Radiation Recall Dermatitis with Cefotetan: A Case Study

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Radiation Recall Dermatitis with Cefotetan: A Case Study

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Key Words. Dermatitis • Radiation-induced • Rash • Cefotetan disodium

ABSTRACT

Radiation recall dermatitis (RRD) is an inflammatory skin reaction that occurs in a previously irradiated body part following drug administration. This phenomenon may occur from days to years following exposure to ionizing radiation. The case of a 54-year-old Caucasian woman who was initially treated with external-beam radiation to the right thoracic region following the diagnosis of a poorly differentiated squamous cell carcinoma of the right lung is reported. She received four cycles of consolidated chemotherapy with docetaxel and carboplatin. Four months later, she was admitted to the hospital for acute cholecystitis and was placed on cefotetan. She developed a tender, erythematous rash on the posterior region of her right thorax 48 hours later. The drug was withdrawn, supportive care was instituted, and the patient subsequently improved. RRD should be suspected in patients who develop an erythematous rash in a previously irradiated region. To our knowledge this entity has not been associated with cefotetan previously.
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INTRODUCTION

Radiation recall dermatitis (RRD) is defined as an inflammatory skin reaction in a previously irradiated body part subsequent to drug administration. This may occur from days to years after exposure to ionizing radiation [1]. This entity is associated with chemotherapy and was originally described with the use of actinomycin [2]. Other antineoplastic drugs have been implicated in the development of RRD. These include the plant alkaloids, docetaxel [3–5], anthracyclines, bleomycin, and alkylating agents including carboplatin [3]. Antiestrogen drugs [6], simvastatin [7], interferon-α2b [8], antituberculous drugs [9], and ultraviolet radiation [10] have also been implicated. While mainly associated with the skin, radiation recall reactions can affect other sites, such as the bowel, esophagus [11], lungs [3], and vaginal mucosa [12].

CASE REPORT

A 54-year-old woman was diagnosed with stage III poorly differentiated squamous cell carcinoma of the right lung. She was treated with external-beam radiation to the right thorax and mediastinum. She received 3,960 cGy at 180 cGy per fraction through anterior and posterior opposed fields. This was followed with an additional 2,520 cGy through off cord oblique fields to bring the total dose to 6,480 cGy. Mixed 6/15 MV photons were used. The skin doses at depths of 2 mm and 5 mm were 4,824 cGy and 5,605 cGy, respectively. The patient also received weekly chemotherapy with docetaxel and carboplatin at 20 mg/m^2 and an area under the concentration–time curve of 2, respectively, and completed 4 months prior to this hospitalization.

This patient was admitted to the hospital with acute cholecystitis. At the time of admission her medications included zolpidem, acetaminophen, and albuterol.

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Hospital Course

Upon admission, she received famotidine, hydromorphone, and cefotetan. The patient also received platelet transfusion, steroids, i.v. immunoglobulin, and HLA-matched platelets in succession for the thrombocytopenia. On the third day of her hospital stay, she developed severe pain in the right scapular region, which she graded as 10/10 and burning in nature. It was sudden in onset and constant with no radiation. The pain was aggravated even with the light touch of a hospital garment. On examination, the right scapular region was erythematous, minimally edematous, nonfluctuant, desquamated, and severely tender (Fig. 1). The pain was not alleviated despite escalating doses of morphine. Subsequently, RRD was suspected, and the cefotetan was felt to be the causative agent and was subsequently discontinued. The tenderness, redness, and swelling began to resolve within 2 days and the patient was completely free of pain 4 days after the discontinuation of the antibiotics.

Discussion

The incidence of RRD is unknown; however, a few retrospective studies have reported a range of 13%–49% [13, 14]. RRD is reported to occur on first exposure to a specific trigger drug [1], but may follow presensitizing episodes in which a drug is administered several times before eliciting RRD [4, 15, 16].

