Cutaneous lupus erythematosus mimicking radiation dermatitis in a patient with breast cancer

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INTRODUCTION

Radiation therapy is a standard therapy for a variety of disorders, including cancer, and results in both acute and chronic dermatologic changes. Radiation dermatitis is a common sequela of radiation therapy, with up to 95% of patients developing moderate to severe skin reactions.[1] However, in a subset of patients, other dermatologic disorders may present concurrently with radiation dermatitis. Here, we report a patient undergoing breast cancer treatment, presenting with treatment-resistant radiation dermatitis that triggered evaluation for an underlying condition. She was eventually diagnosed with cutaneous lupus erythematous. We bring this mimicking clinical diagnosis to the attention of dermatologists.

Abbreviation used:

SCLE: subacute cutaneous lupus erythematosus

CASE REPORT

A previously healthy 58-year-old female with pT3N0M0, estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2-positive right-breast cancer presented with concerns of radiation dermatitis. She had undergone mastectomy, adjuvant radiation (5040 cGy, 28 fractions, January 30, 2019 to March 8, 2019), and treatment with docetaxel, carboplatin, trastuzumab, and pertuzumab (chemotherapy was completed on Ocober 10, 2018, adjuvant trastuzumab was given every 3 weeks for a total of 1 year trastuzumab and pertuzumab, completed on June 27, 2019, last treatment 4-weeks prior to presentation). On examination, the patient was noted to have mottled erythema, desquamative scale, and superficial ulceration on the right side of her chest in the radiation field (Fig 1). Her only complaint was pruritus. Histologic findings included parakeratosis, epidermal erosion, basal vacuolar degeneration with dyskeratosis, prominent melanin incontinence, and a lichenoid chronic inflammatory infiltrate without significant eosinophilia, all of which were nonspecific findings that can be seen in acute radiation dermatitis (Fig 2). A Periodic acid—Schiff stain with diastase was negative for fungal hyphae.

The patient returned 8 weeks later with persistent symptoms despite using topical corticosteroids and was noted to have progression of the dermatitis with several superficial bullae involving skin outside the radiation field. Biopsy revealed lichenoid interface dermatitis (Fig 3). Direct immunofluorescence testing revealed granular deposition of IgG, IgA, IgM, and fibrinogen at the basement membrane. There was also antikeratinocyte nuclear labeling by IgG, which is nonspecific but often correlates with a positive antinuclear antibody test. Direct immunofluorescence revealed a positive lupus band (Fig 4). Additional workup included white blood cell count (2.68×10^3 cells/mm^3; normal range, 3.7-10.4 $\times 10^3$

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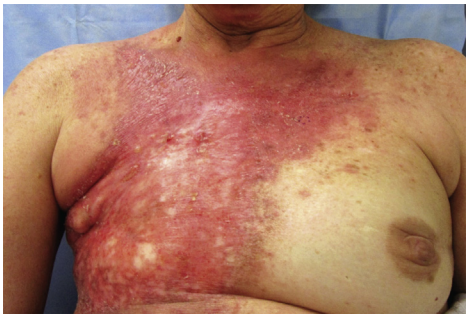

Fig 1. Mottled erythema, desquamative scale, and superficial ulceration on the right aspect of the chest in the radiation field of a patient undergoing therapy for breast cancer.

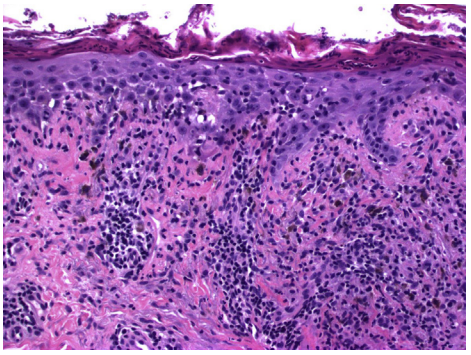

Fig 2. Erosion, basal vacuolar degeneration, dyskeratosis, and lichenoid infiltrate with melanin incontinence. (Hematoxylin-eosin stain; original magnification: ×40).

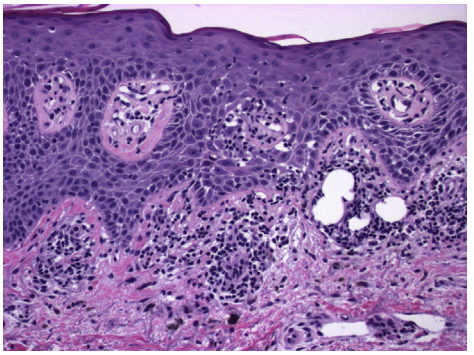

Fig 3. Mild spongiosis, acanthosis, focal basal vacuolar degeneration, dyskeratosis, and mild lichenoid infiltrate with melanin incontinence. (Hematoxylin-eosin stain; original magnification: ×40).

