LETTER TO THE EDITOR

Tamoxifen-induced Radiation Recall Dermatitis

To the Editor:

Radiation recall dermatitis is a phenomenon seen in patients who have received radiation therapy followed by chemotherapy. Tamoxifen, a selective estrogen receptor (ER) modulator, has been implicated in three cases of radiation recall dermatitis (1–3). We report a fourth case, which we believe to be the first reaction documented in the United States.

An 88-year-old woman was diagnosed with infiltrating ductal carcinoma in September 1998. She received 5040 cGy to her left breast with a 1000 cGy boost to the tumor bed for a total dose of 6040 cGy. In October 2000, an ER-positive invasive lobular carcinoma was diagnosed in her left breast. Following quadrantectomy, she began tamoxifen 20 mg/day in November 2000.

In February 2001 she developed asymptomatic edema and diffuse erythema of the skin of her left breast localized to the radiation port used during the management of her September 1998 malignancy. Oral levofloxacin was prescribed for possible cellulitis; however, a skin biopsy was performed 1 week later, as her skin findings were unchanged. Mild fibrosis and perivascular chronic inflammation in the upper dermis were found without evidence of malignancy or infection.

By late February 2001, the skin erythema and edema, while still confined to her radiation port, were markedly improved. By early May 2001, her left breast inflammation had completely resolved. She had continuously taken tamoxifen prior to, during, and after her skin reaction. She was taking no other medications other than levofloxacin.

Radiation recall dermatitis is observed in patients who have received radiation therapy followed by chemotherapy. Via an unknown mechanism, the chemotherapeutic agent produces an inflammatory reaction that has the same appearance as primary radiation exposure and is localized to the previously irradiated tissue (4–6). Although tissue toxicity from radiation exposure is correlated with fraction size and schedule, total dose, and individual patient differences (7), clinically evident radiation damage to healthy tissue is not a prerequisite for the subsequent development of a recall reaction. Although recall reactions have been reported months to years after the completion of radiation treatment (4), the incidence seems to decrease as the time interval between initial radiation and subsequent exposure to chemotherapeutic agents increases (1).

Proposed mechanisms for radiation recall reactions include changes in vascularization, DNA repair, epithelial stem cell function, and drug hypersensitivity reactions. Radiation treatment may produce localized tissue changes that alter the distribution of pharmacologic agents (including tamoxifen) in comparison to surrounding nonirradiated tissues, resulting in a radiation recall reaction (1,8).

Radiation recall reactions have been explained by implicating radiation-depleted or radiation-impaired epithelial stem cells (9,10). Epithelial stem cell sensitivity has also been suggested as a possible mechanism (11). Following radiation exposure, the number of epithelial stem cells present in the skin is depleted. These stem cells may be more sensitive to the effects of drugs aimed at disrupting dividing cells, producing a recall reaction.

Finally, radiation recall reactions may be due to idiosyncratic drug hypersensitivity reactions (12). Reactions experienced after only one dose of the triggering agent suggest drug-induced, nonimmune activation of the body's inflammatory pathways (9). This hypothesis may explain the rarity with which tamoxifen-induced radiation recall reactions have been reported.

Previously irradiated patients who develop findings consistent with radiation recall while taking tamoxifen should also be assessed for infection, breast cancer recurrence, or a new primary malignancy. If tamoxifen-induced radiation recall is believed to be the cause, patients may be able to continue taking tamoxifen. Our patient's experience, and that of a patient previously reported (2), indicate that radiation recall reactions may subside without incident after several weeks, while the patient remains on tamoxifen. If the radiation recall reaction is severe or fails to subside, discontinuation of tamoxifen may be necessary.

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