This recall phenomenon can occur from months to years following the conclusion of radiation therapy. The longest interval was reported with doxorubicin-induced stomatitis, which occurred 15 years after radiotherapy treatment of a palatal sarcoma [17]. RRD occurred in our patient 4 months after the completion of radiotherapy. The relationship between the period of time from radiation to medication exposure and the severity of dermatitis is unclear. It is postulated that the recall seems to be most severe when the duration between the radiotherapy and drug exposure is short [2]. It is also unclear whether the agents carboplatin and docetaxel, which did not cause recall phenomenon in this patient, added to or augmented the reaction by the antibiotic months later.

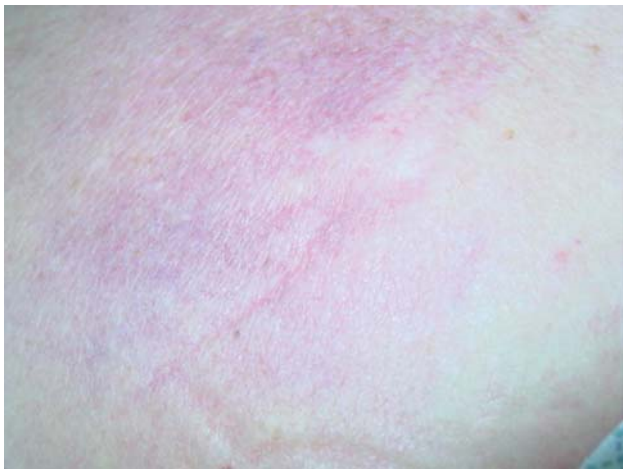

Figure 1. Posterior right upper thorax demonstrating erythematous, desquamating skin rash.

There does not appear to be a minimum dose, nor an established radiotherapy dose relationship in order for RRD to occur [1]. Several authors have suggested radiation doses associated with RRD in the range of 1,000–8,100 cGy [18, 19]. The patient reported here received a tumor dose of 6,480 cGy, and because of the skin-sparing effects, the skin dose of the affected tissue was calculated to be lower—an effect that is related to linear accelerator energy. Typically, cases described in the literature report radiation dosing to the tumor, and not to the skin. Yeo et al. [4] observed that the recall reaction was highest where skin doses were in the range of 1,680–1,870 cGy. Drugs administered by the i.v. route usually produce RRD more rapidly than oral agents. The time to resolution of this dermatitis also differs by the route of administration, with the i.v. route resolving within weeks, while the oral route may last for several months [6]. The discrepancy may be a result of the different pharmacokinetics of the medications administered by different routes.

Garza et al. [20] reported a case of photosensitive recall with the use of cefazolin, while Krishnan et al. [21] reported cases following the use of ciprofloxacin, tobramycin, and piperacillin. To the best of our knowledge, there has been no reported case of RRD in association with cefotetan in the literature. Chemotherapeutic agents are well described as causing RRD, but antibiotics are increasingly associated with this phenomenon. Because of the temporal relationship between the administration of the antibiotic and the onset of the skin reaction, together with the resolution following discontinuation, cefotetan was felt to be the responsible agent. The fact that the skin inflammation was localized to the radiation field would make other diagnoses unlikely.

The pathogenesis of this phenomenon is unclear. The fact that noncytotoxic drugs are associated with RRD led Camidge et al. [22] to speculate that it may represent an idiosyncratic drug hypersensitivity reaction. It has also been suggested that the "trauma" of previous irradiation sensitizes an area of the skin into manifesting immune reactions with little or no overt systemic activation, in a way similar to the Koebner phenomenon [22].

Discontinuation of the offending drug has been the mainstay of therapy. Oral dexamethasone and diphenhydramine [15], or topical hydrocortisone [16], have been used with success, leading to resolution within 7–10 days. Other case reports noted resolution in the same time frame

without the use of antihistamines or steroids [4, 7, 14, 23]. In our patient, complete resolution occurred within 7 days.

Conclusion

RRD should be suspected in a patient who develops an erythematous rash in a previously irradiated region following the use of cefotetan. Prompt recognition and withdrawal are essential for resolution with minimal morbidity.

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Disclosure of Potential Conflicts of Interest

Y.J.L. has acted as a consultant for Genentech and Eli-Lilly.

