Chemotherapy-induced Recall Dermatitis on a Previously Scalded Wound in a Patient with Acute Myeloid Leukaemia

Chia-Yu Chu and Hsien-Ching Chiu*
*Department of Dermatology, National Taiwan University Hospital and National Taiwan University College of Medicine, 7 Chung-Shan South Road, Taipei 100, Taiwan. *E-mail: hcc@ha.mc.ntu.edu.tw*
Accepted April 9, 2003.

Sir,
Chemotherapy-induced "recall" is a phenomenon whereby the administration of a chemotherapeutic agent induces an inflammatory reaction at a previous injury site. Radiation recall is a phenomenon whereby the administration of a chemotherapeutic agent induces an inflammatory reaction at a previously irradiated site (1–3). These reactions are mostly seen in the skin, but they can also develop in organ systems such as the lungs, oesophagus, intestinal epithelium, oral mucosa, bladder mucosa and heart (1, 2, 4). In addition, reactivation of ultraviolet (UV) light-induced erythema (UV recall) is another well-documented sequela of methotrexate therapy (1–3). Both reactions are the prototypes of recall phenomena. However, the concept of "recall" has been extended to include reaction of tissue inflammation evoked by extravasations or phlebitis (2). Here we report a patient with acute myeloid leukaemia (AML) developing recall dermatitis on a previously scalded wound after chemotherapy.

CASE REPORT

A 30-year-old woman was diagnosed as having acute myelomonocytic leukaemia with the initial presentation of intermittent fever and exertional dyspnea. The induction regimen, including idarubicin and cytarabine, was administered and resulted in complete remission status of the disease. Mitoxantrone and high-dose cytarabine were administered 2 months later for consolidation. Four months later, leukopenia, anaemia and thrombocytopenia as well as increased blast count to 7% in the bone marrow aspiration study all suggested an early relapse of the leukaemia. She was therefore admitted to the haematological ward for further therapy. One month before admission, she was accidentally scalded with boiling water at home. The scalded wound was located on the left dorsal hand with erythema and blister formation. She applied a povidone iodine ointment to the wound and it healed uneventfully 2 weeks later. On admission, physical examination revealed a bizarre-shaped scar on her left dorsal hand. The patient received another cycle of consolidation chemotherapy with mitoxantrone 8 mg/m^2 on days 1–3, etoposide 100 mg/m^2 on days 1, 3, 5 and cytarabine 400 mg/m^2 on days 1–5 about 2 weeks after the scalded wound healed. Intriguingly, the scalded wound became erythematous, swelling with local heat and painful several hours after infusion of the drugs on the first day of chemotherapy. At that time, physical examination revealed a hen-egg-sized, well-demarcated, bizarre-shaped, pinkish, slightly infiltrated plaque studded with a few pinhead-sized tiny vesicles just confined to the previously scalded wound area (Fig. 1). In addition, a more erythematous ring peripheral to the scar area was noted. The lesion aggravated after each infusion of the chemotherapeutic agents. Reviewing her past history, no radiation therapy, extravasation insult or sunburn history had been noted on this area. No topical medicament had been applied on the scalded wound in the previous 2 weeks. According to the history and the co-localization of the lesion with the scalded wound scar, we diagnosed the lesion as a chemotherapy-induced recall dermatitis on a previously scalded wound. A tetracycline ointment for the shallow erosions due to rupture of the tiny vesicles and a betamethasone valerate cream for the local inflammation were prescribed. The skin lesion improved significantly after cessation of chemotherapy, leaving only slight hyperpigmentation one month later. Because of complete remission of the leukaemia, the patient

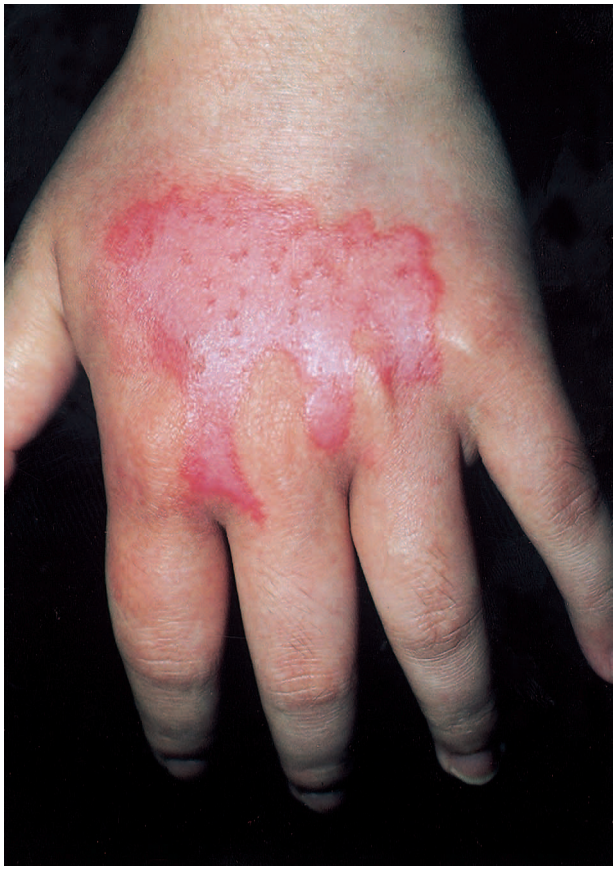

Fig. 1. A well-demarcated, bizarre-shaped, pinkish, slightly infiltrated plaque studded with a few pinhead-sized tiny vesicles just confined to the previously scalded wound area. In addition, a more erythematous ring beyond the scar area was noted.

