

Grade 4 radiation dermatitis presenting with full-thickness ulcerations of the groin after radiation therapy for anal squamous cell carcinoma (SCC): An example of the “bolus effect” of radiation therapy

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Modern radiotherapy techniques for the treatment of squamous cell carcinoma (SCC) of the anus have led to a significant reduction in the incidence and severity of skin toxicity.¹ However, grade 4 radiation dermatitis remains a difficult complication of radiation therapy for malignancies located in skin folds, a phenomenon known as the “bolus effect.” We describe a case of grade 4 radiation dermatitis in an HIV-positive patient after intensity-modulated radiation therapy (IMRT) for SCC of the anus, along with the management of these lesions.

CASE REPORT

A 56-year-old black man with HIV on highly active antiretroviral therapy with stage II SCC of the anus treated with local excision, chemotherapy with 5-fluoruracil and mitomycin, and IMRT (5 times/wk for 5 weeks, total: 50 Gy in 25 fractions) presented with painful ulcers in his groin and perianal region. The patient initiated IMRT 2 months before presentation. Two weeks into IMRT he developed erythematous patches of the perianal region consistent with moist desquamation of grade 2 radiation dermatitis. These areas were treated with saline soaks and antibiotic soaps, and did not erode during the treatment period.

One week after his last dose of radiation, the patient developed increasing pain both perianally and in the inguinal folds. Physical examination revealed malodorous, geometric, sharply demarcated ulcers with central fibrinous exudate

symmetrically along the bilateral inguinal folds (Fig 1, A). He had a similar 1.5-cm ulcer on the glans penis, and a 20-cm ulcer extending confluent from the anus along the bilateral buttocks, perineum, and scrotum (Fig 1, B). There was no surrounding cellulitis, edema, or purulent drainage. A punch biopsy specimen of the inguinal ulcer showed fibrosis and increased vascularity without evidence of SCC, herpes simplex virus, or other infection. The patient underwent debridement in the operating suite, and wound care was performed with wet-to-dry dressings with a plan for eventual split-thickness skin grafting. However, the patient experienced unrelated neurologic decline before skin grafting, and was deemed ineligible for the procedure.

DISCUSSION

Radiation dermatitis is a well-known complication of radiation therapy, and is subtyped into 4 grades based on clinical presentation. Acute radiation damage to the skin is complex and involves inflammation, endothelial cell changes, impairment of functional stem cells, and epidermal apoptosis.² Initially, radiation exposure leads to development of transient, self-limited erythematous patches and dry desquamation, classified as grade 1 radiation dermatitis.^{2,3} After 4 to 5 weeks of treatment, particularly in patients receiving radiation doses of 40 Gy or greater, most patients progress to grade 2 radiation dermatitis, which clinically manifests with painful, erythematous, edematous patches with moist desquamation.^{2,3} Histologic examination at this stage reveals blister formation,

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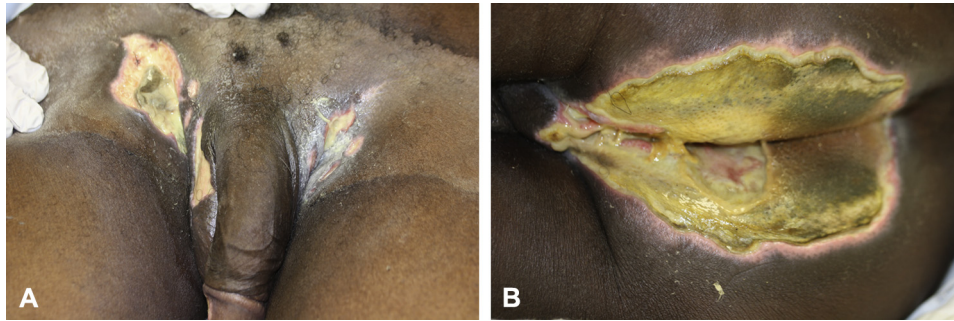


Fig 1. **A**, Grade 4 radiation dermatitis of the groin bilaterally. Ulcerations 10- to 20-mm wide by 6- to 9-mm deep. **B**, Grade 4 radiation dermatitis of gluteal region. A 20- × 15-cm round ulcer extending to the perineum and scrotum.



Fig 2. Transverse view of dose distribution from posterior-anterior axis.

sloughing of the epidermis, and epidermal necrosis.⁴ Progression to grade 4 radiation dermatitis, defined as skin necrosis or ulceration of full-thickness dermis, is rare and usually occurs 2 to 3 months after completion of therapy, often in association with infection or injury to the area.^{2,4}

Although skin necrosis has been seen in up to 10% of patients undergoing radiation therapy for anal cancer,⁵ the use of more advanced radiation delivery techniques such as IMRT has significantly reduced the incidence of both skin toxicity grades 3 or greater and skin toxicity overall, with multiple studies reporting no instances of grade 4 radiation dermatitis using this technique.^{1,6,7} With IMRT, planning software and computed tomography images are used to vary not only radiation intensity, but also beam shape, allowing precise radiation delivery that conforms to the tumor and spares normal tissue.⁶ Dosing can be readjusted on each subsequent treatment for maximum efficacy.

With a total treatment dose of 50 Gy, the patient's initial grade 2 dermatitis at the end of treatment was

expected. The patient's IMRT dose distribution (Fig 2) demonstrates that the highest dose was delivered to the primary tumor site, with an additional focus along the inguinal lymph node chains. However, the patient's rapid progression to grade 4 dermatitis was unexpected, occurring within a month of termination of therapy. This is in the absence of infection on culture and histologic examination.

The severe ulceration of the inguinal folds and gluteal cleft is a manifestation of the so-called bolus effect of radiation therapy. In radiation therapy, "bolus" refers to a tissue equivalent material placed on the skin to concentrate the dose of radiation delivered by scattering entering electrons.⁸ In areas of the body where skin is apposed, such as the groin folds and gluteal cleft, the extra tissue layer acts as an autologous bolus, delivering a higher dose of radiation to the skin at that site, which can lead to more severe skin toxicity.² In addition, this patient's positive HIV status and race may also contribute to his risk for developing severe skin toxicity. Despite

similar overall survival in anal cancer among HIV-positive and -negative individuals, a higher incidence of grade 3 and 4 skin radiation dermatitis has been reported in HIV-positive patients, potentially attributable to a glutathione deficiency that decreases cellular defense, and the radiosensitization effects of highly active antiretroviral therapy.^{9,10} Differences in incidence and severity of radiation dermatitis by race have also been reported, with black patients more likely to experience at least grade 2 radiation dermatitis after radiation.¹¹ This may be because of an increased incidence of a specific genetic polymorphism in this population involving the ATM gene, which encodes proteins for cell cycle checkpoint control and DNA repair and has been implicated as a predictor of late adverse radiation effects, although further study is necessary.^{11,12}

Treatment of radiation dermatitis is dependent upon grade. Treatment for grade 1 is not indicated, as the toxicity is self-limited. Grades 2 and 3 radiation dermatitis are typically treated with basic wound care, with or without topical barrier creams or petrolatum. Grade 4 radiation dermatitis requires specialized, often interdisciplinary wound care with specific recommendations made on an individual basis.¹³ Although radiation dermatitis is most often managed by radiation oncologists in concert with wound-care specialists, dermatologists should also be aware of the natural history and treatment options for complications arising from radiation therapy.

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