References

1 Ristic B. Radiation recall dermatitis. Int J Dermatol 2004;43:627–631.

2 D'Angio GJ, Farber S, Maddock CL. Potentiation of x-ray effects by actinomycin D. Radiology 1959;73:175–177.

3 Schweitzer VG, Juillard GJ, Bajada CL et al. Radiation recall dermatitis and pneumonitis in a patient treated with paclitaxel. Cancer 1995;76: 1069–1072.

4 Yeo W, Leung SF, Johnson PJ. Radiation-recall dermatitis with docetaxel: establishment of a requisite radiation threshold. Eur J Cancer 1997;33:698–699.

5 Camidge DR, Kunkler IH. Docetaxel-induced radiations recall dermatitis and successful rechallenge without recurrence. Clin Oncol (R Coll Radiol) 2000;12:272–273.

6 Bostrom A, Sjolin-Forsberg G, Wilking N et al. Radiation recall—another call with tamoxifen. Acta Oncol 1999;38:955–959.

7 Abadir R, Liebmann J. Radiation reaction recall following simvastatin therapy: a new observation. Clin Oncol (R Coll Radiol) 1995;7:325–326.

8 Thomas R, Stea B. Radiation recall dermatitis from high-dose interferon alfa-2b. J Clin Oncol 2002;20:355–357.

9 Extermann M, Vogt N, Forni M et al. Radiation recall in a patient with breast cancer treated for tuberculosis. Eur J Clin Pharmacol 1995;48: 77–78.

10 Williams BJ, Roth DJ, Callen JP. Ultraviolet recall associated with etoposide and cyclophosphamide therapy. Clin Exp Dermatol 1993;18: 452–453.

11 Jeter MD, Janne PA, Brooks S et al. Gemcitabine-induced radiation recall. Int J Radiat Oncol Biol Phys 2002;53:394–400.

12 Gabel C, Eifel PJ, Tornos C et al. Radiation recall reaction to idarubicin resulting in vaginal necrosis. Gynecol Oncol 1995;57:266–269.

13 Tan CT, Dargeon HW, Burchenal JH. The effect of actinomycin D on cancer in childhood. Pediatrics 1959;24:544–561.

14 Weiss RB, James WD, Major WB et al. Skin reactions induced by trimetrexate, an analog of methotrexate. Invest New Drugs 1986;4:159–163.

15 Castellano D, Hitt R, Cortes-Funes H et al. Side effects of chemotherapy. Case 2. Radiation recall reactions induced by gemcitabine. J Clin Oncol 2000;18:695–696.

16 Stelzer KJ, Griffin TW, Koh WJ. Radiation recall skin toxicity with bleomycin in a patient with Kaposi sarcoma related to acquired immune deficiency syndrome. Cancer 1993;71:1322–1325.

17 Burdon J, Bell R, Sullivan J et al. Adriamycin-induced recall phenomenon 15 years after radiotherapy. JAMA 1978;239:931.

18 Camidge R, Price A. Characterizing the phenomenon of radiation recall dermatitis. Radiother Oncol 2001;59:237–245.

19 Azria D, Magne N, Zouhair A et al. Radiation recall: a well recognized but neglected phenomenon. Cancer Treat Rev 2005;31:555–570.

20 Garza LA, Yoo EK, Junkins-Hopkins JM et al. Photo recall effect in association with cefazolin. Cutis 2004;73:79–80, 85.

21 Krishnan RS, Lewis AT, Kass JS et al. Ultraviolet recall-like phenomenon occurring after piperacillin, tobramycin and ciprofloxacin therapy. J Am Acad Dermatol 2001;44:1045–1047.

22 Camidge R, Price A. Radiation recall dermatitis may represent the Koebner phenomenon. J Clin Oncol 2002;20:4130; author reply 4130.

23 Donaldson SS, Glick JM, Wilbur JR. Letter: Adriamycin activating a recall phenomenon after radiation therapy. Ann Intern Med 1974;81: 407–408.