast cancer has led to a rise in PIM incidence.[10] Estimates have indicated an incidence among previously irradiated breast cancer patients as high as 1 in 500 individuals, appreciably higher than that seen in the general population.[11] Tissue changes occur as early as weeks or as late as 32 years after radiation treatment and are commonly mistaken for mastitis, such as in our case, as well as radiation dermatitis, radiation fibrosis, or malignant conditions.[1,11]

In contrast to other radiation-induced skin conditions, development of PIM is independent of the presence

or absence of adjuvant chemotherapy, type of radiation therapy, or the total radiation dose or fractionation number, with reported doses ranging from less than 20.0 Gy to up to 59.4 Gy and dose fractions ranging from 10 to 30. In 20% to 30% of cases, PIM extends beyond the radiation field, sometimes involving distant sites never exposed to high-energy rays.[1,10,11] This observation suggests a mechanism reliant on more widespread cascade rather than solely local tissue damage.

Prominent culture-negative, lymphoplasmacytic inflammation is another important diagnostic clue. Radiation dermatitis and fibrosis do not have the marked erythematous to violaceous hue seen in early morphea plaques. This color seen in early morphea plaques may be intense enough and in a geographic pattern, emulating a vascular lesion. However, a PubMed search of articles indexed for MEDLINE using the terms *reticulate radiation morphea* and *livedo radiation morphea* yielded no reports linking the reticulate erythema seen in our patient with early PIM. It is important to note that the histopathology findings in our patient were not entirely specific, and although there were some background changes that may have represented a sequela of radiation to the area (ie, the enlarged fibroblasts and increased number of vessels), there were foci suggestive of early sclerosing dermatitis. With clinical correlation, including the extension beyond the radiation field, these changes were best interpreted as early PIM. Therefore, our case demonstrated a novel presentation of a frequently underrecognized trigger for morphea. Although we favored a diagnosis of PIM, a fibrosing chronic radiation dermatitis could not be entirely excluded based on the clinical and histologic features.

There is no standardized treatment of PIM, but traditional therapies for morphea may provide some benefit. Several randomized controlled clinical trials have shown success with pentoxifylline and oral vitamin E supplementation to treat or prevent radiation-induced breast fibrosis.[12] Extrapolating from this data, our patient was started on this combination therapy and showed marked improvement in skin color and texture.

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