Radiation recall dermatitis induced by pegylated liposomal doxorubicin

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A 53-year-old woman was diagnosed in January 1998 with stage IV ductal-infiltrating breast cancer, with multiple lung and bone metastases. She received six courses of cyclophosphamide plus doxorubicin. She remained with stable disease until July 2000 when disease progression was observed, both in the lungs and bones; she received six courses of paclitaxel on a 3-weekly schedule, obtaining a stabilization of her disease. In September 2002, she presented with progressive disease in the lungs and a painful left femoral metastatic lesion. The patient was initially treated with palliative radiation therapy, receiving a total dose of 30 Gy, using an anterior field, with partial pain control (Fig. 1). At the completion of the treatment, no cutaneous reaction was observed. Concomitant medications included omeprazole and ibuprofen. In November 2002, 4 weeks after the completion of radiotherapy, the patient started systemic treatment with pegylated liposomal doxorubicin (40 mg/m^2 i.v. on day 1 every 28 days). Antiemetic prophylaxis consisted of 8 mg of ondansetron given i.v. prior to chemotherapy. Twelve days after the first pegylated doxorubicin infusion the patient experienced localized painful erythema with vesicular eruption in the lateral aspect of her left thigh, in an area limited to the field of previous irradiation (Fig. 1). Physical exam was otherwise unremarkable, with no other cutaneous lesions elsewhere. A biopsy was obtained, and the pathology report was of a vacuolar degeneration of the epidermal basal layer and keratino-

Fig. 1

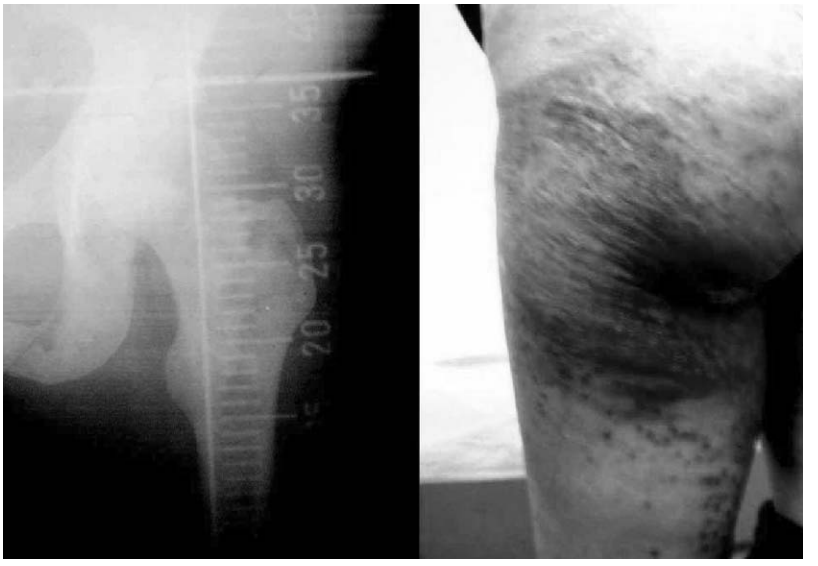

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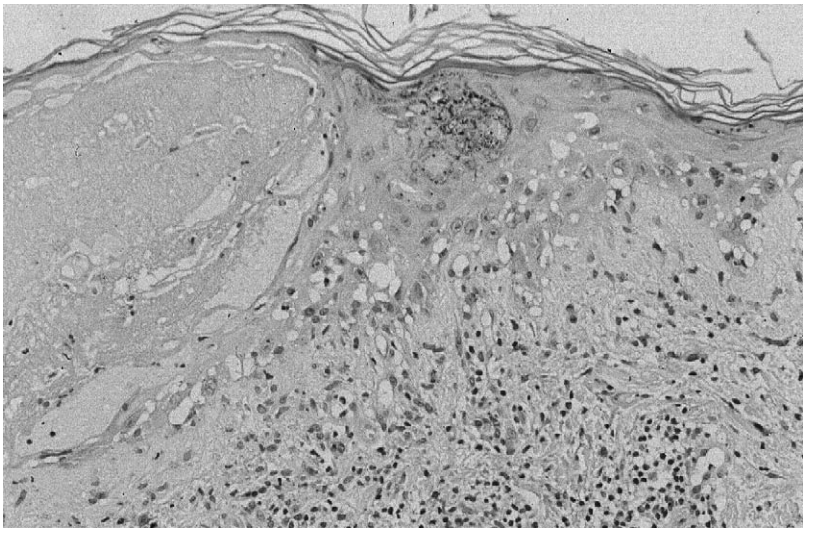
Fig 2



cyte necrosis, suggestive of chemotherapy-induced radiation recall dermatitis (Fig. 2). Concomitant drugs (omeprazole, ibuprofen and ondansetron) are not known to induce dermal recall reactions and other potential causes were excluded.

Treatment was initiated with high-potency topical steroids (betamethasone dipropionate). Fourteen days later, the cutaneous lesions had completely resolved.

Radiation recall dermatitis is a rare toxic effect induced by several chemotherapeutic agents in patients who have received prior treatment with radiotherapy. The recall phenomenon was initially described as erythema, edema, desquamation and blistering that occurred in a previously intact skin area corresponding to the field of irradiation after treatment with doxorubicin [1]. It has been subsequently reported in association with gemcitabine [2,3], docetaxel [4,5], paclitaxel [6,7], oxaliplatin [8,9] and methotrexate [10], among others.

Pegylated liposomal doxorubicin is a novel anthracycline derivative with a markedly distinct toxicity profile from its parent compound, doxorubicin. Whereas cardiotoxicity appears to be reduced, mucosal damage is frequent, and cutaneous toxicity in the form of palmar-plantar erythrodysestesia is dose limiting. It is currently approved for its use as monotherapy in metastatic breast cancer patients who are at increased cardiac risk, in ovarian cancer patients after failure of platinum-based chemotherapy, and in AIDS-related Kaposi's sarcoma.

This case is noteworthy because (i) it is the first report of a radiation recall dermatitis induced by pegylated liposomal doxorubicin, (ii) it shows that the addition of a pegylated liposomal coat does not prevent doxorubicin cutaneous toxicity after radiotherapy and (iii) it was successfully managed with high-potency topical steroids. This potential cutaneous toxicity must be taken into account considering the increasing use of pegylated liposomal doxorubicin in patients who frequently receive radiation therapy, such as stage IV breast cancer patients.

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