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1-1-2019

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#### Recommended Citation

Garrahy, I., & Forman, D. (2019). Nitrofurantoin-induced radiation recall dermatitis.. *J Community Hosp Intern Med Perspect*, 9 (3), 279-281. <https://doi.org/10.1080/20009666.2019.1623627>

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CASE REPORT



## Nitrofurantoin-induced radiation recall dermatitis

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### ABSTRACT

Radiation recall dermatitis (RRD) is an inflammatory skin reaction that develops in a previously quiescent radiation field triggered most commonly by chemotherapy, particularly anthracyclines and taxanes. Radiation-recall dermatitis secondary to antibiotic therapy is quite rare. The patient is 61-year-old female with a history of squamous cell carcinoma of the left breast treated with neoadjuvant carboplatin, paclitaxel, and anthracycline chemotherapy followed by surgery and subsequent whole breast radiation 6040 cGy. Eight years after completion of her radiation she developed diffuse redness of the left breast after two doses of nitrofurantoin taken for a urinary tract infection. On examination, vital signs were stable and she had an erythematous and excoriated rash on her left breast that clinically appeared to be cellulitis. Given her clinical history, coupled with the temporal relationship of starting an antibiotic, strong consideration was given for antibiotic-induced RRD. Nitrofurantoin was discontinued, and the rash resolved completely within several days. This case demonstrates an example of RRD which is the development of an acute inflammatory skin reaction of a previously irradiated area most commonly triggered by chemotherapeutic agents. This case highlights antimicrobial therapy as a rare cause of RRD and underscores the importance of considering RRD in a patient presenting with an acute rash over a previously irradiated area while on antimicrobial therapy.

### ARTICLE HISTORY

Received 1 April 2019  
Accepted 13 May 2019

### KEYWORDS

Nitrofurantoin; breast cancer history; radiation recall dermatitis

## 1. Introduction

Radiation recall dermatitis (RRD) is an acute inflammatory skin reaction that occurs over a previously quiescent irradiated field after administration of certain medications. Most cases of RRD are associated with chemotherapy, particularly the anthracyclines and taxanes [1]. The first radiation recall reaction was described by D'Angio in 1959. It involved dactinomycin which produced a reaction on previously irradiated skin that was identical to the reaction initially produced by radiation [2]. However, RRD has also been reported with tamoxifen, simvastatin, and anti-tuberculosis medication [3–5]. Although antibiotic-induced RRD is rare, associations between quinolones and RRD have been reported. We present a case of a woman who developed RRD after administration of nitrofurantoin.

## 2. Case description

A 53-year-old female developed a urinary tract infection and was started on nitrofurantoin 100 mg twice a day for 5 days by her primary care physician. After two doses of nitrofurantoin, she developed redness and irritation over her left breast (see Figure 1). The patient had had no sunlight exposure to the area nor any changes to her other medications. The patient's only known allergy was hives to dye contrast. On

examination, vital signs were stable, and she had a sharply demarcated erythematous and excoriated rash on her left breast.

The patient has a prior history of squamous cell carcinoma of the left breast treated with neoadjuvant carboplatin, paclitaxel, and anthracycline chemotherapy followed by surgery and subsequent whole breast radiation 6040 cGy. The breast cancer history began in December 2010 when she developed a left axillary mass. CT chest revealed mildly prominent left axillary lymph nodes. With concern for an occult left-sided breast cancer, a follow-up MRI of the bilateral breasts was completed which revealed a 2.2 × 0.9 × 1.7 cm area of heterogeneous non-mass like enhancement within the 2:00 to 3:00 position of the left breast.

She underwent excision of the left axillary mass. Pathology revealed poorly differentiated squamous cell carcinoma of the left breast. The tumor was negative for both the estrogen and the progesterone receptors. She was treated with neoadjuvant chemotherapy with carboplatin, paclitaxel, and anthracycline chemotherapy. A left lumpectomy and axillary node dissection was performed in May 2011. All 18 axillary nodes were negative for metastasis, indicating complete response. Finally, she was treated with adjuvant radiation 6040 cGy in 33 fractions over 6 weeks. She tolerated the radiation course well and only developed mild erythema at the site of the breast irradiation.

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**Figure 1.** Erythematous rash on left breast that occurred one day after first dose of nitrofurantoin corresponding to prior radiation treatment portals.

The patient's rash that occurred following two doses of antimicrobial therapy corresponded to the prior radiation treatment portals. Given the temporal relationship of the rash with the antibiotic administration, the patient was felt to have RRD to nitrofurantoin. Other differential diagnoses included cellulitis and allergic contact dermatitis. However, the patient was afebrile, without leukocytosis, and her only known allergy was to dye contrast. Nitrofurantoin was immediately discontinued, and she was prescribed oral trimethoprim-sulfamethoxazole 160 mg TMP/800 mg SMX twice a day for three days. The rash quickly resolved within one week.

### 3. Discussion

This case demonstrates an example of RRD, which is an inflammatory reaction of a previously irradiated area precipitated by drug administration [6]. There is a wide variety of chemotherapy drugs known to cause RRD, particularly anthracyclines and taxanes. There is growing evidence suggesting the association of noncytotoxic medications with RRD, including tamoxifen, simvastatin, antitubercular drugs. There have been case reports also documenting the association of the antibiotics with RRD, including quinolones, and azithromycin [7–9]. Our patient represents, to our knowledge, the first case of this rare skin reaction to this frequently used antibiotic, nitrofurantoin.

There have been a variety of mechanisms hypothesized for RRD caused by noncytotoxic agents; epithelial stem cell inadequacy and/or sensitivity, vascular damage, and idiosyncratic drug hypersensitivity reactions [10]. Our patient's prompt improvement in symptoms with the discontinuation of nitrofurantoin supports an idiosyncratic drug hypersensitivity reaction

as a likely cause. Such reactions are likely not linked to the immune system. The suggestion is that certain drugs trigger non-immune inflammatory pathways in patients whose inflammatory response threshold has been lowered by radiation. Radiation may induce cells to secrete low levels of cytokines, such as tumor necrosis factor  $\alpha$ , that are responsible for an inflammatory response [9]. When a triggering agent is introduced, the cytokines are upregulated, causing a recall reaction.

The present case report is the fourth involving a radiation recall reaction associated with antibiotic therapy. The first reported radiation recall reaction that occurred with antibiotic therapy was with gatifloxacin [7]. There have also been case reports with levofloxacin and azithromycin-induced RRD. The antibiotic nitrofurantoin, which provoked the reaction, does not belong to the class of fluoroquinolones. Nitrofurantoin is frequently used to treat urinary tract infections due to its convenient oral use, low side effect profile, and low cost. It is important for providers to know that in patients who have been treated with radiation, that a radiation recall reaction can occur with commonly prescribed antibiotics, including nitrofurantoin.

### Disclosure statement

No potential conflict of interest was reported by the authors.

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