Acitretin for Hypertrophic Lichen Planus–Like Reaction in a Burn Scar

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 60-year-old-man sustained a burn in childhood on the lower part of his right leg in a fire in a haystack. The area healed and remained as a stable scar for 50 years. Four months before presentation, he developed a series of hypertrophic papules and plaques measuring up to 12 cm in diameter localized to the burn scar (Figure 1). The individual lesions were violaceous and hyperkeratotic. There were no similar lesions at other skin sites or involvement of his mucous membranes. The patient was taking warfarin sodium and digoxin, and 2 months after the onset of his skin lesions, he began taking lisinopril for hypertension.

Over the following 5 months, 4 skin biopsy specimens were obtained from the most infiltrated areas. All 4 specimens showed an irregularly acanthotic epidermis with focal parakeratosis and prominent lichenoid inflammation (Figure 2) concentrated at the tips of the rete ridges (Figure 3), with liquefaction degeneration of the basal layer. There were scattered eosinophils in the dermis. Three of the skin biopsy specimens, including 2 initial samples, showed no evident squamous cell carcinoma, but a subsequent biopsy specimen showed a hypertrophic epidermis that was associated with large irregular clusters of keratinocytes that projected into the dermis (Figure 4). These keratinocytes showed premature keratinization and focal nuclear atypia and were consistent with an early well-differentiated squamous cell carcinoma.

DIAGNOSTIC CHALLENGE

The clinical presentation and the initial skin biopsy findings were consistent with hypertrophic lichen planus. Our main concern was whether the multifocal epidermal hyperplasia associated with lichenoid inflammation was a harbinger of skin cancer, particularly as the reaction was localized to a long-standing burn scar. The presence of parakeratosis and eosinophils in all the skin biopsy specimens is not a typical feature of lichen planus but can be seen in hypertrophic lesions. A subsequent biopsy specimen showed changes consistent with an early well-differentiated squamous cell carcinoma.

THERAPEUTIC CHALLENGE

Squamous cell carcinoma may develop in the setting of either a long-standing burn scar or hypertrophic lichen planus. Immunosuppressive agents, such as systemic corticosteroids or cyclosporin, are used to treat lichen planus but inhibit cell-mediated immune responses that play a vital role in inhibiting the progression of skin cancers. Clearly, the use of immunosuppressive drugs in our patient, who had both a long-standing burn scar and lesions resembling hypertrophic lichen planus, posed a potential risk of enhancing tumor growth. We were concerned that the apparent absence of squamous cell carcinoma in our patient’s initial biopsy specimens may have represented a sampling problem.

SOLUTION

Acitretin is a synthetic retinoid that has been shown in a double-blind, placebo-controlled study to prevent skin cancers and reduce actinic keratoses in immunosuppressed patients who have undergone renal transplantation. It has also been successfully used to treat lichen planus in a double-blind, placebo-controlled study of 65 patients. Acitretin therapy (20 mg/d) was therefore initiated in our patient, and within 2 months there was marked clearing of his skin lesions. Owing to a rise in his serum triglyceride levels, the acitretin dosage was reduced to 10 mg/d for 1 month, and the decrease in dosage led to an increase in the thickness of 2 of the skin lesions. Biopsy specimens were obtained from both areas and showed lichenoid inflammation with epidermal hyperplasia. One of the biopsy specimens also showed an early well-differentiated squamous cell carcinoma (Figure 4), but this was largely in situ and associated with lichenoid inflammation. As the squamous cell carcinoma was not clinically well defined and the skin lesions had been undergoing progressive regression during acitretin therapy, the acitretin dosage was again...
increased to 20 mg/d. The triglyceride levels were reduced by diet control. Six weeks later, the areas were no longer indurated. A biopsy specimen obtained from the site of the skin cancer 3 months later showed nonresidual tumor. Because of the continued risk of skin cancers developing in the patient’s burn scar, the acitretin therapy was continued at a dosage of 20 mg/d as a chemoprophylactic measure. This regimen has resulted in clearing of the patient’s skin lesions and in residual mottled pigmentation over the burn scar (Figure 5). It has been 1 year since the acitretin therapy was initiated, and no further skin cancers have emerged.

The risk of skin cancer developing in long-term burn scars is well recognized. Cell-mediated immunity is an important factor in controlling the emergence of skin cancers, and its role is illustrated in the marked increase in skin cancers in organ transplant patients who are receiving long-term immunosuppression. In specimens submitted for histological diagnosis, lichenoid tissue reactions and lymphocytic inflammation reflecting host immunological response may be seen in the setting of a broad range of skin cancers, including squamous cell carcinoma and its most frequent precursor, actinic keratosi. Lichen planus, particularly of the oral cavity, and hypertrophic lichen planus may be complicated by squamous cell carcinoma. However, the development of skin cancers usually occurs in long-standing chronic disease and contrasts with the short history of the hypertrophic lichenoid lesions seen in our patient. The limitation of the lichenoid reaction to the burn scar, as well as the presence of parakeratosis and eosinophils in the skin biopsy specimens obtained from our patient, raised our suspicion that we were dealing with an unusual host response directed to preneoplastic changes in a long-standing burn scar. A subsequent biopsy specimen showed changes consistent with an early squamous cell carcinoma. However, the bulk of the lichenoid inflammation in the skin biopsy specimens was associated with an epidermis that lacked evidence of atypia and was consistent with hypertrophic lichen planus.

Acitretin has been used in the chemoprophylaxis of skin cancers and is not recommended as a therapy for established squamous cell carcinomas. In our patient, the decision to postpone surgery was based on the well-differentiated and largely in situ nature of the tumor and the associated lichenoid inflammation, as well as on the
progressive regression of his skin lesions during higher-dosage acitretin therapy. The regression of the skin cancer was probably a reflection of the marked host response occurring in the burn scar that resembled hypertrophic lichen planus, and the role of acitretin may have been a secondary one. Close monitoring of the course of the skin cancer was required in this setting in case surgery was needed.

It is important to distinguish lichenoid reactions occurring in the setting of epithelial dysplasia from lichen planus. Particular caution needs to be taken when reporting on skin samples that have been obtained from localized or solitary hypertrophic lichenoid lesions in patients who lack evidence of lichen planus at other sites. Multiple samples may be required to confirm the presence of a squamous cell carcinoma, as the transition to frank carcinoma may be focal. In certain settings, such as long-standing burn scars, the presence of a lichenoid tissue reaction may represent a host response to early neoplastic changes. Hypertrophic lichen planus developing within a long-standing burn scar is rare, and we were not able to find a previous report of this event.

The mode of action of acitretin in chemoprophylaxis of skin cancer may be related to its ability to promote differentiation of keratinocytes. A recent study indicates that there is aberrant expression of fetal cyto-keratin in lichen planus, which may be one of the reasons that acitretin has been successful in the treatment of lichen planus. The use of agents that are capable of promoting the differentiation of keratinocytes, such as acitretin, may provide an effective treatment strategy when the alternative option is the use of immunosuppressive agents in the setting of increased risk of tumor enhancement. In our patient, the use of acitretin as monotherapy not only cleared the hypertrophic lichen planus-like reaction, but...
it also acted as a chemoprophylactic agent for skin cancers.

Accepted for publication January 31, 2000.

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REFERENCES


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