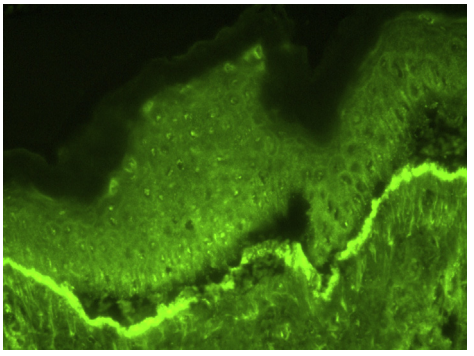

Fig 4. Direct immunofluorescence of IgG demonstrates antikeratinocyte nuclear deposition and irregular basement membrane deposition. (Original magnification: ×40).

cells/mm^3), hemoglobin (11.4 g/dL; normal range, 13.6-16.7 g/dL), and documentation of antinuclear antibodies (1:160, speckled and antiSjögren's-syndrome-related antigen A autoantibody patterns), as well as anti-double-stranded DNA antibodies (56; normal, <40), antiSjögren's syndrome-related antigen A autoantibodies (>8; normal, <1), antiSjögren's syndrome-related antigen B autoantibodies (>8; normal, <1), and ribonucleoprotein (1.7; normal, <1). Taking all these results into account, the patient was diagnosed with lupus and started on hydroxychloroquine. After a short course of therapy, the skin lesions resolved (Fig 5), and no recurrence was noted over the next 15 months of follow-up.

DISCUSSION

Radiation dermatitis is an expected occurrence after radiation treatment, affecting 95% of patients receiving radiotherapy.[1-6] Diagnosis is generally clinical, based upon the finding of erythema and dry/moist desquamation in a patient with a recent history of radiation therapy. Usually, a skin biopsy is not required for the diagnosis of radiation dermatitis. Prophylactic low-to-medium-potency (groups 4 to 6) topical corticosteroids are generally recommended for patients undergoing radiation therapy.

The differential diagnosis of radiation dermatitis includes other skin conditions that can develop during or after completing treatment. Commonly considered diagnoses include allergic contact dermatitis, intertrigo, radiation port dermatophytosis, radiation recall dermatitis, herpes zoster, graft-versus-host disease, and Stevens-Johnson syndrome/toxic epidermal necrolysis. As seen in the case of our patient, a skin biopsy may also be prudent, if the patient is not improving as expected with current management or if dermatitis progresses beyond the field of radiation.

As noted above, the differential includes radiation dermatitis (acute), radiation recall dermatitis, and radiation-induced subacute cutaneous lupus erythematosus (SCLE). Acute radiation dermatitis refers to a side effect of radiation and manifests within a few days to weeks after the initiation of radiotherapy. There are 4 grades, ranging from faint erythema or desquamation to necrosis/ulceration of full-thickness dermis. It is confined to areas of skin

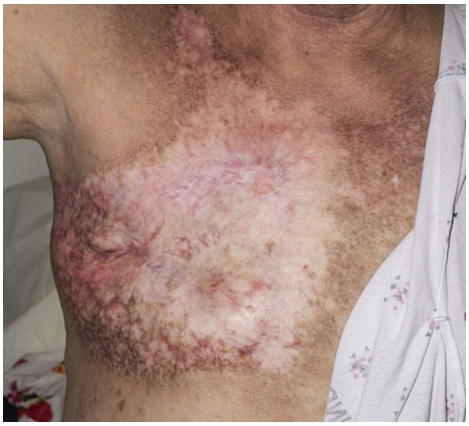

Fig 5. Representative image of right breast after 6 months of hydroxychloroquine therapy.

that have been irradiated, and the skin changes are sharply demarcated. In contrast, radiation recall dermatitis refers to the rare appearance of a maculopapular rash in previously irradiated skin after the administration of drugs; eg, chemotherapy and antibiotics. Finally, SCLE most often presents as a non-scarring papulosquamous eruption. It may be associated with annular plaques with raised erythematous borders and central clearing, peripheral vesicles, crusting, and bullae. Patients typically have positive connective tissue biomarkers, such as antinuclear antibodies, anti-Sjögren's syndrome-related antigen A autoantibodies, antiSjögren's syndrome-related antigen B autoantibodies, antidouble-stranded DNA antibodies, etc. Histologically, there is a lymphocytic interface dermatitis with basal layer degeneration. Epidermal atrophy, apoptotic keratinocytes, perivascular and periadnexal lymphocytic infiltrate, follicular plugging, basement membrane thickening, and dermal mucin can be observed. Direct immunofluorescence reveals a lupus band in 2 out of 3 patients. Radiation recall dermatitis is a less likely consideration in this patient, since she had laboratory and histologic findings that were more consistent with cutaneous lupus. It should be noted that in rare instances, direct immunofluorescence can be background-positive in patients with lupus, even in the absence of cutaneous lupus. However, this is unlikely in this specific patient, since she met additional criteria for the diagnosis of lupus.

There have been previous case reports of SCLE triggered by radiotherapy.[7,8] It was suggested that an autoimmune reaction may have been triggered locally by ionizing radiation functionally altering the immune system and breaking self-tolerance.[7] It should be noted that we cannot definitively identify radiation as the trigger of cutaneous lupus erythematosus in our patient; chemotherapy is a possible trigger as well.

In the past, several case reports of therapeutic radiation causing increased toxicity in patients with systemic rheumatic diseases, such as scleroderma and SCLE, made radiation oncologists hesitant of treating patients with systemic lupus erythematosus.[9] However, additional observational data have also suggested that radiation therapy in patients with systemic lupus erythematosus is not associated with an increased risk of toxicity. There are no specific contraindications for radiotherapy in patients with connective tissue diseases, but a cautious approach for patients with active connective tissue diseases is warranted.

In summary, new-onset cutaneous lupus should be kept in the differential when treating radiation dermatitis that is unresponsive to therapy or progresses beyond radiation field of treatment.

Conflicts of interest

None disclosed.

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