

Inflammatory Actinic Keratoses Secondary to Systemic Chemotherapy

Erum N. Ilyas, MD; Generosa Grana, MD; Justin J. Green, MD

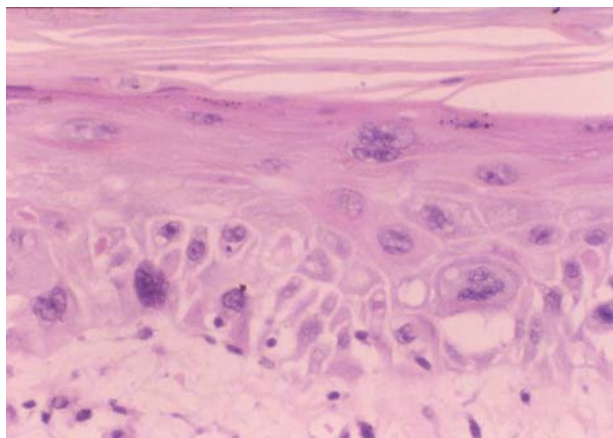
Traditionally, systemic 5-fluorouracil has been associated with a reaction that produces inflammation of preexisting and subclinical actinic keratoses (AKs). We report a case of an inflammatory reaction occurring in AKs secondary to the use of doxorubicin. The cutaneous reaction was successfully managed with the application of high-potency topical steroids over the body and with pain management. When the doxorubicin was discontinued and another agent (paclitaxel) was instituted, the cutaneous reaction gradually diminished.

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Case Report

A 61-year-old woman with a history of carcinoma of the breast presented with painful lesions on her fingers, arms, legs, and back that had persisted for 6 days. There was no pruritus or fever. The patient had undergone a mastectomy and lymphadenectomy, and she had begun chemotherapy one month prior to presentation. Her chemotherapy regimen included doxorubicin and cyclophosphamide administered at 2-week intervals with growth factor (filgrastim) support. The patient's medical history also included basal cell carcinoma treated with Mohs micrographic surgery and one previous attempt at treatment of actinic keratoses (AKs) with topical 5-fluorouracil.

Results of a physical examination revealed numerous rough, keratotic, erythematous, tender papules ranging in size from 0.4 to 1.0 cm in a photodistributed pattern over the dorsal aspect of



Atypical keratinocytes within the basal layer with solar elastosis (H&E, original magnification $\times 100$).

the forearms and hands, central upper chest, upper back, and thighs.

A shave biopsy was performed of a lesion on the thigh. Results of the histologic examination showed atypical keratinocytes within the basal layer with solar elastosis (Figure), bandlike mononuclear cell infiltrate in the dermis, and some larger atypical keratinocytes.

Comment

Traditionally, systemic 5-fluorouracil has been associated with a reaction that produces inflammation of preexisting and subclinical AKs. Similar reactions have been reported in patients receiving doxorubicin.¹ It has been postulated that the selective effect of chemotherapeutics on AKs is secondary to abnormal DNA synthesis in the cells of lesional skin.²

Doxorubicin is an anthracycline antibiotic used as a chemotherapeutic agent in the treatment of carcinomas, including those of the breast, endometrium, ovary, testicle, thyroid, and lung; sarcomas such as Ewing tumor, osteosarcoma, and rhabdomyosarcoma; and hematologic malignancies such as acute leukemias, Hodgkin disease, and non-Hodgkin lymphoma. The mechanism of action of

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Drs. Ilyas and Green are from the Division of Dermatology and Dr. Grana is from the Division of Hematology/Oncology, Department of Medicine, Cooper Health System, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden.

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Reprints: Justin J. Green, MD, 100 Brick Rd, Suite 306, Marlton, NJ 08053 (e-mail: jjgreenjj@hotmail.com).

doxorubicin is through DNA intercalation, thereby blocking the synthesis of DNA and RNA. The drug also has an effect on topoisomerase II. The most common cutaneous side effects associated with doxorubicin include alopecia, stomatitis, hyperpigmentation, radiation recall phenomenon, urticaria, chemical cellulitis, and contact dermatitis.

Cyclophosphamide is an alkylating agent that is not cell-cycle specific. It is an integral part of several chemotherapy regimens, particularly those used in the treatment of breast cancer. It is approved by the US Food and Drug Administration for the treatment of advanced mycosis fungoides and has also been used for management of various types of angiitis, bullous dermatoses, connective tissue diseases, infiltrative diseases, and Langerhans cell histiocytosis. The cutaneous adverse reactions associated with cyclophosphamide include anagen effluvium, pigmented band on the teeth, diffuse hyperpigmentation of skin, transverse ridging of nails, acral erythema, Stevens-Johnson syndrome, urticaria, and mucosal alterations. Cyclophosphamide has been reported to augment the phototoxicity of other chemotherapeutics, including 5-fluorouracil and quinolone antibiotics.³

Our patient's systemic chemotherapy regimen consisted of doxorubicin and cyclophosphamide. We believe that the inflammatory reaction in the AKs was a response to the use of doxorubicin. The cutaneous reaction was successfully managed with high-potency topical steroids applied to the body and low-potency steroids applied to the face. However, the pain associated with the eruption was severe and required aggressive narcotic management. These symptoms occurred after the second cycle of a planned 4-cycle chemotherapy regimen and persisted through each cycle. When the doxorubicin was discontinued and paclitaxel was instituted, the cutaneous reaction gradually diminished.

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