 ISSN 0001-5555

did not receive further chemotherapy during the following 1 year. No recurrence of the skin lesion has been noted.

DISCUSSION

The mechanism of recall phenomenon is currently unknown. Since there has been no previous report of a recall reaction on a scalded wound, we adopt the proposed mechanisms of radiation recall and UV recall to discuss the possible pathogenesis of this "scalded wound recall". As for chemotherapy-induced radiation recall, several mechanisms have been proposed to explain the pathogenesis of radiation recall (1, 4, 5). It has been suggested that the initial radiation therapy leads to a depletion of tissue stem cells within the irradiated field and the subsequent cytotoxic exposure causes a "remembered" reaction among the remaining surviving cells (4). Besides, it could be due to genetic defects induced by the prior irradiation (5). Seymour et al. (6), who suggested that after a dose of radiation some mutations were produced among the surviving cells, proposed that these surviving cells could pass the lethal defects along to their descendants. Furthermore, even though a tissue would be fully reconstituted after the radiation therapy, a significant proportion of the stem cells would be incapable of further proliferation, leading to an enhanced response to the subsequent chemotherapy (4). UV recall could also be caused by structural differences in actinically damaged skin such as vascular fragility or upregulated endothelial adhesion molecule expression that would predispose sun-damaged skin to this particular reaction (1). It could also be related to the effects of the chemotherapeutic agents on the rapidly replicating cell populations just released from the cell cycle blocks induced by UV radiation (5). Therefore, we surmise that a "scalded wound recall phenomenon" might be due to the impaired further proliferation of some stem cells after a severe scalded burn or the effects of the chemotherapeutic agents on the rapidly proliferating cell populations in a recently healed wound. Any previous insult of the skin would result in increased susceptibility of the local area to the toxic effects of subsequent cytotoxic drugs.

Reviewing the literature, the drugs most commonly associated with radiation recall are anti-tumour antibiotics such as anthracyclines, actinomycin D, bleomycin and mitomycin (4, 5). Among the suspected causative agents administered in the present case, mitoxantrone, an anti-tumour antibiotic, has been reported to cause radiation recall reaction (7), and etoposide has been reported to induce UV recall (1, 8) and radiation recall (1, 9), while cytarabine is associated with radiation recall (1).

Cutaneous recall dermatitis may occur at the exact site of previous irradiation from 8 days to 15 years after radiation therapy (1). In contrast, UV recall of methotrexate occurs only when methotrexate is administered 1 to 3 days after UV exposure (1). However, one case of UV recall was reported to be associated with etoposide and cyclophosphamide therapy given one week after mild sunburn (8). Our patient had been scalded one month prior to administration of the chemotherapeutic agents, and the scalded wound had healed 2 weeks before chemotherapy. This is different from an "enhancement" response, in which the administration of a chemotherapeutic agent increases the toxicity of concurrent radiation therapy (1).

Treatment of recall dermatitis is usually symptomatic and application of topical corticosteroids is usually effective. In cases of severe or extensive radiation recall, systemic corticosteroids in conjunction with discontinuation of the causative drugs often produce dramatic improvement (1). In this patient, the lesion of recall dermatitis resolved dramatically after topical treatment and discontinuation of the chemotherapeutic agents.

REFERENCES

1. Susser WS, Whitaker-Worth DL, Grant-Kels JM. Mucocutaneous reactions to chemotherapy. J Am Acad Dermatol 1999; 40: 367–398.
2. Bronner AK, Hood AF. Cutaneous complications of chemotherapeutic agents. J Am Acad Dermatol 1983; 9: 645–663.
3. DeSpain JD. Dermatological toxicity of chemotherapy. Semin Oncol 1992; 19: 501–507.
4. Yeo W, Johnson PJ. Radiation-recall skin disorders associated with use of antineoplastic drugs. Am J Clin Dermatol 2000; 1: 113–116.
5. Smith KJ, Germain M, Skelton H. Histopathologic features seen with radiation recall or enhancement eruptions. J Cutan Med Surg 2002; 6: 535–540.
6. Seymour CB, Mothersill Q, Alper T. High yields of lethal mutations in somatic mammalian cells that survive ionizing radiation. Int J Radiat Biol 1986; 50: 167–179.
7. Sauter C. Radiation recall. Schweiz Med Wochenschr 1997; 127: 2098.
8. Williams BJ, Roth DJ, Callen JP. Ultraviolet recall associated with etoposide and cyclophosphamide therapy. Clin Exp Dermatol 1993; 18: 452–453.
9. Yokel BK, Friedman KJ, Farmer ER, Hood AF. Cutaneous pathology following etoposide therapy. J Cutan Pathol 1987; 14: 326–330.